incf

Neuro Informatics 2010

August 30 - September 1
Kobe, Japan

ABSTRACT BOOK

Neuroinformatics 2010
3rd INCF Congress of Neuroinformatics

Program and Abstracts

August 30 to September 1, 2010
Kobe, Japan

Welcome to the 3rd INCF Congress in Kobe, Japan!

Neuroinformatics 2010 is organized by the INCF in cooperation with the INCF Japan Node. As with the two first INCF Congresses (in Stockholm and Pilsen), the Kobe meeting brings together neuroinformatics researchers from numerous disciplines and dozens of countries. The single-track program includes five keynote speakers, four scientific workshops and two poster and demonstration sessions. In addition, the last half day will be devoted to an INCF Japan Node special session with lectures and discussions on INCF global initiatives and neuroinformatics in the Asian-Pacific circle. We also collaborate with the Neuro2010 conference, which follows immediately and spans a broad variety of neuroscience. In all, we anticipate an exceptional scientific event that will help raise the level of neuroinformatics research worldwide. Please enjoy the many fine presentations, posters, and demos!

David Van Essen

Washington University School of Medicine, USA
INCF 2010 Program Committee Chair

Organizers

Program Committee:

David Van Essen (Chair) - *Washington University School of Medicine*
Richard Baldock - *Medical Research Council, Edinburgh*
Svein Dahl - *University of Tromsø*
Erik De Schutter - *Okinawa Institute of Science and Technology*
Kenji Doya - *Okinawa Institute of Science and Technology*
Mark Ellisman - *University of California at San Diego*
Patric Hagmann - *Ecole Polytechnique Fédérale de Lausanne*
Astrid Prinz - *Emory University*
Idan Segev - *The Hebrew University of Jerusalem*
Shiro Usui - *RIKEN BSI*
David Willshaw - *University of Edinburgh*

Local Organizing Committee:

Chair

Shiro Usui, Director, *RIKEN BSI*
Delegate, INCF Japan-Node

Executive Members

Mitsuo Kawato, Director, *ATR CNL*
Chair, 33rd Annual Meeting of the Japan Neuroscience Society
Kazuhide Inoue, Professor, *Kyushu University*
Chair, 53rd Annual Meeting of the Japan Society for Neurochemistry
Shin Ishii, Professor, *Kyoto University*
Chair, 20th Annual Meeting of the Japanese Neural Network Society
Kenji Doya, Principal Investigator, *IRP-OIST*
Program Chair, Neuro2010
Keiji Tanaka, Deputy Director, *RIKEN BSI*
Delegate, INCF Japan-Node

Committee Members

Yoshimi Kamiyama, Professor, *Aichi Prefectual University*
Chair, Visiome Platform, INCF Japan-Node
Toshio Iijima, Vice President, *Tohoku University*
Chair, BMI Platform in INCF Japan-Node
Ryohei Kanzaki, Professor, *Tokyo University*
Chair, Invertebrate Brain Platform, INCF Japan-Node
Ryoji Suzuki, Specially Appointed Professor, *Kanazawa Institute of Technology*
Chair, Neuroimaging Platform, INCF Japan-Node
Tadashi Isa, Professor, *National Institute for Physiological Sciences*
Chair, Integrative Brain Research Project, INCF Japan-Node
Soichi Nagao, Laboratory Head, *RIKEN BSI*
Chair, Cerebellar PF, INCF Japan-Node
Teiichi Furuichi, Laboratory head, *RIKEN BSI*
Chair, CDT-DB Platform, INCF Japan-Node
Yoko Yamaguchi, Laboratory Head, *RIKEN BSI*,
Chair, Dynamic Brain Platform, INCF Japan-Node
Hidetoshi Ikeno, Professor, *University of Hyogo*
Chair, Simulation Platform, INCF Japan-Node

Advisor

Shun-ichi Amari, Special Advisor, *RIKEN BSI*
Former Vice-Chair, INCF

Congress Manager

Pontus Holm

The International Neuroinformatics Coordinating Facility (INCF, www.incf.org) coordinates and fosters international activities for discovery and innovation in neuroscience and related fields. Established in 2005 through the Organization for Economic Co-operation and Development (OECD) Global Science Forum, the INCF catalyzes global knowledge flow and scientific interaction by developing, maintaining and evaluating worldwide programs, standards, guidelines and infrastructures in neuroinformatics to further our understanding of the human brain and its diseases. With its Secretariat at Karolinska Institutet and Royal Institute of Technology in Stockholm, Sweden, the INCF achieves its international outreach through its national nodes in 15 current member countries across the globe.

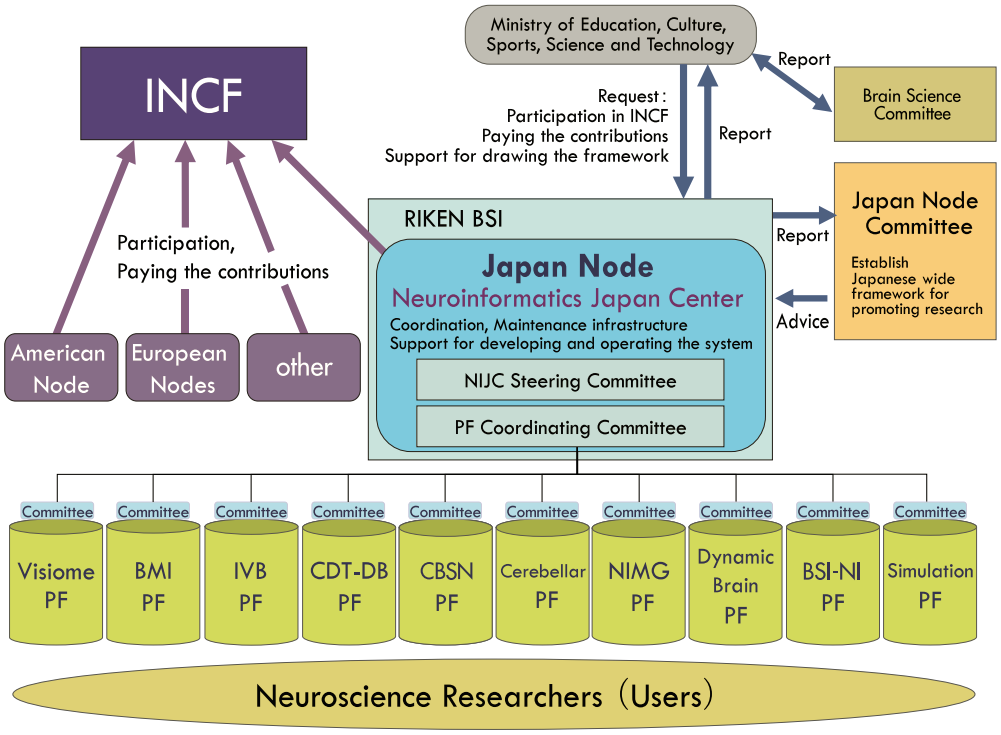
INCF Japan-Node

(http://www.neuroinf.jp/)

The Neuroinformatics Japan Center at the RIKEN Brain Science Institute represents the INCF Japan Node. Together with the Japan Node Committee and the Platform Committees, it promotes domestic activities in neuroinformatics. Platform Committee members collaborate to develop databases that are available for online use. Shared databases are called "platforms" and the Platform Committees are made up of researchers throughout Japan involved in building these platforms.

Platforms in Japan-Node:

- Visiome Platform
- Brain Machine Interface Platform
- Invertebrate Brain Platform
- Cerebellar Development Transcriptome Database
- Comprehensive Brain Science Network Platform
- Cerebellar Platform
- Neuroimaging Platform
- Dynamic Brain Platform
- BSI-NI Platform
- Simulation Platform



※ PF = Platform
※ Some platforms are under development and not released yet

http://www.neuroinf.jp/

Acknowledgements

We would like to express our gratitude to the following organizations for supporting Neuroinformatics2010, the Japan-Node Special Symposium and for co-hosting symposium in Neuro2010.

- OMRON Corporation
- Brain Science Foundation
- Tateishi Science and Technology Foundation
- Portopia '81 Memorial Fund
- Tsutomu Nakauchi Foundation
- Sankyo Foundation of Life Science
- RIKEN BSI
- MEXT (Ministry of Education, Culture, Sports, Science and Technology in JAPAN)

Neuro Informatics 2011

Boston, USA, September 4-6

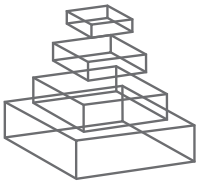
Program Committee

Mitsuo Kawato (Chair, Japan)
Upinder S. Bhalla (India)
Jan Bjaalie (Norway)
Kenji Doya (Japan)
Jeanette Hellgren Kotaleski (Sweden)
Sean Hill (Switzerland)
David N. Kennedy (USA)
Friedrich Sommer (USA)
David Van Essen (USA)

Local Organizing Committee

David N. Kennedy, Chair (UMass Medical School)
Randy Buckner (Harvard University)
Blaise Frederick (Harvard Medical School)
Michael Haselmo (Boston University)
Ron Kikinis (Harvard Medical School)
Jean King (UMass Medical School)
Maryann Martone (UCSD)
Bruce R. Rosen (Harvard Medical School)
Alan Ruttenberg (Science Commons)
Clifford Saper (Harvard Medical School)

www.neuroinformatics2011.org



frontiers

About Frontiers

Frontiers is more than just an open-access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals...

Frontiers Journal Series

The Frontiers Journal Series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the Frontiers Journal Series operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to Quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore,
Frontiers only applies the most rigorous and unbiased reviews.

Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view.

By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

WHY PUBLISH?

World Class Editors - disclosed on all accepted articles
Constructive and Efficient Review - the first real-time review in publishing
Instantaneously Online - claim your discovery with paper pending
Rapid Publication - on average, 3 months from submission to acceptance
Indexing in Major Archives - PubMed Central, Google Scholar and more
Copyright Retention by Authors - freely print and distribute your articles
Global Dissemination - over 240,000 readers in 160 countries
Article Impact - advanced analytics on real-time impact of your article
Democratic Article Tiering - distill the best published research

By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new 21st century generation.

iGroup Asia Pacific Limited based in Bangkok, Thailand, represents a variety of contents and services from a growing number of publishers around the world.

Introducing products for Neuroinformatics 2010:

-Journal of Visualized Experiments

-Life Science Video Library
-Peer Reviewed Video Journal
-Included in Pubmed

-Morgan & Claypool

-Online and Print books
-New Publisher since 2005.

MORGAN&CLAYPOOL PUBLISHERS

-WizFolio

-New Reference Management service
-Manage whole files which was fulltext ,video and MPEG.

WizFolio
Joy of Knowledge Discovery

-Turnitin2

-Plagiarism Checking service on the Internet
-Teaching tool about writing skill

turnitin 2

-PolyVision Interactive Whiteboard

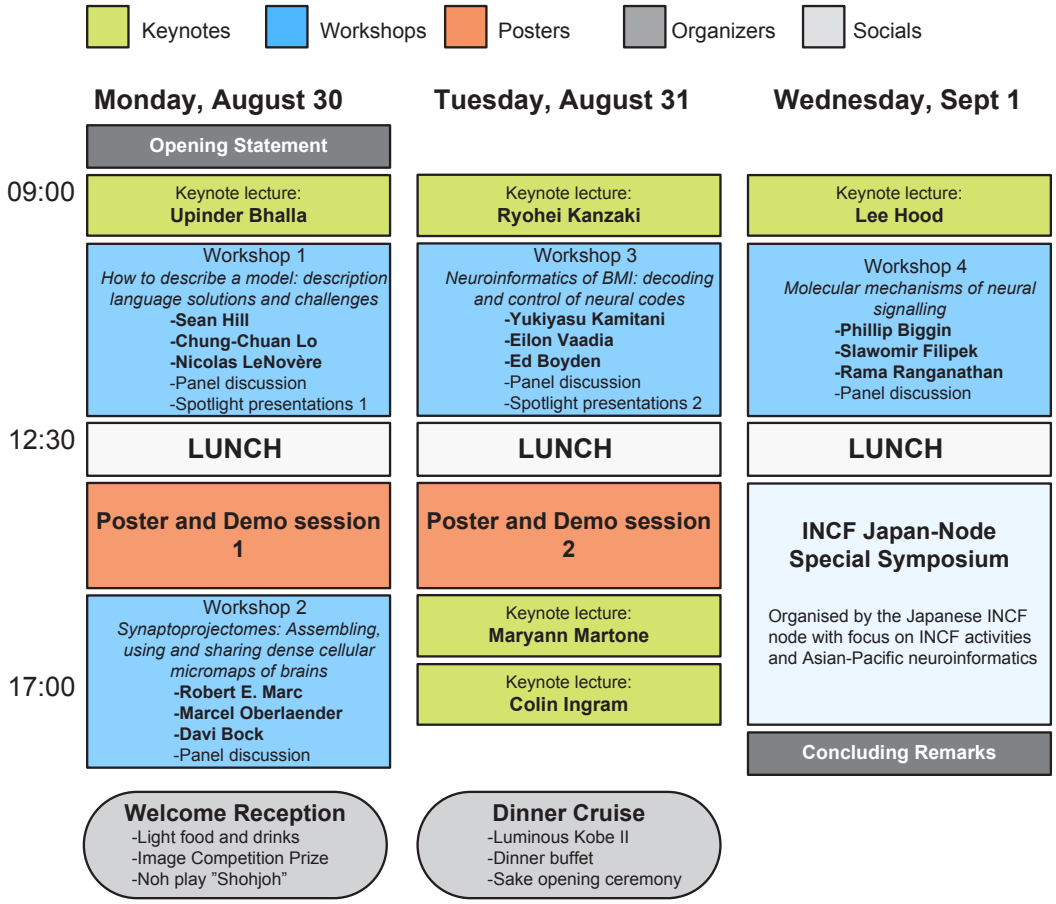
-PolyVision integrates time-tested tools with innovative technologies to bring learning to life.

PolyVision
a steelcase company

iGroup Company, Ltd.
2220/31 Ramkhamhaeng 36/1 Huamark,
Bangkok 10240, Thailand
Telephone: (662) 732-0243 thru 5
(662) 732-1954 thru 8
Fax: (662) 375-2669
Website: http://www.book.co.th/
http://www.igroupnet.com/

iGroup

The Congress at a Glance



Congress Day 1, August 30, 2010

08:45-09:00 **Opening statement**
Sten Grillner (Stockholm, Sweden) and **David Van Essen** (Washington, USA)

09:00-09:50 **Keynote**
Upinder Bhalla (Bangalore, India)
▸ Multiscale models of the synapse: a self-modifying memory machine

09:50-10:20 Coffee break

10.20-12.30 **Workshop 1**
Chair: **Erik De Schutter**
▸ How to describe a model: description language solutions and challenges

10:25-10:50	**Sean Hill**
10:50-11:15	**Chung-Chuan Lo**
11:15-11:40	**Nicolas Le Novère**
11:40-12:10	**Panel discussion**
12:10-12:30	**Spotlight presentations: Honda Naoki, Iain Hepburn, Jaap Van Pelt, and Stephen Larson**

12:30-13:30 Lunch

13.30-16.00 **Poster and Demo session 1**

15:30-16:00 Coffee break

16:00-17:50 **Workshop 2**
Chair: **Mark Ellisman**
▸ Synaptoprojectomes: Assembling, using and sharing dense cellular micromaps of brains

16:05-16:30	**Robert E. Marc**
16:30-16:55	**Marcel Oberlaender**
16:55-17:20	**Davi Bock**
17:20-17:50	**Panel discussion**

19:00 Welcome Reception

Congress Day 2, August 31, 2010

09:00-09:50 **Keynote**
Ryohei Kanzaki (Tokyo, Japan)
▸ Brain mechanisms for the generation of adaptive behavior

09:50-10:20 Coffee break

10.20-12.30 **Workshop 3**
Chair: **Kenji Doya**
▸ Neuroinformatics of BMI: decoding and control of neural codes

10:25-10:50	**Yukiyasu Kamitani**
10:50-11:15	**Hagai Lalazar**
11:15-11:40	**Ed Boyden**
11:40-12:10	**Panel discussion**
12:10-12:30	**Spotlight presentations: David Chik, Makoto Takemiya, Umesh Ghoshdastider, and Takashi Nakano**

12:30-13:30 Lunch

13.30-16.00 **Poster and Demo session 2**

15:30-16:00 Coffee break

16:00-16:50 **Keynote**
Maryann Martone (San Diego, USA)
▸ The possibility and probability of a global neuroscience information framework

16:50-17:40 **Keynote**
Colin Ingram (Newcastle, UK)
▸ Working in the clouds: creating an e-science collaborative environment for neurophysiology

19:00 **Dinner Cruise** (Buses leave from outside the Convention Center at 18:00)

Congress Day 3, September 1, 2010

09:00-09:50 **Keynote**
Lee Hood (Seattle, USA)
▸ A Systems Approach to Neurodegenerative Disease, Emerging Technologies and Proactive Medicine

09:50-10:20 Coffee break

10.20-12.10 **Workshop 4**
Chair: **Svein Dahl**
▸ Molecular mechanisms of neural signalling

10:25-10:50	**Phillip Biggin**
10:50-11:15	**Slawomir Filipek**
11:15-11:40	**Rama Ranganathan**
11:40-12:10	Panel discussion

12:10-13:30 Lunch

13:30-18:00 **INCF Japan Node Session**

INCF Japan Node Session

Congress Day 3, September 1, 2010
How neuroinformatics can revolutionize neuroscience

13:30-13:35 **Opening Greeting by Shun-ichi Amari**

13:35-15:00 **INCF Global Initiatives**
Chairs: **Sten Grillner & Jan G. Bjaalie**

- **Sten Grillner**: What INCF can do for neuroscience
- **Erik De Schutter**: New model description standards to facilitate multi-scale modeling
- **Robert W. Williams**: Global Exploratory Analysis of Massive Neuroimaging Collections using Microsoft Live Labs Pivot and Silverlight
- **Maryann Martone**: The INCF Program on Ontologies for Neural Structures
- **Colin Ingram**: Practical metadata standards: Making data sharing and endurance feasible

15:00-15:20 Coffee Break

15:20-17:10 **New Projects and Impacts from Asian-Pacific Circle**
Chair: **Shiro Usui**

- **David Van Essen**: An informatics perspective on cerebral cortical connectivity and function
- **Gary Egan**: Neuroinformatics approaches for mapping striatal structures and cortico-striatal connections in the human brain
- **Soo-Young Lee**: Perspectives on neuroinformatics as an important tool for an engineering goal - artificial cognitive system
- **Taishin Nomura**: Integrated bioscience with Dynamic Brain Platform
- **Ryutaro Himeno**: Japan's next-generation supercomputer R&D project and grand challenges in life sciences

17:15-18:15 **Panel Discussion**
Chair: **Sten Grillner**
Panelists: **David Van Essen, Jan G. Bjaalie, Upinder Bhalla, Chung-Chuan Lo, Gary Egan, Soo-Young Lee, Kenji Doya**

18:15-18:30 **Concluding Remarks**
Shiro Usui (Wako, Japan) and **Maryann Martone** (San Diego, USA)

KEYNOTES

Maryann Martone

Lee Hood

Upinder Bhalla

Ryohei Kanzaki

Colin Ingram

The possibility and probability of a global neuroscience information framework

Maryann Martone

Department of Neurosciences, University of California at San Diego, San Diego, USA

Understanding the brain strains the limits of current human ingenuity. Perhaps more than any other organ system, the problem of understanding the brain is fundamentally multiscale, with relevant data derived from spatial and temporal scales spanning many orders of magnitude. Because of the complexity and breadth of these networks, unraveling functional circuits underlying complex behaviors or pinpointing the locus of disease processes, even where the genetic defect is known, has confounded scientists, who by the limitations of experimental methods glimpse only a pinhole view of a vast interconnected landscape.

Neuroscientists rely heavily on technological advances to expand our capacity to deal with this enormous complexity. Certainly, neuroscience has been the direct beneficiary of recent revolutions in molecular biology, imaging technology and computational technology. These convergent revolutions are producing views of the brain of increasing size, breadth and detail, as we acquire data spanning multiple scales across increasing expanses of brain tissue. With the concomitant increase in computing power, the increased data generation is leading to production of ever more realistic computational models, allowing scientists to probe the consequences of the structural and biochemical complexity in ways not amenable to direct experimentation.

The potential power of these integrated approaches is exemplified in large-scale projects such as the Blue Brain (http://bluebrain.epfl.ch), the Allen Brain project (http://www.brain-map.org) and Genes to Cognition (http://www.sanger.ac.uk/research/projects/genestocognition). These projects realize huge monetary and manpower investments into the generation of large amounts of data. Because data within these projects are mainly acquired within a single framework, they are able to build powerful informatics infrastructure to serve and analyze these data. Mining these richly integrated data sets is starting to yield new insights into how the brain is organized.

The vast majority of neuroscience, however, is still conducted by individual researchers, who contribute their data and unique insights through less well structured venues such as the literature and websites or the creation of smaller custom databases. Although the amount of data is increasing daily, neuroscience as a whole, with its exceptionally large scope and diverse research community, lacks a coherent community framework for bringing these data together. Because such a framework has not been readily available, each source tends to use its own terminology and is structured, reasonably so, around its own particular data needs. Such customization is a significant barrier to data integration, because it requires considerable human effort to access each resource, understand the context and content of the data, and determine the conditions under which it can be compared to other similar results. The effect of this customization is that much neuroscience data is opaque to modern computational and bioinformatics tools that can operate across vast amounts of data, but require information to be parsed by a machine in order to be accessed and utilized.

Why is the data integration problem so difficult in neuroscience? Neuroscience, unlike molecular biology, does not have a single data type like a gene sequence that is easily stored or exchanged. Nor, like the geosciences, does it have a single well characterized spatial framework in which to place data. Without these types of "hooks", it is difficult to create common tools like Google Earth that "mash up" data coming from diverse sources. Thus, building a successful framework for neuroscience requires a multipronged approach to accommodate the diversity of data and the multiple temporal and spatial scales over which they are acquired. Essentially, a framework should be able to specify for each piece of data what, when and where and provide the means for tying them together; that is 1) a coherent semantic framework encapsulating the concepts that neuroscientists use to communicate about the content of their data, the experimental conditions under which they were acquired and the conceptual and temporal relationships among them; 2) a spatial framework for tying data to its general location in the nervous system; 3) a community infrastructure software base where researchers can share tools and data easily. Building these types of frameworks is hard, but through significant national and international investments in infrastructure over the past decade, the base elements of such a framework are beginning to emerge. However, the promise of these frameworks will only be realized if researchers begin to utilize them to make data and tools more discoverable and interoperable. In this presentation, I will discuss the current landscape of neuroscience resources and our experiences in establishing standards for global neuroscience information exchange through projects like the Neuroscience Information Framework (http://neuinfo.org), the Whole Brain Catalog (http://wholebraincatalog.org) and the INCF programs on atlasing and semantic interoperability.

A Systems Approach to Neurodegenerative Disease, Emerging Technologies and Proactive Medicine

Lee Hood

Institute for Systems Biology, Seattle, USA

The challenge for biology and medicine in the 21st century is the need to deal with its incredible complexity. One powerful way to think of biology is to view it as an informational science requiring systems approaches. This view leads to the conclusion that biological information is captured, mined, integrated by biological networks and finally passed off to molecular machines for execution. Systems approaches are holistic rather than atomistic—and employ both hypothesis-driven as well as discovery-driven approaches. Hence the challenge in understanding biological complexity is that of using systems approaches to deciphering the operation of dynamic biological networks across three time scales of life—development, physiological and disease responses. I will focus on our efforts at a systems approach to neurodegenerative disease—looking at prion disease in mice. We have just published a study that has taken more than 5 years—that lays out the principles of a systems approach to disease including dealing with the striking signal to noise problems of high throughput biological measurements and biology itself (e.g. polymorphisms). I will discuss how we have integrated six different types of data to generate powerful predictive network models. I will also discuss the emerging technologies that will transform medicine over the next 10 years—including next generation DNA sequencing, microfluidic protein chips, single-cell analyses and the capacity to generate stem cells for each individual patient. It appears that systems medicine, together with these transformational technologies and the development of powerful new computational and mathematical tools will transform medicine over the next 5-20 years from its currently reactive state to a mode that is proactive (P4)—medicine that is predictive, personalized, preventive and participatory. P4 medicine will have striking implications for healthcare costs as well as leading to a transformation of the healthcare industry. I will also talk about ISB strategic partnerships that will permit us to bring P4 medicine to the patient.

Multiscale models of the synapse: a self-modifying memory machine

Upinder Bhalla

Neurobiology, Computational Neuroscience and Systems Biology, National Centre for Biological Sciences, Bangalore, India

The human brain expresses some 20,000 genes, 100 billion neurons, and around 10 to the power of 15 synapses that connect up the neurons. Purely on a numerical basis, it seems likely that the synaptic connections would be a good place to store the vast amount of information that makes up our memories. There is now a considerable body of experimental data to show that synapses change in an experience-dependent manner, and increasingly point to these modifications as a key cellular basis for memory. This turns out to be a fertile and challenging arena for multiscale modeling and neuroinformatics. Synapses are precisely at the junction of electrical and chemical signaling. Although there are a plethora of models of signaling in memory, they are small pieces in a multidimensional puzzle. Synaptic memory is one of those processes which demand not just signaling models, but multiscale models that encompass neuronal networks, cellular biophysics, structural change, biochemical signaling, protein synthesis, and gene expression. Some of these domains - like biochemical signaling - are well-represented by simulation tools and standards such as SBML. Others - like structural change - have few, mostly incompatible, tools. I will present the process of modeling the synapse across a few of these multiple scales. There are conceptual challenges here, since we are fundamentally trying to understand how to get immensely stable, life-long changes out of a system that can not only reprogram itself, but also rebuild itself. Other challenges are to see how the synapse balances the requirements for fast switching, against long-term stability in the face of biochemical stochasticity. There are interesting couplings across scales, where electrical events have biochemical effects, and vice versa. I suggest that this cross-coupling at the synapse is one of the key systems where the convergence of neuroinformatics tools and standards can make a huge difference.

Brain mechanisms for the generation of adaptive behavior

Ryohei Kanzaki

Research Center for Advanced Science, University of Tokyo, Tokyo, Japan

For many decades, neuroethology has provided insights into how nervous systems organize and generate behavior. Important contributions from work in invertebrate preparations, particularly insects, have been made to brain research in the past, expanding our general understanding of sensory and motor systems.

Insects are valuable model systems in neuroscience due to the balance between the moderate complexity of their nervous systems, a rich behavioral repertoire, and the cost of maintenance as experimental animals. Insect brains contain on the order of 10^5 to 10^6 neurons. The concept of individually identifiable neurons and small networks composing functional units have been vital for understanding insect brains. Moreover, insects are uniquely suited for multidisciplinary studies in brain research involving a combined approach at various levels, from molecules over single neurons to neural networks, behavior, modeling, and robotics, owing to their seamless accessibility to a wide variety of methodological approaches, in particular genetic engineering, neuroanatomy, electrophysiology, and functional imaging.

Adaptability, the capability to behave properly in accordance with ceaselessly changing environments, is an excellent feature of animals. Insects will become an excellent model for understanding adaptive control in biological systems and in turn, inspire control and communication in engineered systems. In this lecture, focusing on the adaptive behavior in insects, brain mechanisms of the behavior revealed by using multidisciplinary approaches will be shown. Adaptive behavior appears in the interaction between a body, brain and the environment. Therefore, an experimental system for evaluating and understanding adaptive behavior is required to be a closed-loop system, in which environmental information is fed back to an animal. This system must be capable of optionally manipulating the external environment or the properties of the animal, allowing the adaptive behavior to be systematically investigated. We have developed an insect-machine hybrid system, which moves depending on the behavioral or the neural output of an insect, as a novel experimental system. The robot is controlled by the behavior of an insect tethered on the robot or by the neural activity of the insect brain. Therefore, by arbitrarily manipulating the motion system of the robot, changes similar to those done by manipulating the sensory-motor system of the insect are possible.

At first in this lecture, as an example of adaptive behavior of an insect, odor-source orientation behavior of a male silkmoth and its neural basis will be shown. Second, the extent of adaptation in the behavioral strategy, as governed by the neural system and investigated via a robotic implementation, will be shown. Finally, I will demonstrate an insect-machine hybrid system that will lead to great insight for evaluating and understanding adaptive behaviors.

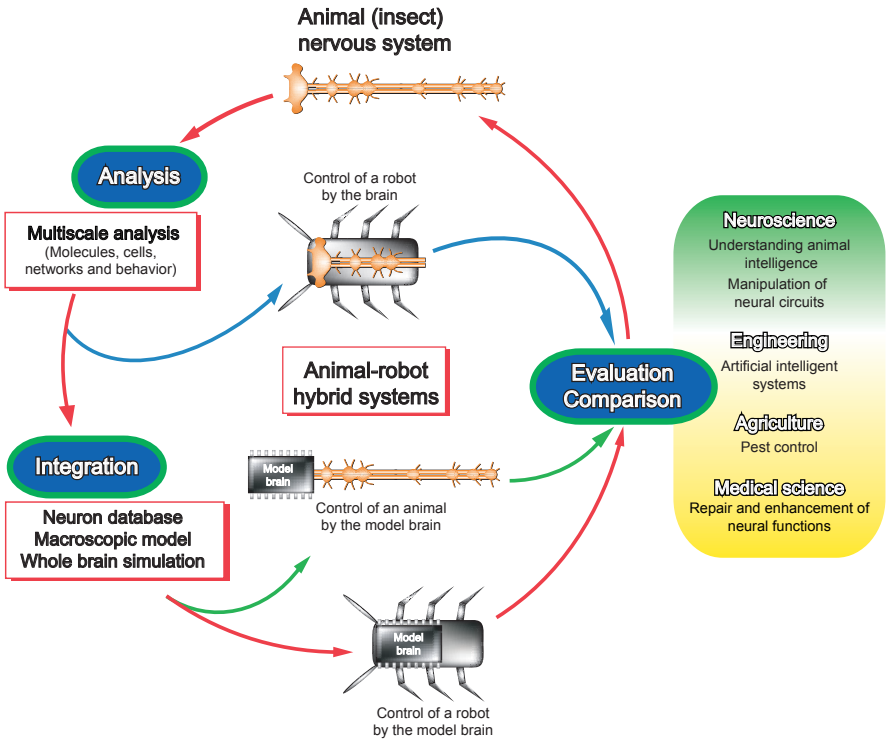


Figure: Concept of the research

Working in the clouds: creating an e-science collaborative environment for neurophysiology

Colin Ingram

Institute of Neuroscience, University of Newcastle, Newcastle, UK

Understanding the way that neural networks function can only be achieved through detailed analysis of the spatio-temporal relationships between activity patterns of neurones within the network. The increasing sophistication of multielectrode and optical recording techniques has provided the means for us to explore the control and organisation of neural networks in ever greater detail. However, whilst developments in neuroinformatics offer new ways in which the large volumes of data generated from such techniques may be manipulated and analysed, there is a growing need to develop an infrastructure to support sharing and collaborative exploitation of these data. Cloud computing provides exciting opportunities for this exploitation with rapidly increasing availability of data storage and compute resource accessed through the web. However, any practical solution to supporting analysis and sharing of time-series neurophysiological data needs to address a number of major challenges, including interoperability of file formats, data visualisation, and effective metadata descriptions. These challenges are being addressed through a number of international research projects, including CARMEN (Code Analysis, Repository and Modelling for e-Neuroscience; www.carmen.org.uk), an open access web platform developed for handling time-series data using distributed computing technology. CARMEN has created a secure collaborative environment in which data can be shared, either between private groups or publicly, and new analysis algorithms can be deployed without restrictions of issues of software and file compatibility. The on-going implementation of an enactment engine is enabling service applications to be linked into more complex and user-defined workflows. The cloud architecture allows the co-location of data and computation and enabling users to conduct their science through a web browser. Furthermore the growing data repository enables maximum exploitation of data that are often difficult and expensive to produce. CARMEN is one example of the shift from small scale science to large scale data integration which will underpin the next major steps in understanding the brain. Infrastructure built on cloud computing will make this integration feasible and will offer new opportunities to build a global community for neuroscience.

Workshop 1:
How to describe a model: description language solutions and challenges

Chair: **Erik De Schutter,** University of Antwerp, Belgium

General adoption of standard model description languages strongly boosts model sharing and software tool development, as witnessed in systems biology. Despite these clear advantages, attempts at creating description standards in computational neuroscience have had limited success so far. In this workshop we present some of the challenges and introduce recent attempts at moving computational neuroscience forward.

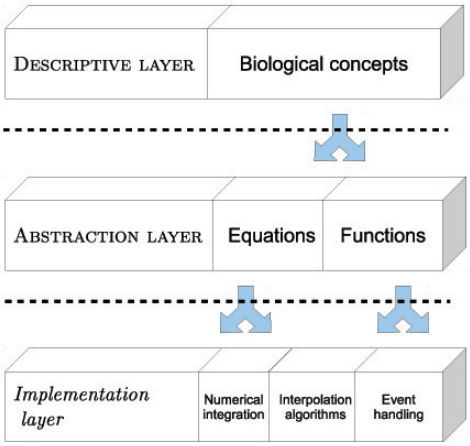
Sean Hill will give an overview of the current state and discuss the challenge of describing a model that spans multiple scales, possibly being simulated using several software packages simultaneously. Chung-Chuan Lo will introduce an INCF initiative to create a new, intrinsically extensible language to describe neural network models. Finally, Nicolas Le Novère will discuss what is needed beyond just model description: how does one document all aspects involved in running simulations and analyzing their output?

Speakers:

Sean Hill, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland
Chung-Chuan Lo, National Tsing Hua University, Hsinchu City, Taiwan
Nicolas Le Novère, European Bioinformatics Institute, Hinxton, UK

Spotlight presentations:

Honda Naoki, **Iain Hepburn**, **Jaap Van Pelt**, and **Stephen Larson**



A layered description language for spiking neural network modeling

Chung-Chuan Lo

Institute of Bioinformatics and Structural Biology, National Tsing Hua University, Hsinchu City, Taiwan

Neural modeling has a long history in the development of modern neuroscience and has greatly enhanced our understanding in principles of neural activity and interactions between neurons. However, as a rapidly growing field, the neural network modeling has reached a level of complexity which makes the exchange of information between research groups extremely difficult. It also becomes more and more unlikely that the modeling results obtained in one lab be exactly reproduced in another lab which uses a different simulator. The problem arises from the fact that the field of computational neuroscience is lacking appropriate standards to communicate network models.

To address this issue, the International Neuroinformatics Coordinating Facility (INCF) has initiated a project: Network Interchange for Neuroscience Modeling Language, or NineML, which provides a standardized machine-readable language for spiking neural network models with an aim to ease model sharing and to facilitate the replication of results across different simulators. In the talk I will introduce the first version of NineML. Its most innovated features includes:

1. Layered: The complete description of a neural network model in NineML is separated into to a user layer and an abstraction layer. The XML-based user layer provides a syntax to specify the instantiation and parameterization of a network model in biological terms. The abstraction layer provides explicitly descriptions of the core concepts, mathematics, model variables and state update rules.
2. Fully self-consistent: All model concepts defined in the user layer are expressed explicitly in the abstraction layer so that a neural network model can be unambiguously implemented by software that fully supports NineML.
3. Highly expandable: future expansions are taken into account in the development of NineML. Hence specific model features that are not supported in the current version of NineML can be easily added in a later version without any major revision to the specification of the language.

In the talk I will also demonstrate NineML using several example models of neural networks. I will show how the description looks like in different layers and how NineML solves some difficult problems.

Using NineML, researchers can describe their neural network models in an unambiguous and simulator-independent way. Furthermore, the models can be reimplemented and simulation results can be easily reproduced by any simulator which fully supports NineML. We believe that this project will have a profound effect on the modeling community and will facilitate research in computational neuroscience.

Describing the whole life-cycle of modelling in neuroscience

Nicolas Le Novère

Wellcome Trust Genome Campus, EMBL, European Bioinformatics Institute, Hinxton, UK

A decade ago, the creation of the Systems Biology Markup Language (SBML) changed the way people exchanged, verified and re-used models in systems biology. The robustness and versatility of this format, coupled to a wide software support, fostered the emergence of an entire area of research centred on model processing such as encoding, annotation, merging, comparison and integration with other datasets. Recently, new languages appeared that complement the model description, such as SED-ML to describe the simulation experiments or SBRML to encode the numerical results. In neurosciences, other fledging efforts cover for instance multi-compartment neurons with NeuroML, and neuronal networks with NineML. More are needed to cover the while spectrum of computational models used in neurosciences. The developers of those initiatives are in contact, and try to improve the interoperability of the languages, for instance by sharing metadata. Similar development guidelines, governance principles and quality checks are needed, in order to provide the community with a serious infrastructure. One can hope to see, in a not too elusive future, the creation of a coherent set of non-overlapping standards that will support not only the various modeling approaches and scales needed to simulate human functions and dysfunctions, but also cover model structure, parametrisation, simulation and numerical output. Such a toolkit will allow bridging genomics, computational neuroscience and drug discovery.

Challenges for Multi-scale Modeling Languages

Sean Hill

Brain Mind Institute, Blue Brain Project, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Understanding the effect of a disease or a treatment on individual brains requires understanding the link between the genetic, subcellular, electric and whole brain scales. Relevant phenomena within the brain span a remarkable range of physical and temporal scales. This includes subcellular activity ranging from the level of individual molecules, protein folding and gene expression to physiological networks governing transcription, signaling and metabolism. Electrical activity ranges from local voltage-gated ion channels and neuron firing behavior to collective network effects, oscillations and whole brain activity. Brain connectivity itself ranges from synapses placed with submicron precision on specific portions of individual neurons to local microcircuitry, mesoscale axonal patterning and long-ranging fiber tracts that connect brain regions across the brain. Other phenomena including plasticity, homeostasis and development occur across timescales ranging from milliseconds to hours, days or years. Mathematical approaches are often already available to model interactions within each scale, however the challenge remains to develop mathematical approaches to describe relationships across scales. Modeling languages also, must be extended to facilitate the description of models within and across spatial and temporal scales. Exploring examples such as linking a molecular-scale synapse model with an electrical-scale neuron model, I will present some of the challenges posed by describing multiscale relationships relevant to brain function and dysfunction.

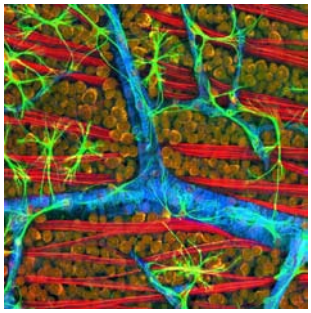
Workshop 2:
Synaptoprojectomes: Assembling, using and sharing dense cellular micromaps of brains

Chair: **Mark Ellisman**, University of San Diego, USA

Understanding the complexities of the brain is a grand challenge, partly because of the wide range of scales involved. Many investigators are now pushing forward to surmount the technical hurdles associated with determining the wiring diagram of specific regions of the brain. Modern light microscopic methods do not provide adequate resolution for tracking the fine details of cellular processes. Higher resolution imaging methods, like 3D electron microscopies, are difficult to apply to the very large volumes of brain tissue, which are required for such mapping. However, recent successes suggest that efforts to accelerate the development of computer-automated methods of both light and electron microscopy may ultimately enable more complete spatial mapping of nervous systems. Presentations in this session will consider these issues and describe progress in imaging cell types and their detailed relationships within key structural domains of nervous systems. The integration of these large and high-resolution multiscale volumes with emerging atlas frameworks will also be discussed. This session will consist of three lectures and a subsequent panel discussion.

Speakers:

Davi Bock, Harvard Medical School, Boston, USA
Robert Marc, University of Utah, Salt Lake City, USA
Marcel Oberlaender, Max Planck Florida Institute, Jupiter, USA

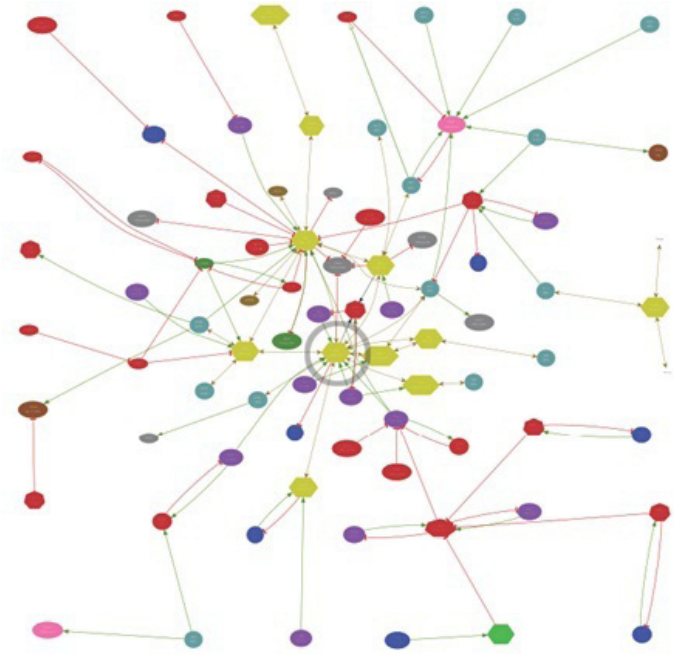


Deerinck and Ellisman, NCMIR - UCSD

Mining retinal connectomes

Robert Marc and James R. Anderson
John A. Moran Eye Center, University of Utah, Salt Lake City, USA

Automated transmission electron microscope (TEM) allows extensive capture of contiguous 2D and 3D imagery, posing challenges for data storage, access, viewing, annotation, tracking and analysis. Such datasets quickly transcend a user's capacity for analysis. And, as annotated anatomical data sets represent significant investment of resources, we argue they should follow Open Data concepts for access and reuse. The Viking application (Anderson et al., 2010, J Microscopy) was our solution to view and annotate RC1, a 16.5 TB ultrastructural retinal connectome volume. Viking is HTTP-compliant, supports concurrent authenticated users, and collaborative annotation strategies, including mining, graphing and rendering neural networks. It demarcates viewing and analysis from capture and hosting and permits applying image transforms in real-time. It also permits the fusion of registered thin-section optical molecular data with TEM image data, augmenting the collection of cell classification metadata. Connectome dataset RC1 was imaged at 2 nm resolution, balancing competing constraints of large-area sampling and fine-scale cell association maps (subclasses of chemical synapses, gap junctions, adherens junctions, organelle patterning). We use a crowd-sourcing strategy for annotation with Viking. This leads to rapid assembly of directed cyclic network graphs, dynamically visualized via a web-services Viz application that also provides network validation, error discovery and correction. The network graph below illustrates the associations of a single class A-II glycinergic amacrine cell (C467, circled) in the rabbit retina tracked through four synaptic "hops". Even if automated tracking and annotation were viable, a Viz-like application would still be critical for finding and correcting network errors. Moreover, crowd-sourcing enables the discovery of novelty (connective, associative and ultrastructural), which automated tools have yet to achieve. In a year of analysis, mining connectome RC1 has uncovered new synaptic pathways and topologies, new non-neural activities, and new signaling states. Intensive mining of connectomics datasets provides the unique opportunity to build realistic system models based on complete synaptic partner maps.
Support: NEI EY02576, NEI EY015128, P30EY014800, NIH T32DC008553, NSF 0941717, Research to Prevent Blindness. Disclosure: REM is a principal of Signature Immunologics, Inc.

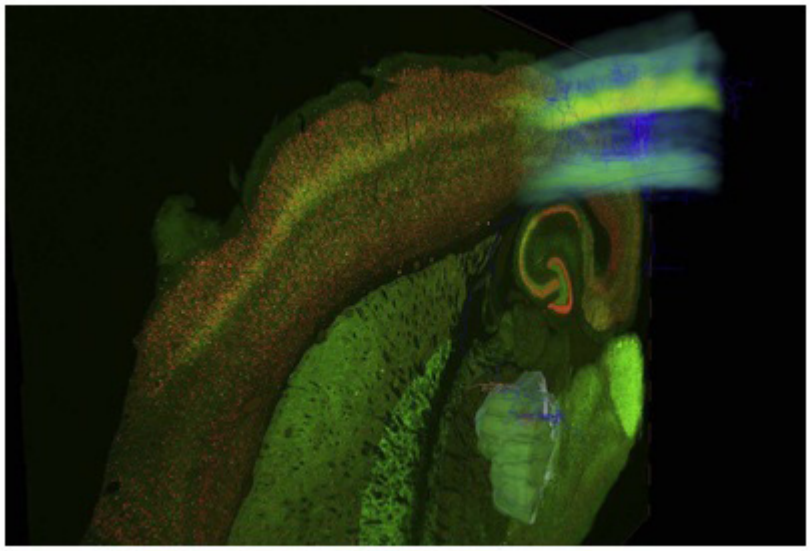


Quantitative anatomy for assembling large scale neural networks

Marcel Oberlaender
Max Planck Florida Institute, Jupiter, USA

Sensory deprivation, as well as neurodegenerative diseases, such as Alzheimer's, cause substantial changes in brain function and anatomy, which ultimately result in behavioral deficits. Therefore, over the last 5 years, Marcel Oberlaender and his colleagues developed methods to image and quantify 3D neuron and neuronal network anatomy. These methods allow determining the number and three-dimensional distribution of all neurons in large volumes of brain tissue, the tracing of all processes from individual neurons, their classification and interconnection to realistic neural networks (see Figure: Illustration of the "Networks in silico project"). High resolution 3D image stacks of the entire brain lay the foundation to quantify the structure and 3D distribution of all neurons within functional neuronal networks. Here, the whisker-related thalamocortical pathway in rats is reconstructed.

So far these methods were limited to certain brain regions such as the somatosensory cortex or thalamus. However, recent developments in imaging techniques and computing power will allow in principle the application of these methods to the entire mouse or rat brain. The department of "Digital Neuroanatomy" at the newly founded "Max Planck Florida Institute for Integrative Biology and Neurosciences" therefore aims to determine the total number and three-dimensional distribution of all neurons in brains of "normal" mice. The resultant "cellular atlas" of the mouse brain will function as an unbiased reference for anatomical changes at cellular level caused by sensory deprivation or disease.



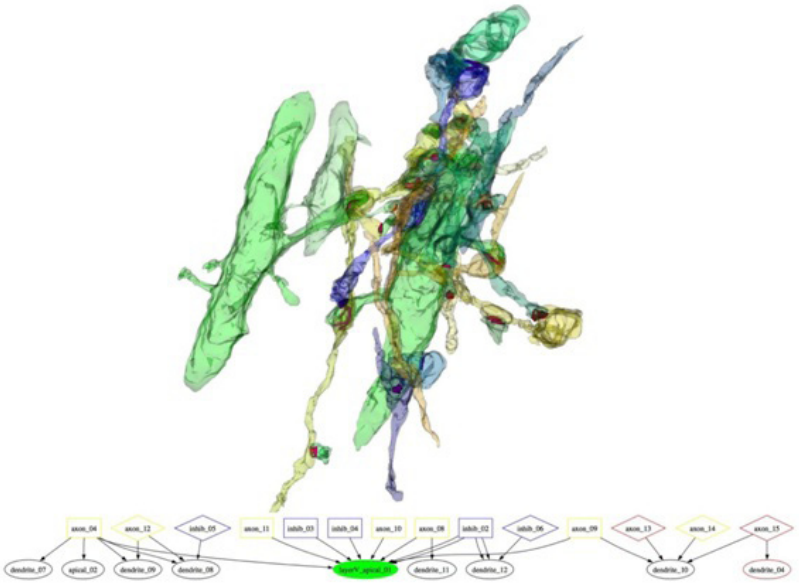
Toward relating wiring diagrams to receptive fields: electron microscopy of calcium-imaged neurons in mouse visual cortex

Davi Bock

Program in Neuroscience, Harvard Medical School, Boston, USA

Our purpose is to combine anatomy and physiology to better understand the operation of neural circuits. We recorded the responses of a cluster of cells in mouse primary visual cortex during presentation of drifting gratings of varying orientation, using in vivo 2-photon calcium imaging. We relocated the physiologically characterized cells at the electron microscopy (EM) level and imaged a 1200 section series of ultrathin (~45 nm) sections using a custom high speed transmission electron microscopy camera array (TEMCA). The imaged field of view per section was ~430 x 300 micron, with a pixel size of ~3.75 nm, resulting in a ~115,000 x 80,000 pixel composite image per section and a ~ 10 TB net image stack. This scale and resolution is sufficient to begin extracting the anatomical connectivity of groups of functionally characterized neurons at the level of individual synapses.

I will present this work, discuss the many data handling issues we have run into along the way, and present a road map for future increases in scale.



Workshop 3:
Neuroinformatics of BMI: decoding and control of neural codes

Chair: **Kenji Doya**, Okinawa Institute of Science and Technology, Okinawa, Japan

Controlling a robot by thought, seeing through silicon retina, connecting brains by wire, or WiFi -- brain-machine interface (BMI) has developed not only as practical technology for neuroprosthetics, but also for real-life testing of our understanding of information coding in the brain. The three speakers of this workshop present the latest developments in non-invasive BMI in humans, multi-electrode BMI in monkeys, and optical stimulation andasensing in genetically engineered animals. Panels will discuss neuroinformatic challenges in BMI, including methods of modeling and decoding, sharing of data and software, and possible social impacts.

Speakers:

Yukiyasu Kamitani, Advanced Telecommunications Research Institute International, Kyoto, Japan
Hagai Lalazar, Interdisciplinary Center for Neural Computation, The Hebrew University, Jerusalem, Israel
Edward Boyden, Massachusetts Institute of Technology, Cambridge, USA

Decoding visual perception from human brain activity

Yukiyasu Kamitani

ATR (Advanced Telecommunications Research Institute International), Kyoto, Japan

Objective assessment of mental experience in terms of brain activity represents a major challenge in neuroscience. Despite its wide-spread use in human brain mapping, functional magnetic resonance imaging (fMRI) has been thought to lack the resolution to probe into putative neural representations of perceptual and behavioral features, which are often found in neural clusters smaller than the size of single fMRI voxels. As a consequence, the potential for reading out mental contents from human brain activity, or 'neural decoding', has not been fully explored. In this talk, I present our recent work on the decoding of fMRI signals based on machine learning-based analysis. I first show that visual features represented in 'subvoxel' neural structures can be decoded from ensemble fMRI responses, using a machine learning model ('decoder') trained on sample fMRI responses to visual features. Decoding of stimulus features is extended to the method for 'neural mind-reading', which predicts a person's subjective state using a decoder trained with unambiguous stimulus presentation. Various applications of this approach will be presented including fMRI-based brain-machine interface. We next discuss how a multivoxel pattern can represent more information than the sum of individual voxels, and how an effective set of voxels for decoding can be selected from all available ones. Finally, a modular decoding approach is presented in which a wide variety of contents can be predicted by combining the outputs of multiple modular decoders. I demonstrate an example of visual image reconstruction where binary 10 x 10-pixel images (2^00 possible states) can be accurately reconstructed from a singe-trial or single-volume fMRI signals, using a small number of training data. Our approach thus provides an effective means to read out complex mental states from brain activity while discovering information representation in multi-voxel patterns.

Sensorimotor control and learning using a Brain-Machine Interface

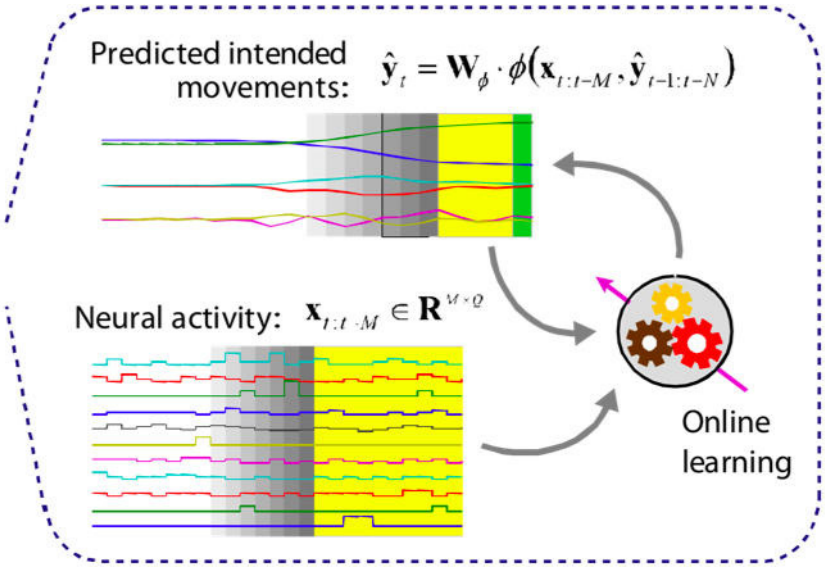
Hagai Lalazar

Interdisciplinary Center for Neural Computation and Department of Medical Neurobiology, The Hebrew University, Jerusalem, Israel

Brain Machine Interface (BMI) is being developed as a therapeutic application to restore motor control to immobilized patients. Neural signals recorded in real-time from the subject's brain are fed into an algorithm which attempts to decipher their motor intentions and convert them into control commands that can guide various devices.

We developed a BMI environment that utilizes an adaptive version of the Kernel Auto-Regressive Moving Average (KARMA) algorithm. This method achieves high accuracy in decoding real arm movements in the offline setting, and smooth, natural-like, and successful movements in the closed-loop paradigm. Moreover, the learning algorithm allows the BMI to be used successfully practically instantly, needs no explicit training, and continually adapts in the background to any changes in neural encodings or recording quality.

In addition to its primary clinical purpose, we are using the BMI setup as a new experimental tool to study sensorimotor control and learning. The advantage of BMI is that it creates a causal and controlled direct link between a sub-population of neurons (all of which are recorded) and the behavioral output. In order to probe the encoding properties of motor cortical neurons, we compared the neural activity of the same neurons when monkeys performed the same task with either real arm movements or the closed-loop BMI. Thus the monkeys had identical motor intentions and similar cursor kinematics in both cases, yet controlled very different effectors. To investigate how such tuning properties initially develop we then let the monkeys learn to control a novel visuomotor task that they had never controlled before with their bodies, over several days. I will show how the population response slowly formed along the several days of learning.

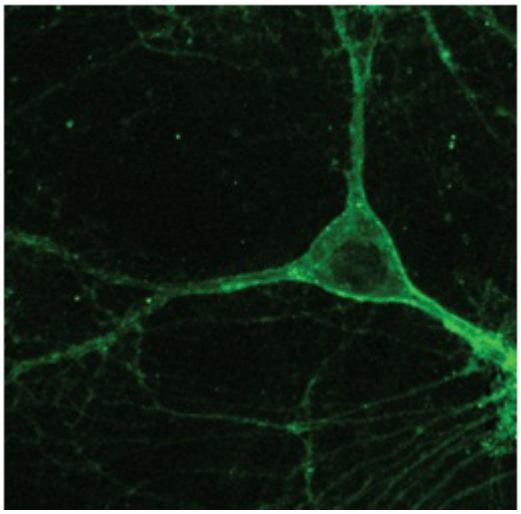


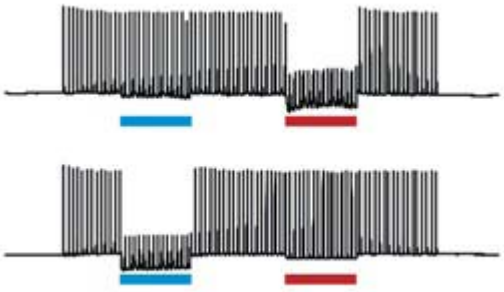
Enabling Systematic Neuroscience with Novel Optical Neural Control Strategies

Ed Boyden

Massachusetts Institute of Technology, Cambridge, USA

Over the last several years our group has developed a rapidly-expanding suite of genetically-encoded reagents that enable powerful neural activation and silencing in response to pulses of light. In order to enable these tools to be used for systematic analysis of the causal contribution of specific cell types, pathways, and brain regions to neural computations, behaviors, and pathologies, we are continually expanding this toolbox in quality and modality of control, and have begun to develop hardware to enable neural circuits to be perturbed in a three-dimensional fashion, and for the network-wide impact to be measured. We explore how these tools can be used to enable systematic analysis of neural circuit functions, exploring the properties of neural circuits that mediate emotion, sensation, and movement, and that play roles in neurological and psychiatric disorders. We also discuss the translational potential of such tools to potentially enable novel ultraprecise neuromodulation therapies.





Workshop 4 :
Molecular mechanisms of neural signaling

Chair: **Svein Dahl**, University of Tromsø, Norway

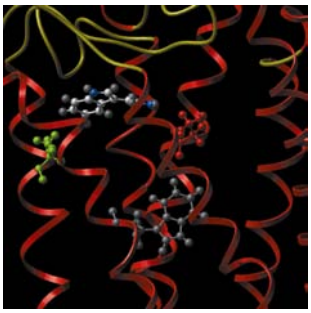
The rapid development of molecular biology over the last 20 years has provided new insight into the molecular mechanisms of signal transduction in the nervous system. The receptors, transporter proteins and intracellular proteins involved in signaling mechanisms have been cloned, and their secondary structures (amino acid sequences) determined. Molecular imaging techniques have demonstrated the dynamics of intracellular signaling mechanisms in amazing detail. Three dimensional crystal structures of some of these proteins have also been determined, and explained their functional mechanisms at the molecular level.

Many of the molecules involved in neural signaling are membrane proteins, which have proven difficult to produce, purify and crystallize. Molecular modeling of such proteins, often based on known crystal structures of other proteins, has gained widespread application as a valuable tool to simulate their three-dimensional structures, molecular dynamics, ligand interactions and functional mechanisms. Neurotransmitter transporter proteins, ligand-gated ion channels and G-protein coupled receptors, all proteins imbedded in pre- or post-synaptic nerve cells, are important molecular targets for existing and yet-to-be discovered therapeutic drugs.

This workshop will demonstrate the results of modeling molecules involved in neural signaling, and simulations of their molecular mechanisms.

Speakers:

Philip Biggin, University of Oxford, United Kingdom
Slawomir Filipek, International Institute of Molecular and Cell Biology, Warsaw, Poland
Rama Ranganathan, University of Texas Southwestern Medical Center, Dallas, USA



Ravna et al, J Mol Model 15:1155-64, 2009

Classification, structure and function of neural membrane proteins

Philip Biggin

Department of Biochemistry, Computational Approaches to Receptor Dynamics and Ligand-Binding, University of Oxford, Oxford, UK

At the very bottom of the enormous complexity that defines neuroinformatics are molecules. An understanding of the detailed nature of these molecules and how they interact with each other is required if we are to be able to not only develop better higher-level models but also improve prospects for rational drug-design.

One of the central problems related to our understanding of neuronal membrane proteins is the fact that they are embedded within a membrane. This has impeded biophysical characterization of these molecules. Nevertheless, in recent years there has been much progress at the molecular level and there is now a substantial amount of structural information available for many neuro-receptors. Complementary to these experimental approaches, there have been significant contributions from computational biochemistry groups using molecular dynamics simulations to gain insight into how these proteins perform their function and undergo conformational change.

In this session we will discuss some of the recent structural and computational work performed at the atomic level and what the future challenges are, including how to link this knowledge into higher-level models.

Systems-level analysis of a G protein mediated signaling pathway

Rama Ranganathan

Green Center for Systems Biology and Dept. of Pharmacology, University of Texas Southwestern Medical Center, Dallas, USA

Photoreceptors of Drosophila compound eye employ a G-protein mediated signaling pathway that transduces single photons into transient electrical responses called "quantum bumps" (QB). While most of the molecular components of this pathway are already known, the system level understanding of the mechanism of QB generation has remained elusive. To address this, we developed a quantitative model explaining how QBs emerge from stochastic nonlinear dynamics of the signaling cascade. The model shows that the cascade acts as an "integrate and fire" device, and explains how photoreceptors achieve reliable responses to light while keeping low background in the dark. Further experimental work shows how different functional properties of the QB –size, shape, and probability of occurrence – can be mechanistically decomposed into distinct molecular mechanisms. This analysis provides a foundation for understanding how the essential biological characteristics of visual signaling arise from systems-level structural and dynamical properties of the underlying signaling pathway.

Ligand binding and action of microswitches in G protein coupled receptors

Slawomir Filipek

International Institute of Molecular and Cell Biology, Warsaw, Poland

G protein coupled receptors (GPCRs) interact with very diverse sets of ligands which bind to the transmembrane segments and sometimes also to the receptor extracellular domains. Each receptor subfamily undergoes a series of conformational rearrangements leading to the binding of a G protein during the activation process. All GPCRs preserved the 7-TM scaffold during evolution but adapted it to different sets of ligands by structure customization. Binding of structurally different agonists requires the disruption of distinct intramolecular interactions, leading to different receptor conformations and differential effects on downstream signaling proteins. The dynamic character of GPCRs is likely to be essential for their physiological functions, and a better understanding of this molecular plasticity could be important for drug discovery. Experiments suggest that agonist binding and receptor activation occur through a series of conformational intermediates. Transition between these intermediate states involves the disruption of intramolecular interactions that stabilize the basal state of a receptor. Such profound changes are evoked by the action of molecular switches (microswitches). The switches proposed so far for different GPCRs include the "rotamer toggle switch" involving the CWxPxF sequence on helix TM6, the switch based on the NPxxY(x)(5,6)F sequence linking helices TM7 and H8, the "3 7 lock" interaction connecting TM3 and TM7 (involving Schiff base-counterion interaction in rhodopsin), and the "ionic lock" linking transmembrane helices TM3 and TM6 and employing the (E/D)RY motif.

To investigate the early activation steps concurrent to ligand binding we used opioid receptors. They belonging to the family A (rhodopsin-like) of GPCRs. For the important role they play in the human body in controlling pain and stress, modulating immune responses and developing addiction the opioid receptors were subject of numerous investigations. We chose a set of rigid ligands with the structural motif of tyramine because ligand flexibility would obscure the very first structural movements induced upon ligand binding. On the basis of conducted molecular dynamics simulations we propose that agonists and antagonists bind to Y3.33 but only agonists are able to move deeper into the receptor binding site and to reach H6.52. The movement from Y3.33 to H6.52 induces breaking of the TM3-TM7 connection D3.32-Y7.43 ("3-7 lock" switch). We also observed a concerted motion of W6.48 and H6.52 suggesting existence of an extended "rotamer toggle switch". Simultaneous action of both switches, the "3-7 lock" and the "rotamer toggle switch", implies a temporal but also spatial (an agonist linking H6.52 and D3.32) dependence between them and possibly other switches on a longer time scales.

References:

1. M. Kolinski, S. Filipek, "Molecular Dynamics of mu Opioid Receptor Complexes with Agonists and Antagonists", TOSBJ (2008) 2, 8-20.

2. M. Kolinski, S. Filipek, "Studies of the Activation Steps Concurrent to Ligand Binding in OR and OR Opioid Receptors Based on Molecular Dynamics Simulations", TOSBJ (2009) 3, 51-63.

3. M. Kolinski, S. Filipek, "Structurally similar pair of agonist and antagonist of kappa opioid receptor studied by molecular dynamics simulations", J. Mol. Model. (2010) in press.

Posters and Demos

Neuroinformatics in India: Building academic and research excellence in the Developing World

Upinder Bhalla[1] and Prasun Roy[2]

1. National Centre for Biological Sciences, TIFR, Bangalore, India
2. National Brain Research Centre, Gurgaon, India

India is the most recent entrant into the INCF, and is rapidly building up its national node and activities. The country node has been named as the "Indian National Node for Neuroinformatics" and more than a dozen institutions have already agreed to participate in national node activities. These institutions span several major disciplines, namely:

(a) The Indian Institutes of Technology at Delhi, Bombay & Madras,
(b) The Indian Institute of Science-Bangalore & Indian Institute of Science Education and Research-Pune
(c) The Indian Institutes of Information Technology at Hyderabad, Allahabad & Bangalore.
(d) The medical institutions as All-India Institute of Medical Sciences-Delhi, National Institute of Mental Health & Neurosciences-Bangalore, and Sree Chitra Medical Institute-Trivandrum.
(e) The mathematical institutions as Indian Statistical Institute-Calcutta & Institute of Mathematical Sciences - Madras.
(f) Scientific institutions as Tata Institute of Fundamental Research-Bangalore/Bombay, Institute of Biotechnology & Applied Bioinformatics-Bangalore, National Centre for Biological Sciences-Bangalore, and National Brain Research Centre-Delhi.
(g) University systems as University of Hyderabad.
(h) Industrial companies as Cellworks, Bangalore.

The first formal activity of the Indian node was the INCF meeting on Multiscale Modeling held in Bangalore in November 2009. A second meeting, to coincide with the National Node meeting, is planned for November 2010. During the November meeting, there evolved two research projects which were enthusiastically supported:

(1) Multiscale models involving biochemical and electrical signalling along with the simulator functionality, the range spanning from dendrite dynamics to network excitation.
(2) Brain as a tissue where cellular and gross imaging methods, biophysical transport processes, and spatiotemporal gene expression profiles, are used for structural and functional studies.

Another key activity of the Node is to promote neuroinformatics research. A first major step toward this was to enlist the active support of the Government of India through its various ministries:

(A) Dept. of Biotechnology, Ministry of Science & Technology: There is a Task Force on "Neuroscience" where the area of neuroinformatics, computational neuroscience, and neuroimaging is an active field of support.
(B)Dept. of Information Technology, Ministry of Communications & Information Technology: There is a special R&D program area on "Perception Engineering", which uses neuromorphic systems and computational neuroscience principles to develop newer clinical, robotic, or technical applications.

The National node will also strengthen ongoing activities in the area. For example there has been an annual workshop on "Computational Neuroscience" that has been held for almost a decade, which the Indian National Node will enthusiastically support. This workshop rotates through major cities in India and takes place in university settings, where students and young faculty from around the country are offered travel fellowships, and are exposed to advanced topics and hands on experience.

As a developing nation, we are keen that the activities of the National Node contribute both to the academic growth in the field, and to eventual biomedical applications supported by data-driven work in neuroscience.

To conclude, Neuroinformatics in India is vibrant and growing, and the fields of computational neurology, neuroimaging (microscale and macroscale), and neuroengineering are seeing a great deal of emphasis from researchers and funding agency alike. We hope to build on the large talent pool in neuroscience and in information technology in India, and are keen to draw on the experience and scientific networking within the INCF to strengthen the field.

The Swedish INCF Node

Jeanette Hellgren Kotaleski

Department of Computer Science and Communication, Royal Institute of Technology, Stockholm, Sweden

The INCF National Node of Sweden is located at the Royal Institute of Technology (KTH) in Stockholm and was established in August 2006. The node functions as a network of research groups, covering primarily computational neuroscience bridging over subcellular networks to large scale networks [1-6]. There is s strong element of software tools for modeling and simulations [7, 8]. Also databases for brain imaging as well as neurorobotics are represented [9]. The node is furthermore coordinating an Erasmus Mundus PhD programme in Neuroinformatics [10]. The node's activities are closely linked with both the Stockholm Brain Institute [11] and Swedish eScience Research Center (SeRC), both with a focus on neurodegenerative diseases.

References highlighting ongoing research:

References

1. Kotaleski JH, Blackwell KT.(2010) Modelling the molecular mechanisms of synaptic plasticity using systems biology approaches, Nat Rev Neurosci. 11(4):239-51.

2. Fransén E, Tigerholm J (2009) Role of A-type potassium currents in excitability, network synchronicity, and epilepsy, Hippocampus (in press)

3. Harischandra N, Ekeberg Ö.(2008) System identification of muscle-joint interactions of the cat hind limb during locomotion, Biol Cybern 99(2):125-38.

4. Lansner A. (2009) Associative memory models: from the cell-assembly theory to biophysically detailed cortex simulations, Trends Neurosci. 32(3):178-86.

5. Kozlov A, Huss M, Lansner A, Kotaleski JH, Grillner S.(2009) Simple cellular and network control principles govern complex patterns of motor behavior, Proc Natl Acad Sci U S A. 106(47):20027-32.

6. Djurfeldt M, Ekeberg O, Lansner A.(2008) Large-scale modeling - a tool for conquering the complexity of the brain, Front Neuroinformatics. 2:1.

7. Mikael Djurfeldt, Johannes Hjorth, Jochen M. Eppler, Niraj Dudani, Moritz Helias, Tobias C. Potjans, Upinder S. Bhalla, Markus Diesmann, Jeanette Hellgren Kotaleski, and Örjan Ekeberg (2010) Run-Time Interoperability Between Neuronal Network Simulators Based on the MUSIC Framework, Neuroinformatics 8(1): 43—60.

8. Brette R, Rudolph M, Carnevale T, Hines M, Beeman D, Bower JM, Diesmann M, Morrison A, Goodman PH, Harris FC Jr, Zirpe M, Natschläger T, Pecevski D, Ermentrout B, Djurfeldt M, Lansner A, Rochel O, Vieville T, Muller E, Davison AP, El Boustani S, Destexhe A. (2007) Simulation of networks of spiking neurons: a review of tools and strategies, J Comput Neurosci. 23(3):349-98.

9. Balkenius C, Morén J., Johansson B and Johnsson M (2010) Ikaros: Building cognitive models for robots, Advanced Engineering Informatics 24:40-48.

Activities of the US INCF Node

Maryann Martone

University of California at San Diego, La Jolla, USA

The US is establishing a distributed series of nodes, recognizing the diversity and size of the neuroinformatics community in the United States. Two such current nodes reside at the Neuroscience Information Framework (NIF; http://neuinfo.org) and the Neuroimaging Tool and Resource Clearinghouse (NITRC; http://nitrc.org), two large projects funded by the National Institutes of Health Blueprint for Neuroscience Research consortium (http://neuroscienceblueprint.nih.gov). The Blueprint is a consortium of the 16 NIH institutes, centers and offices that support neuroscience research that was established to support common programs across institutes. A third node is the Collaborative Research in Computational Neuroscience (CRCNS; http://crcns.org), a joint NIH-National Science Foundation (NSF) initiative that promotes data sharing in the computational neuroscience community. The US node is currently funded by the National Science Foundation which fields a large number of resources for computational neuroscience. The NIF project has established a common mailing list and will encourage all neuroinformatics centers that would like to serve as US node to join in order to foster communication about neuroinformatics in the US and abroad. Both the NIF and NITRC projects have been active partners and contributors to INCF activities. NITRC worked to establish the INCF Software center and provides the source for neuroimaging related tools. The NIF co-hosts the Neurolex wiki, a semantic wiki for viewing the products of the the Structural Lexicon and Neuron Registry task forces for the Program on Ontologies for Neural Structures of the INCF. The US node is also actively involved in creating the underlying spatial services for the INCF atlasing program. The US is excited and pleased to be hosting the 2011 Neuroinformatics meeting in Boston.

INCF Japan-Node and Platforms

Shiro Usui

RIKEN BSI, Neuroinformatics Japan Center, Saitama, Japan

The INCF national node of Japan (J-Node) (http://www.neuroinf.jp) is established at the Neuroinformatics Japan Center (NIJC), RIKEN Brain Science Institute (BSI). Based on the achievement of a Japanese pilot study on Neuroinformatics Research in Vision (1), we developed a base-platform XooNIps (http://xoonips.sourceforge.jp) and several neuroinformatics platforms (PFs). PF committee members collaborate to develop databases that are available for use online, and together with the J-Node committee, we promote domestic activities in neuroinformatics in Japan.

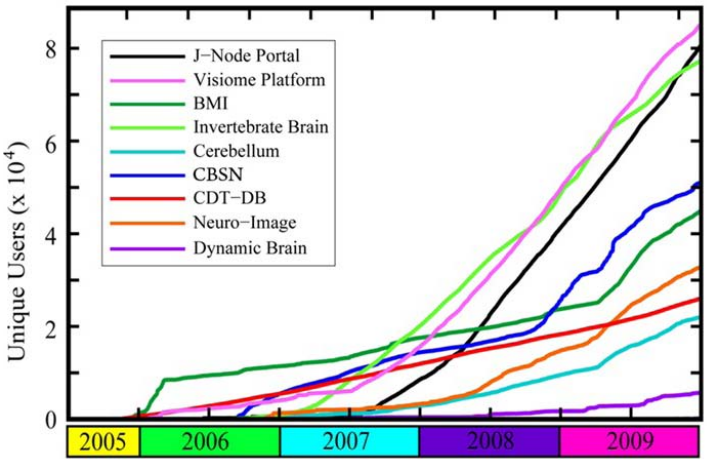
PFs currently running under the J-Node are as follows: Visiome, Brain Machine Interface, Invertebrate Brain, Cerebellar Development Transcriptome, Comprehensive Brain Science Network, Cerebellar, Neuro-Imaging, Dynamic Brain, BSI-NI (under development) and Simulation (under development) (2). We here describe 2 platforms which are under development. The rest of PFs are opened at the J-Node portal.

BSI-NI platform is a general term for several platforms which developed in BSI. RIKEN has been participating in the "Integrated Database Project" which MEXT launched from 2006 to develop and promote life science databases in Japan. To meet the same needs in the brain science, BSI established BSI-NI committee to promote neuroinformatics in April 2008. The following databases are under development to open.

- BSI Microarray Database
- Construction of 3-Dimensional brain atlas of novel experimental rodent "Degu"
- Construction of 3-Dimensional brain atlas of novel experimental primate "Common Marmoset"
- Multichannel EEG data for Brain Machine Interface (BMI) and/or Human Emotions (HE)

Simulation platform (SimPF) provides a common environment for testing, evaluating and sharing computational models via web browser. Users can run a trial of computational models that are registered on PFs and Neuroinformatics databases; no need to install any software on their computers. A user is asked to upload a script of a model to SimPF from a web browser. Once uploaded, SimPF assigns a virtual machine (VM) for the user from SimPF clouds, and connects the VM automatically to the user's browser via VNC (Virtual Network Computing) protocol. We are also providing MPI simulation environment for various kind of neuron and local-circuit simulation. The system consists of portal hosts, ganglia server and execution hosts. Linux and open source software are used for every host and server. Anyone can easily access and use our cloud simulation environment from browser. Install and configuration methods are provided by the PF.

Since the establishment of J-Node and PFs 5 years ago, top-page access statistics of unique users per day for each PF are shown in the Figure. The slopes at the initial phase are about 20 persons/day, which is mostly by the committee members to develop the PF. Once the URL is publicized at large, the slope becomes roughly 100 persons/day, rising by 5 times. This shows the importance of such PFs in neuroscience.



[Figure] Access statistics of unique user for each platform: Cumulative Unique Users/ a day

References

1. Usui S (2003) Visiome: Neuroinformatics research in vision project. Neural Networks 16:1293-1300

2. Usui S, Yamazaki S, Ikeno H, Okumura Y, Satoh S, Kamiyama Y, Hirata Y, Inagaki K, Ishihara A, Kannon Y, Kamiji NL (2010) Simulation Platform: Model simulation on the cloud. Neuroinformatics2010

THE UK NEUROINFORMATICS NODE

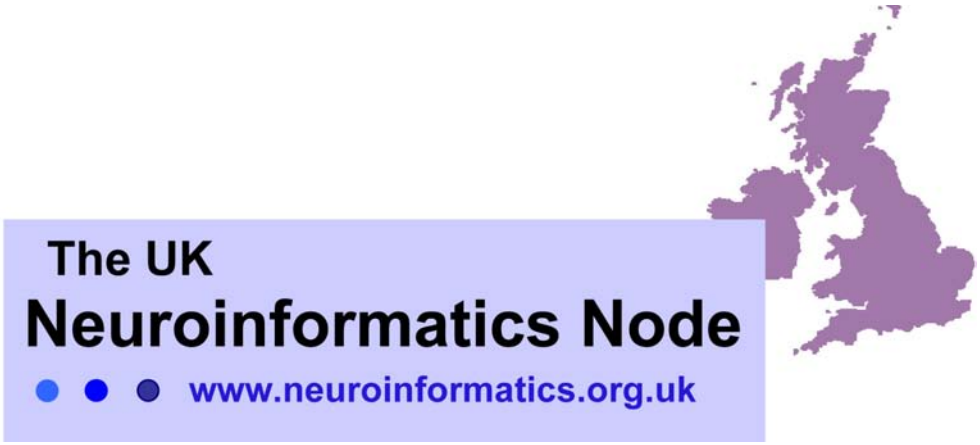
David Willshaw
School of Informatics, University of Edinburgh, Scotland, UK

BACKGROUND
This poster has been created to give an overview of the UK Neuroinformatics Node and to introduce to the participants of the INCF Conference in Kobe what it is that we do.

OBJECTIVES
The UK Neuroinformatics Node developed from the UK Neuroinformatics Network and now acts as the UK link with the International Neuroinformatics Coordinating Facility (www.incf.org), which facilitates neuroinformatics initiatives across the world.
The Node is administered from the University of Edinburgh and brings together practitioners from the basic and clinical neurosciences with those from the mathematics, physics, computing and engineering-based sciences who have a common interest in understanding the organisation and functioning of the nervous system. Its main function is to promote dialogue between neuroinformatics researchers in the UK and related communities in both the UK and worldwide. This poster illustrates what the goals and objectives are and demonstrates the future events and scientific activities of the Node.

CONTACT DETAILS
Chair: Prof David Willshaw, david.willshaw@ed.ac.uk
Administrator: Ewa Maria Henderson, ewa.henderson@ed.ac.uk
www.neuroinformatics.org.uk

FUNDED BY: The Node is a UK-based project funded by UK Research Councils MRC, EPSRC and BBSRC.



Activities of the Polish Node of INCF

Daniel Wójcik[1], Lech Borkowski[2], Piotr Durka[3], Jan Karbowski[4], Maciej Nowak[5] and Andrzej Wróbel[1]

1. Department of Neurophysiology, Nencki Institute of Experimental Biology, Warszawa, Poland
2. Department of Physics, Adam Mickiewicz University, Poznan, Poland
3. Department of Physics, University of Warsaw, Warsaw, Poland
4. Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw, Poland
5. Mark Kac Complex Systems Research Centre, Jagiellonian University, Cracow, Poland

By the Polish INCF node we denote the people engaged in neuroinformatics related activity supporting Polish membership in the INCF. Node activities involve research, education, workshops, infrastructure building.

Education. Two new BSc courses have been created in Poland in the fall of 2009.

- "Neuroinformatics" is a complete BSc program prepared from a scratch in the Physics Department of the Warsaw University. It received 66 applications, 20 students were admitted into the program. Complete description of the program is available at: http://www.neuroinformatyka.pl.

- "Cognitivistics" is a complete interdisciplinary BSc program in the Nicolaus Copernicus University in Torun with neuroinformatics components. It received 160 applications with 75 students admitted into the program. Complete description of the program (in Polish) is available at: http://www.kognitywistyka.umk.pl.

- Two other MSc programs, "Neurocognitivistics", neuroscience-based psychology course in the Warsaw School of Social Sciences and Humanities (SWPS), has some neuroinformatics components, as well as the program in "Neurophysiology" offered in the Biology Department of the Jagiellonian University, http://neuro.iz.uj.edu.pl. A course "Introduction to Neurodynamics and Neuroinformatics" for MSc students at the Department of Mathematics and Computer Science of Warsaw University is offered.

Activities – national.

- A workshop "Neuroscience meets theoretical physics" was organized in September 2008 by the Center of Complex Systems of Jagiellonian University http://www.fais.uj.edu.pl/neurobio.

- Short hands-on course "Introduction to nervous system modeling with Neuron" was organized at the Nencki Institute of the Experimental Biology under auspices of the Polish Neuroscience Society (14-15 April 2009).

http://www.neuroinf.pl/warsztaty_neuron - A symposium on modern data analysis methods in electrophysiology was organized during the 9th International Congress of the Polish Neuroscience Society, 2009.

Activities – international.

- Two Polish-Norwegian Neuroinformatics workshops were organized by the Polish and Norwegian INCF nodes, supported by a grant from the Polish-Norwegian Research Fund and the Nencki Institute. The first one "Modeling of extracellular field potentials" took place on 15-16 January 2009 in Ski, Norway: http://compneuro.umb.no/lfpworkshop/LFP_workshop The Second Polish-Norwegian Neuroinformatics Workshop "How to model neurons and neural systems? Integrating biophysics, morphology, and connectivity" took place on 14-15 January 2010 in Warsaw, Poland: http://www.neuroinf.pl/NIWorkshop2010

- Advanced Scientific Programming in Python Winter School was organized by G-Node and the Physics Department, University of Warsaw, which took place 8-12 February, 2010: http://escher.fuw.edu.pl/pythonschool.

- The Node is taking steps to move the yearly Advanced Course in Computational Neuroscience to Bêdlewo, Poland, for the period of 2011-2013.

A number of international research collaborations, often supported by joint grants, have been established between members of the Node and groups in other countries, in particular Germany, Netherlands, Norway, and USA.

INCF National Node of the Netherlands (NL node)

Jaap Van Pelt[1] and Paul Tiesinga[2]

1. CNCR - Integrative Neurophysiology, VU University Amsterdam, Amsterdam, Netherlands
2. Department of Neuroinformatics, Radboud University Nijmegen, Nijmegen, Netherlands

The Netherlands signed INCF membership in 2007. The coordinator of the NL node is member of the Neuroinformatics Steering Committee with representatives from universities, the Dutch Science Foundation NWO and the Dutch Neurofederation. The NL node aims to promote Neuroinformatics within the context of the International INCF Program. Information exchange is supported by the www.neuroinformatics.nl website. From 2004 on the NL node has been building a neuroinformatics community in the Netherlands through the organization of regular neuroinformatics workshops twice a year. Among the participating researchers most universities and life science research institutes in the Netherlands are represented. For the coming period, the NL node aims to intensify interactions among researchers by organizing local meetings at a more frequent schedule. For this purpose it has identified researchers at locations throughout the country who will act as local hosts. The NL node very much appreciates the wish of the Belgian node to participate in this rotational meeting schedule. The NL node continues to apply for funding, thus far using regular instruments. This year 2010 the Netherlands Node organized its 10th Neuroinformatics Workshop INCF and Neuroinformatics in the Netherlands. The poster summarizes the workshop activities in the past years and introduces those researchers, together with their neuroinformatics research focus, who will implement the rotational meeting program of the NL node.

INCF National node of Norway

Gaute T. Einevoll

Norwegian University of Life Sciences, Aas, Norway

The Norwegian national node is located at the Center for Molecular Biology and Neuroscience (CMBN) at the University of Oslo. Since the upstart in 2007 the running of the node has been funded by a grant from the Research Council of Norway which has allowed for several new activities to support the development of neuroinformatics in Norway. In addition to establishing a national hub for neuroinformatics, the node has so far funded almost twenty small neuroinformatics projects at universities and research hospitals all over Norway. The projects have covered many aspects of neuroinformatics, e.g., atlas development, brain imaging, and modeling, and has engaged both basic and clinical neuroscientists. The aim of this small-project program has been twofold: the stimulation of the use of existing neuroinformatics tools in neuroscience research and clinical practice, and the development of new tools for the national and international neuroscience community. The Norwegian INCF node has established good ties with several other national INCF nodes. In particular, a close collaboration has been developed with the Polish INCF node. Two well-attended Polish-Norwegian neuroinformatics workshops were organized in 2009 and 2010, in a suburb to Oslo and in Warsaw, respectively. Further, the two nodes collaborate on developing neuroinformatics tools for databasing and visualization, as well as for analysis of data recorded multielectrodes. Plans for a future tighter collaboration with Swedish and Finnish INCF nodes have been made.

Czech National Node for Neuroinformatics (CNNN)

Roman Mouček[1], Václav Matoušek[1] and Mirko Novák[2]

1. Department of Computer Science and Engineering, University of West Bohemia, Pilsen, Czech Republic
2. Department of Control Engineering and Telematics, Faculty of Transportation Sciences, Prague, Czech Republic

Czech National Node for Neuroinformatics includes 11 Czech universities, research institutes and industrial enterprises. Approximately 60 people are involved in the neuroinformatics research at the present time. In 2009 they solved four significant domestic projects and research grants supported by the Czech Ministry of education, the Czech Ministry of transportation, The Grant Agency of the Academy of Sciences of the Czech Republic, and the Czech state grant agency. The members of CNNN were mainly interested in the following fields:

- Human interactions with transportation vehicles
- Drivers' behavior
- Database of drivers' records
- Driving simulators
- EEG/ERP experimental database
- ERP analysis in children with developmental coordination disorder
- Methods of EEG/ERP analysis

Electric and metabolic brain activities were detected in parallel using electroencephalography (EEG) and near infrared spectroscopy (NIRS) methods under different physiological and psychological conditions. The obtained results (for more than 40 testing subjects) seem to be promising for analysis of driver behavior conversion from a tolerant to a non-tolerant (aggressive) form and also for possible training of the selected group of drivers for higher resistance to attention decreases and non-tolerant driving. The further research in the area of drivers' behavior is based on the measurement of head muscles tension. More experiments in this field are expected to be performed this year. The database of drivers' records has about 12 specialized parts involving together data of more than 650 people. A special part of this database containing data of drivers' behavior on roads is focused on aggressive events. The database is now extended from the pilot form to a more complex one. The systematic research on the selected representative sample of Czech road network is conducted. In parallel further development of the driving simulators was done. "Vehicle Simulator Axis of the Czech republic" will involve fully functional and frequently used adaptive driver simulators in Prague and Mladá Boleslav. Together with other simulators finished in Brno and Pilsen they will represent the necessary technical basis for wider measuring activities. The database of EEG/ERP experiment is intended for storage, download, and interchange of EEG/ERP data and metadata through the web interface. The system is based on tree layer architecture (MVC pattern) consisting of persistent layer (relational database), application layer (object oriented code, object relational mapping from persistence layer) and presentation layer (JSP). Open source technologies are used. Restricted user policy is applied and user roles are introduced. The possibilities of mapping from the persistence layer (relational database) and from the application layer (object oriented code) to RDF/XML and ontologies is widely tested. The pilot study related to the analysis of evoked potentials in children with developmental coordination disorder is performed. Relation between motor activity and brain response is investigated with the help of electrophysiological methods. The visual, auditory and cognitive evoked potentials (specifically the waves MMN and P300) are used. Dysfunction of differentiation of the complex signals is supposed. It can be confirmed by variance of latency and amplitude of cognitive or sensory evoked potentials. The signal processing methods (Matching pursuit algorithm, Wavelet transform, Huang-Hilbert transform) are modified and tested on EEG/ERP data. Open source library of these methods is implemented in Java language.

Deriving Semantic web structures from EEG/ERP data source

Roman Mouček, Petr Ježek and Václav Papež
Department of Computer Science and Engineering, University of West Bohemia, Pilsen, Czech Republic

Our research group at Department of Computer Science and Engineering, University of West Bohemia in cooperation with other partner institutions within Czech National Node for Neuroinformatics specializes in the research of attention, especially attention of drivers and seriously injured people. We widely use the methods of electroencephalography (EEG) and methods of event-related potentials (ERP).

Recently we have developed our own software tool for EEG/ERP data storage and maintenance. Registration of the system as a recognized data source occasionally requires providing data and metadata structures in the form of ontology in accordance with ideas of semantic web. Representation of data and metadata using ontologies is also supported by scientific effort to integrate data from various data sources and to develop autonomous agents reading and transferring data into an ontology form.

The EEG/ERP data source is based on tree layer architecture (MVC pattern) consisting of persistent layer (relational database), application layer (object oriented code, object relational mapping from persistence layer) and presentation layer (JSP). There is a question which layer is more feasible for mapping of its structure into ontology. Currently we have studied and tested two possibilities:
- Mapping from the persistence layer (relational database)
- Mapping from the application layer (object oriented code)

The standard for expressing semantic web ontologies is nowadays W3C OWL 2 Ontology Web Language (OWL), which is based on description logic. They are various syntaxes available for OWL 2. The RDF/XML syntax is the only syntax that is mandatory to be supported by all OWL 2 tools. OWL is neither a database framework, or a programming language. There are fundamental differences in richness of semantics between OWL (Description Logic based system) and relational database or object oriented systems. On the other hand, there are several approaches how to bridge at least some of these semantic gaps.

There is an analogy between assertional information and database content. An analogy between ontology terminological information and a database schema can be also found. On the other hand, they are important differences in the underlying semantics. If some information is not present in a database, it is considered to be false (closed-world assumption). By contrast, if some information is not present in an OWL document, it may be missing and possibly true (open-world assumption). The ontological representation of objects in OWL is also, syntactically and semantically, very similar to the description of objects, classes and instances. Then the analogy of system analysis in software engineering process with building ontologies leads to the idea of system development based on the description logic, it means formalized ontological description.

There is a number of frameworks and software tools, which are considered to generate OWL (RDF) output from relational database or object oriented code. Some of these frameworks and tools exist only as initial proposals or prototypes described in scientific papers, while some of them have been really implemented. In our case we need to perform only one-sided mapping from relational database (object oriented code) to OWL; therefore we need to use only a subset of semantic richness of RDFS and OWL.

We tried out two parallel approaches. The first approach includes the transformation of relational database into ontology using D2RQ tool and OWL API. The second approach includes the transformation from object oriented classes to OWL using Jenabean tool. The first transformations from the system relational database and object oriented code were performed and integration difficulties were solved.

Acknowledgements
This work was supported by following grants: Grant no. 2C06009 Cot-Sewing; Grant of Czech Republic Ministry of Education, HABILITACE-10 and Grant Agency of the Czech Republic under the grant GA 102/07/1191.

A knowledge based approach to matching human neurodegenerative disease and associated animal models

Sarah M. Maynard[1], Christopher J. Mungall[2], Suzanna E. Lewis[2] and Maryann E. Martone[1]

1. University of California at San Diego, La Jolla, USA
2. Lawrence Berkeley National Laboratory, Berkeley, USA

Many ontologies have been developed covering domains such as anatomy, cell types, and molecular processes. Ontologies for complex entities such as disease have been more difficult to define, but are critical to our pursuit of the subtle relation between clinical disease findings and observations made in model systems. Neurodegenerative diseases have a wide and complex range of biological and clinical features. While diseases share pathological features, they have unique signatures, particularly in targeting cells and subcellular structures. Animal models are key to translational research, yet typically only replicate a subset of indirectly related disease features. In addition, the pathologies occur across multiple spatial and temporal scales, and are expressed using varied vocabularies. Thus, data mining approaches for comparing animal to human conditions has proven challenging.

We take a phenotype-based approach to developing a multi-scale ontology for neurodegenerative disease and model systems, and thereby facilitate comparisons between neurodegenerative disease and model systems. We are defining phenotype to include any observable or measurable feature associated with organism, and, due to the nervous system's complexity, we require knowledge represented in ontologies to bridge the multiple structural scales and neuroanatomical systems in which alterations occur. We constructed a flexible, formal template for structural phenotypes that is amenable to computational logical inference. Rather than a complete specification of a disease process, we focus on measured phenotypes observed in organisms. Humans are treated the same as model systems, yet defined as bearing a disease. Our template draws from the Ontology of Phenotypic Qualities (http://purl.org/obo/owl/PATO) and Neuroscience Information Framework ontologies (NIFSTD; http://purl.org/nif/ontology/nif.owl). The resulting Neurodegenerative Disease Phenotype Ontology (NDPO; http://ccdb.ucsd.edu/NDPO/1.0/NDPO.owl) is encoded in OWL and contains 700 class level phenotypes derived from reviews. The companion Phenotype Knowledge Base (PKB; http://ccdb.ucsd.edu/PKB/1.0/PKB.owl) imports NDPO and contains instances of phenotypes (human and non-human) in primary articles. We loaded our phenotypes into the Ontology-Based Database (OBD; http://berkeleybop.org/pkb), an open access database for ontology-based descriptions where phenotypes, diseases, and models are matched using logical inference and semantic similarity statistical metrics.

The OBD interface performs queries such as "Find organisms containing cellular inclusions", using NIFSTD definitions to connect entities in clinical descriptions of human disease to models, e.g., Lewy body and cellular inclusions. We use OBD to perform similarity comparisons across models and human disease at the level of single phenotypes, e.g., find organisms with aggregated alpha synuclein. Knowledge in the ontology provides phenotype common subsumers. For example, a human with Parkinson's diseas with phenotype "midline nuclear group has extra parts Lewy Body" matches an animal overexpressing alpha synuclein with phenotype "paracentral nucleus has extra parts cellular inclusion" with their common subsumer: Thalamus has extra parts cellular inclusion. OBD uses information content measures to compare aggregate phenotypes to find overall best matches between organisms. Using these queries, we have performed a detailed comparison of organisms and disease related phenotypes.

By using a consistent phenotype model referenced to well-structured ontologies with defined classes, we can aggregate and bridge phenotypes made in animal models from basic research and descriptions of pathological features from clinical preparations. This provides the steps toward a temporal specification of the disease process. We continue to enrich the knowledge base and representations to explore different statistical methods for enhancing the relevancy of the matches.

References

1. Gupta A, Ludascher B, Grethe JS, Martone ME (2003) Towards a formalization of disease-specific ontologies for neu-roinformatics. Neural Networks 16:1277-1292.

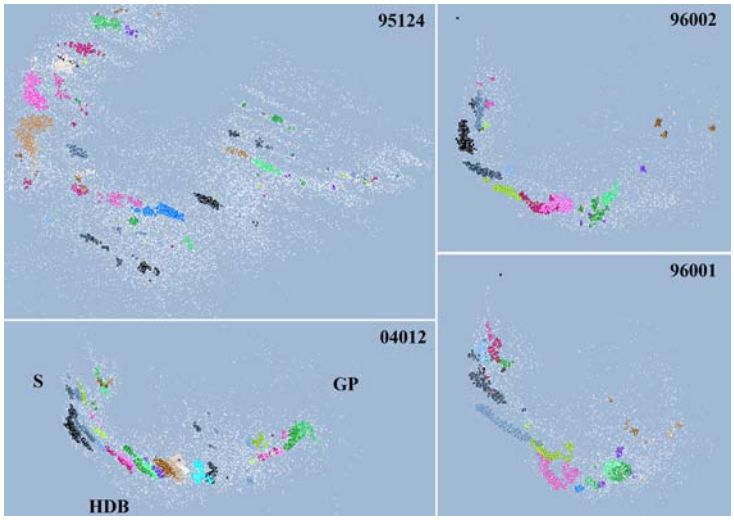
2. Washington NL, Haendel MA, Mungall CJ, Ashburner M, Westerfield M, Lewis SE (2009) Linking human diseases to animal models using ontology-based phenotype annotation. PLoS Biol 7(11):e1000247.

What clustering can teach us about the basal forebrain cholinergic system

Zoltan Nadasdy[1], Peter Varsanyi[2] and Laszlo Zaborszky[2]

1. Seton Brain and Spine Institute and University of Texas at Austin, University Medical Center and Dept. of Psychology, Austin, USA
2. Center for Molecular and Behavioral Neuroscience, Rutgers State University of New Jersey, Newark, USA

Large populations of neurons within brain systems are organized in functional subgroups, which are often difficult to define. To uncover these subgroups by using anatomical methods within considered-to-be "diffuse" structures such as the basal forebrain cholinergic system is a challenging computational task. We utilized the principle that functionally related groups of neurons often clamp together by forming clusters of cell bodies. To detect such groups of neurons from 3D histological data, we developed a clustering method that provides a description of detected cell clusters that is quantitative and amenable to visual exploration. This method is based on bubble clustering. Our implementation consists of three steps: (i) an initial data exploration for scanning the clustering parameter space; (ii) determination of the optimal clustering parameters; (iii) final clustering. We designed this algorithm to flexibly detect clusters without assumptions about the underlying cell distribution within a cluster or the number and sizes of clusters. We implemented the clustering function as an integral part of the neuroanatomical data visualization software Virtual RatBrain (http://www.virtualratbrain.org). We applied this algorithm to the basal forebrain cholinergic system, which consists of a diffuse but inhomogeneous population of neurons (Zaborszky, 1992). With this clustering method, we confirmed the inhomogeneity cholinergic neurons, defined cell clusters, quantified and localized them, and determined the cell density within clusters. Furthermore, by applying the clustering method to multiple specimens from both rat and monkey, we found that clusters in the basal forebrain cholinergic system display remarkable cross-species preservation of cell density within clusters. This method is efficient not only for clustering cell body distributions but may also be used to study other distributed neuronal structural elements, including synapses, receptors, dendritic spines and molecular markers. Grant Support: NIH/NS023945 to L.Z.



A Bayesian parameter estimation and model selection tool for molecular cascades: LetItB (Let It found by Bayes)

Junichiro Yoshimoto, Tomofumi Inoue and Kenji Doya
Okinawa Institute of Science and Technology, Okinawa, Japan

Introduction

Mathematical models of molecular cascade are essential for elucidation of dynamic mechanisms of cellular functions. In constructing such models, an important issue is selection of the model structure and setting of the model parameters, which are often hand-tuned to replicate the known system behaviors by trial-and-error. This is not only time-consuming but also compromise the objectiveness of the results. A theoretically sound and computationally efficient framework to identify them is crucial for making the model-based studies reliable and productive. We previously proposed a Bayesian estimation method to solve the issue (Yoshimoto et al., 2007). Here we present a multi-platform software tool with graphical user interface software to the Bayesian estimation engine, called LetItB (Let It found by Bayes).

Method

We model the chemical reactions within a compartment of interest by a set of ordinary differential equations (ODEs) specifying the concentration changes in the molecular species. The measurements are given by a subset of molecular species at certain time points subject to corruption by noise. In the Bayesian framework, we assume a prior distribution over the parameters of the ODEs and the observation, such as the reaction constants and the variance of measurement noise. Given a set of measurements, the likelihoods of different sets of parameters are evaluated by simulation and the posterior distribution of parameters is computed by integration with the prior distribution. Among a number of methods for Bayesian inference, we adopt Metropolis-Hasting sampling algorithm for our Bayesian estimation engine. Our software tool provides the functions of 1) import/export of cascade models in SBML, 2) graph representation of the model structure and editing the parameters, 3) simulation and visualization of the model dynamics, 4) import and visualization of experimental time series, 5) estimation and visualization of the posterior distribution of the model parameters, 6) evaluation of marginal likelihood for model selection. We used public software libraries: libSBML and SBML ODE Solver for SBML interface, Sundials and GNU Scientific Library for numerical simulation, and QT/QWT for graphic user interface (Top Panel in Fig. 1). LetItB can be compiled and run on multiple platforms including Linux, Mac OS X, and Windows.

Results

We tested the estimation engine and the user interface of LetItB with a number of benchmark problems. The bottom panel in Fig. 1 shows the screenshots for the multiple functions of LetItB. In its application to (an enzymatic reaction) model, the maximal a posterior estimate of the parameters by LetItB was more accurate than those found by conventional genetic algorithms, but we could also visualize the confidence intervals and the dependency between parameters by showing the posterior distribution. It was also verified that the marginal likelihoods computed for a number of candidate models can be used for selection of a model best suited to the given set of observation time courses.

Conclusions

As a solution of system identification problem in molecular cascade modeling, we developed a Bayesian estimation engine and combined it with a graphic user interface so that experimentalists without computational background can utilize the Bayesian system identification framework. LetItB is available from http://www.nc.irp.oist.jp/software. To enhance the computational efficiency, we are incorporating parallelizable Bayesian sampling methods and implementing the LetItB engine for parallel computers.

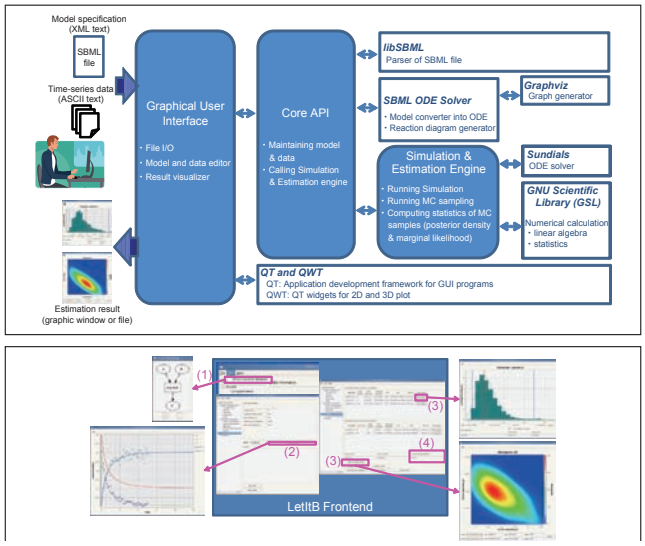


Figure 1 (Top panel) Configuration diagram of LetItB. Blue boxes denote the components implemented by us in C++ language. White boxes with blue descriptions denotes the external libraries required by LetItB. (Bottom panel) Functionality of LetItB.

References

1. Yoshimoto J, Doya K (2007) Bayesian system identification of molecular cascades, International Conference on Neural Information Processing (ICONIP 2007), FAA-5.

A collaborative neuroinformatics platform for distribution and characterization of transgenic mouse lines for cell type specific neuroscience research

Ken Sugino[1], Yao Cheng[2] and Sacha Nelson[1]

1. Department of Biology, Brandeis University, Waltham, USA
2. Department of Computer Science, Brandeis University, Waltham, USA

The brain is the most heterogeneous mammalian tissue consisting of numerous distinct cell types connected via intricate circuits that underlie brain function. Elucidation of brain cell types represents a crucial step in understanding brain function. The identification of neuronal cell types has been a difficult task, often relying on analysis of morphology, electrophysiology, and marker expression using immunostaining. Recently, genetically modified strains of mice have become useful tools for the identification and investigation of neuronal cell types. Multiple efforts to generate mouse lines specifically for this purpose are already underway. A central repository for information on these mouse lines is a logical requirement for optimal use of these resources and advancement of research in this area.

We have developed a web-based database platform for this purpose available at http://www.credrivermice.org. Currently it hosts more than 50 mouse lines mainly generated at Cold Spring Harbor Laboratory (CSHL), Baylor College of Medicine (BCM), The Scripps Research Institutes (Scripps) and Brandeis University (Brandeis). CSHL lines target GABAergic interneurons employing a knock-in strategy to express Cre recombinase from loci known to be important for GABAergic cells including Gad2, somatostatin, parvalbumin and several other genes. Scripps lines are also knock-in lines but mainly target loci related to neural development such as Dcx and Wnt3a. BCM and Brandeis lines employ an enhancer trap strategy, which labels unpredictable but stable and well-defined subsets of cells. Brandeis lines use Tet, rather than Cre as a driver molecule. The web platform, however, is designed to accommodate uploading of information on any mouse line by any registered user, and so will serve as a useful repository for data related to all mouse lines relevant to nervous system research.

The platform offers users basic information on mouse lines including where to obtain the line, information on transgene constructs and associated publications, as well as more general characterization data such as digital atlases of transgene expression, high resolution images for morphology, information on electrophysiological properties and microarray mRNA expression data. The digital atlas is viewable through the web with a custom viewer implemented in Adobe Flex, which also accommodates an annotation facility. The data format for electrophysiology and morphology currently use a flexible wiki format. Affymetrix-based microarray data are searchable and viewable through a custom web-based Javascript application. The Allen Brain Reference Atlas and associated anatomical ontology are used for registering characterization data to anatomical structures and characterization data are searchable using anatomical terms. The platform also has a web based preprocessing facility for digital atlas production and we are now implementing a pipeline to automatically annotate transgene expression pattern.

This web based platform should be useful for facilitating cell type specific neuroscience research. We are also working to extend it to be a platform for constructing a taxonomy of neuronal cell types based on accumulated characterization data. The database is also readily extensible to genetic, genomic and anatomical studies of cell types in other vertebrate species.

Electro-acupuncture upregulate alpha7 nAchR expression in hippocampus improving spatial memory in rats

Jianying Tian[1] and Tianqi Wang[2]

1. Department of Anatomy, Ningxia Medical University, Yinchuan, China
2. Ningxia Medical University, Yinchuan, China

The expression of the alpha7 nicotinic acetylcholine receptor (alpha7 nAchR) diminishes in selected brain regions of patients with Alzheimer's Disease (AD) which may account for pathophysiological abnormalities and some of the deficits in attention and learning and working memory. There is emerging evidence that Yizhi Xingnao needling method have the effects of improveing in attention and memory in traditional Chinese medicine. Purpose: To investigate the effect of electroacupuncture (EA) stimulation at the acupoints on improving learning-memory ability and alpha7 nAchR expression in hippocampus tissue. Methods: SD rats were randomized into control, model group, protective EA (pro-EA) group and EA group, with 10 cases in each. The model was established by administration of methyllycaconitine (MLA), a competitive alpha7 nAChR antagonist, 4.8 mg/kg/d, for 10 days. For the pro-EA group and the EA group, after MLA treated, EA (2 Hz, 1mA)was applied to "Baihui" (GV 20), "Dazhui" (GV 14) and bilateral "Shenshu"(BL 23) and non-acupoint (the chest-abdominal juncture between the first and the second lumbar vertebrae) for 20 min, each time and on alternate days, continuously for 6 weeks. pro-EA group was applied one week additional EA before modeling. Morris water maze test was performed to detect the learning and memory ability. The expression of a7nAchR protein in hippocampal was measured by immunohistochemstry and Dot Blot. Results: The escape latencies on the 2nd day in model group were significantly longer than those of control group ($P < 0.01$) and swimming time in the platform quadrant were significantly shorter than those of control group ($P<0.01$). In comparison with model group, the escape latency of pro-EA group on the 11th day and EA group on 18th day was significantly shorter ($P < 0.05$), and the time in the platform quadrant of EA group was significantly longer ($P < 0.05$). Compared to control group, the expression of alpha7 nAchR in hippocampal CA 3 region, but not CA1 and dentate gyrus in pro-EA and EA groups decreased significantly ($P<0.05$). Compared to model group, the expression level of alpha7 nAchR in the hippocampal CA3 region increased markedly ($P < 0.05$). No significant difference was found between control and non-acupoint groups ($P > 0.05$). Conclusion: EA is able to exert beneficial effects on spatial memory which may be related to its effect on upregulating the expression of alpha7 nAchR in hippocampal CA3 region.

Topology of thalamic axons suggests two developmental modes during innervation of visual cortex

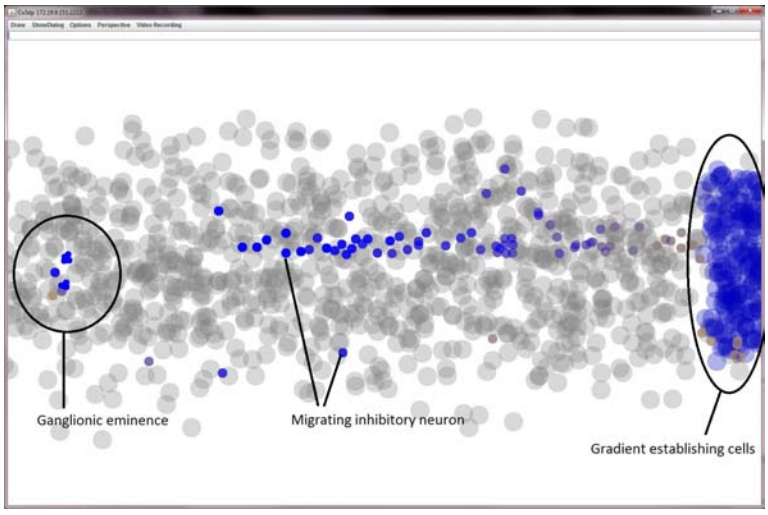
Andreas Hauri, Nuno da Costa, Rodney Douglas and Kevan Martin
Institute of Neuroinformatics, ETHZ/UZH, Zuerich, Switzerland

How does a single axon grow from its cell body to form the arborization pattern seen in an adult brain? Axonal growth cones are responsible for generating these patterns. They produce these patterns based on the genetic instructions they contain, their position, their local chemical environment and other epigenetic factors. The first step to understand this process it is to establish the metrics and topology of adult axons since any model that wishes to describe axonal growth should achieve the same metrics. This study provides such a description for one of the most well studied axonal projections in the cortex the arborization of the thalamocortical axons in the primary visual cortex of the adult cat. During development the thalamic axons innervating the cortical plate divide into different branches that form their main arborization in layer 4. These arborizations form cluster of synaptic boutons that are the basis of the ocular dominance system. We labeled single axons in anaesthetized cats in vivo using intracellular injection of horseradish peroxidase (HRP) or the anterograde tracer biotinylated dextran amine (BDA). After processing for light and electron microscopy, we reconstructed 10 axons. Using a mean shift cluster algorithm we identified the location of the clusters of boutons formed by these axons in layer 4. We named as the 'skeleton' of the axon the branches of the thalamic axon that had their branch-point located outside the cluster, and those that branched inside the cluster the 'florets'. We analysed the axons for several metric and topological properties like Horten-Strahler and Galton-Watson statistics of the 'skeleton" and the 'florets'. These analyses showed properties like branch length, bouton density and probability of branching are different between 'skeleton' and 'florets'. The 'skeleton' seems more directed to find an appropriate target location for making connections, e.g. an ocular dominance slab in layer 4, whereas the 'florets' optimize the coverage of this location with synaptic boutons. These difference in statistics strongly suggests two different phases of growth during the development of the thalamic arbour. An initial set of instructions that leads to ingrowth which is then substituted by a second inducing synaptogenesis. This research was supported by the EU Grant FP7-216593 "SECO".

Simulation of the developmental migration of neocortical inhibitory neurons, using CX3D

Andreas Hauri, Frederic Zubler and Rodney Douglas
ETHZ/UZH, Institute of Neuroinformatics, Zürich, Switzerland

We are exploring the self-construction of the neocortex from its precursor cells by detailed simulations of the cortical developmental process. In previous work we have demonstrated how the laminar organization of pyramidal neurons arises from a few precursor cells. Now we show how the inhibitory cells migrate into this laminar structure. Inhibitory neurons play a crucial role in information processing by the mammalian neocortex. Their range of effect is much more localized than that of typical pyramidal neurons, and so their laminar location in the grey matter is important for their functionality. Their placement is an emergent property of a complex developmental process. Various types of pyramidal neurons are generated successively by precursors in the ventricular and subventricular zone, and migrate radially to create the basic laminar organization of the cortical grey matter. By contrast, the majority of inhibitory neurons arise in the ganglionic eminence at the ventral margin of the cortex. From there they must migrate tangentially through the developing cortex in a dorsal direction, stop at a specific location in the cortical sheet, and finally nest at particular laminar depth. Inhibitory neurons born later in the eminence settle in progressively more dorsal positions in cortex, so providing an even distribution of inhibitory neurons throughout cortex. We have studied this tangential migration using CX3D, which provides tools for the simulating the biology and physics of cell replication, migration, and interaction. We have been able to demonstrate the key features of the migration: cell division in the ganglionic eminence; migration of neurons through cortex; and their settling at their final location in cortex. Younger neurons end their migration earlier than older neurons, as observed in biology. There is no global controller in our simulations. Instead, each cell controls its own behavior based on sensed chemical gradients and concentrations of morphogenic factors. Hence the inherent biological property of inhibitory neurons to localize themselves appropriately for their function is reflected properly in our model. This research was supported by the EU Grant FP7-216593 "SECO".



iSVM: an incremental machine learning approach for recreating ion channel profiles in neocortical neurons

Georges Khazen, Sean Hill, Felix Schürmann and Henry Markram

Brain Mind Institute, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Purpose: Voltage-gated ion channels play an important role in determining the intrinsic firing properties of neurons by regulating the flow of ions and controlling the voltage gradient across the neuronal membrane. Genetic studies have identified nearly 200 different monomeric and heteromeric ion channels expressed throughout the brain. Experimental observations suggest that different sets of ion channels could underlie the same morpho-electrical subtypes. Understanding this molecular diversity is a fundamental goal in neuroscience. Here, we present an incremental Support Vector Machine (iSVM) based model that estimates the expression of ion channel genes in different morpho-electric neurons with a high level of accuracy.

Method: Gene expressions of 135 neurons were profiled for 26 voltage-gated ion channels using single cell RT-PCR measurements and were categorized into three feature classes according to neuron properties: layer, morphology class and electrical firing type. We first identified which channels have a significant change in expression between the classes and then used iSVM to build a predictive model for those channels. The iSVM model is initially trained and tuned using the three feature classes. We then increment the number of features by combining the expression of every gene to the three feature classes and recompute the prediction accuracy of the remaining genes. If the accuracy is improved, we retain the combined gene, otherwise, we reject it. We iteratively combine more genes until the prediction accuracy can no longer be improved.

Results: The results show that most of the channels have a significant change in expression between classes indicating that the layer, morphology, and electrical type of the neuron have an important relationship to the expression of ion channel genes. Although, the correlation coefficients between channels are less than 0.48, the iSVM model can significantly improve the prediction accuracy of some channels by more than 10% when taking into account the expression of other channels. However, the prediction of channels for which the expression frequency was less than 10% could not be improved. Using a 10 fold cross-validation test, the iSVM model obtains an overall average accuracy greater than 83% as opposed to 67% obtained when using logistic regression. Additionally, iSVM was able to recreate the ion channel expression of a test dataset that was not used while building the model with 76% average accuracy.

Conclusion: These results show that it is possible to predict the ion channel diversity for a range of neuronal subtypes in the rat neocortex for which gene expression data has not yet been gathered.

How to build the cognitive network?

Dariusz Plewczynski

Interdisciplinary Centre for Mathematical and Comp, University of Warsaw, Warsaw, Poland

How to build the cognitive network? What is the influence of the learning network on the final quality of information processing in cognitive systems? How a node of such network has to be designed in order to effectively process incoming information that is both time dependent and spatially heterogenous? We address those questions by benchmarking different machine learning algorithms using real life examples (mostly from bioinformatics and chemoinformatics) that mimics the different pattern recognition tasks typically used in various machine learning applications. In the framework of Agent Based Modelling (ABM) the most promising cognitive network appears to be constructed from an sparse ensemble of interacting agents. The cognitive networks are able to successfully combine outcomes of individual learning agents in order to determine the final decision with the higher accuracy than any single learning method used in the construction of a network. We discuss here also the mean-field approximation of the cognitive networks in the limit of the infinite number of learning agents. The ensemble of interacting learning agents, acquires and process incoming information using various types, or different versions of machine learning and clustering algorithms. The abstract learning space, where all agents are located, is constructed here using a randomly connected, sparse model. It couples locally the certain small percentage of similar learning agents, yet also connect remotely about 10% of the other agents with random strength values. Such network simulates the higher level integration of information acquired from the independent learning trials. The final classification of incoming input data is therefore defined as the stationary state of the cognitive system using simple majority rule, yet the minority clusters that share opposite classification outcome can be observed in the system. The cognitive network is able to couple different scales of both space and time patterns by assigning them to different subsets of learning nodes. The probability of selecting proper class for a given input data, can be estimated even without the prior knowledge of its affiliation. The fuzzy logic can be easily introduced into the system, even if learning agents are build from simple binary classification machine learning algorithms by calculating the percentage of agreeing agents. The model is inspired by the large scale cognitive computing models of the brain cortex areas (D. Modha et al., Izhikevich et al.).

References

1. Dharmendra S. Modha, "A Conceptual Cortical Surface Atlas", PLoS ONE 4(6): e5693. doi:10.1371/journal.pone.0005693

2. James S. Albus, George A. Bekey, John H. Holland, Nancy G. Kanwisher, Jeffrey L. Krichmar, Mortimer Mishkin, Dharmendra S. Modha, Marcus E. Raichle, Gordon M. Shepherd, and Giulio Tononi, "A Proposal for a Decade of the Mind Initiative" Science [Letter], Vol 317, Issue 5843, 7 September 2007:1321.

3. Izhikevich E. M. and Edelman G. M. (2008) Large-Scale Model of Mammalian Thalamocortical Systems. PNAS, 105:3593-3598

Sym(p)hony: Towards a dynamic neuroscience information system

Martin Telefont, Eilif Muller, Felix Schürmann, Sean Lewis Hill and Henry Markram
Brain Mind Institute, EPFL, Lausanne, Switzerland

Purpose: There are currently two popular approaches of information access to neuroscientists. 1) Keyword-based searches of unstructured information. Which allows a retrieval of data based on lexicographical properties. 2) Retrieval of information based on structured systems, represented by some controlled terms/classes (e.g. through an ontology). Both methods are effective, however in the neuroscience domain both are unable to capture the information in a sufficient manner, especially due to the dynamic nature of neuroscience knowledge generation. The overlaps between both methods make up only a small area of neuroscience and are not effective at using the strengths that each approach has to offer. Sym(p)hony is a hybrid system, which tries to mend this gap by showing how a computer-aided, systematic evolution of an ontology may be possible, using elements of both approaches.

Method: Sym(p)ony is build on two pillars: 1) elements (which are instances of classes) and 2) relations (which are instances of relationships) between them. The first iteration of the ontology used in the system is based on our current understanding of established classes and relationships that they have to one another. An expansion of classes and relationships is achieved by doing frequency searches of tokens of elements in literature. This process allows the generation of suggestions for classes and relationships, which are lacking from the previous iteration and could be included in a subsequent version.

Results: A first prototype has been implemented that demonstrates the ability of starting from an ontology (based on relationships, which can be reasoned on, and elements, found in neuroscience) that can be augmented based on new elements and relationships. These suggestions are generated from frequency analysis of a subset of the available neuroscience literature.

Conclusion: We present a system that facilitates the maintenance and computer-aided growth of an ontology, which takes the occurrence of new elements and concepts into account by analyzing the frequency with which they occur in the present literature. This offers a possible approach to solve the problem in neuroscience, in which the integration of new concepts and elements lags significantly behind compared to when they become available in the unstructured domain.

Cerebellar Development Transcriptome Database (CDT-DB)

Akira Sato[1], Yukiko Sekine[2], Hirozumi Nishibe[2], Noriyuki Morita[3], Yumi Sato[2], Tetsushi Sadakata[2], Yo Shinoda[2], Toshio Kojima[1] and Teiichi Furuichi[2]

1. RIKEN, Advanced Science Institute, Yokohama, Japan
2. RIKEN BSI, Laboratory of Molecular Neurogenesis, Saitama, Japan
3. Mimasaka Junior College, Okayama, Japan

Cerebellar Development Transcriptome Database (CDT-DB) (http://www.cdtdb.brain.riken.jp/CDT/CDTSearch.jsp) is a neuroinformatics database for sharing and mining large amounts of systematized data regarding the spatiotemporal gene expression profiles which are the basic information on the genetic blueprint of mouse cerebellar development. CDT-DB contains huge amounts of gene expression information in terms of developmental time-series patterns, brain regional and cellular patterns, and tissue distribution patterns obtained by microarray analyses, in situ hybridization analyses, etc. CDT-DB not only provides the easy-to-use interface to cross-search for expression data, but also includes brain image viewers, graph analysis tools, gene ontology search function. All registered genes have hyperlinks to websites of many relevant bioinformatics regarding genome, proteins, pathways, neuroscience and literatures, so that CDT-DB acts as a portal to these bioinformatics websites. CDT-DB has already been demonstrated to be valuable for neuroscience research (for example, identification of several brain genes important for neural circuit development) and has gotten high evaluation by specialists.

References

1. Sato, A., Sekine, Y., Saruta, C., Nishibe, H., Morita, N., Sato, Y., Sadakata, T., Shinoda, Y., Kojima, T., and Furuichi, T. (2008) Cerebellar development transcriptome (CDT-DB): profiling of spatio-temporal gene expression during the postnatal development of mouse cerebellum. Neural Networks 21:1056-1069.

2. Sato, A., Morita, N., Sadakata, T., Yoshikawa, F., Shiraishi-Yamaguchi, Y., Huang, JH., Shoji, S., Tomomura, M., Sato, Y., Suga, E., Sekine, Y., Kitamura, A., Shibata, Y., Furuichi, T. (2004) Deciphering the genetic blueprint of cerebellar development by the gene expression profiling informatics. Neural information processing. Lecture Notes in Computer Science 3316:880-884. Springer-Verlag, Berlin, Heidelberger, Germany

3. Kagami, Y., and Furuichi, T. (2001) Investigation of differentially expressed genes during the development of mouse cerebellum. Brain Research Gene Expression Patterns 1:39-59.

Environment for an integrative model simulation: PLATO

Keiichiro Inagaki[1], Takayuki Kannon[2], Yoshimi Kamiyama[3], Shunji Satoh[4], Nilton Kamiji[2], Yutaka Hirata[5], Akito Ishihara[6], Hayaru Shouno[4] and Shiro Usui[2]

1. Computational Science Research Program, RIKEN, Wako, Japan
2. RIKEN Brain Science Institute, Wako, Japan
3. Aichi Prefectural University, Nagakute, Japan
4. University of Electro-Communications, Chofu, Japan
5. Chubu University, Kasugai, Japan
6. Chukyo University, Toyota, Japan

The brain presides essential roles of human life, and fulfills precise and flexible processing generated by its complicated network. To elucidate the signal processing carried out by our nervous system, numerous physiological experiments and computational studies have been conducted. Those researches have revealed a great deal of brain function; however, a wealth of resources obtained in those experiments and modeling studies were mainly used for publishing articles. Currently, several neuroscience databases (e.g., platforms in INCF Japan-node, modelDB) started managing such resources (experimental data, articles, analysis tools, models) for preserving and sharing. To further elucidate the brain function systematically, the resources available on those databases should be integrated into a large-scale model where anatomical and physiological characteristics are explicitly implemented.

For this purpose, we have been developing a modeling environment called PLATO (Platform for a coLlaborative brAin sysTem mOdeling) which allows computational models to be constructed using several programming languages and connected by means of the common data format (e.g., netCDF, HDF5). It also provides a data management system and programming libraries to systematically build a large scale system model. In the present study, we introduce the PLATO and its newly developed programming libraries, which manage the data exchange and simulation of the large-scale model developed on the PLATO.

The PLATO consists of data management tool (Concierge), the common data format and its programming libraries, and simulation cluster server. The data management tool is utilized for searching and managing the resources to develop models. On the PLATO, the model integration is implemented in the common data format and its programming libraries at the I/O level. The programming libraries for the common data format support development of individual models as well as model integration. The common data format can include both data and its metadata; e.g. modeling convention, which describes the I/O configuration between models such as data name, its dimension and unit, and interval of data storing. Therefore, the common data format itself provides all the necessary information about the data as well as model I/O. It is also independent on operating systems and programming languages, and models can be made pluggable by applying the common data format. This property will be essential to integrate models developed by different programming environment, and be helpful to execute the integrated model on a parallel-processor computer system, especially on cloud computers. When the I/Os in the integrated models complies with the common data format and its programming libraries, an agent system in the library manages the execution of models and data exchange between models during simulation, where the simulation step, data I/O, and its timing are automatically adjusted considering MPI communication in each model.

The PLATO tightly collaborates with the neuroinformatics platforms available on the INCF Japan-node, because numerous models and physiological data are continuously registered on them. That is, the PLATO can provide multidisciplinary modeling environment by this collaboration. Finally, we hope that the PLATO will help researchers to develop models and to integrate them for constructing a large scale brain model in near future.

A multi-scale parts list for the brain: community-based ontology curation for neuroinformatics with NeuroLexorg

Stephen D. Larson[1], Fahim Imam[1], Rembrandt Bakker[2], Luan Pham[1] and Maryann Martone[1]

1. Center for Research of Biological Systems, University of California, San Diego, La Jolla, USA
2. Donders Institute for Brain, Cognition and Behaviour, Radboud UMC Nijmegen, Nijmegen, Netherlands

What makes up the nervous system? What are the inhibitory neurons? What brain regions are they in? What ion channels do they express? Do their dendrites have spines? What fiber bundles do they participate in? These questions and many more could be answered by a multi-scale parts list for the brain, where each part was uniquely indexed and unambiguously defined. Unfortunately, no such standard list has come into widespread use by the neuroscience community. Our effort to address this challenge has resulted in the instantiation of a semantic wiki, NeuroLex.org. For many years we have been building community ontologies for neuroscience, first through the Biomedical Informatics Research Network and now through the Neuroscience Information Framework (http://neuinfo.org) projects. These projects resulted in the construction of a large modular ontology, constructed by importing existing ontologies where possible, called the NIF Standard Ontology (NIFSTD; Bug et al, 2008). It covers behavioral activity, behavioral paradigms, brain regions, cells, diseases, molecules, nervous system function, subcellular components, information resources, resource types, and qualities. NeuroLex.org was originally populated with the NIFSTD in an effort to improve the process of editing and maintaining it. The initial update processes created one wiki page from each ontological "class", which refers to an entity relevant to neuroscience. Content that is added or updated in NeuroLex.org is contributed back to the NIFSTD. This content is not directly added to NIFSTD, but is incorporated into the NIFSTD OWL file by a knowledge engineer after curation by the NIF ontology group. NeuroLex.org's structuring of knowledge allows classes to be rendered using tables, trees, and lists which combine the asserted content of the class with queried content derived from other classes. For example, the page for "Cerebellum" displays a dynamic tree that lists the brain region classes that have been asserted as "part-of" the Cerebellum. This page also lists the neuron classes that have been asserted as "located-in" the Cerebellum. Neither of these property assertions are made on the Cerebellum page itself; rather they are displayed via dynamic queries that find classes related to the Cerebellum throughout the wiki. NeuroLex.org has served as a test bed for a rallying point for the efforts of the Program of Ontologies of Neural System (PONS), an activity of the International Neuroinformatics Coordinating Facility (INCF). In the last year, content and edits have been contributed by several members of the task forces in this activity. In addition, NeuroLex.org has incorporated a lightweight web application for digital atlasing called the Scalable Brain Atlas (http://scalablebrainatlas.incf.org), which generates atlas plate images that highlight a given brain region, in order to more clearly define it. NeuroLex.org has been online since October 2008 and has evolved into a powerful platform for collaboratively maintaining and extending the NIFSTD ontology. It has received 110,000 edits and has 104 registered users. It regularly receives 225 hits per day on average, 80% of which come directly from search engine hit results. NeuroLex.org is built on top of the open source Semantic Mediawiki platform (http://semantic-mediawiki.org) and incorporates several open source extensions such as Semantic Forms and the Halo Extension. We conclude that NeuroLex.org is a good starting point for the collaborative maintenance of ontologies. Other groups are also using a similar approach, e.g., BioMedGT (http://biomedgt.nci.nih.gov). While we are still working through some issues, e.g., synchronizing the NIFSTD with the content on NeuroLex, exporting and importing OWL, and bulk uploading concepts, we believe that semantic wikis are a good tool for providing community contribution and feedback to projects like NIF.

References

1. Bug, W.J., Ascoli, G.A. et al. (2008) The NIFSTD and BIRNLex vocabularies: building comprehensive ontologies for neuroscience. Neuroinformatics 6, 175-194

The Neuron Registry Curator Interface: an Infrastructure for the Collaborative Definition of Neuronal Properties

David J. Hamilton and Giorgio A. Ascoli

Center for Neural Informatics, Structure, and Plasticity, George Mason University, Fairfax, USA

Classifying neurons based on their properties is a fundamental goal in neuroscience (Petilla Interneuron Nomenclature Group: Ascoli et al., Nature Rev Neurosci, 2008). To catalyze progress, the International Neuroinformatics Coordination Facility (INCF) recently organized a Task Force for the creation of a Neuron Registry under the Program on Ontologies of Neural Structures (www.incf.org/core/programs/pons). Our research aims at developing an infrastructure to facilitate the necessary collaboration among the Task Force domain experts. In particular, we describe the implementation of a Neuron Registry Curator Interface (incfnrci.appspot.com) for identifying the necessary and sufficient properties to define neuron types. This web-based database front-end is synchronized with the Neuroscience Information Framework (NIF) vocabularies contained in NeuroLex.Org. The easily learned, broadly accessible, and usage-friendly entry-form with pre-populated vocabularies registered with a robust repository, is meant to funnel the world's forefront expertise on neuronal properties and types to form a consensus on neuron classification.

Supported by NINDS R01 NS39600, by NIDA under the NIH Blueprint for Neuroscience via a NIF sub-contract, and by INCF.

Helmholtz: A modular tool for neuroscience databases

Andrew Davison, Thierry Brizzi, Olivier Manette, Cyril Monier and Yves Frégnac
UNIC, CNRS, Gif-sur-Yvette, France

Databasing of experimental neuroscience data together with the annotations/metadata needed to understand it promises major payoffs both for the scientists who generate the data and for the progress of neuroscience in general. However, systematically putting the annotations and other metadata into a digital form is generally an arduous task at present, and the benefits difficult to realize, so that the cost/benefit ratio for the experimentalist is a poor one, with the corollary that the flow of data shared with the broader community is more a trickle than a flood.

To improve this situation, we are developing tools that aim to make it easier for scientists to put their data into a database, to annotate it appropriately, to obtain some immediate benefit from the effort, and to share the data with others, under terms they control, if they so wish.

The tension between immediate benefit in having a better tool for scientists to manage their own data and longer-term considerations of sharing with others has several implications:

1. the metadata stored should be customizable, since the needs of different labs can vary widely, but there should also be a common core to ensure interoperability if the data are published;
2. we should support storing both raw data and processed/analyzed data, so that the scientist can manage all phases of his workflow and so that the provenance of an individual result or graph can be easily tracked;
3. the same tool should be useable both as a local database and as a public resource;
4. both data and metadata should have fine-grained and easy-to-use access controls.

We are developing an open-source tool, Helmholtz (named after the 19th century physicist and physiologist), implemented mainly as a series of "apps" (applications/components) built with the Django web framework (http://www.djangoproject.com). The advantages of using a web framework are:

1. it makes it easy to setup either a local database (Django comes with a simple built-in web-server) or a centralised repository.
2. a highly modular structure makes the database easy to customize and extend.
3. abstraction of the underlying database layer, so that (i) any supported relational database can be used (e.g., MySQL, PostgreSQL, Oracle or the built-in SQLite); (ii) knowledge of SQL is not required, making it easier for non-database specialists to develop tools and extensions.
4. it is easy to develop multiple interfaces, e.g. a web interface, a web-services interface, interfaces to desktop acquisition or analysis software.

Helmholtz provides core components which handle things that are common to all or many domains of neuroscience: 1. data acquisition: metadata for experimental setups (equipment, etc.), subjects (species, weight, anaesthesia, surgery, etc.), stimulation and recording protocols, for electrophysiology (in vivo and in vitro), optical imaging and morphological reconstructions; 2. databasing of analysis results, linked to the original data on which they are based, and with descriptions of the analysis methods used; 3. access control.

Extension components for different sub-domains of neuroscience will gradually be developed in collaboration with experts in those domains (we currently provide only a visual system component, with functionality for describing and visualising visual stimuli, etc.). It should be straightforward for anyone with some programming experience to develop their own extension components.

The Helmholtz components could be combined with pre-existing Django components (e.g., user management, syndication using RSS/Atom, discussion forums, social-networking tools, a wiki, etc.) to develop a full-scale repository or portal.

The Helmholtz system has so far been used to develop a database of functional and structural data from visual cortex (https://www.dbunic.cnrs-gif.fr/visiondb) within the EU FET integrated project FACETS (http://www.facets-project.org).

The INCF Program on Ontologies for Neural Structures

Maryann Martone[1], Giorgio Ascoli[2], Alan Ruttenberg[3], David Van Essen[4] and INCF PONS Task Force Members[5]

1. University of California at San Diego, San Diego, USA
2. George Mason University, Fairfax, USA
3. Science Commons, Boston, USA
4. Washington University, St Louis, USA
5. INCF, Stockholm, Sweden

The goal of the program on Ontologies of Neural Structures (PONS) of the International Neuroinformatics Coordinating Facility (INCF) is to promote data exchange and integration in the neurosciences by developing terminology standards and formal ontologies for neural structures. PONS was established in recognition that a lack of a consistent or computable terminology for neuroanatomy across structural scales and species is an impediment to data integration in the neurosciences, with its diversity of model systems. PONS has two main subprograms: creation of a lexicon for neural structures and creation of a neuronal registry. These programs are organized into two task forces, comprising an international group of neuroscientists. These task forces are supported by the Representation and Deployment (R & D) Task Force, comprising experts in ontology construction and knowledge representation. The structural lexicon subprogram is creating a lexicon of neural structures in primate and rodent brain from the gross anatomical to the macromolecular scale, including defining criteria by which these structures can be recognized in experimental material. Work to date has established a proposed standard metadata scheme for defining criteria for brain structures that has been implemented within a semantic Wiki (http://neurolex.org). A second subproject is establishing a set of high level consensus structures for mammalian brain to serve as a framework for cross-species translations of major brain regions and for relating more granular parcellation schemes for these brain regions established by different atlas providers and research scientists. The goal is to translate high level concepts such as "cerebral cortex" to a standard set of parts within primates and rodents. This basic upper ontology is also being linked to the Waxholm mouse brain atlas to implement a set of standardized spatial and semantic representations of major brain structures across the INCF atlasing and PONS programs. The neuronal registry subprogram is determining a set of properties for defining neurons in order to create a knowledge base to facilitate comparison among existing and yet to be discovered neuronal types. With the R & D task force, it is reviewing different representations to derive a set of standard relationships that can be used to express properties of neurons in a computable and interoperable form, particularly in the area of connectivity among brain regions, cell populations and individual cells. The two subprograms are designed to work together, with the structural lexicon providing the building blocks to be used by the neuronal registry for building representations of neurons. The R & D Task Force is responsible for establishing a semantic framework for brain structures and neurons that can be used to compute relationships among structures across scales. Initial work has been understanding and aligning the different representations of brain structures and neurons proposed by a variety of groups working in these areas with the aim of harmonization and consolidation. One target is having all terms and relations at least have definitions in, and consonant with, OBO Foundry reference ontologies, and to lay the groundwork for being able to share knowledge on the semantic web. Members of the task force include representatives from several community ontology and database efforts so as to ensure that the results of the PONS program address known needs and are likely to be generally acceptable. As with other INCF programs, the PONS provides a community forum where basic standards, procedures and tools can be established to facilitate interoperability among these different and valuable efforts. All products of the PONS are meant to be evaluated and extended by the larger community. In this way, the neuroscientists can pool their efforts more effectively and add to the growing ecosystem of linked resources within the broader life sciences community.

The Neuroscience Information Framework (NIF): practical experience with large scale integration of federated neuroscience data

Maryann Martone[1] and the NIF Consortium[2]

1. Department of Neurosciences, University of California, San Diego, San Diego, USA
*2. Yale University, Washington University, California Institute of Technology, USA**

The Neuroscience Information Framework (NIF; http://neuinfo.org) was launched in 2008 to address the problem of finding and integrating neuroscience-relevant resources through the establishment of a semantically enhanced framework. The NIF portal provides simultaneous search across multiple information sources to connect neuroscientists to available resources. including:

(1) NIF Registry: A human-curated registry of neuroscience-relevant resources annotated with the NIF vocabulary;
(2) NIF Web: A web index built using the Nutch indexing system from the NIF registry;
(3) NIF Literature: A full text indexed corpus derived from major neuroscience journals, open access literature and specialized bibliographic databases indexed using the Textpresso text retrieval tool;
(4) NIF Database Federation: A federation of independent databases registered to the NIF, allowing for direct query of database content.

NIF has continued to grow significantly in content, currently accessing over 2800 resources through the Registry, 1 million web pages in the Web Index, and 22 million database records contained within 53 independent databases in the data federation, making NIF one of the largest source of neuroscience resources on the web. Search through the NIF portal is enhanced through a comprehensive ontology (NIFSTD) expressed in OWL-DL, covering major domains in neuroscience, e.g., diseases, brain anatomy, cell types, subcellular anatomy, small molecules, techniques and resource descriptors. NIFSTD is used for annotation of resources and to refine or expand queries by utilization of the relationships encoded in the ontology. They are served through Ontoquest, a database customized for storing and serving OWL ontologies. The NIF search interface autocompletes search strings with concepts in the NIF ontologies and automatically expands to synonyms. In NIF 2.5, we have incorporated more automated expansions to provide concept-based searches over classes defined through logical restrictions in the NIFSTD. For example, concepts like GABAergic neuron are automatically expanded to include children of these classes, i.e., types of GABAergic neurons. When such logical restrictions are present, Ontoquest materializes the inferred hierarchy and auto expands the query to include these classes. As the scope and depth of the NIF data federation grows, NIF has been working to create more unified views across multiple databases that export similar information. For example, NIF has registered several databases that provide mapping of gene expression to brain regions or provide connectivity information among brain structures. For these sources, NIF standardizes the database view based on common data elements and column headers. In performing this type of integration across resources, NIF has had to confront the different terminologies utilized by different resources. While we don't change the content of the database, we do provide some mappings to the NIF annotation standards for recognized entities such as brain regions and cell types. We have also started to provide a set of standards for annotating quantitative values such as age and gene expression level. To do this, NIF has defined age ranges for adulthood in common laboratory species such as the mouse and a standard set of categories for expression levels. The latest release of NIF lays the foundation for enhanced semantic services in future releases. In NIF 2.5, entities contained within the NIFSTD are highlighted within the NIF search results display. For anatomical and cell entities, we have introduced the NIF Cards. NIF cards are specialized search applets that draw upon NIFSTD and the NIF data federation to display additional information about an entity and provide customized search options depending upon the domain. As the NIF Cards evolve, they will provide the basis for linking NIF results into a larger ecosystem of linked data.

*Multiple authors in the NIF consortium have contributed to this work: http://www.neuinfo.org/about/people.shtm

Measuring behavioral perfomance in neurosensory experiments: the free tracking-framework (FTF)

Friedrich Kretschmer[1], Malte Ahlers[2] and Jutta Kretzberg[1]

1. Department of Computational Neuroscience, Carl-von-Ossietzky-Universität Oldenburg, Oldenburg, Germany
2. Department of Neurobiology, Carl-von-Ossietzky-Universität Oldenburg, Oldenburg, Germany

One of the main goals of neuroscience is to understand the neuronal basis of animal behavior. To approach this question experimentally, it is crucial to measure the animal's behavior with well-defined stimuli. By using the same stimuli for behavioral and neurophysiological experiments, neuronal responses can be related to behavioral performance. With this approach, it is possible to determine boundaries of the sensory system and to test hypotheses about the neural codes used in neurosensory information processing. For example, the combination of behavioral and neurophysiological experiments is very fruitful for the analysis of genetically modified animals, because it allows to characterize the function of the protein corresponding to the knocked out gene on a systemic level. For this purpose we have developed a universal single camera recording-system suitable for automated tracking of body, head and eye movements in small animals. Combined with a well-defined sensory stimulation, this system allows the reconstruction of the stimulus situation that was present at the receptor neurons during the experiment, providing the basis for neurophysiological experiments. The system tracks artificial and/or natural markers on the animal and estimates their 3D Position. For this purpose the framework combines several techniques from computer vision research, including contour-, region- and pattern-based tracking algorithms. 3D estimation is done by automatically measuring relative distances of at least four static markers attached to the animal in a series of different camera views. This allows the computation of distances to the camera center during an experiment on the basis of the perspective strain (Perspective-N-Point problem). The modular implementation of this software-framework enables the use of different tracking algorithms and the application in many different experimental environments. Tracking is done in on- or offline mode depending on the complexity of the applied algorithms. The free tracking-framework is currently being evaluated in a series of eye- and head-tracking experiments in mice and turtles while visually stimulating with user-defined moving 360° images through a panoramic mirror. At the conference, we will demonstrate the current version of the free tracking-framework. We will show how it is possible to automatically calibrate the camera and how different artificial markers attached to moving objects are tracked and their 3D positions are estimated. The resolution of a standard webcam provides a sufficient preciseness of the 3D estimation for many applications, and the source-code of this academic project will become available in an open source form in the future. Therefore, the free tracking-framework is designed to provide the basis for low-cost experimental setups to track animal behavior to complement studies in neurosensory science.

The Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC)

David Kennedy[1], Christian Haselgrove[2], Nina Preuss[3], Maryann Martone[4] and Jeff Grethe[4]

1. Department of Psychiatry, University of Massachusetts Medical School, Worcester, USA
2. University of Massachusetts Medical School, Worcester, USA
3. TCG, Inc., Washington D.C., USA
4. University of California at San Diego, San Diego, USA

Introduction:
We report on the updates to the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC). Initiated in October 2006 through the NIH Blueprint for Neuroscience Research (1), NITRC's mission is to create a user-friendly knowledge environment for the neuroimaging community. Through the identification of existing tools and resources valuable to this community, NITRC's goal is to enhance, adopt, distribute, and contribute to the evolution of neuroimaging tools and resources.

Located on the web at www.nitrc.org, this site promotes tools and resources, vocabularies, and databases, thereby extending the impact of previously funded, neuroimaging informatics contributions to a broader community. It is anticipated that this will give neuroimaging researchers greater and more efficient access to the tools and resources they need, better categorize and organize existing tools and resources, facilitate interactions between researchers and developers, promote better use through enhanced documentation and tutorials—all while keeping the set of resources up-to-date with the most recent resource upgrades and updates.

Approach:
To meet the disparate needs of resource developers and users, NITRC requires functionality like that found in platforms such as Source Forge, Bugzilla, CVS, Wiki, etc. To unify such functionality, we have chosen to design the knowledge environment using the open-source GForge project. Within the NITRC environment a 'project' is created for each tool or resource that is to be represented. Each project will have independent descriptive content (as projects do currently at IATR, (2)), as well as Wiki, CVS, bug tracking, news forums, and discussion lists associated with it. Descriptions can be housed on the NITRC servers themselves, passed through to an external, preexisting site for content management.

The site was formally launched to the public on Oct. 1, 2007. There are currently 272 hosted projects, and 1611 registered users, and these numbers are increasing daily. NITRC encourages feedback, through surveys of its users to make the site as accessible as possible.

Summary: NITRC, a neuroimaging knowledge environment, is now online. We encourage the neuroimaging community to try it out and provide feedback on its design, tools, resources, and content. The NITRC interface provides a coherent and synergistic environment for the advancement of neuroimaging-based neuroscience research (3).

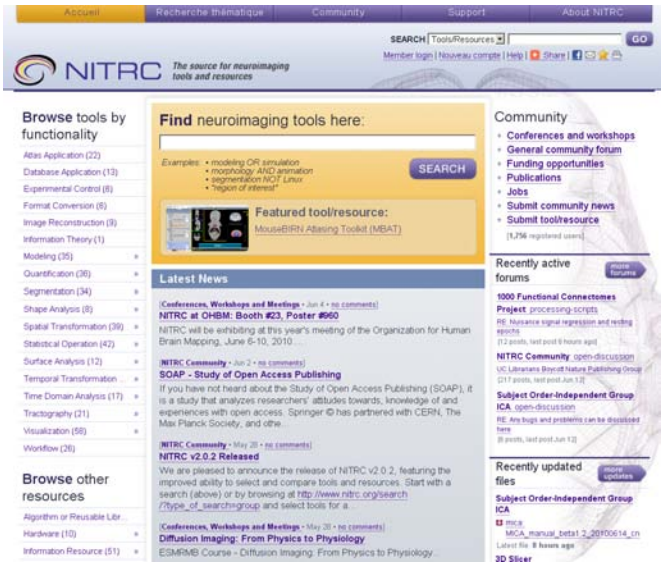
Acknowledgement: This work is supported by Contract No.: N02-EB-6-4281 under the auspices of the NIH Blueprint for Neuroscience Research.

References

1. http://www.nih.gov/news/pr/oct2006/nibib-05a.htm

2. Kennedy & Haselgrove, Neuroinformatics, 2006; 4(3):263-70.

3. Luo XZ, Kennedy DN, Cohen Z., Neuroinformatics. 2009;7(1):55-6.



Neuroinformatics environment for facilitation of brain and neuroscience research

Takayuki Kannon[1], Yoshihiro Okumura[1], Kohji Makimura[1], Nilton Kamiji[1], Keiichiro Inagaki[2] and Shiro Usui[1]

1. RIKEN BSI, Wako-shi, Japan
2. RIKEN Computational Science Research Program, Wako-shi, Japan

To obtain great achievement in neuroscience research, physiological and computational studies should be tightly coupled to systematically analyze the brain function. However it is difficult to harmonize and integrate a wealth of results obtained in those researches because of the variety of style, which makes it complicated to understand the detail of brain function. In order to tackle this difficulty, it is an important task of Neuroinformatics (NI) to provide environment that facilitates integration and sharing of data. NI aims to establish links between brain-related sciences using advances in information technology to achieve better understanding of the brain as a whole. Based on these backgrounds, we have developed and provided an environment for supporting brain and neuroscience research such as XooNIps, Concierge, Samurai-Graph and RAST.

The XooNIps is a NI base-platform system which can be utilized from personal use, to small groups such as laboratories, up to a large community like public platforms. Data in XooNIps are systematically stored in a tree-structured keyword index that allows users to keep track of the progress in their particular research fields. Users can download resources from XooNIps and use them in their research, subject to the license declared by the authors. However, users are often annoyed with the cumbersome registration process to contribute their research resources onto XooNIps. It requires detailed content descriptions (metadata) of resources to ensure their reusability. Thereby, they must enter all the required metadata manually. In general, a browser-based interface is unsuitable for such input operations. Therefore we have been developing a data management tool named Concierge to support the use of XooNIps in searching, downloading, and uploading information.

The Concierge can be utilized for storing, classifying and managing digital resources such as publications, experimental data, presentation files, etc, with its metadata. It also includes laboratory notebook, paper management tool, and experimental data management tool. The paper management tool handles PDF files based upon bibliographic metadata queried from databases such as PubMed. The experimental data management tool handles data files using several common data format (e.g., NetCDF, HDF5) by automatically harvesting information (e.g., experimental conditions). Based on the information stored in the Concierge, users can easily upload files to open databases such as XooNIps based platforms. Moreover, to support the construction of mathematical models, the Concierge can manage mathematical models and resources in cooperation with the modeling environment called PLATO. Samurai-graph is an OS independent graph plotting tool, which provides highly functional and user-friendly graphical user interface. It now supports visualization of netCDF files, a common data format for connecting mathematical models on the PLATO.

RAST is a related abstract search tool based on an extension of the ordinary cosine similarity measure. It lists relevant abstracts on the top of the list, provides feature for keyword suggestion to refine ones search, and manages search results together with the keyword entered for the search. A surprising outcome of this feature was that, when applied to the Japan Neuroscience Society 2009, about half of the abstracts the users has chosen did not contain any of the keywords originally entered. These are the "hidden treasures". Such features might also be applied for searching contents of databases such as XooNIps.

We have developed tools for collecting and managing experimental results, searching, sharing and reusing resources with collaborators, creating, and integrating mathematical models to construct a large scale brain model, whereas visualization tools for viewing the model output. We hope all these tools will support every neuroscientist research life.

Title: Modulation of nociceptive responses induced by VMH-procainization in sucrose fed rat

Manjula Suri[1], Suman Jain[2] and Rashmi Mathur[2]

1. Department of Physiology, University of Delhi, New Delhi, India
2. Department of Physiology, All India Institute of Medical Sciences, New Delhi, India

Modulation of nociceptive response to ad libitum sucrose ingestion (5h) by ventromedial hypothalamus (VMH) has been reported earlier in the same rat. The role of VMH in the pattern of transition from sucrose-fed analgesia to hyperalgesia is not known therefore, we investigated this pattern of transition. Adult male wistar rats were divided into Saline, Procaine and Procaine + Sucrose fed groups. Their phasic nociceptive responses were studied in session I-V(starting at 0, 0.25, 1, 3 and 5h, respectively) by hot plate tests namely, paw lick latencies and escape latency. Saline/procaine was microinjected (1µl/ min) in VMH immediately after session I, to produce temporary reversible lesion in behaving rats. In saline injected group FPL did not vary as a function of time and repeated stimulation. In procaine injected rats, FPL statistically significantly decreased in sessions II and V as compared to session I. (3.25 ± 0.22 to 2.55 ± 0.06 and 2.75±0.16, s). In saline versus procaine injected group the decrease was significant in sessions II, IV and V. In procaine injected sucrose fed group there was a statistically significant decrease in session IV, V versus I. Whereas, statistically significant decrease in session IV, V as compared to saline and in session II as compared to procaine per se was observed. Therefore, the results of our study indicate that procainization of VMH leads to hyperalgesia at 0.25, 3 and 5h, while, sucrose ingestion produces only an attenuation of initial (<1h) analgesia to thermal noxious stimuli suggesting a vital role of VMH in analgesia and in transition from eualgesia to hyperalgesia of biphasic nociceptive response to sucrose ingestion.

INCF Swiss Node: Neural Reconstruction

Mark Longair

Institute of Neuroinformatics, UZH/ ETH Zürich, Zürich, Switzerland

In contrast to many other national nodes of the INCF, active development of the Swiss node began very recently. The goals of this national node are to promote the activities of Swiss research groups working in the field of neuroinformatics, and encourage and facilitate collaborations both between them and with the wider INCF community. Our short term goals are to promote the work of these groups, while in the longer term to provide support for tools to enable collaboration and data sharing, or developing such systems where required. We also plan to arrange a number of events to encourage collaborative work on Open Source software that is used by multiple neuroinformatics groups within Switzerland.

Although the INCF Swiss node will include and promote work in neuroinformatics in very broad terms, we are focusing as a particular theme on neural reconstruction, both from image data acquired via light microscopy and electron microscopy; these data are invaluable for identifying neural circuits and the simulation and modelling of these systems. We present examples of this work from various groups in Switzerland, including reconstructions of very large electron microscope data sets and examples of the combined use of light microscopy and electron microscopy. We particularly feature the software tools that are used for such reconstructions by labs associated with the Swiss node of the INCF.

An algorithm for finding candidate synaptic sites in computer generated networks of neurons with realistic morphologies

Jaap Van Pelt, Andrew Carnell, Alexander De Ridder and Arjen Van Ooyen

CNCR - Dept. Integrative Neurophysiology, VU University Amsterdam, Amsterdam, Netherlands

1. Purpose - Neurons make synaptic connections at locations where axons and dendrites are sufficiently close in space. Typically the required proximity is based on the dimensions of dendritic spines and axonal boutons. Based on this principle one can search for those locations in networks formed by reconstructed neurons or computer reconstructed neurons. Candidate synapses are then located where axonal and dendritic branches come within a certain criterion distance from each other. The present study aimed at developing an algorithm for finding those locations.

2. Method - Both in the case of experimental reconstruction and in the case of model generation, neurons are morphologically represented by piecewise-linear structures (line pieces or cylinders). Proximity tests then need to be performed on all pairs of line pieces from both axonal and dendritic branches. A test based on the shortest distance between pairs of line pieces appears to result in (i) local clusters of synaptic sites where line pieces from axonal and dendritic branches are sufficiently close, and in (ii) a dependency on the typical length scale in the piecewise-linear approximation of the neuronal morphologies. The present study aimed at developing a new algorithm for finding locations of candidate synapses. It is based on the crossing requirement of line piece pairs, while the length of the orthogonal distance between the line pieces is subjected to the distance criterion for testing 3D proximity.

3. Results – The new synapse formation model has been applied to a network of 25 neurons with realistic density (cell bodies generated within a sphere of radius 43 µm with minimum neuron separation of 20 µm). The neurons were generated using the Netmorph simulator (Koene et al., 2009) based on growth parameter values optimized on a data set of reconstructed rat cerebral cortex L2/3 pyramidal neurons made available by Svoboda through the www.neuromorpho.org website (Ascoli et al., 2007). The additional crossing requirement prevented the clustering effect seen in the distance-based approach, while the dependency on the typical length scale was significantly reduced. The remaining dependency may have a fractal origin. For the number of synaptic contacts per neuron-neuron connection, values were obtained that excellently matched the available experimental data.

4. Conclusions – The new algorithm for finding potential synaptic locations in networks of neurons with realistic neuron density and neuronal morphologies eliminated the clustering effect produced when using only a distance criterion, and resulted in highly realistic values for the number of synaptic contacts per connection.

Acknowledgement: This work is supported by EU BIO-ICT Project SECO (216593)

References

1. Ascoli GA, Donohue DE, Halavi M (2007) NeuroMorpho.Org: a central resource for neuronal morphologies. J Neurosci 27(35):9247-51

2. Koene RA, Tijms B, Van Hees P, Postma F, De Ridder A., Ramakers G, Van Pelt J, Van Ooyen A (2009) NETMORPH: A framework for the stochastic generation of large scale neuronal networks with realistic neuron morphologies. Neuroinformatics 7: 195-210.

Forward modeling of extracellular potentials: Results and possibilities

Gaute T. Einevoll, Henrik Linden, Espen Hagen, Janne Fossum, Tom Tetzlaff, Eivind Norheim and Klas H. Pettersen
Norwegian University of Life Sciences, Aas, Norway

Mathematical modelling relies on experimental data to make progress, both to constrain and to test the models. A common experimental method has been in vivo single-unit extracellular recordings: when a sharp electrode is placed sufficiently close to the soma of a particular neuron, the recorded potential reliably measures the firing of individual action potentials in this neuron. This information is contained in the high-frequency part of the recorded potentials. The low-frequency part, that is, the local field potentials (LFP), has proved much more difficult to interpret and has typically been discarded.

Other experimental methods, particularly methods that measure population-level activity in vivo, are needed to facilitate development of biologically relevant neural network models. Large-scale electrical recordings using various types of multielectrodes, i.e., electrodes with many contacts, are one such option. As techniques for such recordings are rapidly improving, there is a need for new methods for extraction of relevant information from such data. Here we present results from projects in our group aimed at elucidating the link between recorded extracellular potentials and the underlying neural activity.

Extracellular potentials in the brain are in general due to complicated weighted sums of contributions from transmembrane currents in the vicinity of the recording electrode. The transmembrane currents accompanying various types of neural activity can be calculated by means of multicompartment models. Given these transmembrane currents, the extracellular potential can in turn be calculated using a electrostatic forward-modelling formula based on the quasistatic version of Maxwell's equations (Holt & Koch, J Comp Neurosci 6:169, 1999) . Several projects where this forward-modelling scheme has been utilized will be presented:

- investigation of how neural morphology and electrical parameters affect the shape and size of extracellular action potentials (Pettersen & Einevoll, Biophys J 94:784, 2008)
- investigation of how the LFP and its frequency content generated by neurons in a population depend on synaptic activity and neuronal morphologies (Pettersen et al, J Comp Neurosci 24:291,2008; Pettersen et al, J Neurosci Meth 154:116, 2006) - introduction of laminar population analysis (LPA) where stimulus-evoked laminar-electrode data from rat barrel cortex are analyzed in a scheme where the MUA and LFP are jointly modelled using physiological constraints (Einevoll et al, J Neurophysiol 97:2174, 2007)
- extraction of thalamocortical and intracortical network models based on laminar-electrode data from barrel cortex and simultaneous recording of thalamic firing activity recorded in the homologous barreloid (Blomquist et al, PLoS Comp Biol 5:e1000328, 2009)
- generation of model data aimed at facilitating the development and objective testing of spike-sorting algorithms for data recorded by multielectrodes
- investigation of the extracellular-potential footprint from synaptic activation of primary sensory cortices from individual thalamic neurons as measured by the so called spike-triggered CSD method (Swadlow et al, J Neurosci 22:7766, 2002)

Supported by the Research Council of Norway (eVita, NOTUR, NevroNor).

An Automated System for Simulating Multi-Compartmenal Models and its Application to Investigate Morphological Properties of a Neuronal Coincidence Detector

Michael Stransky[1], Thomas Wachtler[2], Hans Jürgen Ohlbach[1] and Philipp Lothar Rautenberg[2]

1. Institute for Computer Science, Ludwig-Maximilians-Universität München, Munich, Germany
2. Department of Biology, Ludwig-Maximilians-Universität München, Planegg-Martinsried, Germany

Neuronal morphology plays a fundamental role for the information processing capabilities of neurons. These dependencies can be investigated using compartmental models to simulate functional properties of morphologically characterized neurons. We developed an automated system to investigate the effect of realistic morphologies on the electrophysiological properties of a neuron and applied it to morphologies of neurons of the medial superior olive (MSO) from published data (Rautenberg et al., 2009). The simulation paradigm was designed to be in accordance with electrophysiological experiments conducted by Scott et al. (2005), concerning measurements of input resistance and effective membrane time constant. Simulating neurons from morphological data using compartmental models implies a highly complex parameter space, both in terms of the simulation parameters and the results. To cope with this complexity, we used an integrative approach that employs a database to manage the data, control the simulations, and analyze the results. This yields the requisite for efficient data analysis: Morphologies can be easily exchanged and thus a great variety of analyzes can be performed in a systematic and non-redundant fashion. Even patch-clamp-experiments can be simulated within the database, eliminating the need of performing the same analyses "by hand" again and again for each morphology. This in turn facilitates analysis and visualization of results, and the results are presented in a portable and easy way via direct database access and web interface. For simulating neurons we used the NEURON simulation software (Hines and Carnevale, 1997. Simulations were performed using database and computing services at the German INCF Node (www.g-node.org). Data were stored and simulations were controlled via a PostgreSQL Database. PostgreSQL easily allows to incorporate Python code using plpython, so we could integrate NEURON via Python for simulations and libraries like MDP (Zito et al., 2008) for analysis. In this manner, we performed automated simulations with different morphologies within the database. In addition to the detailed simulation of reconstructed MSO neurons, we performed simulations of simplified models, where the morphology was reduced to three compartments using passive parameters that were estimated with the complex models, like specific axial resistivity constant. Comparison of the simulated responses of the simple model to responses of the morphological complex models enabled us to relate the geometrical properties to functional properties of the neurons. For example, we found that surface area has to change when simplifying the morphology while keeping electro-physiological properties like input resistance constant. Our work demonstrates the efficiency of a unifying approach employing a database for management of both data and analysis tools.

Acknowledgments: The German INCF Node is supported by BMBF grant 01GQ0801

References

1. Hines, M. L., & Carnevale, N. T. (1997). The NEURON simulation environment. Neural Computation, 9(6), 1179-1209.

2. Rautenberg, P. L., Grothe, B., & Felmy, F. (2009). Quantification of the three-dimensional morphology of coincidence detector neurons in the medial superior olive of gerbils during late postnatal development. The Journal of Comparative Neurology, 517(3), 385-396. doi:10.1002/cne.22166

3. Scott, L. L., Mathews, P. J., & Golding, N. L. (2005). Posthearing developmental refinement of temporal processing in principal neurons of the medial superior olive. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 25(35), 7887-7895. doi:10.1523/JNEUROSCI.1016-05.2005

4. Zito, T., Wilbert, N., Wiskott, L., & Berkes, P. (2008). Modular Toolkit for Data Processing (MDP): A Python Data Processing Framework. Frontiers in Neuroinformatics, 2, 8. doi:10.3389/neuro.11.008.2008

Automated analysis of neuronal morphologies via python and (collaborative) open source databases

Nina Hubig[1], Hans Jürgen Ohlbach[1], Thomas Wachtler[2] and Philipp Lothar Rautenberg[2]

1. Institute for Computer Science, Ludwig-Maximilians-Universität München, Munich, Germany
2. Department of Biology, Ludwig-Maximilians-Universität München, Planegg-Martinsried, Germany

Neuronal morphology plays a fundamental role for the information processing capabilities of neurons. To fully exploit the information gained by neuron reconstructions, it is crucial for neuroscientific researchers to analyze a large amount of data in a fast, effective, and automated way. We developed a new system for the analysis of morphological data that is based on a high-level object-oriented programming language that was integrated into an object-relational database management system. This approach enables to connect automatized data analysis procedures directly to the stored data. In our (experimental) system we used Python as object oriented language which is commonly used in the neuroscientific community. It is a versatile language that can be easily applied to solve several tasks that research laboratories face almost every day: data manipulation, biological data retrieval and parsing, automation, or simulations of single cells or neural networks [1]. As a database system we used PostgreSQL [2]. PostgreSQL is a powerful, open source object-relational database system. Its SQL implementation strongly conforms to the ANSI-SQL:2008 standard and therefore is widely compatible with other database systems. For efficient data access, we defined a data schema representing SWC-specifications [3]. Based on this schema, we implemented views and analysis functions in SQL, to enable data analysis directly within the database. Analyses were performed using database and computing services at the German INCF Node (www.g-node.org). Different properties of the morphology of neurons, such as total length, number of branch points, surface area, and volume were calculated and compared across neurons in the database, taking into account other properties, like age or species of the corresponding animal. For example, we found that the ratio between surface area and volume is an important measurement of the influence of a neurons morphology on electrophysiological properties. The results can be accessed from the database for visualization by various well-known software-systems like MATLAB or OpenOffice. Our results are presented in a portable and easy way via database access and web interface. This yields the requisite for efficient data analysis: Morphologies can be easily exchanged and thus a great variety of data analysis can be performed in a systematic and non-redundant fashion. This eliminates the need of doing the same analysis by hand again for each morphology. It also in turn facilitates analysis and visualization of results. The method is not restricted to analysis of neuron morphology, but could also be applied for the analysis of physiological data.

Acknowledgments: The German INCF Node is supported by BMBF grant 01GQ0801

References

1. Bassi, S. (2007). A primer on python for life science researchers. PLoS Computational Biology, 3(11), e199. doi:10.1371/journal.pcbi.0030199

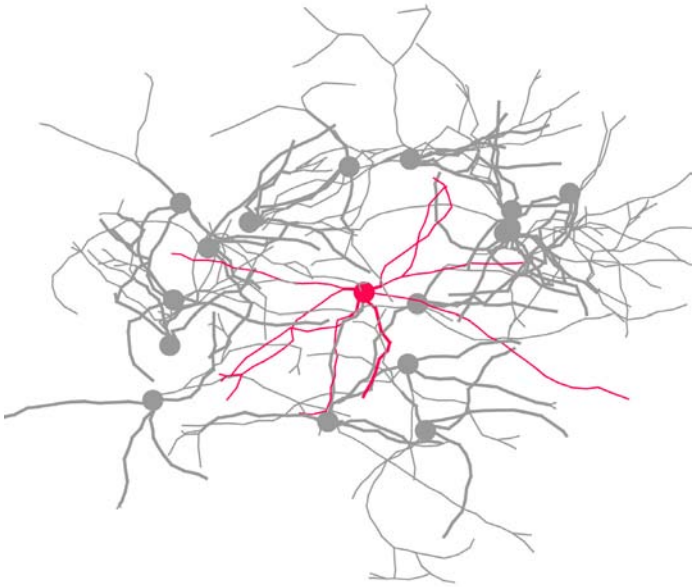
2. http://www.postgresql.org/about

3. http://www.neuronland.org/NLMorphologyConverter/MorphologyFormats/SWC/Spec.html

Self-organizing Winner-Take-All networks

Roman Bauer, Sabina Pfister and Rodney Douglas
Institut für Neuroinformatik, ETHZ/UZH, Zürich, Switzerland

Quantitative studies of the connectivity of cortical neurons have demonstrated that there is a high degree of recurrence between pyramidal neurons in the superficial layers of visual cortex (Binzegger et al., 2004). This recurrence is consistent with the presence of winner-take-all (WTA) behavior, and suggests that the WTA may be a computational primitive of cortical processing (Hahnloser et al., 2000; Maass, 2000; Douglas & Martin, 2004). However, the connectivity and parameters that permit circuits to operate as effective WTAs are rather specific (Hahnloser et al., 2003; Rutishauser & Douglas, 2009), and this raises the interesting problem of how these circuits could be self-organized and -calibrated during cortical development. We are exploring this problem by simulations of cortical development using the simulation framework CX3D (Zubler & Douglas, 2009), operating in conjunction with the spiking neural network simulator PCSIM (Pecevski et al., 2009). Our developmental simulations begin from a single precursor cell. This cell, by replication, differentiation, and axonal growth gives rise to a population of interacting excitatory and inhibitory daughter cells. This developmental process unfolds under the control of gene-regulation like networks. The various neuronal types are generated and randomly arranged in space, and then their neurites extend following growth rules which are implicit in their 'genetic code'. These growth rules induce mechanisms such as directed axonal outgrowth, retraction, and arborization. Based solely on these 'genetic' instructions and the resulting local interactions between developing neurons (e.g. by diffusion of signaling cues or mechanical interactions), we are able to generate biologically observed connection patterns between pyramidal and basket cells in the cortical layers II / III. Using this self-organized circuits, we are able to simulate the WTA behavior of actively selecting the stronger of two input signals, while suppressing the weaker one. Overall, we have shown that we can construct functional networks from a single precursor cell, using developmental processes. This entire self-organizing process arises out of the precursor's genetic code, and it is steered only by local interactions with other cells: There is no global supervisor.



A self-organizing cortical layer 4 model applied to large-scale imaging data analysis

Simon Benjaminsson and Anders Lansner

Computational Biology, Royal Institute of Technology, Stockholm, Sweden

To find useful information in vast amounts of data is what our brains are particularly good at. It is also the ambition of many data analysis applications. Cortical models aimed at capturing the information processing capabilities of the brain are endowed with qualities that are suitable for large-scale data analysis, such as scalability, parallelization and an organization driven by the data statistics through learning.

We have previously suggested a cortical layer 4 model as part of an attractor associative memory system [1]. It allows for transforming raw sensory data into a sparse and distributed code that reflects statistical properties of the input. More specifically, self-organization of the input sensors is facilitated by data dependencies. This leads to their grouping in a hypercolumnar structure. Together with a feature extraction step it underlies a hierarchical and modular cortical architecture.

As well as using sensory data as input, any type of information can be utilized. We demonstrate this on resting-state fMRI data, employing the cortical layer 4 model to explore the statistics in a large multi-subject dataset. The voxels are treated as input sensors and the resulting groupings reflect the resting-state networks. The capability of the model to rapidly form different types of hypercolumnar organizations without excessive computational cost is exploited in this data analysis application to rapidly visualize resting-state networks along with their subnetworks.

References

1. Lansner A, Benjaminsson S and Johansson C (2009) From ANN to Biomimetic Information Processing. Studies in Computational Intelligence 188 (Heidelberg: Springer Berlin), pp. 33-43.

Double frequency synchronization for working memory operation in the brain - a computational study for bridging human scalp EEG data and neural dynamics

Yoko Yamaguchi[1], David Chik[1], Masahiro Kawasaki[2] and Hideki Oka[3]

1. Laboratory for Dynamics of Emergent Intelligence, RIKEN BSI, Wako, Japan
2. Rhythm-based Brain Computation Unit, RIKEN BTCC, Wako, Japan
3. The Center for Advanced Medical Engineering and Informatics, Osaka University, Osaka, Japan

Current studies on brain dynamics in various levels more and more reveal the dynamical brain coordinated by synchronization of oscillations. In the decade, the synchronization hypothesis for dynamical linking was extensively studied in animals and humans. Most of neural systems are known to show various oscillation frequencies in cellular levels and also during cognitive tasks in human scalp EEG. Among them, complexity of synchfonization dynamics provides fascinating problems for understanding neural mechanisms of intellectual properties. According to the dynamical system theory (e.g., the slaving principle by H Haken), slow oscillations of human EEG, such as the delta, theta and alpha can concern with higher cognitive functions to regulate local processes with fast oscillations. We hypothesize that synchronization network in each frequency band has each role in cognitive functions and that their dynamical linking among modules within the same frequency band or through cross-frequency coupling could execute the real-time computation by implementing multiple constraints for cognitive control.

Recently we have reported that EEG theta rhythm related network (4~8 Hz) distributing over frontal midline regions and posterior regions is related with central executive functions (Mizuhara et al. 2007) and furthermore that the theta rhythm network emerges restrictively in manipulation period of working memory(Kawasaki et al. 2010). In the working memory task, alpha rhythm (~10 Hz) around relevant sensory regions is observed in both of storage period and operation period. interestingly, theta and alpha rhythms exhibit one to two phase-locking in the manipulation period. The network mechanism of this double frequency synchronization and its possible functional mechanism are unsolved. In this paper, we propose a alpha-theta cross frequency coupling network model for the working memory task. In the model, alpha oscillation networks are described by flip-flop oscillation networks (Colliaux et al. 2009). A limit cycle attractor in the up state of the associative memory network represents the working memory storage. Theta network is assumed to consist of frontal midline module and sensory modality specific modules with mutual coupling. By introducing a coupling between theta and alpha rhythm units, we show theta network can regulate alpha rhythm synchronization so that dynamically linking among alpha oscillations can retrieve or manipulate memory. This is in agreement with the results suggested by Kawasaki et al. (2010). We conclude that double frequency phase locking between theta and alpha oscillations can work for cognitive control through hierarchical dynamical linking. Then, for the sake of direct comparison with our oscillation network model and human EEG scalp data, we developed a simulation system of scalp EEG by assuming electronic charge in a given location of the brain. Our programming Using InsilicoML and InsilicoDE, showed usefulness of this system on basic simulation and also suggested possible computational neuroscience approach from complex neural dynamics for understanding cognitive functions.

This study was partially supported by Grant-in-Aid for Scientific Research on Innovative Areas No. 4103. The simulation study is supported by physiome.jp and dynamic brain platform (DBPF).

References

1. Mizuhara H, Yamaguchi Y (2007) Human cortical circuits for central executive function emerge by theta phase synchronization. NeuroImage, 36: 232-244

2. Kawasaki M, Kitajo K, Yamaguchi Y (2010) Dynamics links between theta executive functinos and alpha storage buffers in auditory and visual working memory.European J Neuroscience (on-line)

3. Colliaux D, Molter C, Yamaguchi Y (2009) Working memory dynamics and spontaneous activity in a flip-flop oscillations network model with the Milnor attractor. Cognitive Neurodynamics 3:141-151.

Temporal Structure of Incoming Spike Trains Modulate Structure Formation by STDP

Gordon Pipa[1], Marta Castellano[1], Raul Vicente[1] and Bertram Scheller[2]

1. Frankfurt Institute for Advanced Studies, Max Planck Institute for Brain Research, Frankfurt, Germany
2. Clinic for Anesthesia, Intensive Care Medicine and Pain Therapy, Johann Wolfgang Goethe University, Frankfurt am Main, Germany

In order to understand cognitive processes through the cortex it is necessary to have an understanding of its information processing, which depends on the self organization and structure formation on the network. Rich auto-structure has been recorded in spiking activity, ranging from bursty to regular renewal processes and involving very complex spiking patterns. Here we explore the influence of non-Poissonian renewal activity on structure formation by Spike Time Dependent Plasticity (STDP).

We study the impact on non-Poissonian renewal activity on structure formation by STDP. To this end we simulated a conductance based integrate and fire neuron that receives input from 200 up to 2500 neurons, both excitatory and inhibitory. The presynaptic activity was modeled by a renewal process with gamma distributed inter-spike interval distribution (ISI). Using such a gamma process, allowed us to systematically vary the regularity, ranging from Poissonian firing for a gamma process with a shape factor of 1 (coefficient of variation of the ISI distribution $CV_{ISI} = 1$) to extremely regular firing with a shape factor of 100 ($CV_{ISI} = 0.1$).

In the first step we show that the auto-structure of the presynaptic activity (even in the order of thousands mutually independent spike trains) can induce temporal structure in the post synaptic firing, in particular we show an interplay between the pre-synaptic auto-structures which implies a modulation by the rate of the individual processes. This finding raises the question to which degree this dependence between the pre-post synaptic activity can also modulate synaptic plasticity. Thus, in the second step we analyze this impact by using STDP as a synaptic plasticity paradigm. To this end we show that not only the regularity or auto-structure of the renewal process but also the rate of the individual processes modulate the dynamics of the synaptic weights. Both the speed and strength of structural changes induced by STDP can be modulated by the temporal structure of mutually independent spiking activity (i.e., the regularity of the presynaptic activity and its rate).

Our findings give rise to the possibility that the temporal auto-structure of large groups of independent neurons could be used to modulate the sensitivity for spontaneous structure formation in recurrent networks, a novel modulatory effect on structure formation by STDP. Both effects are observed in neuronal recording and had been associated with cognitive tasks. Thus, our findings might be understood as a link between neuronal plasticity and task-modulation of learning and structure formation in recurrent networks.

References

1. Abbott, L. F., & Nelson, S. B. (2000). Synaptic plasticity: Taming the beast. Nature, 1178-1183.

2. Caporale, N., & Dan, Y. (2008). Spike Timing–Dependent Plasticity: A Hebbian Learning Rule. Annual Review of Neuroscience, 31(1), 25-46.

Integration of visuo-motor network models by MUSIC

Aurelien Cassagnes[1], Kenji Doya[2], Jan Moren[3], Junichiro Yoshimoto[4] and Tomohiro Shibata[5]

1. OIST, Kyoto University, Okinawa, Japan
2. OIST, NAIST, RIKEN, Kyoto University, Okinawa, Japan
3. NAIST, Kyoto University, Nara, Japan
4. OIST, NAIST, Okinawa, Japan
5. NAIST, Nara, Japan

1. Introduction A challenging goal in computational neuroscience is to realize a "whole-brain" simulation linking sensory inputs to motor outputs. The visual system is a good instance to approach the goal, because brain parts involved have been well studied and their models have been proposed. Here we aim to connect such models with spiking neurons and close the visual sensor-motor loop.

In connecting multiple models, we often suffer from difficulty in communicating the events among heterogeneous processes, since the models are built by independent groups and implemented on different computer platforms. The MUSIC [1], Multi-Simulation Coordinator, was developed recently to remedy the difficulty. In this study, we implement the visual-oculomotor system by connecting the models of superior colliculi, brainstem integrators, and the eyeballs with MUSIC, on left and right sides.

2. Method

MUSIC

MUSIC [1] is an API allowing large-scale neuron simulators using MPI internally to exchange data during runtime. MUSIC provides mechanisms to transfer massive amounts of event information and continuous values from one parallel application to another. Developed as a C++ library, it is available on a wide range of UNIX systems and Blue Gene/L.

Overall architecture

Fig. 1 shows the schematic diagram of our current implementation, in which the aim is to reproduce the low-level saccadic sensory-motor loop. The visual inputs, which code the target position, are generated by an application module implemented in C++ or Python. The data are delivered to the superior colliculus (SC) model as introduced by Jan Moren [2] and transformed into activation patterns of inhibitory- and excitatory-burst neurons that encode the planned saccade vector. The neural circuit in the SC model consists of leaky integrate-and-fire neurons and is implemented using NEST [4]. The neural activities in the SC are then sent to the brainstem integrator network model [5] to create signal for fixing the eyes still, which is also implemented by NEST. The output is finally transformed into the eye position by the oculomotor plant models implemented in C++. All communication among the modules is handled by MUSIC.

3. Results The entire model consisted of about 40000 spiking neurons. The model reproduced the standard behavior of burst in SC neurons and persistent activities of the integrator neurons. Simulation of the network for 700 ms was run within 9 minutes on a desktop machine running a Linux OS. The projection to the oculomotor plant through MUSIC yields good results.

4. Conclusion

The communication between the several processes was reliably handled by MUSIC and we observed no overload due to the use of the MUSIC API. We now have to observe how the current architecture implementation scales on a richer simulation. We then test its feasibility on large-scale simulation on RIKEN's Next-Generation Supercomputer.

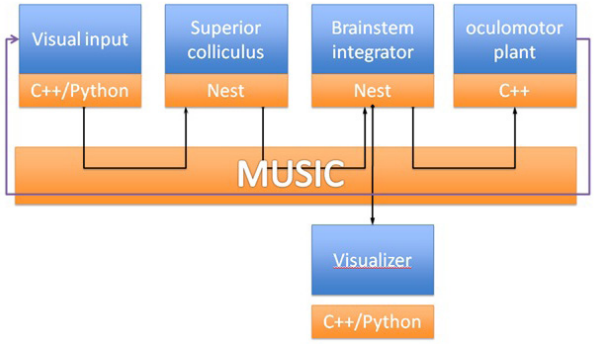


Fig 1 Overall architecture of our oculomotor simulation

References

1. M. Djurfeldt, J. Hjorth, J.M. Eppler, N. Dudani, M. Helias, T. C. Potjans, U. S. Bhalla, M. Diesmann, J. Hellgren K. and Ö. Ekeberg (2010) Run-Time Interoperability Between Neuronal Network Simulators Based on the MUSIC Framework Neuroinformatics 8(1):43-60, DOI 10.1007/s12021-010-9064-z
2. J. Morén, T. Shibata, K. Doya (2010), "Toward a Spiking-Neuron Model of the Oculomotor System". From Animals to Animats: The 11th International Conference on Simulation of Adaptive Behavior.
3. Gewaltig M.-O. & Diesmann M. (2007). NEST (Neural Simulation Tool) Scholarpedia 2(4):1430.
4. Seung H.S., et al. (2000). Stability of the Memory of Eye Position in a Recurrent Network of Conductance-Based Model Neurons. Neuron 26(1): 259-271.

The Connection-set Algebra: A novel formalism for the representation of connectivity structure in neuronal network models

Mikael Djurfeldt

PDC, Royal Institute of Technology and INCF Secretariat, Stockholm, Sweden

The connection-set algebra is a novel notation for the description of connectivity in neuronal network models. Both the connection structure, that is which connections exist, and parameters associated with connections can be described. An elementary set of connection patterns, connection-sets, are provided as well as a set of rules for how to compute new connection-sets from elementary ones. The design goals are to provide a description which is close to how we think about the connection pattern, is expressive enough to describe a wide range of connectivities, and, is still possible to implement in a neuronal network simulator with reasonable time and memory complexity. Special consideration is given to parallel simulators. A C++ version of the algebra has been implemented and used in a large-scale neuronal network simulation.

References

1. Djurfeldt M, Lundqvist M, Johansson C, Rehn M, Ekeberg Ö, Lansner A (2008) Brain-scale simulation of the neocortex on the Blue Gene/L supercomputer. IBM J Research and Development 52(1/2):31-42

NineML-A Description Language for Spiking Neuron Network Modeling: The Abstraction Layer

Ivan Raikov

Computational Neuroscience Unit, Okinawa Institute of Science and Technology, Okinawa, Japan

With an increasing number of studies related to large-scale neuronal network modeling, the International Neuroinformatics Coordinating Facility (INCF) has identified a need for standards and guidelines to ease model sharing and facilitate the replication of results across different simulators. To create such standards, the INCF has formed a program on Multiscale Modeling to develop a common standardized description language for neuronal network models. The name of the proposed standard is Network Interchange for Neuroscience Modeling Language (NineML) and its first version is aimed at descriptions of large networks of spiking neurons. The design of NineML is divided in two semantic layers: an abstraction layer that provides the core concepts, mathematics and syntax with which model variables and state update rules are explicitly described and a user layer that provides a syntax to specify the instantiation and parameterization of a network model in biological terms. The abstraction layer of NineML provides a unified interface to the mathematical and algorithmic tools necessary to express key concepts of spiking neuronal network modeling: 1) spiking neurons 2) synapses 3) populations of neurons and 4) connectivity patterns across populations of neurons. The abstraction layer includes a flexible block diagram notation for describing spiking dynamics. The notation represents continuous and discrete variables, their evolution according to a set of rules such as a system of ordinary differential equations, and the conditions that induce a change of the operating regime, such as the transition from subthreshold mode to spiking and refractory modes. In addition, the abstraction layer provides operations to describe a variety of topographical arrangements of neurons and synapses, and primitives to describe connectivity patterns between neuronal populations, based on structural properties of the populations. The NineML abstraction layer does not merely aggregate the functionality of different modules. It features a flexible interface mechanism that is capable of expressing dependencies between different levels of modeling, as in the case of a neuron model with parameters that vary with physical location. Such flexible interfaces are a necessary step in the design of languages for multiscale modeling that summarize biological knowledge in a broad context.

References

1. Djurfeldt M and Lansner A (2007) INCF report on the 1st Workshop on Large-scale Modeling of the Nervous System. http://precedings.nature.com/documents/262/version/1

Decorrelation of neural-network activity by inhibitory feedback

Tom Tetzlaff[1], Moritz Helias[2], Gaute T. Einevoll[1] and Markus Diesmann[2]

1. Institute of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Aas, Norway
2. RIKEN Brain Science Institute, Wako, Japan

Spatial correlations in spike-train ensembles can seriously impair the en- and de-coding of information in the population rate [1] or in the fine spatio-temporal structure of these spike trains [2]. Recent theoretical and experimental studies showed that spike correlations in neural networks can be considerably smaller than expected based on the amount of shared presynaptic input in such systems [3,4,5]. Here, we demonstrate by means of a simple linear model and simulations of networks of integrate-and-fire neurons that pairwise correlations and hence population-rate fluctuations in recurrent networks are actively suppressed by inhibitory feedback. To investigate the role of feedback, we calculate the power- and cross-spectra of the network response for the intact recurrent system and for the case where the 2nd-order statistics of the feedback signals is perturbed while the shared-input structure and the 1st-order statistics are preserved. In general, any modification of the feedback statistics causes a shift in the power and coherence of the population response. In particular, the neglect of correlations within the ensemble of feedback channels or between the external stimulus and the feedback can amplify population-rate fluctuations by orders of magnitude. This effect can be observed both in networks with purely inhibitory and in those with mixed excitatory-inhibitory coupling. In purely inhibitory networks, shared-input correlations are canceled by negative correlations between the feedback signals. In excitatory-inhibitory networks, the responses are typically positively correlated. Here, the suppression of input correlations is not a result of the mere existence of correlations between the responses of excitatory (E) and inhibitory (I) neurons [4], but is instead a consequence of the heterogeneity of response correlations across different types of neuron pairs (EE, EI, II). If correlations between EE, II and EI pairs were identical, input correlations could not fall below the level imposed by the amount of shared input [6]. We further show that the suppression of correlations and population-rate fluctuations in recurrent networks is in general frequency (time-scale) dependent. The affected frequency range is determined by the population-rate transfer properties: The population response of integrate-and-fire neurons, for example, exhibits low-pass characteristics [7]. High-frequency fluctuations are therefore not affected by feedback.

Acknowledgements:
Supported by the Research Council of Norway (eVITA, Notur), the Helmholtz Alliance on Systems Biology, the Next-Generation Supercomputer Project of MEXT, EU Grant 15879 (FACETS), DIP F1.2, and BMBF Grant 01GQ0420 to BCCN Freiburg. All network simulations were carried out using NEST (http://www.nest-initiative.org).

References

1. Zohary et al. (1994), Nature 370:140-143

2. Tripp & Eliasmith (2007), Cereb Cortex 17(8):1830-1840

3. Tetzlaff et al. (2008), Neural Comput 20(9):2133-2184

4. Renart et al. (2010), Science 327(5965):587-590

5. Ecker et al. (2010), Science 327(5965):584-587

6. Kriener et al. (2008), Neural Comput 20(9):2185-2226

7. Nordlie et al. (2009), Frontiers in Neuroinformatics, doi: 10.3389/conf.neuro.11.2009.08.118

Pyramidal Algorithm for Image Matching and Interpolation

Modest Weinzweig[1] and Witali Dunin-Barkowski[2]

1. Sector of Modeling of Intelligence, Institute of Information Transmission Problems, Russian Academy of Science, Moscow, Russia
2. Department of Neuroinformatics, Scientific Research Institute for System Analysis, Russian Academy of Science, Moscow, Russia

One of the key operations in scene analysis is identification and processing of correspondent visual objects in scenes. Visual object processing usually includes interpolation of images between the fixed given views or forms. Examples of these type of problems are encountered in binocular and/or dynamic stereovision [Marr, 1982]. Also, these types of computational operations might be used in pattern recognition by the way of finding a correspondence of the current input image with a stored template. We have implemented the pyramidal algorithm of matching/interpolation for two visual fields (images) of up to 256x256 pixels with 256 gradations of grey level. The algorithm operates in real time on one-processor PC. The number of algorithm's operations is proportional to the logarithm of image size. The work of the algorithm is illustrated with the following examples:
1. Grey-level portraits of a single person in two distinct angles of view. The sequence of the views of the set of interpolating images in this case yields impression of smooth turns of the subject's head.
2. Two contours of bird wings with strokes up and stroke down. The interpolating images give a complete impression of the bird's flight.
3. Two figures of a contour of a walking figure with the two extreme positions of the limbs. The set of interpolating images represents smooth walking of the contour figure.
4. When the algorithm is applied to matching of the contour circle with a horizontal line inside with the circle with a vertical line inside, it reports that this task cannot be performed.

Thus, the proposed and explored algorithm can effectively provide matching and interpolation of images, which can be matched. Figures, which the algorithm generates for the interpolation of the images, are perceived natural for the human perception. The algorithm also reports impossibility of images matching, when the task cannot be performed. We suppose that this algorithm might be used in systems of artificial intelligence. We also believe that the algorithms, with which neural systems provide matching between pairs of images of the real world, do resemble in substantial features the proposed algorithm.

References

1. Marr D (1982) Vision. Freeman and Company, San Francisco, 1982, pp. 111-159.

Simulations of Mean-Field Equations: Effects of different types of noise

Geoffroy Hermann and Olivier Faugeras
INRIA, Sophia Antipolis, France

Modeling neural activity at scales integrating the effect of thousands of neurons is of central importance for several reasons. First, most imaging techniques are not able to measure individual neuron activity ("microscopic" scale) but are instead measuring "mesoscopic" effects resulting from the activity of several hundreds to several hundreds of thousands of neurons. Second, anatomical data recorded in the cortex reveal the existence of structures, such as cortical columns, containing the same order of magnitude of neurons, and having specific functions.

The mean-field equations are precisely a description of the network at a "mesoscopic" scale. They describe the behaviour of populations of neurons and are obtained assumimg that the number of neurons in each population tends to infinity.

In this paper, we are interested in the simulation of the mean-field equations obtained by Faugeras, Touboul and Cessac (see reference 1). The specificity of this set of equations (consisting in a system of coupled integro-differential equations for the mean and covariance of the membrane potential) is that they take into account two different types of noise. The first type of noise is the stochastic input (corresponding for example to the synaptic noise or to the thermal noise) which leads to a stochastic differential equation for the evolution equation of a single neuron membrane potential. The second type of noise is the variance of the synaptic connectivity matrix. Indeed we assume that the synaptic coupling between two neurons, one belonging to population α and the other belonging to population β obeys a Gaussian law whose parameters depend only on α and β.

In this work, when setting the variance σ of the connectivity matrix to zero, we were able to describe analytically the effect of the stochastic input when the sigmoidal function (converting the membrane potential to a rate) is an erf function: the noise delays the pitchfork bifurcation which occurs when the slope of the sigmoid is increased. We have also simulated the Mean-Field Equations in this case as well as a finite-size network and these simulations match well the theoretical prediction.

However, the most challenging task is to describe the effect of the synaptic variance σ since we expect new behaviours to appear. In this case, the simulations were performed using a Picard method. In the case of two populations, we set the parameters (the mean synaptic weights and external input) such that the noiseless system presents a limit cycle. We observe that when we increase the synaptic varianceσ, the limit cycle is maintained until a certain critical value after which we reach a stationary behaviour. Before this critical value, the covariance matrix also presents a periodic structure. The membrane potential is then a realisation of a Gaussian process whose mean and variance are periodic, with the same period. After this critical value, the mean reaches a fixed point and the variance also reaches a non-zero plateau.

We have corroborated this behaviour by simulating a finite network: interestingly, in this case, finite-size effects appear. Depending on the realisation of the synaptic weights, the network can either present oscillations or converge towards a fixed point.

We are currently working on deriving the bifurcation diagram according to σ analytically; however it requires to use bifurcation theory in infinite dimension, since the system cannot be reduced to a system of ordinary differential equations (see reference 3).

References

1. Faugeras, Touboul, Cessac (2009) A constructive mean-field analysis of multi-population neural networks with random synaptic weights and stochastic inputs. Frontiers in Computational neuroscience.

2. Brunel (2000) Dynamics of sparsely connected networks of excitatory and inhibitory spiking neurons. Journal of Computational Neuroscience 8, 183:208.

3. Kielhoefer (2004) Bifurcation Theory, an introduction with applications to PDEs. Springer.

Organization of Concentric Double-Opponent Receptive Fields in the Primary Visual Cortex by Using Independent Component Analysis

Yasunobu Igarashi[1], Takaaki Aoki[2], Rui Kimura[3] and Shin Ishii[4]

1. National Center for Neurology and Psychiatry, Tokyo, Japan
2. Nara Institute of Science and Technology, Nara, Japan
3. RIKEN Brain Science Institute, Saitama, Japan
4. Kyoto University, Kyoto, Japan

Previous experimental studies showed that neurons in the primary visual cortex (V1) have four firing properties to represent visual information. Four firing properties are named luminance gabor, oriented double-opponent, concentric single-opponent, and concentric double-opponent receptive fields. Previous theoretical studies demonstrated that redundancy compressions like independent component analysis (ICA) and sparse coding can derive basic functions corresponding to luminance gabor and oriented double-opponent receptive fields from natural images. On the other hand, emergences of basic functions cor responding to two concentric receptive fields via redundancy compression of natural images have not been reported. In this study, we propose a low pass filtering function of neurons in lateral geniculate nucleus (LGN) is important to derive concentric basic functions in addition to redundancy compression. Neurons in LGN project their axons to neurons in V1. Therefore, it is plausible that LGN contributes to form receptive fields of V1. We show that the concentric double-opponent basis function can be obtained by applying the low pass filtering and Fast ICA to natural images in a computer simulation. However, the concentric single-opponent basis function cannot be not obtained. This reason is thought that the concentric double-opponent basis function functionally includes the concentric single-opponent basis function from the view point of redundancy compression. We also clarify how shapes of basic functions depend on ones of learning images, and how color components of basic functions depend on a color distribution of learning images.

Stimulus dependent population dynamics in a striatal spiking network model

Adam Ponzi and Jeff Wickens

Okinawa Institute of Science and Technology, Okinawa, Japan

We present a model of an inhibitory spiking network composed of striatal medium spiny neurons (MSN). We show that the network exhibits complex population dynamics produced by the occurrence of episodically firing cell assemblies, and that this occurs for various choices of MSN cell model and is thus a network generated property, while details of cell spiking statistics do depend on the cell model. When excitatory input to the network is dynamically variable we show cell assemblies display stimulus onset dependent dynamics even when the excitatory inputs to each cell are composed of many Poisson spike trains with variable rates, providing the excitatory inputs obey certain conditions. We discuss how this behaviour may relate to striatal cognitive functions in behavioural tasks.

Analysis of the Spike Timing Precision in Retinal Ganglion Cells by the Stochastic Model

Yoshimi Kamiyama and Yuichiro Sakuragi

Information Science and Technology, Aichi Prefectural University, Nagakute, Japan

The ganglion cells of the vertebrate retina form the pathway by which the retina communicates with the visual cortex. The ganglion cells convert the graded potentials into a pattern of spikes whose characteristics is modulated by the synaptic and membrane currents. The ganglion cells respond with precise and reliable spikes to randomly flickering light (Keat et al., 2001). This feature could not be reproduced by the previous models, described with the deterministic differential equations similar to the Hodgkin-Huxley formulation (Fohlmeister and Miller, 1997). We proposed a stochastic model of spike generation in the ganglion cells, based on discrete stochastic ion channels represented by Markov processes. We modeled eight types of ion channels, i.e., Na, Ca(T), Ca(L), Kv, A, K(Ca), h and leakage channels. The proposed model showed precise and reliable spikes to randomly fluctuating current. This result suggested that the stochastic properties of ion channels are critical in determining the reliability of the spike timing in the retinal ganglion cells. However, the underlying mechanisms of the spike timing reliability has not yet been understood. In this work, we systematically analyzed the feature of the spike timing reliability and the role of each channel stochasticity through computer simulation.

We measured the reliability of the spike timing for a wide range of fluctuating input patterns by varying the mean and standard deviation. We applied the event synchronization algorithm (Quiroga et al., 2002) to simulated spikes. The reliability was obtained from all two combinations in the spikes of 30 trials. The reliability of the spike patterns was strongly correlated with characteristics of the fluctuating input as shown in Figure 1. This indicates the existence of optimal input range for the reliability. In order to clarify the role of ion channel stochasticity, we analyzed the contribution of each channel in the spike reliability, by changing the single channel conductance in simulation without changing the total electrical characteristics of the cell membrane. For a particular channel, the single channel conductance was increased by a factor of 20, the channel density was decreased by a factor of 1/20. The simulated results showed that the spike reproducibility is much influenced by the potassium channels, Kv and A, not by the sodium channel, Na. These results suggest that the stochastic properties of Kv and A channels play a key role in determining the precise spike timing of retinal ganglion cells.

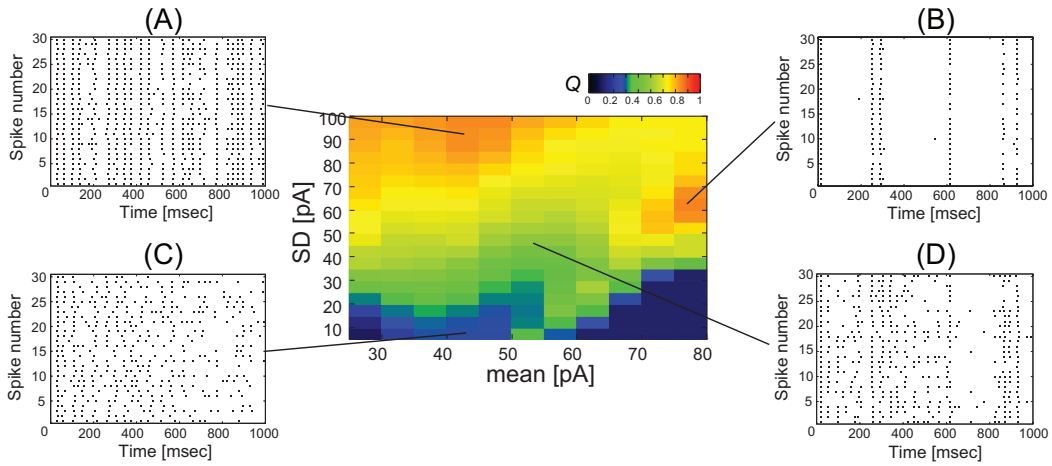


Figure 1 The reliability of the spike timing for a wide range of fluctuating input patterns.

References

1. Keat J, Reinagel P, Reid RC and Meister M (2001): Predicting every spike: a model for the responses of visual neurons, Neuron 30:803-817

2. Fohlmeister JF, Miller RF (1997): Impulse encoding mechanisms of ganglion cells in the tiger salamander retina, J Neurophysiol 78:1935-1947

3. Quiroga, RQ, Kreuz T, Grassberger P (2002): Event synchronization: A simple and fast method to measure synchronicity and time delay patterns, Phys Rev E 66:041904-1-9

The adaptive dynamics of brains: Lagrangian formulation

Chang Sub Kim

Department of Physics, Chonnam National University, Gwangju, South Korea

We present a theory of the adaptive dynamics of brains in the framework of the action principle. The action is defined as time-integration of the Lagrangian of the brains. The action principle states that the adaptive brains select the dynamical path that minimizes the action among all possible configurations of the brain's decision making; action, perception, and learning. The key difficulty here is to know what the brain Lagrangian is. We show that the free energy of Friston may serve as the brain Lagrangian. The Friston free energy is an information theoretical construct through which Friston asserts that brain's adaptive dynamics are designed by nature to avoid undesired surprises caused by the environment [1]. The Friston idea was motivated by von Helmholtz who claimed that the brains are not able to capture a picture of the external world by sensation per se without prior knowledge about the causes. The brains must possess an internal model of the external world [2]. This mechanism is embodied in the mathematical framework of minimizing the free energy. We have reported recently a technical evaluation of the Friston free-energy theory [3]. We report here a generalization of the Friston free energy principle in the language of the Lagrangian in physics. We will argue what the Friston free-energy is as the brain Lagrangian, what is meant by minimizing the action, and what it does associated with the neurobiological implementation. We attempt to unravel Friston's mathematical formulation and put it into a more rigorous physical and mathematical ground. Consequently, it portrays a wealth of structure as an interpretive and mechanistic description toward a unified principle of explaining how the brains may operate.

References

1. Friston K (2010) The free-energy principle: a unified brain theory? Naturereivew Neurosci. 11: 127-138

2. von Helmholtz H (1909) Trietise on Physiological Optics. Vol.III 3rd ed. Voss Hamburg

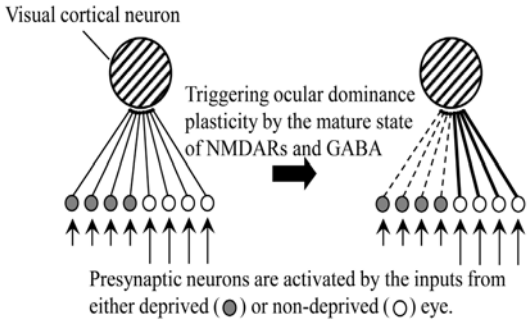
3. Kim C S, Seth A K (2010) The Friston free energy principle: A technical evaluation. preprint.

Activity-dependent synaptic competition by STDP and its role in critical period plasticity

Shigeru Kubota[1], Tatsuo Kitajima[2], Siu Kang[2] and Takao Nakamura[1]

1. Department of Biomedical Information Engineering, Yamagata University, Yonezawa, Japan
2. Department of Bio-System Engineering, Yamagata University, Yonezawa, Japan

Purpose: Sensory experience during a postnatal critical period strongly influences cortical architecture by modifying the neuronal connections. The activity-dependent competition among afferent inputs has been suggested to be highly involved in the induction of such experience-dependent cortical plasticity. This may imply that the mechanisms controlling the competitive state could play a role in determining the timing of critical period. In this study, to study a biological mechanism regulating the competitive behavior of synapses, we theoretically examine the dynamics of synaptic population arising from an spike-timing-dependent plasticity (STDP) model including metaplasticity. Method: We use a conductance-based two-compartment neuron receiving two groups of correlated excitatory inputs following STDP and non-plastic GABA-mediated inhibitory inputs. The magnitude of long-term potentiation (LTP) is dynamically modified by the metaplastic regulation resulting from the activity-dependent desensitization of NMDA receptors (NMDARs). This model also incorporates the effect of developmental alteration in the subunit composition of NMDARs (from NR2B to NR2A), which can alter the strength of the metaplastic modulation through changing the desensitization level of NMDARs. Results: We show that as far as the state of the NMDAR subunit expression and/or GABA inhibition is immature, the synaptic weight distribution of the two correlated groups converges to an identical one. However, when the state of both these developmental systems becomes sufficiently mature, the induction of the correlation-based competition segregates the weight distributions of the correlated input groups at the equilibrium state. This may suggest that the coordinated action of NMDAR subunit and GABA systems can contribute to activating the competitive function of STDP. We also demonstrate that in the presence of competitive mechanism, which group becomes the winning one at the present time depends on the past history of sensory inputs, providing the basis for sensory experience-dependent plasticity. When the input frequency of either one group is transiently suppressed, the group that has not received the frequency modification wins the competition and finally dominates over the group whose activity has been suppressed. This result is reminiscent of ocular dominance plasticity observed in the visual cortex, where, after a brief period of deprivation of vision from one eye, the neuronal response is dominated by the inputs from the eye that has not been deprived of visual stimuli. Conclusions: The present findings indicate that the cortical critical period can be triggered by the functional cooperativity between the NMDAR subunit gene expression and the maturation of GABA inhibition, which activates STDP-mediated correlation-based competition. This hypothesis may simultaneously explain several experimental observations such as the concurrence of the timing of the critical period with the switching in the NMDAR subunit composition as well as the control of this timing by intracortical GABA activity.



Large-scale realistic network simulation of pheromone-processing circuits in the silkmoth brain

Yohei Sato[1], S Shuichi Haupt[2], Tomoki Kazawa[2], Shigehiro Namiki[2], Akira Takashima[2], Hidetoshi Ikeno[3], Ikuko Nishikawa[4] and Ryohei Kanzaki[2]

1. Graduate School of Information Science and Technology, The University of Tokyo, Tokyo, Japan
2. Research Center for Advanced Science and Technology, The University of Tokyo, Tokyo, Japan
3. School of Human Science and Environement, University of Hyogo, Hyogo, Japan
4. College of Information Science and Engineering, Ritsumeikan University, Kyoto, Japan

Pheromone orientation in the silkmoth is a very convenient model system to investigate the neural substrates involved in the generation of behavior. A wealth of behavioral, physiological, and anatomical data has been collected and integrated in our database system (BoND). These data, supplemented by the silkmoth standard brain project, are being used to implement a simulation of the neural circuits in the silkmoth brain processing pheromone information and generating the signals controlling locomotion during pheromone orientation. Reconstructed 3D morphologies of intracellularly labeled neurons are used to automatically generate multi-compartment models for network simulation using NEURON. Connectivities between neurons can be estimated based on physiological information and by mapping the neurons into the silkmoth standard brain, that provides a common geometrical framework for single neuron data collected in a large number of samples in the database (n >1500 identified neurons) and in ongoing experiments. The overview of our system to simulate the multi-compartment network model is shown in Fig. 1. The goal of this project is a comprehensive simulation of the neural circuits generating pheromone orientation behavior to be implemented for running in near-real time on petaflop class hardware that is currently being developed.

The lateral accessory lobe (LAL) / ventral protocerebrum (VPC) complex is a particularly important area for the generation of brain output signals involved in steering. In this area, a particularly prominent type of signal is that of flip-flop descending neurons, thought to control zig-zag walking during pheromone orientation. A pair neurons consisting of a flip-flop neuron (GIIA-DN) and a neck motor neuron (cv1-NMN), that controls turn-associated head movements, is known to be monosynaptically connected. From samples in which these two neurons were identified by double labeling, 13 synaptic locations were identified by overlap in the confocal data and multi-compartment models were created to investigate the signal propagation in this simple network. Synaptic input resulting from simulated current injection at the soma of GIIA-DN or the synaptic locations showed stong attenuation in a passive model of the dendritic tree of cv1-NMN. We investigated the influence of fine arborisations of the dendritic tree of cv1-NMN on voltage changes to currents injected into the dendrite and found that considerable simplification of the morphology resulting in a reduction of the number of compartments had little impact. Thus, these additional compartments may merely be viewed as spatial locations at which connections with other neurons may be made but having negligible significance for the overall electrical behavior of the neurite.

We also simulated the LAL-VPC network using active multi-compartment models based on 72 representative mophologically and physiologically identified neurons. This network consists of 48 bilateral neurons and 24 unilateral local interneurons with 12900 synapses, divided into five areas (upper and lower divisions of LAL, inner and outer VPC, and anterior part of the inner VPC). Upon current injection, activity in this network shows locally confined unilateral as well as bilaterally spreading activation patterns but it was not possible to reproduce phase switching that could generate flip-flop activation. It is possible that the inclusion of short-term synaptic plasticity is a critical feature to allow for the generation of flip-flop activity.

This study is supported by Research and Development of the Next-Generation Integrated Simulation of Living Matter, a part of the development and use of the Next-Generation Supercomputer Project of the MEXT. This work is also supported by the INCF J-Node.

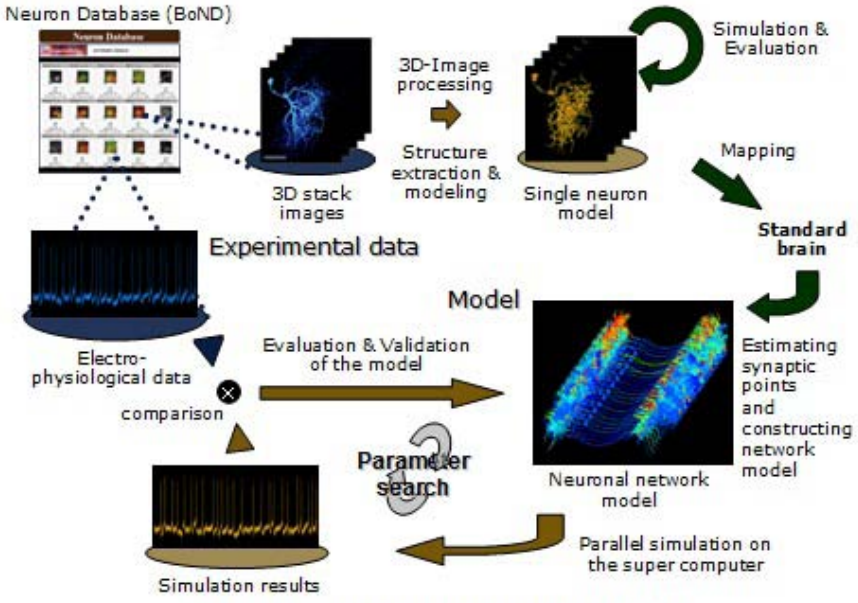


Fig. 1. The overview of our framework to simulate the neuronal network model with multi-compartment models

Joint development of orientation, ocular dominance and binocular disparity maps in a reaction-diffusion based model of V1

M Sultan M Siddiqui and Basabi Bhaumik

Department of Electrical Engineering, Indian Institute of Technology, New Delhi, India

Binocular simple cells in visual cortex (V1) are selective for: orientation selectivity (OR), direction selectivity (DS), binocular disparity (DP) & spatial frequency selectivity (SF); & possesses ocular dominance (OD). Optical imaging technique unveils the relationship between OR & OD maps: OD peaks at pinwheel singularities of the OR map in cat (Crair et al.: American physiology society, 3381-3385, 1997). Recent two-photon calcium imaging technique resorted in capturing the orthogonal crossing relationship between local maps of DP & OD at vertical/near vertical OR sites of V1 in cat (Kara & Boyd: Nature, 458:627-631, 2009). No developmental models till date have attempted to develop DP map in conjunction with OR & OD maps. We present a pre-eye opening receptive field (RF) developmental model based on reaction-diffusion mechanism to jointly develop OR, OD & DP maps in V1 of cat.

Our two eye reaction diffusion model is the extension of Bhaumik & Mathur (J. Computational Neuroscience, 14:211-227, 2003) single eye model. Left & right eye retinal/LGN layers are modeled as two 2D 30 x 30 sheets overlapping ON & OFF center LGN cells one over the other. For the details of retinal cell's spatial receptive field, temporal response functions & mechanism for generation of spikes we have used the model given by Wörgötter & Koch (J. Neurosci., 11(7):1959-1979, 1991). The output layer is modeled as 2D 50 x 50 (n=2500) cortex sheet. Each cortical cell receives synaptic strengths from each 13 x 13 left & right eye retinal/LGN cells centered at their retinotopic center. To satisfy the reported 3:1, horizontal (H) to vertical (V) disparity ratio between left & right RFs centers in cat by Barlow et al. (J. Physiology, 193:327-342, 1967), we assigned left & right RF centers randomly to have: (i) -3<=H<=3 & (ii) -1<=V<=1. Spike response model (SRM) is employed to obtain monocular (left/right) & binocular (left & right) responses of a cortical cell. Drifting sinusoidal gratings with varied relative phase were used to obtain the binocular phase disparity tuning & then disparity sensitivity (DS) & optimal phase was extracted. Disparity map is the optimal disparity phase across the simulated cortex. We use VM ratio to measure interaction between DP & OD maps. VMratio is peak to baseline value of fitted von Mises function to histogram distribution of gradient direction differences between DP & OD map contours. VMratio >3 indicates high interaction & VMratio <2 indicates no interaction. The gradient direction difference at which von Mises function peaks, defines the angle of crossing between DP & OD contours (See Figure 1).

We obtained 55.76% (1394/2500) binocular simple cells having combined features: OR, OD & DP. About 76.04% (1060/1394) of these cells have atmost ±18° (μ=12.8, S.D= 11.7°) difference in their left & right eyes preferred orientations as reported (±15° (S.D=6-9°)) by Blakemore et al. (J. Physiology, 226:725-749, 1972). Our OR, OD & DP maps shows the following interrelation: (i) OD peaks at pinwheel singularities of the OR map (Separation between OD peak & pinwheel: μ=2.1 units, Median=2 units), & (ii) DP & OD map contours cross orthogonally having range from 45° to 135° with median near 90° (VMratio > 3) (See Table 1 & Figure 1), for vertical/near vertical OR sites; which conforms to the experimental findings by Crair et al.: 1997 &, Kara & Boyd: 2009. Also OD & DS are uncorrelated (r=0.07) as reported (r=0.041) by Kara & Boyd: 2009.

Developed binocular simple cells were characterized in terms of orientation difference in left & right eye, OD, & DS. Our model captures the experimentally observed interrelation between OR, OD & DP map. To the best of our knowledge, ours is the first model that yields disparity map.

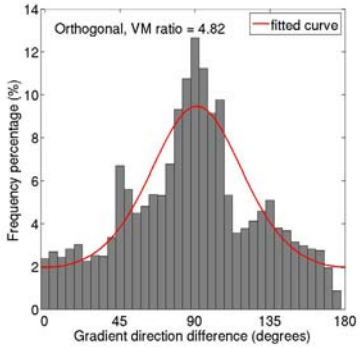


Figure 1 Evaluation of relationship between OD & DP map contours in vertical/near vertical oriented sites.

	Interaction between DP and OD map contours	DP and OD map contours
Vertical/near vertical oriented sites	VMratio	Crossing angle
Site 1	9.03	47°
Site 2	7.3	56°
Site 3	13.69	83°
Site 4	4.82	91°
Site 5	3.2	112°
Site 6	3.31	132°
Site 7	1.12 (No interaction)	-

Table 1 Interaction between DP & OD map contours.

Calcium Signaling in Astrocytes: Modeling Fura-2AM Measurements

Eeva Toivari[1], Tiina Manninen[1], Amit K. Nahata[2], Tuula O. Jalonen[3] and Marja-Leena Linne[1]

1. Department of Signal Processing, Tampere University of Technology, Tampere, Finland
2. Kidney Care Center at DCI, Washington, USA
3. Department of Physiology and Neuroscience, School of Medicine, St. Georges University, St. Georges, Grenada

Purpose:
In addition to wet lab and clinical studies, mathematical models can be used to better understand and verify the hypothesis concerning complex molecular level interactions, including the role of intracellular calcium stores such as endoplasmic reticulum, in cellular functions. Ionic equilibrium in astrocytes can be disturbed by transmitters, for example by serotonin and Alzheimer's disease related amyloid plaques forming amyloid-β peptides (Aβ). We studied the effects of small amounts of Aβ fragments on the neurotransmitter-induced calcium signals in astrocytes by doing Fura-2-acetoxymethyl ester (Fura-2AM) measurements and computer modeling based on calcium-induced kinetic reactions.

Method:
Fura-2AM measurements were done to study the effects of transmitters, such as serotonin and glutamate, on the cytosolic concentration of calcium in astrocytes separately and together with neurotoxic Aβ25-35. Fura-2AM is a membrane penetrating derivative of the radiometric calcium indicator Fura-2 used in biochemistry to measure intracellular calcium concentrations by fluorescence. Aβ25-35 is a synthetic derivative of the longer peptide Aβ42 which predominates in the neuritic plaques. A computational model, introduced by Di Garbo et al. (2007), was adjusted to mimic the calcium signals measured with the calcium imaging technique. The model includes kinetic reaction equations, for example, the effect of both metabotropic and ionotropic receptors, the influx of calcium from/to extracellular matrix, the pumping of calcium from cytosol to the endoplasmic reticulum and the leak back to cytosol, and the release of calcium from the endoplasmic reticulum via inositol 1,4,5-trisphosphate receptors.

Results:
Though serotonin and glutamate have earlier been shown to induce calcium release in astrocytes (Jalonen et al. 1997, Kimelberg et al. 1997), it is shown in this study how serotonin and Aβ25-35, when added together, clearly increase the amplitudes of the calcium signal. Thus, even small amounts of neurotoxic Aβ25-35 can have a severe effect on the intracellular ionic equilibrium. In the modeling part of this study, different experimental setups were computationally simulated using different values of the model parameters and/or different inputs. The model presented by Di Garbo et al. (2007) was found to sufficiently explain the results measured by us using the Fura-2AM technique. For example, phenomena related to unfilled intracellular calcium stores were observed both by calcium imaging and computer simulations. Thus, model simulations support the hypothesis about the importance of intracellular calcium stores, such as endoplasmic reticulum, to calcium signaling in astrocytes.

Conclusions:
We conclude that the experimental results on astrocytic calcium oscillations can be reproduced with the computational model originally proposed by Di Garbo et al. (2007). Modeling the mechanisms of intracellular calcium oscillations in astrocytes is important, as astrocytes have an essential role in regulating the central nervous system microenvironment.

References

1. Di Garbo A, Barbi M, Chillemi S, Alloisio S, Nobile M (2007) Calcium signalling in astrocytes and modulation of neural activity. BioSystems 89: 74-83.

2. Jalonen TO, Margraf RR, Wielt DB, Charniga CJ, Linne M-L, Kimelberg HK (1997) Serotonin induces inward potassium and calcium currents in rat cortical astrocytes. Brain Res 758: 69-82.

3. Kimelberg HK , Cai Z, Rastogi P, Charniga CJ, Goderie S, Dave V, Jalonen TO (1997) Transmitter-induced calcium responses differ in astrocytes acutely isolated from rat brain and in culture. J Neurochem 68: 1088-1098.

Reaction-Diffusion and Membrane Potential Simulation with STEPS

Iain Hepburn, Weiliang Chen and Erik De Schutter

Computational Neuroscience Unit, Okinawa Institute of Science and Technology, Okinawa, Japan

STEPS (STochastic Engine for Pathway Simulation) is a platform we have developed for simulation of neuronal signaling pathways within dendrites and around synapses. The role of spatial organization and morphology in the pathway may be investigated by representing the complex boundaries of reconstructions of neuronal morphology and tissue in 3D tetrahedral meshes, which are particularly well-suited to represent such complex boundaries closely. In order to simulate the discrete, stochastic nature of the chemical interactions together with the diffusion of signaling molecules we implement an algorithm based on Gillespie's Direct Method extended for diffusive fluxes between tetrahedral elements [1].

Creating a suitable mesh can be a challenging task. STEPS supports a number of free and research-licensed powerful mesh generation packages to allow the user some flexibility in how this goal is achieved. In our research this has involved using CUBIT [2] to reconstruct a section of spiny dendrite from simple geometry primitives, such as cylinders and spheres. A mesh can be imported into STEPS with pre-implemented import functions (currently supporting Abaqus and TetGen [3] mesh formats) or user-developed functions by adapting the STEPS element proxy interface. We provide further functionality to retrieve all spatial information from the imported mesh necessary to set the required initial conditions and collect spatial data during a simulation. In addition to this, STEPS provides a preliminary Python-based visual toolkit for displaying meshes and reaction-diffusion simulations.

The transport of key signaling molecules in the pathway may be dependent on voltage-gated ion channels. An important recent addition to our software, therefore, is the EField object, which computes the effect of membrane channel currents on electric potential throughout the same mesh used for the reaction-diffusion computation, including the membranes themselves. Channels can undergo Markov-transitions between states, governed by voltage-dependent rate equations, and ligand binding. Channel currents may be approximated by a simple ohmic current with fixed reversal potential, or relate to a flux of ions based on the GHK flux equation. Voltage-dependent transitions, ligand binding and ionic flux are all extensions to the Direct Method and thus are solved with the reaction-diffusion computation in one framework. This allows for complete simulation of voltage-gated ion channels in the cell membrane along with the intracellular signaling pathways.

The user-interface is in Python, a powerful and versatile scripting language with internal computations in C++ for greater efficiency. STEPS runs on various platforms, including Unix, Max OSX and Windows.

References

1. Wils S, De Schutter E (2009) STEPS: modeling and simulating complex reaction-diffusion systems with Python. Front Neuroinf, 3:15

2. CUBIT Geometry and Mesh Generation Toolkit [http://cubit.sandia.gov/cubitprogram.html]

3. TetGen [http://tetgen.berlios.de]

A Bayesian approach to detecting generalized synchronization

Gordon Pipa[1] and Johannes Schumacher[2]

1. Department of Neurophysiology, Max Planck Institute for Brain Research, Frankfurt am Main, Germany
2. Institute of Cognitive Science, University of Osnabrück, Osnabrück, Germany

During sensory processing, the cortex exhibits self-organizing dynamics with coherent states encoding sensory information. These exhibit oscillation and synchronization, which are frequently studied examples for mechanisms of temporal coding. However, conduction delays in cortex and the dependency on stimulus context allude to the fact that these stable phenomena may often be too restrictive in nature. More general concepts of functional interaction need investigation, such as generalized synchronization:

Two non-identical chaotic systems *x* and *y* are said to be in a generalized synchronization regime if there exists a functional relation $y = \Phi(x)$, such that the state of the response system y can be uniquely determined from *x* if Φ is known. Complete synchronization represents the special case where Φ is simply composed of identity functions.

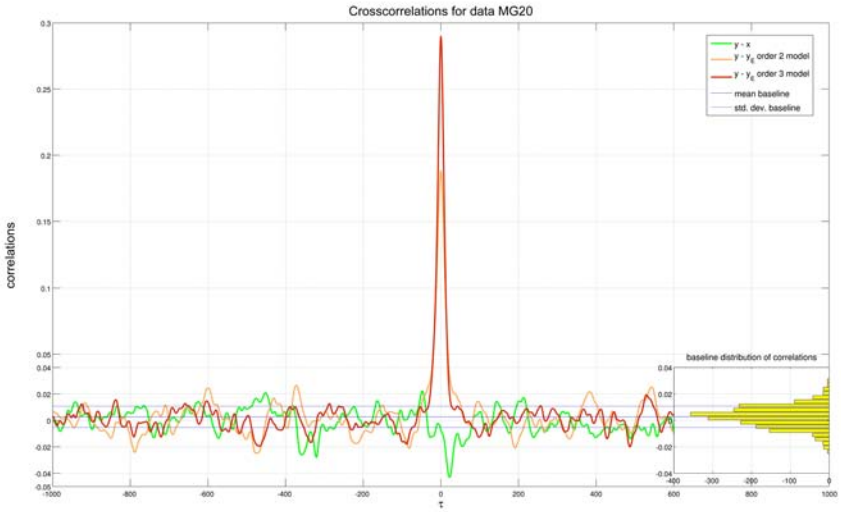
However, Φ may be highly nonlinear, in which case it will remain undetected by the usual quantification of similarities between signals *x* and *y*, such as measures of linear correlation and coherency. Developing reliable tools for detecting this kind of general functional interaction in experimental data therefore has become an important aspect in the investigation of the brain's coding strategies.

We propose a method to detect generalized synchronization in a framework of generative statistical modeling. Truncated Volterra series are used to approximate Φ. The Volterra kernels, weighting monomials of varying degree of the input signal x, are modeled as convolved splines, given by a linear combination of basis splines. The control points of the latter are then estimated with a maximum likelihood approach. The estimated model generates an auxiliary signal yE, which allows a comparison to the original y by means of correlation measures.

The method has been applied to a very large set of synthetic data, produced by a ring of 20 unidirectionally coupled nodes of chaotic 9th order Mackey-Glass systems with a total delay time $\tau = 150$ between the driving system x and the response system *y*. Figure 1 shows results for two models of varying complexity: A model using Volterra kernels up to order two (orange) yields a significant correlation of ~ 0.2 between *y* and y_E, as compared to the initial correlations between *x* and *y* (green). Including a third order kernel into a model (red) boosts the correlation to ~ 0.3, which gives strong indication for the presence of generalized synchronization and demonstrates the power of the Bayesian approach.

The method is based on maximum likelihood, has a unique solution, is computationally efficient, can be implemented by means of convenient MatLab functions and allows to determine the goodness-of-fit. Comparison of different models and parameter setups is possible via statistical criteria such as the deviance or the Akaike information criterion. Furthermore, this generative model approach allows first, decoding and secondly, the generation of new data based on the model.

In a next step we intend to further exploit the Bayesian approach by including regularization techniques. This will allow selection of the estimated parameters with respect to their contribution to the model likelihood. As a result, the model becomes more specific and higher order monomials can be included iteratively, which is expected to greatly increase the model performance (cf. figure 1).



(Figure 1) Green: Driving signal x and response signal y; Orange: Response signal y and estimated signal yE using model with Volterra kernels up to order 2; Red: Model with kernels up to order 3; Histogram: Distribution of correlations between x and time-shifted y as uncorrelated baseline

An agent-based neural computational model with learning

Hideaki Suzuki[1], Hiroyuki Ohsaki[2] and Hidefumi Sawai[1]

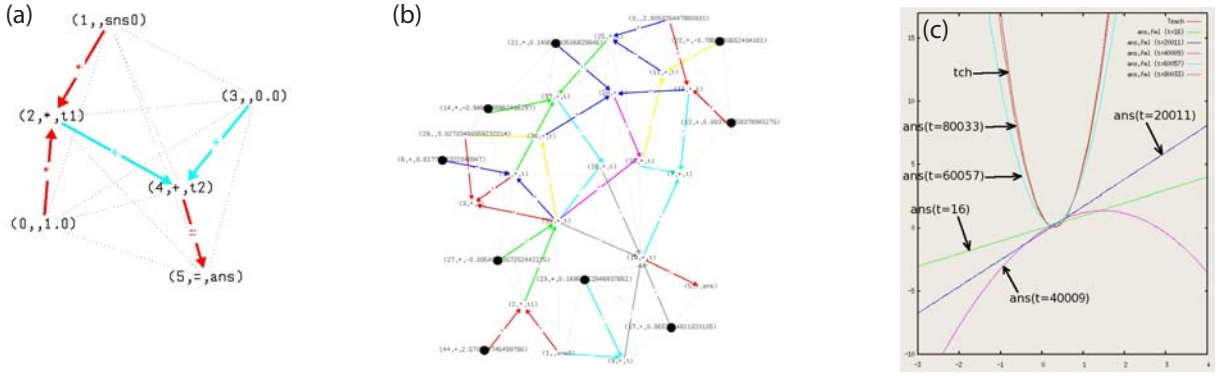
1. National Institute of Information and Communications Technology, Kobe, Japan
2. Graduate School of Information Science and Technology, Osaka University, Suita, Japan

As is well-known, a natural neuron is made up of a huge number of biomolecules from a nanoscopic point of view. A conventional 'artificial neural network' (ANN) consists of nodes with static functions, but a more realistic model for the brain could be implemented with functional molecular agents which move around the neural network and cause a change in the neural functionality. One such network-based computational model with movable agents is 'program-flow computing' [Suzuki 2008], in which programs (agents) move from node to node and bring different functions to CPUs (nodes). This model is also closely related to 'active network' [TennenhouseWetherall 1996] which enables a router (node) to have various functions by delivering packets (agents) with encapsulated programs. Based upon these previous studies, recently, a novel network-based computational model named "Algorithmically Transitive Network (ATN)" was proposed by the authors [Suzuki et al. 2010]. The distinctive features of the ATN are: (1) [Calculation] A program is represented by a 'data-flow network' like the 'data-flow computer' [Sharp 1992]. (2) [Supervised Learning] After the calculation, triggered from the teaching signals, the network propagates differential coefficients of the energy function backward and adjusts node parameters. (3) [Topological Reformation] The network topology (algorithm) can be modified or improved during execution through conducting programs of movable agents. As in the data-flow computer, the ATN's calculation is propelled by the nodes reading the input 'tokens' on their incoming edges, firing, and creating the output tokens on their outgoing edges. Table 1 lists up arithmetic/logic functions a node operation can have. The firing produces not only the arithmetic value X but also the logic (regulating) value R which represent the probability of the token itself existing in the network. Note that for the backward propagation, all the X and R functions have differentiable formulas: sig(z)=1/(1+exp(-z)) and delta(z)=4sig(z) sig(-z). v in node 'c', s in node 'C', and b in judging nodes are node parameters adjusted by the learning.

The learning begins with the evaluation of an energy function at the answer nodes. This causes backward propagation of differential coefficients of the energy function with respect to token variables or node parameters. After the differential coefficients are obtained for all the constant and judging nodes, we revise the node parameters using the steepest descent method. To ensure the convergence of this learning, we also formulate a formula for the learning coefficient (eta). After this, the topological reformation takes place. We prepare six different agents that simplify or complexify the network. The operations create/delete nodes and edges, and renovate the network's algorithm based on the information accumulated during the learning.

To demonstrate the learning capability, the ATN is applied to some symbolic regression problems. Figure 1 shows a representative result for a one-variable quadratic function. In this experiment, we have 6 nodes and 12 agents at first (Fig. 1(a)), but after 80,000 time steps (about 800 forward- and backward propagation), we finally have a 39-node 158-agent network (Fig. 1(b)). Figure 1(c) shows the change of the sensor-answer (input-output) plot during this run. We can see from this figure that the final function of the ATN perfectly agrees with the target function. Using the same parameter setting, we also conducted ten different runs, out of which nine runs succeeded in finding desirable functions. Now we are refining and generalizing the model by incorporating such various program elements as conditional branch, loop, and so on.

Name	Operation code	Input num.	Arithmetic/ Regulating	X	R
Start	S	0	R	–	1
End	E	1	R	–	–
Negative	n	1	A	$-x_0$	r_0
Inverse	i	1	A	$1/x_0$	r_0
Add	+	2+	A	$\sum x_i$	$\min(r_i)$
Multiply	*	2+	A	$\prod x_i$	$\min(r_i)$
Subtract	−	2	A	$x_0 - x_1$	$\min(r_0, r_1)$
Divide	/	2	A	x_0/x_1	$\min(r_0, r_1)$
Less than	<	2	R	–	$R_0 = \mathrm{sig}(\kappa\beta_\mathrm{r}(x_0 - x_1)) \cdot \min(r_0, r_1)$ $R_1 = \mathrm{sig}(\kappa\beta_\mathrm{r}(x_1 - x_0)) \cdot \min(r_0, r_1)$
Greater than	>	2	R	–	$R_0 = \mathrm{sig}(\kappa\beta_\mathrm{r}(x_1 - x_0)) \cdot \min(r_0, r_1)$ $R_1 = \mathrm{sig}(\kappa\beta_\mathrm{r}(x_0 - x_1)) \cdot \min(r_0, r_1)$
Equal to	==	2	R	–	$R_0 = (1 - \mathrm{delta}(\kappa\beta_\mathrm{r}(x_0 - x_1))) \cdot \min(r_0, r_1)$ $R_1 = \mathrm{delta}(\kappa\beta_\mathrm{r}(x_0 - x_1)) \cdot \min(r_0, r_1)$
Not equal to	!=	2	R	–	$R_0 = \mathrm{delta}(\kappa\beta_\mathrm{r}(x_0 - x_1)) \cdot \min(r_0, r_1)$ $R_1 = (1 - \mathrm{delta}(\kappa\beta_\mathrm{r}(x_0 - x_1))) \cdot \min(r_0, r_1)$
Logical AND	A	2+	R	–	$\min(r_i)$
Logical OR	O	2+	R	–	$\max(r_i)$
Logical NOT	N	1	R	–	$1 - r$
Gate	g	2	A	x_0	$\min(r_0, r_1)$
Merge	m	1(a)	A	x	r
Arith. constant	c	1(a)	A	v	r_0
Regul. constant	C	1(a)	R	–	$R_0 = s,\ R_1 = 1 - s$



References

1. Sharp JA (ed.) (1992) Data flow computing: theory and practice. Ablex Publishing Corp

2. Norwood, NJ Suzuki H (2008) A network cell with molecular agents that divides from centrosome signals. BioSystems 94:118-125

3. Tennenhouse DL, Wetherall DJ (1996) Towards an active network architecture. ACM Computer Communication Review 26:5-18

4. Suzuki, H., Ohsaki, H., Sawai H.: A network-based computational model with learning. To be published in: Unconventional Computation, 9th International Conference Proceedings. (2010)

5. Suzuki, H., Ohsaki, H., Sawai H.: Algorithmically Transitive Network: a new computing model that combines artificial chemistry and information-communication engineering. To appear in: Proceedings of the 24th Annual Conference of Japanese Society for Artificial Intelligence (2010)

A computational model of the mouse C2 barrel cortex column

Christian Tomm[1], Michael Avermann[2], Carl Petersen[2] and Wulfram Gerstner[1]

1. LCN, EPFL, Lausanne, Switzerland
2. LSENS, EPFL, Lausanne, Switzerland

In continuation of work done in [Lefort09], we are presenting a model of the mouse C2 barrel cortex column. Our model contains six cortical layers, each consisting of heterogeneous populations of excitatory and inhibitory neurons. To simulate these neurons we use the Adex neuron model [Gerstner09] fitted to experimental datasets collected through electrophysiological recordings. Connectivity probabilities and strengths are drawn from statistics that were fitted to a range of biological observations. Our work aims to understand how spikes are generated and how information is transmitted within a network. Specifically, we are looking at the neural dynamics of our model and compare them to biological recordings that show differences in spike initiation between excitatory and inhibitory populations. Advancing from abstract networks, our goal is to explain differences in network behaviour with respect to the network connectivity and structure.

References

1. W. Gerstner and R. Brette (2009) Adaptive exponential integrate-and-fire model. Scholarpedia, 4(6):8427

2. S. Lefort, C. Tomm, J.-C. F. Sarria, and C. C. H. Petersen (2009) The excitatory neuronal network of the c2 barrel column in mouse primary somatosensory cortex. Neuron, 61(2):301–316

Mesoscopic Network Analysis of the Drosophila Brain

Chi-Tin Shih[1], Jian-Jheng Wu[1], Chih-Yung Lin[2] and Ann-Shyn Chiang[2]

1. Department of Physics, Tunghai University, Taichung, Taiwan
2. Institute of Biotechnology, National Tsing Hua University, HsinChu, Taiwan

Brain structure is believed to have features of complex networks. The physical wiring network for the neuron-neuropil connections of the entire adult Drosophila brain was constructed from the high-resolution images of ~10,000 single neurons. The brain can be divided into 58 regions called LPU (local processing units) which are defined from two characteristics: (i) segregated local interneurons that innervate into the same unit, and (ii) characteristic long-range tracts that are unique for each LPU (Chiang 2010).

In this study, graph theoretical analysis was performed on this complex brain network at the mesoscopic scale, that is, at the LPU level (Bullmore 2009). The main results in this study:

(a) The communities identified by the network analysis revealed the functional modules such as olfactory, auditory, visual, and locomotion systems, and suggested candidates of unknown functional modules.
(b) Centrality analysis predicted the possible provincial and connector hubs.
(c) Distribution of network motifs (Milo 2002) showed that there were many patterns of subgraphs occurring in the real brain network at numbers significantly higher than those in random networks. These motifs might be the building blocks of the brain network.

References

1. Chiang AS et al. (2010) An interactive atlas of the Drosophila brain circuitry at single cell resolution, in preparation.

2. Bullmore, E., and Sporns, O. (2009). Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci 10: 186-198.

3. Milo R et al. (2002) Network Motifs: Simple Building Blocks of Complex Networks. Science 298: 824-827

Random compositional networks of synfire chains dynamically self-tune to the critical state for ongoing percolation of activity

Chris Trengove[1], Cees Van Leeuwen[2] and Markus Diesmann[3]

1. Brain and Neural Systems Team, RIKEN CSRP, Diesmann Research Unit, Saitama, Japan
2. Laboratory for Perceptual Dynamics, RIKEN Brain Science Institute, Wako, Japan
3. Diesmann Research Unit, RIKEN Brain Science Institute, Wako, Japan

Synfire chains are spiking networks with a sequential pool structure that supports the robust propagation of a 'wave' of precisely timed spikes and have been proposed as a mechanism for cognition in which component chains represent features and feature composition (binding) is accomplished by links between chains (Abeles et al. 2004).

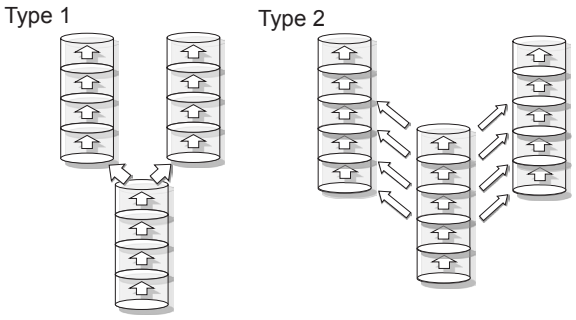
Recent spiking network simulations (Trengove et al. 2010) show that a large number of synfire chains can be embedded in a network the size of a cortical column (~1000 chains of length ~100 in a network of ~100,000 neurons). Activity is stabilized by feedback in the form of balanced excitatory and inhibitory recurrent input ('noise') which limits the number of co-active waves. This set-up opens the door to simulating large-scale compositional systems of synfire chains in which many feature relationships can be represented. As a first step in exploring the dynamics of large compositional systems, we study a compositional network formed by random pair-wise composition of chains. We consider two types of pair-wise composition (as illustrated): Type 1: longitudinal (end-to-end) composition, which results in a feed-forward branching chain structure; and Type 2: lateral composition (with a longitudinal offset) using excitatory cross-links, which supports lateral ignition of waves leading to simultaneous activation of coupled chains by synchronised synfire waves.

Both topologies in principle allow wave activity to multiply and spread through the network. However, due to the regulation by noise, we find that both types of network support a stable equilibrium state that is sustained without external input.

When a distribution of chain strengths is used in the Type 1 model, the equilibrium level of synfire wave activity is tuned to a near-critical level in which the number of chains strong enough to propagate activity is just enough to support ongoing percolation of synfire wave activity through the system. This is because the amount of noise which a propagating wave can tolerate increases monotonically with the strength of the chain. The Type 2 model parameters can be set so that the noise limit for lateral ignition is lower than that for wave propagation, and hence the effectiveness of lateral ignition determines the spread of wave activity through the system. The model can therefore be understood as a random directed graph in which chains are nodes, cross-links are edges, and the effectiveness of an edge is conditional on the global mean activity level. Thus, with a distribution of cross-link strengths, the system equilibrates at the activity level where the effective connectivity is at the percolation threshold: the mean effective out-degree of each node is 1. This dynamic self-tuning to a critical level may relate to the criticality of spike-avalanche phenomena observed both in neural cultures and in vivo (Petermann et al 2009).

The dynamics of the stable state in our models is consistent with observed electro-physiological data, both in terms of the low firing rate and the approximate statistics of membrane potential fluctuations. In simulated recordings replicating the under-sampling of present experimental techniques, the spiking appears irregular and asynchronous, and the precisely organised synfire chain structure and spike timing relationships are not detectable.

Acknowledgements
Partially supported by Next-Generation Supercomputer Project of MEXT, Japan, DIP F1.2, Helmholtz Alliance on Systems Biology, EU Grant 15879 (FACETS), and BMBF Grant 01GQ0420 to BCCN Freiburg. All network simulations were carried out with NEST (http://www.nest-initiative.org).



Pairwise composition: Type 1 (longitudinal) versus Type 2 (lateral + offset)

References

1. Abeles M, Hayon G, Lehmann, D (2004) Modeling compositionality by dynamic binding of synfire chains. J Comput Neurosci 17:179-201

2. Petermann T, Thlagarajan T, Lebedev M, Nicolelis M, Chialvo D, Plenz D (2009) Spontaneous cortical activity in awake monkeys composed of neuronal avalanches. PNAS 106:15921-15926

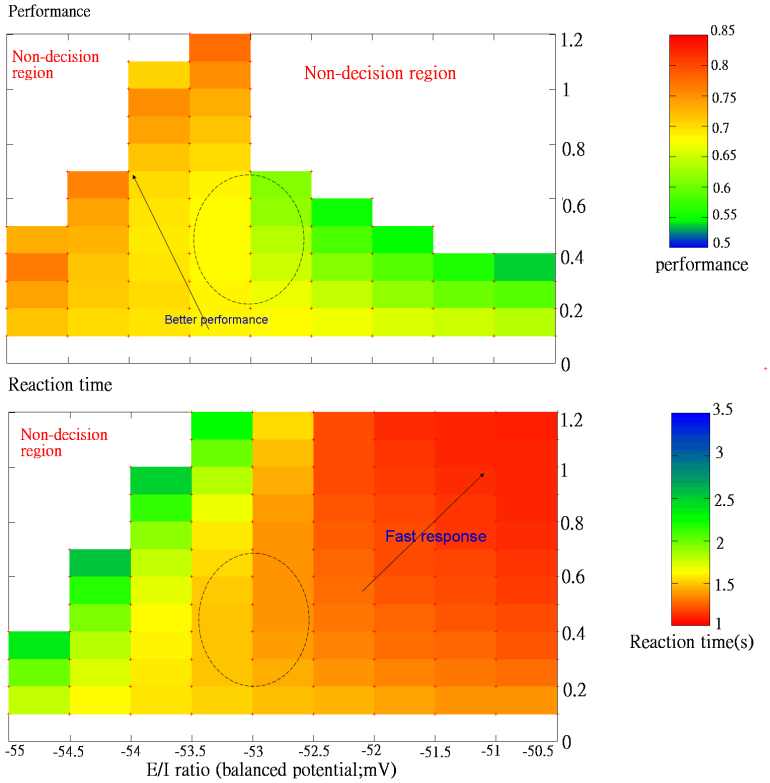
3. Trengove C, van Leeuwen C, Diesmann M (2010) High storage capacity of a random superposition of synfire chains in large-scale cortical networks. 2nd Biosupercomputing Symposium, Maranouchi Japan

Dynamic tuning of perceptual decision making in a cortical circuit model by balanced synaptic input

Cheng-Te Wang and Chung-Chuan Lo

Institute of Systems Neuroscience, National Tsing Hua University, HsinChu, Taiwan

Neurons in the central nervous system are continuously bombarded by noisy excitatory and inhibitory synaptic inputs with balanced intensity. This balanced synaptic input (BSI) is traditionally treated as a source of background noise that increases overall conductance and response variability of neurons. Recent studies demonstrated that the BSI can serve as a mechanism for single-neuron input gain modulation (Chance et al., 2002), which is one of the most important features of information processing in the central nervous system. In a previous study, we found that when BSI is applied to a cortical circuit model of perceptual decision marking (Wang, 2002; Lo and Wang, 2006), its performance is increased but the mean reaction time is prolonged. The result suggests that BSI provides a synaptic mechanism for the behavior of speed-accuracy tradeoff. In the present study, we systemically tested how is the behavior of the neural circuit model is affected by altering the strength of BSI and the ratio of excitation and inhibition in BSI (E/I ratio). We found that when the E/I ratio is high, increasing BSI strength reduces both the performance and the reaction time. When the E/I ratio is low, the performance is improved with increased BSI strength (see Figure). However, the neural circuit dramatically slows down and often fails to reach a decision. Only when E/I ratio is maintained in an intermediate level the neural circuit makes a decent trade-off between the speed and accuracy (dashed circle in Figure). Furthermore, we found that by changing the strength of BSI, we can switch the cortical circuit between different states: (1) a non-functioning state in which the neural circuit ceases to respond to external stimuli, (2) a competition state in which the neural circuit integrates stimuli and performs perceptual discrimination and (3) a bistable state in which the neural circuit acts like a switch that responds to stimuli in an all-or-none fashion. Our result suggests that while the widely studied long-term synaptic plasticity produces slow but long lasting changes to the neural circuits, the balanced synaptic input provides a top-down mechanism for dynamical modulation when a quick and temporal change of the cortical function is needed.



References

1. Lo C-C . Wang X-J, (2006) Cortico-basal ganglia circuit mechanism for a decision threshold in reaction time tasks, Nat. Neurosci. 9, 957-963

2. Wang, X.-J. (2002) Probabilistic decision making by slow reverberation in cortical circuits. Neuron 36, 955;V968 .

3. Chance, F.S., Abbott, L.F. Reyes, A.D. (2002) Gain Modulation Through Background Synaptic Input. Neuron 35:773-782.

Neuronal avalanches of a stochastic sandpile

Chai-Yu Lin and Yi-Duen Wang

Department of Physics, National Chung Cheng University, Chiayi, Taiwan

The slider-block models belonging to a deterministic sandpile model [1,2] have been widely investigated for describing the behavior of integrate-and-fire neurons. However, the slider-block models always exhibit multifractal behavior and then prevent our understanding obtained by numerical simulations. Instead, we propose a stochastic sandpile, called the q-state Manna sandpile model [3], to simulate neuronal avalanche. First, from the simulation of the probability distribution, we demonstrate that the q-state Manna model is in the same universality class for different q. Then, the renormalization-group approach is applied to obtain the property of neural population and the role of leakage current in such a model. Furthermore, we point out the q-state Manna model is equivalent to the slider-block models in the viewpoint of the interactions of each neuron pair. Finally, we extend this model to associate different kinds of feeding in external inputs consisting of information for modeling the integrate-and-fire neurons. We investigate the time behavior of the corresponding dynamical system, patterned firings, synchronization, oscillation, etc. This study may provide a novel understanding of experimental results for multineuronal activity. The potentially rich connection between sandpile models and networks of integrate-and-fire neurons is discussed.

References

1. Cebulla C. (2007) Asymptotic Behavior and Synchronizability Characteristics of a Class of Recurrent Neural Networks. Neural Computation 19:9, 2492 - 2514.

2. Nikitchenko M. and Koulakov A. (2008) Neural Integrator: A Sandpile Model. Neural Computation 20:10, 2379 - 2417.

3. Lin C.-Y. (2010) Renormalization-group approach to the Manna sandpile. Phys. Rev. E 81:2, 021112-1 - 021112-9.

Using Topographica for real-time video input, neural analysis, and reliable control of model parameters in Python

Christopher E. Ball and James A. Bednar
University of Edinburgh, Edinburgh, UK

Topographica is an open-source software project designed to support large-scale computational modeling of the development, structure, and function of topographic neural maps. In this demonstration, we will show two aspects of the Topographica simulation environment that support our neuroscience modeling work: input stimulus generation and model analysis. We will also demonstrate an independent module of Topographica, suitable for use in any neuroscience Python environment, that allows more reliable modeling by providing better control of model parameters.

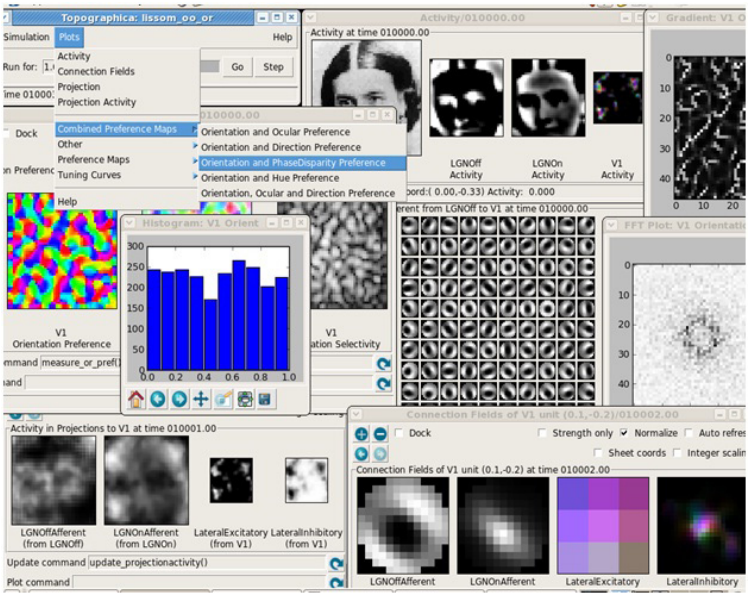
Input stimulus generation and model analysis
Many neuroscience modeling studies require the generation of varied input stimuli for testing or training. Topographica can generate visual and auditory input stimuli from statistical distributions, stored multimedia, and real-time camera or microphone input. We will show how stimuli can be generated and presented to models, focusing in particular on video input (both live and pre-recorded). This capability makes it practical to build models situated in a realistic environment, processing complex real-world inputs.

Topographica also provides a coherent framework for analysing models (both those built with Topographica, and those running in other simulators [1]). We will demonstrate our general-purpose measurement of feature maps, receptive fields, and tuning curves, usable as-is for nearly any model that accepts input patterns, and show how the results of these can be visualized.

Parameter control
While Topographica provides an integrated simulation environment, it is also designed to be highly modular. Some of its modules could independently be useful for any Python-based scientific software. Among these, we have found the Parameters module to be critical for managing large neuroscience simulations. Many parameters of a model should only take values of a particular type within a particular range, but Python's attributes do not normally allow a range or type to be specified. Topographica's Parameters module makes it easy to handle parameter setting robustly, and also allows an attribute to be generated dynamically (from a particular statistical distribution, for example), to have a default value (allowing the modeler to provide sensible defaults), and to be documented easily.

Overall, parameters make simulations more reliable, easier to understand, and easier to run and analyze in large numbers on clusters. We will demonstrate parameters in action, and show how they can vastly simplify code for any scientific software project.
Topographica focuses on easy-to-understand implementation, using a high-level language (Python), while providing high performance through the use of built-in profiling tools and optimization of specific components (by inlining C code or using MPI, for instance). The software runs on Windows, Mac OS X, and Linux, and is freely available from topographica.org.

Development was supported by the US National Institute of Mental Health under Human Brain Project grant R01-MH66991, and by the UK EPSRC-funded Neuroinformatics Doctoral Training Centre at the University of Edinburgh.



Above: sample session from Topographica

References

1. Bednar JA (2009) Topographica: building and analyzing map-level simulations from Python, C/C++, MATLAB, NEST, or NEURON components. Front. Neuroinform. 3:8. doi:10.3389/neuro.11.008.2009

The Schema of the European EPILEPSIAE database for seizure prediction

Matthias Ihle[1], Hinnerk Feldwisch[2], Björn Schelter[2], Jens Timmer[2] and Andreas Schulze-Bonhage[1]

1. Epilepsy Center, University Hospital Freiburg, Juelich, Germany
2. FDM, University of Freiburg, Juelich, Germany

Purpose:
With a prevalence of about 1%, epilepsy is considered to be one of the most common serious brain disorders with profound physical, psychological and social consequences. Characteristic symptoms are seizures caused by abnormal neuronal activity that can lead to temporary impairments of motor functions, perception, speech, memory or consciousness. The possibility to predict the occurrence of epileptic seizures, typically by recording and monitoring the electroencephalographic activity (EEG), could enable new therapeutic strategies for the considerable fraction of epilepsy patients that are not treatable by any state of the art therapeutics like anticonvulsive medication or brain surgery.

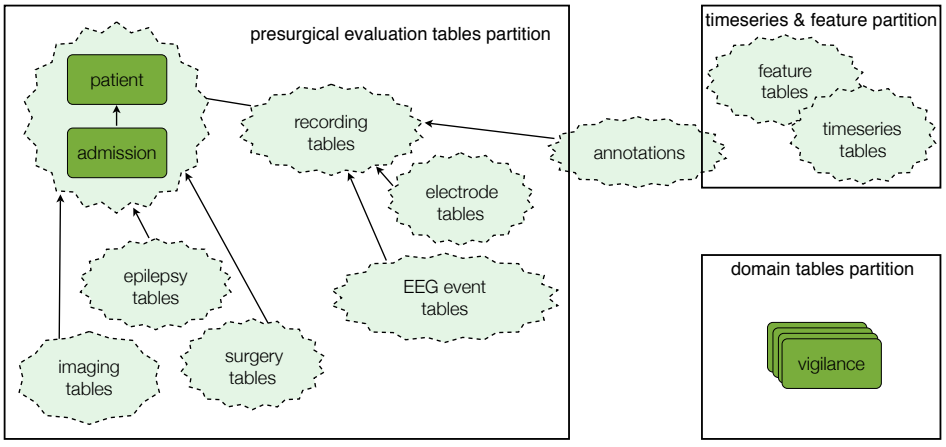
Funded by the European Union, the EPILEPSIAE project, a 7th Framework Programme with seven clinical, academical and industrial partners in Portugal, Germany, France and Italy, was established to develop and advance prediction algorithms and to deploy these algorithms on a small transportable alarming device. So far, the main concern for the development of prediction algorithms have been limitations in the quality and duration of long-term EEG data that are important for the statistical evaluation of prediction methods. Accordingly, the EPILEPSIAE project is currently gathering the largest and most comprehensive epilepsy database existing worldwide to collect and organize a substantial amount of characteristic patient data for research on seizure prediction methods.

Method:
In contrast to previously existing, by orders of magnitude smaller EEG data collections, the EPILEPSIAE database is a relational database, designed for efficient data organization and access and offering extensive searching capabilities.
Therefore, the 250 surface and 50 intracranial epileptic patients datasets are collected and integrated into the database as common effort of all clinical partners. The datasets comprehend multimodal data including raw data as well as different types of metadata:

- raw EEG data recorded from all clinical partners during long-term monitoring of epilepsy patients
- feature data: features derived from the EEG recordings, which are important for the development and testing of prediction algorithms.
- magnetic resonance imaging (MRI) data (skull stripped for reasons of data anonymization)
- standardized EEG annotations covering information visually perceived by experts about the EEG, e.g. about seizures and interictal events
- clinical metadata: information about patients and their diseases including medical history, imaging findings, anti-epileptic therapy, seizure semiology as well as information about EEG recordings and therefore used electrodes
- feature metadata: supplementary information about the feature algorithms and calculations

Results:
Currently, there are working databases at the partner's sites, all in sync with a replicated content of already more than 150 datasets. This makes the EPILEPSIAE database already the by far largest epilepsy database. Although all project partners use an Oracle database, the schema, as it is presented here, is agnostic of the underlying database system and can easily be adapted to other relational databases. We here only outline the general structure of the schema of the EPILEPSIAE database in Figure 1. The complete schema will be visually presented in full detail on the poster.

Conclusions:
Although still work in progress, the EPILEPSIAE database is already the most comprehensive and complete epilepsy database currently existing. Interest for access to the database as well as participation requests from all over the world already give evidence of the emerging acceptance of our database as the de facto standard for databases in the field of epilepsy. This acceptance of our database schema and content is probably the most important impact of the EPILEPSIAE database.



Automated reconstruction of three-dimensional brain structures based on 2D histological atlases

Piotr Majka[1], Grzegorz Furga[2], Ewa Kublik[1] and Daniel Wójcik[1]

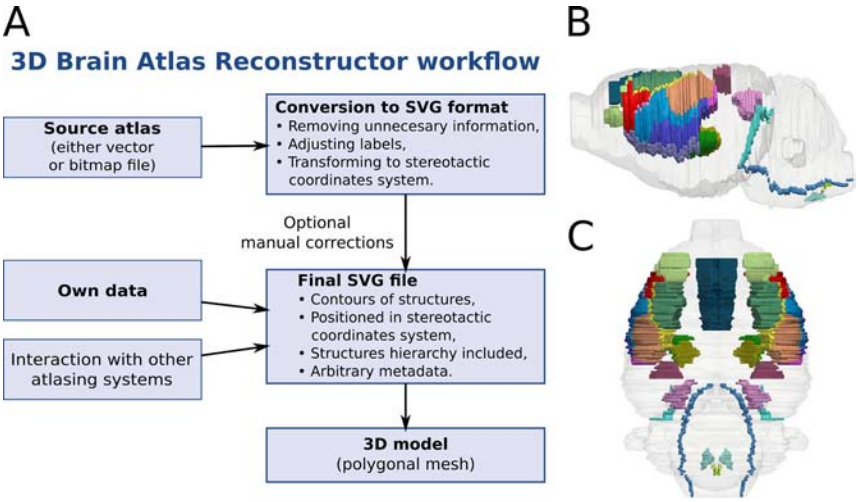
1. Department of Neurophysiology, Nencki Institute of Experimental Biology, Warsaw, Poland
2. Faculty of Mathematics Informatics and Mechanics, University of Warsaw, Warsaw, Poland

Brain activity data obtained with various neurophysiological methods must be precisely localized in neuroanatomical context in order to make the interpretation of the results correct or even possible. Traditionally, such context was provided by 2D planes of the atlases of brain structures. Recent development of modern recording techniques (MRI, PET, multichannel LFP), leading to spatially distributed data, brought a necessity of three-dimensional brain atlases of various species.

Creating three-dimensional atlases is not a new problem in itself (e.g. SMART Atlas, NESYS Atlas3D). However, large part of available software gives only the option of viewing already prepared structures rather than creating new 3D models of these structures. Moreover, common practice in creating such atlases is to do it manually by tracing contours of desired structures on all slices and creating 3D models in commercial software (e.g. Amira). This approach leads to many inconveniences. First of all it is time consuming and tedious task which is hard to record and repeat afterwards by other people or by computer. It is also not customizable as constructing the 3D model again means conducting the whole manual process from scratch. All of those disadvantages result in difficulties in spotting and eliminating reconstruction errors.

Obviously, in case of atypical species the tracing stage is necessary, but for many standard laboratory animals existing 2D atlases could be employed. Here we propose software, 3D Brain Atlas Reconstructor (3dBAR) dedicated to automated reconstruction of three-dimensional brain structures based on 2D histological atlases. Our goal is a framework for generation of 3D models of chosen brain structures based on 2D representations (either vector or bitmap formats) of slices. Implemented methods allow to generate 3D models in reproducible and configurable way as well as track and review the whole reconstruction process in order to find and correct errors. Some typical simple errors which may be noticed in 2D digital atlases, such as open boundaries between regions or incorrectly placed labels, can be highlighted or eliminated by the software. Our workflow allows for manual corrections when automatic reconstruction is not good enough.

The software takes into consideration many collaborative features: it allows exchanging content (complete models as well as data from intermediate stages of processing) and may easily integrate with other atlasing systems by using open file formats (SVG, XML, VRML). The framework allows for adding new public or proprietary content and supports an open file definition based on SVG for 2D input data. Moreover, on-line service with dedicated API will be created allowing downloading desired structures via http queries. At present, our software package consists of graphical interface for generating and previewing models and it contains wrappers for two atlases: Paxinos and Franklin Mouse atlas and Paxinos and Watson Rat atlas. We are working towards integrating other data in particular in collaboration with Scalable Brain Atlas project. Ultimately, the tools will be published as open source. Supported from grant POIG.02.03.00-00-003/09.



A) Outline of implemented workflow, B, C) Lateral and ventral views of selected structures reconstructed with 3dBAR based on 2D planes from standard rat brain atlas (Paxinos G, Watson C (2007) The rat brain in stereotaxic coordinates. Academic Press).

Standard brain of silkworm moth, Bombyx mori, based on the brain and neuron database

Stephan Haupt[1], Hidetoshi Ikeno[2], Tomoki Kazawa[3], Shigehiro Namiki[3], Ikuko Nishikawa[4] and Ryohei Kanzaki[3]

1. Graduate School of Informatics Systems, University of Tokyo, Tokyo, Japan
2. School of Human Science and Environment, University of Tokyo, Himeji, Japan
3. Research Center for Advanced Science and Technology, University of Tokyo, Tokyo, Japan
4. College of Information Science and Engineering, Ritsumeikan University, Kusatsu, Japan

Understanding the brain mechanisms controlling behavior in natural environment is one of the principal aims in neuroscience. One approach directed towards this goal is to rebuild neural systems by simulation. However, the simulation of mechanisms in a whole brain has not yet been achieved because of factors such as complexity and individual variations in experimental data. Several brain functions resulting from interactions with the environment, such as adaptive information processing can conveniently be investigated by using a simple model system, which can be simulated as a whole from the sensory mechanisms to the generation of behavior. We aim to reconstruct and simulate neuronal circuits in the silkworm moth brain and to reveal the design principles of the brain by focusing on this simple model system. We are examining to integrate their morphological profiles with a standard brain based on whole brain and single neuron data in our database, BoND (Kazawa et al., 2008) and IVB-PF (Ikeno et al., 2008). As a first step of our study we are constructing a detailed standard brain model, focusing on whole brain shape and key regions, such as the antennal lobe, the lateral accessory lobe (LAL) and the ventral protocerebrum (VPC) (Iwano et al., 2009). These areas are related to the sensory information processing and behavioral control generating. Confocal images of whole brain are downloaded from the database. Anterior and posterior sectional images are stained by anti-synaptic antibody for intensifying neuropile and neural tracts. Anterior and posterior sectional images are concatenated and adjusted brightness and contrast. Deconvolution process with the point spread function is applied for blurring of confocal images. The whole brain profiles are extracted from these image data. In this analysis, the origin of the coordinate system in the map is set to the center of the oesophageal foramen. The individual difference between brains is measured and compared based on the size and position of characteristic regions, such as the central body and the antennal lobe. To construct a standard brain shape, we applied rigid and non-rigid transformations to produce an average shape. At the same time, we have extracted morphological structures of interneurons in the LAL-VPC and other regions. Extracted results are registered to the database and shared through a Virtual Private Network. They are classified into two groups, bilateral interneurons and local interneurons. We can provide a simulation environment of neurons and networks based on their morphologies properties. Strength of synaptic connections between neurons is estimated by measuring the overlap volume of the arborizations of neuritis. Several research groups have integrated neuron morphology obtained from different animals into the standard brains, such as honeybee, drosophila and locust. We are following same approach, but we are going to estimate the sources of variability and errors by examination of the mapping of the same identified neurons from different brain samples. It is indispensible to evaluate the spatial resolution of such geometrical normalization process to determine the scale at which it can be utilized. The standard brain map for silkworm moth will be published as a content of IVB-PF under the Japan-node in near future.

High Resolution Diffusion Tensor Atlas of the Mouse Brain

Yi Jiang and G. Allan Johnson

Center for In Vivo Microscopy, Duke University Medical Center, Durham, USA

Introduction

Eight diffusion tensor imaging (DTI) datasets of normal adult mouse brains were acquired at 43 μm isotropic resolution by using a streamlined protocol, including specimen fixation and staining, image acquisition, reconstruction, and normalization to a common reference brain (Waxholm Space). The normalization accuracy was evaluated by measuring landmarks displacement between individual brains and the reference brain. Mean values of DTI parameters, e.g., anisotropy and diffusivity, were computed in 9 white matter (WM) structures to determine if the current protocol is able to provide consistent data and distinguish anatomical difference between WMs.

Method

8 normal adult male C57BL/6 mouse brains were actively stained. T1 and T2*, one b0, and 6 diffusion-weighted images were acquired on a 9.4 T magnet using a spin-echo sequence at 43 μm resolution. The T1 and T2* images were used with DiffeoMap to register each individual brain to a reference brain, using rigid transformation, affine transformation, and two-channel LDDMM. The transformation matrix was then applied to properly map and reorient the diffusion tensors. Eigenvalues, where the primary eigenvalue is axial diffusivity (AD), eigenvectors, fractional anisotropy (FA), radial diffusivity (RD), and color-coded orientation map of the primary eigenvector (ev0) were calculated in DTIStudio.

80 landmarks were manually selected on each brain and the reference brain. The landmarks on individual brains were mapped on to the reference coordinate with the corresponding transformation matrix. Displacements between landmarks mapped from individual brains and landmarks of the reference brain were measured to quantify registration accuracy.

Nine WM structures including lateral lemniscus, anterior commissure, cerebral peduncle, internal capsule, optic tract, fimbria, corpus callosum, fornix, and spinal trigeminal tract were manually defined in the reference brain. The averaged values of FA, AD, RD, and angular difference of ev0 were calculated in the 9 WMs in each individual brain. One-way ANOVA and post hoc Tukey-Kramer tests were used to examine regional variations of each parameter across 8 brains and across 9 WMs. To decide if the quality of manual delineation has any influence on the statistical findings, a white matter probability atlas (WMPA) was constructed by averaging the 8 thresholded FA maps of individual brains. The same statistical tests were applied on the core regions (e.g., with WM probability of 0.5, 0.625, 0.75, 0.875, or 1) of the manually defined WMs.

Results

The figure shows group average of FA, AD, RD and colormap of 8 brains providing visual feedback on the normalization quality. Mean displacement of the 640 landmarks is only 1.5±1.0 pixels.

The table lists p-values of the ANOVA test of FA, AD, RD, and ev0 across 8 brains or across 9 WMs. No significant difference was found across the 8 brains for any parameter. In contrast, there exists significant difference across the 9 WMs for all parameters. Subsequent Tukey-Kramer tests provide additional information, such as the lateral lemniscus was found to have significantly lowest anisotropy, while the cerebral peduncle exhibits the highest anisotropy. Analysis of core regions of WMs with probability level of 0.5, 0.625, 0.75, 0.875 or 1 does not change the statistical findings (data not shown).

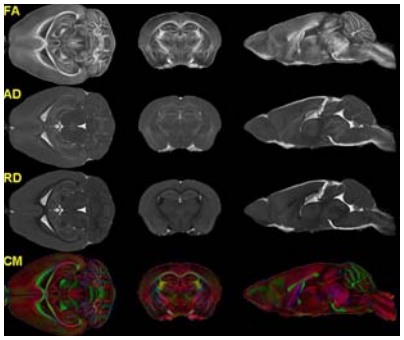
Conclusions

This protocol is able to acquire high-resolution DTI data of mouse brain in a robust and repeatable fashion, allowing us to normalize individual brains onto a common reference with high accuracy, lending validity to atlas-based representation of DTI parameters. It will serve as a foundation to quantitatively study mouse brain integrity and white matter architecture, at what we believe to be the highest spatial resolution yet attained.

Acknowledgement

All work performed at the Duke CIVM, an NCRR National Resource (P41 RR005959).

p-value of ANOVA test	Across 8 brains	Across 9 WMs
FA	0.94	0*
AD	0.84	0*
RD	0.34	4.6e-13*
Angular difference of ev0	0.28	3.3e-13*



References

1. Jiang Y, Johnson GA (2010) Microscopic diffusion tensor imaging of the mouse brain. NeuroImage 50: 465-471

2. Johnson GA et al (2007) High-throughput morphologic phenotyping of the mouse brain with magnetic resonance histology. NeuroImage 37: 82-89

3D MRI Data Viewer System on Neuroimaging-platform

Keiji Matsuda[1], Noriyuki Higo[1], Takao Oishi[2], Kazuhisa Niki[1], Ryoji Suzuki[3], Shinobu Masaki[4], Kazuhisa Ichikawa[5] and Shiro Usui[6]

1. Human Technology Reserch Institute, AIST, Tsukuba Ibaraki, Japan
2. Primate Resesarch Institute, Kyoto University, Inuyama, Japan
3. Kanazawa Institute of Technology, Nonoichi, Japan
4. ATR-Promotions, Kyoto, Japan
5. Osaka University, Osaka, Japan
6. RIKEN, Wako, Japan

Purpose: It is important in neuroscience research and education to visualize three-dimensional brain structures. We have developed 3D MRI Data Viewer System, which enables viewing 3D or 2D MR images by using ordinary Web browsers. This 3D MRI Data Viewer is utilized in "Brain Explorer" of NeuroImaging-platform (http://nimg.neuroinf.jp) to demonstrate a Japanese (Adult, male) brain that was provided by Tohoku University's "The Japanese brain database" and a Japanese monkey (3 years 8 months old, male) brain that was scanned in AIST (National Institute of Advanced Industrial Science and Technology). Brain Explorer is intended not to be glanced at but to be used as an interactive visual dictionary. For this purpose, this Viewer has many functions to promote the use in study. DATA specification: Human MRI data are reconstructed from T1 weighted images (FOV 250mm, slice thickness 1.5mm). We removed the skin from scanned images. When we reconstruct volume data from MRI data, we interpolate them to obtain isotropic voxels. Voxel length is 0.9766mm. This volume data is adjusted on Talairach coordinate system. The origin is the posterior margin of the anterior commissure (AC) at the midsagittal plane. Horizontal zero plane includes AC-PC (posterior commissure) line. Japanese monkey data are reconstructed from sagittal T1 weighted images (FOV 120mm, slice thickness 1.2mm). We show both head and brain (skin removed from data) images. We reconstruct the volume data in the same way as for the human's. Voxel length is 0.46875mm. The volume data are adjusted on Horsley-Clarke coordinates by using spatial markers scanned with the head. Horizontal zero plane is 10 mm superior to the Frankfurt zero plane including the center of ear canal and inferior rim of the orbit. Coronal zero plane includes the straight line passing the center of ear canals. The origin is the point of intersection of horizontal, coronal and sagittal zero-planes. Web application: This Viewer system is implemented as the client-server model. Any workstations or personal computers installed with Apache (httpd server), PHP (Lightweight scripting language) can be a server of this system. Proper operation was checked on Linux, Windows XP/Vista/7 and Mac OS X. NIMG-PF uses Linux machine as a server. Users can access the server and view data with Web browsers. Image processing programs on the server create slice images and surface-rendered 3D images of the selected data on demand from the user's Web browser. We confirm that this Web application works by usual Web browsers such as IE7, IE8, Safari3, FireFox3.5, Opera10, and Google Chrome. We build the user interface using JavaScript and DHTML, so users can operate this application interactively. Clicking a point on the image leads to getting cross sections at an arbitrary point (a cursor, red cross). Dragging the cursor leads to getting the positional information on the tip tool or to moving the cursor, depending on modes. The title of control area has hyper-link of presently displayed images. A user can share what one see with another person by sending the URL. Summary: We have developed 3D MRI Data Viewer System on NIMG-PF, which enables users to view slices and rendered surface image of the brain from arbitrary angles, and to measure the position of arbitrary brain structure on standard anatomical coordinates. We hope that users use this web application as a visual dictionary in their studies.

Validation of landmark sets and their use for registration in mouse brain imaging

Marina Sergejeva[1], Alexandra Badea[2], Asif Menon[3], Jyl Boline[4], Seth Ruffins[5], Albert Burger[6], Ilya Zaslavsky[3], Allan Johnson[7], Fons Verbeek[8] and Andreas Hess[1]

1. I. f. Pharmacology, Erlangen, Germany
2. Center for In Vivo Microscopy, Duke University Medical Center, Durham, USA
3. University of California at San Diego, San Diego, USA
4. Informed Minds, Inc., Wilton Manors, USA
5. California Institute of Technology, Pasadena, USA
6. MRC and Heriot-Watt University, Edinburgh, UK
7. Duke University, Durham, UK
8. Leiden Institute of Advanced Computer Science, Leiden, Netherlands

In the time when genetic engineering is flourishing, and numerous strains of mutant mice are being created for research purposes, a world-wide accessible reference system which would enable comparison of the data of various types from different working groups is very desirable. Several attempts have been made for such mouse brain atlases ranging from the gold standard of the Paxinos printed atlas (2nd edition 2001) to ABA (www.brain-map.org) etc. The INCF (incf.org) has launched the Digital Atlasing Program (incf.org/core/programs/atlasing) which came up with the Waxholm space (WHS: 2008), which is an up-to-date computer-based common reference space for adult C57BL/6J mice. This reference space, available to the public, consists of very high resolution undistorted MRI datasets of different contrasts (T1: 21,5 µm, T2, T2*, 43 µm) together with Nissl histology (20 µm) of the very same specimen, all fully 3D from A. Johnson (Duke, www.civm.duhs.duke.edu/). Very recently, population based datasets including DTI have been made available by A. Johnson (www.civm.duhs.duke.edu/neuro200902/index.html). One desirable application of a computerized digital atlas is to bring one's own data into this reference system to gain full advantage of the information available in the system. This process is called registration. Fully automatic registration processes only exist for very limited use of datasets with hard constrains (dimensionality, modality, contrast etc.). Moreover, the parameterization of these algorithms is complex and high computational power (up to several hours) is needed. An alternative approach, which I) is much faster, II) can be performed by everybody, III) leads to sufficient accuracy for many applications, is a registration based on landmarks or fiducials. In imaging technology, a fiducial is part of an image serving as a point of reference, i.e., characteristic internal anatomic structure of the brain easily identified. Practically and to enhance the spatial precision, the fiducials are often reduced to a single point. Defining a corresponding set of fiducials in a source and target (reference) dataset determines the transformation of the source to the target dataset. Moreover, this landmark based registration may first, enhance performance of the computational intense automatic registration and second, these fiducials allow for validation of any other registration procedure. Therefore, the aim of this study is to identify set(s) of fiducials primarily allowing the registration of any 3D datasets to WHS. These should be unambiguously recognizable:

- to different individuals
- in different image modalities (T1, T2, T2*)
- in various specimens
- in different cutting directions
- in different image resolutions
- in various mouse strains.

Consequently, we started with "medium" resolution MR datasets (T1, T2, T2*, 256x256x128, 80 µm). Using ImageJ (rsbweb.nih.gov/ij/index.html) and its point identification tool, anatomical experts defined an initial set of fiducials (T1: 36, T2: 65, T2*: 51). Next a group of 13 subjects (among them anatomical novice, physicists, vets and biologists) identified these landmarks on the same dataset, using a guide to find and set the fiducials. We achieved a very high precision of around 1.5 voxel deviation across all fiducials. In addition, the same group of people had to identify these fiducials on different datasets of the same mouse strain. In this case, for T1-90 %, T2-100%, and T2*-97% of these same fiducials could be found. A web-based version of our fiducial point effort is online to encourage user participation (http://smartatlas.crbs.ucsd.edu:8080/mapserver-services/pages/imageviewer/incf1.html). This study allows us to get insight into accuracy of manually identifiable fiducials, and therefore their reliability. Establishing an easy to use landmark registration to WHS should facilitate cooperation of mouse imagers all over the world.

Releasing species in spaces: Waxholm Space and its connection to other model systems

Fons Verbeek[1], Dome Potikanond[1], Peng Yang[1] , A. Alia[2], Herman Spaink[3], Jyl Boline[4] and Ilya Zavlavsky[5]

1. Leiden Institute of Advanced Computer Science, Leiden University, Leiden, Netherlands
2. Leiden Institute of Chemistry, Leiden University, Leiden, Netherlands
3. Leiden Institute of Biology, Leiden University, Leiden, Netherlands
4. Informed Minds, Inc., Wilton Manors, USA
5. San Diego Supercomputer Center, San Diego, USA

The Waxholm is space specifically developed for interoperability in the rodent mouse brain (Hawrylycz et al., 2009). Model systems are used in terms for their possibilities of high-throughput applications. In vertebrate research the zebrafish and medaka are good candidates in high-throughput analysis. This is extremely valuable in applications where one intends to screen large component libraries as zebrafish embryos (Brittijn et al., 2009) can be obtained in large amounts and are easily processed. Interoperability amongst species is a long whished item developmental and related biology research (Verbeek et al., 1999). The interpretation of the results is important in the field of zebrafish research, however, only if it can be related to higher vertebrates it will gain importance tremendously. In order to understand effects of compounds one needs a proper atlas in which data can be projected and effects on the phenotype can be understood. To relate effects to the higher vertebrates, so that ultimately a prediction to human can be made, the step from the zebrafish to the rodent need be made first. For the zebrafish a number of atlases (http://bio-imaging.liacs.nl/ZFAtlasServer) and datasets are available. Defining interoperability between mouse and zebrafish is a challenging endeavor as it requires relating fish embryology with adult mouse; in the case of the high-throughput. Alternatively, a route via the adult zebrafish can be considered; here we have to use adult datasets in which the spatial resolution is much lower than the spatial resolution that can be accomplished in the embryo. Moreover, one has to consider the granularity of the annotations in datasets. Atlases are made to depict as much detail as possible, experimental data are not imaged with the highest possible resolution and compromise to resolution. All these effects have to be taken into account in finding a sensible interoperability between databases (Belmamoune & Verbeek, 2008). The INCF Digital Atlasing Program can contribute in accomplishing the interoperability in the Waxholm space by further extending services (Zavlavsky, 2010). An effort has been made to extend these services. These services have been adapted and made congruent with services that are offered in Leiden. The attempt to map zebrafish data to mouse data via services stands as an interesting case study; it serves as a paradigm for future developments in interoperability of model systems. The INCF Digital Atlasing Program is a community effort and requires input from the scientific community. A demonstration of early results will be given at the conference. Considerations on mapping of spatial data through ontological concepts are presented.

References

1. Hawrylycz M, et al. (2009) The INCF Digital Atlasing Program Report on Digital Atlasing Standards in the Rodent Brain. Nature Preceedings.

2. Brittijn SA, Duivesteijn SJ, Belmamoune M, et al. (2009) Zebrafish development and regeneration: new tools for biomedical research. Int. J. Dev. Biol. 53: 835-850

3. Belmamoune M. and Verbeek, F.J. (2008) Data Integration for Spatio-Temporal Patterns of Gene Expression of Zebrafish development: the GEMS database. Journal of Integrative BioInformatics, 5(2):92

4. Verbeek, F.J., Lawson, K.A., and Bard, J.B.L. (1999). Developmental BioInformatics: linking genetic data to virtual embryos. Int. J. Dev. Biol. 43, 761-771.

Coupling Existing Client and Server Software for Integrating Waxholm Space

Seth Ruffins[1], Richard Baldock[2], Daren Lee[1] and Arthur Toga[1]

1. Laboratory of NeuroImaging, University of California Los Angeles, Los Angeles, USA
2. Western General Hospital, Human Genetic Unit and IGMM, MRC, Edinburgh, UK

The INCF Digital Atlasing Infrastructure (DAI) task force is developing a canonical three-dimensional representation of the mouse brain called Waxholm Space or WHS. The WHS model is based on high resolution (21 μm^3 isotropic voxels) T1, T2 and T2* MRI scans and 3D registered Nissl stained serial sections of a single C57Bl/6 male adult mouse brain. In addition to these image volumes, an indexed label image of segmented brain regions has also been generated to sub-divide the model brain. This data set acts as common space for mapping features, properties and the distribution of molecules in the brain. Such mappings results allow WHS to be a common spatial framework for accessing multiple mouse brain resources. Software for accessing and delivering online image databases have been developed independently of the INCF DAI. Rather than construct new tools de novo, straight forward extensions to the WoolzIIP server and MBAT have been written to accommodate WHS. The MouseBIRN project at LONI-UCLA and EMAP (Edinburgh Mouse Atlas Project) at the MRC-Human Genetics Unit, have brought together MBAT (MouseBIRN Atlasing Toolkit) and Woolz IIP server (a modified version of the Internet Imaging Protocol server) to deliver the the five image volumes comprising WHS mouse brain model. The Woolz IIP server allows rapid navigation and interaction with the model brain image within MBAT without the user having to download the entire set of image volumes to their local computer. MBAT's viewer permits the user to display the model data concurrently with images from the local file system and/or other online resources. MBAT also allows registration of 2D images to the WHS model allowing the user to explore their data in the context of other resources mapped to WHS.

Building on Waxholm Space (WHS) and the INCF Digital Brain Infrastructure (DAI)

Jyl Boline[1], Richard Baldock[2], Rembrandt Bakker[3], Janis Breeze[4], Albert Burger[5], Christian Haselgrove[6], Michael Hawrylycz[7], Andreas Hess[8], G. Allan Johnson[9], Stephen Larson[10], Lydia Ng[7], Seth Ruffins[11], Fons Verbeek[12] and Ilya Zaslavsky[13]

1. Informed Minds, Inc., Wilton Manors, USA
2. MRC Human Genetics Unit and IGMM, Edinburgh, UK
3. Radboud University, Nijmegen, Netherlands
4. INCF Secretariat, Stockholm, Sweden
5. MRC Human Genetics Unit and Heriot-Watt University, Edinburgh, UK
6. University of Massachusetts Medical Center, Worcester, USA
7. Allen Institute for Brain Science, Seattle, USA
8. Institute of Experimental and Clinical Pharmacology and Toxicology, Germany, Germany
9. Duke Center for In Vivo Microscopy, Durham, USA
10. University of California at San Diego, USA
11. Laboratory of NeuroImaging (LONI), University of California, Los Angeles, USA
12. Leiden Institute of Advanced Computer Science, Leiden University, Leiden, Netherlands
13. San Diego Supercomputer Center, University of California, San Diego, USA

The *INCF Digital Atlasing Program* (incf.org/core/programs/atlasing) was formed in the fall of 2007 as an international neuroinfomatics collaborative effort (incf.org) to create an atlas-based framework to make the rapidly growing collection of multidimensional data of the rodent brain more widely accessible and usable to the research community (Boline et al. 2007). This led to the formation of the *INCF Digital Atlasing Program Standards Task Force*, which produced a common space for the adult C57BL/6J mouse called Waxholm Space (WHS), via a high-resolution WHS dataset, and the initial specifications and prototype of a hub-based distributed interoperable INCF Digital Atlasing Infrastructure (DAI). The initial vision, perceived challenges and results of this effort is discussed in Hawrylycz et al. 2009. The plans and deliverables of this group were presented to an international panel of experts in the fall of 2009 for feedback and suggestions for future directions. Since then, this effort has evolved into two task forces, the *WHS Task Force*, which focuses on improving and circulation of WHS datasets, labels, and registrations between atlases used in the DAI, and the *DAI Task Force*, which focuses on technical aspects of interoperability within this framework.

These groups continue to build on this framework on multiple fronts:

- Evolving and building the DAI by developing atlas hubs in conjunction with development of the standards that tie these hubs together (abstracts: Zaslavsky, Representation of coordinate reference systems for the rodent brain in the INCF Digital Atlasing Infrastructure, and Zaslavsky, Development of community standards for brain atlas interoperability)
- Development of fiducials and a standard operating procedure for finding them in certain data types, which will be used to validate registration between the current atlases registered to WHS and for registering additional datasets to WHS (abstract: Sergejeva, Validation of landmark sets and their use for registration in mouse brain imaging)
- Bringing new data into WHS (abstract: Jiang, Diffusion Tensor Atlas of the Mouse Brain)
- Creation of a forum for community access and feedback to this work (abstract: Haselgrove, Demonstration of INCF Digital Atlasing Program Resources)
- Development of standards for registration transformations to enable transparency and sharing of these transforms to the community

In addition to this core group work, members of the task forces are incorporating the services offered through the DAI to build on the functionality of existing atlasing tools. These include Scalable Brain Atlas (SBA, scalablebrainatlas.incf.org, abstract: Bakker, Scalable Brain Atlas: From Stereotaxic Coordinate to Delineated Brain Region), Whole Brain Catalog (WBC, wholebraincatalog.org, abstract: Larson, An open Google Earth for neuroinformatics: The Whole Brain Catalog), and Mouse BIRN Atlasing Toolkit (MBAT, mbat.loni.ucla.edu, abstracts: Ruffins, MBAT, at the confluence of Waxholm Space, and Baldock, Coupling Existing Client and Server Software for Integrating WHS). Tying these to the DAI allows them to access diverse information and data from distributed resources, which results in powerful tools for neuroscientists. These new tools will enhance research in the internet age, and pave the way for efficient data sharing and interoperability of data. The taskforces are very engaged in preparing, facilitating and developing this platform for community collaboration.

The INCF digital atlasing program is a community effort and requires input from the scientific community. A workshop highlighting the advances of this program will be held September 2nd 2010 at the Portopia Hotel in Kobe, Japan; all are encouraged to attend.

References

1. Boline J, et al. (2007) 1st INCF Workshop on Mouse and Rat Brain Digital Atlasing Systems. Nature Preceedings, doi:10.1038/npre.2007.1046.1

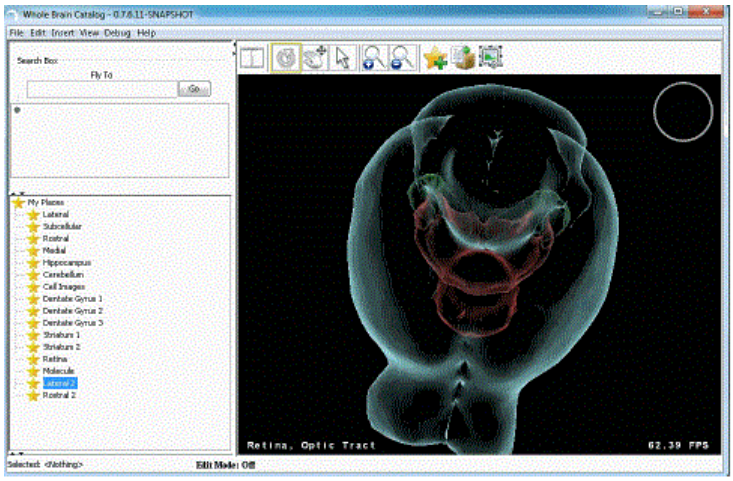
2. Hawrylycz M, et al. (2009) The INCF Digital Atlasing Program Report on Digital Atlasing Standards in the Rodent Brain. Nature Precedings doi:10.1038/npre.2009.4000.1

An open Google Earth for neuroinformatics: The Whole Brain Catalog

Stephen D. Larson, Christopher Aprea, Jesus Martinez, David Little, Vadim Astakhov, Han S. Kim, Ilya Zaslavsky, Maryann E. Martone, and Mark H. Ellisman

Center for Research in Biological Systems, University of California at San Diego, La Jolla, USA

The brain is a deeply intricate structure with important features of organization occurring at multiple spatial scales. Relevant data can be derived from subcellular junctional connectivity, cytoarchitectural local connectivity, and long-range topographical connectivity, just to name a few. This fact forces investigators to use a variety of different techniques to observe its structure, each of which tend to reveal only pieces of a vast puzzle. Because of this, neuroscience faces challenges to understanding the structure of the nervous system, including the problem of assembling structural data collected from the neuroscience community. To address this challenge, it would be useful to have a single system that is capable of the following functions: 1) upload data into a common data environment where it can be easily discovered and retrieved, 2) contextualize data by superimposing and combining related data from multiple scales, and 3) create hypothetical, synthetic views of structures of interest by stitching data together or generalizing patterns found in data. The framework would allow researchers to deal with their data both spatially, placing it in register in a common brain space, and semantically, annotating and tagging it with standard ontological terms. These two dimensions of data - spatial and semantic - create a key basis for organizing the heterogenous, scattered knowledge of the brain's structure into a cohesive whole. Inspired by Google Earth (an online virtual globe system that allows the superimposition of satellite and map imagery), we have created the Whole Brain Catalog (WBC; http://wholebraincatalog.org), an open source virtual brain system that allows the superimposition of multiple neuroscience imagery data, data sources and modalities. Goals of the Whole Brain Catalog include the ability to facilitate insight into data by putting it back within the context of the anatomy of the whole brain, and to allow investigators to make new connections between their data and other intersecting data sets and resources. The Whole Brain Catalog is composed of the following key elements 1) a 3D game engine that allows real-time rendering and interaction with 2D and 3D multi-scale data, 2) a user interface and a set of navigation controls that allow the user to make specific data sets visible, zoom to them, and manipulate them, 3) a spatial registry layer built in concert with services provided by the INCF Digital Atlasing Infrastructure task force that allows users to connect to additional data sources such as the Allen Brain Institute and the University of Edinburgh's EMAP system via spatial query, 4) a semantics layer built in conjunction with the INCF Program on Ontologies of Neural structures task force that allows users to connect to additional data sources such as NeuroLex.org via semantic query, 5) a simulation service that allows users to upload models to a cluster running a parallel version of the NEURON simulation engine, retrieve results, and render them as an animation, and 6) back-end web services and a data management layer that tie these elements together. While the Whole Brain Catalog is still a beta system, it is currently available for use and evaluation. The Whole Brain Catalog displays data in forms such as 3D meshes of subcellular scenes and of brain region territories, 3D volumetric data from MRI, EM tomography, and serial section EM, large 2D image sets from both EM and light level microscopy, and NeuroML / Neurolucida 3D neuronal reconstructions. The 3D brain region atlas is taken from the Allen Institute's mouse atlas, with the option to display the INCF Waxholm space brain regions, provided by the Duke Center for In Vivo Imaging, as an alternate atlas. We conclude that this platform takes a step forward to producing a shared knowledge environment for neuroscience that can handle the multiple scales and modalities of data within this complex domain.



Scalable Brain Atlas: From Stereotaxic Coordinate to Delineated Brain Region

Rembrandt Bakker[1], Stephen D. Larson[2], Sandra Strobelt[3], Andreas Hess[3], Daniel Wòjcik[4], Piotr Majka[4] and Rolf Kötter[1]

1. Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, Netherlands
2. Department of Neurosciences, University of California at San Diego, La Jolla, USA
3. Department of Pharmacology, Friedrich-Alexander-University, Erlangen, Germany
4. Nencki Institute of Experimental Biology, Warsaw, Poland

The Scalable Brain Atlas (SBA) is a web-based interactive brain atlas. It displays brain atlas templates (parcellations) for a variety of species and atlas providers. Brain regions can be selected to launch queries to other web-based resources or, websites can use the SBA to visualize sets of brain regions. The atlas templates are stored as a set of (preferably coronal) slices in Scalable Vector Graphics (SVG) format.

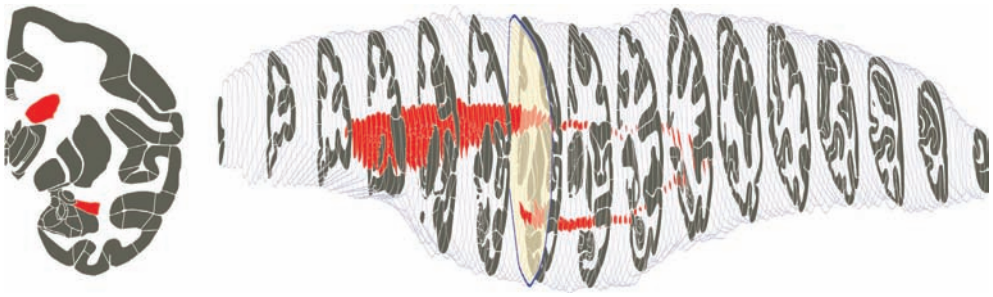
In support of the INCF Taskforce on Digital Atlasing Infrastructure (DAI), a number of services are built on top of the SBA. A user guide is available at http://scalablebrainatlas.incf.org/howto.

1] Thumbnail Service, which allows other websites to embed visual representations of a named brainsite in their code. This service is called as http://scalablebrainatlas.incf.org/thumbnail.php?Q, where Q contains parameters specifying brain atlas, structure name and appearance of the returned image. Internally, the service generates a quasi 3D representation of the brain region, and performs an SVG-to-PNG conversion using the GraphicsMagic php-module. An image cache is maintained to reduce server load. This service is extensively used by the NeuroLex Semantic Wiki pages at http://neurolex.org.

2] Coordinate to Brain Region service, which translates a stereotaxic coordinate to a named brain region. This service is called with parameters specifying the atlas space, and the X, Y and Z stereotaxic coordinates. It is implemented by first finding the slice nearest to coordinate X. The SVG image of this slice is converted to a color-coded PNG image. The Y,Z coordinate is then rescaled to a pixel value; the color value of this pixel provides the key to the brain region name. We plan to also support probabilistic brain atlases, returning a list of region names sorted by probability.

3] Atlas Template to Atlas Space Projection service, which projects an atlas template onto a non-native atlas space. 'Atlas template' refers to the segmentation of the brain in distinct regions, whereas an 'Atlas Space' represents the shape of an individual or averaged brain, typically derived from MRI data, CT scans and/or from stacks of histochemically prepared slices. This service relies on warping services provided by other hubs in the DAI framework. The warping can be guided by the gray/white matter contours, or by sets of fiducials: landmarks that are clearly distinguishable in both spaces. Two use cases are supported: (a) Display a stereotaxic coordinate from a non-native space on a chosen atlas space. For example, a Paxinos-Franklin mouse coordinate can be displayed in Waxholm space. This service finds the brain region at the warped coordinate, and opens the SBA with the brain region highlighted and the coordinate marked. (b) Display an entire template in non-native space. This service relies on precomputed template transformations. It can be combined with (a) to display a stereotaxic coordinate onto the warped template.

The SBA and its services are open source, and not species- or atlas specific. We actively search for new atlas templates to be imported into the SBA. The first and featured template is the Paxinos et al. Macaque atlas, manually traced by the Rolf Kötter group. In addition to this we are importing a number of Macaque parcellations provided by the David van Essen lab, using their Caret software, as well as the Martin-Bowden atlas. For the mouse, we have imported the Allen reference brain atlas from their application program interface, and we acquired an automatically labeled coarse partitioning of the Waxholm space. We are currently working with Sandra Strobelt and Andreas Hess to get the Paxinos and Franklin (2nd ed.) template into the SBA, based on manually redrawn polygons. Finally, the group of Daniel Wójcik is developing algorithms to replace the tedious process of manually creating polygons from scanned atlas templates by automated parsing of pdf/eps source files.



Construction of database of the 3-dimentional digital brain atlas of a rodent Degu (Octodon degu)

Noriko Kumazawa[1], Mariko Katayama[1], Shiro Usui[2], Tsutomu Hashikawa[3] and Atsushi Iriki[1]

1. Laboratory for Symbolic Cognitive Development, BSI, RIKEN, Saitama, Japan
2. Neuroinformatics Japan Center (NIJC), BSI, RIKEN, Saitama, Japan
3. Support Unit for Neuromorphol Analysis, BSI, RIKEN, Saitama, Japan

Purpose: The Caviomorph rodent degu (*Octodon degu*) is native to highland of Chile. Their social systems are unique and quite different from those of rats and mice. The degus live in tight-knit, extended family unit with complicated social behaviors, such as vocal communications. They are diurnal, so that they are well-sighted. We demonstrated that Degu can be trained to use a tool, T-shaped rake. Thus, degu has recently become increasingly important as experimental animals in researches of higher cognitive brain function. There exists only a line-drawing brain atlas of degu, but not histological or MRI brain atlases. So, we constructed stereotaxic histological and MRI brain atlases of degu to make it easier to find their anatomical structures by constructing 3-dimentional model with various functions such as the rotating and sectioning functions. Methods: To confirm the stereotaxic orientation of sections in the brain used for the atlas, reference tracts were made perpendicular to the horizontal (1 mm anterior and 2 mm right lateral from ear bar zero) and coronal (4mm upper and 1.5mm right lateral from ear bar zero). The animal's head was removed and stored for a minimum of 2 days in 4% Paraformaldehyde (PFA). After fixing the brain, the MRI images are acquired by Bruker 400 Ultrashield (9.4T). The frontal and parietal bones were removed to expose the brain. Gelatin-embedded brain was coronally cut on a freezing microtome at 50μ of thickness. A series of Nissl sections were prepared for microscopic imaging. The photographs of stained brain sections were taken with the Olympus virtual slide system (VS-100). After trimming of brain pictures using Adobe Photoshop, we have constructed 3-dimentional digital volume-rendering brain model of degu by a software "SG-eye" which we originally developed with company "Fiatlux". We have annotated the brain regions according to the anatomical terms in "The Rat Brain in Stereotaxic Coordinates" by Paxinos, G. and Watson, C. We have constructed database of stereotaxic 3-dimensional brain atlas of degu with the Neuroinformatics Base Platform System "XooNIps" which have developed by Neuroinfomatic Japan center (NIJC) of Brain Science Institute (BSI). This project is supported by BSI-NIJC. Results: We have constructed database of stereotaxic 3-dimensional brain atlas of degu with Xoonips. In the 3-dimentional model, we are able to see histological images and MRI images at the same cross sections of the 3-dimentional model in the same screen. The advantages of this brain atlas are axis readjusting, freely rotating and sectioning function. These functions help us to see the model from any angels we want, and make 3-dimensional brain atlas of degu more useful. Conclusions: Newly developed 3-dimensional stereotaxic histological brain atlas of degu will be very useful for researchers working in various fields of neuroscience, such as electrophysiological recordings, lesion studies, tract tracing, drug administration experiments, behavioral examination, and so on.

Demonstration of INCF Digital Atlasing Program Resources

Christian Haselgrove[1], Janis Breeze[2], G. Allan Johnson[3], and Jyl Boline[4]

1. University of Massachusetts Medical Center, Worcester, USA
2. INCF Secretariat, Stockholm, Sweden
3. Duke University, Durham, NC, USA
4. Informed Minds, Inc., Wilton Manors, USA

The INCF Digital Atlasing Program was formed to review the state of mouse and rat brain digital atlasing systems and recommend next steps to make rodent brain data more widely accessible and usable. At this stage the program is moving forward on two fronts, the Waxholm Space Task Force addressing a standard space for rodent brains (considering both its definition and reference data) and the Digital Atlasing Infrastructure Working Group developing ways of making the atlas available to end users and making it possible to apply the benefits of a common space to users' data. While both fronts have resulted in numerous best practices and lessons learned, tangible results of the atlasing program have, to date, been mainly proof-of-concept in nature. We present here the first demonstration of the publicly available resources resulting from the Digital Atlasing Program.

We present waxholmspace.incf.org, which hosts the following products of the Digital Atlasing Program:

* Information about the program and task forces
* Meeting schedule, timelines, and goals
* News and updates
* A description of Waxholm Space (WHS), the WHS atlas, and best practice documents
* The canonical WHS dataset, labels, and links to derived datasets
* Transformation services and information about hubs
* The Scalable Brain Atlas
* An embedded viewer to navigate high-resolution images and download those of interest
* Reports and publications
* Movies and figures

as well as:

* Links to other tools that interact with WHS and other Digital Atlasing Program resources
* Links to other INCF programs, including PONS and the Metadata Task Force
* A forum for community participation and feedback

The site is itself a product of the Digital Atlasing Program and has provided its own opportunities for best practices and lessons learned. Making these diverse resources available in a coherent and usable way has involved bringing together subject matter experts, technical experts, and usability experts in ways that have been as novel to the average individual researcher as have been the challenges in meeting the primary goals of the atlasing program. As such, we hope that the best practices and lessons learned from designing and building waxholmspace.incf.org will be as useful as the products of the Digital Atlasing Program that are made available on the site.

MBAT at the Confluence of Waxholm Space

Seth Ruffins[1], Daren Lee[1] , Stephen D. Larson[2], Ilya Zaslavsky[3], Lydia Ng[4], and Arthur Toga[1]

1. Laboratory of NeuroImaging, University of California Los Angeles, Los Angeles, USA
2. Department of Neurosciences, University of California at San Diego, La Jolla, USA
3. San Diego Supercomputer Center, University of California at San Diego, La Jolla, USA
4. Allen Institute for Brain Science, Seattle, USA

The INCF Digital Atlasing Infrastructure (DAI) task force is developing a canonical three-dimensional representation of the mouse brain called Waxholm Space (WHS). The WHS model is based on high resolution(21 µm3 isotropic voxels) T1, T2 and T2* MRI scans of a single C57Bl/6 male adult mouse brain. The model also contains brain parcellations which act as gross organizational bins. The WHS model set acts as common space for mapping features, properties and the distribution of molecules in the brain. Such mappings allow WHS to be a common spatial framework for accessing multiple mouse brain resources. The MouseBIRN Atlasing Toolkit (MBAT), developed at LONI provides an easy to use interface for accessing online resources spatially mapped to WHS. A workflow using MBAT in conjunction with INCF DAI spatial registry and the INCF Program on Ontologies of Neural Structures, has been developed to demonstrate how novel experimental data can be examined with respect to online resources. We will demonstrate the common task of identifying where a biological signal resides in the brain and what other information is known about that region using the following scenario: An investigator wants to know where in the mouse brain a probe accumulates in the brain and what genes are highly expressed in these regions. 1- The image and WHS model is loaded into MBAT's registration workspace as a source and template images respectively. 2- Correspondence points are selected in the template image and matched in target. The registration is performed. 3- The user selects point on the registered experimental image where signal is apparent. 4- The user then selects the source(s) (such as Allen Reference Atlas, ABA, AGEA, MGI, Paxinos mouse brain atlas, etc.) to be queried and sends the point coordinates to the spatial registry. 5- Selected source(s) return a list of entries for the selected points and anatomical terms. This scenario is a common real world task that can greatly expedited with the use MBAT as an integration hub for INCF DAI using WHS.

Representation of coordinate reference systems for the rodent brain in the INCF Digital Atlasing Infrastructure

Jyl Boline[1], Richard Baldock[2], Seth Ruffins[3], Lydia Ng[4], Fons Verbeek[5], Albert Burger[6], Rembrandt Bakker[7], Stephen D. Larson[8], Asif Memon[8], Ilya Zaslavsky[8] and Michael Hawrylycz[4]

1. Informed Minds, Inc., Wilton Manors, USA
2. MRC Human Genetics Unit and IGMM, Edinburgh, UK
3. University of California Los Angeles, Los Angeles, USA
4. Allen Institute for Brain Science, Seattle, USA
5. Leiden University, Leiden, Netherlands
6. MRC Human Genetics Unit and Heriot-Watt University, Edinburgh, UK
7. Radboud University, Nijmegen, Netherlands
8. University of California at San Diego, San Diego, USA

Digital atlases of rodent brain contain large volumes of 2D and 3D imagery, gene expression, electrophysiological and other information. Federating these atlases is one of the goals of the INCF Digital Atlasing Infrastructure (INCF-DAI) Task Force. To enable such federation, we rely on a collection of spatial and semantic translations that convert location and structure name information, respectively, between atlas-specific coordinate systems and semantic conventions. Transforming coordinate information, in turn, requires that the spatial reference system (SRS) of each atlas is formally described. We present an initial specification of coordinate reference system that can be applied across different rodent brain atlases, which has been developed in the course of INCF-DAI work on infrastructure for brain atlas interoperability.

Construction of reference coordinate systems for the brain is not straightforward as we have to deal with variations in the anatomy (size/shape) of individual animals; not to mention dependency of the spatial-temporal pattern information on specific procedures for sample preparation. Existing atlases present brain information in either 2D or 3D, and often differ with respect to coordinate system origin and coordinate axis orientations, while metadata about metric units or neuroscience interpretation of coordinate dimensions is often scattered over various textual descriptions. In addition the assumption of a simple cartesian axes valid over the whole is an approximation for the adult brain but completely inappropriate for the developing brain where curvature of the posterior-anterior axis changes dramatically as the brain develops.

In geodesy, where thousands of coordinate systems for different parts of the world have been developed and systematized over centuries, the community came to a common treatment of spatial reference systems. Standard SRS metadata is cataloged in an authoritative registry (http://www.epsg-registry.org/): each SRS is assigned an identification code which is used by researchers and software developers to find coordinate system description and invoke coordinate transformations.

Our goal is to create a similar authoritative registry for the brain, containing standard descriptions of spatial reference systems used in neuroscience. We present a prototype of such registry, which at the time of writing contains formal descriptions of several SRS for the mouse brain, including those used in the Allen Brain Atlas, the reference Waxholm Space, the Paxinos and Watson stereotaxic system, and coordinate descriptions used in the Edinburgh Mouse Atlas Project. The prototype information model of rodent brain SRS includes the following components:

1) Key SRS metadata, in particular SRS origin, units, coordinate axes specified with respect to common directions in the brain (ventral, dorsal, anterior, posterior, left and right)
2) Anatomical structures segmented in 2D or 3D, including information about the ontology in which the structure is described and a pointer to respective spatial representation of the feature
3) Fiducials (landmarks): points or higher-dimensional features related to the segmented anatomical structures, which can be used to relate this SRS with other systems
4) Orientations: specification of coordinate axes when they do not align with common neuroscience orientations but can be presented as a function of the latter (e.g. for the developing brain)
5) Slices: list of plates in a 2D reference atlas with their characteristics (if the atlas represents a set of 2D plates)

We will demonstrate how such anatomical structure-based characterizations of mouse brain coordinate systems are catalogued and managed within the emerging INCF infrastructure for digital brain atlases. We also demonstrate how this information is used to support on demand coordinate transformations, when a researcher needs to discover and analyze information available for a given point of interest in various atlases.

Dynamic causal modelling reveals involvement of premotor cortex during speech perception

Karsten Specht and Berge Osnes

Department of Biological and Medical Psychology, University of Bergen, Bergen, Norway

Several reports of pre-motor cortex (PMC) involvement in speech perception have been put forward. However, the functional role of PMC and impact on speech perception processes remains unclear and divergence exists between theoretical interpretations (see Scott et al., 2009 for review). The controversial discussion on PMC involvement in speech perception was recently supplemented by corresponding findings in nonhuman primates, summarized by Rauschecker and Scott (2009). They suggest a functional, bi-directional loop linking areas for speech perception and speech production. This hypothesized loop originates in the auditory cortex and runs through the superior temporal gyrus (STS), inferior frontal cortex, pre-motor cortex, and inferior parietal lobe back to the auditory cortex, thus connecting also the assumed "dorsal" and "ventral" stream for speech processing (Hickok and Poeppel, 2007). Rauschecker and Scott (2009) propose that the loop have different computational functions. The loop generates 'forward models' that predict consequences of actions, important in perception and imagery Secondly, the system generate 'inverse models' to decide on which motor commands are appropriate for a required result. However, such dynamic and interactive processes are difficult to delineate with conventional imaging analysis alone.

In order to test such a PMC involvement, we designed a parametric study where we presented parametrically varied speech stimuli in a functional Magnetic Resonance Imaging (fMRI) study. White noise was transformed over seven distinct steps into a speech sound. As control condition served a transformation from white noise into a music instrument sound. The fMRI data were modelled with Dynamic Causal Modelling (DCM) where the effective connectivity between Heschl's gyrus, planum temporale, superior temporal sulcus and pre-motor cortex were tested.

The fMRI results revealed a graded increase in activation in the left superior temporal sulcus. Pre-motor cortex activity was only present at an intermediate step when the speech sounds became identifiable but were still distorted, but was not present when the speech sounds were clearly perceivable and were not involved at all when the sounds evolved into a sound from a music instrument. The applied DCM models differed in the type of modulation and the directionality of their respective influence. A Bayesian model selection procedure favoured a model which contained beside significant interconnections between Heschl's gyrus, planum temporal and superior temporal sulcus also significant bidirectional connections between pre-motor cortex and superior temporal sulcus, but only a unidirectional connection from planum temporale to pre-motor cortex when speech sounds were processed. When music sounds were processed all connections to pre-motor cortex became non significant. Since the highest level of motor activity was observed when participants listened to distorted speech and diminished as the sound became more easily identifiable as speech sounds, it is concluded that pre-motor cortex is not generally necessary for speech perception but may facilitate interpreting a sound as speech when phonological information is sparse.

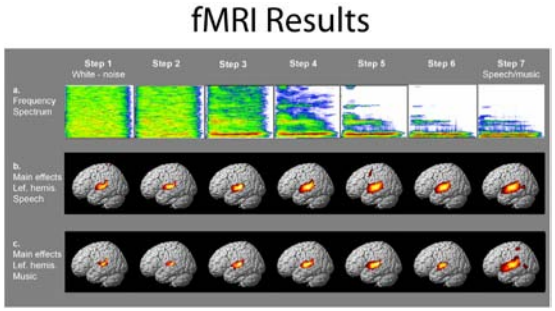


Figure 1

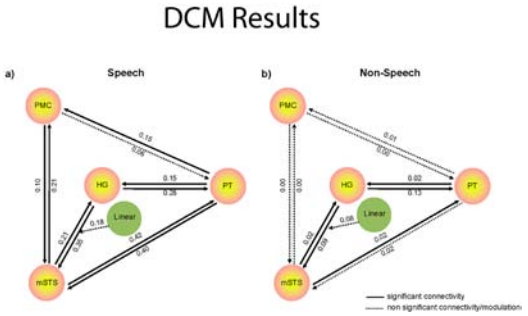


Figure 2

References

1. Hickok G, Poeppel D (2007) The cortical organization of speech processing. Nat.Rev.Neurosci. 8:393-402

2. Rauschecker JP, Scott SK (2009) Maps and streams in the auditory cortex: nonhuman primates illuminate human speech processing. Nat. Neurosci. 12:718-724.

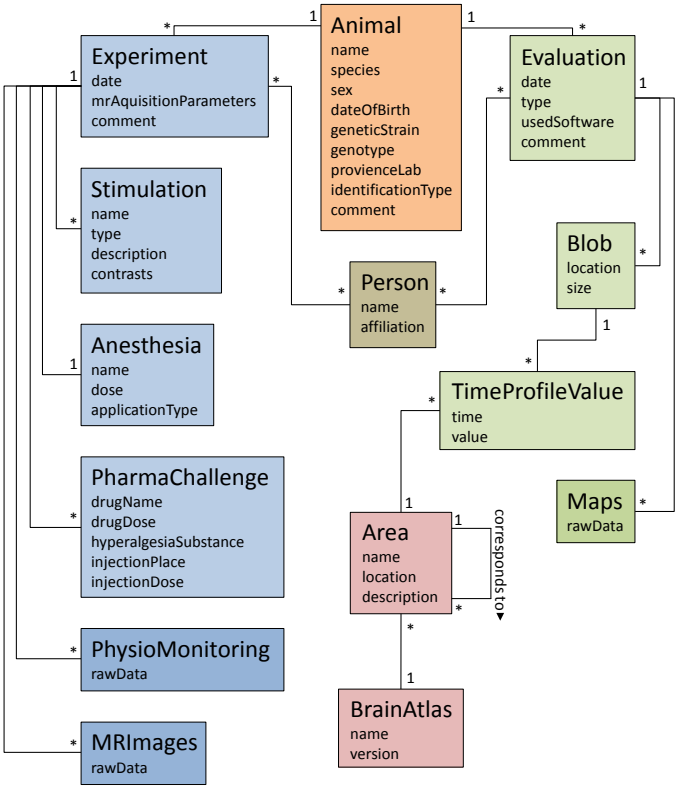
3. Scott SK, McGettigan C, Eisner F (2009) A little more conversation, a little less action--candidate roles for the motor cortex in speech perception. Nat.Rev.Neurosci. 10:295-302

RodImAnD: a MySQL-Database for analysing functional MRI Data from rodents in drug research

Andreas Hess[1], Laura Konerth[1] and Manuel Andre Gaudnek[2]

1. I. f. Pharmacology, Erlangen, Germany
2. Neural Information Processing Group, Technische Universität Berlin, Berlin, Germany

Purpose
Neuroscience has been revolutionized by two superior technologies: Functional brain imaging by MRI (fMRI), allowing repetitive, non-invasive observation of CNS functions, and mouse genomics, providing mice with defined deviations giving insight into molecular processes of brain function. The combination of these cutting-edge technologies opens a new avenue in brain research: Defining the role of gene products for delineating brain regions involved in information processing, in our case pain research in hypo- and hyper-algesic transgenic mice. The investigation of gene-drug-interactions incorporates the exploration of a high-dimensional space spun by variables like mouse strain, stimuli (i.e., different painfulness), analgesic drugs and differential response of brain regions of the pain matrix. Here even the pure administration of the huge amount of generated data is a complex task. Therefore, we aimed at developing a database allowing for (1) structured organization of the fMRI-data and (2) dynamic and interactive access to the data for performing statistical evaluation. Moreover, the integration of various other data sources like ABA, INCF WHS (see contributions on this meeting) becomes easily possible. This integrated database for brain function in transgenic mice strongly supports data sharing and collaboration with other working groups. Method We developed a database using the relational MySQL database management system, which works on many different system platforms and allows access from every SQL-aware application. The free integrated environment MySQL Workbench is used for database engineering. The database scheme reflects the workflow of the experiments (Fig. 1). The tables contain information about MRI measurement, experimental animals (including physiological monitoring), stimuli and pharmacological substances used during acquisition. Moreover, the database keeps track of the analysis tools used, their parameterisation and versions. Our major image analysis tool (MagnAn) is based on IDL (® ITTVIS), a high-level development environment for data analysis and visualization. Data is passed from the database and vice versa via a Java-based bridge component, which could easily be ported to other Java-capable environments, e.g. MATLAB. After acquisition the data are stored in the database alongside a first analysis grouping activated voxels into so-called blobs. The user can then select a group of experiments, e.g. different transgenic mice for same stimulation conditions, including already present analysis results and perform higher order analysis like average map generation on these data. The results are passed back to the database and linked to the original measurement. Results We obtained a data management system that allows for more efficient data handling, reading and processing. Compared to earlier storage in file folders, which implies a data organisation hierarchy complicating searches beyond the folder structure, lookups based on complex filter criteria are now easily possible. The laborious and error-prone manual assembly of interrelated data is eliminated. Search results include old matching experiments which might have been overlooked without a central database, effectively enlarging the base of statistical analysis and possibly reducing the need for new experiments. Furthermore, compared to file system based storage, interrelated datasets cannot be displaced, renamed or cleared accidentally. Conclusion: The presented database allows for an effective storage and retrieval of the huge amount of f MRI data and their subsequent analysis. It is more robust than pure file system based storage and simplifies and encourages the reuse of formerly acquired results. The possibility of reusing results will largely increase as other groups start to incorporate their data into the database. This will hopefully further decreasing the need for new animal experiments and thereby supports animal welfare (3R concept).



Pressure-induced performance decrement in verbal fluency task through prefrontal overactivation: A near-infrared spectroscopy study

Hiroyuki Ito[1], Hoshiko Yamauchi[1], Hitoshi Kaneko[2], Toru Yoshikawa[3] and Kenji Nomura[2]

1. Graduate School of Education and Human Development, Nagoya University, Nagoya-shi, Japan
2. Center for Developmental Clinical Psychology, Nagoya University, Nagoya-shi, Japan
3. Department of Psychiatry for Parents and Children, Nagoya University, Nagoya-shi, Japan

Purpose
Pressure to perform well can paradoxically decrease performance. Researchers in various fields of psychology—social facilitation and inhibition, test anxiety, and choking under pressure—are investigating this phenomenon. There are 3 possible explanations for the paradoxical effects of pressure. Arousal theories (Cottrell, 1972; Zajonc, 1965) suggest a motivation-based explanation that pressure-induced performance decrement is mediated by excessive drive or arousal. Thus, performance decrement is possibly associated with the autonomic nervous system (ANS) activities—representative indices of arousal. On the other hand, attentional-distraction (Landers, 1980; Nideffer, 1992) and explicit-monitoring (Carver & Scheier, 1978; Jackson & Beilock, 2008) theories suggest a cognition-based explanation that pressure to perform at optimal levels causes top-down interference, which consumes working memory load or interrupts proceduralized routines. Thus, pressure-induced performance decrement is possibly related to excessive cortical activity, especially in the prefrontal area, which is highly involved in the working memory systems.

To test these contradictory hypotheses, we investigated the relationship between autonomic arousal, prefrontal activation, and performance in a letter cancellation task (LCT) and verbal fluency task (VFT) under evaluative pressure. Our previous study with n-back tasks revealed that pressure-induced performance decrement was related to prefrontal activation and not to the ANS activities (Yamauchi, et al., 2009). Therefore, in this study, we further tested these hypotheses by using different tasks.

Method
Twelve undergraduate students executed the LCT and VFT under high- and low-pressure conditions. During the tasks, prefrontal activation was measured using near-infrared spectroscopy (NIRS)—a noninvasive hemodynamic technique to measure human cortical activities. Skin temperature, skin conductance level, heart rate, and blood volume pulse amplitude were also measured to assess ANS activities. In high- but not in low-pressure conditions, the participants were informed that their performance would be compared with that of other students; moreover, they would receive an incentive of up to 500 Japanese yen (approximately 5 USD) depending on their rank. They executed the 2 tasks once in each pressure condition. In the LCT, they crossed out the given target letters from a list of random letters for 80 seconds in each condition. In the VFT, they generated Japanese words beginning with the given letters for 120 seconds in each condition.

Results
The performance in the LCT did not significantly differ between the 2 pressure conditions. However, performance in the VFT was poorer in the high- than in low-pressure condition. Consistent with these behavioral data, oxyhemoglobin concentration (oxy-HB)—the main indicator of cortical activation on NIRS—was not influenced by pressure in the LCT but increased with increase in pressure in the VFT. On the other hand, the levels of 4 ANS indicators increased with increase in pressure in the both tasks. A correlation analysis revealed that pressure induced performance decrement in the VFT correlated with oxy-HB ($r = -.62$, $p < .05$; Figure 1), and not with ANS measures.

Conclusions
Pressure-induced performance decrement occurred only in the high cognitive load task—the VFT. Similarly, prefrontal activation increased with pressure only in the VFT. On the contrary, ANS activities increased with increase in pressure, regardless of the task. Moreover, pressure-induced performance decrement in the VFT correlated with prefrontal overactivation and not with ANS activities. These results are consistent with our previous findings (Yamauchi, et al., 2009) and support the cognition-based explanation and not the motivation-based explanation of pressure-induced performance decrement.

Yamauchi H, Ito H, Yoshikawa T, Nomura K, & Kaneko H (2009) Prefrontal activation, autonomic arousal and task performance under mental pressure: A near-infrared spectroscopy study. The 11th European Congress of Psychology.

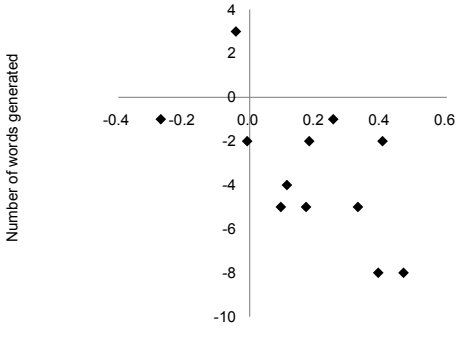


Figure 1 Correlation of pressure-induced performance decrement in verbal fluency task with prefrontal overactivation

The brain correlates of subsequent recollection: what can activation likelihood estimation meta-analysis tell us about memories formation?

Lionel Landré[1], Christophe Destrieux[2], Caroline Hommet[3] and Michel Isingrini[1]

1. UMR-CNRS 6234 CeRCA, University of Tours, Tours, France
2. Hospital of Tours, UMRS Inserm 930, University of Tours, Tours, France
3. Hospital of Tours, UMRS Inserm 930, CMRR Région Centre, University of Tours, Tours, France

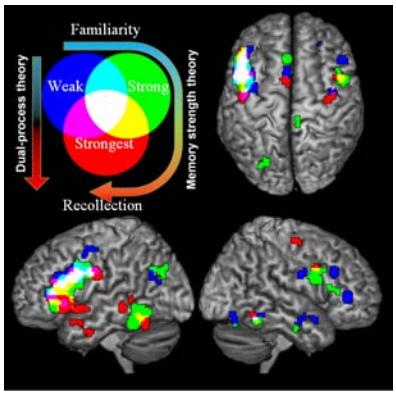
Background
Neural correlates of memory encoding represent a central question in neuropsychological field, especially for stroke or dementia assessment. The extensive investigation of functional brain correlates of memories formation has allowed consensual localisationist models of this phenomenon to be put forward, with a particular accent on mediotemporal and frontal sites. However, most of these studies relied on blocked paradigms that do not allow to differentiate between successful and unsuccessful encoding attempts. Moreover, it has been recently proposed that two distinct processes, with specific brain correlates, may support effective memories retrieval: familiarity and recollection. Still, little is known about the neural networks implied in these processes at encoding, and these neurocognitive dissociations may be attributed to memory strength effect, recollective memories being retrieved with higher levels of confidence. Event-related fMRI advance from the past decade has allowed to disentangle encoding-stage activities depending on subsequent retrieval state in various memory paradigms (Subsequent Memory Effect; SME), enabling direct comparison between the neural correlates of successful and unsuccessful memories formation. Moreover, encoding brain activity can be further differentiated on the basis of subsequent confidence judgements or memories elaboration level, allowing to compare the neural correlates of both dual process theory and memory strength effects. We here propose to address these particular issues using systematic whole-brain Activation Likelihood Estimation (ALE) analysis of verbal subsequent memory encoding studies, contrasting between weak and strong memories item-based activities versus familiar and recollective ones.

Methods
29 studies comprising non-ROI based, whole brain SME activation contrasts in healthy, mid-aged participants were selected for analysis. Data for the corresponding 43 contrasts were further classified according to subsequent confidence and recollective states. For each resulting set, peak coordinates were registered in a common stereotaxic space, and spatially filtered using a gaussian function. Statistical signifiance was then tested at $p < 0.05$ (FDR corrected) using 10000 permutations and cluster-wise thresholding. Results were eventually plotted on a generic brain template for comparison.

Results
Results broadly confirm the implication of a widespread frontal, mediotemporal and parietal network in successful memories formation. However, some structures characteristically activated in blocked paradigms, such as unimodal occipital areas, were not found to underlie encoding effectiveness. Conversely, areas thought to underlie non-memory-specific processes, such as word identification in the fusiform gyrus, were found to be involved in successful encoding.

Considering memory strength effects and recollective states, left inferior frontal gyrus was found to be massively implied in all kinds of successful encoding, with no distinction for weak and strong, or familiar and recollective subsequent memories. Parietal sites were found to be implied in familiarity-based encoding of either weak and strong memories, and left anterior hippocampus and perirhinal cortex were related to recollective-only memories, supporting a dual-process theory of memories formation. Conversely, left fusiform gyrus activity was associated with strong memories of either familiar or recollective type.

Conclusion
This meta-analysis enlightens the implication of a wide fronto-parieto-temporal network in effective memories formation, and futher questions current models of memory. While some regions activity is best described by dual-process theory, memory strength theory is found to be more congruent with others. Taken together, these results point out potential bridges between the two, depending on which "fragment of a larger whole" is considered.



Neuroimaging evidence of demand — reservation balance change in the aging brain: An analysis of hemodynamic response function during motor execution

Toshiharu Nakai[1], Epifanio Bagarinao[1], Makoto Miyakoshi[1], SH Annabel Chen[2], Wen-Yih I Tseng[3] and Kayako Matsuo[4]

1. Neuroimaging & Informatics Lab, National Center for Geriatrics and Gerontology, Ohbu, Japan
2. School of Humanities and Social Sciences, Nangyang Technorogical University, Singapore, Singapore
3. Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan
4. Department of Psychology, National Taiwan University, Taipei, Taiwan

Purpose

It was pointed out that the additional recruitment of brain areas in the elderly was consistent with the compensation hypothesis and characterized neuroplasticity at the systems level [1]. The difference in age-related changes of the BOLD signal (hemodynamic response function: HRF) among the visual areas suggested its physiological background of neuronal network adaptation in the elderly [2]. In this study, we investigated whether such age-related HRF change can be observed in the motor regulation network in order to further confirm the neuroimaging evidence of demand-reservation balance change. The sequential finger tapping task was employed, since it strongly demands activities of both primary and higher motor areas organizing the motor execution network. Method: Twenty-two healthy normal young subjects (< 50 years old, 11 males) and 22 healthy normal elderly subjects (60 - 75, 11 males) gave written informed consent to participate in this study. Two fMRI sessions were performed: 1) TAP: Sequential finger tapping task (2-3-4-5) at 1.5Hz paced by a prompting visual cue, 3 task blocks for each of the right and left sides interleaved with rest blocks, each 18 sec, 2) GRIP: gripping-opening movement of bilateral hands paced by visual presentation of the hand posture for each condition, 3 sec for each movement, 5 task and 6 rest blocks, each 18 sec. Functional data were obtained using a GRE-EPI sequence (TR = 2000 ms, TE = 24 ms, 39 axial slices, 3 mm thick, FOV = 19.2 cm) on a 3T MRI scanner. Functional images were processed using SPM5, and the center coordinates of the ROI (3x3x3 pixels) were determined (2nd level analysis, $p<0.001$). The BOLD signal was extracted using a Matlab module (BAX [3]). Results: The total cluster size of the elderly subjects was significantly larger than that of the younger (GRIP-R, GRIP-L and TAP-L; $p < 0.003$, TAP-R; $p < 0.015$). Activation in the following areas was augmented in elderly subjects ($p < 0.01$). 1) TAP-R: right d/vPMA, SMA, BA3, SPL; 2) TAP-L: left anterior operticulum, SPL, BA4, right SMA, vPMA, BA46/10, CG/ACG, para-hippocampal gyrus; 3) GRIP: bilateral IFG, SMA, SPL (BA7), SOG (BA19), IOG/LOG (BA37). In both experiments, the disappearance of mid-dip (transient HRF amplitude decrease between initial and post-stimulus peaks) was observed at differential peaks in the elderly subjects. In M1, differential activation was not significant between the two age groups ($p<0.01$) and mid-dip was not observed on the contralateral M1, although the averaged % HRF change was reduced on the contralateral side and augmented on the ipsilateral side in the elderly subjects. These results were compatible with the previous observations in visual areas [2]. Conclusions: The results suggested that brain activation was augmented to support the demand for cognitive processing of motor regulation rather than for motor execution itself. Age-related augmentation of brain activation in the higher motor areas, including the associated cortex, depended on the disappearance of mid-dip rather than the increase of % HRF. Mid-dip may represent the stand-by status of the higher motor areas during task performance, even if the demand was low in young subjects. Based on these observations, we hypothesize that the primary and higher motor areas always control a neuronal network unit with different degrees of activation, although the t-statistics for some may be under the threshold of detection using a standard HRF reference. It should also be noted that different HRF shapes between age groups or across brain areas might cause biases in statistical evaluation; for example, differential activation in ACG/CG may be underestimated because of the constant level of the initial-peak.

References

1. Heuninckx S et al., J Neurosci 28, 91-, 2008

2. Nakai T et al., in Early Detection and Rehabilitation Technologies for Dementia, 2010 (in press)

3. Bagarinao E et al., Neuroinformatics 6, 109-, 2008

CANDIShare: A Resource for Pediatric Neuroimaging Data

David Kennedy[1], Jean Frazier[2], Christian Haselgrove[2] and Steven Hodge[2]

1. Department of Psychiatry, University of Massachusetts Medical School, Worcester, USA
2. University of Massachusetts Medical School, Worcester, USA

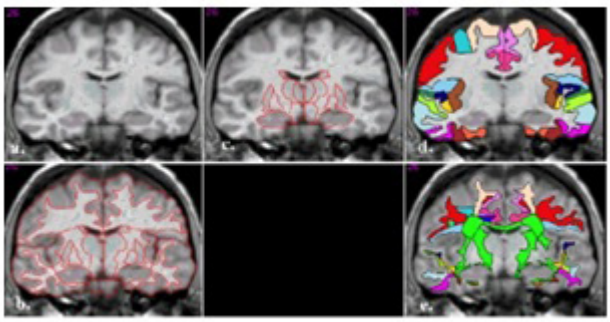
Introduction
There are numerous psychiatric disorders that can plague the development of children. Each of these disorders manifests as a distinct pattern of clinical, behavioral, etiological, neuroanatomic and neurofunctional characteristics that challenge the management of the individual patient, as well as the development of successful intervention and prevention strategies. In the area of neuroimaging, a substantial number of studies have been performed to date; and while much has been learned from this investment, this represents only the tip-of-the-iceberg of the information that can be gleaned from the data. Unfortunately, most of this additional, untapped information resource is lost due to ineffective use of the principles of data sharing and integration.

Approach
Using the existing resources of the eXtensible Neuroimaging Archive Toolkit (XNAT) and the Internet Brain Segmentation Repository (IBSR) we are making a large set of MR image and anatomic analysis data available to the general neuroinformatics community. These data include: a) Image data - including structural and diffusion imaging at 1.5 and 3.0 Tesla, where each subject includes a comprehensive set of clinical, demographic and behavioral measures; b) results for general segmentation (subdivision of the imaged brain in terms of gross neuroanatomic subdivisions of gray, white and CSF tissue classes) and parcellation (regional compartmentalization of cortex and white matter); and c) the creation and dissemination of static and dynamic probabilistic atlases from specific subsets of these data for use in other segmentation and analysis frameworks.

The dataset to be released has been collected over the past 10 years by the investigators at the Child and Adolescent Neurodevelopment Initiative (CANDI), now at the University of Massachusetts Medical Center. This is one of the largest collections of neuroimaging studies in child psychiatry. These data include 263 subjects, span the ages of 3-21 years, and include normative subjects (70) as well as children with ADHD (31), bipolar disorder (130) and childhood onset schizophrenia (32). 150 of these subjects have complete general segmentation, and 123 of these cases also have complete parcellation.

It is of fundamental importance to facilitate interactive sharing of data amongst neuroscience investigators, in general, and within the child psychiatry community in particular. This project seeks to apply existing data sharing mechanisms, and develop domain-specific sharing resources that connect the related aspects of the info-ome that are tailored to the needs of researchers in child psychiatry.

Conclusion
This release of information is dramatically greater than merely 'making the images available': each image is associated with substantial analytic results, many of which have been utilized in the preparation of various publications and comparisons. Moreover, these data will be most effectively shared with the research community when shared in a way that preserves the linkages between the images, the resultant analytic data and meta-data, and it's relationships to other public sources of related information. In short, this represents a 'Knowledge Management' environment that will facilitate traversal of these data and linkages.



A brain-behavior phenotype database consisting of data derived from comprehensive behavioral analyses of genetically engineered

Keizo Takao[1], Kazuo Nakanishi[2] and Tsuyoshi Miyakawa[3]

1. Center for Genetic Analysis of Behavior, National Institute for Physiological Sciences, Okazaki, Japan
2. Frontier Technology Center, Graduate School of Medicine, Kyoto University, Kyoto, Japan
3. Institute for Comprehensive Medical Science, Fujita Health University, Toyoake, Japan

Since 99% of mouse genes have homologous in humans, a large-scale project that is aimed to encompass knockouts of every gene in mice is in progress. Approximately 80% of all genes are expressed in brain and, to investigate their function in individual organisms, we should investigate their functions in the brain. We can identify the genes that have significant impact on the brain functions efficiently by examining the final output level of gene function in the brain, that is, behavior. The influence of a given gene on a specific behavior can be determined by conducting behavioral analysis of mutant mice lacking that gene. In brain-behavior phentoyping, phenotype data should be obtained systematically with reasonably standardized methods, and the data obtained in such projects should be included in a public database. Here, we introduce the development of a brain-behavior phenotypes database of mutant mice by using comprehensive and standardized phenotyping methods. The test battery covers sensori-motor functions, emotion, learning and memory, attention and so on. We have been constructing a relational database consisting of such data. So far, raw data of 164 indices in 19 tests from 120 strains, more than 7000 mice are stored in a FileMaker file. Raw data for each strain that was published in articles are available in the Mouse Phenotype Database (http://www.mouse-phenotype.org/). The utilization of our database may provide a progress in understanding gene-brain-behavior relationship. The database was developed as a part of Integrated Brain Research platform (IBR-PF), which has been succeeded by Comprehensive Brain Science Network platform (CBSN-PF), with support from INCF J-Node.

Probabilistic classification of presynaptic gene function using low-throughput generated functional data from genetic perturbation studies

Lennart Niels Cornelisse[1], Evgeni Tsivtsivadze[2], Tjeerd Dijkstra[2], Tom Heskes[2] and Matthijs Verhage[1]

1. Functional Genomics, Neuroscience Campus Amsterdam, VU University, Amsterdam, Netherlands
2. Intelligent Systems, Institute for Computing and Information, Radboud University, Nijmegen, Netherlands

Classification of gene function based on functional data from genetic perturbation studies is generally hampered by the fact that this data is often generated in different labs under different experimental conditions using technical challenging low-throughput experiment. Here we propose a novel probabilistic method to cluster genetic perturbations based on experimental parameters from low-throughput data, which can handle experimental variation between studies, incompleteness of data sets and different accuracy levels. The method uses mixtures of probabilistic principal component analyzers to cluster log-transformed perturbation data normalized to internal controls. We have applied this method to classify genes expressed in the synaptic terminal using electrophysiological data on synaptic transmission from genetic perturbation studies in Hippocampal autapses. Our analysis revealed three main functional clusters. In addition, we show that the majority of the genes affect spontaneous release and action potential induced release in a similar way suggesting both forms of release are recruited from the same vesicle pool. Finally, we find that some genes seem to have one main function whereas in other genes different domain mutations end up in different functional clusters.

Evolution-guided engineering of serine protease specificity

William Russ and Rama Ranganathan

Pharmacology / Green Center for Systems Biology, University of Texas Southwestern Medical Center, Dallas, USA

Proteins are remarkable for their ability to evolve new functional specificity over relatively short mutational paths. This process is poorly understood, and attempts to alter specificity based on structural intuition rely heavily on trial and error and lack an underlying principle. We have recently described a statistical analysis of coevolution in proteins (Statistical Coupling Analysis, or SCA) that suggests a novel approach to specificity engineering. In the family of S1A Serine Proteases, SCA has identified a set of coevolving residues (a "sector") that predicts and controls substrate specificity, but has evolved independently of sectors influencing stability or catalytic activity. Thus, SCA provides a clear prediction of residues that can be used to alter specificity independent of these other properties. Furthermore, the pattern of coevolution between positions suggests a structurally non-intuitive path of mutagenesis that could recapitulate an evolutionarily plausible route for functional divergence in this family. We are testing these hypotheses by designing proteins with mutations in the SCA specificity sector and assaying their functional properties in the laboratory.

References

1. Lockless SW, Ranganathan R (1999) Evolutionarily conserved pathways of energetic connectivity in protein families. Science 286(5438):295-9.

2. Halabi N, et al. (2009) Protein sectors: evolutionary units of three-dimensional structure. Cell 138(4):774-86

Molecular Dynamics Simulations of NMR structure of C-Terminal Fragment of Presenilin 1

Umesh Ghoshdastider[1], Krzysztof Mlynarczyk[1], Wojciech Pulawski[1], Michal Kolinski[1] and Slawomir Filipek[1,2]

1. Laboratory of Biomodelling, International Institute of Molecular and Cell Biology, Warsaw, Poland
2. Faculty of Chemistry, University of Warsaw, Warsaw, Poland

Purpose
Presenilin 1 (PS1) is a catalytic component of ã-secretase complex which plays a pivotal role in the development and progression of Alzheimer's Disease (AD) that affects more than 25 million people worldwide. It cleaves the Amyloid Precursor Protein into Amyloid â peptides which aggregate in the brain of the Alzheimer's patients. It also has other substrates like Notch which is involved in cell signaling. The ã-secretase complex comprises of four proteins: PS1, nicastrin, APH-1, and PEN-2.

PS1 belongs to intramembrane proteases which process its substrates inside the lipid bilayer. Many of the mutations linked to the Early-onset Alzheimer's Disease is linked to PS1. During activation PS1 is proteolytically cleaved into N-terminal (NTF) and C-terminal fragments (CTF) each containing one catalytic aspartate residue. Although the topology of the NTF is well accepted, it is somewhat controversial for CTF. Here we have validated the first structure of CTF obtained from NMR studies in SDS micelles by performing molecular dynamics (MD) simulations in detergent micelles and lipid bilayer.

Method
To achieve a large simulation time required for micelles formation and proper sampling of conformational space, a coarse grained MARTINI forcefield was used in Gromacs program. For micelles simulations, we used 200 DPC (dodecylphosphocholine) coarse-grain molecules in the periodic box 12 nm x 12 nm x 10 nm filled with water grains. Additional coarse-grain simulations using MARTINI forcefield were performed in dilauroylphosphatidylcholine (DLPC) and dipalmitoylphos-phatidylcholine (DPPC) bilayers. The all-atom MD simulations of CTF were carried out using the Implicit Membrane Model in CHARMM program.

Results
During the 3 µs MD simulation of the CTF in detergent the micelles were created and the central one formed around the protein contained about 80 molecules of detergent. The rearrangement of PS1 were also visible especially in extracellular loop region which grouped in one area. The angles between transmembrane helices stayed similar to those in NMR structure indicating that this part is stable in micelle environment as shown in Fig 1.

The CTF structures obtained in bilayer simulations (both coarse-grain and all-atom) showed larger difference to that of NMR structure. The angle between helices 7 and 8 remained relatively stable but dependent on membrane width, whereas that between partial helices 9a and 9b were changing. It suggests that micelles environment is better for CTF rather than lipid bilayer in absence of other components of ã-secretase complex.

CTF structure revealed by NMR studies has three membrane spanning regions which is in agreement with the nine transmembrane domain model of presenilin 1. However, it has novel characteristics in order to facilitate intramembrane catalysis. It contains a putative half-membrane-spanning helix N-terminally harboring the catalytic aspartate, a severely kinked helical structure toward the C terminus as well as a soluble helix in the assumed-to-be unstructured N-terminal loop.

Conclusions
As shown in the molecular dynamics simulations, the structure obtained after simulation in micelles is structurally close to that of NMR structure in SDS micelles. However, to get insight into the whole structure of ã-secretase complex the additional investigations are required for structure of other parts of the complex and also to reveal molecular role of AD mutations and substrate recognition.

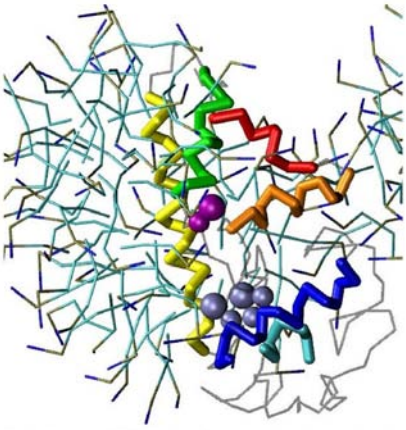


Fig 1: Structure of CTF after 3µs of coarse grain molecular dynamics simulation in micelles. *Coloring scheme:* hα in cyan, hβ in blue, h7 in green, h8 in yellow, h9a in orange and h9b in red. Catalytic residue Asp385 is shown as purple spheres (two spheres in CG representation) while PAL motif is shown as cold-blue spheres.

References

1. Sobhanifar S, Schneider B, Löhr F, Gottstein D, Ikeya T, Mlynarczyk K, Pulawski W, Ghoshdastider U, Kolinski M, Filipek S, Güntert P, Bernhard F, Dötsch V (2010) Structural investigation of the C-terminal catalytic fragment of presenilin-1. PNAS, In Press

2. Marrink SJ, Risselada HJ, Yefimov S, Tieleman DP, de Vries AH (2007) The MARTINI force field: Coarse grained model for biomolecular simulations. J Phys Chem B 111:7812–7824

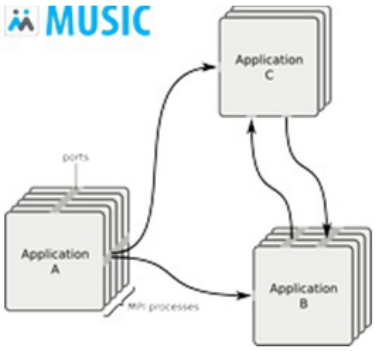
3. Lazaridis T (2003) Effective energy function for proteins in lipid membranes. Proteins 52:176–192

MUSIC software enabling runtime data exchange between parallel neuronal simulators

Mikael Djurfeldt[1], Örjan Ekeberg[2], Tobias Potjans[3] and Markus Diesmann[4]

1. PDC, INCF and Royal Institute of Technology, Stockholm, Sweden
2. CB/CSC, Royal Institute of Technology, Stockholm, Sweden
3. Institute of Neurosciences and Medicine, Research Center Jülich, Jülich, Germany
4. Brain Science Institute, RIKEN, Wako-shi, Japan

MUSIC is an API allowing large scale neuron simulators to exchange data within a parallel computer during runtime. It promotes interoperability between models written for different simulators and allow these to be re-used to build a larger model system, a multi-simulation. MUSIC provides mechanisms to transfer massive amounts of event information and continuous values from one parallel application to another. Since the API enforces independence of the applications, the multi-simulation can be built from pluggable component modules without adaptation of the components to each other in terms of simulation time-step, data allocation strategies or topology of connections between the modules. Special care has been taken to ensure that existing simulators can be easily adapted to MUSIC. A prototype implementation of the API in the form of a C++ library was released under the GPL license early 2009. It is part of major Linux distributions and can be downloaded from the INCF Software Center.



Three applications (A, B, and C) execute in parallel while exchanging data via MUSIC. The software interface promotes interoperability by allowing models written for different simulators to be simulated together in a larger system. It enables re-usability of models or tools by providing a standard interface. As data are distributed over a number of processors, it is non-trivial to coordinate data transfer so that it reaches the correct destination at the correct time.

References

1. Djurfeldt M, Hjorth J, Eppler JM, Dudani N, Helias M, Potjans T, Bhalla US, Diesmann M, Hellgren Kotaleski J and Ekeberg Ö (2010) Run-Time Interoperability Between Neuronal Network Simulators Based on the MUSIC Framework. Neuroinformatics 8:43-60

NineML – A description language for spiking neuron network modeling: The user layer

Anatoli Gorchetchnikov
Boston University, Boston, USA

With an increasing number of studies related to large-scale neuronal network modeling, the International Neuroinformatics Coordinating Facility (INCF) has identified a need for standards and guidelines to ease model sharing and facilitate the replication of results across different simulators. To create such standards, the INCF formed a program on Multiscale Modeling with a goal to develop a common standardized description language for neuronal network models. The name of the proposed standard is Network Interchange for Neuroscience Modeling Language (NineML) and its first version is aimed at descriptions of large networks of spiking neurons.

The design of NineML is divided in two semantic layers: an abstraction layer that provides the core concepts, mathematics and syntax with which model variables and state update rules are explicitly described and a user layer that provides a syntax to specify the instantiation and parameterization of a network model in biological terms.

The user layer of NineML is intended to be primarily machine-readable and uses XML syntax. It is designed with a focus on ease of parsing, verification, and automatic model construction. This does not prevent advanced users from editing the user layer XML descriptions by hand, but the primary means for creation of these descriptions is expected to be software tools that will convert GUI- or script-based representations of objects and properties into valid XML.

The user layer provides the syntax for specifying the model and parameters to be used to instantiate the key elements of a spiking neuron network. This includes descriptions of individual elements (cells, synapses, inputs) and the constructs for describing the grouping of these entities into networks. In addition the user layer defines the syntax for specifying a range of connectivity patterns.

NineML aims to provide a tool to explicitly define a spiking neuron network model both conceptually and mathematically in a simulator independent manner. In addition, NineML is designed to be self-consistent and highly flexible, allowing addition of new models and mathematical descriptions without modification of the previous structure and organization of the language. To achieve these goals, the language is being iteratively designed using several seminal papers (see [1-3] for examples) as test cases.

References

1. Morrison A, Aertsen A, and Diesmann M (2007) Spike timing dependent plasticity in balanced random networks. Neural Computation 19:1437-1467.
2. Hill SL, Tononi G (2005) Modeling sleep and wakefulness in the thalamocortical system. J Neurophysiol 93:1671-1698.
3. Vogels TP and Abbott LF (2005) Signal propagation and logic gating in networks of integrate-and-fire neurons. J Neurosci 25(46):10786-10795.

Modeling realistic morphologies of genetically labelled layer 5 pyramidal neurons

Patrik Krieger and Risto Laakso

Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

The feasibility of computational construction of realistic morphologies with NETMORPH was studied in case of genetically labeled layer 5 pyramidal neurons from mice cerebral cortex (Groh et al 2010). The NETMORPH-framework for stochastic generation of realistic neuronal morphologies has been recently introduced by Koene et al (2009). Morphological data of layer 5 pyramidal neurons from different neocortical areas was quantitatively analyzed for dendritic and axonal shape patterns and their frequency distributions were used to optimize parameters of the dendrite and axon growth process. The computationally generated morphologies were compared with experimental data and model parameter values were compared between neurons from different neocortical areas. Optimized model parameter values were then used to generate large scale networks of neurons.

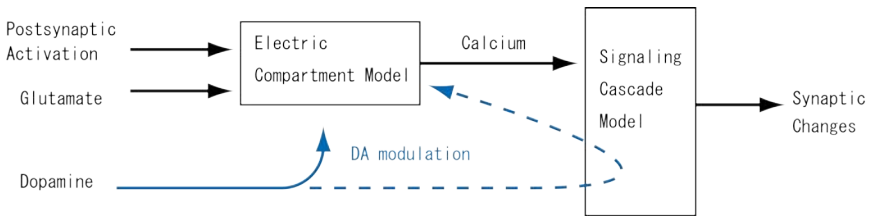
Electrophysiological and molecular mechanisms of synaptic plasticity in the striatum: multi-scale simulation of molecule and cell

Takashi Nakano, Junichiro Yoshimoto, Jeff Wickens and Kenji Doya

Okinawa Institute of Science and Technology, Onna, Okinawa, Japan

The striatum receives glutamatergic input from the cortex and dopaminergic input from the substantia nigra. These inputs, acting together, induce long-term change of corticostriatal synaptic strength, which plays a critical role in learning from reward. Although a number of laboratories have investigated corticostriatal synaptic plasticity, contradictory results and properties have been reported and it is difficult to elucidate the dependence of corticostriatal synaptic plasticity on dopamine, as well as the timing of presynaptic inputs and spike output only by experimentation. To clarify electrophysiological and molecular mechanisms behind the plasticity of striatal synapses, we have constructed models of medium spiny neurons at cellular and molecular levels: an electric compartmental model with a realistic cell morphology (Nakano et al., 2009), and a molecular signaling pathway model (Nakano et al., 2010). These two models operate at different time scales and spatial scales. There are interactions between the two levels. For example, the activation of a postsynaptic signaling cascade is affected by the whole cell electric activity. This makes it difficult to understand the mechanisms only by single models and we need to construct a multi-scale model. In this study, we connected the two models serially, as shown by the solid line in the Figure.

First, we constructed an electric compartment model with realistic morphology obtained from our experiments, to investigate the glutamate and dopamine timing effects on the calcium responses and its electrophysiological mechanisms. The parameters were adjusted based on electrophysiological data. The model prediction was that the calcium response is maximal when the glutamate input leads the postsynaptic spike, and that this spike-timing-dependent calcium response was facilitated when the dopamine preceded the glutamate. This suggests the possibility that dopamine timing regulates corticostriatal spike-timing dependent synaptic plasticity (STDP) through its effect on the calcium response. Second, we constructed a signaling pathway model of synaptic spines expressing D1-type dopamine receptors and examined the mechanisms of dopamine- and calcium-dependent plasticity. The model predicted the synaptic changes induced by dopamine and calcium inputs. The positive feedback loop including dopamine- and cAMP-regulated phosphoprotein of molecular weight 32 kDa (DARPP-32) shows bistability and its activation by dopamine input induces dopamine dependent long-term potentiation (LTP). Calcium input alone also caused synaptic efficacy change through several pathways as CaMKII and PP1. The model predicted that the timing of calcium and dopamine inputs has only minor effect on the synaptic change. Finally, by connecting the two models, we predicted synaptic efficacy change induced by a variety of strength and timing of glutamate and dopamine inputs. Although dopamine modulation of channels and receptors is mediated through signaling cascades (blue dashed line in the figure), here, for simplicity, we used output of the electric compartment model as a calcium input for the signaling cascade model. To connect two models, the output data from the electric compartment model was fed as the input to the cascade model. The model reproduced some types of synaptic plasticity which were reported by experiments: 1) High-frequency stimulation (HFS) induces calcium influx, which leads to long-term depression (LTD). 2) HFS in up-state induces a strong calcium response and LTP. 3) LTP is also induced by HFS with dopamine input. 4) STDP is reproduced when NMDA receptors currents are enhanced. The major new findings from the combined system were that the time integral of the calcium response is a good indicator of the synaptic plasticity and that the major effect of the dopamine timing is through its modulation of the calcium response rather than through the temporal response of the molecular signaling cascade.



References

1. Nakano T, Doi T, Yoshimoto J, Doya K. (2010) A kinetic model of dopamine- and calcium-dependent striatal synaptic plasticity. PLoS Computational Biology, 6(2): e1000670

2. Nakano T, Yoshimoto J, Wickens J, Doya K. (2009) Calcium responses model in striatum dependent on timed input sources. 19th International Conference on Artificial Neural Networks (ICANN), Part I: 249-58

Energetics-based simulation of 3D neuronal network: neurogenesis-inspired structure generation

Ashutosh Mohan[1], Venkateswaran Nagarajan[2], Sudarshan Sekhar[2], Sharath N K[2], Subbu Ramanathan[2]

1. JCSMR, Canberra, Australia
2. Waran Research Foundation, Chennai, India

Our work at WARFT is to create a simulation model for the human brain which encompasses properties and dynamics from the molecular to the large-scale intercortical processing level. Such a simulation model in addition to furthering noninvasive study of human brain will also help in disease modelling and drug discovery. Two important challenges to this project that are currently being addressed are generation of detailed neuronal circuits and energetics-based simulation of these circuits. The former is discussed in this poster while the latter is addressed in a companion poster. A summary of previous work on these problems can be found in the references. In this poster, we propose a novel and biologically realistic neurogenesis-based for structure generation and computation study of the developmental aspects of human brain. Heuristics are developed from the experimental studies in the development of brain circuits. This is a young and burgeoning field and not much is understood about the link between neurogenesis and eventual structure of adult brain circuits and their functionality. Thus, in order to develop a complete and representative set of heuristics, massive collaboration with experimental studies is required. The developed heuristics are then encoded in the form of a gene sequence. Using these gene sequences we generate large neuronal circuits. Any perturbation in the gene sequence results in a faulty circuit and helps in the study of developmental diseases of the human brain. In order to validate the method, we also form a set of plausible and biologically realistic heuristics. In addition, have formulated gene sequences using optimal encoding schemes because of the lack of experimental data. Armed with heuristics and gene sequences, we generate large circuits and study the impact of alteration in gene encoding on the structure and properties and eventually the functionality of neuronal circuits. A neurogenesis-based approach hasn't been proposed before and it can lead to interactive collaboration between computational studies and experiments studying developmental aspects of human brain.

References

1. N.Venkateswaran et al, "Towards Predicting Multi-Million Neuron Interconnectivity involving Dendrites-Axon-Soma Synapse: A Simulation Model", 7th International Conference on Computational Intelligence and Natural Computing in conjunction with 8th Joint Conference on Information Sciences (JCIS 2005) July 21 - 26, 2005, Salt Lake City, Utah, 2005

2. N.Venkateswaran and R Rajesh, "Partitioned Parallel Processing Approach for Predicting Multi-Million Neuron Interconnectivity in the Brain: Involving Soma-Axon-Dendrites-Synapse", BICS 2004 Aug 29 - Sept 1 2004

3. Nagarajan V and Mohan A (2009). Towards linking blood flow and neural activity: Petri net-based energetics model for neurons. Frontiers in Systems Neuroscience. Conference Abstract: Computational and systems neuroscience 2009. doi: 10.3389/conf.neuro.06.2009.03.337

Energetics based simulation of large-scale 3D neuronal network: Energetics-Based Models

Ashutosh Mohan[1], Venkateswaran Nagarajan[2], Sudarshan Sekhar[2], Sharath N K[2] and Subbu Ramanathan[2]

1. Department of Neuroscience, JCSMR, Canberra, Australia
2. Waran Research Foundation, Chennai, India

The MMINi-DASS project is a reverse engineering attempt to predict brain interconnectivity by statistical comparison of simulated and experimental BOLD maps. The benefits of such a project include non-invasive study of human brain and fault-simulation to better understand brain diseases. In the long run, the MMINi-DASS project will facilitate drug discovery and testing for brain diseases. Generation of a simulated BOLD map is a hard problem. We propose an energetics-based model with a petrinet representation for large-scale neuronal simulation that makes this problem easier to solve. See references for an initial overview of MMINi-DASS and energetics-based simulation. Petrinets are used to model single neuron energetics involving mitochondrial placement and energy production, ATP trafficking to various cellular entities - especially those involved in neuronal signal generation and neuron-capilary interaction. Thus, a single unified model describes both the signal processing and energy budget of a neuron. This, we believe will simplify the generation of BOLD maps. Using petrinets to represent the energetics model also simplifies its simulation at the network level with an event-based simulator like MMINi-DASS. Thus, the model developed is not only biologically detailed but is also amenable to large-scale simulation studies. Some major challenges have been addressed. It is a hard problem to build petrinets which produce non-trivial and interpretable results without oversimplifying and making as few assumptions as possible. While the Krebs cycle is easy to represent with a petrinet, energy trafficking in the cell in conjunction with signal production is not well-characterized because we do not yet completely understand the biological underpinnings. There are two reasons though to believe that such an exercise is not premature. Firstly, The optimization-based approach of the MMINi-DASS project might lead to some clues about single neuron energetics. This might in turn lead to predictions which can be experimentally verified. Secondly, the petrinet representation is very general and isn't tied down to the particular details. It is a holistic representation of the system. Current and continuing work is to refine the petrinet and make it more precise.

References

1. N.Venkateswaran et al, "Towards Predicting Multi-Million Neuron Interconnectivity involving Dendrites-Axon-Soma Synapse: A Simulation Model", 7th International Conference on Computational Intelligence and Natural Computing in conjunction with 8th Joint Conference on Information Sciences (JCIS 2005) July 21 - 26, 2005, Salt Lake City, Utah, 2005

2. Nagarajan V and Mohan A (2009). Towards linking blood flow and neural activity : Petri net-based energetics model for neurons. Frontiers in Systems Neuroscience. Conference Abstract: Computational and systems neuroscience 2009. doi: 10.3389/conf.neuro.06.2009.03.337

NEST: Science-driven development of neuronal network simulation software

Susanne Kunkel[1,2], Jochen M. Eppler[1,2], Hans Ekkehard Plesser[3,4], Marc-Oliver Gewaltig[5], Markus Diesmann[4,6] and Abigail Morrison[1,2,4]

1. Functional Neural Circuits Group, Albert-Ludwig University of Freiburg, Freiburg i. Br., Germany
2. Bernstein Center Freiburg, Freiburg i. Br., Germany
3. Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Aas, Norway
4. RIKEN, Brain Science Institute, Wako, Japan
5. Honda Research Institute Europe, GmbH, Offenbach am Main, Germany
6. Brain and Neural Systems Team, RIKEN Computational Science Research Program, Wako, Japan

NEST is a simulator for heterogeneous networks of point neurons or neurons with few compartments (e.g. stick-and-ball models) [1]. It is suited for a broad range of neuronal network modeling approaches and computer architectures: from single- or multi-threaded simulations of small and medium sized networks on standard desktop computers, to distributed simulation of large networks on computer clusters or HPC facilities such as BlueGene. Distributed simulations exhibit excellent scaling up to the order of one thousand processors, and research is ongoing to extend the scalability into the range of ten thousand processors and beyond [2,3]. NEST is developed by the NEST Initiative, an international contract-based collaboration between academic and industrial research institutes.

NEST is subject to continuous development to provide its users with cutting-edge features and respond to the demands of current questions in neuroscience. Recent features include the incorporation of new neuron models such as the MAT(2) model [4] and spike-timing and neuromodulation dependent plasticity [5,6]. To increase its user-friendliness and exploit software trends in the neuroscience community, NEST enables users to extend its functionality through dynamically linked modules and interact with the software using a Python-based user interface PyNEST in addition to the native simulation language SLI [7]. NEST also supports the MUSIC interface to communicate with other simulators [8] and provides visualization tools [9] and a topology module that facilitates concise specification of spatial structure [10]. The developers also continually improve the underlying algorithms, e.g. for the calculation of 'off-grid' spike times and the integration of non-linear neuron models such as the AdEx model [11,12,13].

Frequent releases of the NEST software provide the users with the newest technology and the developers with feedback about bugs and potential improvements. Release stability is supported by an automated test suite [14]. The NEST user community is active and growing, in part due to its use in large national and international projects, such as the Next-generation supercomputing project of MEXT and FACETS as well as at summer schools, for example, the Advanced Course in Computational Neuroscience and the Okinawa Computational Neuroscience Course. A list of neuroscientific publications that use NEST is available on the website, as is the current release of the source code (www.nest-initative.org). A convenient option for those wishing to try out NEST is the LiveCD, which enables easy, platform-independent testing of our simulation software.

Acknowledgements:
Partially supported by Next-Generation Supercomputer Project of MEXT, Japan, DIP F1.2, Helmholtz Alliance on Systems Biology, EU Grant 15879 (FACETS), BMBF Grant 01GQ0420 to BCCN Freiburg, the Research Council of Norway under grant 178892/V30 (eNeuro), the Junior Professor Advancement Program of Baden-Württemberg, and the Honda Research Institute Europe GmbH.

References

1. Gewaltig M-O & Diesmann M (2007) Scholarpedia 2(4):1430

2. Plesser HE et al. (2007) Springer-Verlag LNCS 4641, 672-681

3. Kunkel S et al. (2009) Front. Neuroinform. doi: 10.3389/conf.neuro.11.2009.08.044

4. Kobayashi R et al. (2009) Front. Comput. Neurosci. 3:9

5. Morrison A et al. (2007) Neural Comput. 19, 1437-1467

6. Potjans W et al. (2010) Implementing neuromodulated plasticity in distributed simulations. (submitted)

7. Eppler JM et al. (2009) Front. Neuroinform. 2:12

8. Djurfeldt M et al. (2010) Neuroinformatics 8(1):43-60

9. Nordlie E & Plesser H (2010) Front. Neuroinform. 3:39

Brain-scale simulations with NEST: supercomputers as data integration facilities

Tobias C. Potjans[1,2], Susanne Kunkel[3,4], Abigail Morrison[3,4,5], Hans Ekkehard Plesser[6,5], Rolf Kötter[1,7] and Markus Diesmann[2,5]

1. Institute of Neuroscience and Medicine, Research Center Juelich, Juelich, Germany
2. Brain and Neural Systems Team, RIKEN Computational Science Research Program, Wako, Japan
3. Bernstein Center Freiburg, Freiburg, Germany
4. Functional Neural Circuits, Faculty of Biology, Albert-Ludwigs-University, Freiburg, Germany
5. RIKEN Brain Science Institute, Wako, Japan
6. Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Aas, Norway
7. Donders Institute for Brain, Cognition and Behaviour, NeuroPi.org, Radboud University Medical Centre, Nijmegen, Netherlands

Neural network simulations are currently making a qualitative leap, leaving the regime of highly specialized "single-scale" models that incorporate only limited aspects of biological data, but focus on the multi-scale nature of the brain. These developments are fueled by the advent of computing power at the peta-scale which is increasingly becoming available to computational (neuro-)scientists all over the world (see e.g. http://www.prace-project.eu/, http://www.nsc.riken.jp/, http://www.ncsa.illinois.edu/BlueWaters). In order to optimally employ this computing power in the context of neural network modeling, we identify two main requirements:

(1) Suitable simulation technology has to be made available that can efficiently represent multi-scale brain networks on supercomputers and rapidly solve the network's activity dynamics.
(2) A new class of models needs to be developed comprising multiple scales from the local microcircuit to the macroscopic brain network consistently with available data.

In the past years, simulation technology development focused on the representation of the local cortical network consisting of approximately 100,000 neurons and 1 billion synapses on standard HPC clusters (http://www.nest-initiative.org). The construction of models resolving the layer- and type-specific connectivity structure of the cortical microcircuit integrated a large body of experimental data ranging from anatomical and electrophysiological studies to photostimulation and electron microscopy [1]. The comparison of the simulated network activity and experimentally observed *in vivo* cell-type specific activity reveals the consistency as well as potential shortcomings of the available data and models. We show that this class of models successfully captures prominent microscopic activity features such as layer-specific spike rates and the interplay of excitation and inhibition in the propagation of transient feed-forward inputs as observed *in vivo* (e.g. [2]).

In order to address the activity dynamics and the function of the local network in the context of the embedding in a network of multiple cortical areas, next generation multi-scale neural network simulations have to simultaneously represent the local microcircuit and the macroscopic connectivity structure (e.g. [3]). These brain-scale network simulations approach a regime where the number of cores is larger than the number of synapses per neuron. Therefore, corresponding data structures for the network representation have to make use of the sparseness of connections but nevertheless allow rapid network construction and spike delivery to target neurons. Models on this scale drastically increase their self-consistency and explanatory power because they explicitly incorporate most of the long-range inputs to neurons that were previously modeled as abstract external inputs but make up around 50% of all synaptic inputs. The advanced data integration now not only combines multiple methods but also multiple scales, linking microscopic and macroscopic connectivity.

Here, we present the scale-up of the NEST simulation tool (http://www.nest-initiative.org) up to tens of thousands of processors on the JUGENE supercomputer (http://www.fz-juelich.de/jsc/jugene) and quantify time-memory trade-offs. Furthermore, we summarize our efforts in the construction of brain-scale network models that integrate a vast amount of data on multiple scales. In this concept supercomputers are utilized as data integration facilities.

Partially supported by the Next-Generation Supercomputer Project of MEXT, Japan, the Helmholtz Alliance on Systems Biology, EU Grant 15879 (FACETS), McDonnell Foundation Collaboration Grant, Research Council of Norway Grant 178892/V30 (eNeuro) and JUGENE Grant JINB33.

References

1. Potjans TC, Diesmann M (2008) Consistency of in vitro and in vivo connectivity estimates: statistical assessment and application to cortical network modeling. Proc. 38th SfN Meeting, 16.1.

2. Sakata S, Harris KD (2009) Laminar structure of spontaneous and sensory-evoked population activity in auditory cortex. Neuron 64:404-418.

3. Reid AT, Krumnack A, Wanke E, Kötter R (2009) Optimization of cortical hierarchies with continuous scales and ranges. NeuroImage 47:611-617.

Multi-physical simulation for cellular morphogenesis based on dynamic cytoskeleton

Seigo Nonaka, Honda Naoki and Shin Ishii
Graduate School of Informatics, Kyoto University, Uji-shi, Japan

During embryonic development, cells differentiate to various kinds with specific morphologies which are reflected by cellular functions. For examples, motile cells have structures of lamellipodia and filopodia and neurons have prominent polarized morphology with axon and dendrites. The cellular morphogenesis is a complicated phenomenon, during which a cell receives extracellular signals, processes this information through intracellular signal transduction, and regulates the reorganization of cytoskeleton such as actin filament and microtubules, which directly control the cell shape. Although microscopic properties of cytoskeleton such as (de-) polymerization, capping and branching have been identified, filament-based understanding for macroscopic morphogenesis remains largely unclear. To fill in this hierarchical gap between micro- and macro-scopic phenomena, we have constructed a multi-physical simulator for dynamics of cellular morphology, integrating reaction-diffusion, actin filament and plasma membrane. In this simulation, reaction-diffusion field and membrane are discretized as compartments and nodes, respectively. Actin filament is addressed as a rigid line segment and is assumed to generate driving force against the membrane based on elastic-ratchet model. Using this simulator, we demonstrated chemotactic migration. For realistic simulation, there was a problem of computational cost, because a number of actin filaments are expressed inside a cell (#10^8). The highest-cost calculation is collision detection between actin filament and membrane nodes. To resolve this problem, we adopt parallelization technique (in computer science) to allocate the partial simulation processes related to actin filament to multiple CPUs and calculate the collision detection independently. Then, it successfully accelerated the run-speed almost proportional to the number of CPU in the limited condition. In this presentation, we will report the mathematical model for simulation and some biological applications.

Learning spatio-temporal visual features by a large-scale neural network model

Naoto Yukinawa and Shin Ishii

Graduate School of Informatics, Kyoto University, Uji, Kyoto, Japan

The cortical (re)organization of the primary visual cortex induced by environmental scenes is fundamental for obtaining efficient representations of various features of natural images which are utilized in the further information processing. There have been extensive studies which investigated relationships among visual stimuli, neural development, and the plasticity by several approaches including physiology and computational modeling. However, quantitative analysis by feasible amount of measurements or models which reflect biologically examined neural structures is still difficult and has not been largely explored. In this study, our goal is to model and simulate receptive filed organization of V1 and the spatio-temporal dynamics by a realistic-scaled network consisting of biologically sufficient numbers of spiking model neurons in order to capture macroscopic cortical modification due to the synaptic plasticity induced by visual experience during developmental stages. Assuming the primary visual pathway including retinal ganglion cells (RGCs), LGN cells, and simple cells in V1, we modeled a neural network architecture based on the two-layered model including ON-center and OFF-center RGCs and cortical simple cells (Thorpe, Delorme, and Van Rullen, 2001). Our model has an additional layer which consists of LGN cells with or without lagged input from retinal cells in order to incorporate temporal dynamics of input stimuli. The cortical neurons are implemented by spiking neuron model and retinotopically organized into neuronal maps in which they shared the same synaptic weights. Whenever the synaptic weight of a neuron is modified, the same modification is applied to the entire population of neurons within the map. Inhibition is also presented between neuronal maps. We implemented and simulated our model by means of the NEST (Gewaltig and Diesmann, 2007). We show that our model obtains spatio-temporal receptive fields after some exposure to video sequences. We will validate our model from both quantitative and qualitative aspects by simulation analysis using natural visual stimuli assuming developmental stage learning and later stage learning such as perceptual learning in near future.

References

1. Thorpe S, Delorme A, Van Rullen R (2001) Spike-based strategies for rapid processing. Neural networks 14:715-725 Gewaltig MO, Diesmann M (2007) NEST. Scholarpedia 2(4):1430

A thalamocortical network model in NeuroML

Padraig Gleeson, Matteo Farinella, Guy O. Billings and Angus R. Silver

Department of Neuroscience, Physiology and Pharmacology, University College London, London, UK

NeuroML (http:/www.neuroml.org) is a language based on XML for expressing biophysically detailed neuronal network models. The most recent version of this language (Gleeson et al., 2010) can be used to express models of voltage and ligand gated ion channels, fixed and plastic synaptic mechanisms, complex neuronal morphologies with distributed conductances and network connectivity in 3D space.

NeuroML is being developed as part of an international initiative with the aim of making compartmental neuronal and network models more accessible, to allow such models to be validated across a wider range of simulators and to facilitate exchange and reuse of model components between researchers.

The network model developed by Traub et al., (2005) is one of the most advanced multicompartmental network models created to date. This model features principle cells and interneurons from multiple layers of the cortex and the thalamus connected according to anatomical data. We have converted all of the cell models from Traub et al. (2005) to NeuroML and have successfully reproduced the spiking behaviour of the cells across the neuronal simulators NEURON, GENESIS and MOOSE. We have also created a Layer 2/3 network model based on Cunningham et al., (2003) using these cell models. This and more advanced network models will be shown in this demonstration.

NeuroML based network models can be created, reconfigured and visualised using neuroConstruct (http://www.neuroConstruct.org). Moreover, simulations can be automatically generated and run on the above mentioned simulators. The network models can also be generated for execution in parallel computing environments using Parallel NEURON significantly speeding up run time.

Our results show that even in complex networks featuring multiple cell types and thousands of excitatory, inhibitory and electrical synapses, convergence in the behaviour of subcellular variables and spike times between simulators is possible. However, this agreement often only occurs at the limits of spatial and temporal discretisation. This highlights a strong dependence of the exact spike times of a cell model on the method of numerical integration and illustrates the benefit of NeuroML enabled model validation across simulators.

Making highly detailed cell and network models such as this available in a simulator independent language, coupled with simulator and graphical development environment support will allow a wider range of neuroscientists to use, build on and improve these complex models in their investigations.

The work on converting this model to NeuroML has been funded by the Welcome Trust, Medical Research Council and the EU Synapse project. Details on funding for the NeuroML initiative are at http://www.neuroml.org/acknowledgments.

References

1. Gleeson P, Crook S, Cannon R, Hines M, Billings GO, Farinella M, Morse TM, Davison AP, Ray S, Bhalla US, Barnes SR, Dimitrova YD, Silver RA (2010) NeuroML: A Language for Describing Data Driven Models of Neurons and Networks with a High Degree of Biological Detail PLoS Computational Biology, in press

2. Traub RD, Contreras D, Cunningham MO, Murray H, LeBeau FE, Roopun A, Bibbig A, Wilent WB, Higley MJ, Whittington MA (2005) Single-column thalamocortical network model exhibiting gamma oscillations, sleep spindles, and epileptogenic bursts. J Neurophysiol 93: 2194-2232.

3. Cunningham MO, Whittington MA, Bibbig A, Roopun A, LeBeau FE, Vogt A, Monyer H, Buhl EH, Traub RD (2004) A role for fast rhythmic bursting neurons in cortical gamma oscillations in vitro. Proc NatlAcadSci U S A 101: 7152-7157.

Kernel Current Source Density method: CSD estimation for arbitrary distribution of contacts in one, two, and three dimensions

Jan Potworowski[1], Wit Jakuczun[2], Szymon Łęski[1] and Daniel Wòjcik[1]

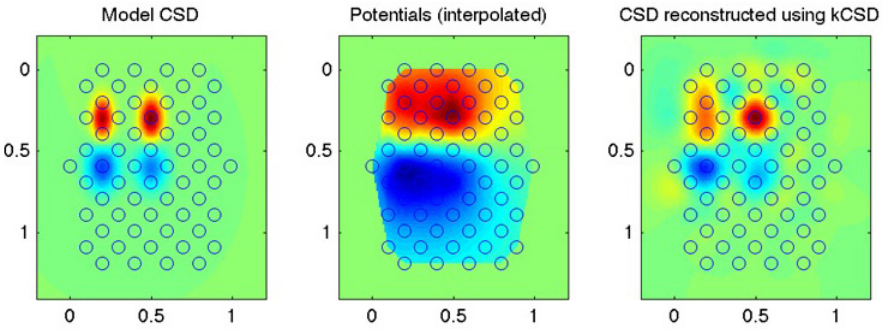
1. Department of Neurophysiology, Nencki Institute of Experimental Biology, Warszawa, Poland
2. WLOG Solutions, Warszawa, Poland

Extracellular recordings of electric potential are an important technique in the studies of neural activity in vivo and in vitro. In the last few years we observe rapid development of technology for large scale electrical recordings. Various types of multi-electrodes were devised to simultaneously record extracellular potentials from multiple spatial locations. The low-frequency part of these recordings, the local field potentials (LFP), is considered to be a signature of the dendritic processing of synaptic inputs. Since LFP is a non local measure of neural activity, with contributions from neurons located more than a millimeter away from the electrode, its direct interpretation is difficult. Thus if only possible it is useful to estimate the current source density (CSD), the volume density of net transmembrane currents, which is the source of the LFP. CSD is directly related to the local neural activity and current source density analysis is a popular tool in the analysis of multivariate LFP.

In homogeneous and isotropic tissue CSD is given by the laplacian of the potentials, so discrete differentiation is the simplest estimate if we have a set of potentials measured on a regular grid. However, if we interpolate so obtained values and ask if the sources which generated the potentials we measured can be given by the interpolated CSD, the answer is usually negative. To find a better answer to the question of possible generating source recently a new method for CSD estimation has been developed, called the inverse CSD (iCSD) method. The main idea behind iCSD is to assume a specific parametric form of CSD generating potentials, calculate the LFP in a forward-modeling scheme to obtain the values of CSD parameters. The iCSD framework developed so far requires an assumption of a specific geometry of contacts and new calculations are needed for every new electrode distribution. All the variants up to now assumed recordings on regular, rectangular grids. Moreover, the complexity of the reconstructed CSD distribution was limited by the number of observations.

Here we present a new, nonparametric method for CSD estimation. The kernel CSD method (kCSD) is based on kernel techniques, widely used in machine learning. kCSD lets the user specify the family of allowed CSD distributions in more intuitive way through over-complete bases. It also makes it possible to employ knowledge of anatomy and physiology of the probed structure, such as laminar structure. The assumption of regular electrode arrangement is not necessary, we show how kCSD can be applied to recordings from electrodes distributed at any positions on one-, two-, and three-dimensional sets with equal ease. Moreover, it turns out that kCSD is a general non-parametric framework for CSD estimation including all the previous variants of iCSD methods as special cases.

Partly supported from grants POIG.02.03.00-00-003/09 and PBZ/MNiSW/07/2006/11.



Left: model CSD, superimposed are the positions of recording contacts of a multi-electrode array used in (Wirth and Luescher, 2004). Middle: potentials which would be measured on the grid (interpolated using splines). These are the data one would work with without employing current-source density analysis. Right: CSD as reconstructed using the kernel CSD method.

References

1. Pettersen, KH, et al. (2006) Current-source density estimation based on inversion of electrostatic forward solution: effects of finite extent of neuronal activity and conductivity discontinuities. J Neurosci Meth 154: 116-33.
2. Wirth, C, Luscher, HR (2004) Spatiotemporal evolution of excitation and inhibition in the rat barrel cortex investigated with multielectrode arrays. J Neurophysiol 91: 1635.
3. Łęski, Szymon, et al. (2007) Inverse Current-Source Density Method in 3D: Reconstruction Fidelity, Boundary Effects, and Influence of Distant Sources. Neuroinformatics 5: 207-222.

odML Format and Terminologies for Automated Handling of (Meta)data

Jan Grewe, Thomas Wachtler and Jan Benda

Department Biology II, Ludwig-Maximilians-Universitaet Muenchen, Planegg-Martinsried, Germany

For analysis, management, and sharing of experimental data, metadata that provide information about data acquisition and experimental conditions are indispensable. Computer-based analysis and data management requires this meta information to be stored and exchanged in machine-readable form. We propose a simple format, the "Open metaData Markup Language" (odML) for metadata. This format specifies a hierarchical structure for storing arbitrary meta information as extended key-value pairs, so called properties, which can be logically grouped into sections and subsections. The odML defines the format, not the content, so that it is inherently extensible and can be adapted flexibly to the specific requirements of any laboratory. This freedom, however, is in conflict with the goal of data sharing: there, a correct understanding of metadata and data is only possible if the annotations apply the same terms or, if mappings between the terminologies applied by sender and receiver are provided.

To facilitate the usage of a common standard terminology we started to define collections of terms and respective definitions for neurophysiology. A terminology is an odML section, for example, the Subject terminology, which contains the terms to describe an experimental subject. Further terminologies are defined, e.g., to describe cells, stimuli, or the properties and settings of used hardware items. They all define names of metadata items not the contents. These terms are meant to be recommendations which should be used if appropriate, but may also be ignored or extended, if necessary. The odML format, however, does not force the scientist to use the suggested terms. The format further offers two ways of customization to meet individual requirements or tastes: (I) It is possible to define synonyms for properties and sections that can be used instead of the originally defined names, or, (II) through individual terminologies which provide mappings to the standard terminologies, custom sets of terms can be created. In both ways, freedom and flexibility is gained without softening the approach of a common standard. The odML is open source and all resources can be found on www.g-node.org/odml. Especially, for the terminologies community feedback is required and highly appreciated.

To completely describe the conditions that led to a certain dataset requires a vast number of metadata and is thus considered a tedious business. We propose that metadata acquisition should start as early and, as the actual data acquisition, as automated as possible. In order to facilitate this, we provide odML-libraries in some common programming languages that allow easy integration of metadata handling into the laboratory workflow, automatically collecting metadata information where it becomes available.

Acknowledgments: Supported by BMBF grant 01GQ0801.

Practically trivial parallel data processing gives neuroscience laboratories easy access to advanced analysis methods

Michael Denker[1], Bernd Wiebelt[2], Denny Fliegner[3], Markus Diesmann[1] and Abigail Morrison[2]

1. RIKEN Brain Science Institute, Wako, Japan
2. Bernstein Center for Computational Neuroscience, Freiburg, Germany
3. Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany

In addition to the increasing amounts of data gushing out from neuroscientific experiments, the complexity of modern data analysis techniques places new demands on the computing infrastructure required for data processing. In particular, the observation that neuronal data typically exhibit non-stationary statistics complicates the task of finding the correct null-hypothesis to assess the significance of a variety of test parameters. Modern computer resources enable a data-based approach to tackle significance estimation: surrogate techniques. In this framework the original data is modified in a specific way so as to keep some aspects of the data (e.g., the non-stationary nature of the data), while deliberately destroying others (i.e., those described by the test parameter). Repeating this procedure many times estimates the distribution of the test parameter under the null hypothesis.

However, the required resources exceed the speed and memory constraints of a classical serial program design and require scientists to parallelize their analysis processes on distributed computer systems. Here, we explore step-by-step how to transform on-the-fly a typical data analysis program into a parallelized application. This approach is facilitated by the observation that a typical task in neuronal data analysis constitutes an embarrassingly parallel problem: the analysis can be divided up into independent parts that can be computed in parallel without communication. In particular for surrogate-based analysis programs, finding the decomposition of the analysis program into independent components is often trivial due to the inherent repetition of analysis steps. On the conceptual level, we demonstrate how in general to identify those parts of a serial program best suited for parallel execution. On the level of the practical implementation, we introduce four methods that assist in managing and distributing the parallelized code. By combining readily available high-level scientific programming languages and techniques for job control with metaprogramming no knowledge of system-level parallelization and the hardware architecture is required. We describe the solutions in a general fashion to facilitate the transfer of insights to the specific software and operating system environment of a particular laboratory.

The details of our technique accompanied by concrete examples form a chapter of the new book "Analysis of parallel spike trains" edited by Sonja Grün and Stefan Rotter and published at Springer 2010.

Behavioral context dependent modulation of pre-stimulus activity underlies the high quality sensory representation in rat taste cortex

Takashi Yoshida and Donald Katz

Department of Psychology, Brandeis University, Waltham, USA

Neurons in sensory cortex show organized activities even in the absence of sensory input, which often affect subsequent sensory responses. Thus, it is reasonable to expect that awake animal actively control the ongoing activity dependent on the context, and that the modulation of pre-stimulus activity could play a key role in adaptive sensory processing with a task demand such as a sensory discrimination. We tested this idea in the cortical taste processing in behaving rat. In primary taste cortex (also called gustatory cortex: GC), pre-taste stimulus activity is known to be modulated specifically when the animal is able to anticipate the upcoming stimuli. However, few studies have examined how the pre-stimulus activity modulation affects taste responses. The goal of this study is to examine the modulation of pre- and post-stimulus activity during a task in which taste served as a discriminative cue, and relationship between the pre- and post stimulus activity. GC local field potentials and single unit activities were recorded from freely moving rats. GC activities were compared between two different behavioral contexts within a session: taste discrimination task (Task) and passive taste administration (Passive). In Task, rats conducted a two-alternative forced choice task in which tastes solutions were used as discriminative cues and two taste solutions were mapped to each of two behavioral responses. In Passive condition, rats were presented taste solutions without any predictable cue and without any behavioral demands. In both conditions, taste solutions were delivered through cannulae implanted in the oral cavity. We found that local field potential power in beta and gamma frequency in Task decreased in both pre-and post-stimulus epochs, suggesting that GC network states were modified by the behavioral context. Consistent with the results of LFP, GC single neuron activities were modulated by the context in both pre- and post-stimulus epochs. In pre-stimulus epoch, firings of single neurons were modified dependent on their firing rates; relatively low firing neurons decreased their activities, while high firing neurons increased their activities in Task. Trial-to-trial variability, estimated by Fano factor, also decreased even prior to the stimulus in Task, whereas the variability decreased after stimulus in Passive. These changes had large impact on the subsequent taste responses; weak, low-firing taste responses were suppressed further, while strong, high-firing responses were maintained. This firing rate change resulted in the slight increase in taste selectivity in Task. Modulations of pre- and post-stimulus firings were positively correlated, and the increase in taste selectivity was mainly attributed to the neurons in which pre-stimulus firing decreased. These results suggest that control of pre-stimulus activity improve the quality of taste representation during the task condition in rat primary taste cortex.

Optimal control of false discoveries for multiple testing of phase locking values in EEG synchrony analysis

Archana Singh[1], Hideki Asoh[2] and Steven Phillips[1]

1. Mathematical Neuroinformatics Group, Human Techonoly Research Institute, AIST, Tsukuba, Ibaraki, Japan
2. Information Technology Research Institute, AIST, Tsukuba, Japan

Recently, much of the neuroimaging research has shown an increasing shift towards measuring the functional connectivity in the brain. As EEG conveniently allows such measurements, it remains as one of the popular techniques for measuring phase synchrony. The standard methods for functional connectivity, e.g., phase locking value (PLV), require imaging the dynamics of phase synchrony from the signals distributed across the brain, at a high temporal resolution. The accompanying increase in data dimensionality incurs a serious multiple testing problem for determining PLV significance. Conventional methods fail to detect even the true significant effects, so more recent advances for controlling false discoveries, such as hierarchical FDF (hFDR, Yekutieli, 2008) were adopted (Singh and Phillips, 2010). Here, we evaluate another method called optimal discovery procedure (ODP, Storey, 2007). To date most of the work on evaluating these methods has been conducted on microarray data, where the knowledge about the distribution of p-values may be exploited to set the tuning parameters that effectively increase their power without compromising on FDR. We evaluate ODP with respect to EEG measures of brain synchrony acquired from a visual search study. This synchrony analysis involves detecting significantly synchronized electrode pairs, by comparing PLVs between efficient and inefficient visual search conditions, across different time-frequency windows. After applying ODP for multiple testing correction, we found significantly greater synchrony between EEG signals during inefficient than efficient condition in the lower gamma band (22-44 Hz) at the expected post-stimulus intervals, consistent with our previous findings. The results reveal that this method can effectively detect more significantly synchronized EEG signals while strongly preventing FDR.

References

1. Singh A. K., Phillps S. (2009) Hierarchical control of false discovert rate for phase locking measures of EEG synchrony, Neuroimage, 50(1), 40-47

2. Storey, J. D. (2007) The optimal discovery procedure: a new approach to simultaneous significance testing. J. R. Statist. Soc. B, 69, 347-368

3. Yekutieli, D. (2008) Hierarchical false discovery rate controlling methodology. J. Am. Stat. Assoc., 103 (481), 309–316

High speed ganglion cell responses in archer fish retina

Viola Kretschmer, Malte Ahlers and Josef Ammermuller

Department of Neurobiology, Carl-von-Ossietzky-Universität Oldenburg, Oldenburg, Germany

Archer fish have the ability to down aerial prey with shots of water matched to size and distance of the prey. On the basis of estimated prey weight, size and motion, each member of a swarm can calculate the point of impact on the water, turn towards it and match its swimming speed to the distance in order to be the first reaching that point. This very complex computational task is accomplished in a very short time (down to 40ms) and therefore has to be achieved by a very compact neural circuitry. Fast turning and acceleration is probably triggered by the archerfish's C-start escape network which is known for fast responses to visual information for life saving purpose. The short latencies until the precisely aimed predictive start require high speed processing and transferring of visual information at all processing stages, including the retina. In this study we examined the underlying high speed processing within the retina by extracellularly recording retinal ganglion cell responses with a 10x10 multi-electrode array, while applying visual stimuli mimicking the natural situation of falling prey. Ganglion cells showed very short latencies down to 19ms in response to white, full-field light flashes. This was compared to other bony fish species like carp and gold fish. Stimulation with moving edges unveiled strong directional sensitivity in several cells. Because of the low latencies it is very likely that a lot of computation is directly accomplished by a retinal network of such specialized cells. Our goal is to understand both the network and its underlying coding strategies.

Recording retinal waves with a 4,096 electrodes array: novel analytical and data sharing tools

Evelyne Sernagor[1], Alessandro Maccione[2], Mauro Gandolfo[3], Stephen Eglen[4], Matthias Hennig[5] and Luca Berdondini[2]

1. Institute of Neuroscience, Newcastle University Medical School, Newcastle upon Tyne, UK
2. Department of Neuroscience and Brain Technologies, Italian Institute of Technology, Genova, Italy
3. Department of Biophysical and Electronic Engineering, University of Genova, Genova, Italy
4. DAMTP, Centre for Mathematical Sciences, Cambridge University, Cambridge, UK
5. Institute for Adaptive and Neural Computation, University of Edinburgh, Edinburgh, UK

In order to decipher information processing in neural networks, it is imperative to understand neural connectivity between individual neurons as well as global network communication. To achieve this goal, neural activity must be studied in very large cell populations using high spatiotemporal resolution recording tools, resulting in the generation of rich datasets that necessitate the development of powerful computational analytical tools. We are using the Active Pixel Sensor (APS) multielectrode array (MEA) to record spontaneous waves of activity that propagate across the ganglion cell layer in the neonatal mouse retina. The APS MEA consists of 4,096 electrodes with near cellular resolution (21 µm x 21 µm electrodes, 42 µm centre-to-centre separation), where all channels (integrated on an active area of 2.5 mm x 2.5 mm) can be acquired from synchronously at high enough temporal resolution (7.8 kHz) to detect single spike signals reliably. Activity was recorded throughout the first postnatal week, when the dynamics of the waves undergo significant changes. Thanks to its high spatiotemporal resolution, the APS MEA system allows us to decipher wave properties with great precision. A major advance is that these data sets contain large, unbiased samples of the whole retinal ganglion cell population, for the first time allowing a comprehensive quantitative analysis of retinal development. Signals are analyzed using several approaches. These include the analytical tools provided with BrainWave, the software package available with the APS MEA. BrainWave offers powerful activity visualization tools as well as all the standard approaches allowing spike extraction and dataset format translation (e.g. to Matlab), enabling analysis using different platforms. Burst and network connectivity analysis is also available with BrainWave. We have also refined existing computational tools that have been developed (in R and in Matlab) to analyse activity from standard commercial 60 channels MEAs and we have optimized them for APS MEA acquired data. These include visualisation tools and standard methods of spike train analysis such as spike statistics and correlation analysis. To enable sharing of the novel retinal data acquired with the APS MEA system between different laboratories (e.g., Genova, Newcastle, Cambridge, Edinburgh), we are using the resources provided by CARMEN (Code Analysis, Repository and Modelling for e-Neuroscience, a new data sharing facility developed in the UK with funding from the Engineering and Physical Sciences Research Council- http://www.carmen.org.uk/). CARMEN allows us to share data and analytical codes over the internet. Our existing tools (written in R) that were originally developed to analyse neural activity from 60 channels MEAs have been deployed on the CARMEN portal. These tools provide online analysis for MEA data generated by several platforms, including the APS MEA system. In summary, we have demonstrated that the APS MEA system is a powerful tool to record and analyze activity patterns in small neural networks. Moreover, the rich datasets generated by the system present us with new computational challenges, and this will yield to the development of new powerful analytical tools. Finally, we have demonstrated that CARMEN offers a highly useful neuroinformatic platform to develop our collaboration.

References

1. Berdondini L, Imfeld K, Maccione A, Tedesco M, Neukom S, Koudelka-Hep M, Martinoia S (2009) Active pixel sensor array for high spatio-temporal resolution electrophysiological recordings from single cell to large scale neuronal networks. Lab Chip 9(18):2644-2651.

2. Hennig MH, Adams C, Willshaw D, Sernagor E (2009) Early-stage waves in the retinal network emerge close to a critical state transition between local and global functional connectivity. J Neurosci 29:1077-1086.

Educational and Research Tools for Vision Science on Visiome Platform

Izumi Ohzawa, Kota Sasaki and Takayuki Nakazono

Graduate School of Frontier Biosciences, Osaka City General Hospital, Toyonaka Osaka, Japan

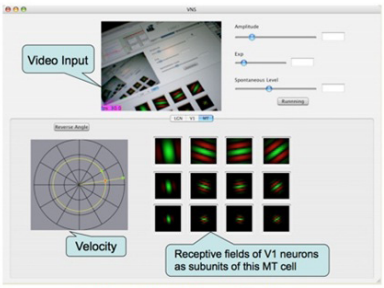
Visiome Platform (http://visiome.neuroinf.jp) is a web-based database system with a variety of digital research resources in Vision Science. With the support provided by the INCF J-Node (http://www.neuroinf.jp), we have developed and contributed experimental data, and various research and educational tools to the Visiome Platform. Here we introduce some of our representative contributions from each category.

1. Experimental data recorded from neurons in the visual cortex
A subset of raw data from our electrophysiological experiments is available from the Platfrom. The data consists of action potential records from neurons in the cat primary visual cortex and includes both the waveform, time of occurrence and experimental parameters. Since the data are recorded in a custom format, an application and its source code for decoding the binary data format are also available as one of the contributed tools.

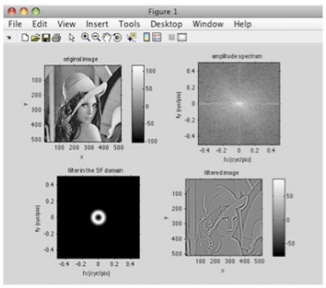
2. Visual Neuron Simulator: a research and educational tool for vision science
We have developed and contributed an application for simulating a visual neuron in real time. The package includes an executable binary for the MacOS X and its entire source code the Apple's Cocoa development environment as an Xcode project. The application has been developed originally as a research tool for debugging and testing the system for conducting electrophysiological experiments without live animals. However, it is also extremely useful for demonstrating how visual neurons respond to real-world stimuli in a classroom and exhibits. It uses a standard video camera as input (USB or FireWire), and generates action potentials via the audio output port. Internally, it contains models for V1 simple and complex cells and an implementation of an MT neuron. The application provides a camera view for showing the visual input, and the neuron's receptive field model. Some of the neuron's operating parameters are adjustable via sliders. For example, the preferred velocity for the simulated MT neuron may be adjusted via a two-dimensional selector in the polar domain.

3. Matlab scripts for research and educational uses
A variety of Matlab scripts and software written in other programming languages are available for downloading from the Platform. The example presented here, "Two-dimensional spatial frequency filtering by FFT using Matlab" is the most frequently downloaded item of all available items on Visiome Platform. The Matlab script is very short: the key part is merely about 30 lines of code, and demonstrates well how the image filtering may be performed efficiently using Matlab. Therefore, it is easily incorporated into more complex scripts for research purposes as well.

We believe that a database such as Visiome Platform fills a unique need as a place to exchange ideas and actual implementations of ideas for the vision research community.



Real-time Visual Neuron Simulator



Matlab Script for 2-D Spatial Frequency Filtering

References

1. Sasaki KS, Ohzawa I (2007) Internal spatial organization of receptive fields of complex cells in the early visual cortex. J Neurophysiol 98:1194-1212.

2. Nishimoto S, Arai M, Ohzawa I (2005) Accuracy of subspace mapping of spatiotemporal frequency domain visual receptive fields. J Neurophysiol 93:3524-3536.

INCF National Node of Finland: Activities and Pilot Projects

Marja-Leena Linne and Ulla Ruotsalainen
Tampere University of Technology, Tampere, Finland

The INCF National Node of Finland (INCFF) was established in 2007. It is hosted by the Department of Signal Processing at Tampere University of Technology. The activities of INCFF are funded through the Academy of Finland [1], the prime funding agency for basic research in Finland. In addition to the chair and coordinator the node has a nine-member steering group with representatives from the fields of neuroscience and computer science in Finnish universities. Funding for the first two years (2008-09) was used to initiate the INCF activity in Finland. The work included organizing two national workshops on neuroinformatics, promoting national and international networking, and performing a survey of Finnish research groups associated with neuroinformatics studies. Based on the survey Finland has approximately ten larger research groups in neuroimaging, three middle-size computational neuroscience groups, and one research group in neurotechnology.

The node was awarded a continuation of funding for 2010-11 with a mission to set up strong networking and collaboration between Finnish neuroscientists and computer scientists. The anticipated activities of the node are focused on education and networking. The activities focused on education in neuroinformatics can be summarized as follows: organization of workshops on national level, providing support for the new pilot projects, organization of Nordic Course on Neuroinformatics, and preparation of the web-based learning material. This learning material will be initially prepared for the Nordic Course, but will be publicly available and regularly updated after the course in order to be used for independent training of researchers. In all of its activities the node is addressing both national and international networking. We will continue visiting and interviewing the Finnish neuroscience and neuroinformatics groups. We will also continue participating INCF activities, including workshops and node meetings. We have also plans to promote collaboration with other INCF nodes in the form of joint pilot tool projects. In 2009, INCFF initiated a small pilot project for testing data storage, sharing, and browsing. XooNIps platform (http://xoonips.sourceforge.jp/; [2]) was selected as a potential candidate. Main goal of the pilot project is to examine the suitability of XooNIps user interface and database for storing and linking PET research related information (publications, measured data, simulated data, phantom data, human data). This kind of information is not only needed by the research laboratories themselves for sharing and browsing information but also by the whole research community to more effectively share research resources. As a result it was concluded that XooNIps platform is able to perform well in basic data uploading and linking tasks. The system will be taken into full use in M2oBSI research group (http://www.cs.tut.fi/sgn/m2obsi) at Tampere University of Technology in the near future.

References

1. Academy of Finland, project # 137349

2. Yamaji K, Sakai H, Okumura Y, and Usui S (2007) Customizable neuroinformatics database system: XooNIps and its application to the pupil platform. Comput Biol Med 37(7):1036-41.

Tools for Neurophysiology Data Management and Analysis at the German Neuroinformatics Node

Andrey Sobolev[1], Philipp Rautenberg[1], Jan Benda[1], Jan Grewe[1], Martin Nawrot[2], Willi Schiegel[3], Tiziano Zito[4], Andreas Herz[1] and Thomas Wachtler[1]

1. Ludwig-Maximilians-Universitaet Muenchen, Planegg-Martinsried, Germany
2. Freie Universitaet Berlin, Berlin, Germany
3. Humboldt-Universitaet zu Berlin and Technologit, Berlin, Germany
4. Technische Universitaet Berlin, Berlin, Germany

Scientific progress depends increasingly on collaborative efforts that involve exchange of data and re-analysis of previously recorded data. A major obstacle to fully exploit the scientific potential of experimental data is due to its complexity which leads to a considerable effort to access both data and metadata for application of specific analysis methods, for exchange with collaborators, or for further analysis some time after the initial study was completed. To cope with these challenges and to make data analysis, re-analysis, and data sharing efficient, data together with metadata should be managed and accessed in a unified and reproducible way, so that the researcher can concentrate on the scientific questions rather than on problems of data management.

At the German INCF Node (G-Node, www.g-node.org), an infrastructure focusing on cellular and systems neuroscience is being developed to improve these key ingredients of neuroscientific research: data access, data storage and exchange, and data analysis. G-Node collaborates with other INCF national nodes, the INCF secretariat, other neuroinformatics initiatives, and with individual researchers. G-Node provides a data management platform where neuroscientists can upload and organize their data for long-term storage, sharing, and analysis. The system is designed to support scientists in dealing with the diverse needs and experiment-specific properties. We recommend that researchers collect metadata in machine readable form and propose a flexible XML-based format, odML (www.g-node.org/odml), together with recommended terminologies, for metadata transfer. Data, together with metadata, can be grouped into datasets, and datasets can be flexibly assigned to experiments and projects, achieving an organization that reflects the structure of the scientific approach and defines data units for analysis or data sharing.

Complementing these features, we develop tools and interfaces for a variety of applications. This enables the researchers to embed our data management platform into their individual research environment.. It allows for seamless integration of data access into the laboratory workflow and yields the requisite for efficient data analysis: Datasets can be selected for sharing or for analysis based on experimental parameters, properties of the recording, or other information that is provided by the metadata. Analyses can be performed in a systematic and automatized fashion. For example, analysis software can be applied to different datasets with analysis parameters adjusted to each dataset, such as number of channels, etc., based on metadata information. This eliminates the need of selecting datasets or adjusting parameters by hand for each analysis. Analysis results, together with documentation of the analysis, can readily be integrated with the data and metadata. This in turn facilitates further analysis or visualization of results.

This approach offers the individual scientist a tool to integrate data management and computational solutions into the daily experimental workflow, thus fostering rapid scientifc progress through neuroinformatics.

Acknowledgments: Supported by BMBF grant 01GQ0801.

NDF: A Data Standard for the CARMEN system

Bojian Liang, Thomas Jackson and Jim Austin
University of York, York, UK

Introduction
CARMEN (Code Analysis, Repository and Modelling for e-Neuroscience, Flecher et al.) is an environment for sharing neurophysiological experimental data and algorithms through an internet portal. There is a wide range of incoming data types used in electrophysiology as well as derived data from the output of system applications/services. They are often unreadable without the original software or knowledge of the format encoding. This presents a real barrier for data sharing and reuse of algorithms and software in neuroscience system. This paper describes Neurophysiology Data translation Format (NDF) developed for CARMEN that overcomes some of these problems.

The NDF data format
NDF provides a standard for sharing data, specifically for data transfer between the various analysis applications/services on the CARMEN system. NDF can be also a useful data format on a researcher's desktop.

An NDF dataset consists of a configuration file in XML format which contains metadata and references to the associated host data files. Using a separated header allows services or users to extract the necessary information about the data set from a small size of header file without need to download the full data set over the network. This also provides means for the system to display detailed meta-data of a remote NDF data without need to access the binary data file remotely. The NDF specifies a set of the most commonly used experimental data entities as "NDF internal data types". NDF can include images and image series data as a basic NDF data type. NDF also supports annotation/marker event data in XML format as a special experimantal event data type.

Data processing services can output data types that may not be represented by formats used for primary data. NDF provides two extandable "semi-defined" data types for applications to create a new data type as its output. The configuration file provides seamless access to these different representations based on the applications used to read the data.

A special XML data element, History, is designed within the header file for data processing history recording. This element contains the full histroy record chain of the privious processing and provides important information for both users and machines to understand a particular experiment, validation of algorithms and for other researchers to accurately repeat an experiment reported.

The NDF API and tools
The NDF API has been implemented as a C library. The NDF API translates the XML tree/node into C style data structures and insulates the data structures of the binary data file from the clients. The API also provides a standard way for data structure memory management for NDF data application programming. Currently, the NDF API has been applied to a data analysis/visualization tool (the SDE) and the CARMEN web based data processing services.

A MATLAT toolbox for NDF has also been implemented. This toolbox has been used as the data input/output pre-processor for the CARMEN services. It can also be used a set of convenient tools on a researcher's desktop for data I/O, independent of CARMEN.

The system currently uses the NeuroShare library as the data input module and will be extended to other input modules.

Conclusions.
It has been shown that a standard data format is crucial in a system like CARMEN where data, tools and algorithms are shared. A single data format standard greatly reduces the work load on system and tool implementation. The efforts of neuroscientists can therefore be concentrated on research work rather than being consumed with the intricacies of transferring data from one format to the others.

From Bombyx neuron database to Invetebrate brain platform - toward a virtual invertebrate neuroscience lab

Tomoki Kazawa[1], Namiki Shigehiro[1], Akira Takashima[1], Stephan Shuichi Haupt[1], Sakiko Siga[2], Hiroyuki Ai[3], Hitoshi Aonuma[4], Masakazu Takahata[5], Ryohei Kanzaki[1], Hidetoshi Ikeno[6] and Shiro Usui[7]

1. Research Center for Advanced Science and Technology, University of Tokyo, Tokyo, Japan
2. Department of Biology and Geosciences, Graduate Science, Osaka City University, Osaka, Japan
3. Division of Biology, Department of Earth System Science, Fukuoka University, Fukuoka, Japan
4. Research Institute for Electronic Science, Hokkaido University, Sapporo, Japan
5. Department of Biological Sciences, Hokkaido University, Sapporo, Japan
6. School of Human Science and Environment, University of Hyogo, Himeji, Japan
7. BSI, RIKEN, Wako, Japan

Brains of invertebrates like arthropods are good model systems for neuroscience because they have simpler structures than vertebrate brains but display a variety of sophisticated properties like multimodal integration, learning, and memory. Compared to vertebrates, the impact of individual neurons in information processing in invertebrates is much more prominent and neurons can often be identified individually in each member of a given species due to their characteristic morphological and physiological properties. Invertebrate neural circuits are mostly studied using intracellular recording and labeling that allows determining the physiological and morphological properties of the cells. Usually, one neuron per sample is recorded, thus the importance of integrating data from different experiments is paramount. Morphological and physiological data of single neurons from silkmoth brains have been fed into BoND (Bombyx neuron database) since 2000, initially using commercial database systems. Analyzing single neuron data from several experimenters consolidated in BoND is very useful for systematic analyses and classifications of neurons especially in 3D morphology when analyzing projection neurons (Kanzaki et. al 2003) and command neurons (Wada and Kanzaki 2005). We thus proceeded to reimplement our database system as a module of a Content Management system (Kazawa et.al 2008) to expand the power of the system. We started Invertebrate Brain Platform (IVB-PF) project organized by J-Node of INCF for accumulating more information about invertebrate brain. By now the contents of Invertebrate Brain Platform (IVB-PF; http://invbrain.neuroinf.jp) are not restricted to single neuron data from silkmoth, but include information on neurons from other arthropods, mathematical models, and research tools relevant to the study of invertebrate brains, information on behavior, brain images and many ancillary documents. The Database software of BoND and IVB-PF was developed as a web software module described by PHP in XOOPS. Xoops (The eXtensible Object Oriented Portal System) is a web server CMS. Access and administration rights are set through a flexible permission system based on user groups. Binary data can be uploaded by the user that registered the data and utilized by users with access rights. Each data set is represented by a thumbnail image and standardized keywords. The database module can be publicly accessed as CosmoDB (http://www.cosmodb.sourceforge.jp). Document pages that describe the contents systematically support the organization of database content. XOOPS is multi-platform based and has a modular structure that allows extension beyond database functionality such as for communication tools. As of April 2010, IVB-PF includes the following public data: 52 images of invertebrate brains of different species, 474 individual neuron data sets from silkmoth, 34 movies of arthropod behavior, several manuals for physiological and behavioral experiments, 21 single neuron data sets from crayfish, and 52 histological brain images from fly. Each lab participating in the IVB-PF project operates a local cosmoDB server. In one of them, BoND, more than 1400 individual neuron data sets, including 3D image stacks of the morphology and physiological responses to pheromone have been accumulated and are prepared for public release. Data mining is one important aspect of the pooling of resources. We are currently implementing a silkmoth standard brain, into which data from the database can be mapped for integration and subsequent creation of a model that will eventually lead to whole-brain simulation in the silkmoth. It is highly effective to manage and share research resources by networked facilities in neuroscience. The environment for data analysis in collaboration with the database can enhance the collaboration among researchers in various fields, including physiology, information science, and engineering and be used efficiently for educational purposes

References

1. Kanzaki R, Soo K, Seki Y, Wada S. (2003), Projections to higher olfactory centers from subdivisions of the antennal lobe macroglomerular complex of the male silkmoth. Chem Senses 28, 113-130.

2. Wada, S. & Kanzaki, R. (2005). Neural control mechanisms of the pheromone-triggered programmed behavior in male silkmoths revealed by double-labeling of descending interneurons and a motor neuron. J. Comp. Neurol. 484, 168-182.

3. Kazawa T, Ikeno H, and Kanzaki R.(2008), Development and application of a neuroinformatics environment for neuroscience and neuroethology Neural Networks 21, 1047-1055

Development of community standards for brain atlas interoperability

Ilya Zaslavsky[1], Richard Baldock[2], Jan Bjaalie[3], Albert Burger[4], Mark Ellisman[1], Michael Hawrylycz[5], Sean Hill[6], Stephen Larson[1], Maryann Martone[1], Lydia Ng[5], Raphael Ritz[7], Fons Verbeek[8] and Jyl Boline[9]

1. University of California at San Diego, San Diego, USA
2. MRC Human Genetics Unit and IGMM, Edinburgh, UK
3. Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway
4. MRC Human Genetics Unit and Heriot-Watt University, Edinburgh, UK
5. Allen Institute for Brain Science, Seattle, USA
6. Brain Mind Institute, EPFL, Lausanne, Switzerland
7. INCF, Stockholm, Sweden
8. Leiden Institute of Advanced Computer Science, Leiden University, Leiden, Netherlands
9. Informed Minds, Inc., Wilton Manors, USA

One of the key goals of the International Neuroinformatics Coordinating Facility is the development of a sustainable global infrastructure for collaborative neuroscience research [1]. To support the integration of diverse neuroscience resources (datasets, applications, services, workflows, models, published research results) this infrastructure shall rely on standardization of service interfaces, data exchange formats and nomenclatures across neuroscience projects as its central unifying activity.

We summarize the main challenges of creating a standards-based infrastructure, and review recent efforts of the INCF Digital Atlasing Infrastructure (INCF-DAI) task force in the development of standards for integrating rodent brain data. Within INCF-DAI, and in communication with other INCF task force teams, we identified several scenarios for standards-based data exchange, for example:

- When exploring an atlas of a mouse brain, a researcher wants to know what information is available for a location in the brain, or for an anatomic structure, in other atlases, gene expression databases, publications, etc.
- When simulating a neocortical column, a brain modeler needs to bring in additional datasets to constrain the model for more realistic simulations, and wants to make sure these additional data can be unambiguously interpreted and seamlessly integrated in the model.
- When analyzing gene expression patterns, a researcher needs to compare these patterns as expressed in adult mouse brain, adult brain of rat (and other species), and in the developing brain.
- When creating software for analyzing and visualizing neuroscience data, a software developer wants to ensure that it will be able to process different datasets and thus have a wider audience.

Based on the notion of a service-oriented architecture (SOA), the INCF data infrastructure is envisioned as a network of computational neuroscience hubs linked with the central INCF server. Hubs host a collection of standards-compliant services which can be registered at INCF Central, so that their metadata is harvested into the central catalog, to support resource discovery across the hubs. A hub can host any combination of atlasing services, image visualization services, ontology services, collection management services, services for connectivity data, simulation services, etc., as long as each of these services is standards-compliant and declares its capabilities and supported functions to the central server.

The emerging INCF-DAI infrastructure for sharing brain atlas data follows this model. A standard set of atlas services is specified and implemented to integrate information from the Allen Brain Atlas, the Edinburgh Mouse Atlas, images and image mosaics assembled at UCSD in the course of the SMART Atlas and the Whole Brain Catalog projects, and the Waxholm Space, with the latter being used as the spatial reference system against which most spatial transformations are computed. The methods include core capability information about an atlasing hub service, descriptions of available spatial reference systems, coordinate transformations, structure lookup, and other methods that may be specific for a particular hub and provide access to the hub's information based on an anatomic structure name (as defined in an ontology) or a point of interest (as defined in a spatial reference system). The output XML schema used by the atlas services is referred to as Waxholm Markup Language.

Further development of this model for standards and services and extending it to other areas of neuroscience requires that the neuroscience community establishes a consensus mechanism to identify areas appropriate for standardization, endorse existing standards where possible or develop new standard specifications where justified, and to maintain a system for governing and evolving the specifications. We will present a prototype of such a mechanism, which is currently being approbated for brain atlas interoperability

References

1. INCF Strategic Plan, 2011-2015 (2010) (http://incf.org/documents/incf-core-documents/StrategicPlan-Web.pdf, last accessed 4/20/2010)

A Web Portal and Search Engine to Promote Collaboration in Brain-Machine Interface Research

Makoto Takemiya, Satoshi Murata and Yukiyasu Kamitani

Department of Neuroinformatics, ATR Computational Neuroscience Laboratories, Kyoto, Japan

Brain-machine interface (BMI) research is a new field of neuroinformatics that combines algorithms and information processing methodologies from computer science with the emphasis on empirical physiological data analysis from neuroscience. One of the goals of BMI is to be able to recognize brain signals so that simply by thinking, a computer can decode the contents of the brain to perform a task. Since its goal is to improve everyday life through practical applications of neuroscience, BMI provides an avenue for neuroinformatics to have a dramatic impact on our society. However, collecting data to test new algorithms is not only time consuming, but also very costly. Furthermore, people with a solid background in algorithms and theoretical computer science may not have the skills or resources necessary to carry out neurophysiological experiments. Since there is still much that is not understood about information coding by the brain, it is important that new algorithms are created and tested by as many people as possible, not just neuroscientists. If data can be made readily available, it can have a profound effect on advancing our understanding of the brain, since more researchers will be able to build and test computational models with empirical data.

To make data readily available and to promote interdisciplinary collaboration, we created a web portal and search engine to facilitate BMI data sharing as part of a project for the Japanese Ministry of Education, Culture, Sports, Science and Technology. Our system allows users to search for, upload, and download data. To advance BMI research by combining behavioral and physiological data, we also allow users to upload documents and videos describing their data and experiments. We use a uniform file format for physiological data, which allows us to develop software that can be used to process and extract important features. We are currently working on a time-alignment tool to combine behavioral information, such as experimental stimuli, with physiological data. To the best of the authors' knowledge, this is a feature that other neuroinformatics databases do not have. Additionally, we have a web-based data previewer that allows users to preview data in their web browser before they download it.

Since it is important to connect data with the people that need it, our system offers free-text search capabilities, similar to contemporary Internet search engines. By entering text describing data that a user is looking for, our search engine will find matching files and experiments. We are also working on an experiment recommender system that will suggest experiments to users based on their download history and ratings given to experiments. This is similar to how e-commerce web sites recommend products to users. Through licensing the data with a Creative Commons license, we allow users who upload data to specify any required citations of their work, while also allowing people who download data to freely use it. This promotes data sharing while still protecting the scientists that create new data and allowing them to gain citations from work that uses their data. In future work we will provide a data-driven search tool that will allow users to search for data by inputing some of their own data. Features of the data, such as spiking patterns, will be compared in order to find similar data.

System for storage EEG/ERP data and metadata

Petr Ježek and Roman Mouček
University of West Bohemia, Plzen, Czech Republic

In our research group at Department of Computer Sciences and Engineering, University of West Bohemia we widely perform experiments focused on attention, especially attention of drivers or seriously injured people.

Because during experiments a lot of data are produced and there is not a widely spread and generally used standard for EEG/ERP storing data/metadata we have developed own system for management of experiments. Our system enables clinicians and various communities of researchers to storage, download, update, manage and share EEG/ERP experiments. Experiments are stored in the relational database (Oracle 11g), user interface is web based to ensure easy interaction with user. Since system is thought to be finally open to the whole community there is necessary to protect personal data of tested subjects. Hence we have designed system of users' accounts and system groups with assigned user roles (Anonymous user, Reader, Experimenter, Group administrator, Supervisor). Anonymous user can see only homepage with essential information about the system. Reared has created his/her account yet and he/she can download public experiments. Experimenter can insert his/her experiments. Group administrator is a user who established group and he/she can accept new members (Each user has to be a member at least of one group). Supervisor has an extra privilege to remove users or whole groups.

The System is based on three-layer architecture (according to MVC design pattern). The used design pattern is directly supported by used technologies (Java EE with Spring, Spring MVC, Spring Security, Hibernate, Hibernate Search, etc.). It ensures a high level of abstraction (system extensibility) as well as a long term existence of the system as an open source.

To enable registered users to search experiments easily we have implemented a full-text search engine. Simultaneously we have prepared an engine providing data in the semantic web form (OWL or RDF representation) existing tools were widely tested.

When semantic web engine is implemented and data in the semantic web form are available we will register our system in the Neuroscience Information Framework. Nowadays the system is available at http://eegdatabase.kiv.zcu.cz for testing. We will be delighted if we would appreciate any feedback from users.

A system for rapid development and easy sharing of accurate demonstrations for vision science

Kazushi Maruya[1], Kenchi Hosokawa[2], Eisuke Kusachi[3], Shinya Nishida[1], Masao Tachibana[4] and Takao Sato[4]

1. NTT Communication Science Laboratories, Kanagawa, Japan
2. Intelligent Modeling Laboratory, University of Tokyo, Tokyo, Japan
3. Freelance, Tokyo, Japan
4. Department of Psychology, University of Tokyo, Tokyo, Japan

With the rapid expansion and fusion of the vision research fields, there has been increasing emphasis on the importance of public sharing of various research resources, especially demonstrations of visual phenomena or stimuli that can be used in actual experiments. However, the amount and range of the contents currently shared in actual web-based platform systems for vision science are far from satisfactory despite prodigious efforts of several user groups. Research resources and demonstrations require precise control of the timing and quality of presented stimulus. To reduce costs of developing fine demonstrations that usually require vast amount of time and research resources, we have developed a new C++ library based on Open GL, named "Psychlops". This library enables users to develop fine demonstrations using generic consumer PC systems without any special applications. In Psychlops, the procedures for preparing to establish a connection with an operation system are completely wrapped with common, non-OS-dependent command sets. It is equipped with several preset routines for commonly used experimental methods, demonstration interfaces, and stimuli. Furthermore, the program runs on generic consumer PCs, including laptop machines. These key features of Psychlops enable users to easily make demonstrations for multiple operating systems, such as Windows and MacOSX without changing any lines in the program. Psychlops is available at our website (http://psychlops.sourceforge.jp) for free. Using Psychlops in combination with a free integrated development environment, e.g., CodeBlocks (http://www.codeblocks.org) or Xcode (http://developer.apple.com/technologies/tools/xcode.html), users can prepare the development environment on their own computers without any financial cost. We have also developed a branch site to complement the Psychlops demonstrations in the Visiome Platform (http://visiome.neuroinf.jp). This Platform is a web-based database system with a variety of digital research resources in vision science and is promoted by Japan Node (J-Node, http://www.neuroinf.jp). Numerous demonstrations uploaded to the Visiome Platform cover a broad range of visual phenomena and illusions. However, browsing users may not easily access the specific contents of each demonstration until they download it because a demonstration developed with Psychlops is an executable application. To mitigate this problem, we have developed a branch site, named "Visitope" (http://visitope.org), where a summary of the uploaded demonstrations is displayed. At Visitope, users can browse items in a friendly manner and access the uploaded demonstrations. Besides these demonstrations, we are planning to make various other contents available at Visitope, including non-academic issues, such as introductions of workshop activities relating to vision science or design resources for web creators. These extra contents are aimed at promoting visits by non-academic people. Thus, Visitope may also work as an introduction to the Visiome Platform itself and to vision science for the general public (Figure 1). We believe that these achievements will contribute to the diversification of user groups and to the formation of a new user group where professional researchers and the general public can engage in constructive conversations. Such a new user group is expected to accelerate progress in vision science in the near future.

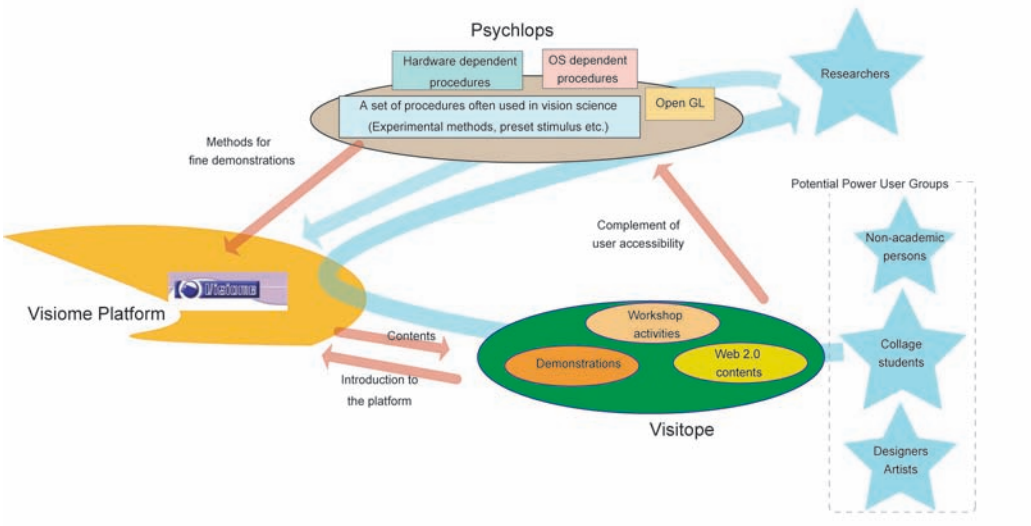


Figure.1

Simulation Platform: Model simulation on the cloud

Shiro Usui[1], Tadashi Yamazaki[1], Hidetoshi Ikeno[2], Okumura Yoshihiro[3], Sato Shunji[4], Kamiyama Yoshimi[5], Hirata Yutaka[6], Inagaki Keiichiro[1], Ishihara Akito[7], Kannon Takayuki[1], Kamiji Nilton[1] and Akazawa Fumihiko[3]

1. RIKEN BSI, Wako, Japan
2. School of Human Science and Environement, University of Hyogo, Himeji, Japan
3. RIKEN, NIJC, Wako, Japan
4. Graduate School of Informatis Systems, University of Electro-Communications, Chofu, Japan
5. School of Information Science and Technology, Aichi Prefectural University, Aichi-gun, Japan
6. Faculty of Engineering, Chubu University, Kasugai, Japan
7. School of Information Science and Technology, Chukyo University, Toyota, Japan

Various kinds of data analysis methods and computational models have been proposed and utilized in neuroscience fields. In this regard, theoretical approach is indispensable for further advance in neuroscience. Recently, a number of software packages for data analysis and scripts/programs for computational models have been provided on the Internet, and many of them are open-access for researchers to validate and reuse. Neuroinformatics Japan Center (NIJC) has been supporting these activities and hosting neuroinformatics database sites called platforms. The platforms contain various research resources, such as experimental data, data analysis tools and computational model scripts/programs as well as research papers to share the knowledge and technique for accelerating computational neuroscience researches. Although a number of resources are available on the platforms and other databases, preparations to review experimental data and execute model simulation on ones own computer still remain burdensome. If a model script is constructed on a neural simulator such as NEURON or GENESIS, one has to install these simulators in our computers even just for a trial use. If a model is written in programming language such as C, C++ or Python, one has to prepare the programming environment including compiler like gcc, g++ and other tools and libraries. Furthermore, if a model is provided in a commercial product, such as MATLAB or Mathematica, one may have to purchase even just on trial. Therefore, we propose a novel framework to avoid these difficulties and provide user-friendly environment to execute model simulation and data analysis programs registered in the platforms without any preparation on a user's computer. Here, we present our on-going project on launching a web service called Simulation Platform (SimPF) as one of the Japan-node platforms (http://www.neuroinf.jp). SimPF provides two types of virtual computing environment for neuroscientists via web, one is virtual machine (VM) and another is grid computing. VM environment is realized by VirtualBox (http://www.virtualbox.org/) running on CentOS. A variety of neural simulators, application and developmental tools, including NEURON, GENESIS, ImageJ, C, C++ and MATLAB, are installed in VM. By using VM, users can review the experimental data with less effort and run the computational model programs that are registered on the platform and database such as ModelDB. It is no need to install any application software or compiler on own computer. That is, when a user clicks the start button of VM, appropriate model program with control script for automatic execution (auto-run script) is sent to the SimPF. Once these files are uploaded, SimPF assigns a VM for the user from SimPF clouds and connects the VM automatically to the user's browser via VNC (Virtual Network Computing) protocol. The desktop screen of the VM appears on the browser, and then the auto-run script starts model simulation automatically. It is true that computational neuroscientists want to have high performance computing environment, such as grid computing, in their laboratories. Usually, each laboratory has several computers, but it is still needed to have technical know-how for constructing own cloud computing system. SimPF also provides a grid computing environment and several model programs for it. The SimPF grid environment is based on open source software such as Globus toolkit and Ganglia. The SimPF, not only lets users be free from preparing the environment to carry out simulation, but also allows simulation for reviewing and analyzing existing models, as well as for reviewing newly presented model submitted for publication. We expect that the SimPF will further support education and research in neuroscience fields.

The development of the ability to read emotion by content and prosody in the language

Young-ok Park

Department of Psychology, Chungbuk National University Graduate School, Cheongju, South Korea

People use a lot of cues to read other's mind. To date many studies have been using behavior and facial expression as a cue to read other's emotion. But prosody of language could be an important cue, too. Prosody of language is expressed differently by different kind of emotion, which is universal in every culture. Language contains verbal cue (content) and voice cue (prosody). In case that the content conveys conflicting information with the prosody, to infer others' mind, it's necessary to separate the prosody from content and focus on the prosody. The aim of this study is to investigate how the ability to read emotion in the prosody develops according to the age. The task presenting Neutral sentence containing happy prosody and fear prosody (condition 1), happy sentence containing happy prosody & fear sentence containing fear prosody (condition 2) and happy sentence containing fear prosody & fear sentence containing happy prosody (condition 3) was conducted by 7-year, 9-year and adult. EQ, SQ and AQ questionnaires were conducted by adults to investigate whether the ability to read emotion in the prosody is relevant to systemizing, empathizing and autism spectrum tendencies. Every response inferring emotion from the prosody scored 1 and every response inferring emotion from the content scored 0. The result showed condition 1, 2, 3 has the main effect according to the age. In condition 1, 2 7-year children performed worse than 9-year children and adults, while in condition 3 more 9-year children infer the emotion by the prosody than 7-year children. The result of this study indicated that there was a difference in the ability to infer emotion by content and prosody between 7-year children and 9-year children & adults.

The Effect of Visual Suggestion on the Perception of Voluntariness in Confession

Ji Min Pyo and Kwang B. Park

Department of Psychology, Chungbuk National University, Chungbuk, South Korea

Previous research found that video-recorded confessions made with the camera focused on the suspect would lead observers to assess that the suspect's statements were more voluntary and conclude that the suspect was more likely to be guilty than if the camera focused on the interrogator or on both the suspect and interrogator equally. It was hypothesized that an observer may tend to assess the confession of the suspect focused in a video-recorded interrogation as voluntary because the video showing the frontal view of the confessing suspect conveys a suggestion of voluntariness to the viewer. The task for the subjects in the experiment consisted of listening to an audio, as opposed to video, recording of custodial interrogation, evaluating the voluntariness and truthfulness of the confession made by the suspect during the interrogation, and determining the ultimate guilt of the suspect. While instructing the subjects about the experimental task, a still photo showing a typical interrogation room as an example was used to manipulate the suggestion (independent variable); no visual illustration of custodial interrogation for the subjects in the No Suggestion condition; a still photo showing the full frontal view of the suspect for the subjects in the Suspect-Focused Suggestion condition; a still photo showing the full frontal view of the interrogator for the subjects in the Interrogator-Focused Suggestion condition; and a still photo showing the profiles of a suspect and an interrogator sitting face to face to each other for the subjects in the Equally-Focused Suggestion condition. After the instruction was given to the subjects, the still photo was removed from the visual field of the subjects. And the subjects in all conditions listened to an audio recording of a custodial interrogation. At the end of the audio recording which contained the suspect's confession, the subjects rated voluntariness and truthfulness of the confession and the guilt of the suspect in the audio recording. As predicted, the results provided a support for the hypothesis that a subtle suggestion conveyed by a still photo affects the judgments regarding the voluntariness and veracity of the confession, and the determination of the suspect's guilt.

References

1. Lassiter, G. D., & Irvine, A. A. (1986). Videotaped confessions: The impact of camera point of view on judgments of coercion. Journal of Applied Social Psychology, 16, 268-276.

2. Lassiter, G. D., Andrew L. Geers, Patrick J. Munhall, Robert J. Ploutz-Snyder, and David L. Brietenbecher (2002) "Illusory Causation: Why it Occurs, Psychological Science 13: 299-305.

MPTP-induced Animal Model of Parkinson's Disease Dementia: There are Species Differences

Shih Chun Ho and Ying Jui Ho

School of Psychology, Chung Shan Medical University, Taichung, Taiwan

Animals treated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) are used as models of Parkinson's disease. This study analyzed changes of motor, anxiety, recognition, and learning in MPTP-lesioned Wistar rats and C57BL/6 mice, which was intended to establish a useful model of Parkinson's disease dementia. MPTP was bilaterally infused into the substantia nigra pars compacta (SNc) of male Wistar rats. Starting one day after the MPTP lesion, the rats were subjected to a battery of behavioral tests for measuring motor function in the rotarod, anxiety level in the elevated plus-maze (EPM), learning and working memory in the T-maze, and recognition in the object recognition task. Male C57BL/6 mice receiving intraperitoneal injection of MPTP were subjected to a battery of behavioral tests for measuring motor function in the open field, anxiety level in the EPM, learning function in the active avoidance task (AAT), and recognition in the object recognition task. Both rats and mice showed motor deficits in the rotarod and open field test, respectively, one day after MPTP lesioning. However, such impairments in the rats were reversed to control levels 7 days after the MPTP lesion, which were assessed by measuring percentage of movement time on the rotarod.Similarly, analyzing total distance and movement time in the open field, motor impairments of the mice were also reversed to control levels 11 days after the MPTP lesion. Decreased exploration time to novel objects in the object recognition test was observed in both rats and mice treated by MPTP. MPTP lesion suppressed open arm time and open arm entry in the EPM test in rats, but not in mice. In addition, MPTP-lesioned rats showed lowered correct responses in the T-maze test. However, no effect of MPTP lesion was found on learning ability in the AAT in mice. In summary, MPTP lesion in rats caused deficits in motor, anxiety, recognition, and learning ability. MPTP-treated mice showed impairments in movement and recognition, but not in anxiety level and learning ability. These results provide evidence for taking the species differences into account when animal models for studying symptoms of early phase of Parkinson's disease dementia.

A suggestibility scale for children

Yeong Rok Oh, Kwang B. Park and Ji Min Pyo

Department of Psychology, Chungbuk National University, Cheongju, South Korea

The present study was to develop a measurement scale of suggestibility for children which was defined as a personality trait independent of memory and/or attentional capacity. The procedure employed by Gudjonsson (1984a, 1987) to measure the suggestibility of adults was modified so that the confounding effect of memory and/or attentional capacity on the score can be controlled for. Specifically, the subjects heard the story and recalled the contents of the story repeatedly until 2/3 of the content was successfully recalled before responding to the questions designed to measure the suggestibility. As a result, the variability in the suggestibility scores due to differential capacity of memory and attention was eliminated. In order to test the validity of the suggestibility scores obtained with the modified procedure, two groups of the subjects were selected: one with the subjects who obtained high suggestibility scores and the other with the subjects who obtained low suggestibility scores. Each of the selected subjects experienced a situation in which he/she interacted with an adult before being questioned about the experience by another adult. The subjects with high suggestibility scores made more errors in answering leading and misleading questions about the experience than did the subjects with low suggestibility scores. The result was discussed for its theoretical implications for the construct of suggestibility and its practical implications for the investigations of crimes committed against or by children.

References

1. Gudjonsson G. H (1984). A new scale of interrogative suggestibility. Personality and Individual Differences. 5, pp. 303-314.

The Relationship among Peer Statue, EQ (Empathy Quotient), SQ (Systemizing Quotient), and AQ (Autism Spectrum Quotient)

Hwa-Jung Cha, Chan-Ok Park, Seung-Bok Lee and Hei-Rhee Ghim

Department of Psychology, Chungbuk National University, Chungbuk, South Korea

This study aimed at investigating whether the scores of social preference and social influence were related to empathy quotient (EQ), systemizing quotient (SQ), and autism spectrum quotient (AQ), and whether five groups of children by peer statue (i.e., the popular, controversial, average, neglected, and rejected groups) were classified by peer nominations had differences on the scores of EQ, SQ, and AQ. The participants were school-age children who began to extend their social relationships to peer relationships out of their families and were in the sixth grade of elementary school. They are expected to be most stable developed and stable on empathy among elementary school students. For the assessment of the peer social statue of children, the Sociometrix test (Coie & Dodge, 1983) was applied. The test was performed to measure the five peer statues: the popular, controversial, average, neglected, and rejected groups. The Korean versions of children's versions of the Empathy Quotient (EQ-C)(Chapman, Baron-Cohen, Auyeung, Knickmeyer, Taylor, & Hackett, 2006), children's versions of the Autism Spectrum Quotient (AQ-C) (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2007), and children's versions of the Systemizing Quotient (SQ-C) (Auyeung, Baron-Cohen, Chapman, Knickmeyer, Taylor, & Hackett, 2006) were used to measure empathy, systemizing, and autistic inclination. Participants: 126 boys and 115 girls from seven classes of an elementary school participated in the study. The range of age of participants was from 10.8 to 12.9 years (mean age = 12.2 years). Measures: The Korean versions of EQ-C (Chapman, Baron-Cohen, Auyeung, Knickmeyer, Taylor, & Hackett, 2006), AQ-C (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2007), and SQ-C (Auyeung, Baron-Cohen, Chapman, Knickmeyer, Taylor, & Hackett, 2006) were used to measure empathy, systemizing, and autistic inclination. The Sociometrix test (Coie & Dodge, 1983) was used for the assessment of the peer social statues of children. In the Sociometrix test, the number of positive nominations was converted to the standard scores using the mean and standard deviation of positive nomination numbers of whole class, and these standard scores were used for the score for Like More (LM). The scores of negative nomination (Like Least, LL) were calculated by the same process. Social preference (SP=LM-LL) and social impact (SP=LM+LL) were calculated using LM and LL. The condition of classification of peer statue is presented in the table1. Procedure: Before the experiments begun, the participants completed EQ, SQ, and AQ presented by computer screens in the lab. Next, the Sociometrix was begun. In the test, children were given a sheet of paper and asked to write down three names for positive nomination and three names for negative nomination on it. This procedure took about 25 minutes. The results showed that the popular, controversial, and average groups had stronger empathetic inclination than the rejected group, and the neglected and rejected groups were disposed toward more autistic tendency than the popular group. In addition, it was revealed that the social preference increased when EQ was high, and the social preference was decreased when AQ was high.

References

1. Coie, J.D., Dodge, K.A., Kupersmidt, J. D. (1983) The behavior analysis of emerging social status in boy's group. Child Development 54(6):1400-1461.

2. Baron-Cohen, S., Wheelwright (2004) The empathy quotient: an investigation of adults with Asperger syndrome of high-functioning autism, and normal sex differences. Journal of Autism and Developmental Disorders 34(2):164-175.

Neuroprotective Effects of estradiol on antioxidant status, calcium homeostasis and glucose transporter in aging female rat brain

Pardeep Kumar, R K Kale, S M Cowsik and N Z Baquer

School of Life Sciences, Jawaharlal Nehru University, New Delhi, India

During normal aging, brain experiences structural, molecular, and functional alterations. Aging in females and males is considered as the end of natural protection against age related diseases like osteoporosis, coronary heart disease, diabetes, Alzheimer's disease and Parkinson's disease. Protection from age-related disorders is provided by several factors, including estrogens. These changes increase during menopausal condition in females when the level of estradiol is decreased. The objective of this study was to observe the changes in activities of superoxide dismutase (SOD), glutathione S-transferase (GST), Ca2+ATPase, intracellular calcium levels, DNA degradation and glucose transporter 4 (GLUT4) occurring in brains of female albino Wistar rats of 3 months (young), 12 months (adult) and 24 months (old) age groups, and to see whether these changes are restored to normal levels after exogenous administration of estradiol (0.1 µg/gm body weight for one month). The results obtained in the present work revealed that normal aging was associated with significant decrease in the activities of SOD, GST, Ca2+ATPase and GLUT4 levels in the brains of aging female rats, and an increase in DNA degradation and intracellular calcium levels. Administration of estradiol brought these changes to near normalcy. It can therefore be concluded that estradiol's beneficial effects seemed to arise from its antioxidant and antilipidperoxidative effects, implying an overall neuroprotective and anti-aging action. The results of this study will be useful for pharmacological modification of the aging process and applying new strategies for control of age related disorders.

INCF Japan-Node Special Symposium
"How Neuroinformatics Can Revolutionize Neuroscience"

SPEAKERS

Sten Grillner

Erik De Schutter

Robert W. Williams

Maryann Martone

Colin Ingram

David C. Van Essen

Gary F. Egan

Soo-Young Lee

Taishin Nomura

Ryutaro Himeno

What INCF can do for Neuroscience

Sten Grillner

International Neuroinformatics Coordinating Facility (INCF) and Nobel Institute for Neurophysiology, Karolinska Institute, Stockholm, Sweden

The goal of the International Neuroinformatics Coordinating Facility, INCF, is to facilitate neuroinformatics research aiming at an understanding of the brain - from the molecular to the cognitive level - and the pathogenic factors underlying the many different diseases of the nervous system, including both psychiatric and neurological aspects [1]. As a consequence, ,INCF is at a cross-road between neuroscience and informatics/physics.

Neuroinformatics provides a very important tool in the analyses of the nervous system. It can be claimed that complex dynamic processes whether at the intracellular or systems level, in which a number of different factors interact, are not understandable without modeling at the single or multi-scale level, nor can the interpretations of such processes and data be tested rigorously without modeling. Similarly, databases with regard to the nervous system are of critical importance for the development and bridging of knowledge in different specific areas, and provide an investigator with easy access to experimental findings in areas which are far outside the investigator's primary competence. A basic scientist may thus with the help of appropriate data bases relate a finding on for instance an ion channel subtype pathology to a rare clinical condition if the data are accessible – otherwise this connection may take years to discover and the development of therapy will be unnecessarily delayed.

The primary aim of INCF is to develop neuroinformatics infrastructure with regard to modeling, data bases and tool development. To achieve this INCF has developed particular programs in different areas that include multi-scale modeling, digital brain atlasing, standards for metadata and the development of data base friendly hierarchical arranged terminology (ontology). Each program includes the leading international experts in its area, and focuses on scalable, portable and extensible solutions to identified neuroinformatics infrastructure problems and bottle-necks.

The INCF Programs are long-term strategic undertakings. Establishing a program is a multi-step process, which starts with a workshop intended to identify the key issues in the area, and continues into the formation of an oversight committee and task forces. Each program delivers products and services, and develops standards and guidelines for its particular field – through these actions the INCF contributes to the development and maintenance of specific database and other computational infrastructures and support mechanisms. These measures are intended to facilitate the flow of information between researchers in both academia and industry.

The INCF also develops initiatives to coordinate and foster international activities in neuroinformatics, and maintains a web portal to make neuroinformatics resources – research tools and information as well as events, training and jobs – more accessible to the community [2].

By facilitating and strengthening neuroinformatics research, INCF can contribute to a rapid progress in all brain sciences and related fields, and to an understanding of the mechanisms underlying different brain disorders and insights into new potential treatments. Another important role for Neuroinformatics is to form an interface between neuroscience and information technology and robotics – the brain is able to solve many of the problems that man-made technologies still seek to master.

References

1. Bjaalie, J. G., & Grillner, S. (2007), Global Neuroinformatics: The International Neuroinformatics Coordinating Facility. J Neurosci 27(14), pp 3613- 3615.

2. INCF 2011 – 2015 Strategic Plan (2010), available on www.incf.org, and in hard copy from the Secretariat, pp 1-16.

New model description standards to facilitate multi-scale modeling

Erik De Schutter[1,2]

1. Okinawa Institute of Science and Technology, Kunigami-gun, Japan
2. University of Antwerp, Antwerp, Belgium

Multi-scale modeling is a tool of critical importance for neuroscience. As computational modeling techniques become integrated with experimental neuroscience, more knowledge can be extracted from existing experimental data. Quantitative models assist in generating experimentally testable hypotheses and in selecting informative experiments. One major challenge in the field is that, because of a wide range of simulation tools being used in the community, it is unlikely that one laboratory can reproduce the results obtained by another group, even if the model is deposited in an openly accessible database. The absence of widely adopted standards for model description also hamper efforts to make existing programs more compatible, reduce opportunities for innovative software development and for benchmarking of existing simulators.

The INCF has started a project to develop a new standard markup language for model description. Based on lessons learned with previous efforts in computational neuroscience and in other fields like systems biology, a concerted effort is made to develop a well-defined but flexible syntax for a self-documenting markup language that will be easy to extend and that can form the basis for specific implementations covering a wide range of modeling scales. The initial effort focuses on describing a growing area of computational neuroscience, spiking networks. This language, called NineML (Network Interchange format for NEuroscience) is based on a layered approach: an abstraction layer allows a full mathematical description of the models, including events and state transitions, while the user layer contains parameter values for specific models. The user layer includes concepts from the four major areas of neuroscience network modeling: neurons, synapses, populations and network connectivity rules. The abstraction layer includes notations for representing hybrid dynamical systems, combining differential equations with event based modeling to describe integrate-and-fire neurons, and abstract mathematical representations of connectivity rules. These abstractions are capable of describing a vast range of network models from the neuroscience literature.

The first official release of NineML is expected by the end of the year. In a next phase NineML will be improved by incorporating community feedback and by expanding the coverage of different spiking network models. Based on this experience new efforts will be launched in the future, using the same language syntax to cover other areas of computational neuroscience, including compartmental models, synaptic microphysiology, cellular mechanics, electrodynamics. Special attention will be given to interoperability issues relevant to multi-scale modeling, where many separate model descriptions may have to be combined and data interfaces need to be defined.

Global Exploratory Analysis of Massive Neuroimaging Collections using Microsoft Live Labs Pivot and Silverlight

Robert W. Williams[1], Lei Yan[1], Xiaodong Zhou[1], Lu Lu[1], Arthur Centeno[1], Leonard Kuan[2], Michael Hawrylycz[2] and Glenn D. Rosen[3]

1. Department of Anatomy and Neurobiology, Center for Integrative and Translational Genomics, University of Tennessee Health Science Center, Memphis TN, USA
2. The Allen Institute for Brain Science, Seattle, USA
3. Department of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, USA

Introduction: The Mouse Brain Library (www.mbl.org) consists of high resolution images generated for 200 genetically well defined strains of mice, 2200 cases, 8800 Nissl-stained slides, and ~120,000 coronal and horizontal sections of the brain. The MBL includes representatives for most sets of recombinant inbred strains, (BXD, LXS, AXB, BXH, CXB). This collection provides a solid foundation for studies of the genetic control of brain structure, function, and behavior (Lu et al. 2001; Yang et al., 2008; Rosen et al., 2009).

A key challenge is how to deliver massive image collections such as the MBL, Allen Brain Atlas projects, and BrainMaps using modern web services. In this work we tested Microsoft Live Labs Pivot (www.getpivot.com) as an image distribution portal. Pivot provides a unique method for delivering and exploring very large collections of high-resolution images.

Methods and Results: Large slides of 30-µm celloidin sections were imaged using a 20x objective (NA 0.75) and an Aperio Scanscope CS scanner at an in-plane resolution of 1-µm/pixel and at 150-µm steps along the cutting axis. Images were segmented to extract single sections. SVS format image were converted into Advanced Forensic format (AFF), JPEG2000, and Silverlight deep zoom (DZI) pyramids. A DVI is 2x larger than its JPEG parent. DZIs were assembled into a set of Pivot image collections. Metadata for sorting and display were extracted from MBL and GeneNetwork.org data tables. Metadata types include thousands of genotypes and phenotypes for all strains, as well as data for individual cases (sex, age, body weight, brain weight, litter size). Spatial coordinate tags for each section using INCF Waxholm space and BIRNLex neuroanatomical terms are being added.

A Pivot server was installed on a Linux CentOS 5 8-core system (Dell R610) running Tomcat and MySQL. The system was tested on Vista and Windows 7 using a Pivot browser (www.getpivot.com) and runs well on Mac OS X 10.6 using the VMWARE Fusion 3 virtual machine. Link to http://mbl.pivotcollections.org to view the MBL.

The MBL collection is large and unwieldy and our current interface (www.mbl.org) does not provide sufficient sorting flexibility and speed to effectively explore or analyze the collection. A good exploratory interface would provide both forest and tree views and a way to effectively scan the entire collection for variation in traits such as ventricular volume, callosal architecture, cortical lamination, and differences in the cytology in specific nuclei in a matter of minutes, not hours or days. Pivot is optimal for these types of rapid review and exploratory tasks. The collection can be filtered, sorted, and viewed at a wide range of magnifications—from thumbnails of whole slide to full zooms of subnuclei—almost instantly. The collection can be split, filtered, and sorted using a range of continuous and discrete metadata variables (sex, age, strain, genotype, behavior) Limitations with the current Pivot implementation can be divided into two categories: those associated with the interface itself (no nested displays, a limit of 15 displayed categories, no graphic overlay for marking or annotation), and those associated with secondary analytic and statistical functions that would typically be used to test hypotheses (no dynamic output of group statistics nor tests for differences among groups using ANOVA or t tests).

Discussion: Pivot is a superb web service architecture that provides very fluid access to massive neuroimaging databases. It is extremely well suited for both the dissemination of massive 2D collections and direct exploratory analysis as part of a web service. Pivot has also been extremely helpful as part of quality control workflow and has enabled us to search for neuroanatomical differences and patterns of variation among strains of mice in ways that far surpass any other web interface.

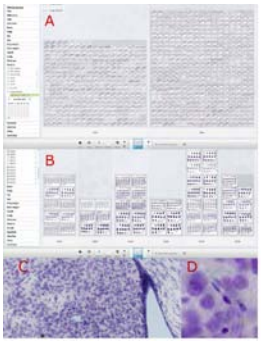


Fig 1. The Pivot interface. A. Forest view of 788 slides in two major categories (1900s, 2000s). B. Tree view of a subset of six strains of mice in which coronal and sagittal sections can be distinguished. C and D are branch and leaf views (progressively higher power zooms) to the level of 1 micron per pixel of a single section (medial striatum).

References

1. Lu L, Airey DC, Williams RW (2001) Complex trait analysis of the hippocampus: mapping and biometric analysis of two novel gene loci with specific effects on hippocampal structure in mice. J Neurosci 2001 21:3503-14

2. Rosen GD, Pung CJ, Owens CB, Caplow J, Kim H, Mozhui K, Lu L, Williams RW (2009) Genetic modulation of striatal volume by loci on Chrs 6 and 17 in BXD recombinant inbred mice. Genes Brain Behav 8:296-308

3. Yang RJ, Mozhui K, Karlsson RM, Cameron HA, Williams RW, Holmes A (2008) Variation in mouse basolateral amygdala volume is associated with differences in stress reactivity and fear learning. Neuropsychopharm 33:2595-2604

The INCF Program on Ontologies for Neural Structures

Maryann Martone

Department of Neuroscience, University of California at San Diego, San Diego, USA

The goal of the program on Ontologies of Neural Structures is to promote data exchange and integration across disciplines, species, developmental stages, and structural scales by developing terminology standards and formal ontologies for neural structures. The current program comprises three task forces: the Structural Lexicon Task Force, the Neuronal Registry Task Force and the Representation and Deployment Task Force. These groups are working on formal definitions for brain regions and neurons through a formal definition of their properties. Demonstrations of the strategies and products will be debuted at the Kobe meeting.

Practical metadata standards: Making data sharing and endurance feasible

Colin Ingram

University of Newcastle, Newcastle, UK

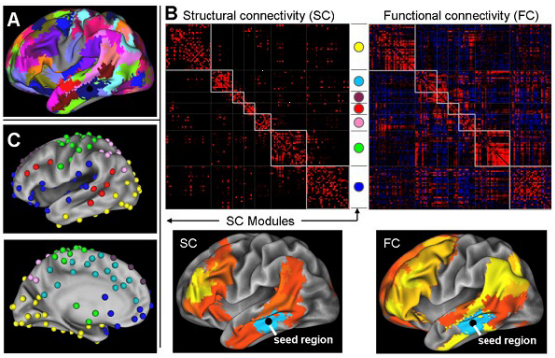
Neuroscience data are associated with a rich set of descriptive information that define the data structure, study design, and conditions of data acquisition (such as device characteristics, experimental protocol and parameters, behavioral paradigms, and subject/patient information) and for analyzed data, the statistical procedures applied. These metadata have a vital role in enabling an understanding of a dataset and without them any shared data have little value. To facilitate data archive, storage, sharing and re-use a number of areas of bioscience have developed agreed minimal metadata standards that have been adopted both by database curators and publishers. The INCF Program on Metadata Standards is examining the issues around developing metadata standards for neuroscience, including methods for efficient acquisition, domain-specific minimal standards, agreed terminology, formats and interoperability. The Oversight Committee has reviewed current schemas used to support neuroscience metadata and identified a number of the challenges associated with implementing an effective metadata structure. The major challenge facing the program is that, whilst it is broadly accepted that 'minimal' metadata are helpful for categorization or indexing of data, in most cases minimal metadata are insufficient to understand a study. On the other hand, describing every condition of an experiment in sufficient detail is difficult, and implementing detailed database schema can burden users and reduce the incentive to contribute, particularly for historical data. Thus, whilst one of the overall aims is to develop generic minimal requirements for reporting metadata, a key principle of the program is to develop approaches that will generate metadata of sufficient detail as to increase the value of the data both now and in the future. To this end we propose to develop metadata extraction tools that can automatically read metadata from acquisition devices or from existing file formats. This metadata extraction will also be applied to the analysis packages used for data processing in order that it is possible to understand the processes used to generate derived data. The program will also evaluate the opportunities for developing standards for the exchange of metadata and new methods for recording metadata at source (e.g. electronic lab books). Such automated extraction will reduce the overhead for generating the metadata whilst implementing a standardized acquisition method. A second principle underlying this program is that specific projects aimed at implementing metadata standards should be user-oriented, with a clear understanding of the value of the available data, the identity of the user community, and the potential outcomes arising from sharing. To this end the Oversight Committee has recommended establishing two Task Forces with a focus around the specific areas of fMRI and EEG where there are large user communities, employing similar methodology and where there can be considerable benefit from data sharing. The first Task Force will focus on the use case of developing a metadata schema to support resting fMRI data, and will develop methods for automating metadata acquisition at the level of the laboratory and ensuring interoperability between different data management systems. The second Task Force will focus on the use case of creating a domain standard for exchanging and describing EEG data, and will develop a framework for defining stimuli which are used in EEG experiments. Over the lifetime of the program these two use cases will be evaluated to determine the extent to which application of metadata standards can increase the access to shared data.

An informatics perspective on cerebral cortical connectivity and function

David C. Van Essen

Washington University School of Medicine, Washington, USA

One of the great scientific challenges of the 21st century is to elucidate how the wiring of the human brain accounts for our unique cognitive capabilities and for individual differences in a wide variety of behavioral capacities. Recent advances on a variety of fronts, from data acquisition to neuroinformatics, will enable rapid progress on this daunting problem. The core data acquisition methods involve two powerful and complementary tools for analyzing human brain connectivity in vivo: tractography, which is based on diffusion imaging (DI), and functional connectivity analysis, which is based on spatial correlations in resting-state fMRI BOLD signals (R-fMRI). This presentation will discuss progress and challenges in using these methods to chart brain connectivity and to parcellate cerebral cortex based on differential patterns of connectivity (Fig. 1). This includes novel methods of data acquisition, analysis, and visualization, plus informatics enhancements for storing and communicating vast amounts of connectivity data. Several approaches to evaluating and validating connectivity data will be discussed. This includes comparisons with tracer-based connectivity maps acquired in nonhuman primates and registered to human cortex using plausible homologies between species. Collectively, these approaches are likely to yield deep insights into the fundamental basis of human brain function in health and disease.



Neuroinformatics approaches for mapping striatal structures and cortico-striatal connections in the human brain

Gary F. Egan[1], India Bohanna[1] and Nellie Georgiou-Karistianis[2]

1. Florey Neuroscience Institute and Centre for Neuroscience, University of Melbourne, Melbourne, Australia
2. Experimental Neuropsychology Research Unit, School of Psychology and Psychiatry, Monash University, Clayton, Australia

Major advances in our understanding of the human brain have resulted from neuroimaging research over the past two decades. The development of novel neuroinformatics approaches for the analysis of large neuroimaging datasets is enhancing our understanding of normal brain function as well as dysfunction in neurological and psychiatric diseases (1). Current models of cortico-striatal circuitry incorporate anatomically distinct parallel neural pathways projecting from the cerebral cortex to the striatum, each subserving a unique motor, cognitive or limbic function. Our current understanding of cortico-striatal functional neuroanatomy has been gained primarily from tract tracing studies in primates, but until recently these circuits have not been comprehensively demonstrated in the human brain (2).

Diffusion Tensor Imaging (DTI) probabilistic tractography has been used to identify the spatial distribution of cortical connections within the human caudate and putamen. Cortical connections were topographically organized within the caudate and putamen, reflecting cerebral cortex organization, with significant spatial segregation between circuits. Both the caudate and putamen connected primarily with the prefrontal cortex highlighting a neuroanatomical difference between humans and primates in cortico-striatal circuitry, and suggests a possible role for the putamen in cognition.

Brain connectivity maps generated with advanced neuroinformatics techniques can facilitate detailed examination of the volume, connectivity and microstructure within individual striatal sub-regions and sub-circuits. Connectivity maps of the caudate and putamen are useful for examining the integrity of individual cortico-striatal circuits and/or striatal sub-regions, and can assist in investigating diseases characterised by regionally selective degeneration of the striatum, such as Huntington's and Parkinson's diseases.

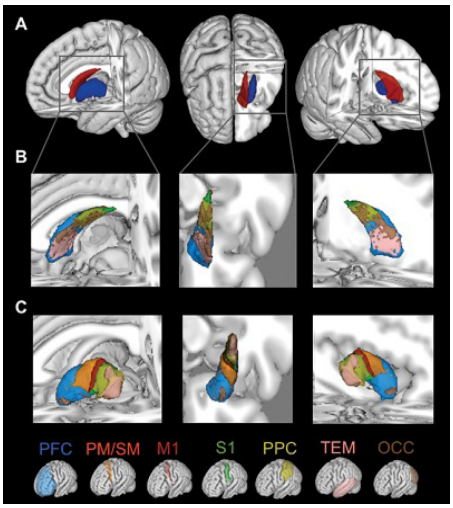


Figure 1: (A) Three-dimensional segmentation of the human caudate (red) and putamen (blue). Organisation of cortical connections within the (B) caudate and (C) putamen. The cortical target regions of interest corresponding to each colour in (B & C) are shown at bottom. All segmentations are overlaid on the standard space MNI152 T1 weighted 1mm structural MR image. PF, Prefrontal; PM, Premotor; M1, Primary motor; S1; Somatosensory; PP, Posterior parietal; OCC, Occipital; TEM, Temporal

References

1. Bohanna I, et al. (2008) MRI identification of neuropathological biomarkers for HD. Brain Research Reviews 58:209-225

2. Alexander GE, et al. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Cited in Barton RA, Harvey PH (2000). Mosaic evolution of brain structure in mammals. Annu Rev Neurosci 9:357-381.

3. Draganski B, et al. (2008). Evidence for segregated and integrative connectivity patterns in the human Basal Ganglia. J Neurosci. 28:7143-52

4. Bohanna I, et al. (2010) Circuit-specific degeneration of the striatum in Huntington's disease: a Diffusion Tensor Imaging study. Neuroimage in press (Proc. 16th Inter Conf Human Brain Mapping)

Perspetives on neuroinformatics as an important tool for an engineering goal - artificial cognitive system

Soo-Young Lee

Brain Science Research Center and Department of Electrical Engineering, KAIST, Daejeon, South Korea

We present two new research projects on neuroinformatics in Korea, i.e., Artificial Cognitive Systems (ACS) and Brain NeuroInformatics and Brain Engineering (BNIBE) projects. Both projects adopt the multidisciplinary integrative approach, and consist of brain signal measurements, computational models, and application test-beds of high-level cognitive functions. The Artificial Cognitive Systems (ACS) will be based on Proactive Knowledge Development (PKD) and Self-Identity (SI) models. The PKD model provides bilateral interactions between robot and unknown environment (people, other robots, cyberspace, etc.). Based on the computational models of PKD and SI, we would like to build functional modules for Knowledge Represenation (Basic units of knowledge, i.e., features, and hierarchical network architecture based on the features), Knowledge Accumulation (Self-learning knowledge accumulation from environment), Situation Awareness (Recognition of unknown environment and situation based on knowledge, previous experience, and self-identity), Decision Making (Decision making based on situation, models of the users, and its own internal states), and Human Behavior (Action model for facial expression, hand motion, and speeches). The developed ACS will be tested against the new Turing Test for the situation awareness. The Test problems will consist of several video clips, and the performance of the ACSs will be compared against those of human with several levels of cognitive ability. The Brain NeuroInformatics and Brain Engineering (BNIBE) project aims for computational models for cognitive functions and its applications to bilaterally-interactive man-machine interface (MMI). At the first phase of the BNIBE emphasizes the recognition of human intention, both explicit and implicit, from EEG, EOG, EMG, and audio-visual data. At the second phase, it will focus on the understanding of human behavior and its applications to real-time MMI.

Integrated Bioscience with Dynamic Brain Platform

Taishin Nomura

Graduate School of Engineering Science, Osaka University, Osaka, Japan

The human genome sequencing was an epoch marking event in reductionist life science, liberating vast amount of experimental data. The challenge for the life sciences in the 21st century is to integrate this information into understanding of human physiology and pathology. In this context, advances in techniques for measurement of human body and functions including brain activities, information technology, and applied mathematics for modeling, simulating, and analyzing nonlinear dynamics continue their remarkable development. The integration of these fields and techniques is now moving the world towards a new generation of life science, where physiological and pathological information from the living human can be quantitatively described in silico across multiple scales of time and size and through diverse hierarchies of organization - from molecules to cells and organs to individuals. The physiome and systems biology in close interactions with bioinformatics and neuroinformatics represent such emerging biosciences. These new trends in biosciences share a common direction, namely "integrative" approach. This integrative approach is in stark contrast to linear and/or static approaches of the reductionist life science, allowing us to understand the mechanisms underlying physiological functions that will emerge through the dynamics of each element and large aggregations of the elements.

Integrative biosciences and engineering in its early stage aims at establishing frameworks and infrastructures for describing biological structure and physiological functions at multiple scales of time and space and then databasing and sharing them. To this end, standardized infrastructures that can deal with dynamics of proteins, cells, tissues, and organs, at multiple scales with multiple physics have been required. International communities such as for systems biology markup language (SBML), CellML, and Virtual Physiological Human (VPH) have promoted pioneering efforts to establish such frameworks. Through communication with these efforts, we have proposed insilicoML (ISML) possessing unique features that are compatible and complimentary to SBML and CellML. It is capable of representing hierarchical, modular, and morphological structure of physiological entities and functional operations of one module onto others. The integrated development environment, insilicoIDE (ISIDE), plays roles as a model composer, a browser, as well as a simulator of models written in ISML, CellML and SBML. The insilicoDB (ISDB) is a set of databases, including ISML-model DB, Morphology DB, and Time-series DB. They can be integrated on the ISIDE. The triplet (ISML, ISDB, and ISIDE) is available in the public domain as the physiome.jp open platform [1]. It can thus be enhancing the stream of model sharing and increasing diversity of building blocks useful for the integration. The physiome.jp has been collaborating with the Dynamic Brain Platform [2], a part of INCF J-Node, to exchange database contents of each platform and to provide standardized methodologies for constructing novel new models of brain functions by integrating models and data provided by the databases.

The development of the integrative biosciences and engineering will change conventional biology and medicine that have been based upon experience and expectation into predictive sciences. The predictive biosciences will have the capability to develop solutions based upon prior understanding of the dynamic mechanisms and the quantitative logic of physiology. Drug discovery, medical and welfare apparatus, and in silico trials for those will improve the development of products with higher efficiency, reliability and safety while reducing cost. They will also impact upon knowledge-intensive industries. It is thus essential for the future development of biosciences, clinical medicine, and industry, to establish infrastructures that are capable of playing core roles in the integration.

References

1. http://www.physiome.jp

2. http://dynamicbrain.neuroinf.jp

Japan's Next-Generation Supercomputer R&D Project and Grand Challenges in Life Science

Ryutaro Himeno

Integrated Simulation of Living Matter Group, RIKEN, Saitama, Japan

MEXT and RIKEN started the Next-Generation Supercomputer R&D Project in 2006, of which goal is to develop a supercomputer with 10 Peta FLOPS in 2011FY. The supercomputer will be installed in a new supercomputer center in Kobe, where the buildings and facilities will be completed by the end of May, 2010. In this R&D project, not only hardware development but also software development in Nano Science and Life Science as Grand Challenge problems are planed and included. The Institute of Molecular Science leads the Nono Science Grand Challenge and RIKEN leads the Life Science one.

As the Life Science Grand Challenge, we have two approaches to achieve comprehensive understanding of life phenomena and to contribute to our society by creating medicine and developing medical/surgical treatment. Those approaches are 1) theoretical simulation approach and 2) data-driven approach. In addition to these approaches, we have a HPC team which is responsible to deliver maximum performance of the 10 Peta FLOPS supercomputer to tune the application software and to develop and provide tools for visualization and parallelization to other teams. These software tools are also available to anyone who will use the supercomputer. In 2007, we have added Brain and Neural Sytems Team lead by Prof. Ishii, Kyoto Universities.

Current status of supercomputer development and the application software development in Life Scinece will be shown in the talk.

INDEX

KEYNOTES

DEMOS

POSTERS

Session 1

Session 2

INCF Japan-Node Special Symposium

Neuro Informatics 2010

Abstract book produced by:

Frontiers
Science Park PSE-D
CH - 1015 Lausanne, Switzerland
T +41(0)21 693 92 02 | F +41(0)21 693 92 01
info@frontiersin.org | www.frontiersin.org

INCF Secretariat, Karolinska Institutet, Nobels väg 15 A, SE-171 77 Stockholm, Sweden
Tel: +46 8 524 87093 Fax: +46 8 524 87 150
E-mail: info@incf.org Web: www.incf.org