Neuro Informatics 2013

August 27 - 29
Stockholm, Sweden

Artwork by Nina Johansson | ninajohansson.se

ABSTRACT BOOK

Neuroinformatics 2013
6th INCF Congress

Program & abstracts

August 27 - 29, 2012
Stockholm, Sweden

International Neuroinformatics Coordinating Facility

The International Neuroinformatics Coordinating Facility (INCF), together with its 17 member countries, coordinates collaborative informatics infrastructure for neuroscience and manages scientific programs to develop standards for data sharing, analysis, modeling and simulation in order to catalyze insights into brain function in health and disease. INCF is an international organization launched in 2005, following a proposal from the Global Science Forum of the OECD to establish international coordination and collaborative informatics infrastructure for neuroscience. INCF is hosted by Karolinska Institutet and the Royal Institute of Technology, and the Secretariat is located on the Karolinska Institute Campus in Solna. INCF currently has 17 member countries across North America, Europe, Australia and Asia. Each member country establishes an INCF National Node to further the development of Neuroinformatics and to interface with the INCF Secretariat. The mission of INCF is to share and integrate neuroscience data and knowledge worldwide, with the aim to catalyze insights into brain function in health and disease.

To fulfill this mission, INCF establishes and operates scientific programs to develop standards for neuroscience data sharing, analysis, modeling and simulation. Currently there are 4 program areas: Digital Brain Atlasing; Ontologies for Neural Structures, Multi-scale modeling, and Standards for Data Sharing. More than 180 leading international researchers are involved in the programs. A cloud-based data federation - the INCF Dataspace - has been developed to enable collaboration between researchers through the sharing of neuroscience data, text, images, sounds, movies, models and simulations.

Learn more: incf.org
software.incf.org
neuroinformatics2013.org

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***as of August 2013**

Welcome to the 6th INCF Congress in Stockholm, Sweden!

The 6th Neuroinformatics Congress returns to where the congress started: Stockholm, the lively capital of Sweden, and site of the INCF secretariat. We expect many attendees, attracted by our exciting congress program and by Stockholm as a nice summer destination.

Neuroinformatics 2013 is organized by the INCF together with the Swedish INCF Node. Overall the program structure is similar to previous years, mostly single track with 6 Keynotes, 4 Workshops, and 2 Poster and Demo Sessions; this year, we have introduced more contributed program content. For the first time, there will be an Oral Presentations Session for which 10 submitted abstracts were selected by the Program Committee out of 39 abstracts that requested an oral presentation. This session will bring you the newest science, and it nicely presents the wide range of research topics that are of interest to neuroinformaticians. Like last year, we also have two concurrent Workshops that were selected among submitted proposals.

Content-wise we have an increased focus on clinical neuroinformatics, an important growth area for INCF and the community, and we end the congress with a Special Session on Large-Scale Brain Initiatives that will present Mindscope, BRAIN and the Human Brain Project. To broaden the scope of the congress, the program committee invited several Keynotes speakers who are not traditionally part of the neuroinformatics community to talk about highly relevant work in related fields.

So while the Stockholm location may seem familiar to regular congress attendees, they will notice that this year's program covers a wider range of neuroinformatics research and applications.

Erik De Schutter
Okinawa Institute of Science and Technology
INCF 2013 Program Committee Chair

Organizers

Program Committee

Erik De Schutter, (Chair) *Okinawa Institute of Science and Technology*
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INCF Secretariat

Congress Program at a glance

Tuesday, Aug 27th

08:30 Opening statement

08:40 Welcome from the INCF Director

09:00 Keynote:
Sophia Ananiadou

09:50 Coffee break

10:20 Workshop 1:
Analysis and interpretation of massively parallel electrophysical data
Chair:
Sonja Grün
Speakers:
Nicholas Hatsopoulos, Robert E. Kass, Jonathan Pillow, Matteo Carandini

12:10 Lunch

13:00 Poster and demo session 1

15:30 Coffee served

16:00 Keynote:
Hiroki R. Ueda

16:50 Presentation by
Huron Technologies

17:00 Keynote:
Randal Burns

17:50 Presentation by
Frontiers

18:00 End

19:00 Welcome reception at Stockholm City Hall

Wednesday, Aug 28th

09:00 Keynote:
Apostolos P. Georgopoulos

09:50 Coffee break

10:20 Workshop 2:
The informatics underlying meta-analysis and reproducibility in neuroimaging
Chair:
Jessica Turner
Speakers:
Satrajit Ghosh, Tal Yarkoni, Gully Burns, Angie Laird

12:10 Lunch

13:00 Keynote:
Barbara Franke

13:50 Poster and demo session 2

15:00 Coffee served

16:30 Oral presentations of selected abstracts:
Stephen Larson, Giorgio M. Innocenti, Gaël Varoquaux, Cameron Craddock, Kit Cheung, Krishnan Padmanabhan, Michele Migliore, Shreejoy J. Tripathy, Gang Yang, Anita Bandrowski

18:20 End

19:15 Banquet at Vinterviken

Thursday, Aug 29 th

09:00 Keynote:
Fred Hamprecht

09:50 Coffee break

10:20 PARALLEL WORKSHOPS

10:20 Workshop 3:
Orion Bionetworks: Predictive models powering the search for cures
Chair:
Magali Haas
Speakers:
Robert McBurney, Philip L. De Jager, Jamie Heywood, Iya Khalil, Stephen Larson

10:20 Workshop 4:
Transfer entropy - an information theoretic tool of choice for brain research
Chair:
Zbigniew R. Struzik
Speakers:
Zbiginiew R. Struzik, Daniele Marinazzo, Damien Battaglia, Michael Wibral

12:10 Lunch

13:00 Special session:
Large scale brain initiatives
Speakers:
Clay Reid, Michelle Freund, Karlheinz Meier

15:30 Coffee break

16:00 INCF Swedish Node special symposium

17:30 Closing remarks

18:00 End

Tuesday, August 27, 2013

08:30 **OPENING STATEMENT**

Jan Bjaalie, University of Oslo, Norway
Erik De Shutter, Okinawa Institute of Science and Technology, Japan

08:40 **WELCOME**

Sean Hill, INCF Executive Director

09:00 **KEYNOTE** ▶ *Integrating and ranking the evidence from pathways to text*

Sophia Ananiadou, University of Manchester, United Kingdom

09:50 Coffee break

10:20 **WORKSHOP 1** ▶ *Analysis and interpretation of massively parallel electrophysiological data*

Chair: **Sonja Grün**, Forschungszentrum Jülich, Germany

10:25 **Nicholas Hatsopoulos**, University of Chicago, USA
10:50 **Robert E. Kass**, Carnegie Mellon University, USA
11:15 **Jonathan Pillow**, University of Texas at Austin, USA
11:40 **Matteo Carandini**, University College London, United Kingdom

12:10 Lunch

13:00 **POSTER AND DEMO SESSION 1**

15:30 Coffee served

16:00 **KEYNOTE** ▶ *Systems and synthetic biology of biological timings*

Hiroki R. Ueda, RIKEN Quantitative Biology Center, Japan

16:50 Presentation by **Huron Technologies**

17:00 **KEYNOTE** ▶ *Data-intensive computing for neuroscience: The open connectome project*

Randal Burns, The Johns Hopkins University, USA

17:50 Presentation by **Frontiers**

18:00 End
18:30 Buses departure from the venue to the Welcome Reception
19 :00 Welcome Reception at Stockholm City Hall

Wednesday, August 28, 2013

09:00 **KEYNOTE** ▶ *Brain function in healthy aging*
Apostolos P. Georgopoulos, University of Minnesota, USA

09:50 **Coffee break**

10:20 **WORKSHOP 2** ▶ *The informatics underlying meta-analysis and reproducibility in neuroimaging*
Chair: **Jessica Turner**, Mind Research Network, USA
10:25 **Satrajit Ghosh**, Massachusetts Institute of Technology, USA
10:50 **Tal Yarkoni**, University of Colorado at Boulder, USA
11:15 **Gully Burns**, University of Southern California, USA
11:40 **Angie Laird**, Florida International University, USA

12:10 **Lunch**

13:00 **KEYNOTE** ▶ *How to make sense of genetics for psychiatric disorders?*
Barbara Franke, Radboud University Medical Centre in Nijmegen, The Netherlands

13:50 **POSTER AND DEMO SESSION 2**

15:00 **Coffee served**

16:30 **ORAL PRESENTATIONS OF SELECTED ABSTRACTS**
Chair: **Erik De Shutter**, Okinawa Institute of Science and Technology, Japan
Stephen Larson, OpenWorm.org, USA
Giorgio M. Innocenti, Karolinska Institute, Sweden
Gaël Varoquaux, INRIA, France
Cameron Craddock, Child Mind Institute/Nathan Kline Institute for Psychiatric Research/The Neuro Bureau Research Institute, USA
Kit Cheung, Imperial College London, United Kingdom
Krishnan Padmanabhan, Salk Institute for Biological Studies, USA
Michele Migliore, Yale University, USA/National Research Council, Italy
Shreejoy J. Tripathy, Carnegie Mellon University, USA
Fan Meng, University of Michigan, USA
Anita Bandrowski, The University of California, San Diego, USA

18:20 **End**
18:30 **Buses departure from the venue to the banquet**
19:15 **Banquet at Vinterviken**

Thursday, August 29, 2013

09:00 **KEYNOTE** ▶ *Electron microscopy circuit reconstruction*

Fred Hamprecht, Ruprecht Karl University of Heidelberg, Germany

09:50 Coffee break

10:20 **PARALLEL WORKSHOPS**

Lecture hall Berzelius:

10:20 **WORKSHOP 3** ▶ *Orion Bionetworks: Predictive models powering the search for cures*

Chair: **Magali Haas**, One Mind for Research, USA

10:25 **Robert McBurney**, Accelerated Cure Project for Multiple Sclerosis, USA

10:45 **Philip L. DeJager**, Brigham & Women's Hospital, USA

11:05 **Jamie Heywood**, PatientsLikeMe, USA

11:25 **Iya Khalil**, GNS Healthcare, USA

11:45 **Stephen Larson**, One Mind for Research, USA

Lecture hall Vesalius:

10:20 **WORKSHOP 4** ▶ *Transfer entropy--an information theoretic tool of choice for brain research*

Chair: **Zbigniew R. Struzik**, The University of Tokyo, Japan

10:25 **Zbigniew R. Struzik**, The University of Tokyo, Japan

10:50 **Daniele Marinazzo**, University of Gent, Belgium

11:15 **Demian Battaglia**, Max Planck Institute for Dynamics and Self-Organization, Germany

11:40 **Michael Wibral**, MEG Unit, Brain Imaging Center, Goethe University, Germany

12:10 Lunch

13:00 **SPECIAL SESSION ON LARGE SCALE BRAIN INITIATIVES**

▶ *Neural coding and project MindScope*

Clay Reid, Allen Institute for Brain Science, USA

▶ *The BRAIN initiative*

Michelle Freund, National Institute of Mental Health, USA

▶ *The EU Human Brain Project - Scientific foundations and plans*

Karlheinz Meier, Ruprecht Karl University of Heidelberg, Germany

15:30 Coffee break

Thursday, August 29, 2013 (cont.)

16:00 **INCF SWEDISH NODE SPECIAL SYMPOSIUM**

Chair: **Jeanette Hellgren Kotaleski**, KTH, KI and INCF, Sweden

16:10 **Per Petersson**, Lund University, Neuronano Center, Sweden

16:40 **Edwin Johnson**, Stockholm Brain Institute, Sweden

17:10 **Linda Lanyon,** INCF Secretariat, Sweden

17:30 **CONCLUDING REMARKS**

Jeanette Hellgren Kotaleski, INCF Swedish Node and **Paul Tiesinga**, INCF Netherlands Node

18:00 **End**

INCF looks forward to welcoming you to the 7th Neuroinformatics Congress in Leiden, the Netherlands, on August 25-27, 2014!

www.neuroinformatics2014.org

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Transactions on Biomedical Circuits and Systems
Reviews on Biomedical Engineering
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Keynotes

Sophia Ananiadou
Hiroki Ueda
Randal Burns
Apostolos P. Georgopoulos
Barbara Franke
Fred Hamprecht

Integrating and ranking the evidence from pathways to text

Sophia Ananiadou

University of Manchester
Manchester, United Kingdom

PathText is a text mining system associating pathway models encoded in SBML with evidence from the literature. The strengths of PathText include integration with text mining semantic search services, Facta+, KLEIO, MEDIE, query generation and document-reaction relevance ranking. These services include event extraction tools (EventMine), faceted search based on named entity recognition, disambiguation components and normalisation. In addition, a one-stop collaborative text processing workflow platform (Argo) includes annotation tools that facilitate curation of pathways.

Systems and synthetic biology of biological timings

Hiroki Ueda

RIKEN Quantitative Biology Center
Kobe, Japan

The logic of biological networks is difficult to elucidate without (1) comprehensive identification of network structure, (2) prediction and validation based on quantitative measurement and perturbation of network behavior, and (3) design and implementation of artificial networks of identified structure and observed dynamics.

Mammalian circadian clock system is such a complex and dynamic system consisting of complicatedly integrated regulatory loops and displaying the various dynamic behaviors including i) endogenous oscillation with about 24-hour period, ii) entrainment to the external environmental changes (temperature and light cycle), and iii) temperature compensation over the wide range of temperature. In this symposium, I will take a mammalian circadian clock as an example, and introduce the systems- and synthetic-biological approaches for understanding of biological timings.

References

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Data-intensive computing for neuroscience: The open connectome project

Randal Burns

Johns Hopkins University
Baltimore, Maryland, United States

High-throughput imaging has created a "Big Data" crisis in neuroscience in which the size and complexity of data exceed the capability of labs to manage it. The Open Connectome Project stores massive imaging data on data-intensive clusters and provides Web services that can be used to extract, store, and analyze neural structure. As a platform for public data, the Open Connectome Project democratizes access to world-class imaging, making data available to researchers in statistics, machine learning, and computer vision. This talk will describe how data-intensive computing is transforming Open (Neuro)-Science. It will cover the hardware and software architecture of the services, including spatial queries, data representations and placement, and integration with parallel computing.

Brain Function in Healthy Aging

Apostolos P. Georgopoulos

University of Minnesota
Minneapolis, United States

In this lecture I will discuss brain function during healthy aging. I will focus on the interaction among neural population signals as a measure of vitality of brain network activity and show that this is well maintained throughout the lifespan. I will argue that, in the absence of disease, brain network function is kept at an adequate performance level even at advanced old age. Finally, I will discuss the influence of genetics on brain function, focusing on the effect of apolipoprotein E gene, as reported in a recent paper from our laboratory.

Leuthold AC, Mahan MYM, Stanwyck JJ, Georgopoulos A, Georgopoulos AP (2013)
The number of cysteine residues per mole in apolipoprotein E affects systematically synchronous neural interactions in women's healthy brains. Experimental Brain Research
DOI 10.1007/s00221-013-3464-x.

How to make sense of genetics for psychiatric disorders?

Barbara Franke

Radboud University Medical Centre in Nijmegen
Nijmegen, The Netherlands

Most psychiatric disorders are highly heritable. Take Attention-deficit/hyperactivity disorder (ADHD), which has a heritability of nearly 80% in both children and in adults. However, ADHD's genetic background is extremely complex, with multiple genetic variants plus the environment contributing to its etiology in most patients. This has hampered the identification of the genes underlying this disorder. The same holds true for other psychiatric disorders like schizophrenia, bipolar disorder and autism.

In my presentation, I will highlight approaches to finding genes for psychiatric disorders, particularly ADHD, including genome-wide genetic association studies, copy number variant studies and next generation sequencing. In this, we often find that statistical/bioinformatics analysis methods lack behind technical advances, however, I will show how we are finally starting to pick up speed in gene-identification.

Importantly, though, the way in which such genes contribute to psychiatric psychopathology is still hardly understood. For this, it is essential that we integrate findings across different types of approaches using bioinformatics. An important tool in the identification of biological pathways is brain imaging. I will show our 'cognomics' studies, in which we link genetics with behaviour by mapping the effects of genes on the brain. Only an effective integration of multimodal data can provide the information needed to map the biological pathways from gene to disease and translate the results from genetic findings into clinically useful information for diagnosis and treatment of psychiatric disorders.

Electron microscopy circuit reconstruction

Fred Hamprecht

Ruprecht Karl University of Heidelberg
Heidelberg, German

The tenet of connectomics is that knowledge of the wiring diagram of a brain will facilitate, or even be prerequisite for, an understanding of its function. Serial sectioning electron microscopy now yields brilliant volume images that allow human tracers to accurately follow all neural processes, as well as identify synapses, in tiny parts of a brain. The race is on for microscopic volume imaging of an entire mammalian brain, and the target is likely to be reached in the foreseeable future.

However, human tracing will not scale to such exceedingly large volumes. Besides the actual image acquisition, automated circuit reconstruction is thus becoming the major bottleneck. Current algorithms do not yield flawless segmentations yet, and buying a larger computer does not solve the issue. Instead, better models are required.

I will survey the state of the art in automated reconstruction and explain why algorithm developers are optimistic to still do their bit in good time.

Special Session on Large Scale Brain Initiatives

Clay Reid
Michelle Freund
Karlheinz Meier

Neural coding and project MindScope

Clay Reid

Allen Institute for Brain Science
Seattle, United States

Local circuits in the cerebral cortex consist of tens of thousands of neurons, each of which makes and receives thousands of connections. A major impediment to understanding these circuits is that we have no wiring diagrams of their interconnections. But even if we had a wiring diagram, understanding the network would also require information about each neuron's function. Recently, we have demonstrated that the relationship between structure and synaptic connectivity can be studied in the cortex by combining in vivo physiology with subsequent network anatomy with electron microscopy (Bock et al., Nature, 2011), leading towards a functional connectome. This research program is continuing as part of a larger program at the Allen Institute, called MindScope, that seeks to examine the computations that lead from visual input to behavioral responses by observing and modeling the physical transformations of signals in the cortico-thalamic visual system of mice (Koch and Reid, Nature, 2012. I will describe other aspects of this program, including calcium imaging experiments to examine the physiological properties of pyramidal neurons that project between different cortical areas: the functional projectome.

The BRAIN initiative

Michelle Freund

National Institute of Mental Health
Bethesda, Maryland, United States

On April 2, 2013, President Obama announced the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, "giving scientists the tools they need to get a dynamic picture of the brain in action and better understand how we think and how we learn and how we remember." This initiative, launched with a proposal for federal funding of $100M in the next fiscal year, will be led by the National Institutes of Health, the Defense Advanced Research Project Agency (DARPA), and the National Science Foundation (NSF), along with additional funds from private partners including the Allen Institute for Brain Science, the Howard Hughes Medical Institute, the Kavli Foundation, and the Salk Institute for Biological Studies.

Earlier versions of such a proposal, called the "Brain Activity Map", were developed at a series of meetings sponsored by the Kavli Foundation, the Gatsby Charitable Foundation, and the Allen Institute for Brain Science. BRAIN will extend that vision, with broad input from the neuroscience community as well as several related disciplines vital for technology development (nanotechnology, materials science, computational science, and many others).

The NIH BRAIN Initiative will begin with a group of 15 external advisors charged to develop a scientific plan that will (a) identify areas of high priority (i.e. improving current tools, identifying new directions); (b) develop some principles for achieving the goals of the BRAIN Initiative (i.e. balance between individual groups and large consortia, balance between problem-solving and technology driven science); (c) suggest opportunities for collaboration with foundations, industry, and other agencies; and (d) deliver specific recommendations for timelines, milestones, and cost estimates.

The EU Human Brain Project, the Human Connectome Project, and the INCF are important complementary efforts. Together these represent an unprecedented global focus on brain mapping with potential not only for a deeper understanding of brain function but for improved diagnostics and therapeutics of neuropsychiatric disorders.

The EU Human Brain Project - Scientific foundations and plans

Karlheinz Meier
Ruprecht Karl University of Heidelberg
Heidelberg, German

The EU has recently approved the Human Brain Project (HBP) as one of 2 European research flagships. The HBP will provide new tools to help understand the brain and its fundamental mechanisms and to apply this knowledge in future medicine and novel computing architectures. Central to HBP is Information and Computing Technology (ICT). The project will develop 6 ICT platforms for neuroinformatics, brain simulation, medical informatics, supercomputing, neuromorphic computing and neurorobotics that will make it possible to federate neuroscience data from all over the world, to integrate the data in unifying models and simulations of the brain, to check the models against data from biology and to make them available to the world scientific community. The ultimate goal is to allow neuroscientists to connect the dots leading from genes, molecules and cells to human cognition and behavior.

Workshops

1: Analysis and interpretation of massively parallel electrophysiological data

2: The informatics underlying meta-analysis and reproducibility in neuroimaging

3: Orion Bionetworks: Predictive models powering the search for cures

4: Transfer entropy--an information theoretic tool of choice for brain research

Workshop 1: Analysis and interpretation of massively parallel electrophysiological data

Chair: **Sonja Grün**, *Forschungszentrum Jülich, Germany*

Probing the organization of interactions within and across neuronal populations is a promising approach to understanding the principles of brain processing. The rapidly advancing technical capabilities to record from hundreds of neurons in parallel open up new possibilities to disentangle the correlative structure within neuronal networks. However, the complexity of these massive data streams calls for novel, tractable analysis tools that exploit the parallel aspect of the data. Due to the fundamental computational and theoretical difficulties in describing interactions within a large set of neurons scientists are in search for the optimal models and mathematical tools to tackle this challenge. This workshop should showcase a few of these different approaches.

Speakers:

Nicholas Hatsopoulos
University of Chicago, USA
Rob Kass
Carnegie Mellon University, USA
Jonathan Pillow
University of Texas at Austin, USA
Matteo Carandini
University College London, United Kingdom

Large-scale spatio-temporal patterns in motor cortex involved in motor control

Nicholas Hatsopoulos
University of Chicago, USA

We have previously documented that motor cortical oscillations in the beta frequency range (~20 Hz) as measured by local field potential recordings propagate as travelling waves across the surface of the primary motor cortex along a rostral-to-caudal axis while monkeys perform a variety of visuo-motor tasks including simple reaching tasks and more complex reach-to-grasp tasks. We demonstrate here that simultaneously recorded neurons in non-human primates coordinate their spiking activity in a sequential manner that mirrors the dominant wave propagation directions of the local field potentials. We are beginning to test the hypothesis that this pattern of propagation may serve to sequentially recruit neurons representing different limb segments in a coordinated fashion.

Point process regression models of neural synchrony

Rob Kass
Carnegie Mellon University, USA

Over roughly the past 10 years point process regression models, often called generalized linear models or GLMs, have become a standard tool for relating neural spiking activity to putative causes, such as features of stimuli, network dynamics, and intrinsic dynamics of neurons. I will begin by discussing the virtues of this modeling approach, and will then turn to the problem of assessing neural synchrony. Synchrony is widely believed to play a fundamental role in neural computation, but its statistical assessment is subtle. I will describe how point process regression models generalize what are commonly called maximum entropy models, and can accommodate the kind of time-varying firing rates that typically appear in stimulus-driven (or action-driven) neurons, as well as non-Poisson or network effects. One of the problems faced in large array recordings is the statistical control of false discoveries. A Bayesian method for controlling false discoveries has yielded interesting physiological results from Utah array recordings in primary visual cortex.

Scalable nonparametric models for large-scale neural datasets

Jonathan Pillow
University of Texas at Austin, USA

Statistical models for binary spike responses provide a powerful tool for understanding the statistical dependencies in large-scale neural recordings. Maximum entropy (or "maxent") models, which seek to explain dependencies in terms of low-order interactions between neurons, have enjoyed remarkable success in modeling such patterns, particularly for small groups of neurons. However, these models are computationally intractable for large populations, and low-order maxent models do not accurately describe many datasets. To overcome these limitations, I will describe a family of ``universal" models for binary spike patterns, where universality refers to the ability to model arbitrary distributions over all possible 2^M binary patterns. The basic approach, which exploits ideas from Bayesian nonparametrics, consists of Dirichlet process combined with a well-behaved parametric "base" model, which naturally combines the flexibility of a histogram and the parsimony of a parametric model. I will explore computational and statistical issues for scaling these models to large-scale recordings and show applications to neural data from primate V1.

Looking for canonical neural computations in the visual system

Matteo Carandini
University College London, United Kingdom

The primary visual cortex (V1) codes fundamental attributes of visual stimuli, representing them in the coordinated and dynamically-changing activity of populations of neurons. Does this representation follow simple mathematical rules? Are these rules stable or do they change according to stimulus properties such as a recent history, strength, or configuration? Working with Andrea Benucci and Neel Dhruv, we addressed these questions in a series of experiments performed in cats and mice, where we recorded from populations of V1 neurons using multielectrode arrays. In response to sequences of stimuli of different orientations, the cortex adopts a very simple linear coding scheme, with a stereotyped response that is simply applied additively to different groups of neurons depending on the stimulus orientation. This basic linear representation, however, is only the scaffolding for more complex, nonlinear operations that make the cortex extremely adaptive. First, in response to sums of stimuli of different contrast, the cortex engages in a range of behaviors, from simple summation to winner-take-all competition. A simple model based on divisive normalization summarizes all these effects. Second, the cortex shows a marked ability to adapt to the statistics of the stimuli: it changes the selectivity and responsiveness of neurons just as needed to counteract any biases in the recent history of stimulation. A simple model based on equalization summarizes these effects. These nonlinear operations cascade from area to area: adaptation to the statistics of the stimuli in one stage of the visual system has profound effects on the inputs to the subsequent stage, and these effects can be predicted by a very simple model based on summation with fixed weights. We have great hope and reasonable expectation that the rules that we have uncovered are not specific to area V1 but are rather canonical rules of operation of cortical populations. These rules may act as guide to research in the underlying mechanisms and circuits and in the neural computations that lead to perception and behavior.

Workshop 2: The informatics underlying meta-analysis and reproducibility in neuroimaging

Chair: **Jessica Turner**, *Mind Research Network, USA*

The desire to do large-scale meta-analyses or mega-analyses across human neuroimaging datasets quickly runs into the issues of differences in study design, implementation, analyses, and reporting of results. Reproducibility of studies and analyses is a cornerstone of the scientific enterprise, yet methods sections in the published literature are usually woefully incomplete, lacking the needed detail to re-do the experiment. The data-sharing and meta-analytic efforts should facilitate replication in various senses of that term. The speakers in this workshop address the challenges of representing this information in data archives or semantic frameworks.

Speakers:

Satrajit Ghosh
Massachusetts Institute of Technology, USA
Tal Yarkoni
University of Colorado at Boulder, USA
Gully Burns
University of Southern California, USA
Angie Laird
Florida International University, USA

Enabling knowledge generation and reproducible research by embedding provenance models in metadata stores

Satrajit Ghosh
Massachusetts Institute of Technology, USA

Reproducible research requires that information pertaining to all aspects of a research activity are captured and represented richly. However, most scientific domains, including neuroscience, only capture pieces of information that are deemed relevant. In this talk, we provide an overview of the components necessary to create this information-rich landscape and describe a prototype platform for knowledge exploration. In particular, we focus on a technology agnostic data provenance model as the core representation and Semantic Web technologies that leverage such a representation. While the data and analysis methods are related to brain imaging, the same principles and architecture are applicable to any scientific domain.

Automated annotation and meta-analysis of the fMRI literature: promises and challenges

Tal Yarkoni
University of Colorado at Boulder

This talk reviews recent efforts to represent and synthesize the published fMRI literature on a large scale. I begin by discussing the pros and cons of existing methods in this area, ranging from fully automated "bag-of-words" approaches to more effortful manual approaches. Particular attention is focused on the fundamental trade-off between data quality and data quantity. I then review a number of applications demonstrating the utility of large-scale synthesis-oriented approaches in helping to map the neural substrates of cognition. Finally, I conclude with a discussion of several open challenges for data mining effort in this area, including better extraction of key metadata from published articles, development of empirically validated cognitive ontologies, and successful hybridization of automated and manual annotation efforts.

Using experimental design to design neuroinformatics data structures

Gully Burns
Information Sciences Institute, University of Southern California, USA

The interdisciplinary nature of neuroscience research leads to an explosion of different informatics tools, data structures, platforms and terminologies. A central difficulty faced by developers is that knowledge representations for any neuroscience subdomain must serve the domain-specific needs of that specified sub-community. Related representations overlap, they contradict each other, they have competing standards. The process of standardization is itself difficult to organize within the community and even harder to enforce in practice. This involves complex issues involving ease of use, computability, data availability as well as scientific correctness and philosophical purity.

In this talk, I present a novel, relatively simple conceptual design that makes a clear distinction between interpretive and observation knowledge to build a general framework for scientific data. Our methodology (called 'Knowledge Engineering from Experimental Design' or KEfED) uses an experiment's protocol's to define the dependencies between its independent and dependent variables. These dependencies support the construction of a data structure that can capture (a) data points, (b) mean values, (c) statistical significance relations and (d) correlations. We will describe the underlying formalism of the KEfED approach, the tools we provide to help researchers build their own models, our approach to unify and standardize the definition of variables, the application of KEfED to complex neuroscience knowledge and possible research directions for this technology in the future.

Data-driven approaches for deriving a semantic framework for cognitive paradigms

Angie Laird
Florida International University, USA

A massive amount of functional neuroimaging data is being acquired, analyzed, and published to provide a more complete understanding of the organization and interactions between cortical and subcortical brain regions that enable human cognition. Two decades of progress in neuroinformatics research is now coming to fruition, as neuroimaging databases are being used to aggregate, synthesize, and mine the collective work of the neuroimaging community. In my talk, I will discuss a BrainMap-based approach for knowledge representation in functional neuroimaging data, and will describe the development of a cognitive paradigm ontology. In addition, I will highlight recent findings for developing a novel method for determining paradigm sub-classification in an automated, data-driven fashion, based on the premise that meaningful segregations in tasks should result in observable dissociations in brain activation patterns. Exemplar results will be provided in the context of paradigm classifications during face perception and discrimination.

Workshop 3: Orion Bionetworks: Predictive Models Powering the Search for Cures

Chair: **Magali Haas**, *One Mind for Research, USA*

Orion Bionetworks is a unique collaborative partnership that leverages the value of disease-area expertise, high-quality data and computational modeling to transform our understanding of diseases and accelerate the search for cures. Our initial effort focuses on multiple sclerosis and includes alliance partners from leading organizations in patient care, computational modeling, translational research, and patient advocacy.

Orion Bionetworks is creating a framework for integrating diverse high-dimensional genomic, proteomic, and phenotypic data to foster the development of multi-scale computational bio-informatics models using highly parallel supercomputing, machine learning and simulation. Disease models will be iterativley refined, validated, and improved through prospective collection of refined phenotypic and molecular datasets through networks of patient-driven and academic bio-repositories and registries.

Creation of predictive causal disease models in an open-science model may fundamentally change how researchers study and discover new treatments for MS, as well as inform how clinicians and their patients make treatment decisions. Further, we anticipate that our work in MS will serve as a "case study" for other endeavors that seek a deeper understanding of complex human biological systems and disease modalities.

Speakers:

Robert McBurney
Accelerated Cure Project for Multiple Sclerosis (ACP), USA
Philip L. De Jager
Brigham & Women's Hospital, USA
Jamie Heywood
PatientsLikeMe, USA
Iya Khalil
GNS Healthcare, USA
Stephen Larson
One Mind for Research, USA

Orion Bionetworks: An innovative alliance for Multiple Sclerosis Disease Modeling

Robert McBurney
Accelerated Cure Project for Multiple Sclerosis (ACP), USA

Despite great strides in medicine over the past century, only a very small fraction of the more than 12,000 diseases separately classified by the World Health Organization can currently be cured or prevented. What we don't know about health and disease far exceeds what we do know. We have a fundamental need for models that can explain the contributions of the components of a biological system to its healthy or diseased state. Such models must also enable exploration of the effects of altering those components, in order to reveal novel targets for drug discovery and predict treatment outcomes.

Highly valuable disease models can be constructed with the following essential building blocks:

- Advanced clinical knowledge of the disease
- High-quality, comprehensive clinical, functional, environmental, and lifestyle data from people with the disease, people with other related or unrelated diseases, and healthy people (control subjects)
- High-quality, comprehensive molecular data obtained from body fluids and tissue (biosamples) from people with the disease, people with other related or unrelated diseases, and control subjects
- Outcomes data and biosamples from people with the disease who have been treated with drugs (system perturbagens) — preferably, perturbagens with different mechanisms of action
- Multiple approaches to creating the disease model, which can be employed in parallel
- Model development and validation datasets

The Phase 1 goal of Orion Bionetworks is to develop an initial disease model for MS, which ultimately will become publicly available. An additional goal is to create and evaluate a framework for establishing alliances in other disease areas.

Why we need disruptive innovation to accelerate MS research

Philip L. De Jager
Brigham & Women's Hospital, USA

Multiple sclerosis (MS) is a disease of the brain and spinal cord that has two components: inflammation, with recurring episodes of acute damage, and slowly progressive neuronal loss, which manifests as a gradual decline in cognitive and other functions. Although we know much about the inflammatory component of MS, our treatment options are imperfect and we currently have no tools with which to predict individual disease course. There is a tremendous heterogeneity among individuals with a syndromic diagnosis of MS.

Biomarker studies to date have identified modest associations with different aspects of the disease, but no single biomarker is informative. Further, we currently do not understand the pathophysiology of the neurodegenerative component of the disease. Thus, to address the issue of personalizing MS care and gain insights into disease progression that could lead to novel therapeutics, we need a new paradigm for MS investigation and analytics that is capable of considering multiple dimensions of information.

What we have learned from the patient's experience

Jamie Heywood
PatientsLikeMe, USA

PatientsLikeMe is a patient-powered research network that collects both free-text and computable health data from patients with specific diseases. By connecting with each other to share their experiences, PatientsLikeMe members generate data about the real-world nature of disease, treatments, and medical care. These data include tens of thousands of reports on the Multiple Sclerosis Rating Scale (MSRS), a measure of functional disability progression caused by MS, as well as reports on symptoms such as fatigue and spasticity. As part of Orion Bionetworks, PatientsLikeMe performed an exploratory analysis of these phenotypic MS data.

Because many MS patients use PatientsLikeMe to report data much more frequently than the typical clinical interval of 3-6 months, we were able to explore disease dynamics over a relatively short time period. We found that even at a scale of weeks, the disease is highly variable, with few predictive factors for future MSRS status other than the patient's current MSRS score.

Because PatientsLikeMe includes a large population of MS patients who have had the disease for varying lengths of time, we were also able to explore longer-term trends, which we will discuss in this workshop. One finding is that during the first 20 years after disease onset, progression along the MSRS seems more tied to the accumulation of disease domains than of increasing severity in already-present domains. This finding may have implications for theories about the underlying biophysical mechanisms of MS.

Applying causal inference modeling in multiple sclerosis

Iya Khalil
GNS Healthcare, USA

We have the opportunity today to harness the power of computer modeling and shared data to create a paradigm shift in our understanding of the mechanisms underlying disease. The work I will describe leverages multiple types of data from patients with multiple sclerosis –genetic, molecular, phenotypic, and clinical – to build models in an unbiased way. Causal disease models developed directly from data provide the predictive power we need to improve clinical outcomes for patients. Knowledge of the essential factors that drive the disease course in individual patients allows us to provide the right treatment at the right time to each patient.

Our approaches to computer modeling include reverse engineering of networks directly from data, followed by in-silico simulations to generate predictions. We also embed clinical validation and iterative improvements in our paradigm in order to continually refine our models.

Applying hierarchical modeling principles to MS Research

Stephen Larson
One Mind for Research, USA

Multiple sclerosis (MS) is an inflammatory disease that damages myelin sheaths around the axons of neurons. Although much effort has been invested in understanding the cellular processes, lipids, and proteins putatively involved in MS, there is currently no cure. A lack of understanding of how fundamental processes interact to give rise to MS phenotypes is the greatest challenge we face in making progress towards a cure.

We live in an information age and are deluged by data generated by many different individual studies. However, our ability to integrate this information into complex holistic models that enable deep hypothesis generation is still lacking. Recently, the first major whole cell in silico model that predicts phenotype from genotype was developed in the open source (Karr et al., 2012). This model includes a comprehensive set of mechanisms of cellular activity. Although their target organism was Mycoplasma genitalium, a microorganism with a small fraction of the number of human genes, the basic cellular processes in this organism are largely conserved in other animals. Thus, this effort has provided an important foundation for future in silico predictive models.

In this session we will review the Karr model as a foundation for modeling MS, and discuss what methods need to be applied to move forward.

Workshop 4: Transfer entropy--an information theoretic tool of choice for brain research

Chair: **Zbiginiew R. Struzik**, *The University of Tokyo, Japan*

The brain processes information. This statement borders on trivial rhetoric, yet it is only within the past decade that brain research has adopted the information theoretic methodology to address the problem of how information is processed in the brain. Transfer entropy is such an information theoretic measure, adopted from physics, allowing for detection and characterisation of inherently nonlinear coupling between dynamical systems exchanging information. In addition the methodology of transfer entropy allows for the determination of the directionality of this coupling and, in effect, the directionality of the flow of information. Numerous studies using this methodology have already shown the unique suitability of the methodology for revealing the brain's informational connectivity. The workshop will be devoted to reporting recent progress and forecasting future prospects of the method developed around the concept of transfer entropy. In particular, the possibility of applications of transfer entropy to reveal the modular and multiscale organisation of the brain's topological and functional connectivity will be addressed.

Speakers:

Zbiginiew R. Struzik
The University of Tokyo, Japan
Daniele Marinazzo
University of Gent, Belgium
Demian Battaglia
Max Planck Institute for Dynamics and Self-Organization, Germany
Michael Wibral
MEG Unit, Brain Imaging Center, Goethe University, Germany

Untangling the informational network of the brain-wide web

Zbigniew R. Struzik
The University of Tokyo, Japan

The brain is perhaps the most profound example of a biological system of inherentcomplexity. A system where complexity is attained from its adaptive functionalresponse to environmental information, through its hierarchical and modularorganisation and through the non-linear forms of inter- and intra-modularinteractions. Interactions, which process information, since the brain is - arguably -the most advanced information processor known.I will give an introduction to the concept of the methodology of information flowanalysis - transfer entropy, discuss the state of the art and consider the possiblefuture (or futuristic) prospects that transfer entropy gives for the exploration offunctional and topological connectivity and information flow in the brain.In particular, I will confront the possibility of applications of transfer entropy to revealthe modular and multiscale organisation of the brain's information flow.

Information transfer in the brain: insights from a unified approach

Daniele Marinazzo
University of Gent, Belgium

Measuring directed interactions in the brain in terms of information transfer is a promising approach, mathematically treatable and amenable to encompass several methods. I will present two results obtained in this framework.I will first show how implementing simple dynamical models on different architectures will reveal the limited capacity of nodes to process the input information. For a given range ofthe parameters, the information flow pattern is characterized by exponential distribution ofthe incoming information and a fat-tailed distribution of the outgoing information, as asignature of the law of diminishing marginal returns.A similar behavior is observed when dynamical models are implemented on the humanconnectome structural matrix and in EEG recordings. This suggests that overall brain effective connectivity networks may also be considered in thelight of the law of diminishing marginal returns.I will then propose a formal expansion of the transfer entropy to put in evidence irreduciblesets of variables which provide information for the future state of each assigned target.Multiplets characterized by a large contribution to the expansion are associated toinformational circuits present in the system, with an informational character (synergetic orredundant) which can be associated to the sign of the contribution.This approach allows an efficient and reliable reconstruction of directed networks andreveals specific patterns of informative multiplets in different physiological states.

Function follows dynamics: state-dependency of information flow in neural circuits

Demian Battaglia
Max Planck Institute for Dynamics and Self-Organization, Germany

Brain function require the control of inter-circuit interactions on time-scales faster thansynaptic changes. In particular, strength and direction of causal influences and informationexchange between neural populations (described by the so-called effective connectivity)must be reconfigurable even when the underlying structural connectivity is fixed. Suchinfluences can be quantified analyzing time-series of neural activity with tools like GrangerCausality, delayed Mutual Information or Transfer Entropy. But how can manifold functionalnetworks stem from fixed structures? Considering model systems at different scales, likeneuronal cultures or cortical multi-areal motifs, we show that ``function and informationfollow dynamics", rather than structure. Different dynamic states of a same structuralnetwork, characterized by different synchronization properties, are indeed associated todifferent directed functional networks, corresponding to alternative information flowpatterns. Here we discuss how suitable generalizations of Transfer Entropy, taking intoaccount switching between collective states of the analyzed circuits, can provide a pictureof causal interactions and information flow in agreement with a ``ground-truth" descriptionat the dynamical systems level.

Graphical analyses in delayed interaction networks

Michael Wibral
MEG Unit, Brain Imaging Center, Goethe University, Germany

Network or graph theory has become a popular tool to represent and analyze large-scale interactions in the brain. To derive a network representation from recorded time series we have to identify the structure of the interactions between these time series. This is commonly done by pairwise bivariate analysis as a fully multivariate treatment is often not possible due to limited data. Furthermore, a true multivariate analysis would consist of the analysis of the combined effect of all possible subsets of network components (their power set), leading to a combinatorial explosion (i.e. a problem that is computationally tractable). Pairwise bivariate analysis introduces the possibility of the detection of spurious interactions between network components due to cascade effects and common drive effects. Spurious connections in a network representation may introduce a bias to subsequently computed graph theoretical measures as these measures depend on the reliability of the graph representation from which they are computed (e.g. clustering coefficient or centrality).Strictly speaking, graph theoretical measures are meaningful only, if the underlying graph structure can be guaranteed to consist of one type of connections only, i.e. connections in the graph are guaranteed to be non-spurious. We propose an algorithmic approach to flag potentially spurious edges due to cascade effects and "simple" common drive effects in a network representation of bivariately analyzed interactions. This approach is based on the detection of directed interactions and the weighting of these interactions by their reconstructed interaction delays. We demonstrate how both questions can be addressed using a modified estimator of transfer entropy. Transfer entropy is an implementation of Wiener's principle of observational causality based on information theory, and detects arbitrary linear and non-linear interactions. Using a modified estimator that uses delayed states of the driving system, we provide a mathematical proof that transfer entropy values peak if the delay of the state of the driving system equals the true interaction delay. From this analysis, we derive a delay weighted network representation of directed interactions. The proposed algorithm may be used to partially prune spurious edges from this network, improving the reliability of the network representation itself and enhancing the applicability of subsequent graph theoretical measures. For the detection of complex common drive effects, a theoretical but no implemented solution exists, yet. This post hoc correction may be a computationally less demanding alternative to a fully multivariate analysis of directed interactions, in cases were a multivariate treatment of the data is not possible.

Oral presentations

Giorgio M. Innocenti, Karolinska Institute, Sweden

Fan Meng, University of Michigan, USA

Shreejoy J. Tripathy, Carnegie Mellon University, USA

Stephen D. Larson, OpenWorm.org, USA

Anita Bandrowski, The University of California, San Diego, USA

Michele Migliore, Yale University, USA/National Research Council, Italy

Krishnan Padmanabhan, Salk Institute for Biological Studies, USA

Gaël Varoquaux, INRIA, France

Cameron Craddock, Child Mind Institute/Nathan Kline Institute for Psychiatric Research/The Neuro Bureau Research Institute, USA

Kit Cheung, Imperial College London, United Kingdom

OP01 A dynamic approach to brain connectivity

Giorgio M Innocenti[1]
1. Karolinska Institutet, Stockholm, Sweden

Over the last 40 years histological methods based on axonal transport of tracers, have generated an impressive amount of connectivity data in experimental animals, revolutionizing concepts of brain organization. Impressive as they are those studies provide an essentially static image of brain connectivity. A more dynamic view of connectivity is encouraged by the revived realization, that neural connections are implemented by axons of different diameter, hence conducting impulses at different speeds. Speed and length of axons generate conduction delays, which together with parameters of postsynaptic integration provide the time frame for brain dynamics. This new approach is generating new images on brain connectivity based on graph theory but which significantly upgrade what has been thus far available (Fig.1).

The results are obtained by injecting an axonally transported anterograde tracer (BDA) into several cortical areas of the macaque and then measuring the diameter of axons to the various targets, and the length of the axonal trajectories using the Neurolucida and the Neurolucida Explorer software (MBF Biosciences, Williston, VT, USA). From these parameters the conduction velocity of axons and the delays they generate from the site of origin to the termination are computed. The histological data on pathway lengths have been confirmed by DTI approaches in monkey and human. Computed delays are compatible with the available electrophysiological data, but experiments in progress are meant to extend the available electrophysiological data.

The results thus far emphasizes the complexity of neural networks when examined from this new point of view.
Comparison of monkey data with human data indicates that human brain has become comparatively slower than the monkey brain and that this may have expanded the dynamic range generated by the connections. Both the monkey and the human work suggest that cortical areas may be arranged in a hierarchy of processing speeds, with motor and somatosensory connections being the fastest.

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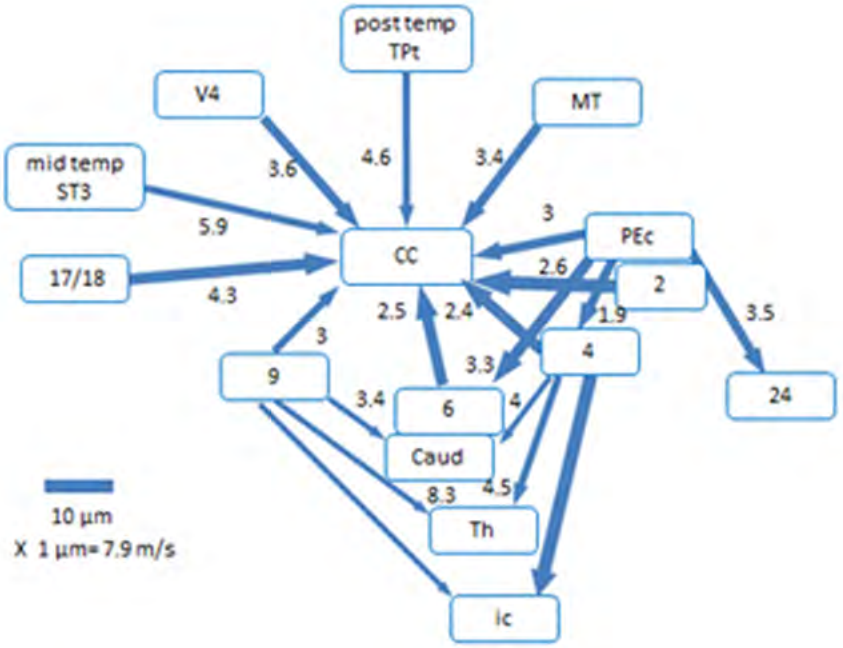
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OP02 PubAnatomy 3D: Integrating medline exploration with the Allen mouse brain atlas

Yang Gang[1], Manhong Dai[1], Jean Song[2], Barbara Mirel[3], Fan Meng[1,4,5]
1. Molecular and Behavioral Neuroscience Institute, University of Michigan, Ann Arbor, USA
2. Health Sciences Library, University of Michigan, Ann Arbor, USA
3. School of Education, University of Michigan, Ann Arbor, USA
4. Psychiatry Department, University of Michigan, Ann Arbor, USA
5. Center for Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, USA

Neurobiology data generated by the big science approaches, such the Allen brain atlases and the NIH Human Connectome Project, provide the opportunity for understanding how brain works at both molecular and anatomical levels with unprecedented resolution and completeness. For example, researchers can now use the Brain Explorer and the NeuroBlast tools developed by the Allen Institute for Brain Science to explore genes and their spatial expression pattern across the whole brain for learning the potential biological implications of genes identified in their experiments as well as designing follow-up experiments, such as knockout/knockin mouse for modeling human diseases. However, since it is impossible for individual scientists to grasp all the known functional roles of genes, anatomical structures and the functional relationships among them, researchers frequently need to perform literature searches to guide such big brain data set explorations. Similarly, literature exploration can also benefit significantly from the relationships among genes and anatomical structures presented in such data sets. The need to use two separate data exploration tools such as the Brain Explorer and PubMed leads to technical hurdles as well as gaps in the thinking process that can significantly constrain the hypothesis development process.

PubAnatomy is 3D is designed to provide a seamless exploration environment across the Allen Mouse Atlas data and the Medline literature for iterative data- and literature guided hypothesis development. We mapped genes and anatomical structures in the Allen Mouse Atlas data set to individual Medline records and developed a flexible web-based search interface for iterative Medline and mouse atlas data exploration. A typical use case is a researcher starting with Medline search for their interested topic, such as diseases and brain structures (Fig 1, upper part), to obtain a list of Medline records, which is annotated with different concept categories such as genes as well as summary statistics such as number of Medline records associated with each gene in the search results (Fig 1, lower part). Researchers can use the summary statistics, various filtering criteria as well as the content of relevant Medline records to select genes and anatomical structures they want to explore through simple drag-and-drop for 3D brain exploration (Fig2). Besides displaying the voxel level data for selected brain structures, users can also select multiple arbitrary 2D intersections in the coronal and sagittal directions to view the raw in situ images together with brain structure annotations for each 2D intersection (Fig 3). Two or more

genes can be displayed side-by-side for detailed raw in situ data inspection (Fig 4). Users can use new structures or additional genes identified in the exploration process to filter Medline research results or start new search/modify existing search through simple drag-and-drop, greatly facilitating the iterative literature and data exploration during hypothesis development.

Pubanatomy3D is available at http://brainarray.mbni.med.umich.edu/PubAnatomy3D/. We plan to define and publish the Application Programming Interface for Pubanatomy 3D to enable third party developers to access data and functions PubAnatomy as well as passing their own data such as gene or SNP lists to PubAnatomy 3D. We will also integrate more data sets, such as connectome, pathway and protein interaction, Gene Ontology, etc. into PubAnatomy to further enhance its usefulness for hypothesis development in neurobiology.

OP03 Towards reusable experiments: making metadata while you measure

Shreejoy Tripathy[1], Anita de Waard[2], Richard Gerkin[1], David Marques[2] and Shawn Burton[1] and Nathaniel Urban[1]
1. Carnegie Mellon University, Department of Biology, Pittsburgh,USA
2. Elsevier, Elsevier Labs, Amsterdam, Netherlands

Using research data acquired in other labs requires that the metadata, that define the conditions and manipulations of each experiment are well documented. Usually, this metadata is not stored with the experimental data itself, and is often written within the experimenter's lab notebook and therefore is not easily searched or compiled. When scientists upload data files to a central repository (like crcns.org), metadata are often not included. For domain-specific databases (such as neuromorpho.org), metadata are added by expert curators in an expensive and painstaking process that does not scale up to the large amounts of scientific data produced every day. An effective way "scale-up" is to convince researchers to create digital metadata in real-time during their experiment. Here, we have developed an electronic lab notebook application (running on tablet computers and smartphones) to annotate in vitro electrophysiological recordings with essential methodological details.

We tailored our system to the workflows used in the collection of electrophysiology data by the Urban, Gittis, and Barth Labs at Carnegie Mellon University. These labs study a variety of brain areas, addressing hypotheses from neural coding and synaptic plasticity to the mechanisms underlying neurological disorders; however, they share a core set of methodologies associated with recording neural activity from brain slices. Using the developed app, individual experimenters enter details (like the animal strain used or the neuron type recorded) through a series of drop-down menus (see Figure 1 for a screenshot). This structured data entry approach allows us to enforce a common metadata format and the usage of INCF standards and terminologies. Additionally, we designed the app's interface to ensure simple, efficient data entry by the user.

The collected metadata is uploaded directly to a relational database and combined with the acquired electrophysiology data files into a semantically-enriched, reusable format that allows for creative data exploration. This data can be used by the person collecting the data or others in the lab for testing hypotheses and analyzing collections of data from his or her own lab, in a web-based 'Data-Dashboard'. Rather than being limited to datasets collected within a single lab, researchers can now find (using metadata as a search filter) and analyze relevant data collected in other labs. Through improving data organization, archiving, and sharing practices, this system will show clear benefits to the scientists performing and analyzing research data and, we hope, will empower demonstrably better neuroscience research.


Shreejoy Tripathy
CMU Urban Labs
Experiment ID: A7766603-26E2-4A60-9886-F7D10D472F02 P1 S1 C1 E2 ???
07 April 2013
Goals, Motivation & Hypotheses
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OP04 Beyond the connectome hairball: Rational visualizations and analysis of the C. elegans connectome as a network graph using hive plots

Pedro Tabacof[1] and Tim Busbice[1] and Stephen Larson[1]
1. OpenWorm.org, San Diego,USA

The C. elegans connectome (White et al., 1986) is currently the most detailed connectome data set at the neuronal circuit level that is publicly available. Represented as a network graph, it consists of edges that distinguish between gap junctions and chemical synapses, weighted by synapse count, with nodes that represent neurons whose identities are unambiguous and well known.

Within the OpenWorm project (Palyanov et al., 2012), we have previously transformed this data set into NeuroML as the foundation for a computational simulation framework for C. elegans (Busbice et al., 2012). In the course of analyzing this data set, we have applied the hive plot methodology for visualizing complex networks (Krzywinski et al., 2012). Hive plots provide a rational and transparent visualization method for making complex networks by laying out nodes on radially oriented linear axes with a coordinate system based on nodes' structural properties. While previous articles have explored the structure of the C. elegans connectome graph quantitatively (Chatterjee & Sinha, 2008; Sohn et al., 2011), to the best of our knowledge this is the first application of the hive plot visualization technique to any connectome data set.

We have created multiple hive plots based on the C. elegans complex graph to depict various aspects of its underlying structure via the JHive tool (http://hiveplot.net). Simple hive plots of the sensory, inter-, and motor neurons on different axes reveals strikingly dense connections for the top four interneurons compared to the rest. Hive plots show that the connections mediated by gap junctions that run between sensory neurons and interneurons are less dense than the connections between interneurons and motor neurons. This asymmetry is not present in the network of chemical synapses. Additionally, hive plots reveal that edges with high degree (10 synapses or greater) are present between motor neurons but not between sensory neurons (Fig 1). These findings have been verified with independent analysis of the connectome with the NetworkX complex network graph library (http://networkx.github.io/documentation/latest/overview.html).

We have found exploration of the C. elegans connectome using hive plots to lead to the discovery of interesting qualitative structure that was previously not obvious, enabling this structure to be further pursued quantitatively using complex network mathematics.

Figure 1. Hive plot of C. elegans connectome. Nodes on axis marked a3 are sensory neurons, nodes on a1 are interneurons and nodes on a2 are motor neurons. Only edges with connection weight greater than 10 are rendered (thin orange), and include connection

weights greater than 15 (medium-thick cyan) and greater than 20 (thick green). Axes are duplicated to display edges between nodes on the same axis. This example shows the absence of connections between sensory neurons (between the a3 axes) and the presence of many high degree connections between motor neurons (between the a2 axes)."

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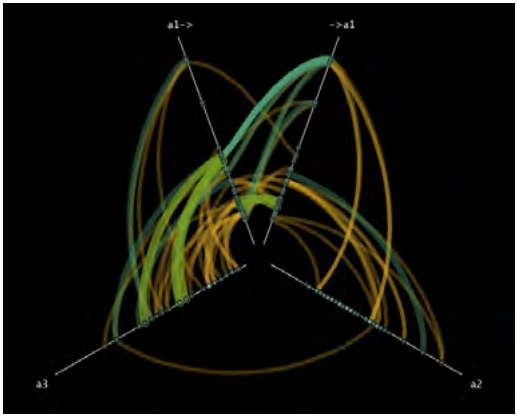

OP05 A unified research resource layer; experiences from the Neuroscience Information Framework

Anita Bandrowski[1], Yueling Li[1], Davis Banks[1], Jeffrey Grethe[1] and Maryann Martone[1]
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The Neuroscience Information Framework, (NIF, http://neuinfo.org), catalogs research resources important to biological science, but the creation of these deceptively simple catalogs turns out to be non-trivial.

After hundreds of years, scientists have some idea of what types of information can be asked from bibliographic catalogs (e.g., PubMed), but catalogs that list research resources can vary significantly from bibliographic catalogs. For example, resources such as transgenic mice, cell lines, MRI data sets, software tools or academic databases are important to research, but the types of information indexed in catalogs of these sorts of resources may not be the same as the information about published work. For example, a cell line may have a patient whom the cell line derives from, the surgeon who removed it, and an organization that maintains the cell line in storage. In this case, the question of who is the author of the cell line makes little sense. Similarly, authorship of an academic database may be less informative than it is in the case of a publication because databases change content over time making statements about the content or an individual responsible for database maintenance a temporally dependent statement. When we consider some of the very successful academic database projects like the mouse genome informatics project, they tend to have a large and revolving number of contributors, curators and programmers. However, the number of these projects, their quality, and the amount of time researchers devote to them is generally increasing making tracking them very useful to both researchers and governmental bodies interested in impact of their research dollars.

Of the thousands of academic resources cataloged in various registries including the NIF Registry, the INCF tool registry, BioSiteMaps (which seeded the NIF Registry), Eagle i, BioDBCore, EBI, and NITRC many share bits of information about those types of entities, but they each look at the cataloging effort in a slightly different way, keeping slightly different pieces of information about each project. Furthermore, most projects duplicate the efforts of others even though the scope of a unified, world-wide registry of research resources is likely to be far beyond any one group. This means that many of the registries have overlapping resources, in somewhat different schemas and can't easily be integrated. The goal of several groups, including ours, has been that a uniform yet very flexible registry schema be created for all online biomedical resources allowing many groups from various countries to add information without the need to duplicate effort. The data that has been generated by many groups has been made available in a uniform format by the NIF system.

NIF at its' core is a catalog of research resources that takes advantage of the work of NIF

curators and many individuals who painstakingly cataloged resources, interlinked these with ontologies and standard data sets in a rich representation of the resource landscape. Over the 5 years during which NIF has been cataloging resources, we have had to adapt our criteria for defining, including and curating resources. In order to allow for flexible representation of resources within the NIF, we opted to code NIF's catalog using the Neurolex semantic wiki (http://neurolex.org) so that we could easily expand the schema and we could link curation and tagging to the NIF core vocabularies. NIF has created a curation document which details for procedures for registering and curating resources for the NIF. We will present NIF's current resource catalog and lessons learned in creating and maintaining a comprehensive resource catalog. By working with various standards and many groups, we hope to reduce duplication, enhance both discoverability and transparency of research resources, which are often very highly sought-after outputs of scholarly research.

OP06 Building a 3D model of the mitral-granule cell network in the olfactory bulb

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2. National Research Council, Institute of Biophysics, Palermo, Italy

We are interested in studying the basic mechanisms involved in odor recognition, a widely studied experimental model of sensory information processing. Recent findings have shown that odors may activate spatially distributed sites in the olfactory bulb with a sparse, columnar-like organization of mitral and granule cells. This organization challenges the classical center-surround organization, and there is thus a need to identify a new paradigm for signal discrimination that could have general implications as well for other brain regions. The possible underlying circuitry and the computational properties of the olfactory bulb have been widely investigated experimentally, especially in terms of odor selectivity and dynamics of cell responses. However, experiments are usually carried out in single cells or in small randomly selected sets of cells. This has prevented a clear understanding of the spatio-temporal organization of the mitral-granule cell network in representing an odor input, which requires simultaneous recording from a relevant subset of mitral and granule cells activated by an odor. The functional effects of a network-wide process such as lateral inhibition, in relation to the patterns of glomeruli activated by different odors, remain thus relatively unknown and difficult to explore experimentally.

The main challenge we are addressing here is the development of a 3D model of the mitral-granule cell network, allowing direct input of the experimental data for individual glomerular activation, in order to demonstrate and predict the learning mechanisms that will ultimately be responsible for the early processing stages of the sensory inputs. For this purpose, we implemented a 2mm^2 3D model of the olfactory bulb (about 1/20th of the entire system). Several 3D reconstructions of mitral cells with full dendritic trees (from Igarashi et al., 2012) were analyzed to extract morphological parameters to generate a population of some 700 synthetic mitral cells, 5 for each glomerulus. Approximately 20000 granule cells were then randomly inserted into the network and connected using a collision detection algorithm. The input activity elicited in 127 glomeruli in the dorsal olfactory bulb during presentation of 19 natural odorants (kindly provided by Alan Carleton, from Vincis et al., 2012) was then used to drive self-organization of the network under different conditions of odor input. This is the first 3D simulation of the olfactory bulb microcircuit using realistic cell properties and network connectivity. It provides a new framework for investigating the functions of a brain system.

The figure shows a rendering of the olfactory bulb 3D model. Green spheres: glomeruli; red spheres: activated glomeruli; white lines: mitral cell dendrites.

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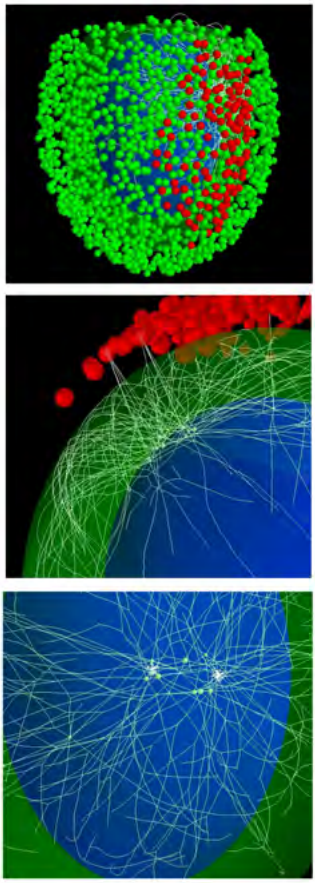

OP07 Large scale whole brain mapping of inputs to the main olfactory bulb

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1. Salk Institute for Biological Studies, La Jolla, USA

An important prerequisite to understanding how neural circuits generate behavior is to understand the structure of those circuits, including the connectivity between the neurons. In sensory systems, a key component of that connectivity is the top down projections from higher cortical regions to primary sensory areas. For example, in mammals, projections from olfactory cortical regions, including piriform cortex, represent a major input to the inhibitory granule neurons in the main olfactory bulb. Inhibitory granule cells play a central role in how odor information is transformed and represented by the principal neurons of the bulb, the mitral cells. Projections from higher odor areas including the accessory olfactory nucleus and the piriform cortex are known to impact the firing of both the granule cells and the mitral cells, highlighting their importance in shaping how odors are represented. However, little is know about the organization of top-down inputs to these inhibitory cells in large part because of the experimental and computational challenges of single cell mapping across a whole brain. To provide a complete portrait of the monosynaptic inputs to inhibitory cells in the main olfactory bulb, we employed the rabies virus trans-synaptic tracing technique and developed an imaging platform that allowed us to visual every single labeled cell across the entire mouse brain. Labeling spatially distinct populations of inhibitory granule cells in the bulb with the modified rabies allowed us to trace the patterns of innervation from a number of higher processing areas, including the accessory olfactory nucleus and the olfactory cortex. From these injections, we were able to reconstruct, identify and classify the presynaptic partners to inhibitory cells in the bulb across the entire mouse brain at single cell resolution. Our data reveal the complex patterns of innervation to the inhibitory neurons of the bulb, and provide a map of the spatial organization of feedback projections for higher brain areas to their lower processing counterparts. By integrating the connectivity maps of inputs into the bulb on the scale of the whole mouse brain with models of activity patterns within the bulb, we hope to provide insight into how cortical feedback may play a role in shaping the representations of odor information.

OP08 Mining resting-state and task-activation fMRI databases: models and software

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P08,Mining resting-state and task-activation fMRI databases: models and software,," INRIA,,Gif sur Yvette,France",,0,Oral presentation,Neuroimaging,"There is an increasing number of databases comprising a very large number of fMRI images: ranging from heterogeneous collections of resting-state acquisitions performed across centers (1000 functional connectomes project), to rich cohort studies bringing in cognitive labels via task-evoked mapping in addition to intrinsic functional and anatomical connectivity (Human Connectome Project, or the cognitive pillar of the Human Brain Project).

We present recent progress in mining these datasets to extract a high-level description of brain organization. We discuss not only models, but also software efforts to make the models available as a data-processing tools to a wider public.

Uncovering unknown structure from these massive fMRI datasets is a challenging problem. Independent component analysis and clustering have been successfully used on rest and task-evoked meta-analytic databases [Smith 2009, Laird2011], but their success is not easily linked to neuroscientific hypothesis, and it is unclear how they can be adapted to profit from the richer cognitive information that is present in new databases.

The hypothesis of functional segregation, central in neuroscience, can be used mine fMRI images for functionally-specialized systems, for instance using clustering [Tononi1998]. In particular, it implies that each cortical subsystem responds primarily to a small number of elementary cognitive tasks. Given a large dataset of images, this hypothesis can be use to ground a sparse dictionary-learning procedure to extract both cognitive latent factors and the corresponding brain maps. Indeed, sparse dictionary learning is a modern machine learning tool that seeks a components in the data that are expressed in a small number of observations. The procedure can be enriched with a explicit model of inter-subject variability, or spatial constraints to extract regions.

On resting-state data, sparse dictionary learning can be used to extract an atlas of networks of intrinsic brain function [Varoquaux2011]. Although the corresponding time-courses have no associated cognitive labels as they are drawn from uncontrolled resting-state experiments, the large amount of rest imaging data available is a good candidate to capture the spatial structure of the fMRI image. Recent methodological progress adding a region-extraction prior to dictionary learning [Abraham2003] yields a brain parcellation (Fig 1) that is more stable and more suited to explain the data than clustering approach when drawing randomly subjects from a large population.

On large databases of task-activation fMRI maps, dictionary learning can extract cognitive atoms to single out specialized brain regions or networks [Varoquaux 2013]. These cognitive atoms can be expressed as loadings on the experimental conditions or the corresponding contrasts (Fig 2). As opposed to resting-state data processing, dictionary learning applied to task-evoked data enables cognitive labeling of brain structures.

Dictionary learning thus provides a common model to analyze large fMRI datasets drawing from rest and from task, by building upon functional specialization. Suitable priors must be applied to model the specificities of each experiments [Varoquaux 2011, Varoquaux 2013, Abraham 2013]: this generic machine-learning tool must be adapted to fMRI data and neuroscience goals.

The corresponding algorithms are challenging to implement and out of reach of most neuroscientists. To provide tools and building blocks to mine large-scale fMRI databases, we develop the core machine learning algorithms in the Python machine learning library ""scikit-learn"" [Pedregosa] and are in the process of building a neuroimaging-specific adaptation layer to it (http://nisl.github.com). Beyond dictionary learning, this software strategy gives to the neuroimage community access to many machine-learning and data-mining tools. We expect these tools to be instrumental in getting the most out of the increasingly large neuroimaging databases.

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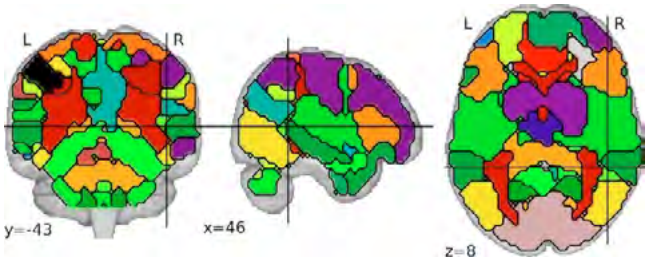
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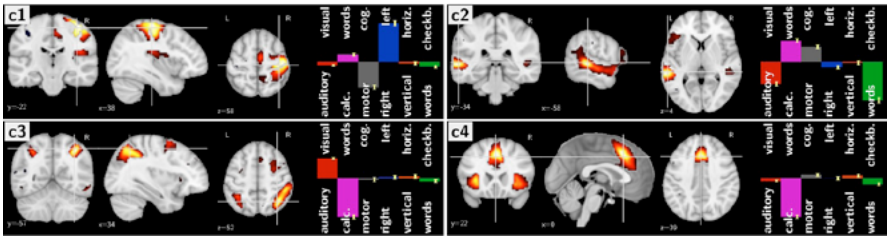
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OP09 The Neuro Bureau Preprocessing Initiative: open sharing of preprocessed neuroimaging data and derivatives

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6. McGill University, Montréal Neurological Insitute, Montréal, Canada
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8. Université de Montréal, Département d'informatique et de recherche opérationnelle, Montréal, Canada

Introduction
Grass-roots initiatives such as the 1000 Functional Connectomes Project (FCP) and International Neuroimaging Data- sharing Initiative (INDI) [1] are successfully amassing and sharing large-scale brain imaging datasets, with the goal of recruiting the broader scientific community into the fold of neuroimaging research. Unfortunately, despite the increasing breadth and scale of openly available data, the vast domain-specific knowledge and computational resources necessary to derive scientifically meaningful information from unprocessed neuroimaging data has limited their accessibility. The Neuro Bureau Preprocessing Initiative [2] has taken on this challenge, generating and openly sharing preprocessed data and common derivatives for the large-scale ADHD-200 dataset [3]. This initiative has grown to include preprocessed DTI data and derivatives for 180 healthy individuals from INDI's Beijing Enhanced Sample [4]. The next planned release will include resting state and structural data from the 1,112 subject Autism Brain Imaging Data Exchange (ABIDE) dataset [5].

Methods
Four teams are currently participating in the preprocessing initiative, each one using different toolsets and preprocessing strategies (fig. 1). Preprocessed data, derivatives, and quality control metrics are made openly available for download through the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) [6]. The ADHD-200 release included two fMRI preprocessing pipelines as well as maps of grey matter density for voxel-based morphometry (fig. 1). The Beijing diffusion imaging release includes DTI scalars along with voxel specific diffusion distributions for performing probabilistic tractography. Figure 2 illustrates various derivatives generated through these initiatives. The future ABIDE preprocessing initiative will incorporate three functional preprocessing piplines and cortical measures (fig. 3). The analytical procedures employed in the preprocessing are extensively documented on the NITRC website [2].

The Neuro Bureau preprocessing initiative also includes an on-going working group to release derivatives, which can be readily compared across different preprocessing strategies, so that investigators can directly test the impact of the method- ological choices on the scientific outcome of a study. Most of the ong-going work consists of improving and harmonizing the quality control procedures and the derivatives generated by different processing pipelines. Interested teams are welcome to join the effort and contribute new analytical pipelines for future release.

Results

Intended to buttress the ADHD-200 Global Competition [7] and accelerate ADHD imaging research, the ADHD-200 preprocessing effort has yielded more than 6,500 downloads from 780 unique IP address globally (see fig. 4), inspired a team of biostatisticians to win the competition and resulted in eight peer-reviewed publications - with many more in preparation or submission. The DTI preprocessing initiative has resulted in 572 downloads from 134 unique IP addresses. Based on the success of the previous preprocessing efforts four teams have agreed to continue this effort by preprocessing the recently released ABIDE dataset (fig 3).

Conclusion

By openly sharing a wide range of preprocessed data and derivatives, the Neuro Bureau Preprocessing Initiative seeks to make neuroimaging research accessible to a wider audience of researchers. It has already enabled computer scientists, mathematicians, and statisticians who lack neuroimaging expertise to develop and test novel data analysis strategies. We see several important benefits to our initiative: (1) facilitate the generation and test of novel hypotheses about brain function, (2) provide a resource to train future generations of neuroimaging researchers and, (3) facilitate the replication of published results by providing a benchmark set of test images. By providing a breadth of derivatives and preprocessing strategies, we also hope to establish a platform for comparing their relative merits, as well as testing the robustness of neuroscientific findings. This already broad resource will soon be enhanced by the inclusion of the phenotypically rich ABIDE dataset which consists of data from an important clinical population.

References

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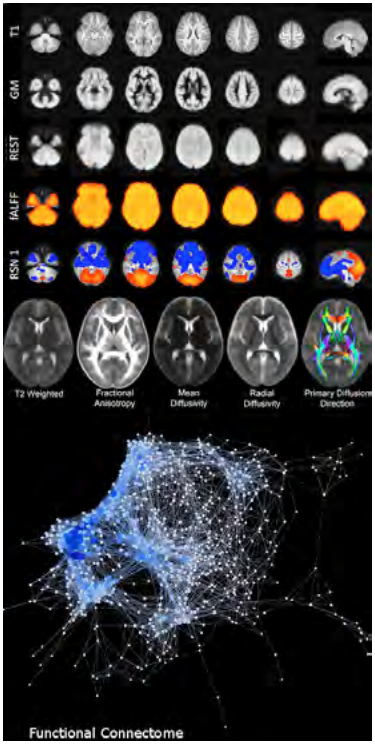
[4] http://fcon_1000.projects.nitrc.org/indi/retro/BeijingEnhanced.html [5] http://fcon_1000.projects.nitrc.org/indi/abide
[6] http://www.nitrc.org
[7] http://fcon_1000.projects.nitrc.org/indi/adhd200/index.html

A. Functional Derivatives

Pipeline	Athena	NIAK
Tools	FSL and AFNI	NIAK, MINC, and PSOM
Dataset	ADHD-200	ADHD-200
Analyses	VBM and R-fMRI	R-fMRI
Infrastructure	Virginia Tech Athena HPC	CBRAIN pan-Canadian HPC network

B. Structural Derivatives

Pipeline	Beijing DTI	Burner
Tools	FSL	SPM
Dataset	Beijing Enhanced	ADHD-200
Analyses	DTI	VBM
Infrastructure	Swiss Federal Institute of Technology HPC	

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Libya
Egypt
Pakistan
Saudi Arabia
India
Thailand
Mexico
Mali
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Nigeria
Ethiopia
Venezuela
Colombia
Kenya
Indonesia
Papua New Guinea
DR Congo
Tanzania
Brazil
Peru
Angola
Bolivia
Namibia
Madagascar
Indian Ocean
Chile
Botswana
Australia
South Pacific Ocean
South Atlantic Ocean
South Africa
Argentina
New Zealand

OP10 NeuroFlow: FPGA-based spiking neural network acceleration with high-level language support

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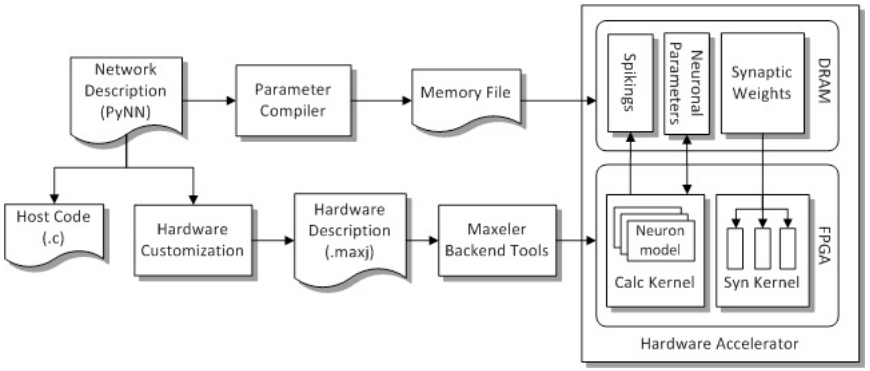
2. Imperial College London, Department of Bioengineering, London, United Kingdom

Spiking neural networks are a useful tool for cortical modelling and robotic control, but simulating a large network in real-time requires high-performance computers or specially built accelerators. Traditional accelerators for large-scale spiking neural network accelerators developed previously use Graphics Processing Units (GPUs) or Application-Specific Integrated Circuit (ASIC) chips. While ASICs deliver high performance, they lack the flexibility to reconfigure and hence are unable to adapt variation in the design and models employed. On the other hand, GPUs provides a decent speedup over multi-core CPUs and good flexibility, but it lacks scalability to handle larger networks.

In this work we present NeuroFlow, a Field Programmable Gate Array (FPGA)-based spiking neural network accelerator consisting of 4 FPGAs. It supports the use of PyNN, a high-level simulator-independent network description language, to configure the hardware. A major novelty of the system is the capability to provide custom hardware configuration based on various simulation requirements, such as precision and time delay. The accelerator is implemented on an off-the-shelf MPC-C500 from Maxeler Technology which employs a streaming architecture in the FPGAs. The accelerator achieves the performance gain primarily by parallelizing the computation of point-neuron models and employing low-level optimization for synaptic data memory access. The accelerator currently supports basic PyNN functions such as spike-timing-dependent plasticity (STDP) and arbitrary postsynaptic current kernels.

The system is able to support simulation of network of approximately 800,000 neurons, and achieve a real-time performance of 400,000 neurons for a network firing at 8Hz with random connections. With a single FPGA running at 150MHz, the accelerator delivers a throughput of 1.9 times to 3.5 times the performance of one of the most recent GPU-based accelerators in terms of postsynaptic potential delivery rate (Fidjeland et al., Neuroinformatics, 2012 Dec), subject to the simulated network and the GPU model used.

In conclusion, while harnessing low-level customization and fine grained parallelism in FPGA, NeuroFlow is also able to provide the flexibility of a high-level platform such as GPUs and high-performance computers. It provides a promising alternative to accelerate spiking neural network simulations.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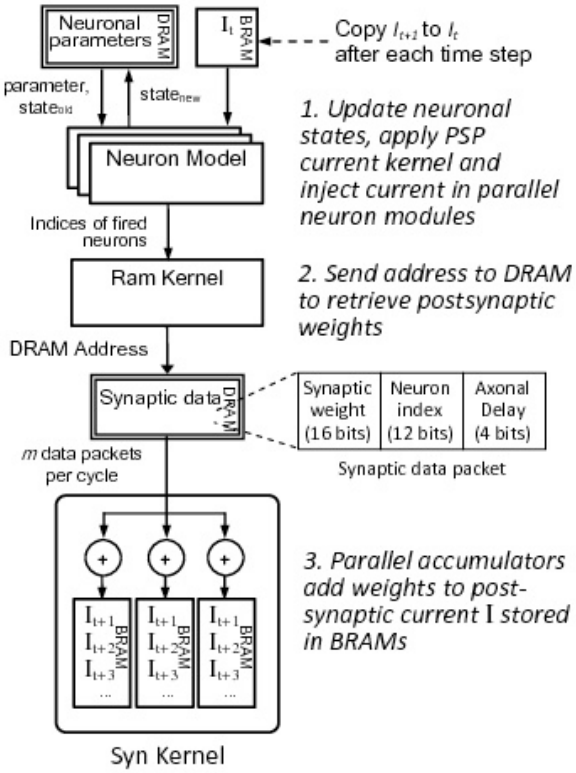
DRAM
Neuron model
Calc Kernel
Syn Kernel
FPGA
Hardware Accelerator


Neuronal parameters
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Copy I_{t+1} to I_t after each time step
parameter, $state_{old}$
$state_{new}$
1. Update neuronal states, apply PSP current kernel and inject current in parallel neuron modules
Neuron Model
Indices of fired neurons
Ram Kernel
2. Send address to DRAM to retrieve postsynaptic weights
DRAM Address
Synaptic data
Synaptic weight (16 bits)
Neuron index (12 bits)
Axonal Delay (4 bits)
Synaptic data packet
m data packets per cycle
3. Parallel accumulators add weights to post-synaptic current I stored in BRAMs
Syn Kernel

Posters and demos stay up during the full meeting. Presentation of posters is however divided into two sessions for practical reasons.

Poster session 1 (day 1): *odd* poster numbers
Poster session 2 (day 2): *even* poster numbers

Abstracts

Topics:

P: poster
D: demo
OP: oral presentation

P96 Recognition of human implicit intention based on fMRI and EEG

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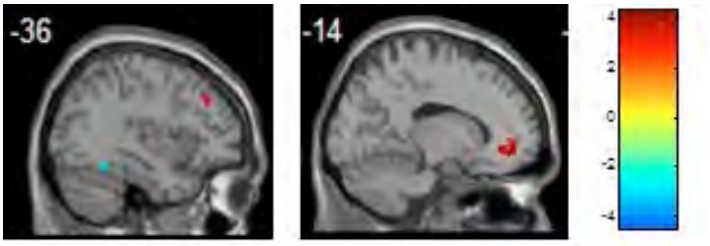
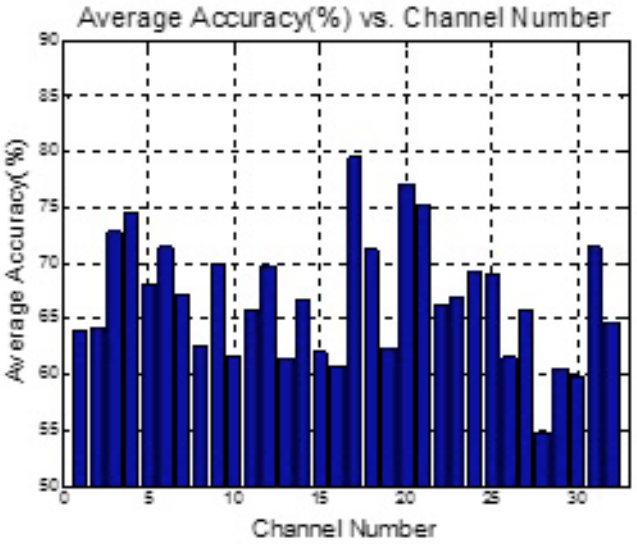
We are trying to understand implicit (un-represented or hidden) human intention, which may be different from explicitly-represented one. Although the taxonomy of the implicit intention is not clear yet, we hypothesize that the implicit intention domain consists of two axes, i.e., the sympathy for one's represented intention and the sympathy for one's counterpart. The former had been studied in the framework of lie detection, while the latter is the new interest in this research. When the subjects read statements on computer screen, we measured fMRI, EEG, and pupil dilation. Also, the subjects were asked to reply as 'Yes' (Sympathy/Agreement to the statement) or 'No' (Non-sympathy/Disagreement). At this moment we focus on two obvious statement categories, i.e., statements of obvious agreement and obvious disagreement. In the future, we will try to understand implicit intention of non-obvious cases for personal and sensitive statements.
For the fMRI experiments nineteen healthy right-handed Korean subjects (12 males and 7 females) were recruited from the student community in KAIST. They are all KAIST undergraduate students, and voluntarily participated. All participants did not have a history of psychiatric disorder, significant physical illness, head injury, neurological disorder, and alcohol or drug dependence. After complete explanation of the study, written informed consent was obtained from all subjects. The study was submitted to the regular review in the KAIST institutional review board and approved. Experiments were held with 3T MR scanner (Siemens Magnetom Verio, Germany) at KAIST fMRI Brain Science Research Center. The Sympathy cases have higher neural activation than the Non-sympathy cases in the left superior frontal gyrus and left anterior cingulated (Fig.1), which are known to be related with self-knowledge. Also, the Non-sympathy cases have higher neural activation that the Sympathy cases at the left fusiform gyrus, which is known to be related with unfamiliar words and faces. This fMRI experiments approve our hypothesis on the 2nd axis of the implicit intention space, i.e., Sympathy vs. Non-sympathy to once counterpart.
For the EEG experiments thirteen subjects (10 males and 3 females) were recruited and their EEG was recorded from 32-channel BrainAmp system (Brain Products GmbH, Germany). Twenty-nine electrodes were placed on the scalp according to the International 10-20 system. One electrode for recording eye movement (EOG) was positioned below subject's right eye. Two electrodes dedicated to the electrocardiogram (ECG1 and ECG2) were placed on subject's collarbones in both sides. Data were acquired with a sampling rate of 500Hz, along with 60Hz notch filtering. We work on two different electrode selection approaches, i.e., one based on the fMRI results (the left fontal electrodes such as F3 and Fp1) and the other with Fisher's linear discriminant analysis. Both ERP and frequency-band analysis are conducted. We had also trained Support Vector Machine (SVM) classifiers to classify single ERP from each channel. Figure 2 shows the classification accuracies of each channel, of which maximum is 78% at the central frontal electrode, Fz.

In conclusion we had successfully tested a hypothesis on the implicit intention axis, i.e., Sympathy/Non-sympathy to the counterpart, with fMRI experiments. Also, we showed that SVM classifiers are capable of classifying single-trial EEG on the axis.





P12 Bioinformatics molecular dynamics and docking pipeline analysis for high-throughput genome analysis and drug discovery oriented to personalized pain therapy in non-responsive patients

Silvia Santoro, Pasqualina D´Ursi, Nadia Galluccio, Martina Landini, Alessandra Mezzelani, Alessandro Orro, John Hatton, Matteo Gnocchi, Andrea Manconi, Luciano Milanesi.
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Some functions of the nervous system are pain transduction and pain perception. These functions are directly involved in many chronic diseases due to the pain condition to which they are associated. Peripheral and central nervous system are the main targets of pain therapy. Pain therapy uses variety of drugs in relationship of severity of the illness and the degree of the patient's response. The individual variability in response to drugs depends on different variables such as pathological (timing and severity), physiological (age, gender and weight), genetic and environmental aspects involved in pharmacokinetics and pharmacodynamics. Although patients can be classified as poor, intermediate, normal or extensive responders, 30% of patients do not respond to pain treatments.
Our aim is to collect and analyse DNA samples in terminal patients to define their drug response phenotype. A bioinformatics analysis of the GWA DNA samples will be performed to identify mutations in candidate genes. A molecular dynamic study will be used to investigate the misfolding structures and the molecular docking will be applied for testing the binding activity of the drugs in use. Variants with low binding affinity will be submitted to virtual screening to identify all the potential leads by using the ZINC database of UCSF with over 21 million ligands.

We have developed the molecular dynamics and docking pipeline analysis based on the High-Performance and Distributed Computing (eg. GPU and GRID clusters) to perform large scale of analysis. Data will be collected in a portal infrastructure organised in three layers: a Portal layer, an Application layer and a Data layer. The Application layer is a variety of java portlets, each of which allow the end user, depending on its permissions, to add and retrieve records stored in the Data layer. The Data layer will be subdivided into three layers: the first is a database that interacts with the Portal layer, the second contains all patients clinical data, the third and last contains personal data of the patients. The infrastructure will use a unique retrieval system that randomly codes patients information to prevent users to obtain a correlation between pathologies and personal data of the patients. This procedure will be used to support high-throughput genome analysis and drug discovery oriented to personalized pain therapy in non-responsive patients.

D01 neuroVIISAS: The integration of atlases and connectomes for modeling

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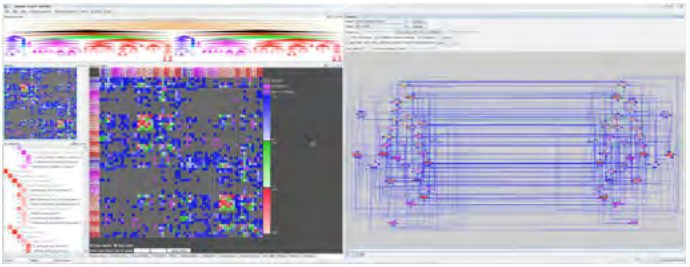
Modeling supports the understanding of complex biological systems like nervous systems and whole organisms. The building blocks to generate models of organisms are heterogeneous and involve multiple structures (organs and their subdivisions, regions of the CNS and their connections) and functions (motor action, perception, dynamics of the stimulus-response behavior). neuroVIISAS (neuro Visualization, Imagemapping, Information System for Analysis and Simulation) is build to allow the integration of structures in terms of 3D-reconstructions, connections and modeling of neuron populations (Schmitt and Eipert, 2012). It is an open environment with regard to import and export of data and a generic tool that can be used for the development of digital atlases, brain mapping, connectome and simulation projects of all types of nervous systems. For the modeling of populations of neurons the NEural Simulation Tool (NEST v 2.2.1) is used (Gewaltig and Diesmann, 2007). This approach enables the modeler to use more realistic connectome data for an accurate definition of connections between populations of neurons in NEST. How this is achieved will be demonstrated with examples of basal ganglia networks (Fig. 1). Furthermore, the interactions of visualization, simulation and analysis of complex neuronal networks will be shown. In addition to high level analysis and visualization functions of neuroVIISAS the import of connectivity data will be explained. The software can be downloaded from http://neuroviisas.med.uni-rostock.de/index-Dateien/Page455.html.



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P97 CircuitML: a modular language for modeling local processing units in the drosophila brain

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The brain of the fruit fly Drosophila melanogaster is an attractive model system for studying the logic of neural circuit function because it implements complex sensory-driven behaviors with a nervous system comprising a number of neural components that is five orders of magnitude smaller than that of vertebrates. Analysis of the fly's connectome, or neural connectivity map, using the extensive toolbox of genetic manipulation techniques developed for Drosophila has revealed that its brain comprises about 40 distinct modular subdivisions called local processing units (LPUs) [1], each of which is characterized by unique internal information processing circuitry. LPUs can be regarded as the functional building blocks of the fly brain because almost all identified LPUs have been found to correspond to anatomical regions of the fly brain associated with specific functional subsystems such as sensation and locomotion. We can therefore cast the task of emulating the entire fly brain as requiring the accurate modeling and integration of its constituent LPUs [1].

Although our knowledge of the internal circuitry of many LPUs is far from complete, analysis of those LPUs comprised by the fly's olfactory and vision systems suggests the existence of repeated canonical subcircuits [2] that are integral to the information processing functions provided by each LPU. The development of plausible LPU models therefore requires the ability to specify and instantiate subcircuits without explicit reference to their constituent neurons and internal connections. To this end, we have devised a neural circuit specification language called CircuitML for construction of LPUs. CircuitML has been designed as an extension to NeuroML [3] and LEMS [4], XML-based neuronal model description languages for data-driven specification of neural circuit models; it provides constructs for defining subcircuits that comprise neural primitives supported by NeuroML and LEMS. Subcircuits are endowed with interface ports that enable their connection to other subcircuits via neural connectivity patterns. We have used CircuitML to specify an LPU-based model of the fly olfactory system [2] that we simulated using a GPU-based CircuitML processor.

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D03 WM: an integrated framework for modeling the visual system

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Visual neuroscience is a broad field consisting of many sub-specialities, covering a range of experimental paradigms, visual modalities, and scales of description. Forging links between experimental findings across subfields is important for advancing our understanding of visual function. Across and within these subfields many models have been built, but they vary widely in their fundamental architecture, level of physiological detail, the nature of their inputs, and the types of responses or outputs that they generate. These differences make it difficult or impossible to directly test the models with novel visual stimuli, to make direct comparisons between models, or to compare model output with the wealth of experimental data.

To address these issues, we have developed a framework for building working models (WM) of the visual system based on the following principles: (1) models should be able to operate on any visual input, so they can be tested in a variety of ways, with stimuli relevant to color, motion, form and depth processing, (2) models should produce outputs like those recorded in experimental studies (spikes, membrane voltages, conductances) to facilitate direct comparison to experimental data and to make clear predictions that can be tested experimentally, (3) models should be fast and easy to run online by anyone, otherwise they will never be tested enough to be thoroughly understood.

This framework supports simple L-N (linear-nonlinear) models with only a few parameters, which can be used for elucidating basic principles (Heess and Bair, 2010), as well as large-scale population models (Baker and Bair, 2012) that implement physiologically plausible networks. Thus, conceptually minimal as well as plausibly elaborate models can be fruitfully studied within the framework. Within WM, users can vary model parameters, select and design stimuli, choose responses to record, and run the model in parallel across a cluster of CPUs. The software is developed in C and MPI for computational speed, and Java for platform-independence and web-based interaction.

The building blocks of the population models are physiological cell classes connected by realistic synapses. The units in the model, from retinal ganglion cells (RGCs) onward, generate spikes and can be switched between Poisson generation and conductance-driven integrate and fire units, so model outputs include spike trains, membrane voltages, and synaptic conductances. Cells in LGN and cortex are organized topographically for receptive field position, and maps for attributes such as orientation, SF and ocular dominance are easily defined. Model neurons can be synaptically connected not just probabilistically between populations or over spatial extent, but on the basis of these mapped visual attributes.
We have built an online portal to the framework at http://www.iModel.org. It gives

investigators the the ability to explore model architectures online, view visual stimuli, select models, stimuli and responses to use in simulations, run those simulations on our own cluster, and display and analyze simulation output. All of this functionality is freely available to users and requires only a web browser and internet connection for access. We will present examples of models built within this framework and prototypes for tools for online access and simulation in the cloud.

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D04 Large-scale synapse detection using CAJAL3D

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Recent advancements in high-throughput electron microscopy (EM) allow for imaging hundreds of cubic microns of cortical tissue at nanometer-scale resolution [1, 2]. The resulting data afford neuroscientists the opportunity to reverse-engineer cortical microcircuits at an unprecedented level of detail. However, the scale of this data necessitates considerable systems engineering and infrastructure to store, analyze, and share data products efficiently. For example, a cortical column at the resolution of currently available large datasets (e.g. 4x4x45nm voxels) is on the order of 1 petabyte when stored on disk. To address this issue, we have developed the Connectome Annotation through Joint Analysis of Large 3-dimensional Data (CAJAL3D) framework, which has several main components:

1) An object model to standardize data products, specifically annotations, and facilitate the interoperability of algorithms and analysis between different institutions. This model, the Reusable Annotation Markup for Open coNnectomes (RAMON), defines a set of data types and associated metadata fields that can be used to describe and annotate massive 3D EM image volumes.
2) Web services to expose an underlying optimized 3D spatial database that stores both image and RAMON-compliant annotation data. Examples of the services provided include arbitrary 3D cuboid cutouts of image and annotation data, creation and manipulation of RAMON objects, and spatial and metadata queries of RAMON objects [3].
3) An Application Programming Interface (API) in MATLAB to simplify developers' use of the web services
4) A distributed processing framework built on the LONI Pipeline [4] to facilitate large-scale automated analysis of EM data.
5) Visualization of EM image data and RAMON annotations via Rambo3D, a GPU based 3D viewer, and CATMAID [5], an open source web-based 2D viewer.

To demonstrate the utility and efficacy of the CAJAL3D framework, we have used its components to identify synapses within the largest dataset available: a 12 terabyte, 450x350x50 _m region of mouse visual cortex [1]. Estimating synapse locations at scale is fundamental to mapping the structure of the brain [6]. Previous work [7-10] has shown that automated synapse detection is tractable, but current state-of-the-art methods do not trivially scale to large volumes. We therefore implemented a simple, efficient synapse

detector, which processed this volume in 2 days on a small, 256-core cluster. The detector located and stored approximately 20 million RAMON synapse objects, which is more than 4 orders of magnitude greater than the largest previous spatial synapse analysis on EM data [11]. An example of RAMON synapse annotations is shown as an overlay on the original EM data in Figure 1. A subset of the detected synapse field is visualized in Movie 1. Although the current detection results are imperfect, they do provide a perspective on the distribution of synapses in mammalian cortex at a scale never before seen.

* DMK and WGR contributed equally to this work",,Yes,http://www.frontiersin.org/Journal/MyEditingViewDetails.aspx?stage=100&articleid=54775&submissionid=54878

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OP01 A dynamic approach to brain connetivity

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Over the last 40 years histological methods based on axonal transport of tracers, have generated an impressive amount of connectivity data in experimental animals, revolutionizing concepts of brain organization. Impressive as they are those studies provide an essentially static image of brain connectivity. A more dynamic view of connectivity is encouraged by the revived realization, that neural connections are implemented by axons of different diameter, hence conducting impulses at different speeds. Speed and length of axons generate conduction delays, which together with parameters of postsynaptic integration provide the time frame for brain dynamics. This new approach is generating new images on brain connectivity based on graph theory but which significantly upgrade what has been thus far available (Fig.1).

The results are obtained by injecting an axonally transported anterograde tracer (BDA) into several cortical areas of the macaque and then measuring the diameter of axons to the various targets, and the length of the axonal trajectories using the Neurolucida and the Neurolucida Explorer software (MBF Biosciences, Williston, VT, USA). From these parameters the conduction velocity of axons and the delays they generate from the site of origin to the termination are computed. The histological data on pathway lengths have been confirmed by DTI approaches in monkey and human. Computed delays are compatible with the available electrophysiological data, but experiments in progress are meant to extend the available electrophysiological data.

The results thus far emphasizes the complexity of neural networks when examined from this new point of view.
Comparison of monkey data with human data indicates that human brain has become comparatively slower than the monkey brain and that this may have expanded the dynamic range generated by the connections. Both the monkey and the human work suggest that cortical areas may be arranged in a hierarchy of processing speeds, with motor and somatosensory connections being the fastest.

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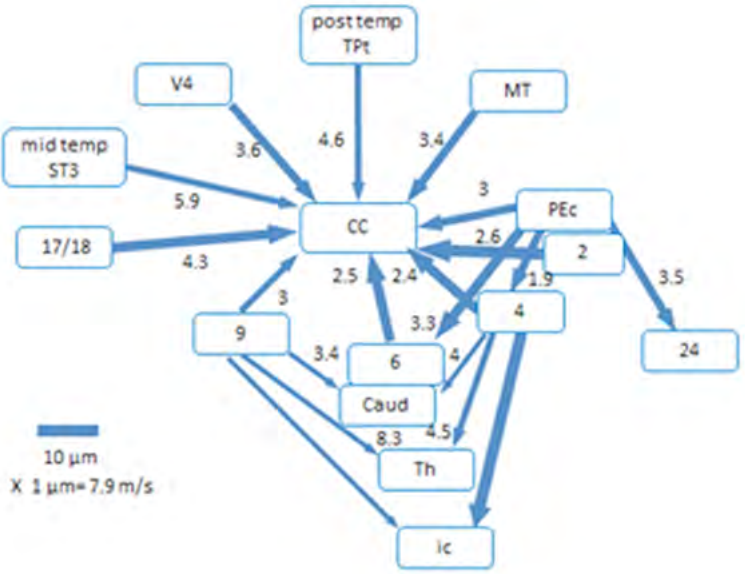
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P13 PhysioDesigner for multilevel neural system modeling

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PhysioDesigner [1,2] is an open platform that supports multilevel modeling of physiological systems in the field of integrated life sciences and systems biology, including physiology and neuroscience. Users can combine and build mathematical models of biological and physiological functions on PhysioDesigner. Users can also integrate morphometric data on a model, which is used, for example, to define a domain in which partial differential equations (PDEs) are solved. PhysioDesigner is capable to build a model including PDEs as well as ordinary differential equations.

Physiological systems are modeled based on modules on PhysioDesigner. Hence a model is represented as an aggregate of modules. There are modules called "capsule modules" which involve several other modules (called "functional modules") so that it is possible to create a kind of sub-package in the model. Users can reuse the encapsulated modules just by copy and paste in other part of the model or in the other model.

One of distinguished features of PhysioDesigner is a capability to create SBML-PHML hybrid models. SBML is a widely prevailing language to describe subcellular phenomena such as gene expressions and protein-protein interactions. PHML is a language natively used in PhysioDesigner to describe models, and was designed to describe a network of functions based on the hierarchical structure of physiological systems. Combining these two languages to describe one single model is a novel method to build a hierarchical model of physiological systems.

Another feature is the template/instance framework, which supports users to create large size models. Encapsulated modules can be defined as a template. Then instances are created according to the template having the completely the same information with the template. However the instances are not merely copies of the template. Once the properties of the template was changed, the changes are immediately applied to all instances. In addition to that, constants and initial values of instance modules can be changed individually, so that each of them can have a personal quality. This would be helpful for example to create a neural network models.

PhysioDesigner has also a capability to process medical imaging data, such as extraction, smoothing, and changing the resolution. By these processing, for example, it is possible to create an 3D object representing the brain conductivity from CT images of grey,

white matters, cerebrospinal fluid and skull. This can be applied to simulate EEG (electroencephalogram) [3].

Combining those features of PhysioDesigner, it can be one of the most powerful tools to support multilevel modeling processes in computational neuroscience. PhysioDesigner is available at http://physiodesigner.org.",,

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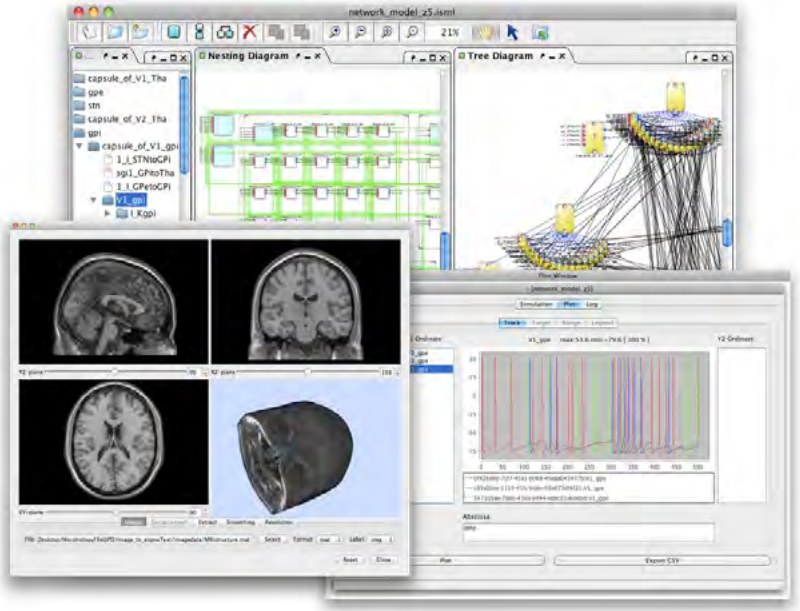

P14 Modeling extracellular potentials in microelectrode array recordings

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Microelectrode Array (MEA) measurements from in vitro slices has become an important research tool in neuroscience, however the interpretation of such recordings is not always straightforward. We have developed a modeling framework for emulating in vitro MEA recordings that takes into account both the measurement physics of the MEA set-up, and the underlying neural activity of the slice, resulting in simulated data that closely resembles experimental recordings. Our modeling framework may aid interpretation of experimental data by reproducing the experimental procedure in silico, make experimentally testable predictions, and produce test-data for validating various analysis methods such as CSD estimates and spike-sorting algorithms.

Our simulations are separated into two domains; the first step is simulations of neuronal activity in populations of multi-compartment model neurons, and secondly solving the electrostatic forward problem in the extracellular space. For the neuronal simulations we employ LFPy [1], a Python module built upon NEURON's Python interface [2] to obtain the transmembrane currents in every compartment of the model neurons. Then the Finite Element Method (FEM) is used to solve the Poisson equation from electrostatics and calculate the extracellular potentials in the 3D volume including the electrode sites, and test various approximation schemes. Hence, the effects of the electrodes can be assessed together with the impact of inhomogeneities and anisotropies of the extracellular medium in recordings. The approach is in principle applicable to any multicompartment neuron model (from e.g. ModelDB [3]), any neuron number or any MEA electrode set-up.

We will present our modeling framework, together with an investigation of the electrode effects on the measured signals. Then we will go on to present two different applications. Firstly, we have produced spike-sorting test-data to benchmark automated spike-sorting algorithms [4] used on MEA recordings. This project is part of an international coordinated effort where such test-data will be collected and made available at http://spike.g-node.org, allowing exchange of synthetic and experimental test-data with known underlying activity, and systematic benchmarking and comparison of spike-sorting algorithms applied to such data [5]. Secondly we will present a project where we have been studying the LFP signature of single neurons receiving varying, sub-threshold sinusoidal current input measured by MEAs in an acute brain slice setting [6]. The model output is compared to corresponding experimental data, which includes the detailed reconstruction of the excited neuron.

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P15 Do you recognize me? The neural marker to familiar faces

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Previous psychophysiological investigations on visual perception have led in depth understanding of relationship between memory and processing of faces in human brain. Various evidences suggest that the representation of faces especially; human faces follows a highly dedicated and complex neuronal circuitry. It has been well established that brain follows a top-down approach for decoding of the previously stored visual images. However, despite the notwithstanding research efforts, it is largely unknown the neural mechanism to distinguish familiar from unfamiliar faces. The aim of this research is to develop a conjectural model for comprehending and discussing how we distinguish familiar from unfamiliar faces. The experimental procedure required the participants to precisely categorize the three types of visual stimuli into familiar, personally familiar and completely unfamiliar human faces behaviourally. Secondly, Event-Related Potentials (ERPs) were recorded from sixteen healthy subjects ranged in age from 20 to 24 years (22.31±1.40; 10M, 6F). Results indicate the structural encoding of faces reflected by face-specific N170 component was elicited for all three categories of faces; while time-locked activity of ERPs evidenced by N400 component was elicited only for familiar faces. The significant occurrence of high latency for the unfamiliar category of faces suggests the inability to extract unique spatial information (required for face recognition) from novel images to recognise as familiar or personally familiar.The observations highlight the behavioural correlation with neural signature obtained from ERP study for the classification and final identification of faces.

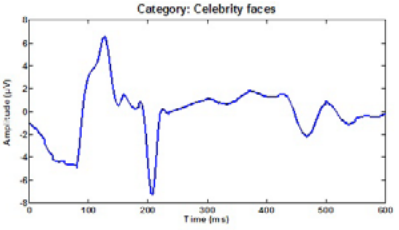

Figure 1. ERP observed for celebrity faces category of stimuli

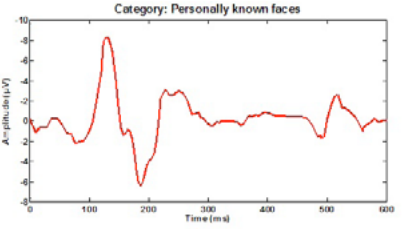

Figure 2. ERP observed for personally known faces category of stimuli

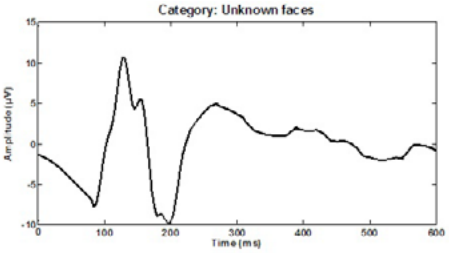

Figure 3. ERP observed for unknown faces category.

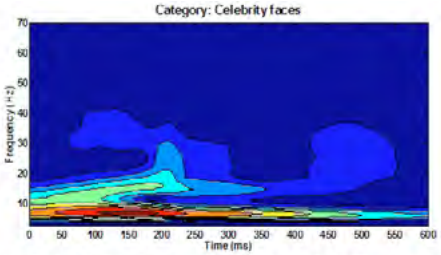

Figure 4. Time vs. Frequency complex wavelet transform plot for celebrity faces category.

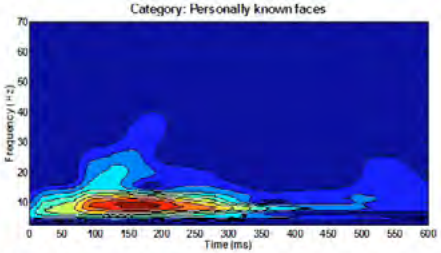

Figure 5. Time vs. Frequency complex wavelet transform plot for personally known faces category.

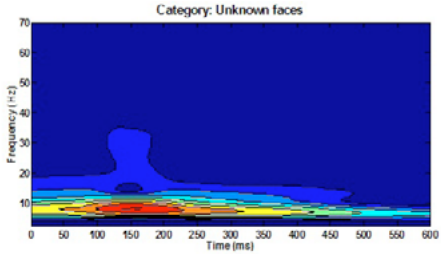

Figure 6. Time vs. Frequency complex wavelet transform plot for unknown faces category.

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P16 NeuroUnit: Validation tests for neuroscience models

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Rigorous validation of a scientific model's explanatory power requires comparing the model's predictions against all relevant experimental data. Model validation is an ongoing process -- models must not simply be validated against data available when the model is initially peer reviewed, but also to data gathered after it has been published. Today, model validation remains an informal and incomplete process. We argue, by drawing an analogy between scientific model validation and software testing, that precise validation criteria that allow model validation to be partially automated are essential for assessing model validity and scope. While modern journal articles tell us clearly how a model works, they provide only incomplete and quickly dated outlines for telling us which observations it aims to explain and how well it achieves them. To overcome this problem, we propose formalizing the model validation process by creating a collection of software tools and associated cyberinfrastructure dedicated to scientific model validation. This validation framework will exist in parallel to the publication system: publications can focus on answering how and refer to the testing framework for answering how well.

In software engineering, a unit test is a function that validates a single component of a computer program against a single correctness criterion. The core of our proposal is the analogous concept of a validation test -- an executable function that validates a provided model implementation against a single empirical observation to produce a score that indicates agreement between the model and a single piece of data. Suites of these tests will be developed via a distributed cyberinfrastructure that enables 1) collaborative construction and curation of tests by members of a scientific community and 2) the execution of tests and the reporting of their results continuously as new data is gathered and new models are developed. We describe a core pythonic framework, SciUnit, that begins to fulfill this vision, and NeuroUnit, a library of SciUnit tests and associated standards for the neurosciences. Visual summaries of aggregate NeuroUnit test results will provide neuroscientists with an up-to-date report of progress in neuroscience modeling, illustrating the merits and deficiencies of competing models, benefiting both ongoing efforts and informing new theoretical and experimental directions. To illustrate the generality of this approach, we consider the result of subjecting historical models of planetary motion to tests derived from empirical observations throughout history (Table 1)

P17 Hybrid scheme for modeling LFPs from spiking cortical network models

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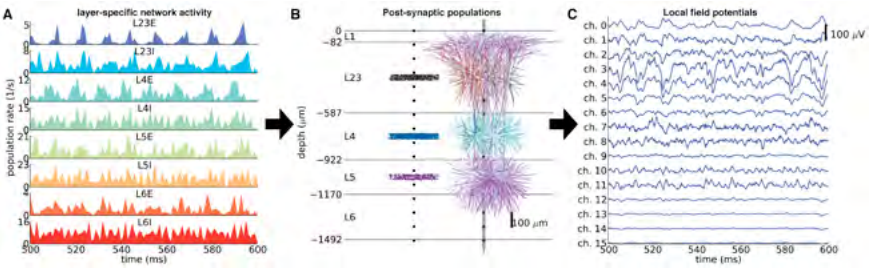
While recordings of extracellular potentials remain a common method for experimentally measuring neural activity, the interpretation of the low-frequency part, the local field potential (LFP), is not straightforward. Cortical LFPs seem to mainly stem from synaptic inputs, but the net LFP signal from several contributing laminar populations is difficult to assess, as the individual contributions will depend on their locations, the morphologies of the postsynaptic neurons, the spatial distribution of active synapses, and the level of correlations in synaptic inputs [1]. While most comprehensive cortical-network simulations are done with single-compartment models [2], multicompartmental neuronal modeling is in general required to calculate LFPs [1]. Here we present a hybrid LFP modeling approach where a network of single-compartment LIF neurons generates the spiking activity (Fig. 1A), while detailed multicompartment neuronal models are used to calculate the accompanying LFP (Fig. 1B-C). Our model describes a 1mm2 patch of cat V1, and we incorporate spatially specific pre- to post-synaptic inter- and intra-layer connectivity constrained by experimental observations [3] using reconstructed neuron morphologies of excitatory and inhibitory neurons in layers L2/3-L6 with passive membrane properties. Model specifications of neuron and synapse numbers within populations are taken from [2], while spatial connectivity profiles are based on [3]. Our hybrid simulation framework allows detailed analysis of how the LFP correlates with network activity and connectivity, and how spatially specific synapse distributions influence the LFP. Spiking network simulations [2] were implemented in NEST (www.nest-initiative.org), while simulations of LFPs from morphologically realistic neurons used LFPy (http://compneuro.umb.no/LFPy) along with NEURON [4].

Figure 1: Schematic illustration of the hybrid scheme. (A) Spiking activity generated in network simulations using single-compartment neurons [2] are used as input to multicompartmental neuron models to generate LFPs (B). LFP contributions from each postsynaptic population are calculated and superimposed (C).



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P18 Evaluating dendritic impact using complex and reduced models of medium spiny neurons

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Current advances in both experimental and theoretical fields have found that synaptic signals are not simply relayed passively to the soma or the axon; instead, dendrites, the main structure to receive synaptic inputs, can act as ""computing units"", performing arithmetic operations by themselves. However, to model neurons with active dendrites will lead to dramatically increased computing costs. In contrast, simple point-like artificial neuron models do not capture the full dynamics of individual neurons as they do not take into account dendritic computation. This lost accuracy, on the other hand, might play an important role in the overall dynamics of neural networks. To bridge this gap between the point-neuron models and very complex neuron models and to better understand how dendritic computation might affect signal integration at more macroscopic levels, we recently developed a biophysically detailed model of medium spiny neuron (MSN) in dorsal striatum with 634 compartments. An early version of this model has been confirmed to reproduce experimental findings [Evans et al. (2012)]. We derived a series of simplified versions of the model with a reduced number of compartments but conserved 3-dimensional morphology. With the complex model and its reduced offsprings, we explore the importance of dendritic morphology and synaptic topology on the input-output relationship of MSNs.

For this purpose, we adopt a novel method by [Chen et al. (2011)], which combines metric space analysis and multidimensional scaling analysis, to quantify the impact of the dendrites. We also apply this method, as well as select techniques from information theory to verify the reduced models' behaviour.

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P19 Spike synchronization in hippocampal cultures using Hebbian learning

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The use of dissociated cortical neurons cultured onto microelectrode arrays represents a useful experimental model to characterize both the spontaneous behaviour of neuronal populations and their activity in response to electrical and pharmacological changes. Learning is a natural process that needs the creation and modulation of sets of associations between stimuli and responses. Many different stimulation protocols have been used to induced changes in the electrophysiological activity of neural cultures looking for achieve learning [1-11] and low-frequency stimulation has brought good results to researchers enhancing bursting activity in cortical cultures [8,9]. Hebbian learning describes a basic mechanism for synaptic plasticity wherein an increase in synaptic efficacy arises from the presynaptic cell's repeated and persistent stimulation of the postsynaptic cell. The theory is commonly evoked to explain some types of associative learning in which simultaneous activation of cells leads to pronounced increases in synaptic strength. Basically the efficiency of a synaptic connection is increased when presynaptic activity is synchronous with post-synaptic activity. In this work, we use different stimulation protocols following Hebb's Law to create adjacent physical or logical connections between adjacent electrodes in the connectivity graphs. The connected electrodes show synchronized activity before and after a new stimulation is applied.

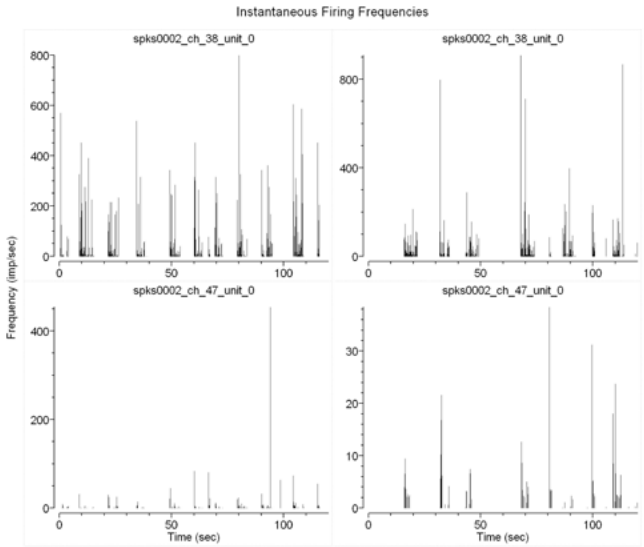
Dissociated cultures of hippocampal CA1-CA3 neurons were prepared from E17.5 sibling embryos. Microelectrode arrays (Multichannel systems, MCS) consisted of 60 TiN/SiN planar round electrodes (200 _m electrode spacing, 30 _m electrode diameter) arrange in a 8x8 grid were used. A total of 24 cultures were used in five experiments of 2-3 weeks duration. In every experiment 4-5 cultures were stimulated with a specific electrical stimulation protocol. Low frequency current stimulation and tetanization voltage stimulation were the main protocols used in this study. Experiments were started when neural cultures had 14 Days in Vitro (DIV) and were carried out during 2-3 weeks. In every experiment, the electrophysiological activity of the cultures was previously analysed and connectivity diagrams based on cross-correlation were obtained for each culture. Two pairs of electrodes with an acceptable spiking activity and no logical connections between them were selected for stimulation.

Low-frequency current stimulation and tetanic stimulation had both an impact on the electrophysiological responses of the cultures. Raster plots showed that all of the stimulations provided induce changes in the firing frequency of the cultures. Instantaneous

firing frequency graphs shows that stimulated electrodes start firing in more separated period of times after stimulation but each firing period last longer. In addition, interspike intervals show the same results observed in the spiking periods but also it can be seen analytically the ISI decrease both in value and dispersion. Both effects are related to the neural stimulation, which modulates the firing capabilities of the cultures.

Connectivity diagrams based on cross-correlation between electrodes showed some kind of connections reorganization after stimulations, concentrating them in a few electrodes. Furthermore, adjacent physical or logical connections in the connectivity graph following Hebb's law appeared in some pairs of stimulated electrodes. Electrodes with created connections between them can distinctly be detected with the instantaneous firing frequencies graphs (Figure 1). The firing periods of the electrodes from the connected pairs follow exactly each other, whereas the firing periods of the not connected pairs of electrodes do not match. Furthermore, the electrodes of connected pairs change both the firing periods after stimulation. This features indicates that there exits a strong connection between them.

Low-frequency stimulation induces permanent changes in most experiments using different values of current amplitude and stimulation patterns. Persistent and synchronous stimulation of relevant adjacent electrodes may be used for strengthen the efficiency of their connectivity graph. These processes may be used for imposing a desired behaviour over the network dynamics.



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P20 Dynamic changes in direction and frequency range of inter-areal cortical interactions revealed by non-parametric Granger causality

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Models suggest that communication between brain areas could be mediated by oscillations in specific frequency bands. This hypothesis is supported by electrophysiological measurements wherein the direction and frequency of the interaction between brain areas varied during the different stages of a cognitive task. Frequency-resolved granger causality (GC) is used often for this analysis, but it has been derived for stationary linear processes, which may not be appropriate for brain activity. Our goal was to determine whether for nonlinear processes conditional GC could still distinguish direct connections from indirect ones and to what extent dynamic changes in the frequency & direction of interaction could be accurately detected. For this the properties of the GC determined parametrically, through fitting an autoregressive process of a fixed order, were compared to those obtained via non-parametric GC, which only uses the measured spectral matrix.

Oscillations in each cortical area were represented by a low-dimensional nonlinear model driven by white noise, whose standard deviation represented the level of activity in the respective areas. In addition, we analyzed the responses from two coupled networks of spiking neurons in the same way. We found that the direction of interaction between reciprocally connected cortical areas was determined by the level of activity, going from areas with high activity to those with low activity, which could be modulated on fast time scales. The frequency band of interaction was determined by the sending area.

For linear processes, the parametric GC had the lowest bias and variance compared to non-parametric GC (Figure 1), but was not appropriate for the nonlinear model and network model, because the oscillations could not be modeled accurately by autoregressive processes of a reasonable order. The non-parametric GC correctly represented the ground truth connectivity when multi-taper spectral estimates were used, but when multi-tapering made the spectral peaks too broad, artifacts emerged.

Taken together, the GC analysis revealed a simple rule for the direction and frequency band of communication between cortical areas, specifically "the loudest area gets heard", which can account for recent experimental results in which the frequency band of communication was direction dependent.

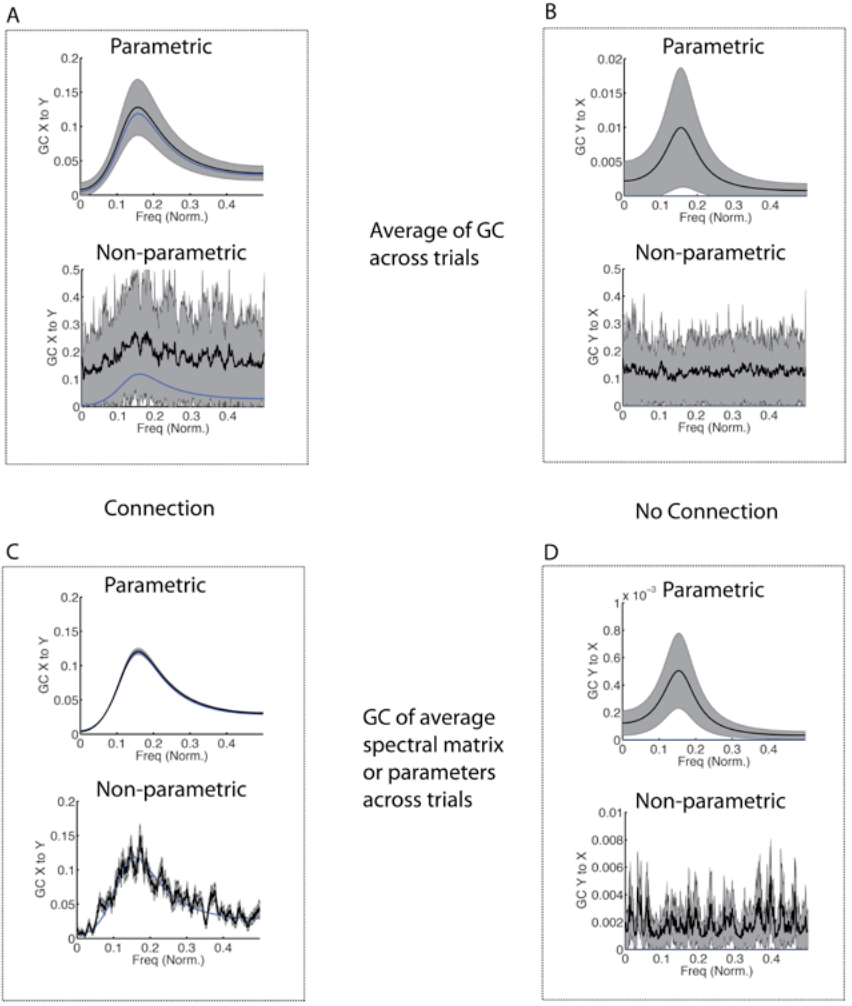

Figure 1. The parametric Granger Causality (GC) had a lower bias than the non-parametric GC. The lowest bias was obtained when the spectral matrix or parameters of the autoregressive process were averaged before calculating the GC. In each panel the top graph is the parametric GC and the bottom graph is the non-parametric GC. The blue line is the analytical result, the black solid line is the calculated result. The gray bands represent the standard deviation of the mean. For the left panels (A,C) there was a connection from X to Y (but no Y to X connection), whereas for the right panels (B,D) there was no connection. For the top panels (A,B), the GC was calculated for each trial and then averaged, whereas for the bottom panels (C,D) the spectral matrix or parameters were averaged first and then the GC was calculated.

P21 Influence of different modeling protocold for calcium currents in the AHP features of a type-S motoneuron

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A mathematical model of a type S motoneuron (MN) was developed to evaluate the influence of different modeling protocols for calcium currents and calcium reversal potential in the soma of the MN. The dendritic tree was modeled as a passive structure with a stem cylinder and two asymmetrical branches using a tapering cable model (Figure 1). Ionic channels in soma were associated with the leakage, delayed-rectifier potassium, calcium-dependent potassium (SK), sodium fast, hyperpolarizing, A current, N-type and P-type calcium-currents, according to the Hogdkin-Huxley (HH) formalism (Hogdkin and Huxley, 1952). The parameters were adjusted to represent the physiological responses of cat motoneurons (Zengel et al., 1985). The calcium currents were modeled with the HH formalism and a reversal potential for calcium set as 140 mV (HHEs model). Then, the reversal potential was calculated according to the Nernst equation (HHEv model). This change resulted in a magnitude decrease of the AHP in response to a current pulse in the soma of 50 nA and 0.5 ms of duration, but still within the values reported in experimental data. This is due to the decrease in the calcium drive potential (ECa –Vs) and hence a decrease in the calcium current, intracellular calcium concentration and in the potassium SK, responsible for the AHP. It was also built two models using the Goldman-Hodgkin-Katz (GHK) (Goldman, 1943; Hodgkin and Katz, 1949) formalism for the calcium currents: one with AHP values with the same magnitude of HHEs (0.040% of difference – model GHKEs) and another with the same as in HHEv (0.042% of difference – model GHKEv). The magnitude of the currents (type-P and type-N calcium, potassium SK) were similar (<1%, except for the type-N in the HHEv and GHKEv, which was 6.92% different), but the time course was different. The N-type calcium currents of the GHK models have a rising time ≈ 25% larger than the correspondent HH models and a half-decay time ≈ 23% larger (Figure 2A). The type-P calcium current have a rising time ≈ 39% larger and a half-decay time ≈ 14% larger (Figure 2B). The same happens with the variables that depend on the calcium concentration. Using GHK or HH formalism in the passive model altered the time course of the currents, but it did not affect the final behavior of the model.

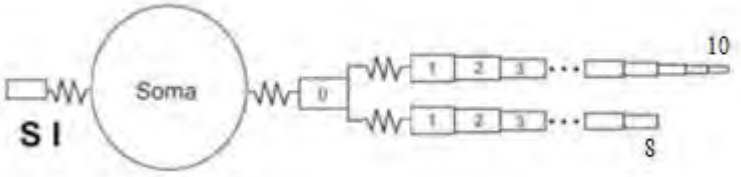

Figure 1: Geometry of the type-S MN model. The SI is the cylinder representing the initial segment, a spherical soma, a stem dendrite and two asymmetric branch, with 10 and 8 cylinders.

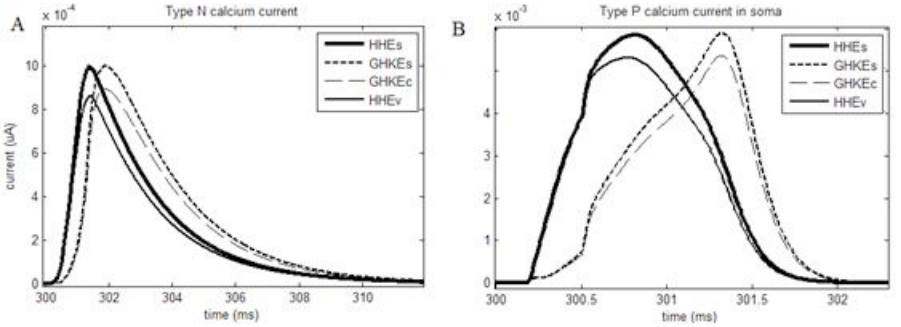

Figure 2:Type-N (A) and type-P (B) calcium currents in response for a current pulse of 50 nA and 0.5 ms of duration applied in the soma.

P22 Modeling a developmental switch of spontaneous calcium oscillations in neural progenitors

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Spontaneous calcium (Ca2+) activity is a hallmark of neural development. Recently we demonstrated spontaneous Ca2+ and membrane potential oscillations in neural progenitors both in vitro and in vivo and furthermore established necessary molecular players (1). Here we propose a mechanism of its generation by implementing a mathematical model of coupled ordinary differential equations describing the time course of Ca2+ concentration and membrane potential in multiple interconnected cells. The spontaneous activity is based on a plasma membrane oscillator for Ca2+ and membrane potential as well as an ER-cytosol oscillator. The non-linear connection between these two oscillators result in a much higher frequency of membrane potential oscillations compared to Ca2+ oscillations (167 times faster). We treat gap junction permeability and conductance of voltage dependent Ca2+ channels as bifurcation parameters and identify regions of parameter space necessary for spontaneous oscillations. A corresponding parameter space is experimentally investigated during differentiation of neural progenitor cells by applying quantitative real-time PCR and real-time Ca2+ imaging. Intriguingly, the shape of the experimental developmental path is highly analogous to the in silico landscape (Figure 1). In summary, the network of interconnected neural progenitors starts to spontaneously oscillate once a sufficient level of gap junction and VDCC conductivity has been acquired. Interesting, this means there is no need for specialized cells to act as pacemakers, but is rather a matter of difference in maturity. The bifurcation analysis for VDCC conductance reveals two Hopf bifurcations, meaning there exists an upper limit of conductance for spontaneous oscillations. One could imagine the role of functional pacemaker as a commitment that is ambulating within the group of differentiating cells. Conclusively, the modeling results comply well with former and new experimental data and we identify a developmental switch of spontaneous Ca2+ oscillations in neural progenitors.

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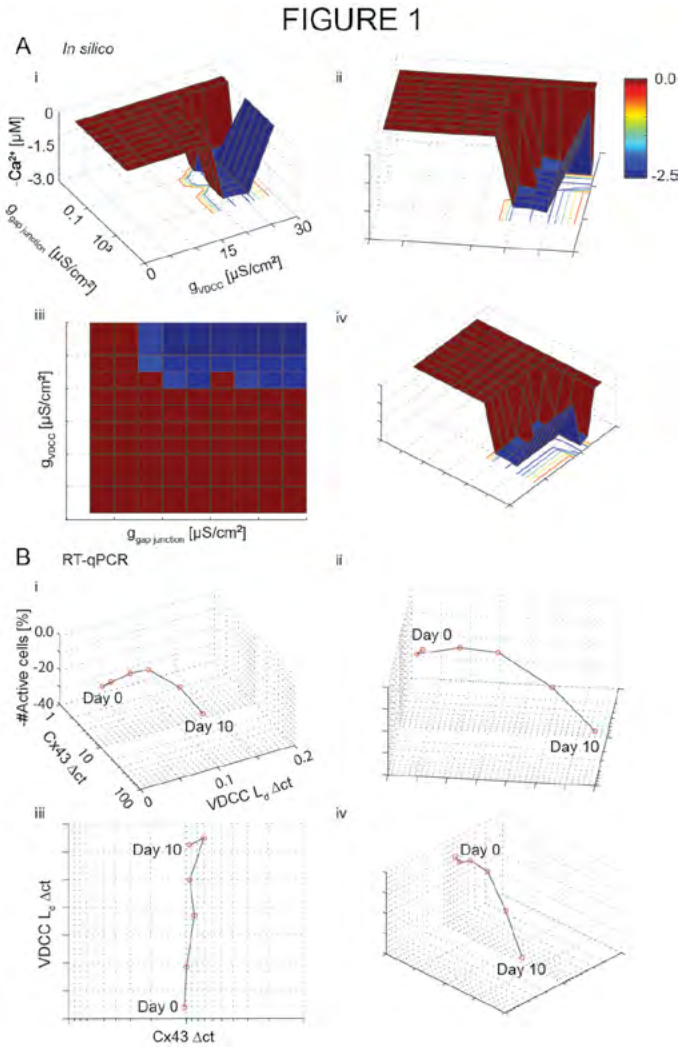
FIGURE 1
A
In silico
i
ii
iii
iv
-Ca²⁺ [µM]
0
-1.5
-3.0
0.1
10³
0
15
30
g_gap junction [µS/cm²]
g_VDCC [µS/cm²]
0.0
-2.5
g_VDCC [µS/cm²]
g_gap junction [µS/cm²]
B
RT-qPCR
i
ii
iii
iv
-#Active cells [%]
0.0
-20
-40
Day 0
Day 10
1
10
100
Cx43 Δct
0
0.1
0.2
VDCC L_α Δct
Day 0
Day 10
Day 10
Day 0
VDCC L_α Δct
Cx43 Δct
Day 0
Day 10

P23 1D-3D hybrid modelling: From multi-compartment models to full resolution models in space and time

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The sub-cellular architecture of neurons is composed of numerous organelles that fill the intracellular space and play an active role in signal translation and signal transfer in neurons, from the electrical to the biochemical scale. Organelles like mitochondria and the endoplasmic reticulum form a complex and filigreed three-dimensional neuronal subarchitecture, that strongly influences how signals in the cell are encoded and transported long distances through the neuron. The inhomogeneous occupation of cytosolic space also affects how fast ions can travel through the cytosol. In order to make use of established 1D simulation methods for electrical signaling in neurons [1], [2], [3] such as multi-compartment modeling with NEURON [4] or GENESIS [5], and to integrate the three-dimensional neuronal sub-architecture, that needs to be included in a model to fully understand the detailed dynamics of important signaling events, we developed a 1D-3D hybrid modeling framework, that allows us to couple established multi-compartment models, e.g. [6], and full three-dimensional models for subcellular signaling. These can include the detailed morphology of the cell and its organelles. By reconstructing the three-dimensional morphology from, e.g. .hoc geometry files and a mapping algorithm to map the membrane potential data from a multi-compartment model simulation onto the detailed three-dimensional cell, we are able to use established and published models within this novel framework [7], [8], [9]. We demonstrate how this framework can be used and how the neuronal sub-architecture strongly influences sub-cellular signaling events. In particular we show a proof-of-concept which highlights the benefits of our approach, i. e. we shed light on the effect of differently sized intracellular obstacles, voltage gated calcium channel densities (Borg-Graham [10]) as well as a variable diffusion tensor on the intracellular calcium dynamics [9].

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P24 Employing NeuGen 2.0 to automatically generate realistic morphologies of hippocampal neurons and neural networks in 3D

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Detailed cell and network morphologies are becoming increasingly important in Computational Neuroscience. Great efforts have been undertaken to systematically record and store the anatomical data of cells. This effort is visible in databases, such as NeuroMorpho.org [1]. In order to make use of these fast growing data within computational models of networks, it is vital to include detailed data of morphologies when generating those cell and network geometries. For this purpose we developed the Neuron Network Generator NeuGen 2.0, that is designed to include known and published anatomical data of cells and to automatically generate large networks of neurons. It offers export functionality to classic simulators, such as the NEURON Simulator by Hines and Carnevale [2]. NeuGen 2.0 is designed in a modular way, so any new and available data can be included into NeuGen 2.0. Also, new brain areas and cell types can be defined with the possibility of constructing user-defined cell types and networks. Therefore, NeuGen 2.0 is a software package that grows with each new piece of anatomical data, which subsequently will continue to increase the morphological detail of automatically gen- erated networks. Here we introduce NeuGen 2.0 [3] and apply its functionalities to the CA1 hippocampus [4]. Runtime and memory benchmarks show that NeuGen 2.0 is applicable to generating very large networks, with high morphological detail (cf. [3]). For demonstration purpose a network containing 15.000 cells can be generated within ten minutes. The complexity for interconnecting the cells in the worst case demands O(n^2) CPU time, but may be much better depending on the maximum distance dmax between cells selected for synaptic interconnection (for algorithmic description refer to [3]). For our test case roughly 2 GiB of memory was required - a smaller network is depicted in Fig. S1. NeuGen 2.0 also renders appealing for other projects, as e. g. in our novel 1D/3D hybrid modelling approach, utilizing NeuGen 2.0 as a preprocessing tool for the generation of a volume grid which is subject to numerical treatment by our PDE solver framework UG4 [5] in e. g. a reaction-diffusion equation system in the intracellular space of the geometry respectively network. Nota bene: NeuGen 2.0 is written entirely in standard Java thus beeing available for a broad user audience.

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P25 Partial Granger causality analysis for brain connectivity based on event related potentials

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Partial Granger causality is a measure of direct functional connectivity that takes into account both environmental (exogenous) inputs and unmeasured latent variables as two main confounding parameters [1]. The concept underlying this approach is that the influences reflected in correlations among the residuals can partly be factored out analogous to partial coherence. In our present work, partial G-causality is applied to Event Related Potentials (ERPs) to examine the timing of distributed brain processes involved in perception and cognition.

In this work a synthesized model consisting of five time series in different conditions was extensively tested to validate partial G-causality approach. The aim was to separate effects of confounding variables in the data. A time-domain multiple-trial partial G-causality was applied to a 128 channel ERP data [2] based on a mismatch negativity auditory oddball paradigm. Bayesian Information Criterion (BIC) measure was used to model order estimation of multivariate autoregressive model. A total of 120 trials of target response signal from -100 to 400 milliseconds after stimulus onset were selected. Data were subsampled to 125Hz and limited to 19 general EEG channel locations. A 3D source reconstruction was employed to interpret and confirm the causal interactions in ERP data. More specifically, a full channel inverse analysis was performed which consisted of steps such as source space modelling, data co-registration, forward computation using EEG beam forming, and inverse reconstruction. The inference was done using non-parametric bootstrapping test in both simulated and experimental data.

The technique showed the robustness to input and latent influences on the simulated data. The ERP results disclosed two major bilateral signal propagations close to primary auditory cortex and superior temporal gyrus in both the right and left temporal areas, which were consistent with previous literature [3]. Expectedly, source localization analysis showed considerable bilateral activities in the temporal lobe. In addition, significant bidirectional connectivity was found between C3 and FC5 channels which may reflect a perturbation of neuronal dynamics by forward-backward processing [3].

The present results using partial G-causality analysis opens up promising perspectives to the study of functional connectivity. One prominent advantage of employing this technique is to identify the influence of specific brain regions to provide a priori hypothesis for the effective connectivity analysis and its related techniques such as dynamic causal modelling [4].

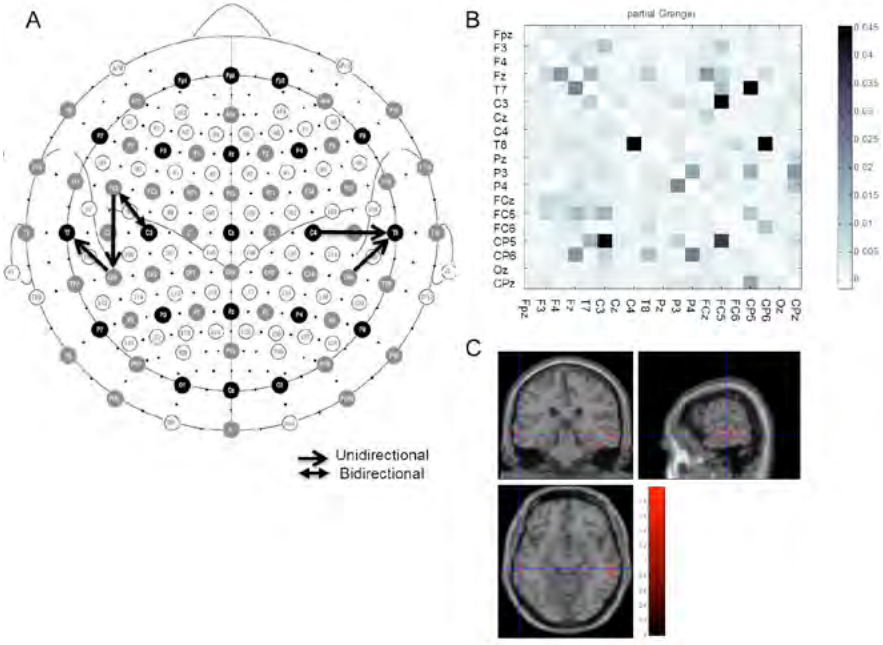

Figure 1. Results of applying partial G-causality analysis to ERP from a mismatch negativity auditory oddball experiment. (A) Significant causalities of the target responses. (B) Significant corresponding connectivities. (C) Reconstructed sources using imaging approach.

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P26 A multivariate data-driven approach for decoding emotions

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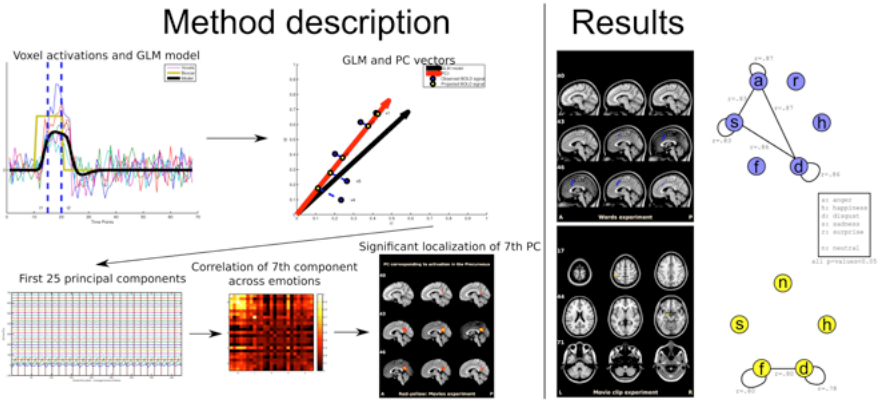
Brain basis of discrete emotions, such as disgust and fear, has been studied extensively. However, the subjectivity of emotional feelings makes it difficult to consider any a priori model that would apply for all subjects and experimental runs. Furthermore, as different emotions involve complexly intertwined brain circuitries, it is precarious to consider e.g. a GLM model to fit all experimental conditions.

To overcome the limitations of classic stimulus-model-based techniques we implement a data-driven approach, which is efficient in detecting signal components in a similar sense as a set of basis functions (e.g., PCA). Although interpretation of such components is non-trivial, the approach provides numerous advantages. First, correlation analysis can reveal temporal consistency across different runs. Second, localization of the components may unveil functional connectivity of the involved brain regions.

We applied a PCA-based analysis procedure to two fMRI data sets to detect signal components that correlate with discrete emotions. The first experiment (n = 20 subjects) involved free viewing of video clips that elicited four basic emotions (disgust, fear, happiness, and sadness) and a neutral emotional state. In the second experiment (n = 14), the participants were triggered by single emotion words to mentally induce six basic emotions (anger, disgust, fear, happiness, sadness, and surprise).

For the movie experiment our method extracted an fMRI-signal component involving right amygdala and right supra-marginal gyrus ($p < 0.001$, uncorrected, cluster size > 100). This component showed significant temporal correlation with experiences of fear and disgust ($p < 0.05$). In the mental imagery experiment, the words angry, sad and disgusting had significant temporal correlation ($p < 0.05$) with a component involving the anterior cingulate cortex ($p < 0.001$, uncorrected, cluster size > 100).

In conclusion, our new approach that overcomes some critical limitations of conventional fMRI analysis could provide novel insights into the brain basis of emotional processing. . It can be used for both block-designed experiments and model-free naturalistic-stimulation experiments, such as free viewing of a movie.",,Yes,http://www.frontiersin.org/Journal/MyEditingViewDetails.aspx?stage=100&articleid=54673&submissionid=54776



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P27 A nonlinear coupling between the firing threshold and the membrane potential enhances coding of rapid signals

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In the field of computational neuroscience it is of crucial importance to dispose of simplified spiking models that carefully capture the spiking activity of real neurons. Generalized Integrate-and-Fire (GIF) models have recently been shown to predict the occurrence of individual spikes of both inhibitory and excitatory neurons with millisecond precision. However, while the f-I curves of inhibitory fast-spiking neurons are in good agreement with the ones predicted by GIF models, the same is not true for excitatory pyramidal neurons. In particular, standard GIF models do not capture saturation at relatively low rates. Moreover, in contrast to what has been observed in pyramidal neurons, the firing threshold of standard GIF models does not depend on the speed at which the membrane potential approaches this threshold.

To solve this problem, we propose a new model in which a stochastic GIF model equipped with both a spike-triggered current and a spike-triggered movement of the firing threshold is extended with a subthreshold adaptation mechanism consisting of a nonlinear coupling between the firing threshold and the membrane potential. This additional mechanism can be interpreted as a phenomenological model of sodium channel inactivation. Importantly, all the model parameters, including the timescale and the functional shape of the nonlinear coupling, are not assumed a priori but are extracted from in vitro recordings using a convex optimization procedure.

Our results demonstrate that, in pyramidal neurons, the firing threshold and the subthreshold membrane potential are indeed nonlinearly coupled. Consistent with the dynamics of sodium channel inactivation, we found that this mechanism operates on a relatively short timescale (5 ms) and makes the firing threshold dependent on the speed at which the threshold is approached. The precise shape of the nonlinear coupling extracted from the experimental data accounts for both the saturation at low rates and the noise sensitivity observed in pyramidal neurons. Moreover, accounting for sodium channel inactivation significantly improved the ability to predict individual spikes with millisecond precision.

Our results suggest that the firing threshold dynamics enhances sensitivity to rapid fluctuations of the input and makes pyramidal neurons respond as differentiate-and-fire rather than integrate-and-fire.

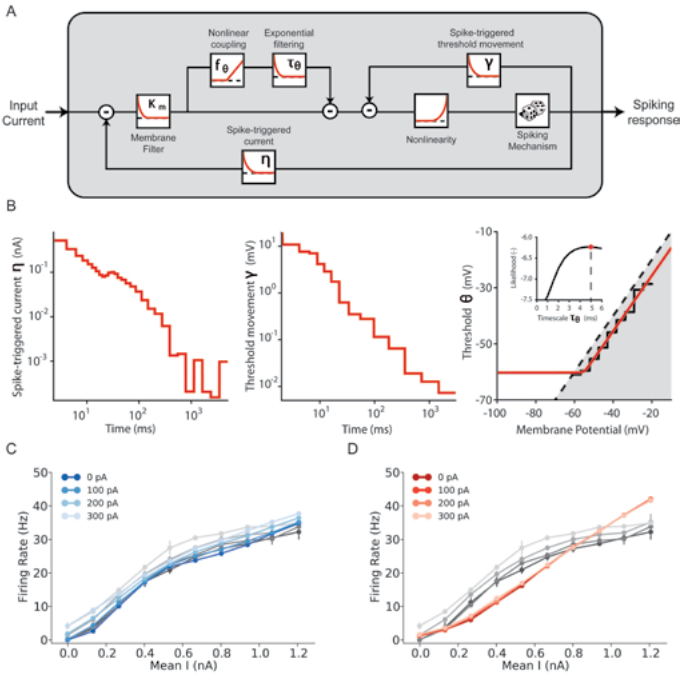

Figure 1: A generalized integrated-and-fire model extended with a nonlinear coupling between the firing threshold and the subthreshold membrane potential captures the f-I curves observed in L5 pyramidal neurons. A: Schematic representation of the model. The input current is first low-pass filtered and then transformed into a firing intensity by an exponential nonlinearity. Spikes are emitted stochastically and trigger both an adaptation current $\eta(s)$ and a movement of the firing threshold $\gamma(s)$. The firing threshold is also coupled to the subthreshold membrane potential V. The nonlinear coupling is defined by the function $f_\theta(V)$ and has a characteristic timescale τ_θ. B: Model parameters extracted from intracellular recordings performed in L5 somatosensory pyramidal neurons. Left: Adaptation current $\eta(t-\hat{t})$ triggered after the emission of an action potential at time $\hat{t}$. Middle: Spike-triggered movement of the firing threshold $\gamma(t-\hat{t})$. Right: nonlinear coupling $f_\theta(V)$ between the firing threshold and the subthreshold membrane potential. Inset: the nonlinear coupling is characterized by a timescale τ_θ =5 ms. C: The average firing rate of a L5 pyramidal neuron in response to noisy currents is plotted as a function of the mean input (gray). Different curves correspond to different levels of noise. Model prediction is shown in blue. D: The prediction of a GIF model fitted under the assumption that the firing threshold and the membrane potential are not coupled (i.e. $f_\theta(V)=0$) is shown in red.

P28 A parameter identification toolbox for two-dimensional integrate-and-fire neuronal models based on electrophysiological data

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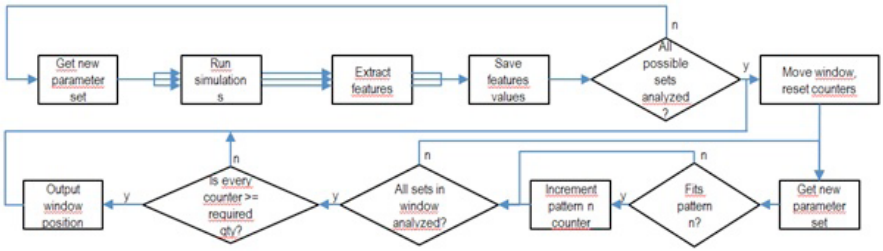
Two-dimensional integrate-and-fire neuronal models, such as the adaptive exponential[1] or quadratic integrate-and-fire[2] (AdEx or Izhikevich) model, compromise between computational efficiency and the ability to generate diverse realistic spiking patterns ([1–3]). However, when searching for model parameters to fit the neuronal spiking patterns observed in electrophysiological recording, it often requires expert knowledge e.g. in dynamical systems theory, or a tedious trial-and-error approach.

In this work, we offer a systematic computational approach towards solving this problem. First, for each free parameter, a list of plausible values is defined. Then every possible parameter set is analysed, and the features of the simulated neurons are extracted and saved. The second step is to define the target spiking patterns. The user also needs to define a window size, and a required number of instances for each target pattern. The program then uses a sliding window approach on the feature map built in the first step, counting the instances of each pattern, and provides the list of parameter sets that fit the description. The computer program is written in C++ to generate results efficiently.

To test our approach, we focus on the AdEx model parameters to replicate the electrophysiological data of neurons in the lateral habenula (LHb). Experimental data has shown that although LHb neurons can have different morphologies, their basic electrophysiological characterizations are very similar[4]. They also display time-dependent inward rectification and distinct afterhyperpolarization. Furthermore, LHb neurons can exhibit distinctive spontaneous spiking patterns: silent, tonic regular spiking, tonic irregular spiking, and rhythmic bursting. Importantly, rebound bursts can be activated upon brief membrane hyperpolarization. In the model, the essential features to be considered are the adaptation rate, sag, spontaneous spiking frequency, number of spikes per burst, and regularity of the pattern, but other features like spike width, after-hyperpolarization potential could also be extracted. Our toolbox allows us to identify a small region in the parameter space containing the right neuronal proportions for the observed spiking patterns. As a result, we can reproduce the diversity of LHb spiking patterns with small parameter variations within a single model. Although the current implementation considers only two-dimensional integrate-and-fire models, it can be modified or expanded to other types of neuronal models.



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P29 Preliminary results on statistical group analysis of probabilistic tractography: Application to major depression disorder

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Introduction
Diffusion tensor imaging (DTI) is an ideal tool to investigate white matter abnormalities. Several disorders, including major depression disorder (MDD) present white matter abnormalities for which disturbance of global connectivity must be investigated. The objective of this work is to propose a new method, augmented with a new visualization technique to carry out group based DTI analysis for connectivity based hypothesis testing.

Method
We propose a new DWI analysis pipeline consisting of preprocessing, tractography, visualization and analysis. Preprocessing: T1, T2, DWI b0 and DTI images are registered on to each other; grey and white matter masks are constructed and neuroanatomical labeling is performed. Tractography: PICO probabilistic tractography [1] is used where the seed points are chosen as grey-white matter boundary voxels for each selected grey matter structure. Using the tracts and parcellation data connectivity maps are generated for seed regions (ex. Amygdala) and the maximum common sub-graph is calculated among all patients and control subjects (Figure 1). Visualization and Analysis: Two types of visualization are performed. First, FA value of each voxel is associated with the arc-length of all tracts that pass through that voxel. Using this information, a graph that shows arc-lengths on the x-axis and FA values on the y axis is constructed. For example, if FA value of voxel x is 0.3 and 4 tracts pass through this voxel; and voxel x happens to be 5, 20,35,155 voxels away on these 4 tracts from the chosen seed point, then for the FA value 0.3 and for the arc-lengths 5,20,35 and 155, the corresponding grid box is incremented by one. When this is performed for all subjects, we obtain the graphs presented in figures 2 and 3. Second, for each grid box at a specific FA value and arc-length, a t-test is performed between group graphs. The associated p value is stored within this grid box as shown in figures 4 and 5. Using these graphs, it is easy to indicate how populations differ with respect to arc-length and FA values for tracts that originate from the same region such as amygdala.

Results
DTIs are collected with 7 b0 and 45 directions on 10 subjects (5 MDD patients, 5 control). Cortical–subcortical neuronal networks, especially limbic and frontal–subcortical neuronal circuits play an important role in the pathogenesis of MDD [1]. When amygdala and its connections are investigated, the most common connections in both groups are found as temporal pole, insula, hippocampus, medial-orbito frontal cortex, putamen, lateral-orbito frontal cortex and entorhinal cortex. The connections that differ statistically between patients and controls are detected in graphs constructed between left amygdala and temporal pole, insula and hippocampus, as well as in graphs between right amygdala and

MOFC, putamen and hippocampus. The connection length and FA values differed between these regions in the range of 0-300 mm and 0.1-0.6 respectively.

Conclusion

The method we propose not only enables hypothesis testing of probabilistic tracts but also provides multi-resolution visualization to view FA versus fiber length correlations. This method can be utilized for connectivity related group studies of white matter abnormalities.

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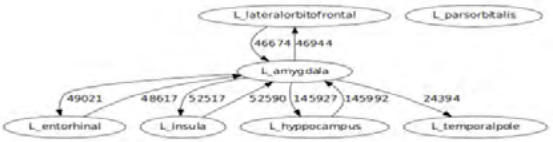

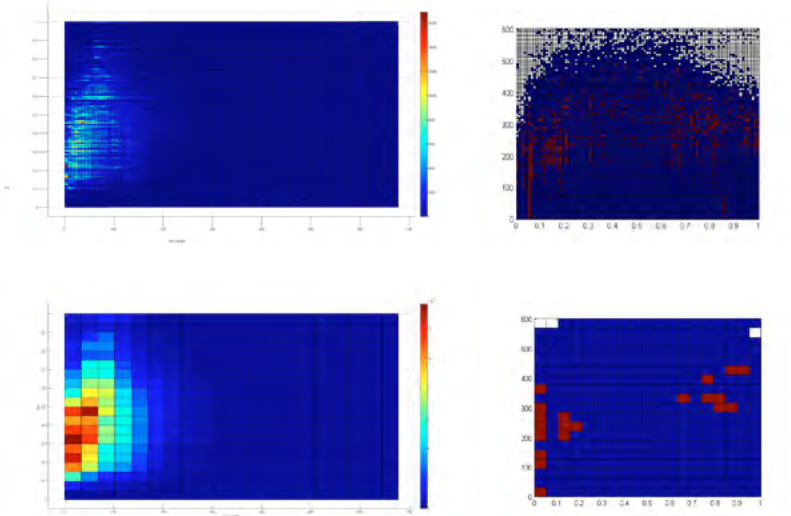

P30 Engineering the mind: a system engineering approach to modelling the brain

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System engineering techniques, in particular those used for software engineering, have been developing over a number of years to support the design of highly complex Man-made systems. System engineers build a top down hierarchical design of a system that abstracts complexity, allowing engineers working on individual parts of the system to have a common view of how their own elements interact with others. To do this the system is decomposed into subsystems, and the definition of the interfaces between each subsystem is rigorously maintained. This paper proposes the use of the same techniques to reverse engineering a model of the brain. It uses a system engineering approach to develop a theory of the high level functional (as opposed to physical) architecture of the brain, and from this decomposes the system in to a number of specialised subsystems with defined interfaces. Reverse engineering the mind has the added complication that not only is the architecture unknown, but so is the underlying technology used to build the architecture. An expandable framework for these underlying technologies has therefore been defined. This includes a generic model of a spiking neuron, and its specialisations. Neurons can be connected together in networks and the arrangement of the neurons in these networks has also been included in the framework. These have been called design patterns, a term which is used in software engineering to denote a general reusable solution to a commonly occurring problem. As part of the research a first iteration of the model that uses the framework has been developed in C#. This has already provided an interesting insight into the way thoughts could be orchestrated, and may help to explain some of the basic characteristics of the mind.

D05 TissueStack: an Open Source HTML5 web based imaging viewer

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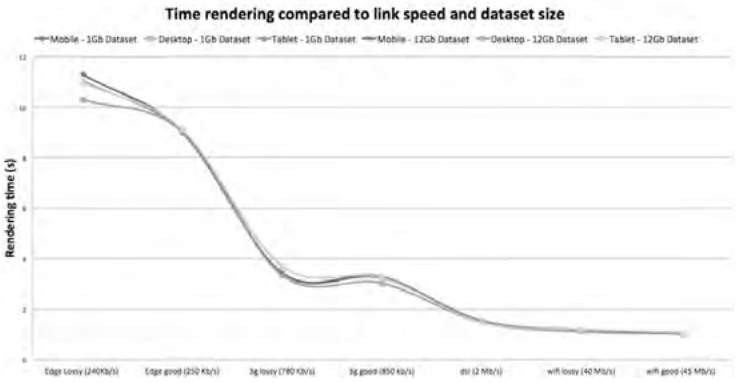
Web based viewing of large 3D datasets is now a critical part of imaging research. This has been driven by multiple efforts to make available large collections of histological, optical and electron Microscopy data. It is critical that the web applications to view and serve this data are robust, available on multiple platforms, have a scalable view of data and are intuitive to use for novel users. Existing tools that are capable of presenting tri-planar views of large datasets rely upon custom web extensions such as Adobe Flash, have restrictive dataset size limitations and as such are not tractable on mobile devices.

The TissueStack project was born from these goals and is now a mature product. The original use case was a large multi-site study with geographically distant generators of imaging data. This leads to the problem in which no one is sure where or how to access the current version of all the data without having to download TB's of data and trawl through it. This problem is not unique to the neuroimaging field and as such in TissueStack we made extensice use of techniques from the very closely related field of GIS (Graphical Information Systems – ie: online mapping).

The server and viewing application have a number of features: Image tiles can be either generated on the fly or Pre-tiling can be initiated via the interface. The tool is HTML5 based and thus runs on mobile devices (iOS, Android, etc). We have tested the TissueStack server on 3D datasets up to 12GB in size over a mobile data link with no significant increase in rendering time (See Figure). It supports embedding, direct links to dataset features, dataset colour mapping, intensity range adjustments, multiple views of datasets, overlays and load balancing across multiple servers. The current server has a plug in architecture and can load files in either MINC or NifTI format. An example server running on a virtual appliance in the Australian Research Cloud can be viewed at http://caivm1.qern.qcif.edu.au.

Tissuestack has so far been successfully used for neuroimaging, chemical engineering, electron microscopy, digital curation by museums and animal atlasing data. The main website and more information is available at www.tissuestack.org

TissueStack is an Open Source project and is available on GitHub (github.com/NIF-au/TissueStack). All code is licensed via the GPL v3.


Time rendering compared to link speed and dataset size
Mobile - 1Gb Dataset
Desktop - 1Gb Dataset
Tablet - 1Gb Dataset
Mobile - 12Gb Dataset
Desktop - 12Gb Dataset
Tablet - 12Gb Dataset
Rendering time (s)
Edge lossy (240Kb/s)
Edge good (250 Kb/s)
3g lossy (780 Kb/s)
3g good (850 Kb/s)
dsl (2 Mb/s)
wifi lossy (40 Mb/s)
wifi good (45 Mb/s)


Tissue Stack - Desktop
Data
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Zoom Level: 3
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P31 Multimodal stereotactic template of the gray short-tailed opossum's brain

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The gray short-tailed opossum (Monodelphis domestica) in an increasingly popular laboratory animal due to the early stage of development of its newborns born at 14 PCD, which makes this species particularly useful in developmental and comparative neurobiology. However, while a number of studies were performed on the opossum brain, still, a consistent and comprehensive neuroanatomical reference is not available. Moreover, there is no stereotactic coordinate system defined which makes procedures like brain lesions or tracer injections more difficult to perform and less accurate. The aim of this study is to provide a multimodal stereotactic template of the Monodelphis opossum brain to enhance usefulness of this species as a convenient model in neurobiological research.

Data of four modalities were acquired from a single one-year old male specimen preserved in formalin: (1) T1/T2* magnetic resonance image collected using Bruker BioSpec 9.4T imaging system with the isotropic resolution of 50um. (2) Photographs of the tissue block taken during cryosectioning ('blockface' images) acquired with the camera placed in front of the cryostat. (3 and 4) Series of 40um thick coronal Nissl- and myelin stained slices across the whole brain, 264 slices each.

During the data integration process, the blockface images were rigidly coregistered to one another to remove cryostat shaft's jitter and were stacked into a single volume. Then, reconstruction of the brain from both series of stained slices was performed. First, images of the stained slices were rigidly registered to corresponding blockface images, then the slices' images were sequentially aligned to a reference slice from the middle of the stack. However, the rigid alignment did not correct distortions of individual sections like tearing, folding or loosing some of its parts. Therefore, deformable reconstruction routine was used to assure a smooth shape of the histological volumes. By iteratively deforming consecutive slices towards the average of their neighbors, the procedure corrected the most distorted slices, forced smooth reconstruction of the brain outline, and significantly improved the shapes of the internal brain structures. Computed deformation fields were then visualized and quantitatively analyzed to highlight the areas with the highest amount of deformation. Finally, blockface volume, and those based on series of stained slices were affinely aligned to the MRI volume which resulted in the complete multimodal template.

The stereotactic coordinate system was established by examining microtomography (micro-CT) image of the opossum's skull acquired with the X-Tek (Nikon) Benchtop CT160Xi microtomograph with the 41um isotropic resolution. Coronal, Lambdoid and Sagittal

sutures were identified as well as ear canals and dental chiasma, which allowed to locate bregma and lambda anatomical points, define interaural line and thus, to express locations within the brain with respect to the defined landmarks.

The obtained template allows for slicing the brain at arbitrary planes and for performing any other type of volumetric analyzes. Four data modalities constituting the template facilitate the ongoing process of delineating individual brain structures. Moreover, other experimental results like data acquired from various immunohistochemical stains will be mapped into the template in the future.

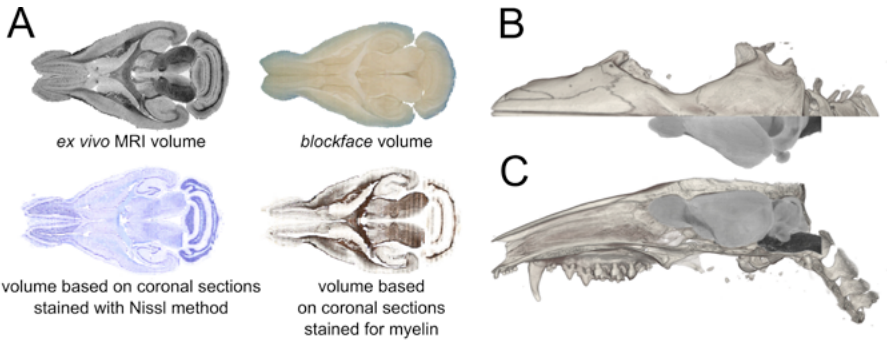

Figure 1: A summary of the performed steps of data integration; A) Horizontal cut through volumes of various data modalities acquired from the brain of a single specimen. B) Illustration of the method of determination of the stereotactic coordinate system by coregistering 3D skull image with MRI volume of the brain; horizontal view. C) Saggital view.

P32 The INCF Digital Atlasing Program, a look back and to the future

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The International Neuroinformatics Coordinating Facility (INCF, http://incf.org/) formed the Digital Atlasing Program in the fall of 2008, in response to a workshop and report[1] that recommended INCF create a framework for digital atlas data sharing and related recommendations and standards.

In 2009, INCF formed a Standards Task Force (TF) led by Mike Hawrylycz. They generated a detailed report[2] outlining the design of an atlas-based data sharing framework that allows researchers from individuals to large groups share data from a variety of rodent based experimental modalities from distributed locations, and ultimately to view and perform comparative analyses of the results. It includes the recommendations and specifications of an infrastructure capable of reaching these goals, along with practical issues. This group also created Waxholm Space (WHS) and a prototype of the Digital Atlasing Infrastructure (DAI), together forming the backbone of this atlas-sharing framework[3]. Their work was reviewed later that year with a Reference panel. Based on this feedback, the standards TF was dissolved and two others created, a WHS TF (led by Mike Hawrylycz) to improve reliability and access to WHS, and a DAI TF (led by Ilya Zaslavsky) to develop and refine infrastructure and supporting standards and services. Since then, these groups have tackled a number of projects that facilitate data sharing of multiple types with this framework.

In late 2010, an Atlasing workshop was held, highlighting the atlasing framework and deliverables. At this time, it was clear the community needed registration workflows, tools, and expertise. Thus, registration experts were recruited to the TFs and potential data sharing use cases were solicited. Since 2011, creating primarily 2D image registration workflows and tying them to DAI has been a main focus of both TFs, which crosses into areas dealing with metadata, provenance, and ontologies. In late 2012, Ilya Zaslavsky's group successfully created a 2D image registration tool tied to the INCF DAI. Work is underway to develop registration workflows for high-throughput 2D images. Work continues in supporting project areas, such as registration fiducials, pan-mammalian delineations, standards, metadata, provenance, rat WHS, and data management and handling.

In late 2012, a workshop was held to evaluate the outcomes of the INCF Atlasing Program. This group confirmed that user-friendly data registration should be a top priority for the program. Usability, visibility, and the ability to collaborate with other related projects are key to the success of this program. To this end, the program welcomes input from the

community, and requests expert recommendations in our project areas. Please contact any of the authors for further information.

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P33 Extending the INCF digital atlasing infrastructure to include online image registration to atlas references spaces

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The INCF digital atlasing infrastructure (DAI) is being developed to assist neuroscientists with discovery, access and integration of information from multiple atlases based on location in the brain. The backbone of the DAI service-oriented architecture is a collection of atlas web services, which provide access to location information including anatomic feature labels at a given point of interest, registered images, gene expression data, annotations, etc. A registry of formally defined atlas reference spaces for widely used atlases and coordinate transformation functions between them are the foundation for spatial integration. The atlas web service interface is an implementation of the Web Processing Service (WPS) standard, and the information exchanged via services is encoded in Waxholm Markup Language (WaxML) which is an application schema of ISO 19136 and provides standard constructs for representing coordinate systems, transformations, names and locations of brain structures, etc. Standard-compliance of atlas web services enables DAI to leverage a number of standard components developed elsewhere, including client libraries and online portal interfaces. The current operational system of services incorporates reference spaces for several mouse brain atlases (the ABA voxel space, ABA reference plates, Allen Gene Expression Atlas (AGEA), WHS, and Paxinos-Franklin atlas) as well as for atlases of the rat brain (the Paxinos-Watson atlas, WHSrat, and Wistar-Rat).

While the DAI framework enabled neuroscientists to access information from existing atlases, easy integration of user imagery into the system remained a challenge. To address it, we developed a workflow for spatial registration of 2D images and 2D image collections. The workflow can be invoked from the DAI atlas portal. In the current implementation, users upload their image collections to the INCF DataSpace, an online data grid environment for managing and sharing distributed data using iRODS. The uploaded images are processed to generate a number of derivate representations used in the registration process. Presented with a gallery of uploaded images, users then align image slices to reference spaces and establish fiducial reference points for thin plate spline computation using online software called Jibber. Coordinate system descriptions and coordinate transformation functions for the added image or image collection are then generated automatically based on the spline coefficients, using the workflow's Jetsam component. As a result, users have the ability to immediately query available atlas hubs via atlas services using spatial locations on their own images to retrieve structure names, other registered images, gene expression and other data associated with user-defined points of interest.

This work was conducted within the DAI Task Force of the INCF Program on Digital Brain Atlasing.

P34 Developmentally conserved brain designs quantifiable with transcriptome tomography

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We have invented a framework for gene expression density mapping on the whole three dimensional (3D) anatomical context, transcriptome tomography, in which tissue sections in each of three orthogonal planes are fractionated (fractions), and gene expression densities in them measured with microarrays (fraction data) are then reconstructed to generate 3D maps (PLoS One 2012; 7, e45373). The fractions are exactly in the same thickness, so the fraction number of a coronal section, for instance, represents the distance from the starting point of the sections, the spino-cerebral (SC) border. Thus, besides 3D reconstructed maps, comprehensive expression densities along the body axes are measurable in the fractions. This unique feature of the data has encouraged us to test how gene expression gradients along the anterior-posterior (AP) body axis can be measured in the framework. Homeobox gene family members, Hox genes, are sequentially activated in time and space in a way of evolutionally conserved co-linear genomic position of the paralog genes (Figure 1A) and are participated in definitions of positional information along the AP axis in developmental stages of wide ranges of animals including mammals. Using the fraction data, we would show that the spatially co-linear expression patterns of Hox genes along the AP axis were also observed in the adult mouse brain. Intriguingly, the expression densities exponentially declined when plotted against the fraction numbers representing distances of from the SC border (Figure 1B), and the inclination was correlated to the genomic location of the paralogs. We would also show co-linear density gradients of Dlx genes that belonged to another homeobox gene family. The 3D expression maps of Hox and Dlx genes in the adult brain were seen in the ViBrism-DB for the first dataset created with transcriptome tomography (http://vibrism.riken.jp/3dviewer/ex/index.html ; some seen in Figure 1C). Quantified expression density data exclusively produced with our framework provided evidences of the direct co-relation of them to the genomic organization. This may contribute to clarify a developmentally conserved regulatory mechanism underlying complex brain function.

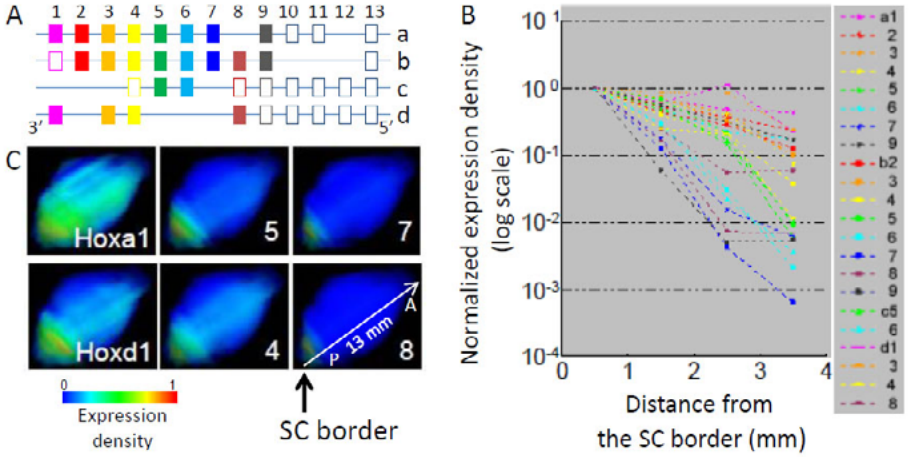

Figure 1. (A) The genomic organization of the mouse Hox genes. Genes are clustered in four groups (a-d) and in each group they are located in the order of paralog numbers (1-13) from the 3′ to the 5′ of the genome. This order regulates the co-linear gene expression in time and space of the embryonic stage (Deschamps and van Nes J., 2005). Solid bars indicate the presence of gene expression in the dataset. **(B) Expression densities of Hox genes plotted against the distances from the SC border.** Log transformed densities normalized to the values of first section data are plotted. Color codes are the same as those in Figure 1A. Genes in the 3′ position less declined than genes in the 5′ position in posterior to anterior gradients of the brain. **(C)Typical expression maps of Hox genes in the 3D anatomical space.** Expression densities are shows as the color code. Orientation of the brain, the SC border and the map scale are indicated in the map of Hoxd8.

P35 Brain-wide atlas of amyloid-beta distribution in transgenic amyloid precursor protein mouse model of Alzheimer's disease

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Genetic animal models are powerful tools for preclinical experimental investigations of pathogenic processes, diagnostic markers and identification and evaluation of novel interventional approaches. Numerous genetic animal models reflect important characteristics of different diseases, but none reproduce the full spectrum of pathological changes seen in human patients. The selection of appropriate models is a considerable challenge and requires knowledge about the genetic background, behavioral alterations and neuropathological phenotype. For neurodegenerative diseases, such as Alzheimer's disease, detailed information about the morphology, spatial distribution and amount of key pathological hallmarks, such as aggregation of amyloid-_ plaques in the brain. A considerable general challenge for the field is that most studies are typically restricted to selected brain regions, and document their observations journal figures as representative selected examples. This poses an important limitation to the knowledge that can be gained from morphological phenotyping studies, and there is a growing awareness about the need for new resources allowing researchers to share large amounts neuroanatomical data image data describing important features of genetic disease models. We have developed a database infrastructure for efficient dissemination of serial microscopic image data from rodent brains, and here present an atlas showing immuno-labeled amyloid-_ plaques in 12 month old female and male transgenic mice carrying the Arctic (E693G) and Swedish (KM670/6701NL) amyloid precursor protein mutations. Our atlas system (http://www.rbwb.org/, see tg-ArcSwe atlas) allows online inspection of the histological characteristics and spatial distribution of immuno-labeled amyloid plaque. We demonstrate how the image collection facilitates brain-wide characterization and quantitative image analysis of labeled neuropathological features. We argue that accumulation of comprehensive morphological data on multiple animal models in digital brain atlas systems will allow better characterization and more efficient selection of animal models for future resource-demanding interventional investigations.

P36 Volumetric Waxholm Space atlas of the rat brain for spatial integration of experimental image data

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Brain atlases are important tools for understanding complex brain anatomy and widely used for planning of experiments and interpretation of experimental data. Several volumetric atlas templates based on magnetic resonance imaging (MRI) data have been developed for the rat brain to facilitate assignment of anatomical location to data and comparison across experiments. Important limitations of these atlases have been the lack of a standardized spatial reference given by internal landmarks and a lack of anatomic delineations directly corresponding to underlying image features. Recently, a standard reference space (Waxholm Space) was defined for the mouse brain by the International Neuroinformatics Coordinating Facility (INCF), connecting several mouse brain atlases for spatial integration of experimental data. As a contribution to a novel atlasing resource for the rat brain, we have implemented Waxholm Space in the rat, and created a volumetric atlas of the Sprague_Dawley brain based on ex vivo MRI anatomical (T2*) images with 39 _m isotropic voxels and diffusion tensor imaging (DTI) volumes with 78 _m isotropic voxels acquired from an 80 day old male Sprague_Dawley rat. The atlas covers 83 anatomical structures, including 16 substructures of the hippocampus, distinguished on the basis of image contrast observed in MRI and DTI, aided by information from traditional brain atlases and cyto_ and chemoarchitectonic data from other animals. The atlas and the underlying MRI and DTI image volumes are shared via the INCF Software Center. Waxholm Space connects the atlas to a growing infrastructure of interoperable resources and services for multi_level data integration and analysis across reference spaces.

D06 Analyzing electrophysiology and simulation data with Spyke Viewer

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The amount of data generated by electrophysiological experiments and simulations continues to increase. In order to analyze these datasets, researchers need a way to navigate, access and visualize data in various formats. The development environment for new analyses should enable rapid iteration without restricting flexibility. There should be a convenient way to share newly developed analyses and visualizations with collaborators or the community.

We address these requirements with Spyke Viewer [1], an open source, multi-platform graphical user interface (GUI) application for navigating, visualizing and analyzing electrophysiological datasets. It is based on Python and the Neo framework [2], which enables it to load a wide variety of file formats commonly used in electrophysiology. Using Spyke Viewer, researchers can load and navigate Neo object hierarchies and easily perform operations on the data.

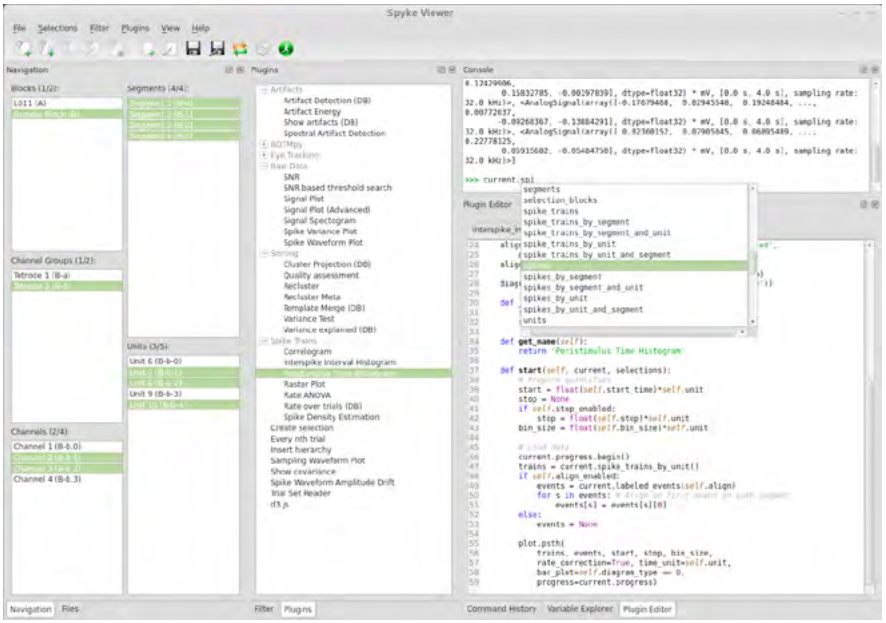
The central design goals of Spyke Viewer are flexibility and extensibility. An embedded Python console allows for interactive exploration of selected data subsets. Users can create filters to control how the data is represented in the navigation view. The filters are regular Python functions that can be edited directly from the GUI. They are stored as annotated Python files so they can be modified using external editors and shared with other users.

A plugin architecture enables users to extend Spyke Viewer. Plugins can be easily created and modified using the integrated Python editor. They are implemented as Python classes, so they can use any existing Python libraries. Analysis plugins can range from simple plots to elaborate analyses and support quick and easy creation of graphical parameter editors using guidata [3]. Spyke Viewer includes several plugins for commonly used plots such as spectrograms, peristimulus time histograms or cross-correlograms. Analysis plugins can also be executed independently of the GUI, e.g. to run on compute servers. Using IO plugins, Spyke Viewer can load file formats and data sources that are not supported by Neo.

While various tools for analyzing electrophysiological data exist, none offer the flexibility of Spyke Viewer. Many are limited to certain file formats or analysis methods and based on proprietary software. In contrast, Spyke Viewer is open source and can run custom analyses with data from arbitrary sources thanks to its plugin system. Users can rapidly develop new analyses and easily share them with the community using a web-based plugin repository.

[1] http://spyke-viewer.readthedocs.org

[2] http://neuralensemble.org/neo/
[3] https://code.google.com/p/guidata/”



D07 Construction and Use of Semantic Repository for Electrophysiological Experiments

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A need to store, organize, share and interpret data and metadata from electrophysiological experiments also emerged during our investigation of developmental coordination disorder in children. If classic data and metadata were successfully stored to the EEG/ERP portal [1], related studies, discussions, and partial interpretations remained unorganized and not searchable. Since the EEG/ERP portal (using a relational database a persistent layer) was not sufficiently prepared to store and process these unstructured texts, it was decided to find an appropriate solution to aggregate and store such data and facilitate subsequent search of relevant information. It was also necessary to use already existing description of data and domain knowledge in a form of semantic web structures.

The OWLIM repository [2] and the KIM platform [3] were finally selected and used to store, annotate and search data. The KIM Platform supports semantic annotation of documents based on ontology, which is stored in the semantic repository. The annotated documents can be searched through; the use of ontological terms ensures more relevant results than a normal full-text search.

To facilitate ontology development, a tool KIM-OWLImport was created. It is able to retrieve the selected ontology into the semantic repository in memory and modify it according to the rules defined by the KIM platform. The ontology then can be used for semantic annotation. To import documents into the KIM Platform a tool KIMBridge was developed. It runs as a service and periodically downloads new documents from selected data sources. Currently, KIMBridge supports downloading PDF documents from Google Drive and downloading discussions from the social network LinkedIn.

Downloaded documents are annotated according to ontological prototype and indexed in the KIM Platform. Subsequent search is made through the web interface. This functionality was verified on a test set of domain documents.

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P37 Modelling mechanotransduction in primary sensory endings

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Mechanotransduction is a process fundamental to life. It underpins a variety of sensory modalities from hearing to blood pressure regulation. However, the molecular components of the mechanosensory mechanisms in primary sensory endings are poorly understood. Experimental approaches to solving this problem are long and laborious. Therefore, a theoretical approach was proposed as an efficient means to circumventing this process.
A mathematical, biophysical model of mechanosensory endings was implemented, which reproduced existing experimental data of the receptor potential of the mammalian muscle spindle primary ending. This probabilistic model combines mathematical representations of different ion channel types to produce an output which is the predicted receptor potential of the sensory ending, given the presence of specific ion channels. The model outputs the tension-dependent electrical response of the receptor, given a stretch stimulus. The parameters required for this model identify the necessary molecular entities required for this behaviour to occur. The dbd (dorsal bipolar dendritic) neuron in D. melanogaster larvae fulfils a similar role to the muscle spindle in mammals. Electrophysiological data was obtained from these neurons via whole-cell patching. It was shown that the dbd neuron can respond to both electrical and mechanical stimuli, but that these responses are noticeably distinct. Furthermore the stretch-evoked data obtained from these receptors was equivalent to that predicted by the model, demonstrating a cross-taxa correlation between the behaviour of neurons in this class. This finding enables simple genetic assays to be carried out in D. melanogaster to ascertain the identity of molecules which are involved in primary mechanotransduction at the sensory terminal. A simple bioinformatics search has yielded a shortlist of candidates which fulfill the criteria of the model predictions. These can now be experimentally tested in a simple and direct approach.

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P38 Including the slice geometry in Current Source Density analysis

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Multielectrode recordings of local field potentials (LFP) from brain slices have become a standard research technique. Because of the long range of the electric fields it is often advantageous to reconstruct the neuronal transmembrane currents from the measured potentials, a procedure known as Current Source Density (CSD) analysis. CSD analysis methods utilize the relation between the transmembrane currents and the potentials (Poisson equation) and have been used succesfully in many contexts. However, CSD methods typically assume that the tissue is isotropic and homogeneous, which is clearly not true in slice recordings.

We have developed a variant of the kernel CSD method which takes into account the finite thickness of the slice and different conductivities of the tissue and the fluid covering the slice. To achieve that, we have employed the method of images and replaced the standard ""1/r"" solution to the Poisson equation with a series. We have tested the new kCSD variant on model data, in which the spread of electric field was thoroughly modelled using the Finite Element Method. We have found that 1) the reconstructed error is smaller when the correct slice thickness and the inhomogeneity in conductivities are taken into account, but the improvement is relatively minor, 2) it is enough to include just the first two additional terms resulting from the method of images.

P39 NeuroElectro.org: a community database on the electrophysiological diversity of mammalian neuron types

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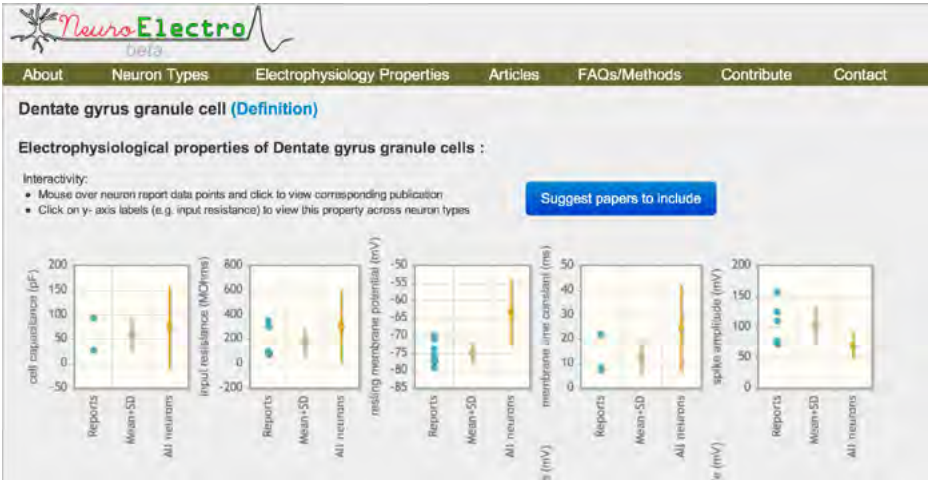
Brains achieve efficient function through implementing a division of labor, in which different neurons serve distinct computational roles. One striking way in which neuron types differ is in their electrophysiology properties. Though the electrophysiology of many neuron types has been previously characterized, these data exist across thousands of journal articles, making cross-study neuron-to-neuron comparisons difficult. Using a combination of manual and automated methods, we describe a methodology to curate neuron electrophysiology information into a centralized repository.

Here, we discuss improvements on our previous methods, in which we have extracted information on neuron-type electrophysiology properties (like resting membrane potentials or action potential widths) from published research articles using Python-based web searching and html parsing tools. Specifically, we have greatly expanded the list of journals we extract information from, now including articles published by the Elsevier, Highwire, Wiley, and Oxford family of journals. We now also use basic text-mining methods to mine details on each study's experimental conditions (like species or electrode type used) from article methods sections. Finally, we also allow users of the web interface, at neuroelectro.org (screenshot in Figure 1), to contribute to the database's content. For example, users can suggest relevant articles on a specific neuron type as well as validate content that has been extracted via our automated algorithms. Furthermore, users can elect to become "content-experts" on a specific neuron type and can then modify the database's content directly.

We are now mining and analyzing the resulting NeuroElectro database to discover unknown relationships on the electrophysiological similarity of different neuron types throughout the brain. For example, we show that there exist but 3 or 4 major neuron classes in terms of electrophysiological properties, which separate largely based on neurotransmitter released and cell size. Furthermore, we are also working with existing neuroinformatics resources, like NIF and NeuroLex (neurolex.org), to integrate our data into the larger neuroinformatics ecosystem, which include databases on neuron morphology and gene expression. Our hope is that greater integration of neuron knowledge will lead to an improved quantitative understanding of the computational function of different neuron types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Dentate gyrus granule cell (Definition)
Electrophysiological properties of Dentate gyrus granule cells :
Interactivity:
Mouse over neuron report data points and click to view corresponding publication
Click on y- axis labels (e.g. input resistance) to view this property across neuron types
Suggest papers to include
cell capacitance (pF)
input resistance (MOhms)
resting membrane potential (mV)
membrane time constant (ms)
spike amplitude (mV)
Reports
Mean+SD
All neurons

P40 Considerations for developing a standard for storing electrophysiology data in HDF5

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11. Blackrock Microsystems, Salt Lake City, USA
12. University of Stirling, Stirling, United Kingdom

The INCF Program on Standards for Data Sharing has a working group that is developing a standard for storing electrophysiology data in HDF5. The impetus for this effort is that many experimentalists are starting to use HDF5 to store data, so a standard would facilitate data sharing significantly.

The most important requirement of such a standard is to accommodate the common types of data used in electrophysiology and also the metadata required to describe them. Neuroshare (an API for accessing electrophysiology data stored in various formats) defines four data types: analog signals, segments, neural events and experimental events; as well as some metadata. A standard needs to efficiently store these data types, and probably also imaging data and some kinds of data generated in the data processing chain, such as features used for spike sorting.

Further, a standard way of storing the metadata must be specified. The set of metadata required to describe electrophysiology data is difficult to determine a priori because the types of experiments are so varied. So, a flexible mechanism must be used which allows referencing and specifying values for currently existing ontologies and also accommodates information not currently systematized. Techniques to include post-experiment annotations of data, and for relating different data parts, are also required.

There are numerous projects relevant to storing electrophysiology data in HDF5. These include: NEO, NeuroHDF, brainliner.jp, klusta-team spikedetekt, BrainVisionHDF5 and

Ovation (ovation.io). A project, NeXus Format (nexusformat.org), uses HDF5 to store particle physics data, but might be adaptable for electrophysiology. It is managed using a well-defined community infrastructure that may be worth emulating.

So far, the working group entertains two approaches towards defining a standard, which may eventually be merged. One, currently named Pandora, defines a generic data model that can be used with HDF5 or other storage back-ends. Due to the generic nature, the data model can be used to store various kinds of neuroscience data. The other proposal, called epHDF, defines domain specific schemata for storing electrophysiology data in HDF5. For any approach, a suite of test data sets to help evaluate a proposed standard is needed, and tools to allow validating data files are desirable.

Details of the above considerations and the current state of the development of a standard will be presented.

P41 EEG/ERP portal for android platform

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We deal with collecting experimental data from Electroencephalography (EEG) and Event-Related Potentials (ERP). Lack of tools for experimental data/metadata management has been solved by developing the EEG/ERP Portal. The advantage of the EEG/ERP Portal is its availability from every computer connected to the Internet. Such solution is sufficient for collecting the most of experiments performed in the laboratory. On the other hand, situations when using a computer is not a viable option are frequent. Many experiments are conducted outside the laboratory with a portable measuring device. In this environment a desktop computer with internet connectivity is usually not available. The other use case is a situation when a researcher discusses the experimental results with colleagues at workshops. A mobile device synchronized with the EEG/ERP Portal seems to be a practical solution.

Facing mentioned needs we have developed a system for collecting experimental data/metadata running on mobile devices. The Android was selected as a mobile operation system because it provides a free SDK with a well-documented API. In addition, the Android is very often used in the current devices.

The system contains a set of forms where a user can fill metadata describing an experiment. The set of metadata is equivalent to metadata that the user can fill in the EEG/ERP Portal. The metadata are described by the internal portal ontology. In addition, the user can upload binary data. The communication of both the mobile EEG/ERP Portal and web EEG/ERP Portal is ensured using RESTfull web services. Server-client architecture is used. A server part is implemented in the EEG/ERP Portal. The server provides access to the database and sends data to the client implemented inside the mobile device. The communication between the server and client is secured using SSL protocol. User credentials are required; the EEG/ERP Portal user account is used to verify the client.

The application is hosted in GitHub repository: https://github.com/NEUROINFORMATICS-GROUP-FAV-KIV-ZCU/eeg-database-for-android. Users are welcome to download and test it.

P42 Laguerre domain estimation of the Elementary Motion Detector based on the fly visual system

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Biological visual systems are generally believed to compute local motion via so called elementary motion detectors (EMDs). The EMD computes local motion by using a non-linear correlation of the luminance change from two neighboring photoreceptors after delaying the input from one. By subtracting the output from a mirror symmetric unit, direction opponency is achieved. A similar underlying computational structure is found in a range of animals, including flies, wallabies, and humans. In the fly optic ganglia, lobula plate tangential cells (LPTCs) spatially pool the output from many EMDs. The physiology of insect LPTCs, and their behavioral output, closely matches the predictions of the EMD. Importantly, however, whereas the EMD model can explain many biological observations, its neural components still remain elusive. The evidence is thus indirect.

In fly motion vision research cathode ray tube (CRT) monitors are commonly used. These provide relatively high refresh rates, up to 200 Hz. Even if this is too fast for our own visual system to detect, the flicker rate is within the detection range of the fly visual system. Since the pulsatile CRT monitor refresh rate is within the fly coding range, it is coded by their photoreceptors and LPTCs. In effect, this flickering stimulus provides a unique opportunity for investigating the influence of high temporal frequencies on the underlying EMD input.

We here use a CRT monitor with a refresh rate of 160 Hz on which we sinusoidally modulate a full-screen stimulus that is known to drive LPTCs strongly. We record the intracellular response of single fly photoreceptors and of LPTCs to sinusoidal gratings with different temporal and spatial frequencies. A single-tone sinusoidal grating does not provide sufficient excitation for accurate parameter estimation of a single EMD, but by adding the extra 160 Hz signal provided by the CRT refresh rate, parameter estimation from individual pulses of the neural response is possible. Note, however, that the measured signal comprises the output of several EMDs.

The pulse-modulated nature of the visual stimuli due to the refresh rate of the monitor lends itself to Laguerre domain system identification. The relationship between Laguerre spectra of the input and output signals of a single EMD model has been derived and serves as a basis of its parameter estimation, see Fig 1. Further, a sparse optimization method is used to evaluate the weights and shifts of multiple EMDs contributing to a layer of EMDs that describes the measured data from LPTCs (Fig. 2).

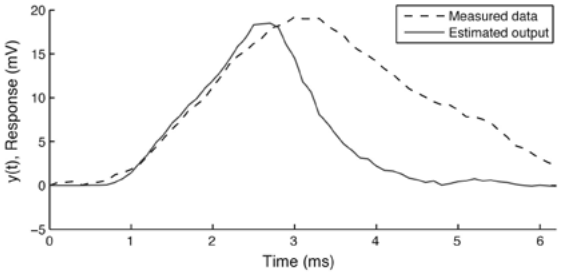

Figure 1: Response of the estimated single EMD model to a single input pulse in comparison with the true output signal, as measured from an LPTC. The rising edge of the estimated model output fits well to the true output signal but not to the decaying part of the pulse, since the measured signal representsa pooled ouputs of multiple EMDs.

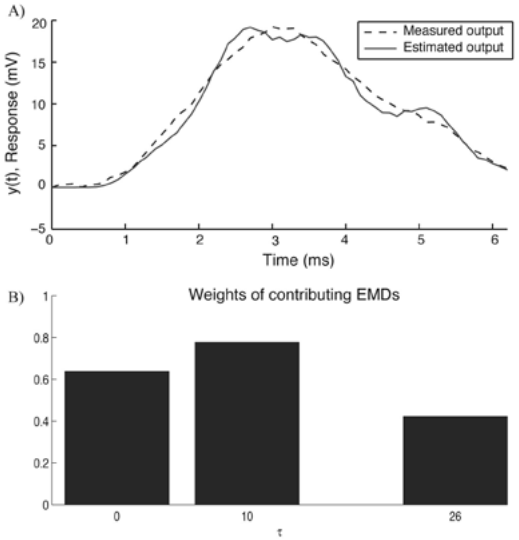

Figure 2: A) Output of three spatially distributed EMDs to a single CRT pulse (single fram on the CRT) with respect to the measured data. The excitation properties of the visual stimuli do not allow for estimation of more complex configurations of EMDs. With the consideration of multiple EMDs, the signal shape of the measured output is reasonably well approximated by the model output. B) The relative weights of the three contributing EMDs. The horizontal axis indicates the temporal shift between the contributing EMDs, where one shift corresponds to one sampling instant (0.1 ms).

P43 A feature extraction and selection procedure for an efficient classification of MEG recordings

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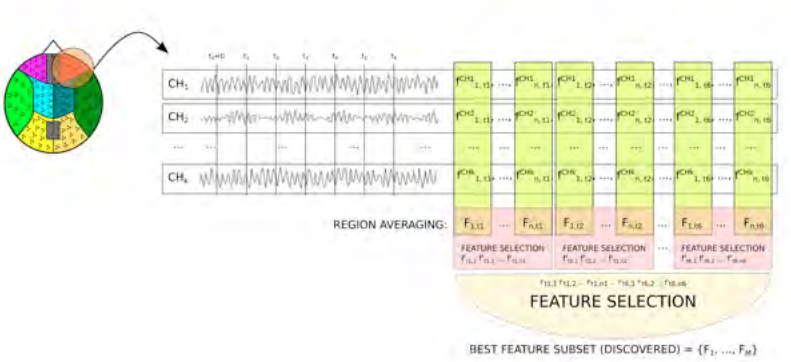
Human brain recordings obtained through electroencephalography (EEG) and magnetoencephalography (MEG) with high temporal resolution yield abundance of data to be interpreted meaningfully. It's important to deal with high-dimensional data (channel - time - frequency), where computational efficiency matters such as in the classification problems for brain-computer interfaces. Our study focuses on feature extraction and selection for a classification task from MEG recordings of two subjects (Chan et al., 2011). We aimed an efficient classification of data obtained by verbal and visual stimuli. We here suggest a novel approach that takes into account spatial, temporal and spectral features (Fig. 1).

Features extracted were curve length, singular band power values (theta, alpha, beta and gamma), mobility, complexity, spectral edge, nonlinear energy and various moments such as variance, skewness and kurtosis (Özkurt et al., 2006). These features were extracted from groups of channels assigned to specific brain regions (temporal, frontal, occipital, parietal for both hemispheres) and averaged for each region. Six different post-stimulus time points were defined: 200, 300, 400, 500, 600, 700 ms. Features were computed for each time point within a centered window of 50 ms.

Feature selection was performed in order to reduce the high dimensional space allowing in the meantime pinpointing the most relevant features. A two-level feature selection approach was implemented. The first level partitioned the feature set in six different subsets (one for every time-point) and feature selection was applied separately on each subset. The second level merged the features retained at level one and applied a further selection.

The following feature selection procedure was performed for both levels: Correlation-based subset evaluation is used in order to assess the quality of the selected features. An optimal feature subset contains features that are highly correlated with the corresponding class while uncorrelated with each other. Accordingly, _features with low correlation are discarded. As features highly correlated with the ones of the given subset do not introduce further advantage, they are also discarded.

Concerning the search for the optimal subset of features, a standard genetic algorithm (GA) was used. GA performs a computationally efficient search through entire space while reducing the risk of being trapped into local optima (Goldberg, 1989). Our algorithm was able to provide accuracy close to 100 % for the classification of verbal and visual material from the brain recordings.",,



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P44 epHDF – a proposed standard for storing electrophysiology data in HDF5

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The HDF5 file format is becoming increasingly popular for storing scientific data including electrophysiology data. The efficient sharing of electrophysiology data using HDF5 will require conventions for how the data are organized within HDF5 files. The determination of such conventions is difficult for at least two reasons. First, it is virtually impossible to anticipate all of the types of data and metadata that will need to be stored. Second, no standard scheme exists for specifying how data in HDF5 files should be organized.

To address both of these difficulties, we propose a layered approach. The first layer, which we call "HDFds" (for "Hierarchical Data Format – data sharing"), provides domain-independent conventions for specifying how the data in HDF5 files are organized. Main features of HDFds: a) Enables associating external schemata to components of an HDF5 file in a manner similar to how name spaces in an XML file identify elements. b) Specifies locations and a format for storing arbitrary metadata in a HDF5 file. c) Allows linking metadata to particular data parts within a file and to external files.

The second layer builds on the conventions in HDFds to specify schemata for storing basic electrophysiology data types. We call this second layer "epHDF", for "electrophysiology HDF". The data types defined in epHDF (time series, time series segment, neural event and experimental event) are based on the entities defined in Neuroshare for covering the most commonly used data types in electrophysiology. For each type, the data can be stored in whatever HDF5 numeric format is most efficient (for example 16 bit integer). For all of the data types, a metadata schema is specified that includes the fields needed to make a plot of the data with correct units.

epHDF does not constrain the location of entities within the HDF5 file and allows defining and reference additional schemata to add new capabilities. This flexibility enables constructing new conventions as needed while still maintaining the capability to interpret the basic electrophysiology data types required for data sharing.

A test was done by converting a sample file, provided by a recording equipment manufacture, from a custom HDF5 format to epHDF. Only minor changes were required to do the conversion and the file size was reduced. The use cases presented in the poster suggest that the epHDF format is simple and also efficient.

References

Neuroshare.org

P45 Spatio-temporal and cortical characterization of EEG changes during motor imagery

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Motor imagery produces similar sensation in the brain as motor execution. Therefore, motor imagery has become an important control paradigm in applications of brain machine interface (BMI) to motor disabled subjects. Most studies focus on EEG oscillations corresponding to alpha (8-12Hz) and beta (13-30Hz) rhythms from electrodes covering motor related areas during a motor imagery task. The distinct spatio-temporal distributions of alpha/beta rhythma make them ideal features for brain decoding. However, cortical sources underlying motor imagery are not known clearly, and are difficult to verify with scalp-based EEG, which cannot provide cortical information and has a limited spatial resolution. In this study, we combine fMRI and EEG to investigate the spatio-temporal distribution and cortical sources underlying event related (de)synchronization (ERD/S) in alpha and beta rhythms (Pfurtschellet et.al, 1999). Here, we present an analysis from five healthy subjects who performed motor imagery by sequential finger tapping using left or right hand. Alpha and beta ERD/S are evaluated from spectrally decomposed and source reconstructed dipole signals using Variational Bayesian Multimodal EncephaloGraphy (VBMEG) hierarchical Bayesian estimation (Sato et.al, 2004). This method incorporates fMRI activity information as a hierarchical prior to localize EEG sensor signals in the subjects' MNI brain space. As the inference requires simultaneous testing of thousands of signals, the statistical significance is optimized against false positives by using hierarchical FDR and optimal discovery procedures (Singh et.al, 2010, 2011). Our analysis reveals a readiness (bereitoschaft) potential with contralaterally dominant mu and beta band de-synchronization, beginning about 0.5s before the imagination onset cue in the expected brain regions, motor and supplementary motor areas. Our results confirm that some of the neural substrates of motor imagery overlap with those of motor execution. Combined EEG/fMRI analysis with VBMEG allowed us to visualize our inference in high-resolution spectral, temporal, and spatial maps. An important advantage of this method is that the same fMRI prior can be used for all subsequent applications of EEG-BMI. We hope that these results revealing motor imagery readiness potential will help in constructing more efficient BMI decoders.

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D09 Identifying and classifying experimental procedures in neuroscience papers – a novel approach to search and discovery

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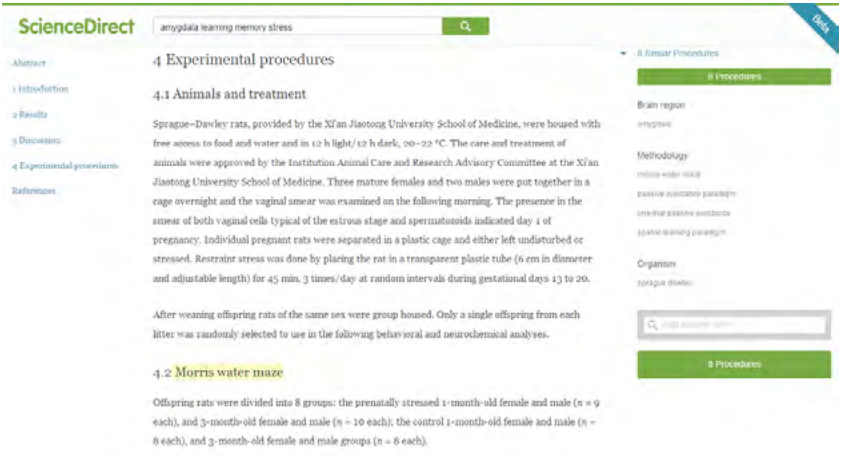
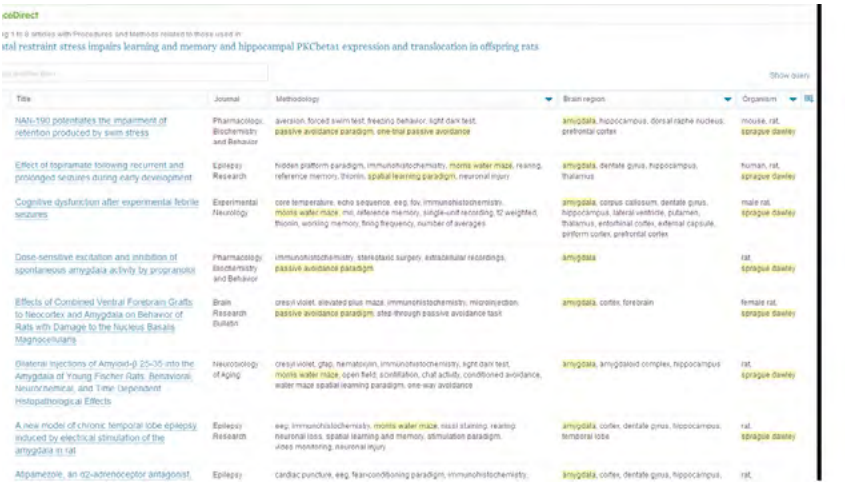
A primary activity of most bench researchers working in neurosciences is setting up and executing detailed experiments in order to understand and measure how the brain contributes to a variety of psychological, behavioral and biological processes. Typically such experiments involve a set of definable factors: a certain strain of mouse, a certain region of the brain being studied, a certain pharmacological treatment, a certain receptor. Consequently, a widespread and important information seeking task of such researchers is finding papers that describe similar experiments to the one the researcher is conducting. However, due to the overwhelming preference of researchers for searching in PubMed (which only contains abstracts), the propensity of researchers to favor few high level keywords related to the topic of study, and the tendency of abstracts to summarize the results of their experiments as opposed to the methods applied, finding papers with certain experimental procedures is incredibly time consuming and inefficient. It is a process in which success literally requires "getting lucky."

To solve this problem we have developed a novel search and discovery tool that categorizes hundreds of thousands of neuroscience papers based on the factors that are most important and unique to the experiments described in the paper; locates papers that describe similar methods based on those factors; and presents the results in a tabular format to facilitate comparison and refinement. Based on insights from studies of researcher information seeking and reading behavior, we present this tool in the context of the methods section of individual papers – the point at which researchers actually evaluate whether the paper they are reading is appropriate for their needs, and are therefore most likely to be interested in finding additional papers that describe similar experiments. The development of this tool has involved a range of information retrieval techniques including development of new neuroscience methodology ontologies, named entity extraction and natural language processing on a variety of biomedical and neuroscience concepts, and development of new methods for scoring relevance of concepts to individual papers and across the corpus. In addition we followed an iterative, agile development process while developing this tool including extensive research on information seeking behavior among neuroscientists, live testing of the tool on Elsevier's full text platform ScienceDirect and continuous improvements to precision, recall and relevance. Development is ongoing, and we will be able to report the results in August.


ScienceDirect
amygdala learning memory stress
Abstract
1 Introduction
2 Results
3 Discussion
4 Experimental procedures
References
4 Experimental procedures
4.1 Animals and treatment
Sprague–Dawley rats, provided by the Xi'an Jiaotong University School of Medicine, were housed with free access to food and water and in 12 h light/12 h dark, 20–22 °C. The care and treatment of animals were approved by the Institution Animal Care and Research Advisory Committee at the Xi'an Jiaotong University School of Medicine. Three mature females and two males were put together in a cage overnight and the vaginal smear was examined on the following morning. The presence in the smear of both vaginal cells typical of the estrous stage and spermatozoids indicated day 1 of pregnancy. Individual pregnant rats were separated in a plastic cage and either left undisturbed or stressed. Restraint stress was done by placing the rat in a transparent plastic tube (6 cm in diameter and adjustable length) for 45 min, 3 times/day at random intervals during gestational days 13 to 20.
After weaning offspring rats of the same sex were group housed. Only a single offspring from each litter was randomly selected to use in the following behavioral and neurochemical analyses.
4.2 Morris water maze
Offspring rats were divided into 8 groups: the prenatally stressed 1-month-old female and male (n = 9 each), and 3-month-old female and male (n = 10 each); the control 1-month-old female and male (n = 8 each), and 3-month-old female and male groups (n = 8 each).
8 Similar Procedures
8 Procedures
Brain region
Methodology
Organism
8 Procedures


ctal restraint stress impairs learning and memory and hippocampal PKCbeta1 expression and translocation in offspring rats
Title
Journal
Methodology
Brain region
Organism

D10 e-NeoTutor: A Novel online intelligent tutoring system for teaching neuroscience curriculums and playing BCI neurogames in the cloud

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Effective clinical research work in the field of neuroscience requires considerable depth in multiple research domains. Researchers have to be cognizant of the latest advances in the fields of mathematics, computer science, neuroscience, neuroinformatics, neuroanantomy, statistics, and the new field of neurogames designed to address different pathologies with novel commercially available brain computer interfaces. Projects like the Neuroscience Information Framework (NIF), the International Neuroinformatics Coordinating Facility (INCF), and the Neuron Registry provide descriptions and additional opportunities to connect disparate data sources for students and researchers. Because of the plethora of available data, models, information, and tool sets, it would be helpful to provide an organizing context to help accelerate the learning process for both students and academic researchers new to the domain. eNeoTutor at www.neuronalarchitects.com/eNeoTutor/is designed to enable graduate students, recent PhDs, scientists, and experts in many diverse fields an opportunity to create, accelerate and translate their expertise. This online intelligent tutor enables users to access the latest information from a wide variety of databases, tool sets, track assignments, lecture course objectives and play different video games associated with commercially available EEG sensing devices such as Neurosky and Emotiv.

Four separate hierarchical sliding panels offer the students the ability to build neuroscientific software in popular languages such as C, .NET. Java, along with statistical languages such as R and mathematical languages like MATLAB; track lecture material, take assessments and notes, track assignments and play HTM5/Javascript and XNA based games; assess their performance with an intelligent dashboard that monitors academic performance and schedules; and the ability to measure sustained and switching multiple brain states associated with gamma and theta wave activity. Using the principle of having everything on one page with a heavy dose of modularity of third party user controls coupled to a hybrid statistical engine called Neural Maestro, students can organize an entire neuroscience curriculum, read and create papers and develop e-book content along with several neuroinformatics knowledge databases. eNeoTutor includes four distinct database models that generate the entity relationships for object oriented modeling, examining and building pathways associated with several neuropathologies: Autism, ADHD, Schizophrenia, Epilepsy and other mental disorders. In addition to the main tutor application, there are three additional navigators for both simulation and predictive analytics: (A) Brain Navigator, (B) EEG Navigator, and a (C) Neural Tissue Simulator. Each designed to process student data sets, aid in project development, provide article and grant proposal generation. Currently, the tutor is being tested and will be available online at the end of April 2013.

D11 DroLIGHT: Real time embedded system towards endogenous clock synchronization of drosophila

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It's been more than 100 years since the Drosophila melanogaster species is well used in the neurobiological studies (especially after mid 1960s), the past research had well contributed in the key findings towards nervous system development and function (Bellen et al., 2010). We are interested in research on photoreception, behavioral biology and circadian clocks (Benzer, 1967; Konopka and Benzer, 1970; Roenneberg and Foster, 1997; Helfrich-Förster et al., 2001) of Drosophila. Here, we briefly present a new solution, might be helpful in synchronizing the endogenous clock of Drosophila to natural-like light-dark cycles.
Meeting the technological research objectives, we introduce a new computational software solution towards neurobiology and photobiology i.e. DroLIGHT (Ahmed et al., 2013); a user friendly, domain specific, intelligent, distributed, real time embedded and data management system. It is capable of controlling and automating the hardware that produces different colors of lights via Light Emitting Diodes (LEDs). The hardware used is a non-commercial, in house and custom engineered device, integrating seven combinations of different colors of LEDs with three brightness ranges.

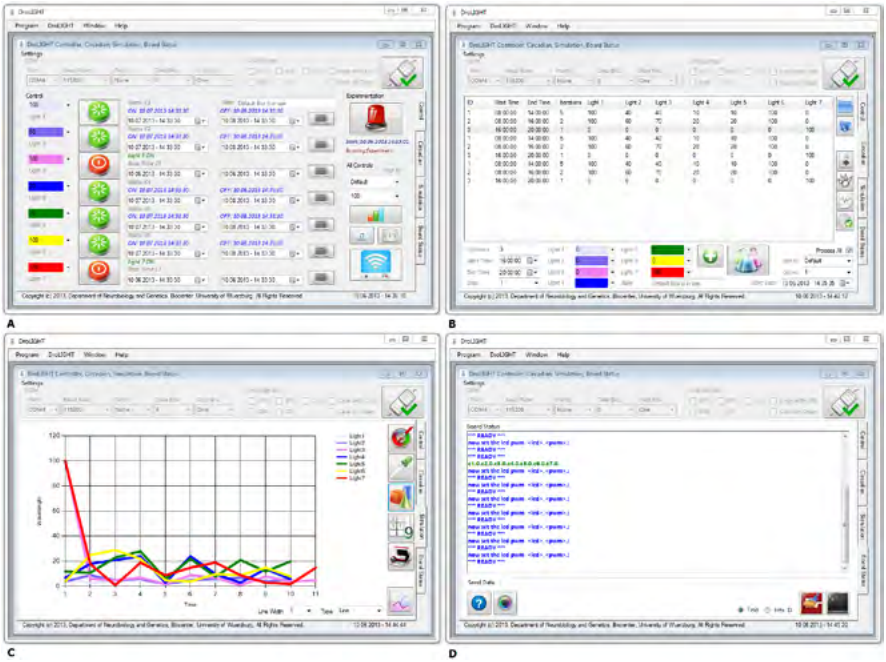
DroLIGHT is a desktop Multiple Document Interface (MDI) application (Fig. 1), capable of doing several tasks: manually controlling multiple hardware devices with variable preliminary specifications, making combinations of different colors with similar and/or different wavelengths, scheduling light operations, generating circadian rhythm, producing different kinds of simulations and allowing user to directly instruct the hardware in string instructions. Moreover, the major developmental benefits of DroLIGHT are: it requires lower hardware cost than other high end platforms, with much smaller memory foot print, faster execution time, based on preprocessed managed object oriented source code, with no heap effect, secure access to the deployed and connected hardware.

DroLIGHT is implemented following spiral software development life cycle, integrating formal unified modelling language to scheme from different perspectives and incorporating human computer interaction guidelines, principles and patterns. Looking at the future perspectives and focusing own scientific system requirements, it is programmed (managed code) in C-Sharp programming language within Microsoft Dot Net Framework 2012. Unlike most of the traditional neuroinformatics and bioinformatics applications or scripts, the deployment procedure of DroLIGHT is very simple. User has to only run the 6 steps installer which provides all kinds of immediate information and automatically configures software settings in the operating system, without requiring any additional third party compilers or interpreters. It is compatible to the Microsoft Windows platform (preferably, 7 or higher).

The most recent, available version of the DroLIGHT is in use (in academic labs) and we are focusing on the future research and development objectives by further enhancing the capabilities of DroLIGHT with the addition of more features to advance the neurobiological experimental processes and improve the hardware control.

Fig. 1: DroLIGHT Graphical User Interface (GUI).

(A) Control; the top left-right part contain settings to establish connection with the hardware, at successful connection the remaining GUI options will be enabled to control LEDs manually and automatically by scheduling the time (example: currently the hardware is connected at COM port 4 at 115200bd, two LEDs are producing lights and all rest are scheduled in an experiment). (B) Circadian; provides interface to create, edit, load and run circadian experiments (example data set is loaded and in editing mode). (C) Simulation; produces visualizations in different styles (example line chart is shown). (D) Board Status; gives the board's operational status as well as the direct access to test and control the hardware with string and hexadecimal instructions.



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D12 Machine-readable representations of hippocampal neuron properties to facilitate investigative analytics

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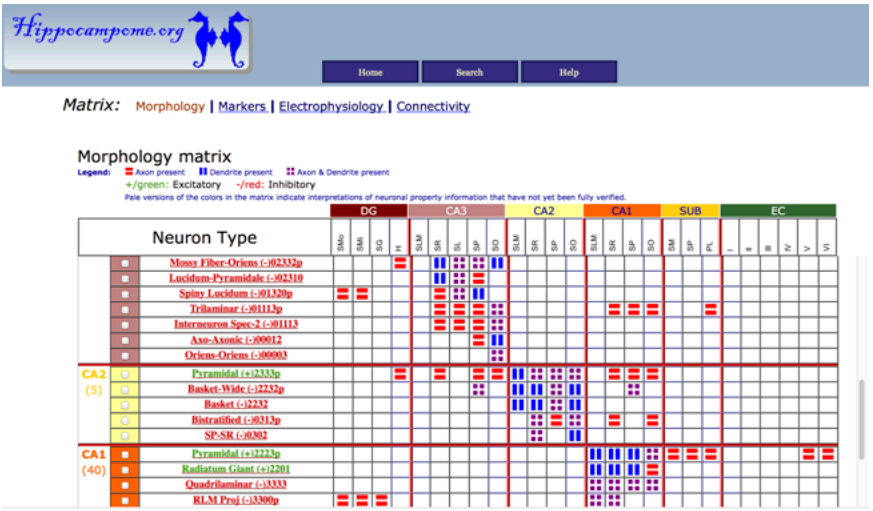
Extensive effort has been expended toward mining books and peer-reviewed articles to establish dense coverage of neuronal types within the hippocampal formation. Experimental evidence includes morphological, electrophysiological, and molecular-marker expression, with morphology providing the primary basis of neuron-type definitions. The motivation for representing literature-mined data in machine-readable form is to facilitate investigative analytics. These may range from the computational modeling of networks gleaned from potential connectivity between neuronal types to the correlation of molecular markers with morphology derived through electronically searchable neuronal properties. Hippocampome.org (Figure 1) is an information portal that makes knowledge of these machine-readable neuron properties accessible via both human and application programming interfaces. Previously intractable analytics of this coverage of hippocampal neuronal property descriptions are now made possible with the advent of the Hippocampome.



D13 Mapping neuroimaging resources into the NIDASH Data Model for federated information retrieval

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Introduction
The astounding influx of human brain imaging data makes data annotation and sharing an essential aspect of modern neuroimaging research. However, no neuroimaging data exchange standard exists that makes consuming and publishing shared neuroimaging data simple and meaningful to researchers. In this work, we use the NIDASH Data Model (NI-DM; [1]), a neuroimaging domain specific extension to the W3C PROV Data Model [2], to create NI-DM Object Models that represent neuroimaging resources from the general context of provenance information. NI-DM is a key component of an effort to build a larger Semantic Web and Linked Data framework for the generation, storage and query of persistent brain imaging data (and associated metadata) in the context of existing ontologies.

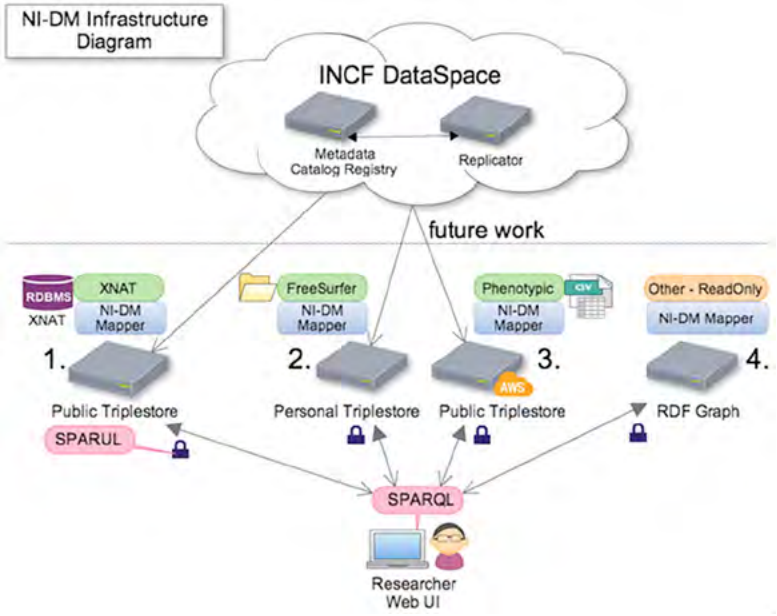
Methods
We developed NI-DM Object Models to integrate three common brain imaging data modeling patterns: 1) database schemas, 2) standard directory structures, and 3) csv/text files (Figure 1). The ADHD200 (973 participants) dataset was downloaded from the NITRC Image Repository [3], an XNAT database [4]. The T1 weighted anatomical scans for each participant were processed using the 'recon-all' tool from FreeSurfer (FS) Version 5.1 [5], and additional phenotypic data was downloaded as a CSV file from NITRC. A NI-DM Object Model was then constructed for each information type.

Results
Three deliverables resulted from this effort. First, we defined NI-DM Object Models that represent information derived from the XNAT database schema, the FS standard subject directory structure, and the contents of FS statistics files (i.e., csv/text files). These Object Models were expressed in a set of IPython Notebooks to demonstrate the encoding process [6]. Second, the ADHD200 dataset was used to instantiate a Linked Data/RDF [7, 8] representation of the NI-DM Object types, each of which was uploaded into an RDF database (Figure 1). This representation is designed to capture data, associated metadata and provenance to allow for distributed storage and federated query. Third, we developed several queries in SPARQL [9], the query language for Linked Data, to evaluate

the information retrieval capabilities of NI-DM. Two types of queries were successfully implemented, single data source and multi-data source federated queries [10]. Using these queries, we were able to successfully federate data sources and retrieve 1) participant demographics, 2) file resources and 3) anatomical statistics.

Discussion

The work presented here is being performed in the context of many other related efforts in defining a terminology for brain imaging and creating ontologies that capture relationships in these vocabularies. By leveraging RDF we broaden the range of biomedical information resources included in the Linked Data enterprise including existing services and libraries that can simplify query generation and speed-up response times. We believe this distributed model will show its usefulness before being fully adopted by the community. We have focused here on demonstrating the utility of NI-DM in the context of brain imaging, particularly in the representation of data processed by FS, but the benefits of the data model will grow as more brain imaging object models are designed for additional analysis packages (e.g., FSL, SPM) and derived datatypes.



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D16 Building the Ferretome

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Databases of structural connections of the mammalian brain, such as CoCoMac (cocomac.g-node.org) or BAMS (brancusi.usc.edu), are a valuable resource for the analysis of brain connectivity and the modeling of brain dynamics in species such as the rhesus macaque or the rat, and have also contributed to the computational modeling of the human brain. Another important model species which is widely used in electrophysiologic or developmental studies is the ferret. However, at the moment no systematic compilation of connectivity is available for this species. Thus, we have begun developing a database of anatomic connections and architectonic features of the ferret brain (the 'Ferretome', www.ferretome.org).

The main goals of this database project are: to assemble structural information on the ferret brain that is currently widely distributed in the literature or in in-house laboratory databases into single resource which is open to the scientific community; to try and build an extendable community resource that is beneficial not only to researchers in neuroinformatics and computational neuroscience, but also to neuroanatomists, by adding value to their data through algorithms for efficient data representation, analysis and visualization; to create techniques for the representation of quantitative and raw data; to expand existing database ontologies in order to accommodate further neuroarchitecture information for identifying essential relations between brain structure and connections. The Ferretome database is being developed in MySQL and has adapted essential features of the CoCoMac methodology and legacy. In particular, its data model is derived from CoCoMac. It also uses a semantic parcelation of ferret brain regions as well as a logical brain maps transformation algorithm (objective relational transformation, ORT). The database has been populated with literature reports on tract tracing observations in the ferret brain using a custom-designed web interface that allows efficient and validated simultaneous input and proofreading by multiple curators.

The database is also equipped with a web interface for generating output data that was designed with keeping in mind non-computer science specialist users. This interface will be extended to produce connectivity matrices in several formats including a graphical representation superimposed on established ferret brain maps. An important feature of the Ferretome database is the possibility to trace back entries in connectivity matrices to the original studies archived in the system. We hope that the Ferretome database will become a useful resource for neuroinformatics and neural modeling, will support studies of the ferret brain in the long-term and facilitate advances in comparative studies of mesoscopic brain connectivity.

OP02 PubAnatomy 3D: Integrating medline exploration with the Allen Mouse brain atlas

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2. Health Sciences Library, University of Michigan, Ann Arbor, USA
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Neurobiology data generated by the big science approaches, such the Allen brain atlases and the NIH Human Connectome Project, provide the opportunity for understanding how brain works at both molecular and anatomical levels with unprecedented resolution and completeness. For example, researchers can now use the Brain Explorer and the NeuroBlast tools developed by the Allen Institute for Brain Science to explore genes and their spatial expression pattern across the whole brain for learning the potential biological implications of genes identified in their experiments as well as designing follow-up experiments, such as knockout/knockin mouse for modeling human diseases. However, since it is impossible for individual scientists to grasp all the known functional roles of genes, anatomical structures and the functional relationships among them, researchers frequently need to perform literature searches to guide such big brain data set explorations. Similarly, literature exploration can also benefit significantly from the relationships among genes and anatomical structures presented in such data sets. The need to use two separate data exploration tools such as the Brain Explorer and PubMed leads to technical hurdles as well as gaps in the thinking process that can significantly constrain the hypothesis development process.

PubAnatomy is 3D is designed to provide a seamless exploration environment across the Allen Mouse Atlas data and the Medline literature for iterative data- and literature guided hypothesis development. We mapped genes and anatomical structures in the Allen Mouse Atlas data set to individual Medline records and developed a flexible web-based search interface for iterative Medline and mouse atlas data exploration. A typical use case is a researcher starting with Medline search for their interested topic, such as diseases and brain structures (Fig 1, upper part), to obtain a list of Medline records, which is annotated with different concept categories such as genes as well as summary statistics such as number of Medline records associated with each gene in the search results (Fig 1, lower part). Researchers can use the summary statistics, various filtering criteria as well as the content of relevant Medline records to select genes and anatomical structures they want to explore through simple drag-and-drop for 3D brain exploration (Fig2). Besides displaying the voxel level data for selected brain structures, users can also select multiple arbitrary 2D intersections in the coronal and sagittal directions to view the raw in situ images

together with brain structure annotations for each 2D intersection (Fig 3). Two or more genes can be displayed side-by-side for detailed raw in situ data inspection (Fig 4). Users can use new structures or additional genes identified in the exploration process to filter Medline research results or start new search/modify existing search through simple drag-and-drop, greatly facilitating the iterative literature and data exploration during hypothesis development.

Pubanatomy3D is available at http://brainarray.mbni.med.umich.edu/PubAnatomy3D/. We plan to define and publish the Application Programming Interface for Pubanatomy 3D to enable third party developers to access data and functions PubAnatomy as well as passing their own data such as gene or SNP lists to PubAnatomy 3D. We will also integrate more data sets, such as connectome, pathway and protein interaction, Gene Ontology, etc. into PubAnatomy to further enhance its usefulness for hypothesis development in neurobiology.

OP03 Towards reusable experiments: making metadata while you measure

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Using research data acquired in other labs requires that the metadata, that define the conditions and manipulations of each experiment are well documented. Usually, this metadata is not stored with the experimental data itself, and is often written within the experimenter's lab notebook and therefore is not easily searched or compiled. When scientists upload data files to a central repository (like crcns.org), metadata are often not included. For domain-specific databases (such as neuromorpho.org), metadata are added by expert curators in an expensive and painstaking process that does not scale up to the large amounts of scientific data produced every day. An effective way "scale-up" is to convince researchers to create digital metadata in real-time during their experiment. Here, we have developed an electronic lab notebook application (running on tablet computers and smartphones) to annotate in vitro electrophysiological recordings with essential methodological details.

We tailored our system to the workflows used in the collection of electrophysiology data by the Urban, Gittis, and Barth Labs at Carnegie Mellon University. These labs study a variety of brain areas, addressing hypotheses from neural coding and synaptic plasticity to the mechanisms underlying neurological disorders; however, they share a core set of methodologies associated with recording neural activity from brain slices. Using the developed app, individual experimenters enter details (like the animal strain used or the neuron type recorded) through a series of drop-down menus (see Figure 1 for a screenshot). This structured data entry approach allows us to enforce a common metadata format and the usage of INCF standards and terminologies. Additionally, we designed the app's interface to ensure simple, efficient data entry by the user.

The collected metadata is uploaded directly to a relational database and combined with the acquired electrophysiology data files into a semantically-enriched, reusable format that allows for creative data exploration. This data can be used by the person collecting the data or others in the lab for testing hypotheses and analyzing collections of data from his or her own lab, in a web-based 'Data-Dashboard'. Rather than being limited to datasets collected within a single lab, researchers can now find (using metadata as a search filter) and analyze relevant data collected in other labs. Through improving data organization, archiving, and sharing practices, this system will show clear benefits to the scientists performing and analyzing research data and, we hope, will empower demonstrably better neuroscience research.


Shreejoy Tripathy
CMU Urban Labs
Experiment ID: A7766603-26E2-4A60-9886-F7D10D472F02 P1 S1 C1 E2 ???
07 April 2013
Goals, Motivation & Hypotheses
Animal Preparation
Slice Preparation
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OP04 Beyond the connectome hairball: Rational visualizations and analysis of the C. elegans connectome as a network graph using hive plots

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The C. elegans connectome (White et al., 1986) is currently the most detailed connectome data set at the neuronal circuit level that is publicly available. Represented as a network graph, it consists of edges that distinguish between gap junctions and chemical synapses, weighted by synapse count, with nodes that represent neurons whose identities are unambiguous and well known.

Within the OpenWorm project (Palyanov et al., 2012), we have previously transformed this data set into NeuroML as the foundation for a computational simulation framework for C. elegans (Busbice et al., 2012). In the course of analyzing this data set, we have applied the hive plot methodology for visualizing complex networks (Krzywinski et al., 2012). Hive plots provide a rational and transparent visualization method for making complex networks by laying out nodes on radially oriented linear axes with a coordinate system based on nodes' structural properties. While previous articles have explored the structure of the C. elegans connectome graph quantitatively (Chatterjee & Sinha, 2008; Sohn et al., 2011), to the best of our knowledge this is the first application of the hive plot visualization technique to any connectome data set.

We have created multiple hive plots based on the C. elegans complex graph to depict various aspects of its underlying structure via the JHive tool (http://hiveplot.net). Simple hive plots of the sensory, inter-, and motor neurons on different axes reveals strikingly dense connections for the top four interneurons compared to the rest. Hive plots show that the connections mediated by gap junctions that run between sensory neurons and interneurons are less dense than the connections between interneurons and motor neurons. This asymmetry is not present in the network of chemical synapses. Additionally, hive plots reveal that edges with high degree (10 synapses or greater) are present between motor neurons but not between sensory neurons (Fig 1). These findings have been verified with independent analysis of the connectome with the NetworkX complex network graph library (http://networkx.github.io/documentation/latest/overview.html).

We have found exploration of the C. elegans connectome using hive plots to lead to the discovery of interesting qualitative structure that was previously not obvious, enabling this structure to be further pursued quantitatively using complex network mathematics.

Figure 1. Hive plot of C. elegans connectome. Nodes on axis marked a3 are sensory neurons, nodes on a1 are interneurons and nodes on a2 are motor neurons. Only edges with connection weight greater than 10 are rendered (thin orange), and include connection

weights greater than 15 (medium-thick cyan) and greater than 20 (thick green). Axes are duplicated to display edges between nodes on the same axis. This example shows the absence of connections between sensory neurons (between the a3 axes) and the presence of many high degree connections between motor neurons (between the a2 axes)."

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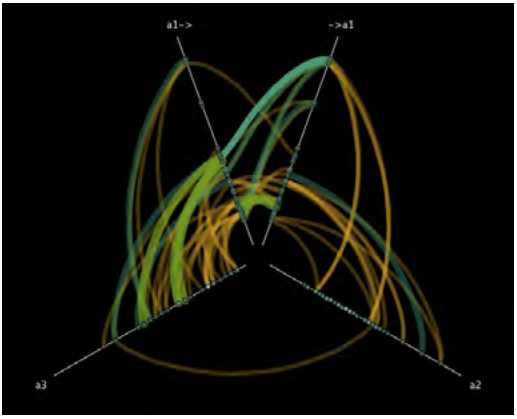

P46 Properties of the intrinsic and extrinsic uni- and bilateral connectome of the spinal cord of the rat

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The spinal cord (SC) of the rat consists of 34 segments from the cervical to the coccygeal level which contain 10 principal layers (Rexed I-X) on the left and the right side surrounded by white matter. Here, efferents to and afferents from peripheral organs as well as intrinsic connections (C) of SC have been investigated in about 800 peer-reviewed tract tracing publications. The connectivity data of these publications have been transfered into the rat connectome dataset in neuroVIISAS (Schmitt and Eipert 2012, Schmitt and et al. 2012). SC regions were organized in a hierarchy to allow multiresolution analysis (Fig. 1).
In the intrinsic bilateral connectome of the SC (891 regions) 26222 C were documented at the level of layers (ipsi: 11297, contra: 805). 5213 C are reciprocal which appears to be significant because in Erdös-Rényi (ER) simulations an average of 437.1 reciprocal connections was found. The small-worldness coefficient (SWC) is 3.598 (ER: 1). Furthermore, the connections of the network have a scale-free distribution. Local connectivity analysis revealed that cervical, thoracic and lumbal layers II-VIII possess most intrinsic connections. The layers III-IX of thoracal segment 3 have the largest eigenvector centrality of 0.709 as well as the largest Katz-index. The extrinsic contralateral (146 regions, C=7405) and ipsilateral connectome (171 regions, C=4178) have been analyzed at the level of segments. In contrast to the intrinsic connectome the SWS increases to 5.207 in the ipsilateral and decrese to 2.19 in the contralateral extrinsic SC connectome. In conclusion, we build the first bilateral connectome of the SC of a mamalian for which the most detailed tract tracing investigations exist and integrated it into the complete rat nervous system connectome.
Figure 1: The regions at the level of segments of the left and right side of the SC are arranged symmetrically. Connections are directed and colors of connections indicate the density of connections, respectively, the weights. CS: cervical, T: thoracic, L: lumbal, Sa: sacral.

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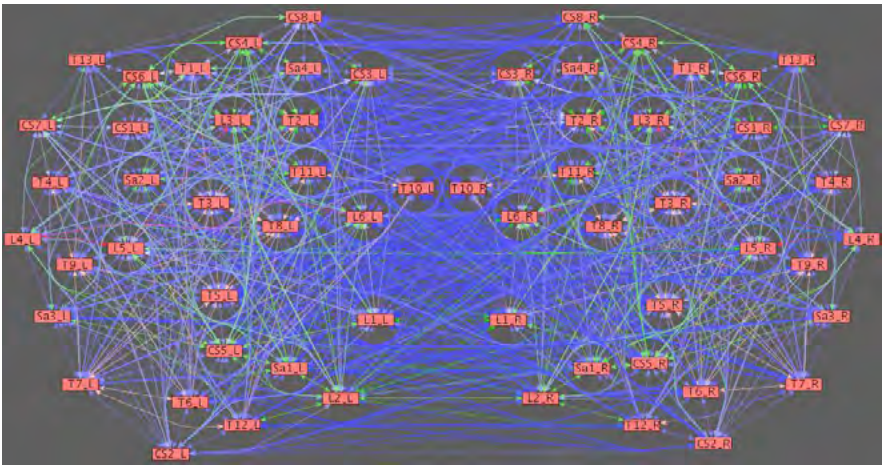
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P47 Analysing behavioral data from IntelliCage system in Python

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IntelliCage is a computerized cage for automated recording of mice behavior [1]. A group of up to 16 mice can be monitored simultaneously, each animal carries a subcutaneously implanted radio transponder for identification. A computer records precise data (time, duration, etc.) about visits of animals to the corners (conditioning units), in which reinforcements (such as sweetened water) or punishments (air puffs) can be administered, possibly with a different protocol for each animal. For each visit also the nosepokes to the sides of the corner and the licks from bottles with liquids are recorded. The system gives a unique opportunity for long-term studies of behavior of animals living in social groups. The size and complexity of the data obtained from IntelliCages call for development of suitable data analysis methods and software. The software bundled with the cages, called Analyzer, allows for basic data processing; however, more advanced analysis has to be performed elsewhere. Typically this has been done using spreadsheets, which is both time-consuming and error-prone. To address the growing need of data analysis we have developed a Python toolbox for processing and analysis of data from IntelliCages. The toolbox is organized in a modular way, with separate modules responsible for 1) loading the data, 2) verification of data integrity, 3) data analysis, plotting, and exporting results. The data loading module allows for loading and merging both the raw IntelliCage data and the data preprocessed with Analyzer. The loaded data are stored in a database and presented via a Python interface, allowing for easy selection of relevant quantities for chosen groups of mice, with optional advanced filtering. Distinct phases of experiment (such as for example adaptaion, learning and extinction phases, or perhaps consecutive days) may be defined in a text file to facilitate the analysis. Next both the behavioral data and the hardware logs can be tested to ensure that the number of errors is below set thresholds. Due to modular structure it is easy to adapt or extend the various tests, so that only the relevant aspects are taken into account. Finally, the data are passed into data analysis modules. Currently implemented modules allow for analysis of 1) place preference learning (the relative number of visits, nospokes and licks in different corners), 2) social interaction between animals, defined as the percentage of visits to a corner which fall in a defined short time window after a visit of different mouse to the same corner. Together, the three steps form a complete workflow for analysis of IntelliCage data."

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P48 Comparison of parallelized gray-scale zonal operations on CPU and GPU

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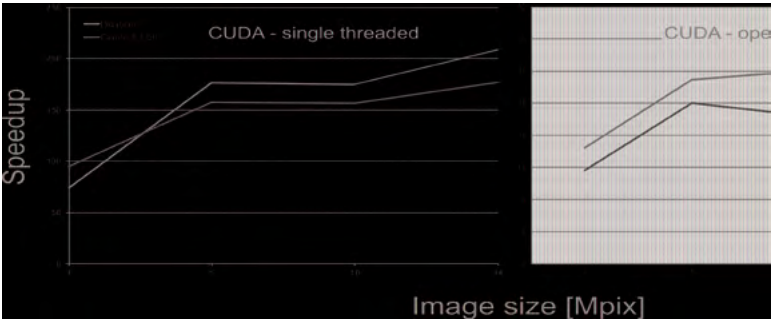
Parallelization of image processing algorithms can be achieved either on the Central Processing Unit (CPU) or on the Graphic Processing Unit (GPU) sides. The availability of cheap computing power together with the increase of image resolution and size makes conceiving parallel algorithms for neuroinformatic applications very attractive. Since the advent of the Compute Unified Device Architecture (CUDA) of NVidia, GPU computing grows in popularity. On the other hand, limitations of the CUDA architecture and the capabilities of hardware need to be considered upfront in software design for achieving maximal performance. The CUDA-enabled GPUs have four types of memory, notably global memory, constant memory, texture memory and shared memory, which have distinct physical properties. The advantages of GPU massively-parallel architecture are penalized by the transfer overheads between the GPU memory and the main RAM memory, which make GPU implementation of certain classes of algorithms not useful. Zonal image processing operators, such as image convolutions, erosions and dilations, have ubiquitous applications in image processing. Such operators have complexity of O(N^2) for non-separable kernels and do not depend on the output of other processed pixels, In such way these operations do not require synchronization between threads and provide ample opportunities for speedup if executed in parallel. This makes zonal operations suitable to exploit as the best case scenario of algorithmic parallelization. In this work we compare CPU and CUDA based implementations for the basic morphological operations and spatial convolution. The CPU-based parallelization was exploited using the OpenMP library in C. For completeness, a parallel Java implementation was also developed. The results indicate that the most advantageous GPU implementation is achieved by using texture memory. Our results show an advantage of GPU parallelization over sequential implementation on the CPU for both convolutions and mathematical morphology operations. The CPU tests were run on a 4 core Intel Core i7-920 CPU with 2.67 GHz clock and 4GM RAM. Using a 3x3 kernel, the speedup of CUDA on a high end NVidia GeForce GTX 470 platform was ranging from 177 to 208 times for convolution and dilation against a sequential implementation, respectively (Fig. 1). On the other hand, the CUDA speedup ranged from 18 to 36 times for the same image sizes against an optimized CPU OpenMP implementation, respectively. Finally, the CUDA-enabled morphology operations functionality was incorporated conveniently into an ImageJ plugin. It was demonstrated that the overhead of Java waz negligible, which presents a viable option for integration of GPU code into Java programs. The wide spread use ImageJ, together with the availability of GPUs makes it attractive to further exploit GPU-parallelization of image processing algorithms on this platform.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Speedup
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P49 ASNeuPI – An algorithm for skeleton-based neuronal polarity identification

Yi-Hsuan Lee[1], Yen-Nan Lin[1] and Chung-Chuan Lo[1]
1. Institute of system neuroscience, National Tsing Hua University, Hsinchu, Taiwan

The direction of signal transmission is crucial for functions of neural networks. Therefore, the direction of signal flow, which is regulated by neuronal polarity, should be included when we analyze neural networks. However, the biochemical method used to identify neuronal polarity is time-consuming and may not be an appropriate strategy for analyzing large-scale neural networks.

To address this problem, we proposed an algorithm for skeleton-based neuronal polarity identification (ASNeuPI). In ASNeuPI, we first morphologically divide a neuron into several substructures and for each substructure we extract seventeen morphological features. Next, K-nearest classifier (KNNC) is applied for identifying the most influential feature combination that correlates with the polarity of the training dataset. Finally, we perform linear discriminant analysis (LDA) to generate an optimal axis that provides highest accuracy for polarity identification. The optimal axis is then used to identify polarity of neurons in the testing set.

We tested this method on neurons innervating protocerebral bridge (PCB) or medulla (MED) in Drosophila. The neuron skeletons were extracted from data obtained from Brain Research Center, National Tsing Hua University, Taiwan. On average, the polarity of more than 85% terminal points in a neuron could be correctly identified. We tested the maximum performance of ASNeuPI on a clean dataset constructed by manually removing artificial branches resulting from noise in raw images. We found that the average accuracy reaches 95% in the best case. Our results show that, as a computer-based semi-automatic procedure, ASNeuPI provides quick polarity identification and is particularly suitable for analyzing large-scale data.

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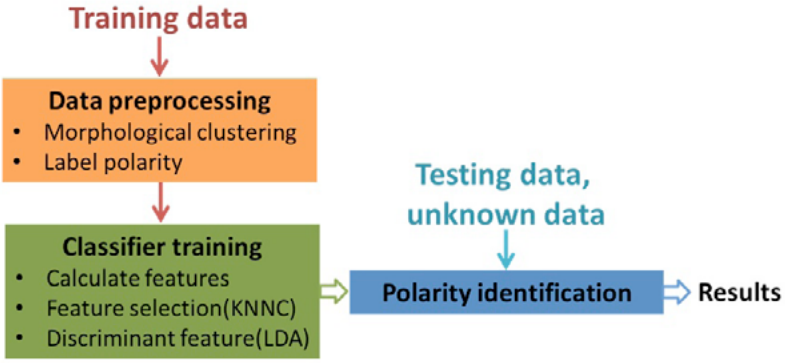

Figure1. ASNeuPI workflow.
Training data are first morphologically clustered into several substructures and the polarity is labeled manually. After the classifier training, an optimal axis is generated and used as discriminant feature for identifying polarity. Once the discriminant feature is decided, polarity of the testing data can be identified by the classifier.

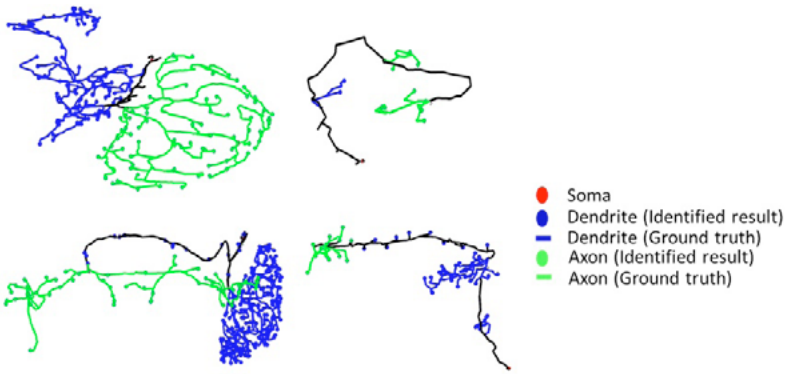

Figure2. Neuronal polarity identification by ASNeuPI.
The colors of backbone indicate real polarity (as identified in experiments), while the colors of dots represent polarity identified by ASNeuPI. The accuracy of ASNeuPI can reach 85-95% dependent on the quality of the data.

P50 Network architecture and information propagation in protocerebral bridge of Drosophila central complex

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The central complex (CX), which consists of four neuropils located in the central brain of insects, is characterized by a complex but highly organized and repetitive circuit architecture. Furthermore, CX has been suggested to participate in a range of functions including spatial working memory, sensory-motor transformation and motor control. However, how these functions are implemented and realized by the complex neural circuits in CX remains unclear. As a first step toward understanding of the functions of the CX neural circuits, we mathematically analyzed connectivity of 662 Drosophila neurons which innervate one of the CX neuropils, the protocerebral bridge. Specifically, each neuron is represented as a high-dimensional innervation vector with each dimension corresponding to a subregion of CX. We found that the seemly complex innervation patterns of the neurons are highly structured and the whole network can be generated or even predicted by applying a generator matrix on a small set of initial neurons. The result implies that the development of the complex CX neural network can be highly efficient because it can be driven by a small set of genes that encode the simple rules, or the generator matrices.

We further investigated a small set of observed neurons with innervation patterns that cannot be generated from the generator matrices. To determine whether these "special" neurons play specific roles in information transduction, we compared the network constructed by neurons from observed data and the network generated from the mathematical model (the generator matrices). Specifically, we studied how signals propagate from a given input neuron to a given output neuron through multiple intermediate neurons. We found that the observed network is characterized by strong recurrence that is several folds stronger than that of the model network for specific input-output neuron pairs. We further identified that only two specific neurons in EIP class are responsible for the major changes in the network recurrence which greatly increases the complexity of network computation. Further analysis indicated that the unique innervation pattern of these neurons plays a key role in maximizing the network recurrence for the specific input-output neuron pairs. The result suggests that a small number of specially designed neurons can greatly improve the complexity of the neural computation. Therefore, our work provides insights into the complex organization of CX neural circuits and may generate specific predictions that can be tested experimentally.

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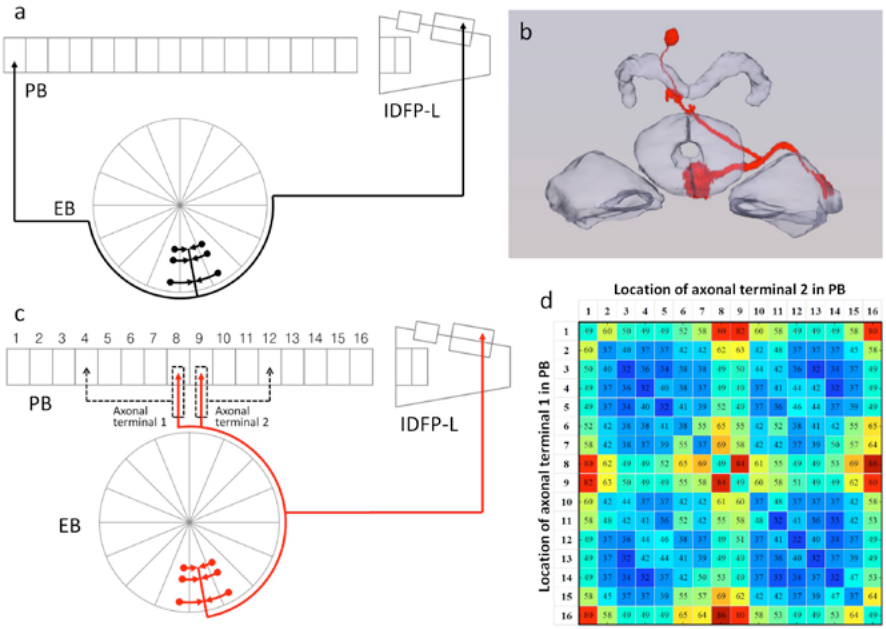

Figure 1 A specific EIP neuron that maximizes the recurrence of the network.

(a) The innervation pattern (arrowheads: axons, filled circles: dendrites) of the type 8 neuron of EIP class in the model network generated by the generator matrices in the model network. EIP neuron class specifies neurons that innervate ellipsoid body (EB), inferior dorsofrontal protocerebrum (IDFP) and protocerebral bridge (PB). **(b)** In the observed network derived from data, the neuron in (a) does not exist. Instead, a specific neuron with the same EB innervation pattern was observed as shown in 3D reconstruction. **(c)** The innervation pattern of the observed neuron shown in (b). To test how the specific innervation pattern affects the network structure, we randomized the locations of the two axonal terminals in PB and calculated the degree of recurrence of the resulting networks. **(d)** We found that most of the re-arrangements of the terminal locations result in very low degrees of recurrence while the recurrence is maximized when the two terminals were placed at the locations 8 and 9, exactly corresponding to the observed neurons. A few other positions, 8 & 16 for example, also lead to large degrees of recurrence but those locations are developmental inefficient and may not occur in the actual neural circuits.

P51 Helmholtz: a customizable framework for neurophysiology data management

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The benefits of capturing the output of neurophysiology laboratories in structured databases are potentially very large, both in improved data management within a laboratory and in easier and more effective sharing of data, whether with close collaborators or in public databases. However, at present the task of systematically annotating every experiment with sufficient metadata to enable the data to be correctly analysed and interpreted is typically an arduous one. Then, once the effort to create a laboratory database has been made, considerable further effort is needed, due to lack of software tool support, to make use of the database in the day-to-day life of the laboratory, and so realise the potential benefits.

To improve this poor cost-benefit ratio requires that both entering data/metadata into a database system and making use of it later in analyses, visualization etc. be made much easier. This in turn will require software tools that can either integrate with or replace the existing software for data acquisition and analysis used in the laboratory, and that provide a smooth and intuitive workflow to minimize the time required for the potentially tedious process of data annotation. Meeting these requirements in the highly heterogeneous fields of neurophysiology and systems neuroscience can be very difficult, since there is very little standardization of data formats, equipment, software platforms or experimental protocols between different labs.

In this presentation we review some general principles that we think should be followed in trying to address these difficulties, and present a specific solution we have developed: Helmholtz, an open-source framework for developing databases that are customized to the needs of an individual neurophysiology lab.

The Helmholtz framework is built on top of the Django web framework (http://www.djangoproject.com/; following the tradition in the web development community of naming Django-based projects after famous jazz musicians, we named our project after a famous physiologist.) Using Django as a basis brings several advantages: (i) it can be used both for a local database, using the simple, built-in webserver and for a centralized repository; (ii) an abstraction layer on top of the underlying relational database allows any of the widely-used database systems to be used interchangeably (e.g. MySQL, PostgreSQL, Oracle, or the built-in, configuration-free SQLite); (iii) the same abstraction layer makes it easier for non-programmers to extend and customize the database: no knowledge of SQL is required; (4) it is easy to build multiple interfaces to the same database, for example interfaces to acquisition or analysis software, using web technologies.

Helmholtz provides core components which handle elements that are common to all or many domains of neurophysiology. For example, information about 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. Another component supports databasing of analysis results, linked to the original data on which they are based, and with descriptions of the analysis methods used. Extension components to support the specific needs of individual labs are straightforward to write, requiring minimal programming experience.

Helmholtz supports multiple interaction methods: via a web interface (with support for tablet computers); batch data import from spreadsheets; programmatic interaction via a web-services API. The API generates and accepts multiple data formats: XML, JSON, YAML and odML; RDF support is planned in the near future.

P52 Large-scale shape analysis of human brain MRI data

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2. ICTEAM, Catholique de Louvain, Belgium, Louvain, Belgium
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Human brain shape databases are useful for morphometric studies of healthy and patient populations. They provide scientists with shape measures for comparison with their own MRI data, as well as to train, test, and provide prior information for algorithms that detect, segment, measure, and classify brain structures. Human MRI shape databases have been restricted in the past to measures of labeled region volumes and cortical region thicknesses. These measures are useful for studies of neurogenesis or atrophy in morphological development, degeneration, and disease progression. However, more subtle shape measures may help us to relate structures to behaviors or phenotypes beyond gender, handedness, and relatedness, and have great potential for use in biomarker discovery for clinical diagnosis. As a part of the Mindboggle project, we have created software to extract brain features (labeled regions, sulci, and fundi), and compute shape measures on these features. Currently our shape measures include: mean, Gaussian, maximum, minimum, and principal directions of curvature, travel depth [1], surface area, volume, Laplace-Beltrami spectra [2], and FreeSurfer software-derived measures of depth and thickness [3]. The recent release of our Mindboggle-101 dataset (http://mindboggle.info/data), the largest and most complete set of free, publicly accessible, manually labeled human brain images [4], gives us an unprecedented opportunity to combine automated feature extraction and shape analysis to a large, manually labeled brain MRI dataset. We will present our findings on these shape measures across 101 healthy brains.

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P53 Senselab databases integrate neuronal data and modeling

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P53,Senselab databases integrate neuronal data and modeling.,Yuguo Yu," Yale University,Neurobiology,New Haven,USA, Fudan University,Center for Computational Systems Biology,Shanghai,China",,0,Poster,General neuroinformatics,"Since 1993, SenseLab has developed a suite of databases using the olfactory system as a model to enable the integration of neuroscience data in molecular biology, cell morphology, electrophysiology, and computational neuroscience. Our open-ended and flexible Entity Attribute Value with Classes and Relationships (EAV/CR) meta-schema facilitate the inclusion of data from multiple spatial scales and diverse areas by making it easy to continue to modify the schema to include new topics as necessary as the databases become populated and adopted more widely.

The current databases include CellPropDB, an archive for neuronal properties such as ion channels and receptors for particular neurons; NeuronDB archives these properties with respect to their spatial distribution in neuronal compartments; ModelDB is a repository of computational neuroscience computer code; MicrocircuitDB is a collection of computer code specific to circuits within brain regions; ORDB archives over 14,000 olfactory receptors; OdorDB archives over 200 odors that interact with ORs, OdorMapDB is an archive of olfactory bulb maps generated by different methods; and BrainPharm aims to archive drug and receptor interactions.

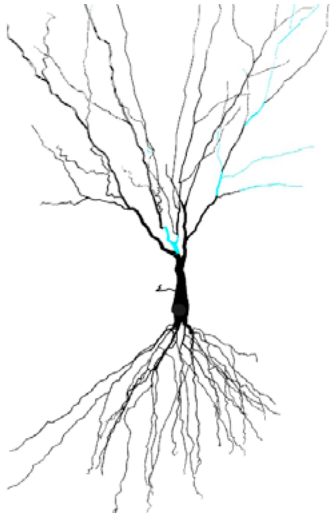
Recent developments in ModelDB include developing new search tools for making it easier for modelers to find models of interest. We recently provided a novel search tool, ModelSearch, available from the ModelDB home page, which combines free text and database pre-defined keyword searches into unique results sorted on model names. In collaboration with Channelpedia, we are developing methods to simplify searching for model components such as ion channels that are sometimes duplicated across different models. To make ModelDB models more easily interpreted, we are developing an HTML5 graphical model viewer (suppl. figure) based on NEURON's Model View tool. This view, accessible by a link from a supported model's page, displays a 3d image of the neuron. The user may select specific ion channel mechanisms or synapses to view their runtime parameters and their distribution across the cell.

We have just created a new SenseLab database NeurosciDataDB for a collaboration to allow more transparent access to microcircuits and other data generated in electrophysiologial

experiments. All data will be cross-linked with models, using a set of ""tags"". Clicking on a tag, for example ""motor cortex"", will bring up a list of both the models and the experimental data that is thus tagged.

Safiulina et al 2010

135 sections; 943 segments
- 1 real cells
  - root soma[0]
    135 sections; 943 segments
    - 14 distinct values of nseg
    - 17 inserted mechanisms
    - 7 subsets with constant parameters
      - ModelViewParmSubset[1] (135 sections)
      - ModelViewParmSubset[2] (134 sections)
      ModelViewParmSubset[3] (1 sections)
      - ModelViewParmSubset[4] (9 sections)
        depth_cacum = 0.2
      - ModelViewParmSubset[5] (6 sections)
      - ModelViewParmSubset[6] (2 sections)
      - ModelViewParmSubset[7] (2 sections)
    - 116 sections with unique parameters
    - 61 Point Processes
- 1 artificial cells of 1 base classes
0 NetCon objects
0 LinearMechanism objects
- Density Mechanisms
  - Mechanisms in use
  - Homogeneous Parameters
  - Heterogeneous Parameters
  - Global parameters for density mechanisms
  KSChan definitions for density mechanisms
- 61 point processes (60 can receive events) of 2 base classes



P54 Single-file solution for storing neuroscience data and metadata

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Formats and data models used in neuroscience are often domain-specific and typically designed to store a certain kind of data, e.g. time series or image data. Furthermore, file formats are often designed for efficiency with respect to recording software and hardware and, in the worst case, the stored data is only accessible via proprietary software. To support community-based tool development and data sharing, a common standard for data storage would be desirable. It is one of the goals of the INCF to specify a recommendation for such a common file format for electrophysiological data that is also able to store various metadata.

Here we present an approach to define a common file format based on a generic data model that can represent and describe multidimensional data. It is able to store time series, spike trains, images, image stacks and also more complex kinds of data. Further, tagging with events or annotating with arbitrary metadata, for example about stimulus conditions or hardware settings, is supported. Due to its flexible design the data model is compatible to other tools and formats and able to represent data from NEO (www.neuralensemble.org/neo) or Neuroshare (www.neuroshare.org) files. One guiding principle of the model is that it guarantees just enough information, including units, sampling rates, array names, to create a plot of the contained data. While the data model is, at this minimum definition, not domain specific, its parts can be typed to represent domain specific entities. This ensures that software working on the data model can always read the data even without knowledge about the domain it is used in. At the same time this offers high degree of flexibility. The same applies to the metadata, which is organized according to the odML model (Grewe et al. 2011). This approach restricts the format but not the content while providing the means to use standardized terminologies. Linking between data and metadata is an integral feature of the approach. In the HDF5 format, the data model is represented in a rather flat hierarchy. A file consists of the two main groups for data and metadata, respectively. Thus, data and metadata are stored in the same file while links can be established between both parts. Though it is of course possible to read these files with the standard HDF5 libraries, specific APIs provide a more convenient way to access the data on a higher abstraction level. Therefore, we started the development of a reference implementation in C++ that can be used to include the format in existing tools and environments and may serve as a guideline for implementations in other languages. For more information see www.g-node.org/pandora

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P55 Systematic spatial independent component analysis to decompose individual fMRI activity during continuous listening to music

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Decoding brain states during real-world experiences through functional magnetic resonance imaging (fMRI) depends a great deal on data analysis methods. This study addresses the decomposition of fMRI data elicited by naturalistic and continuous music using a systematic independent component analysis (ICA) approach, which is performed on individual fMRI datasets. The method mainly includes preprocessing fMRI data using a digital filter, dimension reduction through principal component analysis (PCA) and fast model order selection, ICA decomposition through software analyzing the stability of ICA, selection of the spatial maps whose temporal courses are significantly correlated with those of musical features, and visually checking the common spatial maps across majority of participants from the selected components. Among eleven participants in the experiment, we found nine participants sharing a common spatial map, with activity localized in the (primary and secondary) auditory cortices and in the somatosensory cortex, and a common temporal course significantly correlated with the musical feature 'brightness'. These findings reveal a novel function of the auditory and somatosensory cortices, namely monitoring and processing of polyphonic timbre during listening to naturalistic, continuous music.

P56 Mouse visual cortex dynamics during early postnatal development

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We explored the patterns of population activity during early postnatal development in layer 2/3 of the primary visual cortex of mice expressing Td-tomato in Dlx5/6 + interneurons. Ages P7-P26 were examined. Layer 2/3 neurons in area V1 were stained with OGB-1 calcium sensitive dye and spontaneous events were recorded over several hours under light isofluorane anesthesia. At P7-8 spontaneous activity was dominated by short synchronous events, involving the majority of cells in the field of view (250_m X 250_m). Sparsification of spontaneous activity started to become evident by P10 – P12, shortly before eye opening, as described in Golshani et al. [1,2]. Population events had a complex spatiotemporal structure, with calcium transients appearing sequentially in a restricted number of neurons (neuronal avalanches). After the start of sparsification the frequency of occurrence of avalanches of certain size and duration obeys a power law. The balance between excitation and inhibition may in part determine the properties of neuronal avalanches [3]. We therefore explored the relationship between patterns of activity seen in interneurons and pyramidal cells during the first three weeks of postnatal development. We made the following preliminary observations:

A) Mean correlation coefficients between pairs of pyramidal cells and between pairs of interneurons decrease in a similar fashion during sparsification.

B) A number (1-25) of pyramidal neurons can be identified in the vicinity of each interneuron, whose event rate negatively correlates with the spontaneous calcium events of the interneuron. We call these "pyramidal followers" of the interneuron.

C) Correlation coefficients between "pyramidal followers" of a particular interneuron are typically higher than the mean correlation coefficients computed across other pyramidal cell pairs at comparative distances from each other. Before sparsification (P7-P8) the difference is small, but then it increases gradually to become significant by P10.

D) From P10 onwards (with sparsification) the number of partners with high inter-neuronal correlation coefficient decreases for both pyramidal neurons and interneurons.

In summary, the spontaneous pattern of activity in both L2/3 pyramidal cells and interneurons changes significantly during early postnatal development (P7-P26), as decorrelation sets in. Following sparcification, interneurons remain anticorrelated with a group of pyramidal cells, forming a cortical circuit unit, whose function remains obscure at the moment. Such units may play a role in visual stimulus encoding after eye opening.

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P57 Analysis of High Frequency EEG components in response to predefined realistic visual scenes

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The correlation between EEG and human visual information is presented in this article. EEG tests were performed in order to investigate the response of the brain signals upon passing different images with different textures and colors. Tests are performed on 4 different persons and EEG signals are recorded, processed and analyzed with various signal processing techniques.

Electroencephalography recording sites are applied according to international 10-20 electrode system. High frequency components (70 to 150 Hz) in brain signals were analyzed in correlation to the texture of the shown image, and a correlation function is built.
Results obtained show important affinity between the texture profiles of certain images and the brain response. This affinity could lead in further research works to define a brain stress or anti-stress level related to the image content shown to the subject.

P58 The Ontology for Experimental Neurophysiology: a first step toward semantic annotations of neurophysiology data and metadata

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Analysis of existing ontological resources reveals a lack of terms for accurately and unambiguously annotating electrophysiological data and metadata. With the development of different resources for describing and sharing this particular type of data, the community needs controlled vocabularies to describe the different types of electrophysiology recording paradigms.

To build such vocabulary, or ontology, we created a dedicated workgroup involving relevant initiatives such as the EEGBase (http://eegdatabase.kiv.zcu.cz/home.html), the G-Node (www.g-node.org), the INCF task force on standards for sharing of electrophysiology data (http://www.incf.org/programs/datasharing/electrophysiology-task-force), NIF (www.neuinfo.org) and Neuroelectro.org (www.neurolectro.org).

As the field of electrophysiology is heterogeneous and multifaceted and the corresponding scope of the ontology considerable, the development of OEN has been separated along two main branches: a branch considering devices and methods, and a branch considering neurophysiological concepts. Here, we describe the first version of the Ontology for Experimental Neurophysiology (OEN, https://github.com/G-Node/OEN), focused on devices and methodology, and our strategy for the creation of the neurophysiological concepts.

The device branch terminology is built upon existing ontologies related to neurophysiological experiments or investigation, namely the Ontology for Biomedical Investigation (OBI, http://obi-ontology.org/) and the Neural ElectroMagnetic Ontologies, (NEMO, http://purl.bioontology.org/ontology/NEMO). Existing terms describing neurophysiological devices and methods have been imported using the MIREOT format (Courtot et al., 2011) and the web service Ontofox (http://ontofox.hegroup.org/). The granularity of the ontology has been extended using the odML terminology (http://www.g-node.org/projects/odml/terminologies) and terms from the EEGBase.

To test our ontology, we created a simple knowledge base to describe the content of the EEGBase database. We are showing here some preliminary results and the infrastructure to transform EEGBase into semantic EEGBase.

In parallel we are developing a terminology to describe neurophysiological concepts such as action potential. This work is done in collaboration with other relevant ontologies such as the Phenotypic Quality Ontology (PATO, http://obofoundry.org/wiki/index.php/PATO:Main_Page) and the Gene Ontology, (GO, http://www.geneontology.org). To gather the feedback of the community, we are using Neurolex and web-based surveys to gather and assess the diversity of definitions.

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P59 A pythonic workflow for automated large-scale parameter scans

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P59,A Pythonic Workflow for Automated Large-Scale Parameter Scans,," Norwegian University of Life Sciences,Department of Mathematical Sciences and Technology,Aas,N orway",,0,Poster,General neuroinformatics,"The systematic exploration of the properties of neuronal systems requires parameter scans along several dimensions. The resulting combinatorial explosion in the number of possible parameter combinations entails that hundreds of thousands of parameter sets need to be tested even for a handful of dimenions, with a number of randomized trials for each. While such large-scale scans will remain infeasible for brain-scale models for quite some time, due to overall runtime limitations, they are becoming routine for smaller systems (Nordlie et al., 2010, Heiberg et al., 2013), requiring suitable workflows and software tools for managing automated large-scale parameter scans.

Recent software developments, such as Sumatra (Davison, 2012) and the NeuroTools Parameters package (Muller et al., 2009) have been important steps towards managing research projects involving a large number of simulations. We present here a further step in this direction: a pythonic workflow that allows us to

• generate, aggregate and analyze data from hundreds of thousands of parameter sets and randomized trials;
• progress from coarse-scale to fine-scale scans, continuously monitoring progress and adapting scan resolution;
• avoid re-running any parameter set that has been tested before;
• drop scans along "singular" dimensions (e.g., drop scans along the modulation frequency for those sets with zero modulation amplitude);
• control parameter scans running on large, remote clusters from a personal computer including automated job preparation, submission, and monitoring, and data collection using the Fabric Python library (Hansen and Forcier, 2013);
• and to utilize large clusters with queuing systems efficiently for projects requiring a very large number of very small jobs using distributed shell (dsh) and IPython parallel.

We will discuss our experiences from a real-world project (Heiberg et al., 2013).

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P60 The rat BST-amygdala macroconnectome: a case study of functional-structural modules revealed by network analysis

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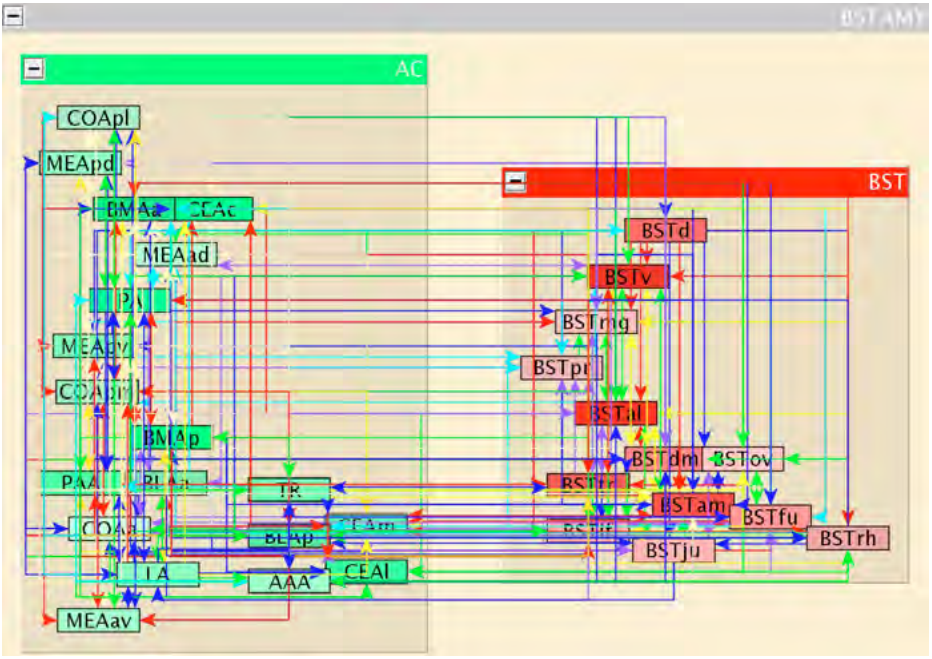
The amygdalar (AMY) nuclei and the bed nuclei of stria terminalis (BST) are heavily interconnected (Dong et al., 1996), and crucial for the behavior of mammals. In rats, the functions of different AMY regions include agonistic behavior and fear conditions, while the anterior part BST is involved in chronic stress, and its posterior part in addiction. Moreover, different roles of individual rat BST nuclei have been postulated (Dong et al., 2004). Thus, the network analysis of the structural connections between BST and AMY may help understanding the functionality of these regions.

We statistically analyzed the neuroanatomical connections reports stored in BAMS, and associated with the AMY and BST regions. The analyzed adjacency-matrix is made of 33 nodes connected by 506 edges (line-density 51%), and it was populated from more than 5000 individual reports of neuroanatomical connections, manually collated from the original research references, and mapped onto the rat nomenclature Swanson 2004 (Swanson, 2004). These data allows graph theoretical analyses of a directed and weighted local BST-AMY-connectome (Figure 1). The results of a weighted modularity analysis yielded functional-topographical groupings of the rat BST and AMY. Thus, the amygdalar nuclei involved in agonistic behavior and those involved in fear and pain are grouped in separate clusters. The majority of BST nuclei grouped in a single cluster, but a second cluster was identified. The members of the latter were also identified as a separate group in a recent statistical analysis of the gene expression patterns of 52 receptors and neurotransmitters in the rat (Bota et al., 2012). Furthermore, motif-analysis revealed a significant amount of motifs containing reciprocal connections (165 reciprocal connections) in the BST-AMY-network. These findings may indicate a regulatory role through positive or negative feedback mechanisms of particular regions (BSTal, BSTtr, BSTov, CEAl).

We will present the results of our analysis over the connectivity data manually collated from all published and original research literature pertinent to the rat BST and AMY, and discuss the functional relevance of our findings. We also propose new experiments, for a more precise identification of functionality of individual rat BST and AMY regions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P61 Parametric and non-parametric system identification of oculomotor system with application to the analysis of smooth pursuit eye movements in Parkinson's disease

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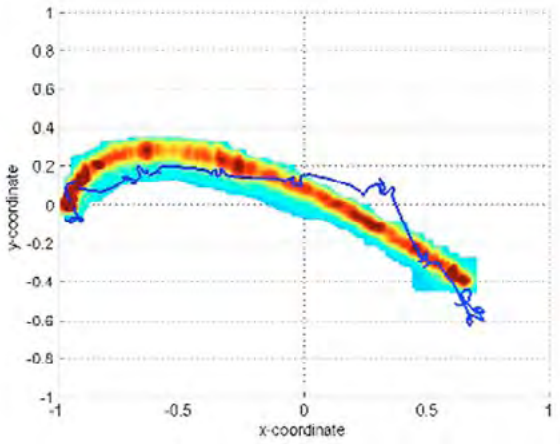
Modern video-based eye-tracking technology has facilitated human eye movement research and opened up for the introduction of advanced mathematical modeling methods. Smooth pursuit is perhaps the most frequently studied type of eye movements. Parkinson's disease (PD) is a neurodegenerative movement disorder, where eye movements typically demonstrate a saccadic pattern with decreased pursuit velocity compared with healthy subjects. The smooth pursuit system (SPS) has been shown to be affected negatively in PD [3], motivating the search for accurate quantification methods that could then be further used as diagnosing or even staging tools.

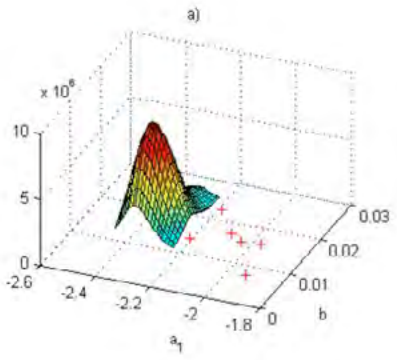
Method: A test subject is presented with specially designed visual stimuli displayed on a computer screen while a video-based eye tracker registers his/her gaze trajectories. Stochastic parametric and non-parametric system identification algorithms are then applied to the trajectorial data. The resulting mathematical models are scrutinized by means of anomaly detection techniques to distinguish between health and disease.
Visual stimuli properties constitute a crucial part of the proposed method and are underpinned by the recent progress in input signal design for best model accuracy. In fact, in most of the related research work as well as commercial products, standard constant velocity or sinusoidal visual stimuli have been utilized. These types of signals are of low temporal and spatial excitation order whose properties inevitably leads to poor performance of the system identification methods.

A parametric and a non-parametric method for modeling of the eye-tracking data are considered. The non-parametric one exploits orthogonal series approximation (OSA) for characterizing the involved probability density functions (PDF). Normal trajectories with associated gaze trajectory distributions are estimated from data to establish individualized eye-tracking profiles. In the parametric method, the SPS is modeled by a Wiener system, whose parameters are estimated from eye-tracking data. Here, parameter estimates from several recorded data sets of healthy individuals are used together with OSA to find an approximate PDF describing the distribution of the 'healthy' parameters. Parameter estimates of other test subjects can then be tested against said distribution to statistically determine whether they belong to it or not. The parametric models can be obtained from a single run of the visual stimuli but characterize the mean tracking performance of the test individual over this particular trial. The non-parametric models need multiple runs of the same stimuli, enabling however the recognition of deviating parts of the trajectories.

Results: The results presented in this abstract are preliminary and are part of an on-going clinical evaluation of the proposed technique. Three patients with PD and four healthy controls have been evaluated. Both the parametric and non-parametric methods distinguish well between the patients and age-matched controls. Fig. 1 illustrates the non-parametric method where the normal trajectory and uncertainty distribution estimated from eye-tracking data of a healthy control are presented vs a gaze trajectory of a PD patient. The heat map shows the OSA estimates of the PDFs of the healthy control tracking a visual stimulus, red indicates high values. The blue line shows a trajectory of the PD patient attempting to track the same stimulus. Only a small fragment of the trajectory is shown. The points of the PD patient's trajectory mostly belong to outliers of the uncertainty distribution of the control. Fig. 2 shows OSA estimates (surfaces) of the probability distributions of healthy model parameters together with parameter estimates (markers) of Parkinson patients. Model parameters were estimated by means of the nonlinear parametric method. a) Parameter distribution of healthy control (age 54) and the parameter estimates of a PD patient (age 57, red plus signs), b) Parameter distribution of healthy control (age 65) and the parameter estimates of two PD patients (ages 65, red plus signs, and 71, red circles).

The distinction both in the obtained trajectories and in the estimated model parameters between the patients and controls is evident and the parametric method appears also to clearly distinguish between the alterations in SPS due to aging and those caused by Parkinsonism.

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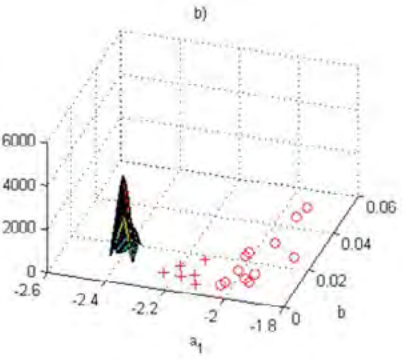
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a1
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b

P62 Cortex-inspired network architecture for large-scale temporal information processing

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The abundance of brain imaging data provides neuroscientists with a strong foundation in their research. With high-performance computing platforms becoming increasingly available and more powerful, large-scale data processing represents an important step towards modeling and understanding the neurophysiological processes in the brain. Since they exhibit intrinsically rich and complex spatio-temporal dynamics, a capability to explore distributed patterns of correlated activity at varying time scales is of considerable relevance to brain imaging data analysis. Some characteristics of such data, especially multi-scale temporal aspects of information, are ubiquitous. Sensory input reaching the brain particularly in the auditory stream is a representative example of a complex spectro-temporal information coding scheme. In the context of brain information processing, generic cortical computations can serve as a model approach to the problem of handling a temporal dimension.

Here we present a general cortex-inspired information processing network architecture aimed at capturing temporal correlations in data and extracting distributed representations in the form of cortical activation patterns. The architecture originally intended as a rudimentary abstract model of cortical layer 4 feature extraction capabilities (Johansson and Lansner, 2006) is implemented in the large-scale massively parallel neural simulator, Nexa (Benjaminsson and Lansner, 2012). We extend the original network (Benjaminsson et al., 2010) into the temporal domain allowing for building sparse and de-correlated representation of spatio-temporal correlations in the input data. The proposed architecture has a multi-layer and modular column-like structure, as conceptually shown in Fig.1. The data is first expanded with time lags to a higher-dimensional space, where significant correlations are sought. With the use of multidimensional scaling and competitive learning the projections to the activation layer are set in a way that multivariate spatio-temporal receptive fields are represented. Each receptive field is then composed of units with varying response properties to code for different attributes.

This network allows for unsupervised sequential processing of multivariate stochastic time series, independently of its origin. In this work, acoustic signals obtained from isolated spoken digits (Leonard, 1984) are used to illustrate the processing and feature extraction capabilities of the proposed architecture. The results indicate that the method is capable of successfully de-correlating the input data and extracting representations suitable for classification. Supervised learning with Bayesian confidence propagation neural networks (Lansner and Ekeberg, 1989) showed performance comparable to modern machine learning methods such as support vector machines. The potential of the proposed scalable cortex-

inspired approach to capture meaningful multivariate temporal correlations and provide insight into the model-free high-dimensional data decomposition basis is expected to be of particular use in the analysis of large brain signal datasets such as EEG or MEG.

Figure 1 – Proposed network architecture with outlined intermediate data processing steps. The input is first expanded using time delays, and then the receptive fields are created by means of multidimensional scaling (MDS) followed by vector quantization (VQ) with competitive selective learning (CSL).

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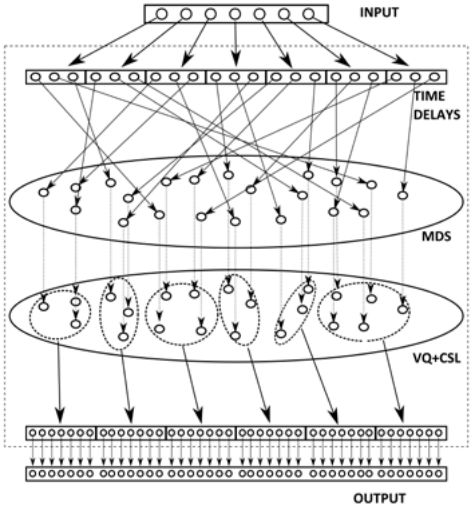

P63 Analyses of topics maps derived from neuroanatomical publications

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Using Latent Dirichlet Allocation (LDA) (Steyvers and Griffiths, 2007) we derived the topical composition of large corpora of full-text neuroanatomical articles that we extracted from PDF documents. Based on the derived topic mixture of each document, we analzed the relationships between documents in a given corpus. We applied Distrivuted Recursive Layout (DrL) (Martin et al., 2011), a graph layout algorithm, to visualize these inter-document relationships. Finally, we replicated this process focusing on different sections of an article (e.g., Abstracts, Methods and Materials) and looked for correspondences between the topics derived from the different sections.

Our poster presents the results of our analyses and describes the details of our methodology. We discus the challenges we faced and how we overcome them. Our ultimate goal is to streamline this procedure and incorporate it into our literature management application to enable other investigators to explore text collections of interest.

We conducted these analyses with articles from two journals: The Journal of Comparative Neurology and Brain Research.

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P64 Connecting brain imaging acquisition protocol, processing and analysis terms to an established lexicon

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6. The MIND Research Network, Albuquerque, USA

Description
For data sharing to be useful, data must not only be easily available and stored in an organized fashion, but the metadata that captures information about how the data was acquired, processed, and analyzed, must also be available. Additionally, metadata must describe this data using unambiguously defined terms. Efforts are underway to provide lexicons of brain imaging terms to the neuroscience community. Two examples are NeuroLex[1] and RadLex[2]; lexicons for the domains of neuroscience and radiology, respectively. While NeuroLex follows the OBO[3] principle of always defining a term, RadLex identifies relationships among terms, but often without definitions.

Often the item to be shared resides in data or tool repositories, which may have a defined schema or a fixed set of terms, but do not provide definitions for those terms. Users may not know precisely what is meant by each term and this makes it difficult to meaningfully combine data from disparate sources. In addition, the lack of standardized terms makes it difficult for query tools to search across collections at different institutions and makes data provenance ambiguous.

The overall goal of this project is to provide definitions for terms used in each stage of the data lifecycle of brain MRI-based experiments and place the terms within NeuroLex. We have begun our efforts with DICOM [4] terms, neuroimaging data processing and analysis terms, and BIRN's Human Imaging Database (HID) terms[5]. In some cases, connecting or parent terms were added to Neurolex to connect the new set of terms with those already in the lexicons.

To date, we have added over 1700 DICOM tag terms to Neurolex. We are currently evaluating systems that allow the creation of Terse RDF Triple Language (Turtle) files of these terms and their relations for importation into other ontologies or lexicons. Work is also ongoing to structure the data processing and analysis terms for addition into Neurolex. This work expands an existing lexicon with terms commonly used in neuroimaging and their inclusion will allow formal data models to refer to these terms through a SPARQL endpoint.

References

1)http://neurolex.org
2)http://www.radlex.org
3)http://www.obofoundry.org
4)http://medical.nema.org/
5)http://www.birncommunity.org/

P65 Optogenetics, electrophysiology and optical-imaging through windows on the brain in nonhuman primates

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3. Vanderbilt University, Nashville, USA
4. Salk Institute for Biological Studies, VCL, La Jolla, USA

Non-human primate (NHP) models are essential for the study of human perception, cognition, motor control, and neurological diseases. Our laboratories study visual perception, and address questions of functional connectivity (within and across cortical areas), interactions between groups of neurons during object perception and attention, the interplay between different image cues (e.g. motion and depth), and cross-modal sensory interactions (auditory-visual). Our studies are conducted in anaesthethized and in awake-behaving NHPs using a diversity of techniques: optogenetics, single-cell electrophysiology, optical imaging, fluorescence imaging, anatomy, and psychophysics.

We describe a new approach, developed in our laboratories, to improve optogenetics in NHPs. Optogenetics combines optics and genetics to control neuronal activity with cell-type specificity and millisecond temporal precision (1-4). Its use in model organisms such as rodents, drosophila, and C. Elegans is now well established. However, application of this technology in non-human primates (NHP) has been slow to develop (5-9). One key challenge has been the delivery of viruses and light to the brain through the thick dura mater of NHPs, which can only be penetrated with large-diameter devices that damage the brain. The opacity of the NHP dura prevents visualization of the underlying cortex, limiting the spatial precision of virus injections, electrophysiological recordings and photostimulation. Our approach replaces the native dura mater with an optically-transparent artificial dura. This artificial dura can be penetrated with fine glass micropipettes, enabling precisely targeted injections of virus into brain tissue with minimal damage to cortex. The expression of optogenetic agents can be monitored visually over time. Moreover, this optical window permits targeted, non-invasive photostimulation and concomitant measurements of neuronal activity via intrinsic signal imaging and electrophysiological recordings. These manipulations and measurements are precisely located in relation with the stable network of blood vessels on the surface of the brain (10, 11).

We also describe our preliminary work to combine this multiple-technique information, and to share it between our laboratories, e.g.: registration of brain-surface images obtained at different times and with different techniques; linking photo-electrophysiological, epifluorescence and anatomical data; querying for specific combinations of sensory and optogenetic responses. We outline the interrelation between our project and other

initiatives, and the possibility of using our artificial-dura implant to develop and test neuroinformatic resources in a medium-scale primate system.

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P66 The NeuroLex Neuron curation project: Practical experience aggregating structured information about neurons on a semantic wiki

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2. Yale University, New Haven, USA

The use of structured information, such as information in databases, ontologies and other machine readable forms, is a critical strategy to dealing with the vast number of neurons, brain regions, and details of neuronal morphology present within neuroscience. Unfortunately it is challenging to create structured data in neuroscience that has a degree of authoritativeness due to the significant practical challenges of aggregating knowledge from experts. Past strategies, including sending emails soliciting help and arranging in person workshops have been useful for some knowledge aggregation, but a sustained effort is usually required to coordinate with experts to create a knowledge base of any significant depth.

Since May 2012, we have engaged in a targeted and sustained curation project for neuronal types. We updated a standard form for neuronal type information to streamline it for curator input. The level of modeling chosen was carefully selected to favor broad population of fewer properties rather than deep population across few cells. Using this resource, we can compile useful information about cell types through the native functions of the wiki, including categories like ""Cholinergic neuron"", ""Spiny neuron"", ""projection neuron"".

We recruited 40 experts throughout the field of neuroscience and have aggregated their knowledge about neuronal types into structured information using the wiki platform NeuroLex.org (Grethe, 2009). In collaboration with these experts, we have added ~50 new neuron types and filled in ~1000 new properties (Fig 1), as well as modified and removed existing neuron types that had inaccuracies. The entire contents of the curation project are available at NeuroLex.org and as structured RDF.

We chose to expose this information through the semantic wiki rather than a relational database or journal article because these pages are readily accessible to search engines and are open to community contribution. Because this platform is also used for modeling brain structures, molecules and parts of nerve cells, the representation is already integrated automatically across these different scales. We believe that this platform serves as a model for exposing neuroscience information in a way that facilitates data integration in the neurosciences.

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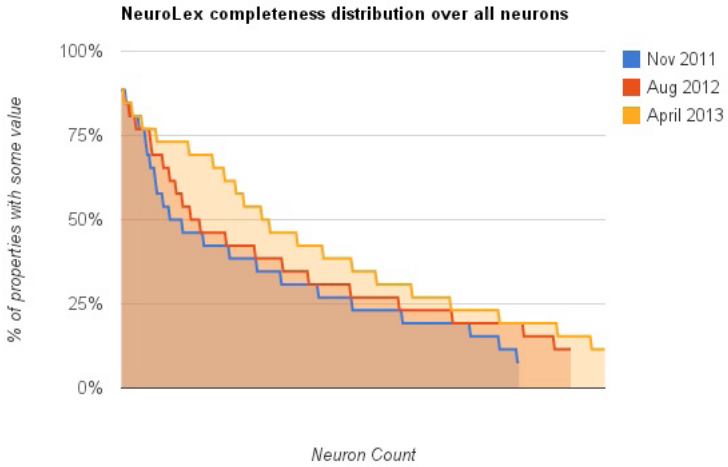

P67 Pupillometry with modern video eye trackers

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Video-based eye trackers have gained popularity over other methods of recording ocular motor behaviour since they are cost effective, non-invasive, and have a high temporal frequency of data collection (up to 2000 Hz). These systems can also perform pupillometry, but pupil recordings face certain challenges. Even when lighting is constant, the pupil size has some constant variability and noise, which is compounded by the effect of conjugate eye movements that change the angle of view of the pupil, and thus alters the number of pixels occupied by the pupil in the image, even with no change in pupil size, as well as vergence eye movements that are accompanied by physiologic changes in pupil size. Furthermore, there are no standardized methods for normalization, analysis and representation of data. Last, with increasing sample size and trial duration, data management becomes a complex issue.
We recently analyzed pupil changes in a monetary decision-making paradigm under constant illumination. On each trial subjects decided between 2 different prospects, one with a higher magnitude of reward but lower probability of winning than the other. Pupil size was recorded monocularly at 1000Hz for the 4 seconds given for the decision.

Analysis of each subject's data was done on a spreadsheet. Repeats of the same trials were first averaged, eliminating gaps in data due to blinks, followed by averaging the pupil size within 250ms time bins. Data were then normalized to the first bin as baseline before analysis across subjects: thus pupil size changes were expressed in terms of ratio of change from the baseline. Using this method we could show that pupil dilation did correlate with the difficulty of decision-making.

We have demonstrated a method for pupillometric data collection and analysis using video eye tracking while addressing concerns of inter individual variability (by normalizing), noise (by smoothing) and representation (by using ratios and relative measures to represent differences). While video eye trackers can provide a substantial amount of pupil data, analysis of this data has to be rigorous. Numerous challenges remain.

P68 Monoamine neuromodulation of cognitive association – a multiscale study: pathway signalling, electrophysiological analysis and fMRI response

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Introduction:

An enduring query in systems neuroscience is the effect of chemical modulators on neural processing and cognitive behavior. We study here these effects under two basal monoamine modulator inputs: noradrenergic and melatonic activations. In the latter, we study the modulation of word-association under noradrenergic-epinephnergic activation or melanonin-estradiol activation. Our goal is to see how alteration of the aforesaid activation level changes the coupling between interacting neural networks,

Methods & Results:

Electrophysiological analysis:

We analyze the effect of the monoamine activation by its modulation of central reticular arousal system (noradrenergic mode), and analyze the effect on interactive networks, such as that on clinical electrophysiological findings of EEG entrainment/detrainment under visual/auditory stimulation. Here, we investigate the effect of noradregenic activation on the linkage node synaptically connecting the two networks. We define the EEG findings showing that increasing noradrenergic activation decreases the interactive coupling between two autonomous neural circuits, such as that between visual perceptual circuit and the occipitoparietal interpretative circuit; this observation is made from our time-domain analysis of experimental findings of earlier investigators, which we interrelate with neuromodulation status.

Systems Biochemistry analysis

We here consider the case of activation by the other monoamine system (the melatonin/estrogen mode) on a neural node. It is known that melatonin signal is the primary actuator of this estrogen activity. Hence we perform a systems biology analysis via GeneGo/MetaDrug platform utilizing the molecular structure of estradiol. We find melatonin actuation enhances ($p<0.01$): (i) cytochrome P-19 upregulation, generating estrogen biosynthesis (ii) G1R-kinase activation, producing electrophysiological changes as in neural deactivation and spiking inhibition.

Neuroimaging analysis:

We perform fMRI study of cognitive association task of 24 healthy subjects (12 male, female each) using free word-association test. We use independent component model and network analysis, and demarcate the task-positive/task-negative networks, found to be linked by a focal internode, precuneus. We observe that in females (fig. 1), the deterministic responsivity of the node is lower by 21% when compared to males ($p<0.05$).

Conclusion

We thus see in females, the monoamine activation process (melatonin, estradiol and adrenergic actuation), can produce deactivation of the linkage node between neural circuits in cognitive operations, as that between task-positive and task-negative networks. This internodal de-activation, and consequent increased autonomy and independence (detrainment) between the circuits, is incisively conserved in neurobiological processes across the different levels: molecular pathway, electrophysiology, behavior, and cognition.

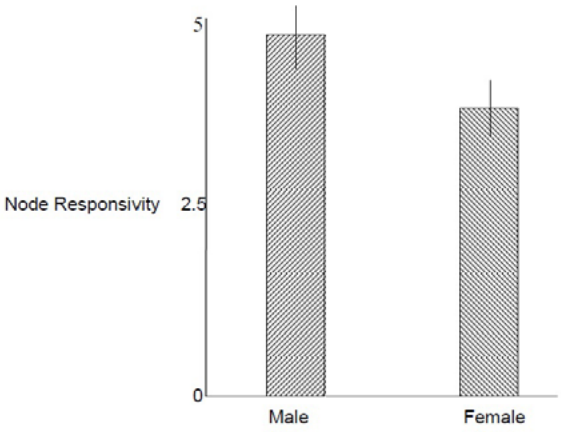

Fig. 1: The deterministic responsivity of focal internode in females is 21% less than in males, as per the fMRI study undertaken.

P69 Dynamics of brain activity underlying working memory for music in a naturalistic condition

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Despite working memory's (WM) critical role in high-level cognitive functions in the integration of information over time, its implementation in the neural tissue is poorly understood. Auditory WM has been mainly studied using vocal stimuli and only recently a few studies have started investigating the neural networks engaged in auditory WM for music. Moreover, in neuroscience WM has not been studied in naturalistic conditions but rather using artificial target detection tasks (e.g., n-back and Sternberg) and simpler, manipulated materials, all of which might create mental states not characteristic of brain's behaviour in more natural, attentive situations. In music, WM allows us to form a coherent representation of the otherwise undifferentiated musical stream, and to emotionally respond to it, i.e., by tracking tonal, rhythmic and timbral dynamics. Our goal was to study the functional neuroanatomy of WM memory for musical motifs as it emerges in the brain while listening to music.

We followed a naturalistic, non-standard procedure: a) participants' (musicians) brain responses were recorded while attentively listening to a piece of music, instead of performing auditory cued tasks; b) we adopted a modern tango as stimulus, containing shifts in tempo, timbre, dynamics, tonality and rhythm, a complex stimulus more representative of the complex auditory scene environment our brains have evolved to respond to; c) we used a behavioural test to identify the stimulus motifs and build a time-course predictor of WM neural responses; d) activation of WM-related neural networks was studied by tracking in the neurovascular responses the temporal evolution of motivic repetition that naturally occurs in Western tonal music, assumed to trigger WM; and e) in order to fine-tune the identification of WM function in the brain, the variance accounted by a set of the stimulus' acoustic features was pruned from participants' brain responses. Correlational analysis revealed a distributed network of cortical and subcortical areas responding to motif repetitions, including a right lateralized dorsal area in the prefrontal cortex, bilateral basal ganglia, and left hippocampus.

The findings suggest that WM encoding of motifs while listening to music emerges from the integration of neural activity spread out over cognitive, motor and limbic subsystems. The recruitment of the hippocampus stands as a novel finding in auditory WM. We hypothesize this activation to be enabled by the use of a realistic listening condition, which might evidence the formation of long-term memories for the music.

P70 The effect of apolipoprotein E (apoE) genotype on synchronous neural interactions (SNI) in healthy brains

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In this study, we analyzed the effect of apolipoprotein E (apoE) genotype on SNI distributions in cognitively healthy subjects of various ages to determine the relations between apoE genotype and neural communication. ApoE is involved in lipid metabolism in the brain but its effects on brain function are not understood. Three apoE isoforms (E4, E3, and E2) are the result of cysteine-arginine interchanges at two sites: there are zero interchanges in E4, one interchange in E3, and two interchanges in E2. The resulting six apoE genotypes yield five groups with respect to the number of cysteine residues per mole (0-4 CysR/mole). The use of the number of CysR/mole to characterize the apoE molecule converts the categorical apoE genotype scale, consisting of 6 distinct genotypes above, to a 5-point continuous scale, allowing the use of statistical analyses suitable for continuous variables. Using such analyses, here we show for the first time that apoE affects in a graded and orderly manner neural communication, as assessed by analyzing the relation between the number of CysR/mole and synchronous neural interactions (SNI) measured by magnetoencephalography (MEG) in 130 cognitively healthy subjects. By investigating the statistical properties along the range of CysR/mole SNI distributions, the 4-CysR/mole (E2/2) SNI distribution was found to have unique properties. The special status of the 4-CysR/mole distribution was reinforced by the results of a hierarchical tree analysis (see figure 1) where the 4-CysR/mole (E2/2) SNI distribution occupied a separate division by itself and the remaining CysR/mole SNI distributions were placed at increasing distances from the 4-CysR/mole distribution, according to their number of CysR/mole, with the 0-CysR/mole (E4/4) being farthest away. These results support the idea that the number of CysR/mole is an important quantitative factor underlying the effect of apoE on SNI. In addition, these findings suggest that the 4-CysR/mole (E2/2) SNI distribution could serve as a reference distribution. When the SNI distributions of individual subjects were expressed as distances from this reference distribution, there was a substantial overlap among subjects of various CysR/mole. This orderly variation of SNI with the number of CysR/mole is in keeping with recent advances and ideas regarding the molecular mechanisms underlying the differential effects of apoE in the brain which emphasize (a) the healthier stability conferred on the apoE molecule by the increasing number of cysteine-arginine interchanges, with 4-CysR/mole (E2/2) being the best case, as opposed to (b) the instability and increased chance of toxic fragmentation of the apoE molecule with lower number of CysR/mole, with 0-CysR/mole (E4/4) as the worst case. Overall, we show for the first time that the apoE genotype affected the SNI distribution in a systematic and graded fashion, according to the number of CysR/mole in the apoE molecule.

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Fig. 1. Dendrogram derived from hierarchical tree clustering of the number of cysteine residues per mole (CysR/mole) SNI distribution distances. Notice the distinct division of E2/2 with 4 CysR/mole, the clustering of all other apoE genotypes, and the orderly placement in the tree of apoE genotypes according to the number of CysR/mole, from zero to four.

D08 Web data storage for management and sharing of neuroscience data

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In neuroscience, technological advancements and improvements in methodology, achieved during the last decades enable scientists to produce growing amounts of increasingly complex data recorded from many species, modalities, and levels of study. Annotation and organisation of these data has become a challenging task, which is not only important for the interpretability and reproducibility of results and analyses, but also essential for collaboration and data sharing. In order to address these issues, the German INCF Node (G-Node) is developing software solutions consisting of several services and tools for experimental neuroscientists, focusing on online data access and organisation of electrophysiological data. The core of this project is a web service representing a centralized data storage system that provides functions for upload, search, and management of data and metadata [1]. The principal design goal of this service was to improve the experimental workflow and to unify data access from different locations and platforms. In addition we develop libraries and client programs providing the full functionality while allowing the scientist to use this service either directly through a web page or from his preferred working environment. Currently this includes a toolbox for the popular numeric computing environment Matlab and a library for the programming language Python. The software supports various techniques and standards used in the field for data analysis and management, including NEO[2], Neuroshare[3], and odML[4]. When files are uploaded to the storage service, they are converted to native objects such as signals, spikes, neural events or metadata objects. All those objects can be searched, selected and manipulated separately. Furthermore, the service implements a versioning system for all stored data objects and allows fine-grained sharing of data from whole datasets down to single signals and files. The service itself exposes its full functionality via a common application programming interface (API). The architecture of the API is based on the Representational State Transfer[5] (REST) pattern, which is a widely used design model for HTTP-based web APIs. As main transfer format the API uses the markup language JSON[6]. This use of common web technologies facilitates the development of other software solutions that interact with the service.

References

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[2] NEO I/O (http://neuralensemble.org/neo)
[3] Neuroshare (https://github.com/G-Node/python-neuroshare)
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[5] R. T. Fielding (2002) doi:10.1145/514183.514185
[6] RFC 4627 (http://tools.ietf.org/html/rfc4627)

D14 The BrainLiner platform for sharing, searching, and previewing time-aligned neurophysiological data

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Performing experiments and recording neurophysiological data requires substantial resources. At the same time, data-driven science requires large amounts of data in order to build statistical models and study the relationships between tasks and complex brain activity patterns. Thus to maximize returns on invested resources and to conduct meaningful research, it is important for scientists not only to publish descriptions about their research, but also to share the data used in such publications.

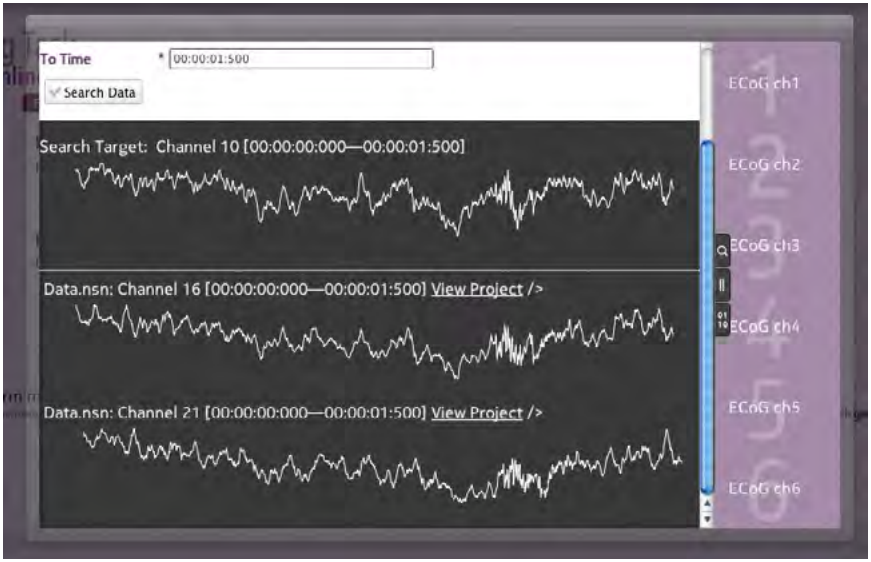
BrainLiner.jp was launched as part of the Japanese Strategic Research Program for Brain Science (SRPBS) to share time-aligned neurophysiological and stimulus data. Using our portal, scientists from all over the world can freely share data that is time-aligned to behavioral information, in a standardized file format. We allow users to upload data as Neuroshare or matlab files in a standardized format. We then convert uploaded matlab files into Neuroshare (.nsn) files and uploaded Neuroshare files into matlab files automatically when a user uploads a data file.

BrainLiner.jp has supported text-based search of project descriptions and documents since the first release. However, we recently added a data-driven similarity search feature to search for data that are similar to input data. Users can select interesting data patterns and then, using our data search, can find similar data that share a similar pattern.

Our data-drive search is implemented as a web service that is accessible programmatically, allowing developers with API access to incorporate our data similarity search into their analyses.

We recently re-implemented our data previewer in HTML5, to allow people without Flash to preview data. As with the data-driven search, the HTML5 viewer is implemented as a modular web service, which is hoped to be extensible in the future.

Finally, to ease data sharing and use, we completely redesigned and reimplemented our web portal with a simpler and more responsive interface.


To Time
* 00:00:01:500
Search Data
Search Target: Channel 10 [00:00:00:000—00:00:01:500]
Data.nsn: Channel 16 [00:00:00:000—00:00:01:500] View Project />
Data.nsn: Channel 21 [00:00:00:000—00:00:01:500] View Project />
ECoG ch1
ECoG ch2
ECoG ch3
ECoG ch4
ECoG ch5
ECoG ch6

D15 Setting up a web-based neuroscience database has never been easier: The CoCoMac engine goes open source

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We present a web-based framework to (1) set up a relational data base; (2) search and browse its contents interactively; and (3) edit/add content to it. Central to the framework is a database definition file: a text file that describes the database structure in a compact (JSON-based) format. This file can either be written from scratch to set up a new database, or be extracted from an existing database. Multiple versions of the definition file can provide different views (intranet/world wide web) of the same database. The platform provides an interactive search/browse wizard that (1) allows the user to compose complex queries without needing to know the database structure; and (2) presents the search results in tabular form, with interactive (AJAX-based) links to related child and parent tables. Adding/editing data is currently a privilege of the administrator; we are developing a module that allows users to own and edit specific rows of a table and all of its children.

The system is being developed for the CoCoMac 2.0 database (Bakker et al. 2012), which collects published tracing studies to compose a complete picture of the wiring diagram of the Macaque brain. In CoCoMac, the end product is a connectivity matrix (Fig. 1), which is not contained in the database but needs to be computed from it. This workflow is supported in the form of temporary tables that can be dynamically integrated with the database definition. CoCoMac also provides an example of how additional, non-standard views can be added for tables of a given class.

To get started, one needs a working instance of the MySQL data base engine, and a web/intranet server with PHP support. The database definition file should contain a list of tables and their field types, or, if a field references another table, the name of that table preceded by a caret symbol. This file can be automatically parsed from an existing database. An optional javascript file is used to define how the system should display table rows in different contexts, such as within a table cell or itemized list. The system can be downloaded from http://cocomac.g-node.org/git, and seen in action at the CoCoMac 2.0 website http://cocomac.g-node.org. It is also in use for a lab automation project (Bakker et al. 2012a) and various internal projects.

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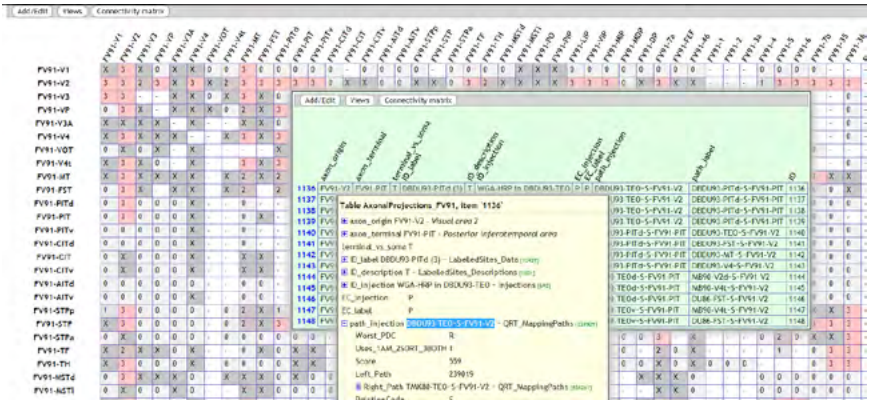

D17 Head in the cloud: accessing distributed data and services through XNAT

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The XNAT open-source imaging informatics platform provides a user-friendly web application for uploading, processing, browsing, searching, and downloading imaging-related data and associated metadata. XNAT also has a RESTful web services API for programmatic access. pyxnat is a Python language library that uses the XNAT REST API to facilitate scripted access to the contents of an XNAT server.

We have extended pyxnat to abstract over the location of the data managed by an XNAT server. Queries against XNAT can be used to access data stored on the server itself; to use a local mirror of those data, either prepopulated (e.g., the Human Connectome Project's ""Connectome In a Box"") or built incrementally by downloading on demand files from the XNAT server; or to index into cloud-based or other third-party network storage (e.g., Amazon S3, INCF Dataspace, NCI TCIA collections).

This abstraction over storage makes it straightforward to write a script that identifies a set of subjects based on search criteria such as age, sex, neurological assessments, or behavioral measures; locates imaging data for those subjects; and applies standard or custom analysis tools to those data, using computing resources nearest to the data or otherwise best suited to the task.

In continuing work we are building an abstraction over computational services, so that only small, parametric script modifications will be required to move data analysis operations between the XNAT server and client-managed computing resources or public clouds.

D18 DANI-Boy: A Data Access and Navigation Interface for Biology

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Biomedical laboratories are producing ever increasing amounts of data, yet tools used to annotate and link the data are not flexible enough to accommodate rapidly evolving community standards and the demands of data integration, analysis and model workflows. Experimenters produce data and annotate parts of a project while performing data gathering and analysis of other part while performing annotation on others. Data integration tools used in the bio-medical domain currently do not provide a flexible enough framework to keep up with evolving ontologies and the daily reality of data generation. The increasing pressure to publish well annotated data and provide links to existing ontologies and data repositories creates the opportunity for a new set of tools.

We present a prototype of a Data Access and Navigation Interface for Biology (DANI-Boy) which support the continuous integration and annotation data by allowing easy access to community developed ontologies while allowing enough flexibility to add information not yet standardized by a wider community. DANI-Boy was build on best data integration practices, allowing to build on existing resources, such as NeuroLex biomedical ontologies. Semantic Media Wiki (SMW) is used in the current version as a graphical user interface to facilitating the continuous refinement of data annotation and linking to ontologically defined entities. Python is used for various background processing tasks to facilitate information extraction, cross ontology matching and in providing an ontology anchored object API. The intent is to provide a more intuitive service model than the standard SPARQL services provided by SMW.

The present prototype offers access to integrated experimental data gathered over the course of multiple years in the exploration of Layer I cells and microcircuitry of the neocortex of a P14 rat. The example implementation shows how morphological, electrophysiological, molecular and connectivity data can be organized, explored, annotated and updated.

D19 The Neuroscience Information Framework (NIF): a unified semantic framework and associated tools for discovery, integration, and utilization of biomedical data and resources on the web

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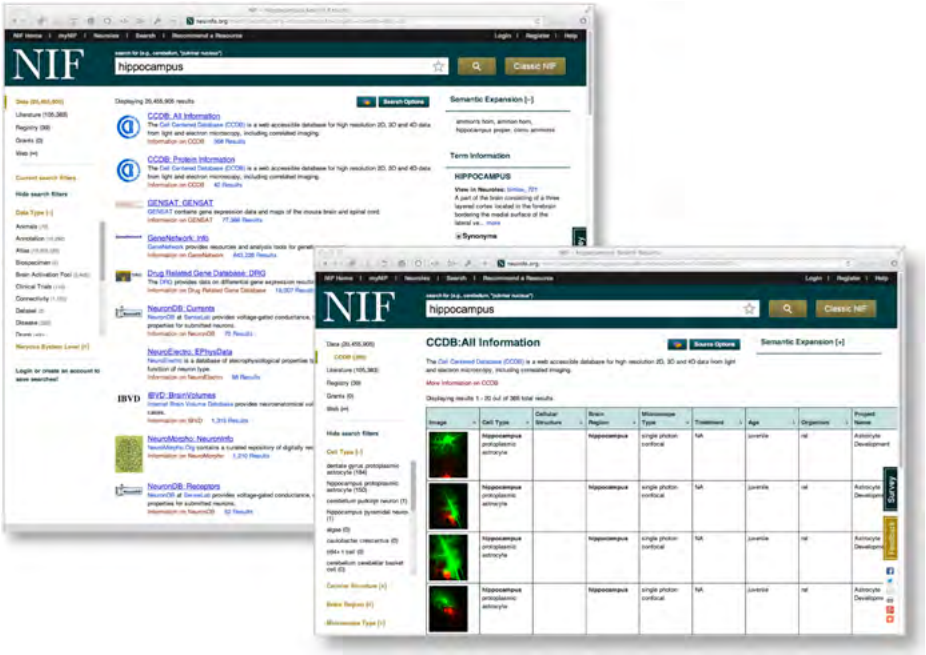
The Neuroscience Information Framework (NIF; http://neuinfo.org) has recently launched a completely re-designed discovery portal for finding and integrating neuroscience-relevant resources, data, and literature. The new portal provides users with new tools to visualize data content (e.g. through analytics that provide a landscape analysis of where data can be found for topics of interest) to more personalized services via myNIF (e.g. the saving of favorite searches). The portal searches across 3 primary collections: (1) NIF Registry: A human-curated registry of neuroscience-relevant resources annotated with the NIF vocabulary; (2) NIF Literature: A full text indexed corpus derived from the PubMed Open Access subset as well as an entire index of PubMed; (3) NIF Database Federation: A federation of independent databases that enables discovery and access to public research data, contained in databases and structured web resources (e.g. queryable web services) that are sometimes referred to as the deep or hidden web.

To further enable the utilization of this vast collection of information, the NIF is applying semantic web technologies to its holdings. By defining a set of standards and best practices for describing and representing data such semantic web and linked data technologies eliminate the barriers between database silos and foster the evolution of the Web into a Web of data. Such technologies are being successfully applied as integration engines for linking biological elements in many domains. Exposing NIF's content as Linked Open Data will enable further integration with the growing amount of information available from the linked open data cloud – thereby providing much richer resources for the neuroscientist. The publication of this content relies on NIF's comprehensive ontology (NIFSTD) that covers major domains in neuroscience, including diseases, brain anatomy, cell types, subcellular anatomy, small molecules, techniques and resource descriptors.

Over the past year, NIF has continued to grow significantly in content, providing access to over 6,000 resources through the Registry, and more than 200 independent data resources in the data federation, making NIF the largest source of biomedical information on the

web. NIF's tools help people find and utilize neuroscience related resources - provides a consistent and easy to implement framework for those who are providing such resources, e.g., data, and those looking to utilize these data and resources.

In this demonstration we will provide a tour of NIF's suite of services, tools, and data:
* Search through NIF's newly re-designed semantically-enhanced discovery portal
* Working with NIF's linked data (e.g. nervous system connectivity) via SPARQL
* Services and tools that provide access to the NIF data federation - the largest collection of Neuroscience relevant information on the web
* Contributing to the NeuroLex – a community resource for neuroscience terminology built on a semantic media-wiki platform
* Curation and normalization of data utilizing NIF's Google Refine services
* NIF's semantically enhanced data and tools for its maintenance
* myNIF and the NIF Digest – personalized services for researchers



D20 BLUIMA, an NLP pipeline for neuroscience

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The growing number of published neuroscientific literature makes it impossible for researchers to read, manually curate and integrate the newly available information. There is a rich landscape of tools to automate knowledge extraction from scientific papers. However, this landscape is fragmented and lacks interoperability. In addition, some tools are focused on the biomedical domain, but few are specific to neuroscience.

BLUIMA is an integrated suite of software components for natural language processing of neuroscientific literature (neuroNLP). BLUIMA is based on the high-performance Apache UIMA framework and provides UIMA components wrapping state-of-the-art NLP tools so they can be used interchangeably in processing pipelines. BLUIMA also includes original models and tools specific to neuroscience and provides corpus readers for neuroscientific corpora.

Corpus readers are provided for several corpora (e.g. WhiteText brain regions corpus). A robust PDF reader module performs precise text extraction from scientific articles in PDF format. BLUIMA also includes pre-processing modules for sentence segmentation, word tokenization and part-of-speech tagging (JulieLab), as well as lemmatization (BioLemmatizer) and abbreviation recognition (BioAdi). The MongoDb module allows storing UIMA documents into MongoDb, the leading NoSQL database. Lexical-based named entity recognizers (NER) are available for organism name, age and sex, for brain regions, cell and subcellular names, protein and gene names. BLUIMA also provides a NER built using the NIFSTD brain ontology, and another using the BioLexicon, a lexical-terminological resource of nearly 2.2 Mio lexical entries from the biomedical domain. Finally, BLUIMA wraps several machine learning-based NERs for chemicals, species and proteins.
The above components are packaged into a freely available, standalone software suite with minimal dependency. Furthermore, a simple scripting language allows configuring the different components in a simple and straightforward format.

Evaluation was performed on a random sample of 10'000 PubMed abstracts containing the MeSH term ""Neuroscience"". On this dataset, 97.0% of all tokens were recognized and mapped by one or more components.

In conclusion, BLUIMA is an effort to integrate available tools and develop new tools for the processing of neuroscientific literature.

OP05 A unified research resource layer; experiences from the neuroscience information framework

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The Neuroscience Information Framework, (NIF, http://neuinfo.org), catalogs research resources important to biological science, but the creation of these deceptively simple catalogs turns out to be non-trivial.

After hundreds of years, scientists have some idea of what types of information can be asked from bibliographic catalogs (e.g., PubMed), but catalogs that list research resources can vary significantly from bibliographic catalogs. For example, resources such as transgenic mice, cell lines, MRI data sets, software tools or academic databases are important to research, but the types of information indexed in catalogs of these sorts of resources may not be the same as the information about published work. For example, a cell line may have a patient whom the cell line derives from, the surgeon who removed it, and an organization that maintains the cell line in storage. In this case, the question of who is the author of the cell line makes little sense. Similarly, authorship of an academic database may be less informative than it is in the case of a publication because databases change content over time making statements about the content or an individual responsible for database maintenance a temporally dependent statement. When we consider some of the very successful academic database projects like the mouse genome informatics project, they tend to have a large and revolving number of contributors, curators and programmers. However, the number of these projects, their quality, and the amount of time researchers devote to them is generally increasing making tracking them very useful to both researchers and governmental bodies interested in impact of their research dollars.

Of the thousands of academic resources cataloged in various registries including the NIF Registry, the INCF tool registry, BioSiteMaps (which seeded the NIF Registry), Eagle i, BioDBCore, EBI, and NITRC many share bits of information about those types of entities, but they each look at the cataloging effort in a slightly different way, keeping slightly different pieces of information about each project. Furthermore, most projects duplicate the efforts of others even though the scope of a unified, world-wide registry of research resources is likely to be far beyond any one group. This means that many of the registries have overlapping resources, in somewhat different schemas and can't easily be integrated. The goal of several groups, including ours, has been that a uniform yet very flexible registry schema be created for all online biomedical resources allowing many groups from various countries to add information without the need to duplicate effort. The data that has been generated by many groups has been made available in a uniform format by the NIF system.

NIF at its' core is a catalog of research resources that takes advantage of the work of NIF

curators and many individuals who painstakingly cataloged resources, interlinked these with ontologies and standard data sets in a rich representation of the resource landscape. Over the 5 years during which NIF has been cataloging resources, we have had to adapt our criteria for defining, including and curating resources. In order to allow for flexible representation of resources within the NIF, we opted to code NIF's catalog using the Neurolex semantic wiki (http://neurolex.org) so that we could easily expand the schema and we could link curation and tagging to the NIF core vocabularies. NIF has created a curation document which details for procedures for registering and curating resources for the NIF. We will present NIF's current resource catalog and lessons learned in creating and maintaining a comprehensive resource catalog. By working with various standards and many groups, we hope to reduce duplication, enhance both discoverability and transparency of research resources, which are often very highly sought-after outputs of scholarly research.

P71 Toward collaboration in NIJC platforms: Standard brain database linked with application server

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We are developing and running a platform, Invertebrate Brain Platform (IVB-PF), to provide various research resources, such as neuronal images, behavioral movies and textbook for comparative studies on sensory processing and behavioral control of invertebrates. In the case of silkworm moth, more than 1,000 neuronal image data have been collected and registered. The standard brain image of moth brain has been created and provided (Ikeno et al., 2012). The morphological models of several neurons have been reconstructed and registered in the standard brain. These are provided as contents of our database in stack images, Wavefront OBJ and SWC formats. It is suitable to provide resources as model file for both provider (experimentalist) and user (modeler), because experimentalists can keep original experimental data in their side even register on the platform and users can immediately apply neuron structure on their model simulation by download from the platform.

We are also providing a virtual machine environment with standard application software, such as Fiji, Neuron and Genesis, in neuroscience research through another platform, Simulation Platform (Sim-PF) (Yamazaki et al., 2011). The platform does not only equip utilities for visualization and simulation, but also the high-speed access to the registered data for retrieving and using large amount of data (Fig.1). As the data viewing and applications on the Sim-PF is accessed by user demands from IVB-PF seamlessly, we provide following operations on the registrations and utilizations of the standard brain by the collaboration of these two platforms.

1. Three-dimensional viewing of confocal laser scanning microscope (CLSM) images of the brain and neurons
2. Three-dimensional viewing of standard brain image from various directions
3. Segmentation and modeling of neuropiles and neuron morphologies from CLSM image
4. Registration of neuropiles and neurons into the standard brain
5. Statistical analysis of neuron morphology

To integrate morphological data of a species and compare with others, the standard brain could be a highly effective tool. It is possible to estimate projection regions and synaptic connectivity of neurons. By collaboration of our platforms, we can provide an environment to use neuron morphological data for construction and application of the standard brain.

The process and software using on the platform can be applied to various kinds of insect and invertebrate brains.

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P72 MorphDepot and its points of interaction for new software developments in the field of single cell research

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Does "being a neuroscientist" imply "being a computer scientist" (or "being a programmer")? Reasonable evidence for that statement provides the fact that neuroscientific progress increasingly depends on data management efforts that involve storing and structuring data, querying and analyzing data, exchange of data, and re-analysis of previously recorded data – all within the digital world. In order to avoid this statement coming true and to enable the neuroscientist to keep focused on neuroscientific questions, we need an ecosystem of scientific software tools that can integrate modern developments fast and that is capable of being integrated into the scientists workbench without deep knowledge of computer science. We present "MorphDepot" [1], a Python package for managing morphological data together with corresponding single cell recordings, that was designed with focus on two aspects: (1) software implementation was as tightly as possible aligned to neuroscientific use cases in order to minimize developmental overhead; (2) we designed various software interfaces in order to maximize impact and usability of the tool. In particular, three levels of interaction for MorphDepot with other software or with the scientist are provided: (1) a file-system level, (2) an application programming interface (API) level, (3) and a graphical user interface (GUI) level. Each level supports specific use cases: (1) the file-system level provides the possibility to use a diversity of software that operates on files and directories, such as file manager, image viewer, specific analysis software, version control systems, or synchronization software; (2) the API level provides the possibility of communication between different software, applications, or scripts, including web services. This allows integration of analysis tools and automation of scientific workflow processes; (3) the GUI-level provides a direct interface of a specific service for a scientist, for example by a web application. As a reference system, MorphDepot supports the GinJang project [2] in managing morphological data successfully between two INCF-nodes, J-Node [3] and G-Node [4].

With this software architecture, we add a tool to the ecosystem of neuroscientific software that integrates smoothly with established tools and allows the scientist to focus on neuroscience instead of computer science.

[1] https://github.com/G-Node/MorphDepot
[2] http://projects.g-node.org/ginjang/
[3] http://www.neuroinf.jp
[4] http://www.g-node.org/

D21 20 years of NEST: A mature brain simulator

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Efficient and reliable simulation tools are essential for progress in brain research. Since the early days of neuronal computing (Farley & Clark, 1954), a wide range of simulators have been developed, each specialized on one or few spatial and temporal scales (Brette et al., 2007). But the reliable and reproducible simulation of such complex systems as the brain is a very demanding challenge. Thus, the Computational Neuroscience community concentrated on a few reliable and widely used simulation tools in recent years. Neuronal network simulation is thus coming of age: Just as our colleagues in electrophysiology, we begin to base our work increasingly on the use of standard tools, with modifications and adaptations for our particular research, instead of building home-brew solutions from scratch. This concentration was not least the result of a series of large-scale EU funded projects, such as FACETS, BrainScaleS and the recently announced Human Brain Project.

From its humble beginnings as a PhD-student project 20 years ago, the Neural Simulation Tool NEST (Gewaltig & Diesmann, 2007) saw its first incarnation as the SYNOD simulator in 1995 (Diesmann et al., 1995), leading to exciting results on synfire chains early on (Diesmann et al., 1999). By tightly coupling software development with computational neuroscience research (Kunkel et al., 2010), simulator technology evolved steadily, facilitating new scientific insight at (nearly) every step. Some key examples were parallelization (Morrison et al., 2005; Plesser et al., 2007), exact integration of model equations (Rotter & Diesmann, 1999), precise spike times in a time-driven simulator (Morrison et al., 2007; Hanuschkin et al., 2010), spike- time-dependent (Morrison et al., 2007) and neuro-modulated plasticity (Potjans et al., 2010), and a Topology module for spatially structured networks (Plesser & Enger, 2013). Streamlined data-structures (Kunkel et al., 2011) allow NEST to efficiently exploit the capabilities of some of the largest computers on Earth for simula- tions on the brain scale (Helias et al., 2012). Systematic quality assurance through testsuites (Eppler et al., 2009) and continuous integration technology (Zaytsev & Morrison, 2013) ensure simulator reliability (within limits). With a user-friendly Python-based interface (Eppler et al., 2008; Gewaltig et al., 2012), integration with PyNN (Davison et al., 2008) for simulator-independent scripting and MUSIC support (Djurfeldt et al., 2010) for integrated multi-scale simulation, NEST is a powerful simulation tool for brain-scale simulations today.

NEST has been publicly available since 2004 and has been taught at summer schools and graduate courses since, training a generation of computational scientists. This has lead to a steady increase in computational neuroscience publications based on NEST simulations in recent years (see http://www.nest-initiative.org for a list), indicating that NEST is

indeed establishing itself as a widely used tool for the simulation of large networks of (comparatively) simple model neurons.

As of the NEST 2.0 release in 2012, NEST is available under the GNU Public License to ensure wide dissemination. The further development of NEST is chaperoned by the NEST Initiative, a non-for-profit organization incorporated in Ecublens, Switzerland, which is open for interested scientists. We are currently preparing to move NEST source code to a distributed version control system, allowing all NEST users "real time" access to bug fixes and improvements, and to facilitate contributions by the NEST Community.

In our demonstration, we will illustrate the capabilities and versatility of NEST. We will in particular focus on three complementary approaches to simulating large-scale cortical networks: A data-driven approach based on detailed connectivity information (based on data from the Blue Brain Project), constructive network generation, based on connectivity patterns (Potjans & Diesmann, 2012), and simulation of advanced 3D topological networks.

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OP06 Building a 3D model of the mitral-granule cell network in the olfactory bulb

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We are interested in studying the basic mechanisms involved in odor recognition, a widely studied experimental model of sensory information processing. Recent findings have shown that odors may activate spatially distributed sites in the olfactory bulb with a sparse, columnar-like organization of mitral and granule cells. This organization challenges the classical center-surround organization, and there is thus a need to identify a new paradigm for signal discrimination that could have general implications as well for other brain regions. The possible underlying circuitry and the computational properties of the olfactory bulb have been widely investigated experimentally, especially in terms of odor selectivity and dynamics of cell responses. However, experiments are usually carried out in single cells or in small randomly selected sets of cells. This has prevented a clear understanding of the spatio-temporal organization of the mitral-granule cell network in representing an odor input, which requires simultaneous recording from a relevant subset of mitral and granule cells activated by an odor. The functional effects of a network-wide process such as lateral inhibition, in relation to the patterns of glomeruli activated by different odors, remain thus relatively unknown and difficult to explore experimentally.

The main challenge we are addressing here is the development of a 3D model of the mitral-granule cell network, allowing direct input of the experimental data for individual glomerular activation, in order to demonstrate and predict the learning mechanisms that will ultimately be responsible for the early processing stages of the sensory inputs. For this purpose, we implemented a 2mm^2 3D model of the olfactory bulb (about 1/20th of the entire system). Several 3D reconstructions of mitral cells with full dendritic trees (from Igarashi et al., 2012) were analyzed to extract morphological parameters to generate a population of some 700 synthetic mitral cells, 5 for each glomerulus. Approximately 20000 granule cells were then randomly inserted into the network and connected using a collision detection algorithm. The input activity elicited in 127 glomeruli in the dorsal olfactory bulb during presentation of 19 natural odorants (kindly provided by Alan Carleton, from Vincis et al., 2012) was then used to drive self-organization of the network under different conditions of odor input. This is the first 3D simulation of the olfactory bulb microcircuit using realistic cell properties and network connectivity. It provides a new framework for investigating the functions of a brain system.

The figure shows a rendering of the olfactory bulb 3D model. Green spheres: glomeruli; red spheres: activated glomeruli; white lines: mitral cell dendrites.

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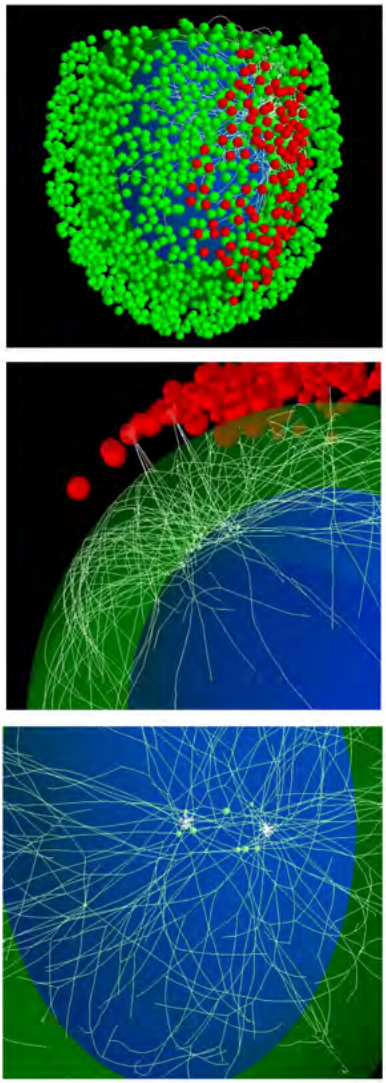

OP07 Large scale whole brain mapping of inputs to the main olfactory bulb

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An important prerequisite to understanding how neural circuits generate behavior is to understand the structure of those circuits, including the connectivity between the neurons. In sensory systems, a key component of that connectivity is the top down projections from higher cortical regions to primary sensory areas. For example, in mammals, projections from olfactory cortical regions, including piriform cortex, represent a major input to the inhibitory granule neurons in the main olfactory bulb. Inhibitory granule cells play a central role in how odor information is transformed and represented by the principal neurons of the bulb, the mitral cells. Projections from higher odor areas including the accessory olfactory nucleus and the piriform cortex are known to impact the firing of both the granule cells and the mitral cells, highlighting their importance in shaping how odors are represented. However, little is know about the organization of top-down inputs to these inhibitory cells in large part because of the experimental and computational challenges of single cell mapping across a whole brain. To provide a complete portrait of the monosynaptic inputs to inhibitory cells in the main olfactory bulb, we employed the rabies virus trans-synaptic tracing technique and developed an imaging platform that allowed us to visual every single labeled cell across the entire mouse brain. Labeling spatially distinct populations of inhibitory granule cells in the bulb with the modified rabies allowed us to trace the patterns of innervation from a number of higher processing areas, including the accessory olfactory nucleus and the olfactory cortex. From these injections, we were able to reconstruct, identify and classify the presynaptic partners to inhibitory cells in the bulb across the entire mouse brain at single cell resolution. Our data reveal the complex patterns of innervation to the inhibitory neurons of the bulb, and provide a map of the spatial organization of feedback projections for higher brain areas to their lower processing counterparts. By integrating the connectivity maps of inputs into the bulb on the scale of the whole mouse brain with models of activity patterns within the bulb, we hope to provide insight into how cortical feedback may play a role in shaping the representations of odor information.

P73 An integration layer for neural simulation: PyNN in the software forest

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Following the principle of separation of concerns, there is a trend in the development of neural simulation software away from monolithic simulation tools and towards an ecosystem of specialized components, each of well-defined scope, that can be combined in different combinations according to scientific need [1]. Examples of such components are CSA [2] for specifying network connectivity, NineML [3] for describing the mathematics of individual neuron and synapse models, NeuroML [4] for specifying neuronal morphology and the placement of functional elements, such as ion channels and synapses, within this morphology, Neo [5] for representing electrophysiological signals recorded from simulated neurons and synapses, NEST [6] and NEURON [7] for performing the simulations, and MUSIC [8] for facilitating runtime exchange of data between different software tools. PyNN [9] is a Python API for simulator-independent specification of spiking neuronal network models and simulation protocols. A script written in PyNN can be run on any supported simulator (or neuromorphic hardware platform) without modification. From its conception, PyNN has had an integrative role, making it easier to use multiple simulators in a single project (for cross-checking, etc.) and to port a model from one simulator to another. Recent developments have emphasized still further the potential of the PyNN approach as an integration layer, simplifying the task of gluing together different software components in order to construct a federated neural simulation platform customized to the scientific problem of interest.

We report here on a number of recent enhancements to PyNN, each of which involves integration of an external software component with the PyNN API: (1) using CSA specifications of neuronal connectivity in PyNN, with automated pass-through of CSA objects to the underlying simulator, where this is supported (NEST), for efficiency; (2) import and export of NeuroML model descriptions into/from PyNN; (3) integration into PyNN of the Neo library for structured handling of electrophysiology data, greatly increasing the number of output data formats available to PyNN and making it much easier

to use the same analysis/visualization tool for both simulation-derived and experimental data; (4) PyNN support for simulator-independent, user-defined neuronal and synapse models defined in NineML (rather than the fixed menu of simulator-independent models previously provided by PyNN); (5) integration into PyNN of the MUSIC library, enabling simultaneous use of multiple different simulators in a single model, defined in a single simulation script. Taken as a whole, these new features are a good illustration both of the merits of Python in general and PyNN in particular as a federation platform/integration tool for neuronal simulation, and of the benefits of a modular approach to neuroscience software development.

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P74 Tracing neural circuits by dynamically simulating whole-brain activity patterns in the human connectome

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How does one unravel neural circuits from whole-brain connectivity data? To answer that we build a large-scale dynamic simulation of the human connectome in virtual reality, that reconstructs whole-brain activity in real-time. Using DTI structural connectivity data from [1] we built an interactive 3D visualization of the human connectome network in an immersive virtual reality environment (Fig. 1) using the Unity 3D gaming engine. Further, the virtual reality brain network in Unity is coupled to a real-time neuronal simulator, iqr [2]. As we see, coupling structural connectivity data with detailed enough neuronal population dynamics is sufficient in predicting functional correlations and large-scale activity patterns. We model neuronal dynamics by a linear-threshold filter (as work in progress, we are currently implementing population dynamics from mean-field models [3]). Each population module is stochastic, having Gaussian noise. The user can stimulate any region or simultaneous regions of the network with external input currents. The simulation then reconstructs reverberating neural activity propagating throughout the network in real-time. As an explicit example, we stimulate the superior parietal areas and watch causal activity propagating in the parietal lobe, indicative of visuo-motor integration (Fig. 2). This is a first step to simulating and mapping large-scale brain activity in real-time. As quantitative analysis methods and data-recording technology in neuroscience make improvements, it is becoming evident large-scale dynamics and whole-brain quantitative measures play an important role. For instance, oscillations across large brain regions are precursors to several cognitive functions. Moreover, the causal map in these interactions is crucial. Compared to functional correlations, large-scale temporal activity maps across directionally connected brain structures serve as a more powerful tools to unravel mechanisms of large-scale neural circuits. Our results show that stimulating brain areas triggers a sequence of causal activations in associated network loops that represent cognitively related functions.

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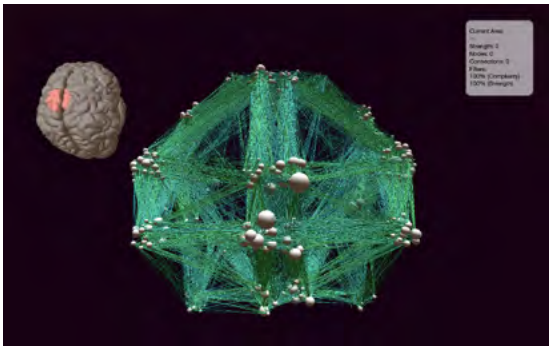

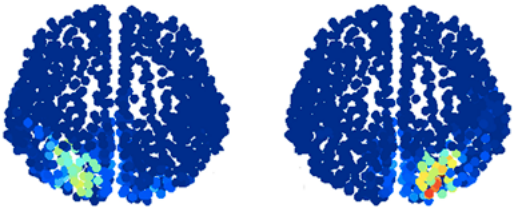

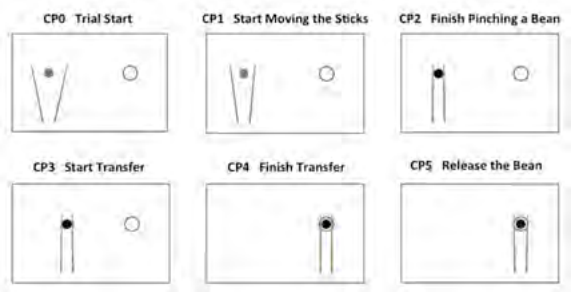
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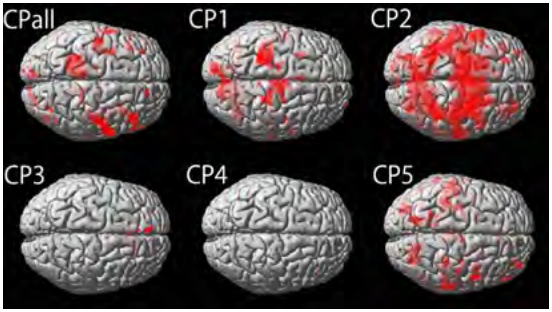
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P75 Mozaik: a framework for model construction, simulation, data analysis and visualization for large-scale spiking neural circuit models

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The increasing amount of computational resources becoming available is causing a shift in computational neuroscience towards increasingly heterogeneous models of neural circuits and brain regions, and more importantly, employment of increasingly complex stimulation and experimental protocols in an effort to bridge the gap between simulations and biological experiments. This growth in complexity of virtual experiments poses a challenge for the existing tool-chains, as the set of tools that are involved in typical modeller's workflow is expanding, with a growing amount and complexity of metadata, describing the experimental context, flowing between them. A plethora of tools is currently available covering different parts of the workflow; however, numerous areas lack dedicated tools, while integration and interoperability of existing tools is limited. This forces modellers to either handle the workflow manually, leading to errors, or to write substantial amounts of code to automate parts of the workflow, in both cases hindering their productivity.

To address these issues, we have developed Mozaik: an integrated workflow system for spiking neuronal network simulations written in Python. Mozaik integrates the model, experiment and stimulation specification, simulation execution, data storage, data analysis and visualization into a single automated workflow, ensuring that all relevant metadata are available to each of the workflow components. It is based on several widely used Python tools, including PyNN [1], Neo [2] and Matplotlib [3]. It offers scientists a declarative way of specifying models and recording configurations, using hierarchically organized configuration files. The models are constructed using topologically organized sheets of neurons and projections between such sheets of neurons. After specifying the model, a user can define the list of experimental protocols to be executed with the model. Each experiment defines a list of stimuli that will be presented to the model, and optionally can also involve direct stimulation of neurons in the model. Using a single command, a user can instruct Mozaik to create an instance of the model and execute the specified experiments. Mozaik will automatically record all data into a datastore and, importantly, also save all the relevant metadata describing the experimental context. The datastore can be accessed via a query interface, allowing for easy and efficient data manipulation. This query system is extensible and already offers a number of operations that are commonly used in analysis or visualization. The analysis and visualization modules operate over the datastore, using the query system. They are written in a modular and extensible way, utilizing the saved metadata to automate numerous processes. This ensures an efficient way to add new analysis and visualization methods.

Mozaik is written in a modular way, making it easy to replace any of its components, while

the existing modules are designed to be extensible with minimal programming effort. Mozaik increases the productivity of running virtual experiments on highly structured neural networks, by significantly automating the whole experimental cycle, while increasing the reliability of modeling studies by relieving the user from manually handling the flow of metadata between the individual stages of the workflow.

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P76 A Python test suite for statistical properties of probabilistic networks with and without spatial structure

Daniel Hjertholm[1] , Birgit Kriener[1] and Hans Ekkehard Plesser[1]
1. Norwegian University of Life Sciences, Department of Mathematical Sciences and Technology, Aas, Norway

The advances in both computer development and simulation technology in computational neuroscience allow us to simulate ever larger and more complex networks of interacting spiking neurons that are in line with neuroanatomical findings (Helias et al, 2012). Even though reconstructions of brain circuitry become more detailed and complete (Potjans and Diesmann, 2012), the exact circuitry will vary between individuals. It is thus general connection rules, such as random connectivity according to measured connection probabilities for individual types of neurons, or also spatially dependent probabilistic connection profiles, that determine network structure in simulations.

As simulations become more complex it is hence of importance to be able to test whether the generated network instantiations are correct with respect to the underlying connectivity rule and neuron distribution. Such tests should be automated, so that they can be executed as part of automated test suites (Eppler et al, 2009; Zaytsev and Morrison, 2013). Randomized operations such as probabilistic network wiring can only be tested statistically and statistical tests may—indeed ought to—fail in a certain number of cases. To still be able to integrate such tests in automated test regimes, adaptive testing strategies have been proposed (L'Ecuyer and Simard, 2007).

Here we present a Python-based test suite for some of the most commonly used probabilistic network types, e.g. random connectivity with fixed probability, or distance-dependent connection profiles in two- and three-dimensional space with open or periodic boundary conditions. The tested factors are characteristic statistical quantities such as the degree-distribution or the distribution of pairwise distances, which are tested against the expected distributions obtained analytically. We discuss the implementation, performance and sensitivity of the tests with respect, e.g., to sample size, number of samples, or the quality of the underlying random number generator. The tests employed are chi-square tests for discrete distributions, such as degree distributions, and Kolmogorov-Smirnov tests for continuous distributions, e.g., the distribution of distances.

Though the test suite is primarily developed for connection routines implemented in the NEST simulation software (Gewaltig and Diesmann, 2007), we emphasize that it can be easily extended to work with data obtained from analogous connection routines in other simulators.

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P77 ImgLib2 for large scale image analysis and visualization

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Today, both connectivity and detailed neuroanatomy of biological nervous tissue are reconstructed from light- and electron-microscopy images. Structures in neuronal tissue span a wide range of scales, they have both fine details and large extent. Accordingly, large volumes need to be imaged at very high resolution resulting in image data of overwhelming and ever increasing size. New approaches to both algorithm development for image analysis and data storage and access management are desperately required.

We propose our Java library ImgLib2 for n-dimensional data representation and manipulation [1] as a valuable tool in this context. ImgLib2 separates pixel-algebra, data access and data representation in memory by virtualization. It makes algorithm development independent of infrastructure design and vice versa, simplifying both lines of development. In consequence, it is easier to express new or existing approaches for image analysis in software. New data sources are immedately available to existing algorithm implementations. ImgLib2 collaborates seamlessly with existing infrastructure. It is typically sufficient to implement one basic accessor to connect an existing data source to the library.

We demonstrate ImgLib2's flexibility in two distinct and relevant contexts: (1) a rich-client visualization and annotation tool for remotely stored image volumes of many terabytes size [2], and (2) as a server-side image processing backend for the browser-based collaborative annotation tool CATMAID [3].

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D22 The Three NITRC's: Software, data and cloud computing for brain science and cancer imaging research

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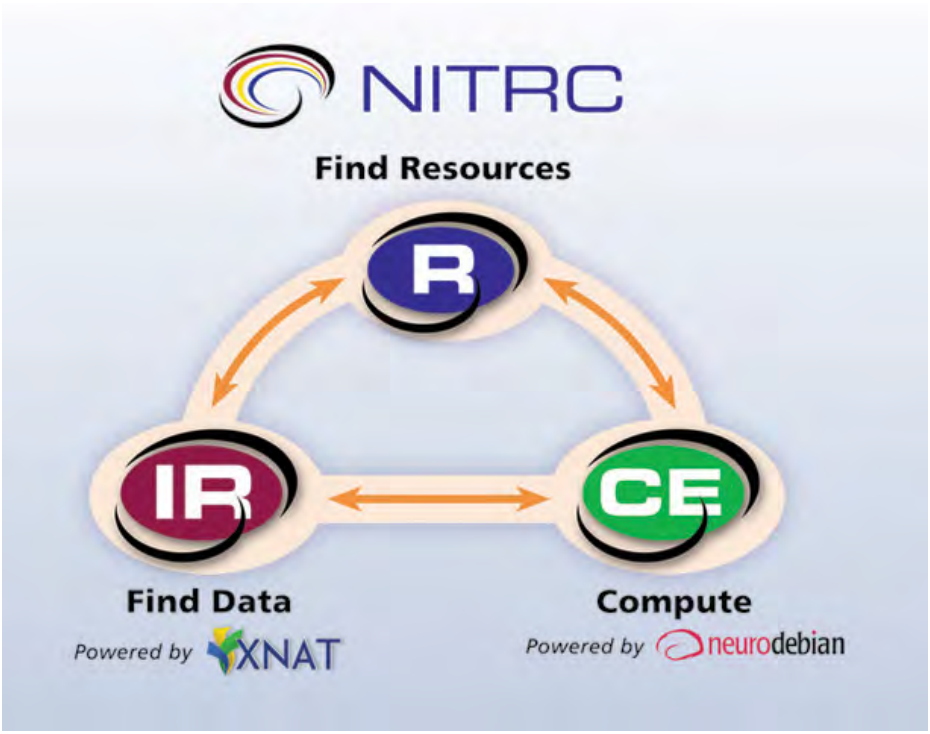
Background: Initiated in October 2006 through the NIH Blueprint for Neuroscience Research, the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) has embarked on a mission is to foster a user-friendly knowledge environment for the neuroscience community. By continuing to identify existing software tools and resources valuable to this community, NITRC's goal is to support its researchers dedicated to enhancing, adopting, distributing, and contributing to the evolution of neuroimaging analysis tools and resources.

Methods: Over the years, the scope of NITRC Resources (NITRC-R) has grown to include resources to support MR, PET/SPECT, CT, EEG/MEG, optical imaging and now clinical neuroinformatics and imaging genomics. NITRC has also expanded its capabilities to support image data sharing and computation. In support of enhanced data sharing, NITRC provides an Image Repository, NITRC-IR (http://www.nitrc.org/ir/), which is built on XNAT and provides sharing infrastructure for images and related data. In this era of ever-mounting shared data resources, neuroimaging scientists and cancer imaging researchers are becoming more challenged to secure sufficient computational resources to execute complex computational analysis on these large data resources. Using AWS EC2 and leveraging NeuroDebian, NITRC produced and released the Computational Environment (NITRC-CE) via Amazon's AWS Marketplace. NITRC-CE is an on-demand, cloud based computational virtual machine pre-installed with popular NITRC neuroimaging tools. A public Amazon Machine Instance (AMI) is also available.

Results: NITRC facilitates access to an ever growing number of neuroinformatics tools and resources (540 to date), many relevant to imaging research, some identify themselves specific to cancer research such as TCIA and MITK Diffusion. NITRC-R averages monthly 17,000 visits and 82,000 pageviews. The NITRC-IR offers 4,764 subjects, and 4,779 MR Imaging Sessions searchable across six projects to promote re-use and integration of these valuable shared data. NITRC-CE provides simplified deployment of cloud-based computation that supports FreeSurfer, FSL, AFNI and many other software resources.

Conclusions: In summary, NITRC is now an established knowledge environment for the neuroimaging community where tools and resources are presented in a coherent and synergistic environment. We encourage the imaging community to continue providing design and content feedback and to utilize these resources in support of data sharing requirements, software dissemination and cost-effective computational performance.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D23 A simple tool for neuroimaging data sharing

Christian Haselgrove
1. University of Massachusetts Medical School, Worcester, USA

Data sharing is becoming increasingly common, but despite encouragement and facilitation by funding agencies, journals [1], and some labs and larger research efforts, there remain political, financial, social, and technical barriers to sharing data [2]. In particular, technical solutions are few for researchers that are not a part of larger efforts with dedicated sharing infrastructures, and social excuses such as the time commitment required to share or the lack of motivation to share can keep data from becoming public [3].

We present a system for sharing neuroimaging data, designed to be simple to use and to provide benefit to the data provider. The system consists of a server at the International Neuroinformatics Coordinating Facility (INCF) and client tools for uploading data to the server. The primary design principle for the client side is ease of use: the user identifies a directory containing DICOM data and provides his INCF Portal user name and (public) identifiers for the subject and imaging session. The client probes the data for metadata and prompts the user for additional or missing information, then anonymizes the data and sends it to the server. The server first checks anonymization of incoming data, deleting data that is not property anonymized. The server then runs quality control routines on the data, and the data and the quality control reports are made public. The user is notified by e-mail when this is complete, and retains control of the data and may delete it from the server if necessary. The result is that in the time required for upload and quality control processing, including a scant minute or two of the user's time, the data is anonymized, made publicly available, and quality control is performed.

Recent enhancements to the system are a GUI uploader to better facilitate preparation and upload of data and the addition of diffusion and structural QA procedures. The system now also presents structural and time series QA measures in the context of other data in the database, giving an indication of relative data quality.

The client tools and access to the public image database are available at http://xnat.incf.org/.

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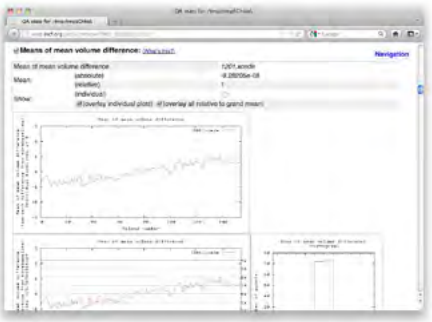
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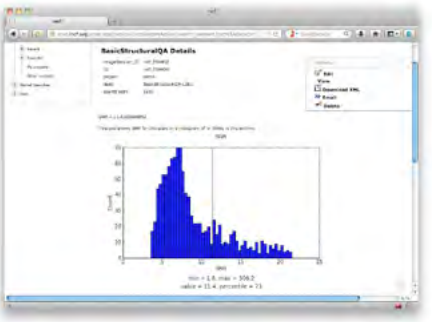
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D24 Mojo 2.0: Connectome Annotation Tool

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A connectome is the wiring diagram of connections in a nervous system. Mapping this network of connections is necessary for discovering the underlying architecture of the brain and investigating the physical underpinning of cognition, intelligence, and consciousness [1, 2, 3]. It is also an important step in understanding how connectivity patterns are altered by mental illnesses, learning disorders, and age related changes in the brain.

Mapping the densely packed network of synaptic connections between individual neurons in the brain is challenging, even when using state-of-the-art microscopy techniques, computer vision algorithms, and analysis software. Using serial section electron microscopy (SSEM), it is possible to image of thousands of neuronal profiles and synaptic connections at the nm scale and acquire terabytes (TB) of image data. Fully automatic computer vision techniques are available to annotate this data, but results are still far from perfect and require additional human annotation to produce an accurate connectivity map [4]. Therefore, it is important to develop tools that allow domain experts to interact with the raw data and ensure correctness. A number of software tools and packages for neuron reconstruction are available [5, 6, 7, 8, 9, 10]. However, tools supporting dense reconstruction and correction of automatic segmentations over TB datasets are under development. User interaction modes are an important consideration for these tools to reduce the amount manual labour required to produce a 3D reconstruction.

In this demonstration we present Mojo 2.0, an open source, interactive, scalable annotation tool to correct errors in automatic segmentation results (Figure 1). Sparse user scribbles are used to correct both split and merge errors for TB scale volumes.

To correct a split error, the user scribbles over objects that should be joined. Any segments touched by the brush stroke are combined into one segment. This operation is performed in 2D or 3D as specified by the user. To correct a merge error the user can use a split brush to paint a broad line over cell membrane in the image. Watershed pixels within this region are used to split the segment in 2D. Mojo 2.0 also predicts how adjacent 2D segments should be split, allowing the user to navigate in 3D and quickly confirm or adjust multiple split operations while retaining 3D connectivity. An adjust mode allows the user to manually draw a region and add it to the selected segment. This mode is useful when a combination of split and merge operations are required to correct a segment.

We demonstrate Mojo 2.0 on SSEM images of mouse brain cortex, automatically labeled by the Rhoana image processing pipeline and compare results with manual tracing methods.

Mojo 2.0 is available online at: http://www.rhoana.org/

Figure 1: Mojo 2.0 is an interactive desktop application for connectome annotation. The Mojo 2.0 interface shown here displays electron microscope images of mouse cortex with segmentations shown as an editable color overlay. Automatic segmentation results can be corrected by sparse user scribbles. Above the editing panel a simple toolbar controls display and annotation options. On the right a list of segments is displayed, ordered by segment size. The application is open source and scalable up to TB scale volumes.

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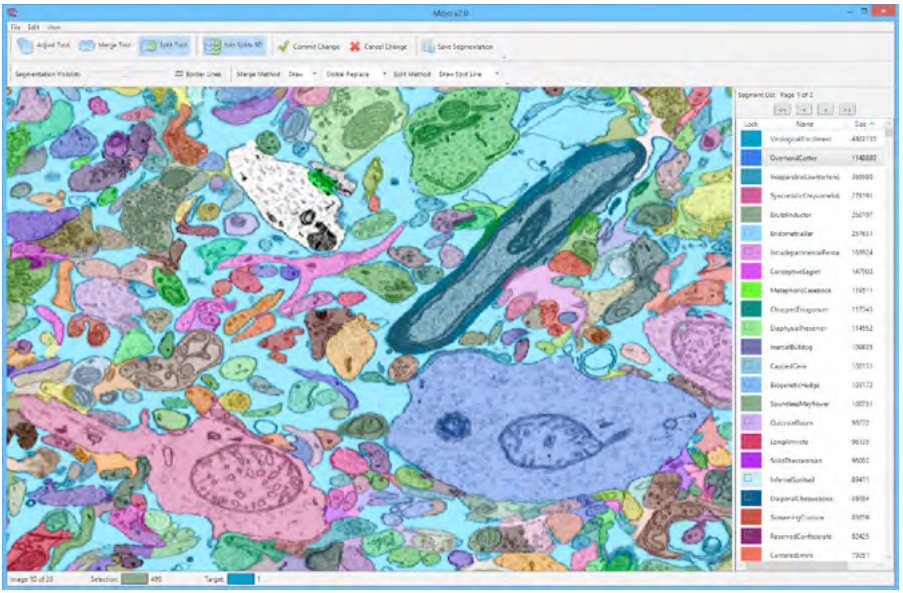

D25 Towards automated analysis of connectomes: The Configurable Pipeline for the Analysis of Connectomes (C-PAC)

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4. Duke University, Departments of Statistical Sciences, Durham, USA
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7. New York University Child Study Center, Phyllis Green and Randolph Cowen Institute for Pediatric Neuroscience, New York, USA

Introduction

To successfully examine the brain's functional architecture (connectome) and its behavioral associations, researchers need tools that facilitate reliable, replicable connectivity analyses. Here we introduce C-PAC, a configurable, open-source, automated processing pipeline for functional MRI data that builds upon a robust set of existing software packages. Users can rapidly orchestrate automated large-scale pre-processing and data analyses, and can easily explore the impact of processing decisions on their findings by specifying multiple analysis pipelines to be run simultaneously. C-PAC can reliably process hundreds or thousands of subjects through a variety of preprocessing strategies in a single run. Thus C-PAC has been optimized for use on large data sets such as those made public by the International Neuroimaging Data-sharing Initiative (INDI, http://fcon_1000.projects.nitrc.org/).

Methods

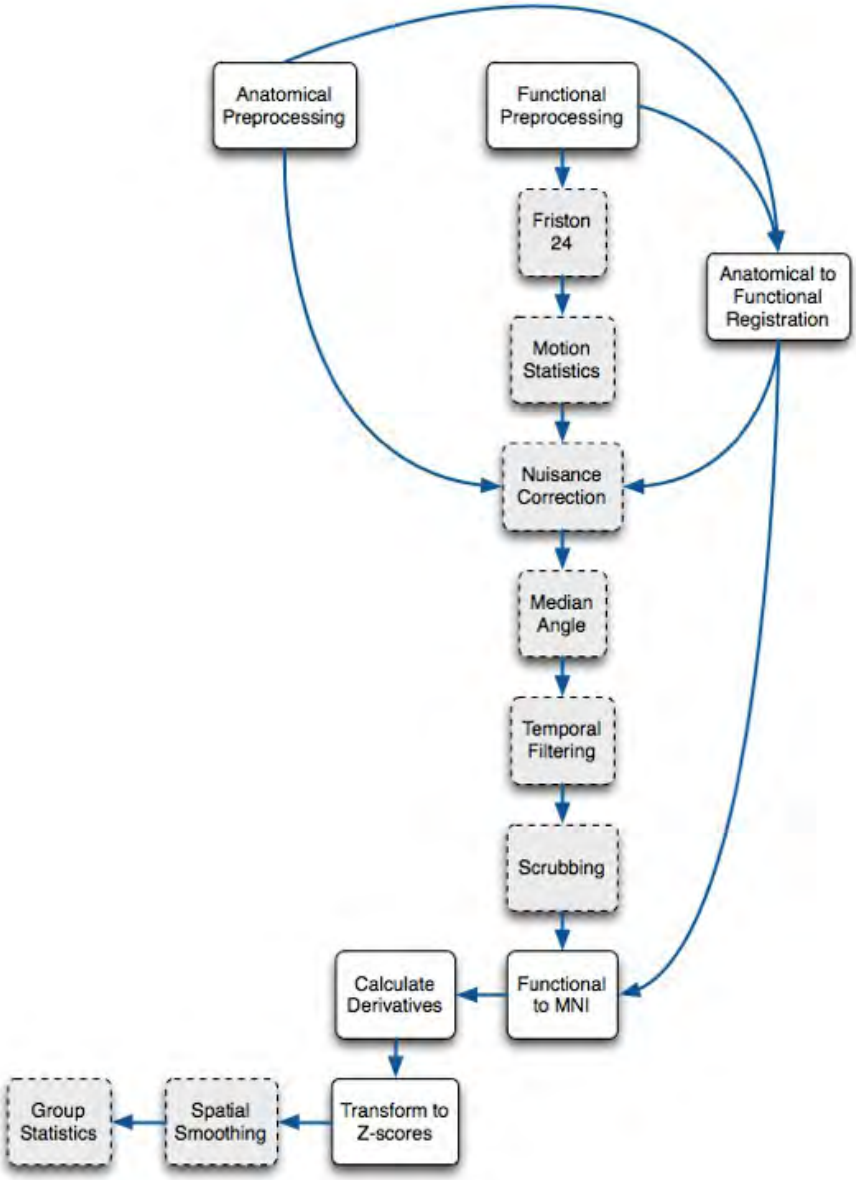
C-PAC has been implemented in Python using the Nipype pipelining library. Nipype provides C-PAC with mechanisms to automatically detect and exploit parallelism present in a pipeline, iterate over several parameter settings, and to restart a pipeline without having to recompute previously completed processing steps. C-PAC extends Nipype functionality by providing workflows specific to connectivity analyses, functional connectivity derivatives and analyses not present in other neuroimaging packages, and a simplified interface for specifying and running pipelines. The CPAC workflows are built from AFNI and FSL tools, as well as algorithms coded in Python using Scipy, Numpy and scikit-learn.

The C-PAC processing and analysis pipeline (fig. 1) is configured through a simple configuration file, which permits the inclusion and exclusion of different steps, and setting of a variety of parameters. A variety of input data organization schemes and subject specific

acquisition parameters (slice acquisition, slice timing information, time point censoring) are easily configured through a subject configuration file. Available preprocessing options include: motion correction, anatomical/functional coregistration, spatial normalization, spatial and temporal filtering, tissue segmentation, slice-timing correction, several variations of nuisance signal removal and volume censoring (motion "scrubbing"). C-PAC also includes a number of advanced analysis methods that facilitate detailed exploration of connectivity patterns, network structure, and brain-behavior relationships. Individual-level measures include: Seed-based Correlation Analysis, Amplitude of Low Frequency Fluctuations (ALFF) and Fractional ALFF, Regional Homogeneity, Voxel-Mirrored Homotopic Connectivity, and Network Centrality (Degree and Eigenvector). At the group level, C-PAC features Connectome-Wide Association Studies, Bootstrap Analysis of Stable Clusters, and integrated group statistics using FSL/FEAT. Additionally, users can easily extract preprocessed time-series data and connectivity matrices for analysis with other packages. C-PAC can seamlessly interact with shared memory (multi-core) and cluster-based (sun grid engine, OpenPBS) high performance computing environments to minimize computation time.

Results and Conclusions

Currently in its alpha release, C-PAC is available as an open source project through github along with user and developer documentation (http://fcp_indi.github.com). Alpha testing is currently being performed in five partner labs and it has already been employed to process and analyze several large (~1000 subject) datasets available through the 1000 Functional Connectomes Project and INDI (e.g., ABIDE, ADHD-200, NKI-Rockland). The beta release is scheduled for early spring and will include feature enhancements including a graphical user interface, a quality assessment interface, and several new functional connectivity derivatives. Future enhancements will include integration with Freesurfer to enable surface based analyses, and the ability to process and analyze diffusion tensor imaging data.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Nuisance Correction
Median Angle
Temporal Filtering
Scrubbing
Calculate Derivatives
Functional to MNI
Group Statistics
Spatial Smoothing
Transform to Z-scores

D26 Informatics Infrastructure for the Australian Neuroscience Community: The Multi-modal Australian ScienceS Imaging and Visualisation Environment and the Characterisation Virtual Laboratory

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1. Monash University, Melbourne, Australia

The "21st century microscope" will not be a single instrument; rather it will be an orchestration of specialised imaging technologies, data storage facilities, and specialised data processing engines. This interactive presentation will detail two unique Australian national projects that are creating an integrated computer environment for researchers who work with imaging data – with a particular focus on the neuroinformatics community.

The Multi-modal Australian ScienceS Imaging and Visualisation Environment (MASSIVE – www.massive.org.au) is a specialised high performance computing (HPC) facility for computational imaging and visualisation. This facility provides the hardware, software and expertise to drive research in the biomedical science, materials research, engineering, and neuroscience communities, and it stimulates advanced imaging research that will be exploited across a range of imaging modalities, including synchrotron x-ray and infrared imaging, functional and structural magnetic resonance imaging, x-ray computer tomography (CT), electron microscopy and optical microscopy.

MASSIVE is a unique Australian facility with a focus on fast data processing, including processing data "in-experiment", large-scale visualisation, and analysis of large-cohort and longitudinal research studies. The facility runs an instrument integration program to allow researchers to more easily process imaging data, and provides a remote desktop environment providing access to common interactive analysis and visualize tools.

A major undertaking under the MASSIVE program, is the NeCTAR-funded Characterisation Virtual Laboratory (CVL), a project that is developing software infrastructure to provide easier access to the tools and techniques that researchers use to process, analyse and visualise imaging data.

MASSIVE has supports over 25 Australian neuroinformatics projects. These include:
• Researchers processing, analysing and viewing data generated by advanced imagingequipment, such as the Australian Synchrotron Imaging Beamline, new generationComputed Tomography (CT), Magnetic Resonance Imaging (MRI), and othertechniques.
• Researchers undertaking large-cohort studies and longitudinal studies such as theASprin in Reducing Events in the Elderly (ASPREE) study and the IMAGE-HDHuntingtons study.
• Scientists applying computer tomography techniques or volume visualisation and analysis techniques.

• Researchers who are applying advanced image processing, image analysis, orvisualisation techniques, or undertaking research in these fields;
• Researchers running or developing modelling and simulation applications, inparticular applications that are suited to fast file system access or GPU hardware;

Neuroinformatics support on MASSIVE and the CVL is provided through two major programs: an Instrument Integration program, and the MASSIVE Desktop.

Instrument Integration
MASSIVE has a dedicated program to integrate imaging instruments with high performance computing capability (Figure 1). The result of this work allows scientists the ability to usecomplex and computationally demanding data processing workflows within minutes of imagecapture. Instruments integrated with MASSIVE include that are of particular interest toneuroscientists include:

• MRI and CT equipment at Australian National Imaging Facility locations acrossAustralia; and
• Beamlines at Australian Synchrotron including near real-time CT reconstruction on the Imaging Beamline.

This work allows scientists to visualise and analyse collected data in near real-time, as theexperiment is in progress or shortly after it completes. In particular, groups that are imaginglive anesthetized animals must be able to establish whether a previous scan has successfullyproduced the desired data – before proceeding with the next step of the experiment. Theseexperiments are typically time-critical as the window of the experiment once begun is short. Insome cases the images captured by detectors at the Imaging Beamline are very large andnecessitate the movement of data sets in the terabyte range. These constraints dictate thatsignificant computing power is available on demand and that the computer is tightly coupled to the instruments and available on-demand by researchers.

Remote Desktop Environment

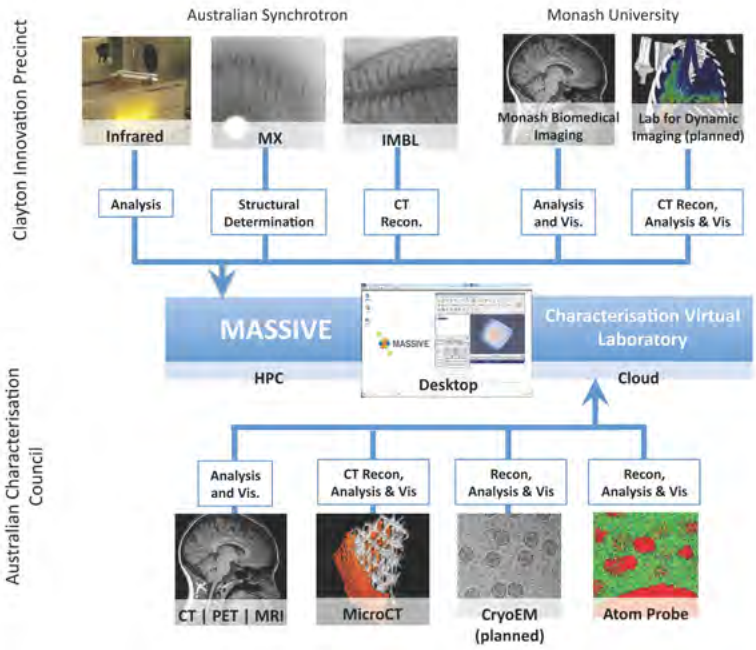
MASSIVE provides users with an easy access managed scientific desktop – an interactiveenvironment for analysis and visualisation of multi-modal and multi-scale data (Figure 2). Thisenvironment provides researchers with access to a range of existing tools and software, including commercial and open neuroinformatics applications.

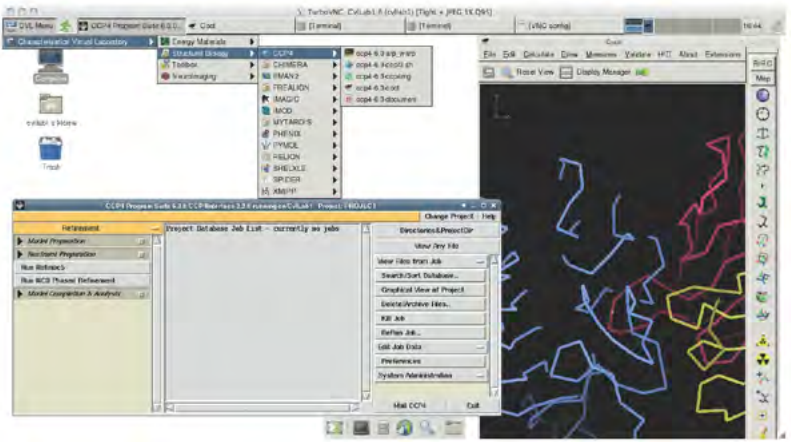
This service has proved to be popular amongst a range of MASSIVE neuroscience users for anumber of reasons:

• The desktop supports a community that is relatively new to HPC, providing arecognizable environment. Common neuroimaging applications such as FSL andSPM have been

integrated to allow users to transparently submit HPC jobs without HPC knowledge;
• As data and study sizes increase it becomes more logical to perform data analysisand rendering at the very location where the data is stored and alongside systemssuch as MASSIVE and nearby storage systems;
• Together with the Instrument Integration program, the desktop provides an end-to end solution – allowing researchers to view and analyze images shortly after capture;
• Performing analysis and visualisation centrally allows researchers to accessperformance hardware, including fast file systems and GPUs;
• A remote desktop allows the CVL to support a wide range of analysis tools anddoes not require wrapping or reengineering of those tools.

Interactive Demonstration
This interactive presentation will demonstrate the work done under these two programs.





OP08 Mining resting-state and task-activation fMRI databases: models and software

Gael Varoquaux[1], Yannick Schwartz[1], Alexandre Abraham[1], Alexandre Gramfort[1] and Bertrand Thirion[1]
1. INRIA, Gif sur Yvette, France

P08,Mining resting-state and task-activation fMRI databases: models and software,," INRIA,,Gif sur Yvette,France",,0,Oral presentation,Neuroimaging,"There is an increasing number of databases comprising a very large number of fMRI images: ranging from heterogeneous collections of resting-state acquisitions performed across centers (1000 functional connectomes project), to rich cohort studies bringing in cognitive labels via task-evoked mapping in addition to intrinsic functional and anatomical connectivity (Human Connectome Project, or the cognitive pillar of the Human Brain Project).

We present recent progress in mining these datasets to extract a high-level description of brain organization. We discuss not only models, but also software efforts to make the models available as a data-processing tools to a wider public.

Uncovering unknown structure from these massive fMRI datasets is a challenging problem. Independent component analysis and clustering have been successfully used on rest and task-evoked meta-analytic databases [Smith 2009, Laird2011], but their success is not easily linked to neuroscientific hypothesis, and it is unclear how they can be adapted to profit from the richer cognitive information that is present in new databases.

The hypothesis of functional segregation, central in neuroscience, can be used mine fMRI images for functionally-specialized systems, for instance using clustering [Tononi1998]. In particular, it implies that each cortical subsystem responds primarily to a small number of elementary cognitive tasks. Given a large dataset of images, this hypothesis can be use to ground a sparse dictionary-learning procedure to extract both cognitive latent factors and the corresponding brain maps. Indeed, sparse dictionary learning is a modern machine learning tool that seeks a components in the data that are expressed in a small number of observations. The procedure can be enriched with a explicit model of inter-subject variability, or spatial constraints to extract regions.

On resting-state data, sparse dictionary learning can be used to extract an atlas of networks of intrinsic brain function [Varoquaux2011]. Although the corresponding time-courses have no associated cognitive labels as they are drawn from uncontrolled resting-state experiments, the large amount of rest imaging data available is a good candidate to capture the spatial structure of the fMRI image. Recent methodological progress adding a region-extraction prior to dictionary learning [Abraham2003] yields a brain parcellation (Fig 1) that is more stable and more suited to explain the data than clustering approach when drawing randomly subjects from a large population.

On large databases of task-activation fMRI maps, dictionary learning can extract cognitive atoms to single out specialized brain regions or networks [Varoquaux 2013]. These cognitive atoms can be expressed as loadings on the experimental conditions or the corresponding contrasts (Fig 2). As opposed to resting-state data processing, dictionary learning applied to task-evoked data enables cognitive labeling of brain structures.

Dictionary learning thus provides a common model to analyze large fMRI datasets drawing from rest and from task, by building upon functional specialization. Suitable priors must be applied to model the specificities of each experiments [Varoquaux 2011, Varoquaux 2013, Abraham 2013]: this generic machine-learning tool must be adapted to fMRI data and neuroscience goals.

The corresponding algorithms are challenging to implement and out of reach of most neuroscientists. To provide tools and building blocks to mine large-scale fMRI databases, we develop the core machine learning algorithms in the Python machine learning library ""scikit-learn"" [Pedregosa] and are in the process of building a neuroimaging-specific adaptation layer to it (http://nisl.github.com). Beyond dictionary learning, this software strategy gives to the neuroimage community access to many machine-learning and data-mining tools. We expect these tools to be instrumental in getting the most out of the increasingly large neuroimaging databases.

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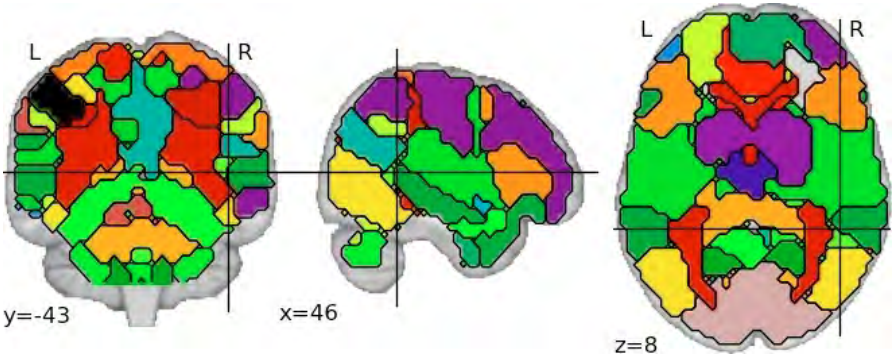
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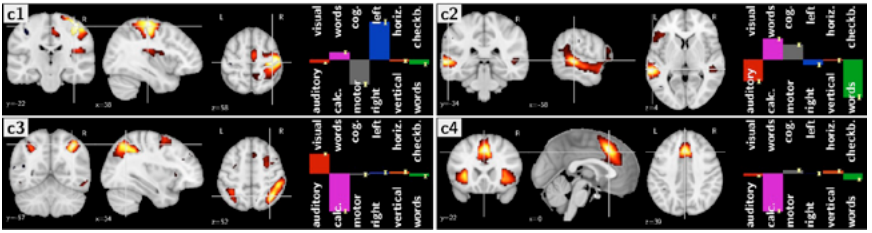
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OP09 The Neuro Bureau Preprocessing Initiative: open sharing of preprocessed neuroimaging data and derivatives

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Introduction
Grass-roots initiatives such as the 1000 Functional Connectomes Project (FCP) and International Neuroimaging Data- sharing Initiative (INDI) [1] are successfully amassing and sharing large-scale brain imaging datasets, with the goal of recruiting the broader scientific community into the fold of neuroimaging research. Unfortunately, despite the increasing breadth and scale of openly available data, the vast domain-specific knowledge and computational resources necessary to derive scientifically meaningful information from unprocessed neuroimaging data has limited their accessibility. The Neuro Bureau Preprocessing Initiative [2] has taken on this challenge, generating and openly sharing preprocessed data and common derivatives for the large-scale ADHD-200 dataset [3]. This initiative has grown to include preprocessed DTI data and derivatives for 180 healthy individuals from INDI's Beijing Enhanced Sample [4]. The next planned release will include resting state and structural data from the 1,112 subject Autism Brain Imaging Data Exchange (ABIDE) dataset [5].

Methods
Four teams are currently participating in the preprocessing initiative, each one using different toolsets and preprocessing strategies (fig. 1). Preprocessed data, derivatives, and quality control metrics are made openly available for download through the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) [6]. The ADHD-200 release included two fMRI preprocessing pipelines as well as maps of grey matter density for voxel-based morphometry (fig. 1). The Beijing diffusion imaging release includes DTI scalars along with voxel specific diffusion distributions for performing probabilistic tractography. Figure 2 illustrates various derivatives generated through these initiatives. The future ABIDE preprocessing initiative will incorporate three functional preprocessing piplines and cortical measures (fig. 3). The analytical procedures employed in the preprocessing are extensively documented on the NITRC website [2].

The Neuro Bureau preprocessing initiative also includes an on-going working group to release derivatives, which can be readily compared across different preprocessing strategies, so that investigators can directly test the impact of the method- ological choices on the scientific outcome of a study. Most of the ong-going work consists of improving and harmonizing the quality control procedures and the derivatives generated by different processing pipelines. Interested teams are welcome to join the effort and contribute new analytical pipelines for future release.

Results

Intended to buttress the ADHD-200 Global Competition [7] and accelerate ADHD imaging research, the ADHD-200 preprocessing effort has yielded more than 6,500 downloads from 780 unique IP address globally (see fig. 4), inspired a team of biostatisticians to win the competition and resulted in eight peer-reviewed publications - with many more in preparation or submission. The DTI preprocessing initiative has resulted in 572 downloads from 134 unique IP addresses. Based on the success of the previous preprocessing efforts four teams have agreed to continue this effort by preprocessing the recently released ABIDE dataset (fig 3).

Conclusion

By openly sharing a wide range of preprocessed data and derivatives, the Neuro Bureau Preprocessing Initiative seeks to make neuroimaging research accessible to a wider audience of researchers. It has already enabled computer scientists, mathematicians, and statisticians who lack neuroimaging expertise to develop and test novel data analysis strategies. We see several important benefits to our initiative: (1) facilitate the generation and test of novel hypotheses about brain function, (2) provide a resource to train future generations of neuroimaging researchers and, (3) facilitate the replication of published results by providing a benchmark set of test images. By providing a breadth of derivatives and preprocessing strategies, we also hope to establish a platform for comparing their relative merits, as well as testing the robustness of neuroscientific findings. This already broad resource will soon be enhanced by the inclusion of the phenotypically rich ABIDE dataset which consists of data from an important clinical population.

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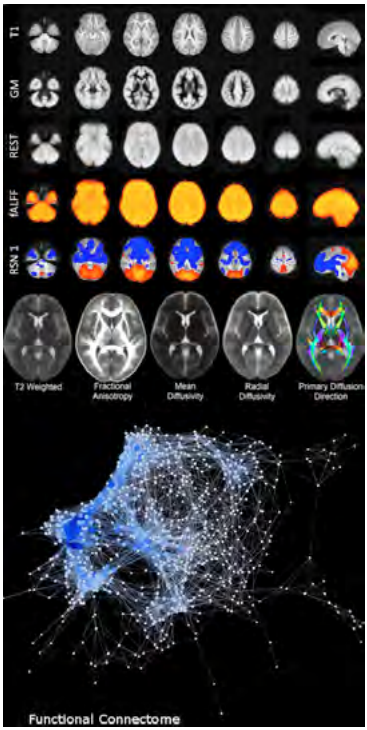
[6] http://www.nitrc.org
[7] http://fcon_1000.projects.nitrc.org/indi/adhd200/index.html

A. Functional Derivatives

Pipeline	Athena	NIAK
Tools	FSL and AFNI	NIAK, MINC, and PSOM
Dataset	ADHD-200	ADHD-200
Analyses	VBM and R-fMRI	R-fMRI
Infrastructure	Virginia Tech Athena HPC	CBRAIN pan-Canadian HPC network

B. Structural Derivatives

Pipeline	Beijing DTI	Burner
Tools	FSL	SPM
Dataset	Beijing Enhanced	ADHD-200
Analyses	DTI	VBM
Infrastructure	Swiss Federal Institute of Technology HPC	

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Nigeria
Ethiopia
Venezuela
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DR Congo
Tanzania
Indonesia
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Angola
Bolivia
Namibia
Madagascar
Indian Ocean
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Botswana
Australia
South Pacific Ocean
South Atlantic Ocean
South Africa
Argentina
New Zealand

P78 Partitioning age-related changes in brain activation using a virtual performance task to simulate complex movements

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Aging has become a serious social issue, especially in Asian countries. In order to maintain the activities of elderly people, social programs to promote physical and mental exercises are conducted. Although some investigations have reported that those activities potentially contribute to the prevention of cognitive decline [1], the neurological background has not been systematically verified. We investigated the availability of a virtual performance task designed from such exercises as a model to test age-related changes in brain function [2].

An event-related fMRI task representing the motor behavior in the bean transfer test (BTT), which is used as one component of the test battery to evaluate the physical ability of elderly in Japan, was designed. The task consisted of two operations using a 2 by 2 turnkey system. With the left-hand key, a small, round object (bean) is pinched with two lines representing chopsticks. Then, the object with chopsticks is moved to a round target (pot) with the right-hand key to put the bean in. The behavioral data were marked with 6 checkpoints (Fig.1). The onset of each trial was determined using the sum of two jittering factors, the execution time for each trial by the subject and periodically altering the interval time before the onset of each trial. fMRI data were obtained using the EPI sequence on a 3T MR scanner, and the data sets were analyzed using SPM8.

fMRI data were obtained from 11 elderly (over 60, 6 females) and 7 non-elderly (under 54) volunteers. In the activation representing the total trial, the network for the upper visuo-spatial transformation tract and higher motor control was observed in the elderly (two-sample t-test, $p<0.05$). Differential peaks between the two age groups were detected as augmented activation in the left BA5 ([-23 -38 59]) and bilateral BA6 ([-60 -2 47], [60 2 38]) in the elderly group (Fig.2, CPall). In the partitioned maps, it was indicated that this difference was mostly contributed to by the first task switching point (CP2) and pinching the object (CP1). Activation of these areas was not significant in the CP3 and CP4 map in the elderly. On the other hand, activation was augmented in the dorsal visuo-motor pathway in the young subjects during these steps. It was suggested that these results represent: 1) a higher demand for visuo-spatial transformation by adjusting the asymmetric (two independent) rotation of the sticks, and 2) a lower frequency of object transference to the goal than pinching it in elderly subjects. By recording self-paced object manipulation in the interactive task, complex brain activation during a combined motor processing could be more precisely attributed to cognitive elements. This feature was useful to further partitioning age-related changes in brain activation.

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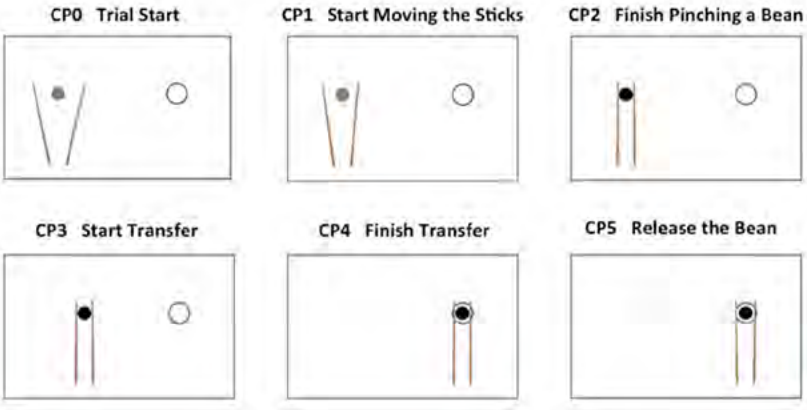

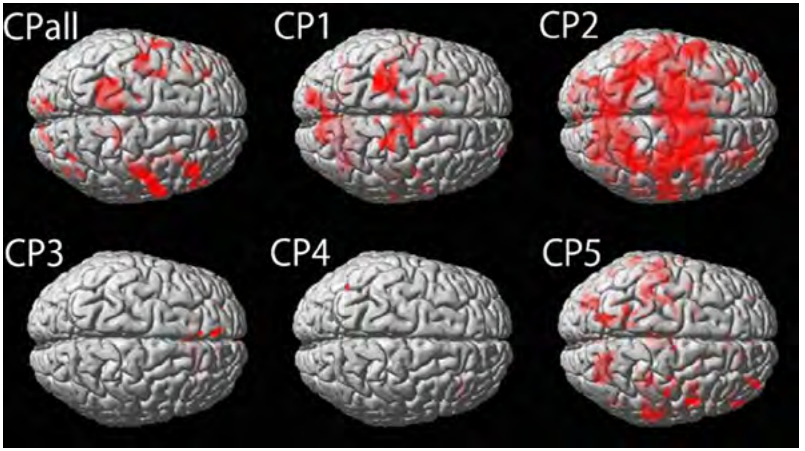

P79 Global Structural Brain Networks underlining Binocular Rivalry

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Introduction: This study reports how the global organization of the structural brain network relates with stability of perceptions in Binocular Rivalry. Binocular Rivalry is a phenomenon which is shown when right and left eyes are presented with different images simultaneously at the same retinal position, then the perceptions of the two images compete, and shift back and forth between them. For many decades, psychophysical and neuroscientific researches have asked where the competing neuron pools exist in our brain: Especially, contributions of low-level visual regions, such as the primary visual cortex or lateral geniculate nucleus, and/or high-level visual regions, such as extrastriate visual regions, were often discussed (Logothetis et al., 1996; Lee, Blake, 1999; Kovacs et al., 1996; Lee, Blake, 2004; Logothetis, Schall, 1989; Tong et al., 1998; Wunderlich, et al., 2005; Haynes et al., 2005). Additional to these researches, several fMRI studies reported that prefrontal and parietal regions also become active at the times when perceptions alternate (Lumer, Friston, 1998; Knapen et al., 2011). Although many studies reported contribution of various brain regions to Binocular Rivalry, there is no study about what structural brain networks lay behind dynamic interactions among these various brain regions. From these backgrounds, we asked how structural brain networks relate with perceptual alternation phenomenon in Binocular Rivalry. Especially, we tried to find properties as the global organization of the structural brain network.

Methods: Ten male and seven female right-handed volunteers (aged from 20 to 29, normal or corrected-to-normal vision) joined the experiment. After informed consents, we performed the Binocular Rivalry experiment for one hour total and DTI recordings. The analysis process consisted of four proceedures: First, we performed noise reductions and co-registrations, and calculated three dimensional maps of Fractional Anisotropy (FA) values. Second, we created 68 cortical and 16 subcortical region of interests (ROIs) in FreeSurfer. Third, we reconstructed fiber tracts connecting between each pair of these ROIs by tracking the vector map of FA values using the FACT algorithm (Mori, Barker, 1999). Fourth, we evaluated correlations between the differences among the mean FA values in individuals' fiber tract bundles and the differences among individuals' speeds of perceptual alternation. Here, the fiber tract bundle showing positive or negative correlation was named positive or negative Correlation Networks (CNs) respectively.

Results: Figure (a) shows a spatial map of these two types of fiber tract bundles, which were entangled with each other. Red lines indicate positive CNs, and blue lines indicate negative CNs. The thick lines represent significantly strong connections because the Correlation 0.7 corresponds with expected value of false discovery rate 0.05 [Benjamini, Hochberg,

1995]. From these entangled networks, we observed the difference of averaged values of the Correlations for cortical regions and for subcortical regions. Figure (b) is the average of the correlations in cortico-cortical connections. Figure (c) is the averaged correlation in subcortico-subcortical connections. Figure (d) is the comparison between averages of all bars in (b) and (c). These results showed that all subcortical regions strongly connect with negative CNs, and that many cortical regions strongly connect with positive CNs. The ratio of number of positive to negative connections also showed the same inverse trend between cortex and subcortex as averages of correlations.

Conclusions: This study revealed, for the first time, the global organization of brain networks relating to stabilization and destabilization of perceptual alternation. Revealing the general contrast between the contribution of the cortical regions to destabilization and the contribution of the subcortical regions to stabilization of perceptions in Binocular Rivalry will help to give deeper understandings of interactions between many brain regions and will further develop this idea of global interaction beyond the individual brain regions previously discussed.

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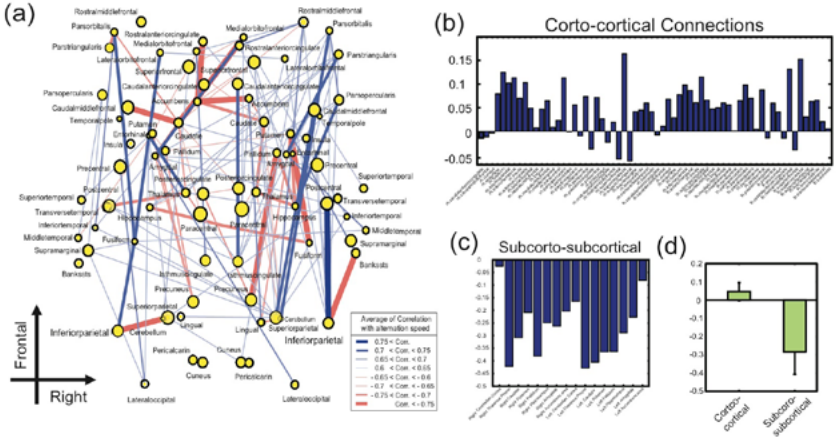
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Subcorto-subcortical
(d)
Cortico-cortical
Subcorto-subcortical

P80 Signal-to-noise rationale in fMRI

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fMRI data are often characterized by their signal-to-noise ratio (SNR). In general, the SNR compares the level of a desired signal to the level of background noise. While this concept is quite straightforward for MRI data, this is not trivial for fMRI data. In the case of MRI data, the determination of SNR is image-based and can be conceptualized by comparing the mean signal of the MRI image to the background noise of the image (Edelstein et al., 1986; Parrish et al., 2000). As Parrish et al. (2000) pointed out, for fMRI data it is not at all clear whether the SNR is image-based or time-based. In essence, the question is how to capture the information related to the signal and the noise based on the 4D fMRI dataset. In the literature, several definitions have been proposed. In these definitions the desired signal is represented for example by the amplitude of the signal (e.g. Joel et al. 2011), or the standard deviation of the activation (e.g. Penny, 2011). The use of these ad-hoc definitions decreases the comparability of fMRI studies. During our presentation we will give an overview of existing definitions based on the fMRI literature. By constructing reference tables, we provide insight in the relations among the definitions. In addition, we will present some simulation results that reveal the connection with the power to detect activation in fMRI data.

To conclude, a unified SNR definition might be unreasonable because the measurement depends greatly on how the signal of interest is defined. Still, for fMRI data, a minimal requirement should be that the definition is directly related to the activation signal.

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P81 EEG-fMRI fusion on the cortical surface using Coupled Tensor-Matrix Factorization: A simulation study

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4. Istanbul Sehir University, Istanbul, Turkey

Although it is a challenging problem in neuroimaging to merge the data coming from different modalities on a common spatial domain, the integration of EEG and fMRI offers us an opportunity to reveal the complex dynamics of brain functions and neuronal interactions (Bayram et al., 2011).

In this study, a novel EEG-fMRI fusion approach based on multilinear methods is developed and applied to simulated data. We treat EEG data as a three-way array with temporal, spectral and spatial dimensions. We perform coupled tensor-matrix factorization (CTMF) to obtain common spatial signatures between fMRI and spectral EEG data (Acar et al., 2011). The EEG inverse problem is also incorporated into the merging process to obtain a common image on the cortical surface. We improve the spatial signature estimation by using the alternating least squares algorithm in a hierarchical manner where the noise and factor covariance are also exploited. Unlike conventional CTMF algorithms where a single dimension is considered to be fully coupled between two datasets, we project part of the datasets on a common and part on discriminative subspaces (Liu et al., 2013). This enables us to deal with the cases in which EEG and fMRI sources differ. By this way, our proposed algorithm is able to show both coupled and uncoupled responses at the same time.

In the simulation, we generated EEG/fMRI data from one deep and two superficial sources. Deep source is common to both modalities and each of the superficial sources is specific to one modality. Results of the simulation show that CTMF algorithm with inverse problem successfully localizes the sources. (Maximum values of the fMRI spatial components overlap with the real sources; common spatial EEG component overlaps with the real source and the distance between the maximum value of the uncommon EEG spatial component with the real one is 11 mm.) Also, algorithm correctly identifies common and distinct sources (See the figure).

Brain activity reflected in different domains is integrated on the same spatial scale by this approach. Our current research focuses on applying the method on real data.

Figure 1: Three different source locations are chosen on the cortical surface. Deep source is located in middle temporal gyrus and superficial source specific to fMRI is on the right superior-frontal cortex and superficial source specific to EEG is on the left superior-frontal cortex. fMRI temporal pattern is constituted by convolving hemodynamic function with a

boxcar. EEG source signal is generated from sinusoids oscillating at 4 and 12 Hz. Channel EEG is obtained by projecting source signal onto the sensor space with lead field matrix. First two rows shows the fMRI spatial and temporal components found from CTMF algorithm. Last two rows are the EEG components. First column is the spatial signature of the EEG in the source space, second column is temporal signature, third is the spectral signature and final column is the spatial signature of the EEG in the sensor space.

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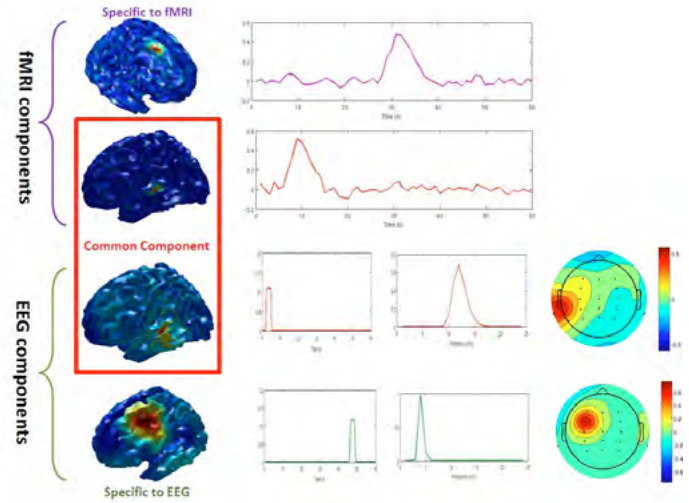

P82 Towards a universal error measure in connectomics using the variation of information

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Connectomics concerns the description and analysis of neuronal wiring diagrams. This is usually accomplished by imaging neuropil (the dense network of neuronal processes) in 3D using serial-section electron microscopy, followed by delineating the neurons in those images. The latter step has been achieved by manual skeleton tracing (ST) [e.g. Helmstaedter et al, 2012] or by semi-automatic volumetric segmentation (VS) [e.g. Jain et al, 2011] (See Figure 1). These methods extract neuronal morphology and connectivity information from the image data, and have different characteristics in scalability, errors, and speed of reconstruction. It is notoriously difficult to compare them. ST accuracy can be measured by the error-free path length (EFPL) [Helmstaedter et al, 2012], while VS accuracy is most frequently estimated with the Rand error [Jain et al, 2011]. These measures, although useful, have limitations that have hampered progress in the field. EFPL is difficult to apply to fully volumetric reconstructions such as those found in [Jain et al, 2011], while Rand error is incomparable even between different datasets reconstructed via VS, let alone ST datasets.

These limitations prevent comparison of accuracy and reconstruction speed between skeleton tracing and volumetric segmentation methods, which makes it difficult to judge which algorithms and tools are most advancing connectomics. Recently, the variation of information (VI) [Meila, 2007] has emerged as a tool to evaluate volumetric segmentations [Kaynig et al, 2013]. VI is an information-theoretic metric defined as the amount of additional information needed to obtain one segmentation given the other. For example, if every neuron obtained by a VS algorithm (A) is actually split in exactly half compared to the true segmentation (T), then when given the true identity of a voxel (3D pixel) in the true segmentation, we need 1 bit of additional information to find the voxel's identity given by the algorithm, so VI(A, T) = 1.

A well-designed, universal error metric is extremely important for neuronal reconstruction; without it, it is difficult to know how to improve existing approaches. The use of VI, however, has remained limited. We show here that VI has many desirable properties that not only overcome the above limitations of Rand error to evaluate VS accuracy, but also allow detailed analysis of the errors encountered by the method being evaluated, enabling rapid iteration and improvement. We further show progress towards demonstrating that VI can translate accuracy between skeletal tracing and volumetric segmentation. This opens for the first time the possibility of placing skeletal tracing tools and VS algorithms on the same speed/accuracy trade-off curve, an advance that would accelerate progress in both areas and thus in all of connectomics.

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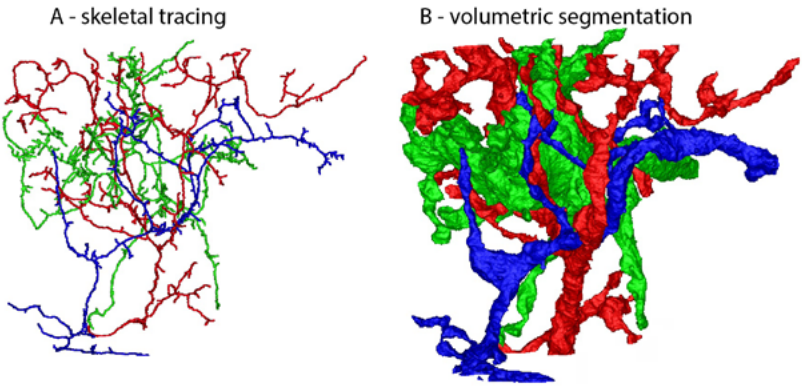

P83 Using the Ontology of Experimental Variables and Values (OoEVV) to model human neuroimaging experiments

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Neuroimaging data is raw material for cognitive neuroscience experiments, leading to scientific knowledge about human neurological and psychological disease, language, perception, attention and ultimately, cognition. The structure of the variables used in the experimental design defines the structure of the data gathered in experiments, which in turn constrains the interpretations of the results that may be presented as experimental conclusions. Representing these interpretational assertions, and the experimental data which support them, in a computable way is needed so that they could be used in logical reasoning environments, i.e. for automated meta-analyses, or linking hypotheses and results across different levels of neuroscientific experiments. Therefore, a crucial first step in being able to represent human neuroimaging results in a clear, computable way is to develop representations for the scientific variables involved in neuroimaging experiments. These representations should be expressive, computable, valid, extensible, and easy-to-use. They should also leverage existing semantic standards to interoperate easily with other systems. We present an ontology design pattern called the Ontology of Experimental Variables and Values (OoEVV). This is designed to provide a lightweight framework to capture mathematical properties of data, with appropriate 'hooks' to permit linkage to other ontology-driven projects (such as the Ontology of Biomedical Investigations, OBI). We instantiate the OoEVV system with a small number of functional Magnetic Resonance Imaging datasets, to demonstrate the system's ability to describe the variables of a neuroimaging experiment. OoEVV is designed to be compatible with the XCEDE/PROV-DM neuroimaging data standard for data collection terminology, and with the Cognitive Paradigm Ontology (CogPO) for specific reasoning elements of neuroimaging experimental designs.

P84 eScience Infrastructure for sharing neuroimaging data and running validated analysis pipelines on a high performance cloud

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Neuroimaging biomarkers are features derived from neuroimaging data that can be used for disease detection, staging, and prognosis, or to monitor the effect of treatment. To discover and validate these biomarkers, sample sizes are needed that exceed the typical size of single-site studies. This is achieved by combining data sets from different medical centers, and requires an eScience infrastructure for standardized image analysis and the exchange of imaging data, meta-data and analysis results. We present a Dutch pilot study to build such an infrastructure, whereby the emphasis is on patient privacy, access control, user agreements and dispatching analysis pipelines to a high performance cloud. The use case is hippocampal volume extraction (Van der Lijn et al. 2008). This analysis pipeline will be validated and applied to a combined data set from four cohorts.

Three types of data need to be stored: (1) Raw medical image data (DICOM), (2) Subject related meta data fields such as age and gender, and (3) derived data which includes the biomarkers. We have selected the XNAT platform (Markus et al. 2007) as a skeleton, and created a java-based tool for client-side anonimization and batch upload of the DICOM files. Patient IDs are first encrypted with a passphrase known to the data-owner, then hashed, following guidelines in Noumeir et al. (2007). Face scrambling is optional, and carried out on the server. A remaining challenge is to refine the XNAT permission system such that (1) data-owners can allow users to run a pre-installed analysis pipeline, without giving them access to the actual data files, and (2) pipeline-owners can allow users to run the pipeline, without making the code open access. Although these features oppose current trends towards open science, they allow inclusion of protected data sets that would otherwise be unavailable.

Biomarker extraction pipelines are often computationally intensive; the hippocampal

volume pipeline takes several hours on a present day compute node for a single image. We will dispatch jobs to a high performance cloud, whereby jobs runs in a virtual machine (VM). This solution has two advantages over traditional grid computing: (1) the pipeline developer can choose the operating system and software running on the VM; and (2) since the VM gets destroyed after the pipeline finishes, no sensitive data can accidentally be left on the compute node.

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P85 VisN: Neuroimaging Toolkit for Medical Image Visualization

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The National Intrepid Center of Excellence (NICoE) performs patient care and research of traumatic brain injury (TBI) and related psychological health conditions for United States armed forces. This research includes multi-modal neuroimaging acquisitions that are not available in current clinical medicine. VisN has been developed to apply existing open-source image processing libraries to demonstrate the potential of next-generation radiology to aid in the understanding of mental health. VisN extends the open-source Medical Image Processing, Analysis, and Visualization (MIPAV) program and uses the ImageJ program (Schneider, 2012) developed at the National Institutes of Health to provide a PACS-like system to radiologists that provides memory management and distributed database access functionality not yet found in clinically oriented software. The result is a familiar interface for the radiologist, as in Figure 1, while still allowing the application of emerging image processing tools. VisN can apply transformation matrices and non-linear volumetric transformation maps ad-hoc to the medical image fusion process. Once overlaid, VisN can define statistical parameters of interest for the visualization of functional activations. Tractography information is available using Camino (Cook, 2006). Finally, regions of interest can be selected and visualized on a volumetric basis, as shown in Figure 2. This provides a focus on real-time image processing tools that are manipulated through an integrated interface shown in Figure 3. VisN provides an open-source framework for emerging neuroimaging needs in radiology software. NICoE's imaging protocol combines clinically useful structural images with images that do not have an immediate clinical application but may provide useful research information. Research images include functional, diffusion, spectroscopy, susceptibility, and perfusion MRI studies. Fluorodeoxyglucose (FDG) positron emission tomography (PET) images, broad electroencephalography data, and spatially localized magnetoencephalography (MEG) are also available. These multi-modal, spatially variable image sets make it difficult for commercially available image processing systems to provide the flexibility needed to conduct this research. VisN advances the state of accessible image processing to provide a viable platform for advanced neuroimaging-related software which can easily be translated into a radiology environment.

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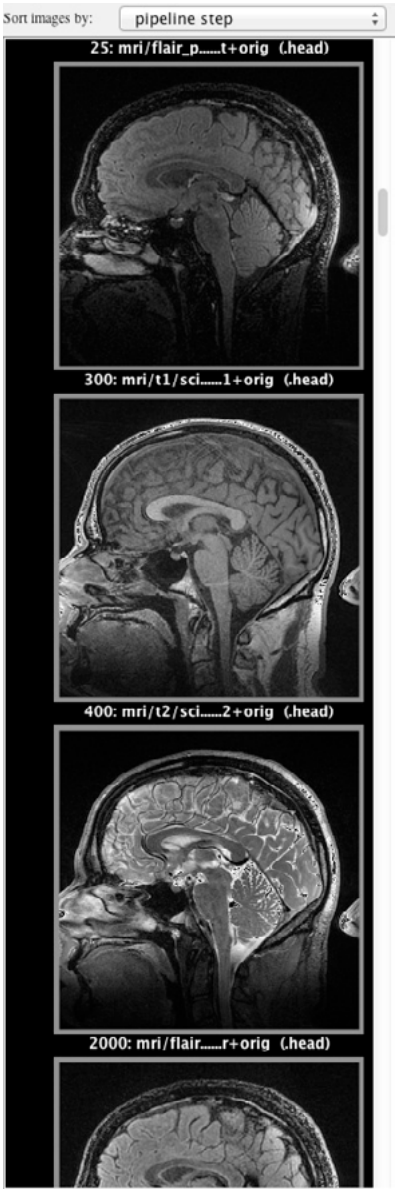
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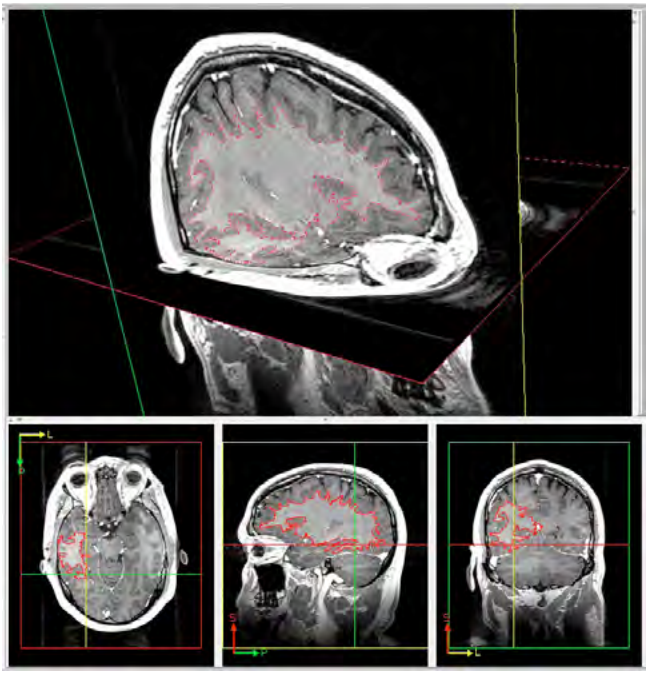

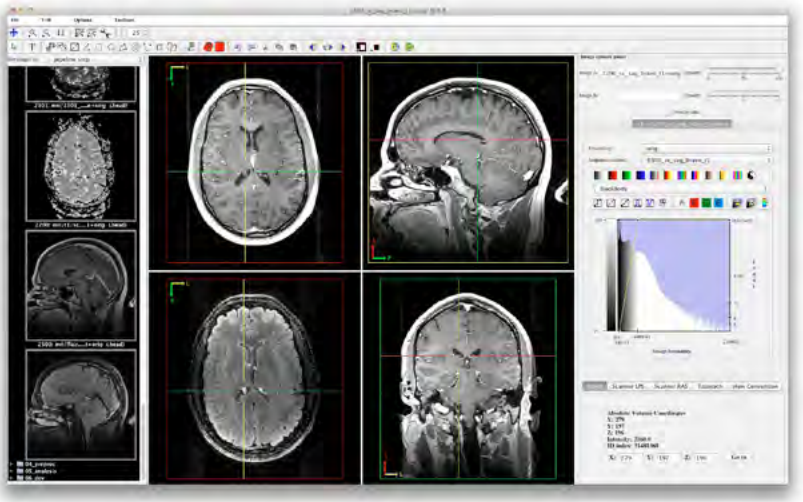

P86 Human brain functional networks during automatic and conscious processing of musical emotions

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Different cognitive strategies, explicit and effortful vs. automatic and implicit, may be involved in the perception and induction of emotions. In the visual domain, implicit emotional responses depend on subcortical neural structures whereas explicit processing of emotions relies on networks of cortical regions. However, virtually nothing is known about explicit and implicit processing of emotions in the auditory domain. In this study, we aimed at determining the neural circuits responsible of affective experiences of music. Also, mindful of the idiosyncrasy of these emotions and their high dependence on the individual's listening biography, internal state and traits, we tested whether the underlying neural circuits of explicit and implicit processing of musical emotions would be modulated by individual factors.

Forty subjects listened to 4-sec clips from film soundtracks, rated as fearful, happy, or sad in a previous behavioral study. We utilized functional magnetic resonance imaging (fMRI) to measure the brain activity during an implicit emotion condition, when subjects focused on distinct aspect of the music (the number of musical instruments), and an explicit emotion condition when subjects classified the emotion perceived in the same musical stimuli.

Implicit emotion processing of the musical stimuli recruited a network of core, subcortical structures, including the amygdala and parahippocampal gyrus, typically involved in the fast, spontaneous affective reactions in other modalities. Explicit processing instead predominantly activated cortical areas previously associated with the cognitive processing of music and emotional recognition and regulation. Investigation of the effects of individual factors in the brain responses to musical emotions revealed an important role for personality, mood, and musical expertise in modulating limbic and cortical activity. Furthermore, by means of a graph-based network analysis, we mapped the interdependence of neural activity among regions of the human brain. Results evidenced enhanced functional connectivity of the subcortical areas during implicit processing of musical emotions.

P87 Naively successful: Naïve Bayes with and without decision trees for automated annotation of human neuroimaging abstracts

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Introduction: We are developing prototype tools for the automated extraction of metadata from collections of fMRI abstracts. The Cognitive Paradigm Ontology (CogPO) defines ontological relationships between terms pertaining to fMRI experiments. BrainMap is a database describing these experiments, which is annotated by human experts guided by the CogPO terms. We explored the performance of a naïve Bayes classifier (with several transformation approaches for this multi-label task) and the combination of the classifiers with decision trees. These efforts aim at improving the workflow for filtering and classification of fMRI papers into usable and relevant groups for further meta-analysis, storage, or annotation within other software frameworks.

Methods: The CogPO annotations for the gold standard corpus were from seven categories: Each abstract had at least one and possibly more labels drawn from Paradigm Class (e.g., Stroop), Behavioral Domain (e.g., Attention), Stimulus Types (e.g., Faces), Stimulus Modalities (e.g. Visual), Instructions (e.g. Remember), Response Types (e.g. Button Press), and Response Modalities (e.g. Foot). Using naïve Bayes and either binary relevance or a label powerset transformation, we trained the classifiers on the gold-standard set of 247 abstracts. Performance using these classifiers was then assessed for each category. To determine whether a hierarchical approach could leverage the internal structure of these categories, we created decision trees for combining these categories of annotations. We trained multiple decision trees based on each of the terms of a given category being chosen as the root node. For annotating new samples from a test set, we determine which of the terms is the likeliest tag using the naïve Bayes results. Then we follow the appropriate decision trees to obtain tags for all the categories.

Results: Our naïve Bayes classifier on annotation terms in each dimension produced surprisingly good results. The integrated F1-micro measure for the various categories and methods ranged from 0.3 to above 0.8; the proportion of abstracts labeled with the exact matching set of labels (i.e. no extra labels, and all the correct labels identified) varied as well across the categories, with a mean of 0.42. The Bayesian decision trees performed slightly better than naïve Bayes on each category alone. Incorporating expert knowledge through identifying correctly one of the category labels (e.g., starting with the correct label for Stimulus Type), improved performance on the remainder of the categories.

Conclusions: We recognize that journal article abstracts will likely not provide adequate

information for complete classification. The ability to identify the correct set of labels in each category was influenced by the number of possible labels (categories with more labels to choose from had worse performance than categories with fewer), and by the number of labels per instance (performance was better for abstracts with fewer labels), as well as by the dependencies captured by the decision tree hierarchies. The methods presented here are generic and can be extended to the full-text of articles (or subsections). Although our algorithms cannot completely replace a human annotator, they can serve as a valuable aid to complement the annotation process for a human expert, and may lead to reduction in time and effort.

P88 The XNAT Ecosystem

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The XNAT imaging informatics platform is widely used to manage a variety of neuroimaging research, from internal research programs to large-scale data sharing initiatives. While XNAT has been open source since its inception and developers from around the world have contributed to its features, the number of contributions has been limited due to the scale and complexity of the XNAT code base. However, with the inclusion in recent releases of XNAT of an open application programming interface (API) based on the REST web services model, many more developers are developing tools that interact with XNAT through the API without needing to learn XNAT's internal code. Examples include pyXNAT, a python library for exchanging data with XNAT; Connectome Workbench, a visualization and analysis platform for structural and functional MRI data; and 3D Slicer, an advanced medical image visualization suite; and LONI Pipeline, a GUI-based application for executing and managing automated processing streams. A variety of additional tools are currently in development. The most recent version of XNAT includes a plugin architecture that enables developers to build new capabilities directly in XNAT with minimal interfacing in the core code. Modules can include visual components as well java code and extensions to the XNAT REST API. As an example, our lab has produced a module that enables users to pull XNAT metadata into iCal calendar feeds. These feeds can be used to assist study monitoring by integrating views of data in scheduling systems (e.g. Google calendar) by the date and time of acquisition in an integrated view with scheduling. To assist in dissemination of XNAT related software, we have developed a sharing resource called XNAT Marketplace (https://marketplace.xnat.org) where developers can contribute and share modules, scripts, and other tools along with documentation. XNAT Marketplace interface and features were designed following patterns established by similar software dissemination sites such as Firefox Add-ons (https://addons.mozilla.org/en-US/firefox/extensions/). Marketplace includes categories, featured plug-ins, a search interface, a tool upload interface, and tool versioning. Together, the API, XNAT plugins, external tools that interact with XNAT, and the XNAT marketplace make up an ecosystem of informatics tools and applications that enable new capabilities in neuroimaging research.

P89 OntoCATI: Towards an ontology of neuroimaging measures in the CATI Platform

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CATI (Acquisition Centre and Image Processing, a French national platform supported by the Alzheimer's Foundation [1]) provides software solutions for automatic measurement of different biomarkers related to specific modalities (Figure 1). CATI provides assistance for acquiring, analyzing, organizing and sharing neuroimaging data in the context of multi-centric clinical research studies. Our goal is to support the scientific study of the different working groups (neurologist, MRI PET physician, quality check operations engineer, engineer developing brain imaging tools) and help them to model the knowledge linked to their domain of interest.

We proposed a structured metadata hierarchy for storing information relevant to various aspects of a project (e.g. study, subject, dataset, etc.) along with derived data and process in order to develop improved semantic request and reasoning tools for knowledge extraction on the derived data (for example we would like to compare the hippocampal volumes obtained on different time points). We developed a database schema CATISchema and an ontology OntoCATI [2]. At this stage, the first module of OntoCATI supports the information concerning acquisition, raw data (clinical and neuroimaging), and image processing. This module uses DOLCE [3] as its upper ontology. The image processing generates a multitude of data and derived measures. These measures are potential biomarkers for the Alzheimer's disease (AD).

In order to build the second module of OntoCATI dedicated to these measurements we first focus on the data issued from the modality T1 MRI and on three types of measures: rate of hippocampal atrophy with the longitudinal version of SACHA [4], cortical thickness reduction with Freesurfer (http://ftp.nmr.mgh.harvard.edu/) and opening of primary cortical folds using the longitudinal version of Morphologist-2012 pipeline [5]. An important point in our modeling consists in distinguishing the concept of measure and biomarker. For example, hippocampal volume is considered as the most widely used and admitted biomarkers in the AD to monitor its progression [6]. Therefore in OntoCATI this measure belongs to the sub-class of biomarker. Concerning the other measures the ontology will allow us to determine what measures become biomarkers using queries.

To model the different measurements that are the assignment of numbers to anatomical entities, we need to describe the brain anatomy (e.g., hippocampus), the measure (magnitude, dimensions (units) and uncertainty) and the disease concepts and their

codification. This module of OntoCATI uses the Basic Formal Ontology (BFO) as its upper level ontology [7]. For the anatomy domain we refer to the Foundational Model of Anatomy ontology (FMA) [8], which adopts and extends into BFO [9], a domain-independent, spatio-temporal theory that provides a rigorous ontological framework. Concerning the pathology domain we rely on ICD-10 [10] and UMLS standard [11]. For example to describe the hippocampus, according to FMA, we define hippocampus as a 'gyrus of limbic lobe' that is a 'segment of cerebral hemisphere' that is a subClass of 'Anatomical Entity' that is a subclass of the BFO concept 'independent continuant'. To represent the volume of the hippocampus we create the relation has for volume that is linking the concept of 'hippocampus' to the BFO concept 'three dimensional region' (Figure 2).

This is the first step in our work. In the future, we will integrate other concepts to represent the other measures (cortical thickness, opening of primary cortical folds, etc.). We will also work on the other modalities presented in Figure 1 and we will develop the queries to cross the frontier between measures and biomarkers.

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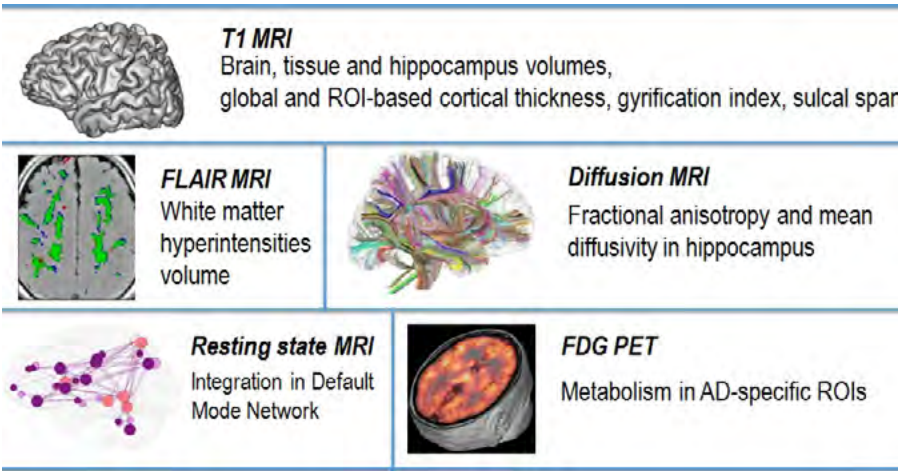
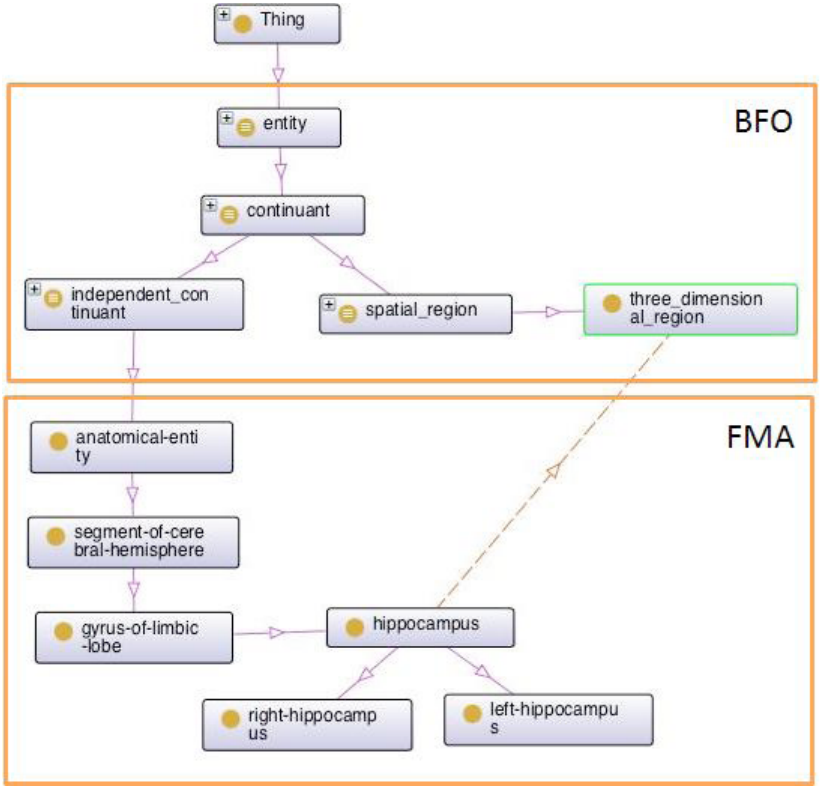

T1 MRI
Brain, tissue and hippocampus volumes,
global and ROI-based cortical thickness, gyrification index, sulcal spar
FLAIR MRI
White matter
hyperintensities
volume
Diffusion MRI
Fractional anisotropy and mean
diffusivity in hippocampus
Resting state MRI
Integration in Default
Mode Network
FDG PET
Metabolism in AD-specific ROIs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P90 Structural MRI predicts biological maturity

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Structural MRI has considerably advanced our knowledge about the complicated process behind brain maturation. Developmental trajectories of grey matter show an inverted-U shaped pattern peaking around puberty, suggesting a biological mechanism of synaptic overproduction followed by pruning [Giedd et al. 1999; Giedd, 2008]. Cognitive milestones happen concurrently with these structural changes, and a delay in such changes has been implicated in developmental disorders such as ADHD [Giedd and Rapoport, 2010]. Accurate estimation of individuals' brain maturity, therefore, is critical in establishing a baseline for normal brain development against which neurodevelopmental disorders can be assessed. In this study, structural MRI scans from a large dataset of normally growing children and adolescents (n = 308) with age ranging from 6 to 22 years were used [Evans, 2006]. Using a completely automated and well-validated pipeline (CIVET), morphological parameters namely cortical thickness and surface area were calculated at 81,924 vertices covering entire cortex. These high-dimensional morphological data were down-sampled to 2,560 points for each morphological parameter and used to build a predictive model to estimate the chronological age via the elastic-net regularized regression [Friedman et al. 2010] that jointly performs variable selection and model estimation. Nested 10-fold balanced cross-validation was used to estimate the model tuning parameters (the inner cross-validation loop) and the prediction error (the outer cross-validation loop). The resultant model accounted for 62% of the sample variance and had mean absolute error of 630 days in the (outer) cross-validation loop (see Figure 1 for a scatter plot where females and males are denoted with blue and green colors) while it provided nearly perfect estimates during the training (variance explained 95% and the mean absolute error of 232 days). In the model averaged over cross-validation folds, we observed that a widely distributed pattern of cortical parameters were utilized in age estimation. The results of our study demonstrate that structural MRI can be used to predict individuals' biological maturity with high accuracy, a critical information that might help in discerning individuals with neurodevelopmental disorders.

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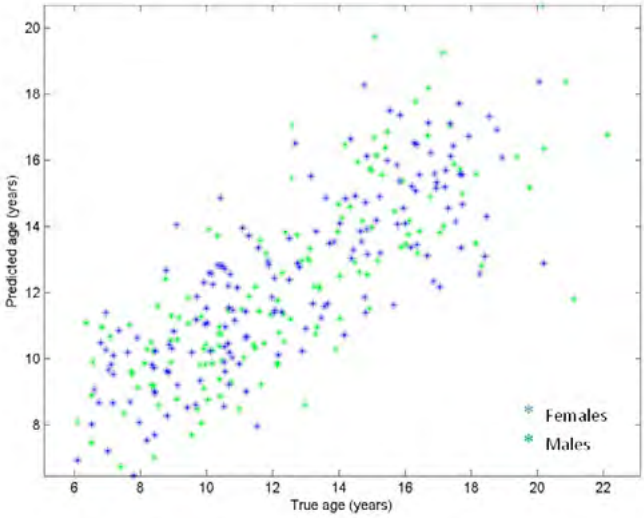
Predicted age (years)
True age (years)
Females
Males
20
18
16
14
12
10
8
6
8
10
12
14
16
18
20
22

P91 Optimizing the task demand to evaluate the activation response in elderly subjects using fMRI

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1. National Center for Geriatrics and Gerontology, Neuroimaging & Informatics, Ohbu, Japan
2. Graduate School of Medicine, Nagoya University, Psychiatry, Nagoya, Japan

It has been reported that eye-finger coordination, which is essential for behaviors in daily life, is potentially impaired in mild cognitive impairment [1] and Alzheimer's disease [2]. The age-related change of brain activation during visuo-motor coordination was studied to explore the possibility to evaluate sub-symptomatic decline of cognitive processing. Twenty healthy young subjects (10 males, 25.2 ± 5.5) and 20 healthy elderly subjects (11 males, 68.2 ± 4.0), all right handed, participated in this study. Bimanual finger-movement tasks were conducted using visual prompting cues to indicate the mode (symmetric or asymmetric) and velocity (1.0, 1.5 and 2.0Hz) of movements. fMRI data were obtained on a 3T MR scanner and processed using SPM8. Behavioral data indicated that not velocity but tapping mode seems to have substantial influence on the task performance. Consistent activation in the precentral gyrus, postcentral gyrus (BA3), inferior parietal lobule (BA37), middle occipital gyrus, and cerebellum was observed in the elderlies. Activation in the middle frontal gyrus (BA9) was augmented depending on the velocity in both age groups. Activation in the primary motor cortex (M1, BA4) was significant under all conditions in the young-elderly contrast, and that in the supplementary motor area (SMA, BA6) was significant in the elderly-young contrasts, respectively. It was suggested that higher M1 activation in the young subjects reflect their accurate motor performance (performance ratio; 0.89 – 1.02) compared with the elderlies (0.49 – 0.65) in this study. This lower performance in the elderlies may explain their higher activation in the SMA. Mode difference efficiently extracted the contrast in the BA9 only in the young subjects, while the activation in the BA9 depended on the velocity in the elderlies. BA9 is one of the areas frequently reported age-related enhancement of brain activation. To conclude, bimanual finger movement within the same mode in the optimized velocity range may be appropriate as a cognitive battery for the elderlies.

References

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P92 OpenCL accelerated connectome analysis in python

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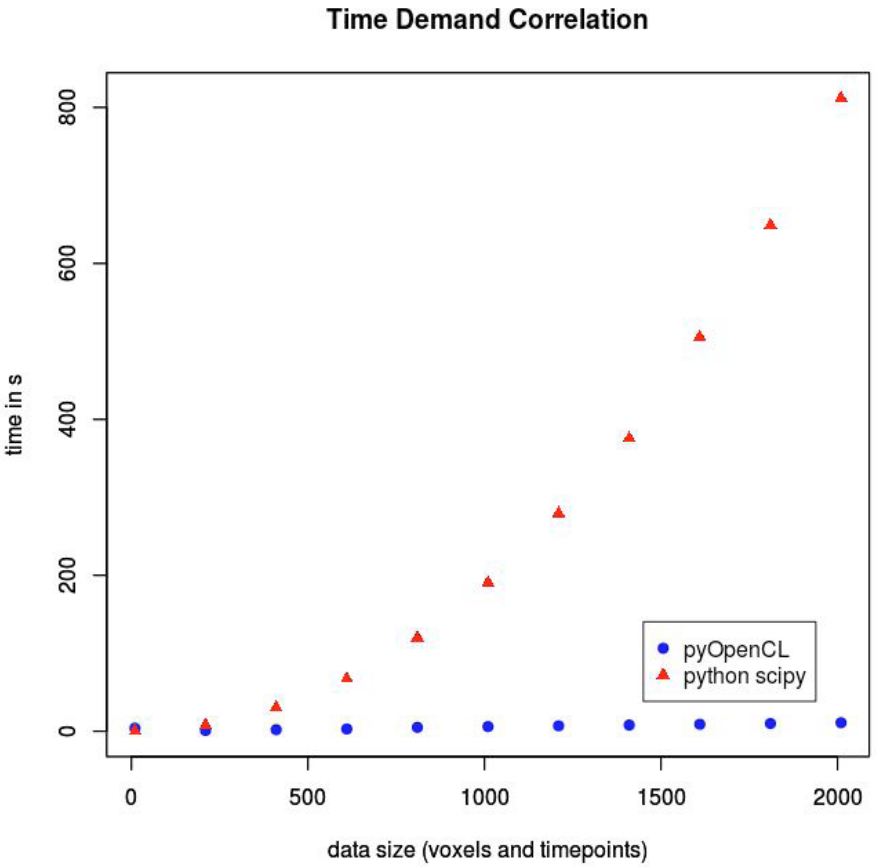
1. Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig,Germany

In the last years there has been an increasing interest in the analysis of human connectome data. Connectivity is naturally at least bivariate since it is computed between each pair of objects. The computational complexity of connectome analysis grows therefore at least quadradic in resolution size. For example, in functional magentic resonance imaging (fMRI) resolution is increasing; not only with higher field strength but also with improved scanner sequences.

To cope with this increasing computational demand researchers have begun to apply two strategies. One strategy uses parcellation techniques to reduce dimensionality. The second approach are simpler and less demanding algorithms. However, both procedures encounter limitations. Here, we suggest an additional approach which concentrates on massive parallelization by exploiting modern and future hardware capabilities. Especially in the context of neuroimaging, many computational problems are easy to parallelize. So far, many parallel programming environments were to hardware specific to be beneficial for a wider user community. In this context we chose the emerging hardware independent OpenCL interface.

One simple and widely applied measure of functional connectivity is the Pearson product-moment correlation between hemodynamic signals. Even so Pearson correlation is relatively fast estimated, the computation on the whole-brain in a high resolution is computationally demanding. Here we show computing connectivity can be accelerated using parallelization in pyOpenCL (Fig. 1). Future GPGPU environments with thousands of cores and fast accessible memory will enable the analysis of larger datasets with even higher throughputs.

To foster brain research we want to further implement standard connectome analysis techniques in an easy accessible (python), hardware independent and well scalable (OpenCL) way.


Time Demand Correlation
time in s
0
200
400
600
800
0
500
1000
1500
2000
data size (voxels and timepoints)
pyOpenCL
python scipy

P93 Spatial Bayesian modelling of neuroimaging meta-analysis data

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Meta-analysis for functional brain imaging is growing in importance as the number of available studies grows. Unfortunately, the only data widely available for meta-analysis are the [x,y,z] coordinates of peak activation foci. Most existing methods convert these coordinate data into images and then apply traditional imaging modelling and inference proceedures. However, these methods are mass-univariate, make inference on individual voxels (or clusters) and require fixed tuning parameters. Such methods do not provide an interpretable fitted model, and cannot produce spatial confidence intervals on location of activation. Using a Bayesian hierarchical point process approach, modelling brain activation as a mixture of latent activation centers, and these activation centers are in turn modelled as off-spring from latent population centers. When our fully Bayesian model fit to multiple groups it is trival to make predictions of the group label for new data and, through an importance sampling trick, leave-one-out cross validation accuracy for the sample studied. This framework provides a method for reverse inferences that account for the spatial structure of the data; in particular, we find dramatic improvements in our classification accuracies over Naive Bayes which does not model the spatial structure.

P94 Co-registration methods for 2D ultrasound and nuclear magnetic resonance images

Yusniel Santos Rodríguez[1], Javier Figueredo[2], Joe Michel López Inguanzo[1], Marlis Ontivero[1], Daylin Gongora[1], Jorge Iglesias Fuster[1] and Maria Antonieta Bobes León[1]
1. Cuban Center for Neuroscience (CNEURO)
2. Center of Medical and Surgical Research (CIMEQ)

Intra-operative MRI and CT images provide information about patient's brain several times during surgery. However, they have serious drawbacks concerning the relatively long image acquisition procedures, high investment and operating costs, a spatially limited workspace and need for special (MR- or CT-compatible) surgical equipment. The optimal solution for neurosurgeons includes a navigation system with high quality images combined with real-time processing and three-dimensional imaging capabilities. Many of these capabilities are available in the ultrasound systems used in neurosurgery for several years. These systems have drawbacks associated with a limited viewing angle, the mixing of study and image data and variable dimensions. However, recent advances has improved the image quality up to a level comparable with intra-operative MRI. Thus, by sorting these limitations, the integration of ultrasound with high resolution MRI represents an efficient and inexpensive procedure for pre-operative surgical planning and intra-operative imaging. Our work combines intra-operative 2D ultrasound images and pre-operative MRI, as well includes fusion with fMRI and DTI images. We present data obtained from surgical procedures in patients with brain tumors. In all cases this procedure allowed the evaluation of 2D ultrasound images combined with MR structural images, fMRI and DTI data, allowing a more efficient surgical planning with successful outcomes.

OP10 NeuroFlow: FPGA-based spiking neural network acceleration with high-level language support

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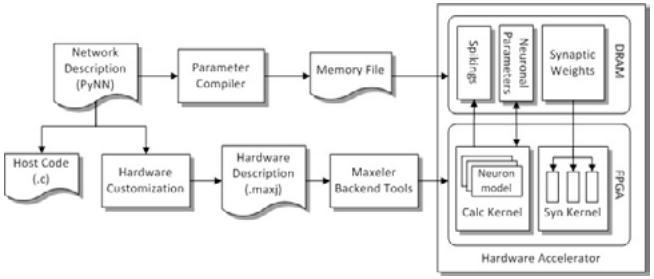
2. Imperial College London, Department of Bioengineering, London, United Kingdom

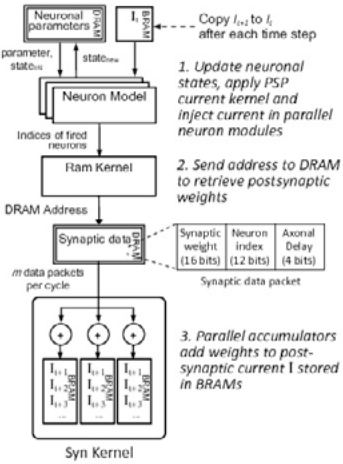
Spiking neural networks are a useful tool for cortical modelling and robotic control, but simulating a large network in real-time requires high-performance computers or specially built accelerators. Traditional accelerators for large-scale spiking neural network accelerators developed previously use Graphics Processing Units (GPUs) or Application-Specific Integrated Circuit (ASIC) chips. While ASICs deliver high performance, they lack the flexibility to reconfigure and hence are unable to adapt variation in the design and models employed. On the other hand, GPUs provides a decent speedup over multi-core CPUs and good flexibility, but it lacks scalability to handle larger networks.

In this work we present NeuroFlow, a Field Programmable Gate Array (FPGA)-based spiking neural network accelerator consisting of 4 FPGAs. It supports the use of PyNN, a high-level simulator-independent network description language, to configure the hardware. A major novelty of the system is the capability to provide custom hardware configuration based on various simulation requirements, such as precision and time delay. The accelerator is implemented on an off-the-shelf MPC-C500 from Maxeler Technology which employs a streaming architecture in the FPGAs. The accelerator achieves the performance gain primarily by parallelizing the computation of point-neuron models and employing low-level optimization for synaptic data memory access. The accelerator currently supports basic PyNN functions such as spike-timing-dependent plasticity (STDP) and arbitrary postsynaptic current kernels.

The system is able to support simulation of network of approximately 800,000 neurons, and achieve a real-time performance of 400,000 neurons for a network firing at 8Hz with random connections. With a single FPGA running at 150MHz, the accelerator delivers a throughput of 1.9 times to 3.5 times the performance of one of the most recent GPU-based accelerators in terms of postsynaptic potential delivery rate (Fidjeland et al., Neuroinformatics, 2012 Dec), subject to the simulated network and the GPU model used.

In conclusion, while harnessing low-level customization and fine grained parallelism in FPGA, NeuroFlow is also able to provide the flexibility of a high-level platform such as GPUs and high-performance computers. It provides a promising alternative to accelerate spiking neural network simulations.


Network Description (PyNN)
Parameter Compiler
Memory File
Host Code (.c)
Hardware Customization
Hardware Description (.maxj)
Maxeler Backend Tools
Spikes
Neuronal Parameters
Synaptic Weights
DRAM
Neuron model
Calc Kernel
Syn Kernel
FPGA
Hardware Accelerator


Neuronal parameters
DRAM
BRAM
Copy I_{t+2} to I_t after each time step
parameter, $state_{old}$
$state_{new}$
1. Update neuronal states, apply PSP current kernel and inject current in parallel neuron modules
Neuron Model
Indices of fired neurons
Ram Kernel
2. Send address to DRAM to retrieve postsynaptic weights
DRAM Address
Synaptic data
Synaptic weight (16 bits)
Neuron index (12 bits)
Axonal Delay (4 bits)
Synaptic data packet
m data packets per cycle
3. Parallel accumulators add weights to post-synaptic current I stored in BRAMs
Syn Kernel

P95 Logarithmic Hybrid Optical Neural Network-type systems: towards digital-optical cognitive models of robust object recognition

Ioannis Kypraios[1]
1. APEM R&D Computing Lab, Begbroke, United Kingdom

By combining the complex logarithmic r-theta mapping of a space-variant imaging sensor [1, 2] with the hybrid digital-optical neural network filter together with a window unit multiple objects of the same class or of different classes can robustly be recognized. The resulted logarithmic r-theta mapping for hybrid digital-optical neural network system or briefly referred to as logarithmic hybrid optical neural network system is shown to exhibit with a single pass over the input data simultaneously in-plane rotation, out-of-plane rotation, scale, log r-_ map translation and shift invariance, and good clutter tolerance by recognizing correctly the different objects within the cluttered scenes. Here, we study the biologically-inspired knowledge learning and knowledge representation [3] achieved by the logarithmic hybrid optical neural network-type of object recognition systems (see Fig. 1 and Fig. 2). We investigate the effects that altering the knowledge representation can have on the problem's learned knowledge and the problem solving process, in overall. Further, we study the logarithmic unconstrained-, logarithmic constrained-, and logarithmic modified-hybrid optical neural network systems architectures' designs [4, 5]. We show how the logarithmic unconstrained-hybrid optical neural network object recognition system applies an unconstrained representation of the problem's knowledge to maximize the search of solutions, how the logarithmic constrained-hybrid optical neural network object recognition system uses a constrained representation of the problem's knowledge to guide the search towards certain solutions over others in the multidimensional search space, and how the logarithmic modified-hybrid optical neural network object recognition system uses memory-like masks to recall certain solutions over others in the multidimensional search space.

Fig. 1. (a) Simplified human retina and visual cortex model used for description purposes only; (b) A digital-optical computational model for the cognitive interaction between the retina and the human visual cortex with the general logarithmic hybrid optical neural network architercture.

Fig. 2. Biologically-inspired knowledge learning and knowledge representation with the logarithmic hybrid optical neural network-type of object recognition systems

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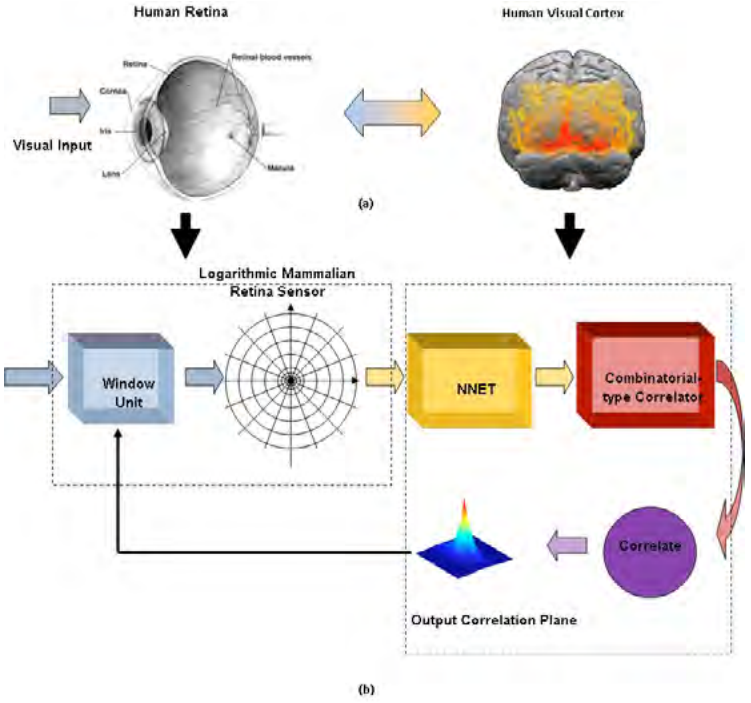
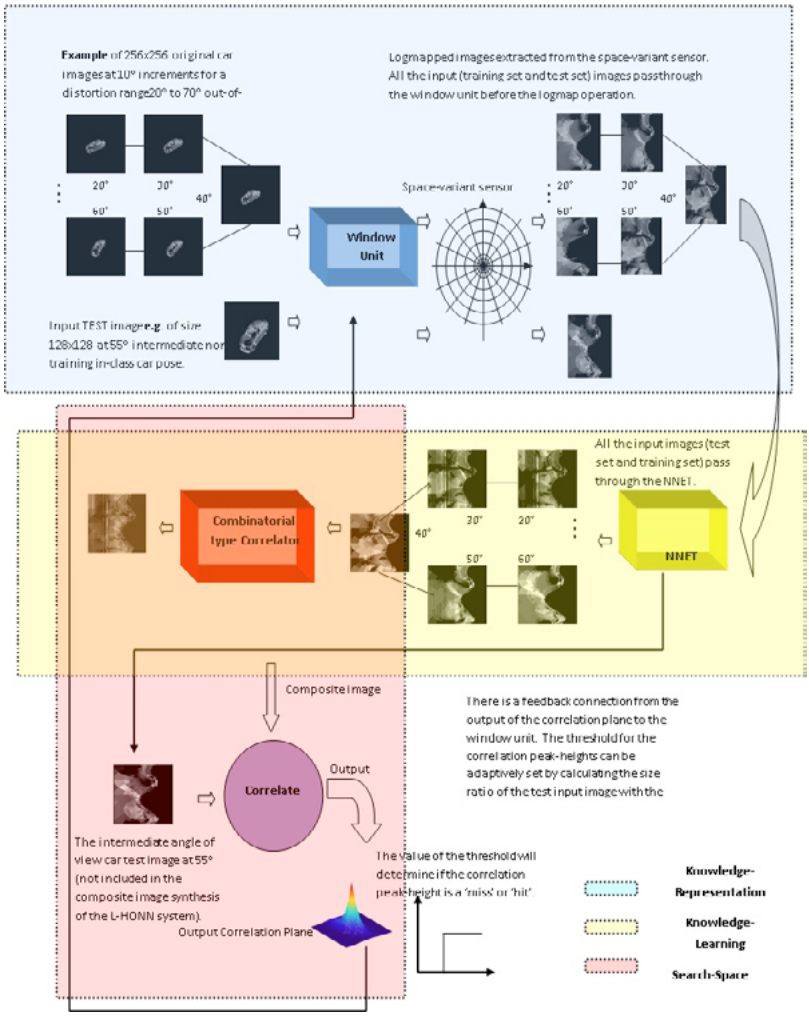

Human Retina
Human Visual Cortex
Visual Input
Retina
Retinal blood vessels
Cornea
Iris
Lens
Macula
(a)
Logarithmic Mammalian
Retina Sensor
Window
Unit
NNET
Combinatorial-
type Correlator
Correlate
Output Correlation Plane
(b)


Example of 256x256 original car images at 10° increments for a distortion range 20° to 70° out-of-
20°
30°
40°
50°
60°
Window Unit
Space-variant sensor
Logmapped images extracted from the space-variant sensor. All the input (training set and test set) images pass through the window unit before the logmap operation.
Input TEST image e.g. of size 128x128 at 55° intermediate non training in-class car pose.
All the input images (test set and training set) pass through the NNET.
NNET
Combinatorial type Correlator
Composite Image
Correlate
Output
There is a feedback connection from the output of the correlation plane to the window unit. The threshold for the correlation peak-heights can be adaptively set by calculating the size ratio of the test input image with the
The intermediate angle of view car test image at 55° (not included in the composite image synthesis of the L-HONN system).
Output Correlation Plane
The value of the threshold will determine if the correlation peak-height is a 'miss' or 'hit'.
Knowledge-Representation
Knowledge-Learning
Search-Space

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Special Session

Workshops

page numbers are clickable!

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Demos

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