Neuro Informatics 2014

ABSTRACT BOOK

Neuroinformatics 2014
7th INCF Congress

Program & abstracts

August 25 - 27, 2014
Leiden, the Netherlands

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, Multiscale 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
neuroinformatics2014.org

INCF Member Countries*

Belgium
Czech Republic
Finland
France
Germany
India
Italy
Japan
The Netherlands
Norway
Poland
Republic of Korea
Sweden
Switzerland
United Kingdom
United States
Victoria, Australia

*as of August 2014

Welcome to the 7th INCF Congress in Leiden, The Netherlands!

The 7th Neuroinformatics Congress meets this year, for the first time, in Leiden, Netherlands. The congress program reflects a growing interest in all aspects of Neuroinformatics and "Big Data" analysis, fueled in part by the EU Human Brain Project and the BRAIN initiative in the US. Speaking for the organizers and for the Program Committee, I hope you enjoy it!

Neuroinformatics 2014 is organized by the INCF together with the Netherlands INCF Node. Overall the program structure is similar to previous years, mostly single track with 6 keynotes, 5 workshops, and 2 poster and demo sessions. The keynote speakers represent a broad range of data-rich neuroscience fields, ranging from epigenetics in the brain to multi-scale modeling of information processing in the whole brain. Two of the workshops are concurrent and were selected from submitted proposals. As last year, there will be an oral presentations session for which 9 submitted abstracts were selected by the Program Committee out of 43 abstracts that requested an oral presentation. This session will bring you the newest science and it presents research topics that are of special interest to attendees.

Mary B Kennedy
California Institute of Technology
INCF 2014 Program Committee Chair

Program Committee

Richard Baldock, University of Edinburgh, UK
Avrama Blackwell, George Mason University, USA
Erik De Schutter, Okinawa Institute of Science and Technology, Japan
Henry Markram, EPFL, Switzerland
Maryann Martone, University of California, San Diego, USA
Russell Poldrack, University of Texas at Austin, USA
Paul Tiesinga, Radboud University, The Netherlands
Yoko Yamaguchi, RIKEN Brain Science Institute, Japan
Mathew Abrams (secretary), INCF Secretariat

Local Organizing Committee

Paul Tiesinga (Chair, NeuroInformatics.NL)
Rembrandt Bakker (NeuroInformatics.NL)
Moniek Lijster (NIHC)
Esther van der Wel (NIHC)
Fons Verbeek (LIACS)
Joris Slob (LIACS)
Erno Vreugdenhil (Leiden UMC)
Niels Cornelisse (Neurofederatie)

GENERAL INFORMATION

VENUE

The congress will take place at Kamerligh Onnes Gebouw (KOG), Steenschuur 25, Leiden Law School, Law library, University of Leiden. For directions, see below.

Exhibits are located outside the lecture halls. Featured exhibitors are listed on page 16-17.

The poster and demo sessions will take place in the C-corridor, on the ground floor in the venue. The sessions are scheduled for Monday, Aug 25 13:00 - 15:40 and Tuesday, Aug 26 14:00 - 15:40.

The poster boards and demo stations will be marked with numbers referring to those stated in the abstract tab, and in the online Abstract book. Materials for putting up the posters will be provided. The meeting staff will remove posters not taken down by Wednesday, August 27, at 16:00. The meeting organizers do not accept responsibility for any materials left behind.

INTERNET

Individual usernames and passwords for the WiFi will be handed out at registration.

LUNCH

Several light lunch options are available in the restaurant located inside the congress venue (price range 4-6 EUR). Coffee will be served in the exhibits area.

CONFERENCE COORDINATORS ON SITE

Rosa Cusato-Sörnäs, INCF +46 8 524 870 16

Helena Ledmyr, INCF +46 8 524 870 35

OPENING HOURS OF THE REGISTRATION DESK

Aug 25	8:00 - 17:30
Aug 26 - 27	8:30 - 18:00

PARTICIPATION, NAME TAGS

Official conference name tags will be required for admission to all conference functions. Participants who lose their name tags will have to pay a fee of 25.00 EUR to obtain a replacement tag.

SOCIAL EVENTS

The City of Stockholm has invited all pre-registered participants to a Welcome Reception in City of Leiden Town Hall on August 25.

On August 26, INCF hosts a Congress Banquet at Hortus Botanicus.

TO THE VENUE

Directions from Leiden train station:

By foot: Cross the station square and keep to the right side of the road. Take the Stationsweg and then the Steenstraat and continue across the Blauwpoortsbrug bridge. On leaving the bridge, turn right and take the Prinsessekade, which will become the Korte Rapenburg. Cross the street and you are on the Rapenburg. Walk along the Rapenburg until it becomes the Steenschuur. You will find the KOG on your left hand side.

By bus: Buses stop in front of the train station. You can take buses no. 15, 16, 31, 40, 42, 187, 185, or 189. You need a bus which drives along the Breestraat. Ask the driver to let you know when you are at the bus stop in the Breestraat. Walk along the Breestraat and turn right at the end of the street. You are now on the Steenschuur. The KOG is on your right hand side.

MAP

Scan the QR code below for a local google map with the venue, hotels, transportations and social events

Monday, Aug 25th

08:30 OPENING STATEMENT
Mary B Kennedy

08:40 WELCOME FROM THE INCF EXECUTIVE DIRECTOR
Linda Lanyon

09:00 KEYNOTE
Daniel Choquet
A nanoscale view into the dynamic of AMPA receptor organization in synapses

09:50 COFFEE BREAK, PROVIDED BY **WILEY**

10:20 WORKSHOP 1
The Neuroinformatics of neuroanatomy
Chair:
Maryann Martone
Speakers:
Trygve Leergard, Jacopo Annese, Douglas Bowden, Mike Hawrylycz

12:10 LUNCH

12:10 *PLOS Data Q&A for neuroscience researchers*. Room: TBD

13:00 POSTER AND DEMO SESSION 1

15:00 COFFEE SERVED

15:40 KEYNOTE
Michael Milham
Emerging models for biomarker identification

16:20 PRESENTATION BY FRONTIERS

16:30 KEYNOTE
Felix Schürmann
In silico neuroscience – an integrative approach

17:20 END

17:30 WELCOME RECEPTION AT THE CITY OF LEIDEN TOWN HALL

Tuesday, Aug 26th

09:00 KEYNOTE
Viktor Jirsa
The Virtual Brain: a simulator of large-scale brain network dynamics

09:50 COFFEE BREAK

10:20 WORKSHOP 2
Building the brain
Chair:
Paul Tiesinga
Speakers:
Geoff Goodhill, Tomomi Shimogori, Rodney Douglas, Nenad Sestan

12:10 LUNCH

13:00 SPECIAL SESSION
Big data in clinical and translational informatics
Chair:
Sean Hill, INCF Scientific Director
Speakers:
Yike Guo, Asla Pitkanen

14:00 POSTER AND DEMO SESSION 2

15:00 COFFEE SERVED

15:40 KEYNOTE
Dmitri Chklovskii
Can connectomics help us understand neural computation? Insights from the fly visual system

16:20 ORAL PRESENTATIONS OF SELECTED ABSTRACTS
Oscar Javier Avella Gonzalez, Anita Bandrowski, Mihail Bota, Tristan Glatard, Lior Kirsch, Camille Maumet, Birgit Plantinga, Miroslav Radojevic, Oliver Schmitt

17:50 END

18:00 BANQUET AT HORTUS BOTANICUS

Wednesday, Aug 27 th

09:00 KEYNOTE
Margarita Behrens
The epigenome and brain circuit changes during postnatal development

09:50 COFFEE BREAK

10:20 PARALLEL WORKSHOPS

10:20 WORKSHOP 3
Synaptic computation
Chair:
L. Niels Cornelisse
Speakers:
Erik De Schutter, Bert Kappen, Alexander Walter, Michele Giugliano

10:20 WORKSHOP 4
Open collaboration in computational neuroscience
Chair:
Angus Silver
Speakers:
Stephen Larson, Padraig Gleeson, Rick Gerkin, Shreejoy Tripathy, Aurel A. Lazar

12:10 LUNCH

13:00 NETHERLANDS NODE SPECIAL SESSION
Population-based neuroimaging

15:10 COFFEE BREAK

15:40 NETHERLANDS NODE SPECIAL SESSION

17:00 INCF VICTORIA NODE
Ramesh Rajan
Welcome to Cairns in 2015!

17:15 CLOSING REMARKS
Jan Bjaalie, INCF Governing Board Chair

17:30 END

INCF NETHERLANDS NODE SPECIAL SYMPOSIUM

August 27, 13:00 - 17:00

Neuroinformatics of population-based neuroimaging

Chair: **Leon Kenemans**, Universiteit Utrecht

Population imaging deals with the systematic acquisition and analysis of medical imaging data in large population cohorts. The aim of population imaging is to discover and develop imaging biomarkers (objective measures of the presence and state of the disease), e.g. to predict or follow the development of disease. There is a large number of ongoing population-based (neuro)imaging studies, and a number of large new initiatives have recently been announced, for an overview see populationimaging.eu.

The goal of this workshop is to look into a number of fundamental neuroinformatics and other methodological issues that arise in setting up population studies, analyze their results and make the data available.

Not all characteristics present in the population can be statistically resolved by a single population-based study, however large it may be. Data sharing across studies is important, and Paul Tiesinga will kick-off the session by presenting the outcome of a workshop on datasharing in the neurosciences that preceded the congress and has the aim of formulating a white paper on datasharing. The next topic is MRI processing. We will cover both the harmonization of MRI acquisition protocols between participating research centers, where maximizing reproducibility across scanners is at least as important as obtaining maximum scan quality, as well as the processing of all those scans. Because of the need for high throughput, manual analyses need to be avoided and automated analysis pipelines for segmentation and biomarker extraction are required, with characterizations that allow for statistical analyses across subjects. **Christian Beckmann** will talk about such analyses in the Human Connectome Project. In addition, metadata such as (fMRI) tasks, cognitive tests and genetic data need to be standardized. Within this context, we introduce and several prominent examples of ongoing population imaging. **Alan Evans** will talk about the CBRAIN and GBRAIN platforms for distributed processing of 3D/4D brain imaging data, and **Aad van der Lugt** will speak about the Rotterdam generation R study. Legacy data is too valuable to be discarded, hence, approaches to integrate and analyze data from multiple studies are important as well. **Rembrandt Bakker** will relate his experiences of populating a database with legacy data sets and constructing a pipeline for their analysis. Finally, recent developments have led to successful prediction of the status of individual subjects based on their MRI scans. **Hugo Schnack** will present some results in this area and discuss the possibilities for their diagnostic use. To wrap up the session we end with a discussion on the requirements for future population studies.

Program: see page 11

Advisory board

Rembrandt Bakker, Radboud University, Nijmegen
Wiro Niessen, Erasmus Medical Center, Rotterdam
Hugo Schnack, University Medical Center, Utrecht
Paul Tiesinga, Radboud University, Nijmegen
Rob Heinsbroek, NIHC

NeuroInformatics•NL

National Initiative Brain & Cognition

Monday, August 25, 2014

08:30 **OPENING STATEMENT**
Mary B Kennedy, Program Committee Chair, California Institute of Technology, USA

08:40 **WELCOME**
Linda Lanyon, INCF Executive Director

09:00 **KEYNOTE** ▶ *A nanoscale view into the dynamic of AMPA receptor organization in synapses*
Daniel Choquet, University of Bordeaux, France

09:50 Coffee break**, provided by** WILEY

10:20 **WORKSHOP 1** ▶ *The Neuroinformatics of neuroanatomy*
Chair: **Maryann Martone**, University of California San Diego, USA

10:25 **Trygve Leergard**, University of Oslo, Norway
10:50 **Jacopo Annese**, University of California , USA
11:15 **Douglas Bowden**, University of Washington, USA
11:40 **Mike Hawrylycz,** Allen Institute for Brain Science, USA

12:10 Lunch

12:10 PLOS Data Q&A for neuroscience researchers. Room: TBD

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

15:00 Coffee served

15:40 **KEYNOTE** ▶ *The Functional Connectomes Project*
Michael Milham, Child Mind Institute, USA

16:20 Presentation by frontiers

16:30 **KEYNOTE** ▶ *In silico neuroscience – an integrative approach*
Felix Schürmann, École Polytechnique Fédérale de Lausanne, Switzerland

17:20 End

17:30 Welcome Reception at the City of Leiden Town Hall

Tuesday, August 26, 2014

09:00 **KEYNOTE** ▶ *The Virtual Brain: a simulator of large-scale brain network dynamics*
Viktor Jirsa, Inserm at Aix-Marseille University, France

09:50 Coffee break

10:20 **WORKSHOP 2** ▶ *Building the brain*
Chair: **Paul Tiesinga**, Radboud University Nijmegen, The Netherlands

10:25 **Geoff Goodhill**, University of Queensland, Australia
10:50 **Tomomi Shimogori**, RIKEN Brain Science Institute, Japan
11:15 **Rodney Douglas**, University of Zurich, Switzerland
11:40 **Nenad Sestan**, Yale University, USA

12:10 Lunch

13:00 **SPECIAL SESSION** ▶ *Big data in clinical and translational informatics*
Chair: **Sean Hill**, INCF Scientific Director

13:10 **Yike Guo**, Imperial College, UK
13:30 **Asla Pitkanen**, University of Eastern Finland, Finland

14:00 **POSTER AND DEMO SESSION 2**

15:00 Coffee served

15:40 **KEYNOTE** ▶ *Can connectomics help us understand neural computation? Insights from the fly visual system*
Dmitri (Mitya) Chklovskii, Howard Hughes Medical Institute Janelia Farms, USA

16:20 **ORAL PRESENTATIONS OF SELECTED ABSTRACTS**
Chair: **Mary B Kennedy,** California Institute of Technology, USA
Oscar Javier Avella Gonzalez, VU Amsterdam, Netherlands
Anita Bandrowski, The University of California, San Diego, USA
Mihail Bota, University of Southern California, USA
Tristan Glatard, McGill University, Canada and University of Lyon, France
Lior Kirsch, Bar Ilan University, Israel
Camille Maumet, University of Warwick, United Kingdom
Birgit Plantinga, Eindhoven University of Technology, Maastricht and University Medical Center, Netherlands
Miroslav Radojevic, Erasmus MC, Netherlands
Oliver Schmitt, University of Rostock, Germany

17:50 End

18:00 Banquet at Hortus Botanicus

Wednesday, August 27, 2014

09:00 **KEYNOTE** ▶ *The epigenome and brain circuit changes during postnatal development*
Margarita Behrens, Salk Institute, USA

09:50 Coffee break

10:20 **PARALLEL WORKSHOPS**

10:20 **WORKSHOP 3** ▶ **Synaptic computation workshop**
Chair: **L. Niels Cornelisse,** University Amsterdam, The Netherlands

10:25 **Erik De Schutter,** Okinawa Institute of Science and Technology, Japan

10:50 **Bert Kappen,** Radboud University Nijmegen, The Netherlands

11:15 **Alexander Walter,** Charité Cross Over, Germany

11:40 **Michele Giugliano**, University of Antwerpen & Neuro-Electronics Research Flanders, Belgium

10:20 **WORKSHOP 4** ▶ *Open collaboration in computational neuroscience*
Chair: **Angus Silver**, University College London, UK

10:25 **Stephen Larson**, MetaCell, LLC, USA

10:45 **Padraig Gleeson**, University College London, UK

11:05 **Rick Gerkin**, Carnegie Mellon University, USA

11:25 **Shreejoy Tripathy**, University of British Columbia, Canada

11:45 **Aurel A. Lazar**, Columbia University

12:10 Lunch

13:00 **INCF NETHERLANDS NODE SPECIAL SYMPOSIUM**
Chair: **Leon Kenemans**, Utrecht University, The Netherlands

13:00 **Paul Tiesinga**, Radboud University Nijmegen, The Netherlands
Outcome of the workshop "Share and Flourish, new standards for data sharing in the neurosciences"

13:20 **Christian Beckmann**, Radboud University Nijmegen, The Netherlands
Automated analysis methods for fMRI datasets and their role in the Human Connectome Project

13:50 **Alan Evans**, McGill University Health Centre, Canada
Big data platforms for distributed processing of 3D/4D brain imaging data

14:30 **Aad van der Lugt**, Erasmus Medical Center Rotterdam, The Netherlands
Population Imaging, the Rotterdam experience

Wednesday, August 27, 2014 (cont.)

15:10 **Coffee break**

15:30 **Rembrandt Bakker**, Radboud University Nijmegen, The Netherlands
Neuroimaging data integration across scanners and protocols: the Biomarker Boosting project

15:50 **Hugo Schnack**, Utrecht University, The Netherlands
Translating neuroimaging findings from research into clinical practice

16:20 Discussion moderated by **Leon Kenemans**, Utrecht University, The Netherlands
Requirements for future population studies

16:45 WELCOME TO CAIRNS IN 2015!
Ramesh Rajan, INCF Victoria Node

17:00 CLOSING REMARKS
Jan G Bjaalie, INCF Governing Board Chair

17:15 End

INCF looks forward to welcoming you to the 8th Neuroinformatics Congress in Cairns, Australia, on August 20-22, 2015!

www.neuroinformatics2015.org

International Neuroinformatics Coordinating Facility

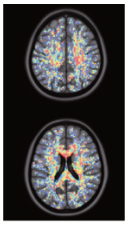
incf | Neuro Informatics 2015

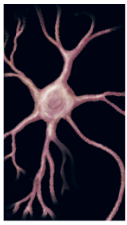
Save the date!

Neuroinformatics 2015 comes to Cairns, Australia, home of the Great Barrier Reef and the Daintree Rainforest!

Join us on 20-22 August for:

- Keynotes from top scientists in the neuroinformatics field
- Workshops and poster/demo sessions
- A one-day special session organized by the INCF Australia Node:
  - Multi-scale integrative neuroscience research in attention circuits in the brain
  - Australian National Imaging Facility - technical developments and applications in the imaging grid




Welcome to Cairns, Australia!

20-22 August 2015

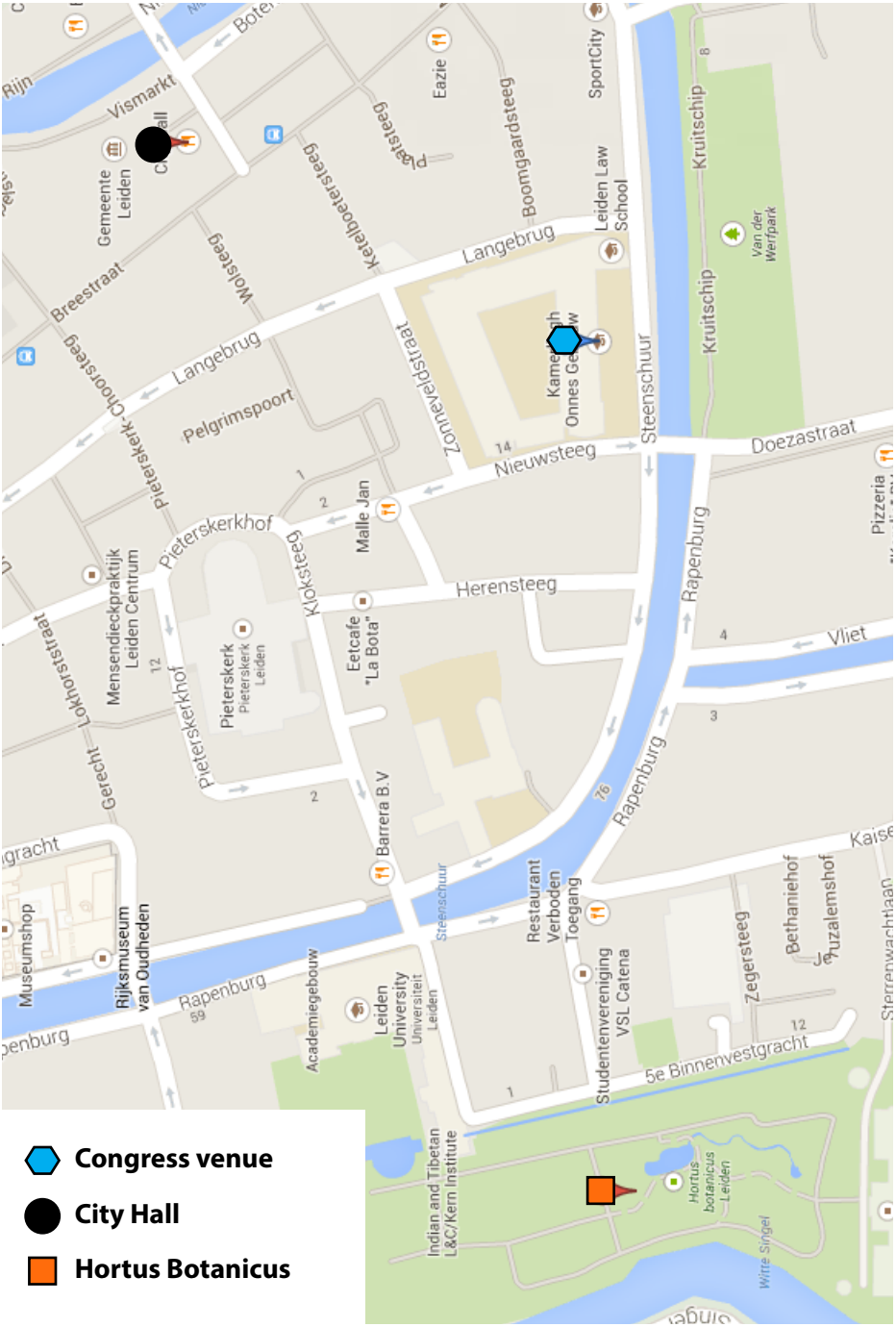
The 8th INCF Congress on Neuroinformatics is co-organized by the INCF Australia Node, hosted by the ARC Centre of Excellence for Integrative Brain Function.

The Congress is an official satellite meeting of the 25th meeting of the International Society for Neurochemistry in Cairns, Australia, on August 23-27.

Australian Research Council
Centre of Excellence for Integrative Brain Function

ISN International Society for Neurochemistry

neuroinformatics2015.org


Congress venue
City Hall
Hortus Botanicus
Rijn
Vismarkt
Gemeente Leiden
Breestraat
Langebrug
Pelgrimspoort
Pieterskerkhof
Pieterskerk
Pieterskerk Leiden
Mensendiecktraktijk Leiden Centrum
Lokhorststraat
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Rijksmuseum van Oudheden
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Universiteit Leiden
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Eetcafe "La Bota"
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Herensteeg
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Steenschuur
Restaurant Verboden Toegang
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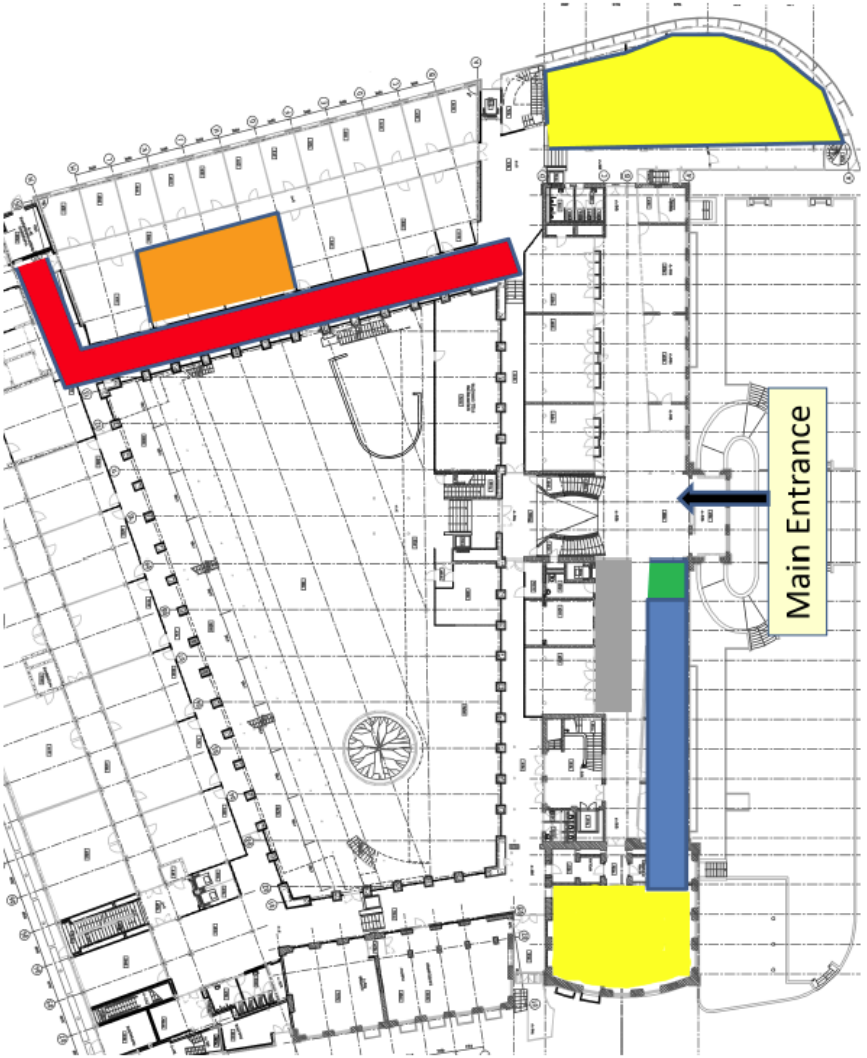
Kruitschip
Van der Werfpark
Doezastraat
Pizzeria
Vliet
Zegersteeg
Bethaniehof
Jeruzalemshof
5e Binnenvestgracht
Indian and Tibetan L&C/Kern Institute
Hortus botanicus Leiden
Witte Singel

Ground floor
Green: Registration
Red: Posters
Orange: Demos, hackathon

First floor
Blue: Exhibitions
Yellow: Lecture halls
Grey: Coffee & lunch cafeteria



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Abstracts

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Scan the QR code to access

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- abstract listing on Frontiers' website

ABSTRACT INFORMATION

The abstract list is sorted in alphabetical order by the corresponding author's last name.

P Poster
OP Poster which will also be presented in the oral session at 16:20 on Tuesday, August 26.
OD Demo which will also be presented in the oral session at 16:20 on Tuesday, August 26.
D Demo

Session 1

Monday, August 25 13:00 - 15:40
Abstracts with even numbers will be presented

Session 2

Tuesday, August 26 14:00 - 15:40
Abstracts with uneven numbers will be presented

All abstract presenters have been asked to be available during both sessions if possible.

Corresponding author	Abstract title	Abstract number
Adebimpe, Azeez	Altered brain functional connectivity in patients with benign childhood epilepsy	P56
Ahmed, Zeeshan	Ant-app-database towards neural, behavioral research on deserts ants and approximate solar estimations	D09
Asai, Yoshiyuki	Interoperability between multilevel modeling platform PhysioDesigner and databases in Physiome.jp and Dynamic Brain Platform through Garuda platform	P45
Avella Gonzalez, Oscar Javier	Inter-network interactions: impact of connections between oscillatory neuronal networks on oscillation frequency and pattern	OP03
Bakker, Max	Efficient generation of large-scale neural connectivity matrices using machine-learning techniques	P49
Bakker, Rembrandt	Do gold standards remain gold standards when compiling a large number of published tract-tracing studies into a connectivity database?	P52
Bakker, Rembrandt	eScience Infrastructure for running validated image analysis pipelines: how to best compare MRI scans from different medical centers	D19
Bandrowski, Anita	Identifying research resources in biomedical literature should be easy	OP04
Battaglia, Demian	First neuronal connectomics challenge: from imaging to connectivity	P05
Beul, Sarah	Cortical cytoarchitecture and distance predict corticocortical connectivity	P17
Bjaalie, Jan	Workflow for integration and analysis of histological data in rodent brain Waxholm Space	P19
Bohland, Jason	Classification of cortical areas using gene expression profiles	P41
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Bosman, Conrado	Low-frequency phase-locking of selective human medial temporal lobe neurons to the local field potential of contralateral lateral prefrontal cortex during visual stimulation	P24
Bota, Mihail	The rat cerebral cortex macroconnectome	OP09
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Djurfeldt, Mikael	MUSIC---a tool for co-simulation of neuronal network models. Current status and future development.	P51
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Güçlü, Umut	A two-stage approach to estimating voxel-specific encoding models improves prediction of hemodynamic responses to natural images	P64
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Hess, Andreas	A new automatic multi seed analysis for fMRI resting state data in animal model: Comparison to ICA	P54
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Kamitani, Yukiyasu	The BrainLiner Platform for sharing and searching time-aligned neurophysiological data	D12
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Leergaard, Trygve	Registration of serial two-photon data to rodent brain Waxholm Space	P22
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Lenk, Kerstin	The effect of longer range connections on neuronal network dynamics	P14
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Linssen, Charl	Can we hear the shape of a neuron? Cell type classification in high density multi-electrode recordings	P23
Lo, Chung-Chuan	The Flysim project – persistent simulation and real-time visualization of fruit fly whole-brain spiking neural network model	D15

Corresponding author	Abstract title	Abstract number
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Mahan, Margaret	Parallel confidence-weighted classification of large-scale, multimodal neural data on MapReduce	P32
Mahfouz, Ahmed	Predicting targets and signaling pathways of steroid hormones using the Allen Brain Atlas	P40
Majima, Kei	The BrainLiner Platform for sharing and searching time-aligned neurophysiological data	D12
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Keynotes

Margarita Behrens
Dmitri (Mitya) Chklovskii
Daniel Choquet
Viktor Jirsa
Michael Milham
Felix Schürmann

The epigenome and brain circuit changes during postnatal development

Margarita Behrens

Salk Institute
La Jolla, CA, United States

During the period between birth and adulthood the brain undergoes profound changes driven by experience-dependent plasticity and the formation of stable neuronal circuits that last for the lifetime of the individual. These changes are driven by changes in transcriptional patterns in each brain cell-type without the creation of new cells, suggesting the possibility that dynamic changes in DNA-methylation (mC) patterns could be driving these transcriptional changes. DNA methylation is a stable covalent modification that persists in post-mitotic cells throughout their lifetime, defining their cellular identity. However, the methylation status at each of the ~1 billion cytosines in the genome is potentially an information-rich and flexible substrate for epigenetic modification that can be altered by cellular activity.

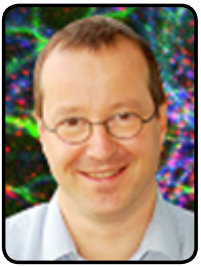
Addressing this question requires integration of large-scale DNA methylation data sets with computational analyses capable of identifying dynamic epigenetic patterns throughout the genome. To do this, we produce whole-genome bisulfite sequencing data, at single-base resolution, from human and mouse frontal cortex throughout their lifespan. Using statistical and machine learning approaches such as high-dimensional cluster analysis, we found widespread methylome reconfiguration during fetal to young adult development, coincident with synaptogenesis. During this period, we found that highly conserved non-CG methylation (mCH) accumulates in neurons, but not glia, to become the dominant form of methylation in the human neuronal genome. We also found an interesting mCH signature that identifies genes escaping X-chromosome inactivation. Finally, whole-genome single-base resolution 5-hydroxymethylcytosine (hmC) maps revealed that hmC marks fetal brain cell genomes at putative regulatory regions that are CG-demethylated and activated in the adult brain.

Can connectomics help us understand neural computation? Insights from the fly visual system

Dmitri (Mitya) Chklovskii

Howard Hughes Medical Institute Janelia Farms
Ashburn, United States

Animal behavior arises from computations in neuronal circuits, but our understanding of these computations has been frustrated by the lack of detailed synaptic connection maps, or connectomes. For example, despite intensive investigations over half a century, the neuronal implementation of local motion detection in the insect visual system remains elusive. We developed a semi-automated pipeline using electron microscopy to reconstruct a connectome, containing 379 neurons and 8,637 chemical synaptic contacts, within the Drosophila optic medulla. By matching reconstructed neurons to examples from light microscopy, we assigned neurons to cell types and assembled a connectome of the repeating module of the medulla. Within this module, we identified cell types constituting a motion detection circuit, and showed that the connections onto individual motion-sensitive neurons in this circuit were consistent with their direction selectivity. Our identification of cell types involved in motion detection allowed targeting of extremely demanding electrophysiological recordings by other labs. Preliminary results from such recordings show time delays confirming our findings. This demonstrates that connectomes can provide key insights into neuronal computations.



A nanoscale view into the dynamic of AMPA receptor organization in synapses

Daniel Choquet

University of Bordeaux
Bordeaux, France

The spatio-temporal organization of neurotransmitter receptors in the postsynaptic membrane is a fundamental determinant of synaptic transmission and thus information processing by the brain. Ionotropic AMPA glutamate receptors (AMPAR) mediate fast excitatory synaptic transmission in the central nervous system. Using a combination of high resolution single molecule imaging techniques and video-microscopy, we had previously established that AMPARs are not stable in the synapse as thought initially, but undergo continuous entry and exit to and from the post-synaptic density through lateral diffusion.

Using three independent super-resolution imaging methods together with modeling, on both genetically tagged and endogenous receptors, we now demonstrate that, in live hippocampal neurons, AMPAR are highly concentrated inside synapses into a few clusters of around seventy nanometers. AMPAR are stabilized reversibly in these domains and diffuse freely outside them. Nanodomains are themselves dynamic in their shape and position within synapses as they can form and disappear within minutes, although they are for the most part stable for at least up to an hour. These results open the new possibility that glutamatergic synaptic transmission is controlled by the regulation at the nanometer scale of the position and composition of these highly concentrated nanodomains.

The Virtual Brain: A simulator of large-scale brain network dynamics

Viktor Jirsa

Inserm at Aix-Marseille University
Marseille, France

We present The Virtual Brain (TVB), a neuroinformatics platform for full brain network simulations using biologically realistic connectivity. This simulation environment enables the model-based inference ofneurophysiological mechanisms across different brain scales that underlie the generation of macroscopic neuroimaging signals including functional MRI (fMRI), EEG and MEG. Researchers from different backgrounds can benefit from an integrative software platform including a supporting framework for data management (generation, organization, storage, integration and sharing) and a simulation core written in Python. TVB allows the reproduction and evaluation of personalized configurations of the brain by using individual subject data. This personalization facilitates an exploration of the consequences of pathological changes in the system, permitting to investigate potential ways to counteract such unfavorable processes. The architecture of TVB supports interaction with MATLAB packages, for example, the well known Brain Connectivity Toolbox. TVB can be used in a client-server configuration, such that it can be remotely accessed through the Internet thanks to its web-based HTML5, JS, and WebGL graphical user interface. TVB is also accessible as a standalone cross-platform Python library and application, and users can interact with the scientific core through the scripting interface IDLE, enabling easy modeling, development and debugging of the scientific kernel. This second interface makes TVBextensible by combining it with other libraries and modules developed by the Python scientific community. Here we describe the theoretical background and foundations that led to the development of TVB, the architecture and features of its major software components as well as potential neuroscience applications.

The Functional Connectomes Project

Michael Milham

Child Mind Institute
New York, United States

Central to the development of clinical tools for developmental neuropsychiatry is the discovery and validation of biomarkers. Resting state fMRI (R-fMRI) is emerging as a mainstream approach for imaging-based biomarker identification, detecting variations in the human connectome that can be attributed to developmental and clinical variables (e.g., diagnostic status). Despite growing enthusiasm, many challenges remain. I will discuss evidence of the readiness of R- fMRI based functional connectomics to lead to clinically meaningful biomarker identification through the lens of the criteria used to evaluate clinical tests (i.e., validity, reliability, sensitivity, specificity, and applicability). Gaps and needs for R-fMRI- based biomarker identification will be identified, and the potential of emerging conceptual, analytical and cultural innovations (e.g., the Research Domain Criteria Project (RDoC), open science initiatives, and Big Data) to address them will be highlighted. The need to expand future efforts beyond identification of biomarkers for disease status alone will be discussed, with a particular emphasis on the importance of identifying clinical variables related to risk, expected treatment response and prognosis.

In silico neuroscience – an integrative approach

Felix Schürmann

École Polytechnique Fédérale de Lausanne
Lausanne, Switzerland

Many areas of science and engineering have adopted simulation-based research as a novel tool for discovery and insight. The sustained performance growth in supercomputer performance allows ever more detailed models, which makes supercomputing nowadays also a viable tool for biology. However, the heterogeneity of neural systems poses particular challenges: the data is multi-modal, multi-scale and often times incomplete; intricate workflows are required for model generation and mathematical formulations are volatile; due to the heterogeneity requirements of memory and compute are demanding. At the same time, neurobiology has potentially a lot to gain: systematically accounting for the data and bringing it together in a unifying computer model provides an integration strategy capable of overcoming the fragmentation of data and identifying gaps in our knowledge. Attempting this ultimate integration is revealing novel design principles of the brain. These principles are in turn helping to predictively fill gaps in data and knowledge. As a proof of concept, the Blue Brain Project built a facility comprised of many key technologies and workflows and used this facility to build and simulate a unifying model of the neocortical microcircuit of the young rat.

Special session on
Big data in clinical and translational informatics

Yike Guo
Asla Pitkanen

Small brain and big data

Yike Guo

Imperial College
London, United Kingdom

Brain research is largely data driven. At Imperial Data Science Institute, we focus on applying modern statistics and machine learning methods for studying drain diseases prediction and monitoring. In this talks, I will cover few of our work in this area including applying deep learning methods for epilepsy prediction, and using a novel regularization method to automatically detect significant voxel activation for fMRI analysis. Also, I will present some of our new work in the area of neuroconnectivity research by applying big data analysis methods.

Common Data Elements: A remedy for cure of underpowered preclinical studies

Asla Pitkanen

University of Eastern Finland
Kuopio, Finland

Due to many failures in translating the promising preclinical treatments into clinic, interest of industry in brain-related diseases is vanishing. This has raised a concern that there will be no novel, more efficient, and better tolerated treatments for many neurological and psychiatric diseases, including epilepsy. The problems in translation have been related to models used, differences in pathophysiology of the disease between species, and importantly, to lack of statistical power and reproducibility of pre-clinical studies. NIH has an initiative that has led to generation of common data elements (CDEs) for over 10 neurological diseases that can be used to harmonize clinical trials. Until recently, there have been very few attempts for harmonization of practices in pre-clinical studies. Epilepsy research community has initiated in 2013 an activity to generate CDEs for preclinical epilepsy research. In smaller scale, individual consortia like FP7 EPITARGET have established CDEs suitable for their experimental designs. Even though there is no experience yet, how the CDEs become applied in experimental laboratories, one can expect that their use will generate more accurate and reproducible large datasets, and reduce the concern related to underpowered pre-clinical studies.

Workshops

1: The neuroinformatics of neuroanatomy

2: Building the brain

3: Synaptic computation workshop

4: Open collaboration in computational neuroscience

Workshop 1: The neuroinformatics of neuroanatomy

Chair: **Maryann Martone**

Neuroanatomy provides one of the unifying frameworks for neuroscience and thus it is not surprising that it provides the basis for many neuroinformatics tools and approaches. Regardless of whether one is working at the subcellular, cellular or gross anatomical level or whether one is modeling circuitry, molecular pathways or function, at some point, this work will include an anatomical reference. The brain is perhaps unique in the number of nomenclatures and strategies for parcellating its anatomy. Yet this diversity creates a headache for current information systems, which must attempt to reconcile the different reference systems developed. This workshop will focus on what is required of those working in neuroanatomy to make their data suitable for and compliant with neuroinformatics systems, so that it can be compared computationally to other work and reused by others, including those who are working in genomics, proteomics, physiology, and other forms of behavior. Thus, the aim is to focus less on exactly how one parcellates a brain and more on how one models this parcellation to make the information usable. We will hear from researchers working on informatics systems that include an atlasing component about their approaches and best practices.

Speakers:

Trygve Leergard
Department of Anatomy, Institute of Basic Medical Sciences, University of Oslo Oslo, Norway
Jacopo Annese
University of California, San Diego, United States
Douglas Bowden
University of Washington, Seattle, United States
Mike Hawrylycz
Allen Institute for Brain Science, Seattle, United States

Navigating the rodent brain by digital atlasing

Trygve B. Leergard
Department of Anatomy, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway

Accurate assignment of anatomical location to rat and mouse brain image data is essential for interpretation and comparison of experimental measurements. Rodent brain atlases therefore rank among the most cited neuroscience publications. New generation open-access atlases now provide volumetric reference templates based on high-resolution MRI data, and recent studies have shown that anatomical regions and subregions to a large extent can be defined on the basis of MRI contrast. Volumetric atlas templates will allow researchers to efficiently accumulate, analyze, compare, and reuse experimental data. But before these promising resources can fulfill their potential, efficient tools and procedures for data registration are needed, and important concerns regarding anatomical precision must be considered. I will here review recent developments in the field of digital atlasing and discuss some challenges ahead.

The digital renaissance of human neuroanatomy

Jacopo Annese
University of California, San Diego, United States

The field of neuroscience is once again looking at the brain as matter. This is due largely to the new power and sophistication of available techniques that are applied to modeling neural architecture. We are at the exciting technological stage where it has become feasible to represent the anatomy of an entire human brain at the cellular level; this is exciting because cytological parameters such as axonal architecture, neuronal number, size, and cortical layer organization are still extremely relevant to the clinical neurosciences. This knowledge, if formalized at the system level, can bridge Connectome-era brain maps with classical architectonic and comparative data produced by histological methods and stereology. Currently, the combination of 2-D and 3-D digital imaging approaches and algorithms for the automated analysis of cellular-level features can be used to build brain models with the potential to demonstrate the structural basis behavioral and pathological phenotypes. The challenge is to make sense of the seemingly insurmountable microstructural complexity within white and gray matter and produce templates that can, in spite of individual variability, be generalized for translational applications. In other words, neuroanatomy, in the XXI Century is less concerned with topography and classification; rather, it has become an effort towards the virtualization and standardization of brain tissue.

Essential features of digital brain models for neuroinformatics

Douglas Bowden
University of Washington, Seattle, United States

The ideal digital brain atlas will allow investigators to map data obtained by any method directly into a canonical atlas where its location can be compared with all other data mapped to the same atlas. The neuroscience community will be best served by adoption of a single atlas per species, because every transcription of data from one atlas to another loses information. For maximal precision the atlas of each species should be based on a high resolution MRI. To maximize utility for neurophysiologists who wish to stimulate, inject, or record in areas of data concentration, the atlas should be registered to a conventional stereotaxic space. Since every investigator's first question will be, "Where are my data located?" the canonical atlas should be segmented to match a widely accepted conventional atlas. Alternative segmentations should be mapped to the atlas like any other data and made available for comparison. The mapping application should enable nonlinear warping of images of brain sections to corresponding planes of section in the atlas using as many landmarks as possible. The atlas application should enable preparation of images of mapped data for presentation and publication. And it should enable investigators to upload mapped data sets to the atlas website: 1) for comparison with existing data, and 2) for deposit in a permanent repository where future investigators can compare it with theirs.

Neuroinformatics and digital atlases of the Allen Institute for Brain Science

Mike Hawrylycz
Allen Institute for Brain Science, Seattle, United States

Neuroinformatics techniques and analysis have played a large role in the development and presentation of many of the atlases of the Allen Institute for Brain Science. Large scale pipelines manage the flow of data from laboratory to the web, using methods of image processing, data analysis, and annotation. In this presentation we survey the neuroinformatics tools and techniques used and their relationship to neuroanatomy for the Allen atlases of the mouse, developing mouse, and mouse connectional atlas.

Workshop 2: Building the brain

Chair: **Paul Tiesinga**

Most approaches within computational neuroscience simulate systems, brain networks, local circuits, as they are now. In recent years, homeostatic regulation has been characterized and modeled; however, for understanding diseases that have their origin in genetic defects that emerge at later age, it is important to understand how these defects interact with developmental processes that occur earlier and last longer that the typical period considered for homeostatic studies. It also important to understand from a basic science standpoint how the brain is built from the ground up and whether that leads to 'shortcuts' to make it possible to build realistic models for the connectivity of the mature brain and characterize the natural variability in brain structure. This workshop will discuss the building of the cortical circuit in terms of neural migration, axonal growth, and the formation of synapses.

Speakers:

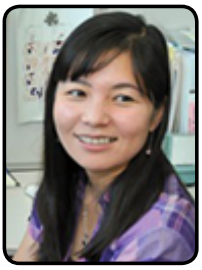
Geoff Goodhill
University of Queensland, Brisbane, Australia
Tomomi Shimogori
RIKEN Brain Science Institute, Tokyo, Japan
Rodney Douglas
Institute of Neuroinformatics, University of Zurich, Zurich, Switzerland
Nenad Sestan
Yale University, New Haven, United States

Computational principles of axon guidance

Geoff Goodhill
University of Queensland, Brisbane, Australia

Correct brain function relies on the accurate guidance of growing axons to their appropriate targets during development. At the tips of developing axons, growth cones are highly dynamic structures with exquisite sensitivity to environmental cues. I will discuss our recent experimental and theoretical work attempting to uncover the computational principles that growth cones employ to detect and respond to environmental chemotactic gradients, focusing particularly on growth cone shape dynamics. I will discuss how just a few shape primitives capture most of the shape variance of growth cones, and that periodic oscillations play a critical role in their shape dynamics.

BTBD3 controls dendrite orientation toward active axons in mammalian neocortex



Tomomi Shimogori
RIKEN Brain Science Institute, Tokyo, Japan

Experience-dependent structural changes in the developing brain are fundamental for proper neural circuit formation. Here, we show that during the development of the sensory cortex, dendritic field orientation is controlled by the BTB/POZ domain–containing 3 (BTBD3). In developing mouse somatosensory cortex, endogenous Btbd3 translocated to the cell nucleus in response to neuronal activity and oriented primary dendrites toward active axons in the barrel hollow. Btbd3 also directed dendrites toward active axon terminals when ectopically expressed in mouse visual cortex or normally expressed in ferret visual cortex. BTBD3 regulation of dendrite orientation is conserved across species and cortical areas and shows how high-acuity sensory function may be achieved by the tuning of subcellular polarity to sources of high sensory activity.

Principles of neocortical self-construction

Rodney Douglas
Institute of Neuroinformatics, University of Zurich, Zurich, Switzerland

Current scientific wisdom in Europe and the USA promotes exhaustive data collection projects as the necessary route to understanding the structure and function of the nervous system, and so of future neuromophic computers. These proposed exa- to zettabyte descriptions stand in stark contrast to the gigabyte of construction information available to the developing brain. This enormous disparity raises the question of how the elaborate information processing circuits of (for example) the neocortex construct themselves using the relatively small amount of information encoded in the genome of neuronal stem cells. Our approach to this intriguing question combines experimental observation of cortical development with simulation of a detailed model of the physical process itself. The entire simulated development plays out under the control of an abstract regulatory network inserted into the initial neuroepithelial cells. These cells then expand by mitosis, differentiation, and morphological specialization into the multi-layered connected neural networks of two example murine neocortical areas, which are composed of about 0.25M neurons. I will explain this process, and show how we are able to infer the control GRN from only sparse experimental data. I will argue that understanding such abstract principles of biological development can provide novel insights into brain organization and function, as well as offering novel approaches to future self-constructing computers and other manufacturing technologies.

Functional genomics of human brain development and evolution

Nenad Sestan
Yale University, New Haven, United States

The mammalian brain develops through a dynamic and prolonged process that depends on the precise regulation of gene expression, and these processes vary across mammals to generate species-specific neural circuits and behaviors. Systematic efforts to map detailed gene expression patterns in the developing human brain have been lacking. In this presentation, I will describe some of our recent efforts to characterize the transcriptome of the developing human brain. I will also introduce the audience to the BrainSpan project (brainspan.org), a rich new open access data resource focused on anatomical, transcriptional and epigenetic analyses of the developing human brain. These data are already being used in a variety of ways. I will demonstrate how they can be used to study the molecular instructions for human brain development, and how there are conserved and divergent features between model organisms and humans that may help explain unique features of human brain structure and function. In addition, they provide a spatiotemporal map of transcript distribution that can be used to complement genetic studies of diseases, providing potential regional and developmental patterns of action for disease-associated genes.

Workshop 3: Synaptic computation workshop

Chair: **L. Niels Cornelisse**

The synapse is often considered to be the basic unit of computation in the brain given its highly nonlinear properties. Last year two decades of exciting molecular and cellular neuroscience on the synapse were acknowledged with the award of the Nobel prize to three pioneers in the field, Rothman, Schekman and Südhof. Despite all insights at the molecular and cellular level, the synapse remains enigmatic when it comes to its role in shaping the computational properties of neuronal networks. With the rapid advancement of computer simulation capacity and initiatives like the Human Brain Project there is a growing need for accurate models of synaptic computation to facilitate more realistic neural network simulations. This will not only results in a better understanding of how the brain processes information, and how certain gene defects in the synapse lead to brain diseases, but may also serve as a source of inspiration for new strategies in artificial intelligence and cognitive computing.

In this workshop 4 speakers will present the latest insights (published and unpublished work) in the processes that underpin both short- and long-term synaptic plasticity, using detailed (stochastic) models for the presynaptic terminal and the postsynaptic site, and the impact of both forms of synaptic plasticity on network behavior, using network models

Speakers:

Erik De Schutter
Okinawa Institute of Science and Technology, Okinawa, Japan
Bert Kappen
Radboud University Nijmegen, Nijmegen, The Netherlands
Alexander Walter
Charité Cross Over, Berlin, Germany
Michele Giugliano
University of Antwerpen & Neuro-Electronics Research Flanders, Antwerp, Belgium

Importance of stochasticity and small molecule number in the induction of synaptic plasticity

Erik De Schutter
Okinawa Institute of Science and Technology, Okinawa, Japan

It is well known that many aspects of synaptic transmission are highly stochastic, the most obvious being the transmitter release process. The experimental induction of synaptic long-term plasticity important in learning is also highly variable. A likely reason is that the signaling pathways involved with synaptic plasticity induction exist in spines that have very small volumes, resulting in small numbers of molecules (range 10 ~ 100) participating in the reactions.

In a study of the induction of cerebellar long-term depression (LTD) at Purkinje cell synapses, which is evoked by a rise in cytosolic calcium activating PKC and a MAP-kinase based feedback loop, we have demonstrated that the stochasticity of the chemical reactions makes the induction probabilistic (Antunes and De Schutter, J. Neuroscience 2012). Though experimentally a sigmoidal relation between calcium concentration and amount of LTD was measured, the model predicts that this average over the induction in 100s of spines does not imply the existence of a calcium threshold. Instead, in single spines the induction is binary and the calcium concentration only sets the probability of induction as expected from stochastic dithering.

In a follow-up study we have discovered that the properties of this system critically depend on the number of Raf molecules in the spine (Jain et al. 2014). Raf is a proto-oncogene and a principal component of the MAP-kinase based feedback loop activated during cerebellar LTD induction. The predicted number of Raf molecules in a Purkinje cell spine is close to the critical minimal number to allow induction of LTD, a decrease by a few molecules prevents the induction of stable LTD while an increase does not cause much more LTD. Assuming free diffusion of Raf, the expected fluctuations in the number of Raf molecules in a spine will strongly influence its capacity to undergo LTD.

Besides the biological implications, these results also point to the need of detailed stochastic simulations that track integer number of molecules, like the Gillespie method implemented in the STEPS simulator (Hepburn et al., BMC Systems Biology 2012). Stochastic differential equations cannot replicate the dependence on molecule number of this system.

Emerging phenomena in neural networks with dynamic synapses and their computational implications

Bert Kappen
Radboud University Nijmegen, Nijmegen, The Netherlands

In this presentation I will review our research on the effect and computational role of dynamical synapses on feed-forward and recurrent neural networks. I will discuss a new class of dynamical memories, which result from the destabilization of learned memory attractors. This has important consequences for dynamic information processing allowing the system to sequentially access the information stored in the memories under changing stimuli. Although storage capacity of stable memories also decreases, our study demonstrated the positive effect of synaptic facilitation to recover maximum storage capacity and to enlarge the capacity of the system for memory recall in noisy conditions. Possibly, the new dynamical behavior can be associated with the voltage transitions between up and down states observed in cortical areas in the brain. We investigated the conditions for which the permanence times in the up state are power-law distributed, which is a sign for criticality, and concluded that the experimentally observed large variability of permanence times could be explained as the result of noisy dynamic synapses with large recovery times. Finally, I will discuss how short-term synaptic processes can transmit weak signals throughout more than one frequency range in noisy neural networks, displaying a kind of stochastic multi-resonance. This effect is due to competition between activity-dependent synaptic fluctuations (due to dynamic synapses) and the existence of neuron firing threshold, which adapts to the incoming mean synaptic input.

A catalytic slot model for exocytosis with a single release sensor effectively explains Ca^{2+} dependent properties of neurosecretion

Alexander Walter
Charité Cross Over, Berlin, Germany

Communication between nerve cells in the brain relies on chemical transmission of signals across synapses, highly specialized cell-to-cell interfaces. At the presynapse, regulated secretion of neurotransmitter-containing vesicles, exocytosis, activates postsynaptic responses. Exocytosis occurs on different timescales: fast (synchronous) release is mediated by high-release probability vesicles, whereas vesicles with low release probability contribute to slow (asynchronous) release. However, to what extent those vesicles differ in molecular composition, placement or state of maturation remains controversial.

While previous models of exocytosis necessitated parallel calcium-sensors to account for the observed remaining slow exocytosis following deletion of the fast calcium-sensor Synaptotagmin, we found that a simpler, sequential model with only a single release sensor suffices to describe previously obtained data in chromaffin cells and neurons: we suggest that during maturation vesicles associate with a catalyst at the release site. This catalyst facilitates priming by a calcium-dependent increase of the interconversion rate between un-primed and primed vesicles without changing the population of those states in equilibrium.

Previous kinetic models describing exocytosis have mainly relied on the numerical integration of chemical kinetic equations, disregarding the quantal nature of vesicle transitions. Given the relatively low number of vesicles contributing to exocytosis at single synapses, this is problematic. To describe the natural condition more accurately, we developed a new approach to model exocytosis from neurons by combining a stochastic simulation algorithm, stochastic placement of release sites and realistic spatio-temporal modeling of calcium-signaling.

Our model can explain salient observations, including calcium-dependence of exocytosis components, their fusion and recovery kinetics as well as statistical features of synapses and their short-term plasticity. It also accounts for a number of observations not easily explained in earlier models, including submaximal release (decreased fraction of fast/slow release at low calcium concentrations), effects of regional SNARE-mutation and the phenotype of synaptotagmin knockouts when stimulated by high-frequency trains.

We provide a mathematical framework that can be used to investigate the impact of changes in calcium-channel-release site topology and suggest that calcium-dependent catalysis is a fundamental feature of the release apparatus, optimizing the refilling of fast vesicles during sustained stimulation.

Emergence of connectivity motifs in networks of model neurons

Michele Giugliano
University of Antwerpen & Neuro-Electronics Research Flanders, Antwerp, Belgium

Recent evidence in rodent cerebral cortex and olfactory bulb suggests that short-term dynamics of excitatory synaptic transmission is correlated to the occurrence of stereotypical connectivity motifs. The cause of these structural differences in excitatory synaptic microcircuitry is unknown.

Supported by modelling and computer simulations, we propose that these connectivity motifs emerge from the interactions between short-term synaptic dynamics (SD) and long-term spike-timing dependent plasticity (STDP). Our study highlights the conditions under which SD-STDP explains the correlation between facilitation and reciprocal connectivity motifs, as well as between depression and unidirectional motifs. These conditions may lead to the design of experiments for the validation of the proposed mechanism.

Workshop 4: Open collaboration in computational neuroscience

Chair: **Angus Silver**

Neuroscience has traditionally been a discipline where isolated labs have produced their own experimental data and created their own models to interpret their findings. However, it is becoming clear that no one lab can create cell and network models rich enough to address all the relevant biological questions, or to generate and analyse all the data required to inform, constrain, and test these models. The success of the open source software development movement suggests that both model building and data collection/curation would be greatly enhanced by public, collaborative efforts to solve these problems. This workshop will highlight several examples of such efforts taking place in neuroinformatics today, and will present open tools and resources that can be instrumental in facilitating further efforts.

Speakers:

Stephen Larson
MetaCell, LLC, United States
Padraig Gleeson
University College London, London, United Kingdom
Rick Gerkin
Carnegie Mellon University, Pittsburgh, United States
Shreejoy Tripathy
University of British Columbia, Vancouver, Canada
Aurel A. Lazar
Columbia University, New York, NY, United States

Open Worm: A community developed in silico model of *C. Elegans*

Stephen Larson
MetaCell, LLC, United States

Stephen Larson will present the OpenWorm project (openworm.org), which aims to create an in silico, data driven model of the nematode C. elegans. This currently unfunded project has been successful in attracting computational and experimental neuroscientists and software developers from around the world towards this common goal.

The Open Source Brain Initiative, enabling collaborative model development in computational neuroscience

Padraig Gleeson
University College London, London, United Kingdom

Computational modelling is important for understanding how brain function and dysfunction emerge from lower level neurophysiological mechanisms. However, computational neuroscience has been hampered by poor accessibility, transparency, validation and reuse of models. The Open Source Brain (OSB) initiative (opensourcebrain.org) has been created to address these issues. This aims to create a repository of neuronal and network models from multiple brain regions and species that will be in accessible, standardised formats and work across multiple simulators. OSB will create a collaborative space to facilitate model creation and sharing, where both computational and experimental researchers can contribute to their development.

OSB combines advanced open source technologies for tracking, annotating and combining models developed across research teams, with software for building, validating, visualising, simulating and analysing models. While models can be developed and shared in any format we actively encourage and support their conversion to open, standardised modelling languages like NeuroML (NeuroML.org) and PyNN (neuralensemble.org/PyNN). OSB will also benefit from close interaction with other important neuroinformatics resources like NeuroMorpho, ModelDB, NIF and NeuroElectro.

Padraig will introduce the aims of the OSB initiative, describe the current functionality of the website and the range of models already available, and present future plans for the project. By increasing the scientific rigour of model construction, improving their robustness and transparency and lowering technological barriers, OSB will increase the power of computational approaches and make them accessible to a wider range of neuroscientists.

NeuroElectro and NeuronUnit

Rick Gerkin
Carnegie Mellon University, Pittsburgh, United States

Rigorously validating a quantitative scientific model requires comparing its predictions against an unbiased selection of experimental observations according to sound statistical criteria. Developing new models thus requires a comprehensive and contemporary understanding of competing models, relevant data and statistical best practices. Today, developing such an understanding requires an encyclopedic knowledge of the literature. Unfortunately, in rapidly-growing fields like neuroscience, this is becoming increasingly untenable, even for the most conscientious scientists. For new scientists, this can be a significant barrier to entry.

Software engineers seeking to verify, validate and contribute to a complex software project rely not only on volumes of human documentation, but on suites of simple executable tests, called "unit tests". Drawing inspiration from this practice, we have developed SciUnit, an easy-to-use framework for developing "model validation tests" -- executable functions, here written in Python. These tests generate and statistically validate predictions from a specified class of scientific models against one relevant empirical observation to produce a score indicating agreement between the model and the data. Suites of such validation tests, collaboratively developed by a scientific community in common repositories, produce up-to-date statistical summaries of the state of the field. Here we aim to detail this test-driven workflow and introduce it to the neuroscience community. As an initial example, we describe NeuronUnit, a library that builds upon SciUnit and integrates with several existing neuroinformatics resources to support validating single-neuron models using data gathered by neurophysiologists.

Semi-automated approaches for drawing inferences from the vast neurophysiology literature

Shreejoy Tripathy
University of British Columbia, Vancouver, Canada

Over the past decade, neurophysiology saw a data explosion as groups worldwide have published thousands of articles on the biophysical properties of a rich diversity of neuron types. In this talk, I will discuss NeuroElectro.org, an effort to extract this information by employing semi-automated literature text-mining algorithms. I will describe approaches for normalizing and structuring such heterogeneous data. I will also describe meta-analyses where we have combined this data with other data sets, such as Allen Institute gene expression atlases, to explore the scope and genetic origins of brain-wide neuronal electrophysiological diversity. Lastly, I will discuss example use cases of NeuroElectro data, including using the public API to provide parmaters to help build and constrain generic computational neuron models.

Neurokernal: Emulating the drosophila brain on multiple GPUs

Aurel A. Lazar
Columbia University, New York, NY, United States

The brain of the fruit fly Drosophila melanogaster is an extremely attractive model system for reverse engineering the emergent properties of neural circuits because it implements complex sensory-driven behaviors with a nervous system comprising a number of components that is five orders of magnitude smaller than those of mammals. A powerful toolkit of well-developed genetic techniques and advanced electrophysiological recording tools enables the fly's behavior to be experimentally linked to the function of its neural circuitry.

To enable neuroscientists to use these strengths of fly brain research to surmount the structural complexity of its brain and create an accurate model of the entire fly brain, we have developed an open source platform called Neurokernel designed to enable collaborative development of comprehensive fly brain models and their execution and testing on multiple Graphics Processing Units (GPUs). Neurokernel's model support architecture is motivated by the organization of the fly brain into fewer than 50 functional modules called local processing units (LPUs) that are each characterized by a unique population of local neurons. By defining communication interfaces that specify how spikes and neuron membrane states are transmitted between LPUs, Neurokernel enables researchers to collaboratively develop and refine whole-brain emulations by integration of independently developed processing units. Neurokernel will also empower researchers to leverage additional GPU resources and future improvements in GPU technology to accelerate model execution to the same time scale as a live fly brain; this will enable in vivo validation of Neurokernel-based models against real-time recordings of live fly brain activity.

We will demonstrate Neurokernel's module interfacing feature by using it to integrate independently developed models of olfactory and vision LPUs based upon experimentally obtained connectivity information.

Oral presentations abstracts

Topics:

OD - oral demo
OP - oral presentation

OD01 Central and peripheral monosynaptic, polysynaptic and collaterals connectivity in the rat

Oliver Schmitt[1], Peter Eipert[1], Rene Hoffmann[2], Paulinne Morawska[1], Ann-Christin Klünker[1], Jennifer Meinhardt[1], Felix Lessmann[1], Julia Beier[1], Kanar Kadir[1], Adrian Karnitzki[1], Jörg Jenssen[1], Lena Kuch[1], Linda Sellner[1] and Andreas Wree[1]
1. University of Rostock, Anatomy, Rostock, Germany
2. University of Rostock, Mathematics, Rostock, Germany

Most stereotaxic tract-tracing studies were performed in the laboratory rat. Therefore, the most comprehensive knowledge of central and peripheral nervous system connectivity is available for this tetrapode vertebrate. The rat connectome project is a long term metastudy that aims to collate all connections described in peer reviewed articles documenting neuronal connections detected by stereotaxic tract-tracing techniques in juvenile and adult normal rats (non-genetically and non-experimentally modified). So far, connections of 4300 reports have been collated and currated by experts in neuroanatomy. These data, have been imported in the generic framework neuroVIISAS (neuroviisas.med.uni-rostock.de) for advanced connectome analysis and simulation. To combine the different granularities of the collated connections, an extensive hierarchy of parts of the nervous system of the rat was created, containing all the regions participating in the imported connections and distiguishing the different hemispheric parts. This hierarchical approach and the extend of collated data is unique and allows the most precise connectome analysis on different levels of granularity with regard to ipsi-, contra-, bi- and unilateral specifications of connections. The hierarchical terminology is directly related to brain regions defined in different stereoteaxic atlases of the rat central nervous system. 2D- and 3D-atlas data are directly available and are used to visualize connectivity spatially. In addition 223 single neuron parameters of the Senselab database (neuroelectro.org) have been related to types of neurons used in neuron models implemented in NEST. In neuroVIISAS an interface to NEST (nest-initiative.org) is available that allows to use all NEST neuron models and moduls of the simulation engine in combination with real world connectivity and neuron parameters. To complete the number of critical parameters of realistic simulations we will present first results of a high-throughput-high-resolution identification of single cells of a terabyte virtual-slide dataset. For the first time, the rat connectome project also includes collateral connections from multi-tracer reports as well as pathways from transneuronal tract-tracing publications. This different type of connectivity data can be efficiently seperated from the conventional monosynaptic non-collateral one and integrated in population simulations. Currently the connectome consists of 232688 ipsi- and contralateral weighted (connection strength) and directed connections, completed by 2253 transneuronal pathways and 605 collateral sources. In conclusion, a nearly complete collation of consistent multiscale connectivity data of a whole nervous system of the rat is available (neuroviisas.med.uni-rostock.de). The laboratory rat is a well known vertebrate of which a huge amount of neuroscientific data exist. Such an outstanding source of connectivity, neuroanatomical, neurophysiological and behavioral data could be a promising starting point for multimodal large scale simulations in order to understand cognition and behavior of a complex vertebrate nervous systems.

OP02 Critical points detection in neuron microscopy images

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Measuring the morphology of neuronal cells is an essential step towards understanding neuronal cell and network functionality. Fluorescence microscopy is a powerful tool for capturing detailed information about neuronal cell morphology and connectivity. The enormous amount of image data acquired in typical experiments is not used to its full potential due to the fact that automated neuron reconstruction methods are still very far from being perfect and expert manual image annotation is too laborious. Hence the development of computational image analysis methods that allow accurate and efficient neuron reconstruction is imperative [1-3]. Neurons are tree-like structures whose accurate representation depends critically on the bifurcations and end-points. Automatic identification of these critical points in the images provides important clues for neuronal reconstruction. We have developed a novel method that automatically detects and characterizes bifurcations [4] as well as end-points in microscopy images of neuronal cells. Several challenges emerge when processing such images, such as nonuniform intensity (caused by inhomogeneous staining), the complexity and diversity of the image structures, and the fact that many of these structures are below the optical resolution limit. To address these issues, our method combines a newly developed directional filtering algorithm and a fuzzy-logic [5] rule-based reasoning scheme to decide about the presence and the type of critical point at each image location. We have carefully designed a set of fuzzy-logic rules that leverages the local image context at each point to make accurate decisions. The developed method has been successfully applied for critical points detection in preliminary experiments involving fluorescence microscopy image data sets from various labs in order to test robustness. The presented results (see attached figure) illustrate the potential of the method (with bifurcations and end-points shown as red and yellow dots, respectively, where larger diameters indicate higher reliability). We are in the process of developing a fully automated system for neuronal reconstruction that takes advantage of the sparseness of the image data and at the same time exploits local image context to achieve both high efficiency and high accuracy. The presented critical points detection method provides essential input to the system and will prove useful to existing neuron tracing methods as well.

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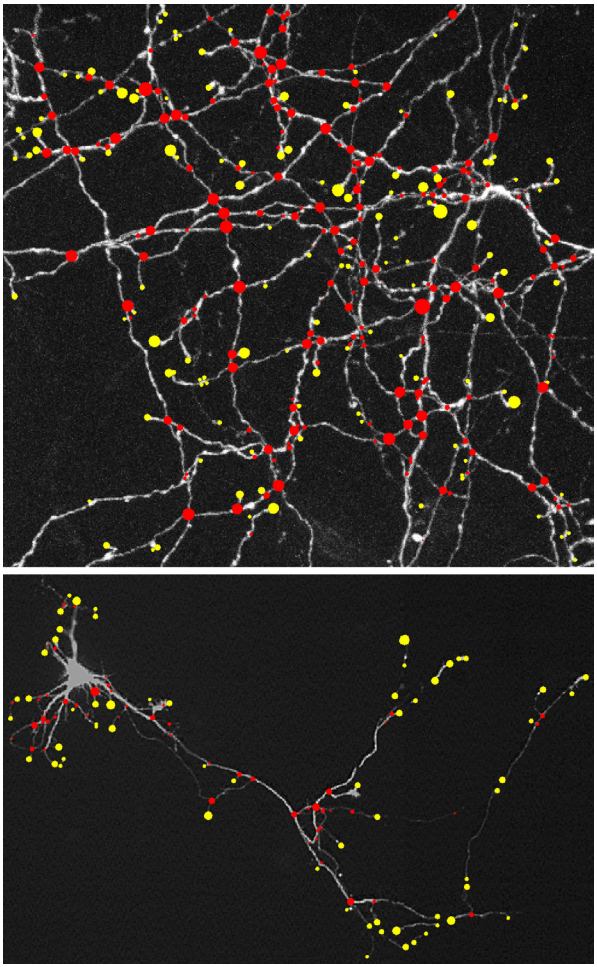

OP03 Inter-network interactions: impact of connections between oscillatory neuronal networks on oscillation frequency and pattern

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Oscillations in electrical activity are a characteristic feature of many brain networks and display a large variety of temporal patterns. A network may express a single oscillation frequency, alternate between two or more distinct frequencies, or continually express multiple frequencies. In addition, oscillation amplitude may fluctuate over time. The origin of this complex repertoire of activity remains unclear. Interactions between oscillatory networks may contribute, but the effects of these interactions are poorly known. Here, we created two model networks, one generating on its own a relatively slow frequency (slow network) and one generating a fast frequency (fast network). Taking either the slow or the fast network as source network projecting connections to the other, or target, network, we systematically investigated how type and strength of inter-network connections affected target network activity. For high inter-network connection strengths, we found that the source network could completely impose its rhythm on the target network (see figure 1). Interestingly, the slow network was more effective at imposing its rhythm on the fast network than the other way around. The strongest entrainment occurred when excitatory cells of the slow network projected to excitatory or inhibitory cells of the fast network. The fast network most strongly imposed its rhythm on the slow network when its excitatory cells projected to excitatory cells of the slow network. Strikingly, for lower inter-network connection strengths, multiple frequencies coexisted in the target network. Just as observed in rat prefrontal cortex, the target network could express multiple frequencies at the same time, alternate between two distinct oscillation frequencies, or express a single frequency with alternating episodes of high and low power. Together, our results suggest that input from other oscillating networks may markedly alter a network's frequency spectrum and may partly be responsible for the rich repertoire of temporal oscillation patterns observed in the brain.

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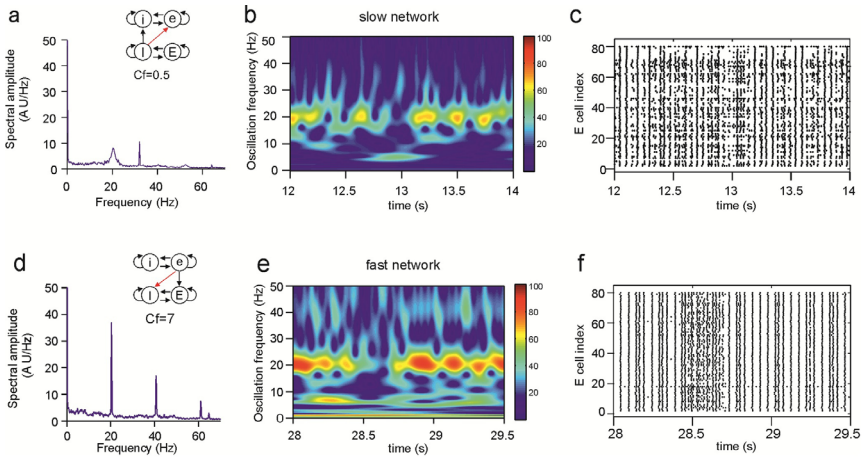

OP04 Identifying research resources in biomedical literature should be easy

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The published literature is where researchers go to build upon previous work; however, the reproducibility of this research has recently been scrutinized in the scientific community and even the popular media. A central tenet of reproducibility is a clear and unambiguous description of the data, methods, and material resources in publications. While research resource identification is an important step towards promoting reproducible and efficient science, we recently attempted to identify research resources (model organisms, antibodies, knockdown reagents, constructs, and cell lines) in the biomedical literature. The results showed that only 54% of resources were uniquely identifiable, regardless of domain, journal impact factor, or reporting requirements (Vasilevsky et al., 2013; peerj.com/articles/148). This was largely due to a lack of unique identifiers such as a catalog numbers in the publications. To address this issue, the Resource Identification Initiative (RII) was formed by a dedicated group of academics, government and non-government institute officials, publishers and commercial antibody companies. This initiative aims to enable resource identification within the biomedical literature through a pilot study promoting the use of unique Research Resource Identifiers (RRIDs). In the pilot study, authors are asked to include RRIDs in their manuscripts prior to publication for three resource types: antibodies, model organisms and tools (including software and databases). RRIDs meet key criteria: they are unique, they are machine readable, free to generate and access, and are consistent across publishers and journals. The intention is to provide a central resource for journal submission systems to access shared resource identifiers and conversely link to the various nomenclature and data authorities. To facilitate access to the RRIDs, we aggregated data for the three resource types into the Resource Identification Portal (scicrunch.com/resources). The portal pulls data from antibody catalogs from over 200 vendors, transgenic organisms from sources such as MGI, IMSR, ZFIN, ZIRC, CGC, WormBase, and RGD; and additionally, the portal contains the NIF Resource Catalog, which contains over 3,700 software tools and over 3,300 academic databases. Accessibility from a single portal, with integrated help features and a "cite this" button enables researchers to quickly find their resources and include the RRID in the methods section or as a keyword in their publications. The pilot study included 25 participating journals over a 3-month time span, and had a stated goal to determine if authors could improve the way they identify their resources. While the pilot study is still underway, the preliminary data shows authors are using the Research Identification Portal (as of 4/11/2014 there were 10,878 sessions on the portal from 8,822 unique users, more than 100 user help requests, and 73 databases/software tool and 186 antibody registration requests were documented). An initial search for RRIDs in the literature indexed in PubMed showed there were 3 papers that had been indexed into PubMed that contained a total of

7 unique identifiers, 6 for software tools, 1 antibody, while google scholar shows 19 papers that contain at least one RRID. We anticipate the numbers of RRIDs in the literature will increase over the upcoming months as the papers continue to be published.

References

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OP05 Human areal expression of most genes is governed by regionalization

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The human brain is organized in multiple anatomical substructures, whose morphology and circuitry are believed to allow each substructure to carry out their distinct function. While the physiological and histological differences and similarities between structures have been intensively studied, the molecular profiles giving rise to those differences are far from being understood. Specifically, it is not known which principles govern the expression patterns of genes across the adult brain and what determines their spatial organization. Recent high-resolution genome-wide transcriptome profiling studies allow addressing these questions.

Here we study the relation between regional expression patterns of individual genes and the developmental origin of each region. We analyzed two genome-wide mRNA expression datasets from post-mortem adult human brain, with a total of 26 subjects and 4193 samples. For each gene, we computed an index that measures how strongly its expression pattern agrees with the brain-region developmental ontology.

We find that 94% of human genes exhibit a regional expression pattern that agrees with the known brain-region ontology. This effect is particularly strong in neuron-specific genes and is also present in astrocytes- and oligodentrocytes-specific genes. Importantly, the same effect is found in many genes that are not cell-type specific, including housekeeping genes, and genes involved in embryonic development. This suggests that gene expression in the adult brain is regionally tuned, even for genes that participate in brain-wide functions, and for genes whose function is known in embryonic development but not in the adult brain. Furthermore, when performing the same analysis over subregions of the neocortex, 25% of genes show distinct expression patterns across different cortical areas. This suggests that cortical regions are far more heterogeneous in terms of their transcriptome than believed before.

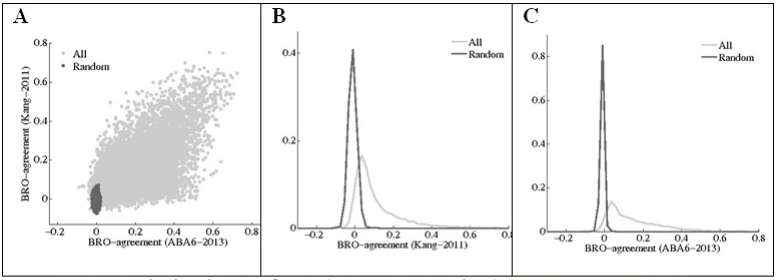

Figure 1. The distribution of BRO (Brain region ontology)-agreement scores. **(A)** A scatter plot showing BRO-agreement scores for 16 regions of the *ABA6-2013* dataset (absica) and the *Kang-2011* dataset (ordinate). Each light-grey dots corresponds to a single genes (a total of 17K genes). Dark-grey dots correspond to permuted data. The two BRO scores are significantly correlated (Spearman , ρ = 0.53, n=16947, *p*-value<10^{-16}). **(B)** Marginal distribution of BRO scores in the *Kang-2011* dataset. BRO scores for most genes are significantly greater than randomized scores. **(C)** Same as B, for the *ABA6-2013* data.

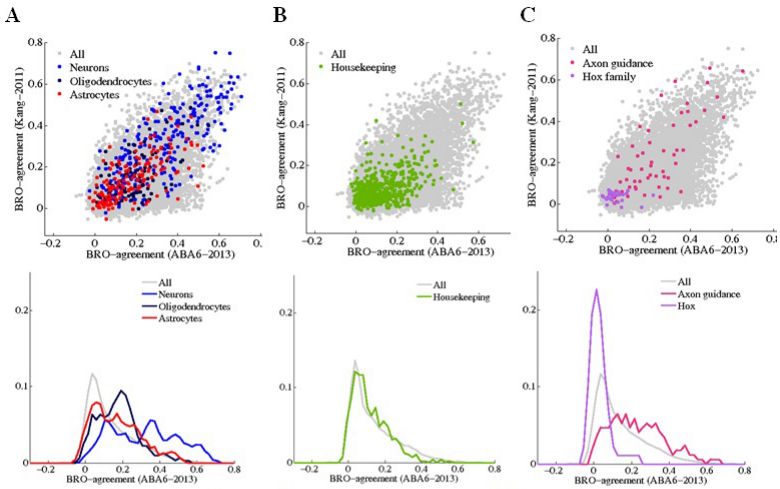

Figure 2. The distribution of BRO-agreement scores on different subsets of genes. The images in the upper row show the spreading of BRO scores in *ABA6-2013* and *Kang-2011*. The images below show the distributions in the *ABA6-2013* dataset. **(A)** Cell type specific genes receive higher agreement scores than all genes (Wilcoxonone tail test; neurons: *p*-value = 10^{-70}, oligoodendrocytes: *p*-value = 10^{-5}, astrocytes: *p*-value = 10^{-3}). **(B)** The distribution of BRO scores for housekeeping genes considerably overlaps with the BRO-scores distribution across all genes and the two are not significantly different (Wilcoxonone two-tail test: *p*-value = 0.25). **(C)** Axon guidance genes receive higher scores than general genes (Wilcoxon; *p*-value = 10^{-7}). Hox genes are less in agreement with region-ontology than the full set of genes. Comparing to the randomized scores we find that 21 Hox genes are BRO significant (67%).

OP06 Interoperability between the CBRAIN and VIP web platforms for neuroimage analysis

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Accessing substantial amounts of computing resources is required by several neuroimaging studies. CBRAIN (Sherif et al, 2014) and VIP - Virtual Imaging Platform (Glatard et al, 2013) - are two web portals offering access respectively to the Canadian and European Grid Infrastructures for neuroimage analysis. They provide services to launch and monitor experiments with state-of-the-art neuroimaging tools (e.g., FSL, Freesurfer and CIVET), and to trigger the required data movements accordingly. We are developing mechanisms to facilitate the interoperability between these portals, which would help users share and access larger data sets, access more computing resources, and access richer application catalogs. In this work, we describe our solutions to (i) harmonize authentication (ii) exchange data files (iii) share computing resources (iv) exchange applications between CBRAIN and VIP. We enabled single sign-on authentication to CBRAIN and VIP using Mozilla Persona, a secure, easy-to-implement, easy-to-use system respecting users' privacy. As a result, users can log-in to both VIP and CBRAIN using their email address only. Data sharing was enabled by developing synchronization robots between the Canadian and European infrastructures. With these robots, large data sets can be exchanged asynchronously between European and Canadian infrastructures, masking most of the transfer times. Regarding resource sharing, we are interfacing CBRAIN with the DIRAC task scheduler (Tsaregorodtsev et al, 2009) so that computing resources of the European Grid Infrastructure can be leveraged in CBRAIN. Exchanging applications is more ambitious due to the difficulty to automatically deploy neuroimaging applications on heterogeneous computing systems, and due to potential reproducibility issues resulting from such cross-system deployments (Gronenschild et al, 2012). To address these issues, we are developing an architecture based on the deployment of virtual machines on clusters, grids and clouds. Our prototype (Glatard et al, 2014) implemented in CBRAIN allows to register applications in virtual disk images, to run analyses with specific disk images, to deploy VMs uniformly and automatically on clusters and clouds, and to control the performance-cost trade-off associated to the deployment.

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OP07 Ultra-high field tractography and functional mapping of the subthalamic nucleus

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2. Maastricht University Medical Center, Department of Neuroscience, Maastricht, Netherlands
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Introduction
The basal ganglia are a group of deep brain gray matter nuclei that are involved in the pathophysiology of Parkinson's disease. The subthalamic nucleus (STN), is one of these nuclei and an important target for deep brain stimulation (DBS) surgery; a treatment that involves the stereotactic placement of an electrode, which is known to relieve motor symptoms. Although the location of the electrode has great influence on the clinical outcome, with current clinical MR imaging techniques, this small nucleus cannot be identified accurately enough to solely rely upon for targeting. However, with the introduction of ultra-high field (7T or higher) MRI scanners, higher resolution, and higher contrast imaging becomes available with shorter scan times. Furthermore, it offers the option to investigate the subject-specific structural connectivity and thereby the functional subdivisions of the STN in high detail. This is important to improve targeting of only the motor region of the STN and to improve our so-far limited understanding of basal ganglia functionality. In this study we investigate this high-resolution structural connectivity of the STN based on ultra-high field MRI data.

Methods
This study was approved by the local ethics committee of the Maastricht University Medical Center. Five healthy subjects were scanned on a 7T MRI scanner (Magnetom 7T, Siemens, Erlangen, Germany). The scan protocol consisted of 0.5 mm isotropic gradient echo (GE), and 1.5 mm isotropic diffusion weighted images. The STN was manually delineated from the GE scan. Constrained spherical deconvolution tractography was used to reconstruct the fibers emerging from the STN. Its projections were then used to functionally subdivide the structure.

Results
Scans are currently being performed and results will be presented during the meeting. Preliminary results show that fibers running from the STN to frontotemporal brain regions, which are known to be involved in cognitive and emotional functions, emerge from the ventromedial part of the STN. Fibers running from the STN to the premotor areas however emerge from the dorsolateral side of the STN (see Figure 1).

Conclusion

These results suggest that a high-resolution partition can be identified with the aid of ultra-high field MRI. With the planned inclusion of more subjects we expect to be able to also investigate the inter subject variability of these results.

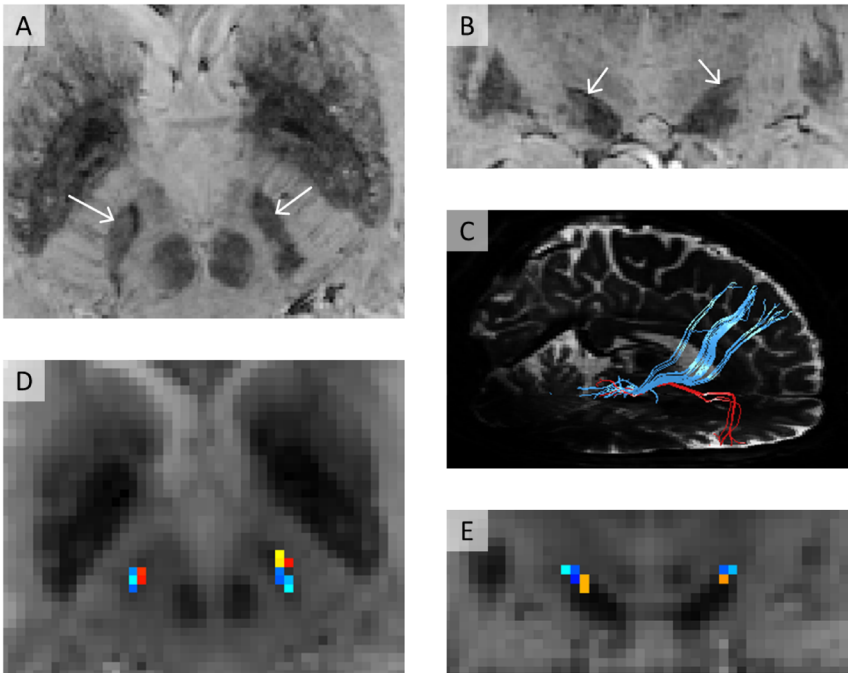

Figure caption

Figure 1. Axial (A) and coronal (B) high-resolution 7T gradient echo images of the human basal ganglia. The arrows denote the subthalamic nucleus (STN). Fibers emerging from the STN running to the premotor areas are shown in blue, those running to the frontotemporal brain regions are shown in red (C). Origins of these fibers in the STN with corresponding colors in axial (D) and coronal (E) plane.

OP08 IBMA: An SPM toolbox for NeuroImaging Image-Based Meta-Analysis

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Introduction
While most neuroimaging meta-analyses are based on peak coordinate data, the best practice method is an image-based meta-analysis that combines the effect estimates and the standard errors from each study [7]. Various efforts are underway to facilitate sharing of neuroimaging data to make such intensity-based meta-analysis possible (see, e.g. [4]). When image data is available for each study, a number of approaches (see [6] for a review) have been proposed to perform such meta-analysis including combination of standardised statistics, just effect estimates or both effects estimates and their sampling variance. While the latter is the preferred approach in the statistical community [1], often only standardised estimates are shared, reducing the possible meta-analytic approaches. In view of the increasing availability of image data for neuroimaging analyses, we introduce IBMA, a toolbox for SPM [8] providing a set of tools for image-based meta-analysis. The toolbox is freely available at: github.com/NeuroimagingMetaAnalysis/ibma.

Method
Using the IBMA toolbox, we studied six meta-analytic approaches based on:
- contrast estimates only: Random-effects General Linear Model (RFX GLM);
- contrast estimates and standard errors: Fixed-effects General Linear Model (FFX GLM);
- Z-statistic: Fisher's [2], Stouffer [9], Mixed-effects (MFX) Stouffer [7];
- Z-statistic and sample size: Weighted-Z [5,10].

Out of these six approaches, two are random-effects methods (RFX GLM, Stouffer MFX) and therefore offers the possibility to deal with studies heterogeneity. The fixed-effects approaches are strictly only appropriate if the between-study variance is null.

Using 21 studies of pain in control subjects, we visually compared the results obtained at $p< 0.05$ FDR corrected using the six meta-analytic approaches. The reference results were computed with the best-practice analysis: a 3-level hierarchical model: level 1, subject FFX; level 2, study MFX; level 3: meta-analysis MFX, using FSL's FLAME method [3].

Results and conclusion
Fig. 1 presents the detection obtained at $p< 0.05$ FDR corrected in a one-sample meta-analysis of pain using the IBMA toolbox. Further work will investigate the validity of each meta-analytic approach in the context of neuroimaging.

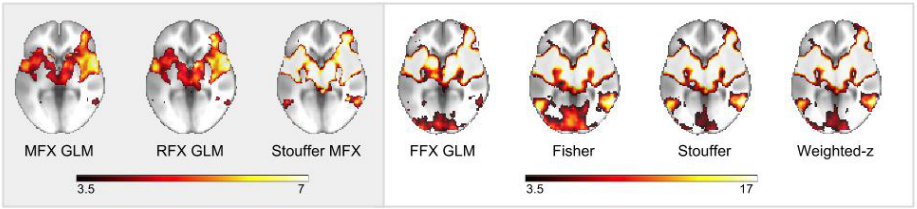

Fig. 1: Result of a meta-analysis of 21 pain studies for 4 fixed-effects (FFX GLM, Fisher, Stouffer, weighted-z) and 2 random-effects (RFX GLM, Stouffer MFX) meta-analytic approaches compared to the reference (MFX GLM) at a threshold of p<0.05 FDR corrected.

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OP09 The rat cerebral cortex macroconnectome

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The neuroanatomical circuitry of the cerebral cortex is the structural substrate for cognition. Even though the rat cerebral cortex (RCC) is one of the most investigated gray matter parts in neuroanatomy, there is no unitary and comprehensive view of its circuitry. In order to provide this, we have expertly annotated and inserted in the Brain Architecture Management System (brancusi.usc.edu) the brain-region level connections of the RCC, as reported in the primary research literature.

We report here the extensive completion of the RCC association connections (macroconnectome) as reflected from the published literature. The BAMS RCC macroconnectome is constructed from a total 75,000 connections reports inserted in the system, associated with more than 560 neuroanatomical tract tracing experiments, and curated from more than 450 references. It includes 1,923 association connections between 73 cerebral cortex regions, as defined in the Swanson 2004 Atlas. The BAMS RCC matrix has 82% coverage, and the connections are weighted on a ranked qualitative scale with 11 values. This matrix was statistically analyzed, using a method for weighted and directed networks.

The main results of our analysis are as follows: a) the RCC is divided in four modules that are structurally and functionally relevant; b) each module has distinct topographical and topological relationships with the other three; c) the network has the small-world and the rich-club properties; d) the cortical regions included in the RCC's rich-club are organized in two distinct poles, and e) the entorhinal lateral cortex is the hub of the RCC macroconnectome.

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

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

Demo abstracts

Topics:

D01 Spyke Viewer and the cloud: quick algorithm development and large scale data analysis for electrophysiology

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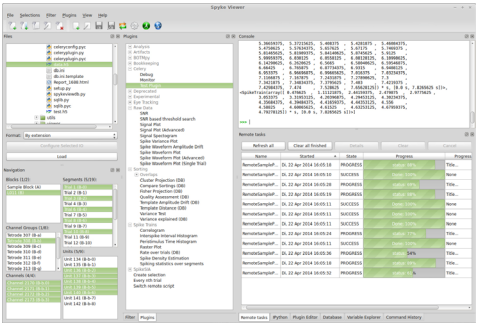
Effective analysis of the increasingly large amounts of data generated by current electrophysiological experiments and simulations requires powerful new tools. Spyke Viewer (Pröpper and Obermayer, 2013) is an open source, multi-platform application for navigating, visualizing and analyzing such data. Based on Python and the Neo framework (Garcia et al., 2014), Spyke Viewer supports reading and writing a wide variety of file formats. The loaded Neo object hierarchy is represented in a graphical object browser. Together with user-defined filters, the object browser is used to select data for visualization and analysis. Operations on the selected data can be performed using an integrated Python console or with plugins. Spyke Viewer includes a number of plugins for common plots and basic analyses. Users can easily create their own plugins using the integrated Python editor or external tools. Plugins are implemented as Python classes and can use any existing library. Spyke Viewer now supports executing plugins on computing or cloud servers using Celery [1]. Plugins, even with local code changes, can be submitted for remote execution with a single command. An arbitrary number of compute nodes can be used and new nodes can be added during runtime. Spyke Viewer includes a remote execution manager where users can manage queued, running and finished plugins or view parameters, progress and results. This allows quick iteration during development and simple execution even for large scale analyses.



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D02 Developmental coordination disorder in children – experimental work and data annotation

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Developmental coordination disorder (DCD) is described as a motor skill disorder characterized by a marked impairment in the development of motor coordination abilities that significantly interferes with performance of daily activities and/or academic achievement [1]. Since some electrophysiological studies suggest differences between children with/without motor development problems, we prepared an experimental protocol and performed electrophysiological experiments with the aim to make a step towards a possible diagnosis of this disorder using the event related potentials (ERP) technique. The second aim is to properly annotate the obtained raw data with relevant metadata and promote their long term sustainability. The experimental protocol is based on auditory stimulation using the stimuli representing animals and their sounds: bleating goat (80% probability of occurrence), barking dog (5%), meowing cat (5%), meowing dog (5%), and barking cat (5%); 600 stimuli are used in total during the experimental session. The tested subjects were children of younger school age from elementary schools in Pilsen. They were preliminary divided into three groups based on the level of their developmental coordination disorder identified by a motor test. During the experimental session, children were asked to reply to each target stimulus (dog or cat sound) by pressing one button for sounds of barking dog or meowing cat, and the other button for sounds of barking cat or meowing dog. All experiments were performed in a sound and electrically shielded booth placed in an electrophysiology lab. EEG/ERP activity was recorded using standard 10-20 international system with the reference electrode placed above the nose. Raw data were filtered and cleaned from artifacts; currently they are further analyzed. The data were collected and annotated respecting the current outcomes of INCF Program on Standards for Data Sharing, Task Force on Electrophysiology and the group developing the Ontology for Experimental Neurophysiology (OEN, github.com/G-Node/OEN). The data with metadata will be stored in the EEGbase database (eegdatabase.kiv.zcu.cz) after several conceptual and technological changes (deployment of noSQL database, changes in the user interface) in this web application. The experimental data and metadata will be also provided in the HDF5 format.

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D03 K-Surfer: A KNIME-based tool for the management and analysis of human brain MRI FreeSurfer/FSL Data

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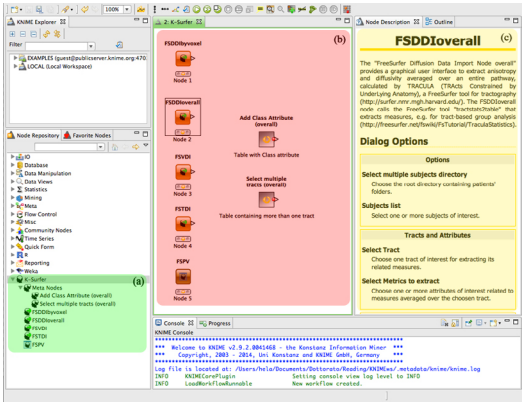
Diagnostic imaging techniques such as positron emission tomography (PET), magnetic resonance imaging (MRI), functional MRI (fMRI) and diffusion tensor imaging (DTI), represent nowadays the primary source of information in Neuroscience. A new challenge for neuroscientists is discovering knowledge by merging multi-source and multi-format data from imaging, genomics, proteomics and clinical evidences. As data size and complexity grow, the manual workflow for such analysis becomes time consuming and errors prone. Several software for neuroimaging processing aim to automatize the pre-processing of neuroimages by using a modular approach. FreeSurfer [1] and the FMRIB Software Library (FSL) [2] are popular examples of tools that can be used in conjunction for conducting both volume-based and surface-based analysis of human brain MRI. However extracting the multi-dimensional data (volume, thickness, diffusion indices) generated by FreeSurfer and FSL is not straightforward and requires an accurate and detailed knowledge of their tools, conventions and file formats. Furthermore, statistical analysis and data mining have to be performed by using external analytics platforms and the importing of neurological data into such tools, represents a crucial phase. Among several commercial and open-source software for data analytics, the Konstanz Information Miner (KNIME) [3,4], has received high satisfaction ratings in the last edition of the largest survey of data mining, data science and data analytics professionals in the industry [5]. This work presents K-Surfer , a novel and unique KNIME plug-in for brain MRI data. K-Surfer facilitates the design and deployment of fully automated workflows for extracting, managing and mining FreeSurfer and FSL data. It also integrates the FreeSurfer tool for the visualisation of 3D brain tracts into KNIME to allow an immediate comparison of numerical and visual findings. K-Surfer consists of five new KNIME modules (nodes), available in the Node Repository of KNIME (Fig. 1.a), with specific functionalities: (i) the node FSDDIoverall (FreeSurfer Diffusion Data Import overall) extracts anisotropy and diffusivity values averaged over an entire pathway; (ii) the node FSDDIbyvoxel (FreeSurfer Diffusion Data Import by voxel) extracts several measures as a function of the position along the trajectory of the pathway; (iii) the node FSVDI (FreeSurfer Volume Data Import) extracts the volumes of specific structures, as determined by the subcortical segmentation; (iv) the node FSTDI (FreeSurfer Thickness Data Import) extracts several measures, including the thickness of specific structures, as determined by the cortical segmentation; (v) the node FSPV (FreeSurfer Pathways Viewer visualises the probability distribution of single white-matter pathways or all white-matter pathways simultaneously. K-Surfer also includes two meta nodes that extends the previous functionalities: (i) the node Add Class Attribute (overall) can be used for adding a new column containing the class attribute to a diffusion data table; (ii) the node Select multiple tracts (overall) can be

used for extracting the diffusion values of more than one tract at once. A sample KNIME workflow demonstrating the K-Surfer nodes and meta nodes is depicted in Fig. 1.b and in the Fig.1.c the Node Description for the selected node is visualised. The nodes have user-friendly configuration dialogs (see Fig. 2 for an example) and do not require the user to write UNIX shell commands and scripts as required when using FreeSurfer and FSL directly. The main goal of K-Surfer is to extend KNIME so to provide a specific environment for the study of neurological data, reducing time costs and human errors. Furthermore, K-Surfer extends some current functionalities of FreeSurfer scripts for extracting data, adding new features such as importing measures related to more brain tracts, selecting subjects from different studies, and merging demographic, genomics and proteomics data. The KNIME extension K-Surfer is freely available at sourceforge.net/projects/ksurfer for non-commercial use.



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D04 Extending NI-DM to share the results and provenance of a neuroimaging study: Implementation within SPM and FSL

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Introduction
We propose a model for communicating functional brain imaging analyses results and associated provenance for enhancing data sharing, conducting meta-analyses, and for use by software and database developers. A typical neuroimaging study is divided in several steps including: data acquisition, pre-processing, statistical analysis and eventually publication. At each of these steps, new data is produced and a set of parameters, referred to as meta-data, must be recorded to facilitate reproducibility and meta-analyses [22]. The pre-processing and statistical analysis steps are usually performed inside a single analysis software (e.g. SPM [26] , FSL [6], AFNI [3]) or pipeline (e.g. Nipype [20], LONI pipeline [13], aa [1]). Further, a number of databases devoted to the storage of raw (ADNI [2], LORIS [14], XNAT [28], Shanoir [25], HID [11], COINS [5], IDA [29], etc.) and derived data (OpenFMRI [21], Neurovault [19], BrainMap [4], SumsDB [27], NeuroSynth [18]) have emerged and greatly encourage data sharing across the community [23].

However, in the absence of a common format to encode the meta-data, the communication between neuroimaging software is limited and databases are forced to query the user for or manually annotate missing meta-data (e.g. Neurovault, SumsDB, brainmap.org) or to use data mining approaches to automatically extract this information from the published papers (e.g. NeuroSynth, Brainspell).

In [7] and [12], we introduced the Neuroimaging Data Model (NI-DM), a domain-specific extension of the recently-approved W3C recommendation, PROV-DM [24]. Our work initially focused on the description of the dataset-experiment hierarchy [7,16] and provenance in Freesurfer [17]. Along with these models, a lexicon of DICOM terms was defined to capture the precise meaning of each entity [8, 9, 10]. Recently, we extended NI-DM to model the results of statistical parametric mapping studies, such as fMRI brain mapping results, and their provenance [15]. Here, we review our recent progress in implementing NI-DM to share the statistical results of a neuroimaging study in both FSL and SPM.

Methods

As presented in Fig. 1, this NI-DM extension focused on the final steps of a neuroimaging study including statistical estimation (computing the effects estimates and their standard errors) and inference on the statistical map (producing a thresholded map of regionally specific effects usually included in the result section of a neuroimaging study). We defined a recommended minimal set of neuroimaging metadata to be reported for functional MRI analyses, by engaging experts in neuroimaging data analysis in a series of weekly video conferences and focused workshops. In conjunction with the software development team, for both SPM and FSL, we implemented a native export in NI-DM as part of the analysis software.

Results

Fig 2 provides an overview of the proposed NI-DM extension. This result provides a formal model of the statistical inference in brain imaging, and is therefore also a first attempt to provide a unified view of this activity across software.

Conclusion

Further work will extend the data model to AFNI and other image analysis software, and integrate with NeuroVault.org API. This will allow developers to submit NI-DM description of the inference along the statistical maps thus providing rich metadata crucial for performing accurate meta analyses. Having a standardised and community driven way of adding and accessing data will improve usability and utility of NeuroVault.org. This initial test bed will allow to evaluate and refine the NI-DM standard in a practical context.

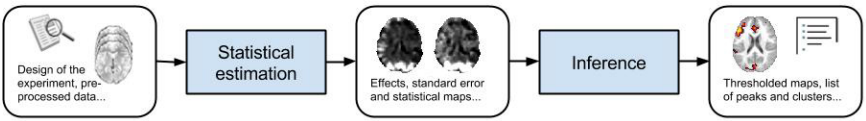

Fig. 1: Modelling the results of a neuroimaging study: from statistical estimation to inference.

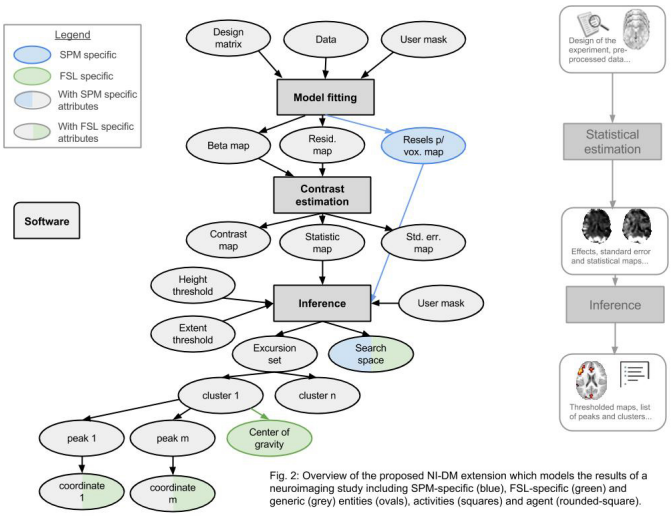

Fig. 2: Overview of the proposed NI-DM extension which models the results of a neuroimaging study including SPM-specific (blue), FSL-specific (green) and generic (grey) entities (ovals), activities (squares) and agent (rounded-square).

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D05 A Docker image for spiking neural network simulators

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Docker is a container engine that permits to deploy any application in the form of a container. Like virtual machines, it permits to build a tested environment in which a given software stack is guaranteed to work. However, unlike virtual machines, it also permits to dynamically use all the computing resources available on the host computer. This is essential for neural network simulations that are becoming everyday more heavy and that run in parallel.

The usefulness and future developments of spiking neural network simulators depend on the fact that the software is open source, on the sharing of experimental data and on the sharing of neural network models. It also depends on the spreading of the concepts of spiking neural networks in neuroinformatics and in the scientific community as a whole. For this to happen, there are two types of negative behaviors to deal with: One one hand, first-time users can be driven away from using the existing spiking neural network simulators by the mere installation of the simulators in their own computer. On the other hand, expert users may not want to try a new software stack to avoid corrupting their existing installations.

Docker images are an answer to both these problems. Indeed, first, it permits to run applications without any installation. Second, through the versioning system of the containers and of the images, it permits to try any new software without breaking a working software stack.

That's why we have publicly released a docker image containing all the spiking neural software simulators used in the European project BrainScaleS [1,2]. We placed it in the docker index. With this, you will be able to run NEST, Brian, NEURON, PyNN and the multi-simulation coordinator MUSIC on any host computer supporting Docker. Given their ubiquity and their strength, we want to promote the widespread use of Docker images in the neuroinformatics community.

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D06 The UrbanLegend Project: A system for cellular neurophysiology data management and exploration

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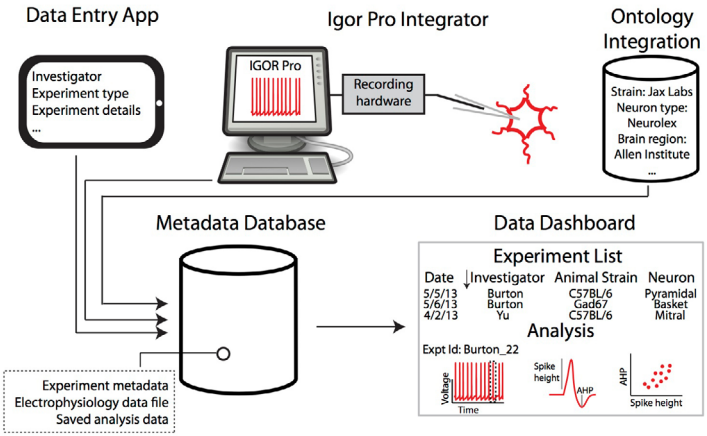
A challenge in neuroinformatics is translating developed tools like standards, best practices, and ontologies to experimental laboratories. While experimentalists generally agree that such standards are useful and can potentially help mitigate issues of scientific reproducibility, integrating these tools into scientists' existing workflows has been difficult. Using the example of cellular neurophysiology, experimentalists use a combination of technologies for acquiring and storing electrophysiological data including custom acquisition software (e.g., IGORPro or AxoClamp) and pen-and-paper lab notebooks to store relevant methodological details. While these laboratory-specific workflows are quite effective within each lab, the heterogeneous nature of how these data are stored and annotated makes within- and cross-lab data compilation extremely difficult. Here, we describe the UrbanLegend Project, a collaboration between the lab of Nathan Urban at Carnegie Mellon University and Elsevier Research Data Services (researchdata.elsevier.com), designed to improve in-lab practices of neurophysiological data annotation and standardization.

The UrbanLegend project is composed of the following primary components (schematic in Figure 1): 1) a web-based electronic lab notebook application for annotating in vitro electrophysiological recordings with essential methodological details; and 2) a data browser for visualizing and performing metadata-based searches of recorded data and analyses. Using the lab notebook app while performing an experiment, electrophysiologists enter details like the animal strain used or the neuron type recorded via a series of drop-down menus. This structured data entry approach allows enforcing a common metadata format and the usage of INCF standards and terminologies. Following experiment completion, the collected metadata is uploaded to a relational database and combined with the acquired electrophysiology data files into a semantically-enriched, reusable format for creative data exploration. Specifically, the web-based "Data Dashboard" allows for finding and sorting experiments using metadata as a search filter (e.g., find experiments with animals of age P10-12 and where olfactory bulb mitral or granule cells were recorded). Additionally, the dashboard facilitates interactive visualization of the collected sweeps as well as simple analyses.

While the UrbanLegend Project is currently implemented within the Urban Lab, we are actively seeking to scale-up its utilization to additional in vitro neurophysiology labs at Carnegie Mellon and beyond. We hope that by improving data organization, archiving,

and sharing practices, our system will show clear benefits to the scientists performing and analyzing research data and ultimately empower demonstrably better neuroscience research.



D07 Mobile metadata: bringing neuroinformatics tools to the bench

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The complexity of experimental paradigms in neuroscience results in corresponding complexity of recorded data and associated metadata. This poses a challenge to data annotation and metadata capture in the lab. Often, crucial experimental information is hand-written in lab notebooks or entered manually in various text files or spreadsheets. This process is both time-consuming and error prone, and the information is not easily accessible for data processing. Moreover, the diversity of formats hampers the development of common software solutions to further manage and re-use the metadata. To address this problem, odML, a flexible data model for metadata, was proposed (Grewe et al., 2011) that supports efficient organization of metadata. While such a machine-readable format enables to automatize metadata capture to large extent, in every experiment there is information that needs to be recorded manually. For these cases, we here present a standalone mobile app that enables scientists to acquire seamlessly and efficiently their metadata in a structured format at the bench, independent of lab environment, or even outside in the field. The tool was inspired by, and is similar in concept to, the pioneering solution for clinical assessment, CARAT (Turner et al., 2011), but uses odML as a standard data model, which enables acquisition of metadata from various scientific domains, and offers features for designing templates and managing metadata structures. The strength of this approach is to hide the complexity of odML structures from the user while providing the necessary control over the data entry process. The mobile app runs on the most frequently used platforms, iOS and Android. An intuitive and simple user interface allows researchers to create metadata forms that can be either directly filled in with acquired values, or saved as templates for re-use. When designing templates the user can, for example, define whether a certain field is required, or in which order the fields are presented and should be filled. Thus, one can design fillable forms that are adapted to the specific experiment and can be re-used in later experiments. Experimental records are stored as odML files and therefore can be integrated with other experimental metadata. This mobile application thus provides an important element in a toolchain for metadata management that facilitates the recording of metadata in machine-readable form.

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D08 Automatic recovery of Z-Jumps for neuronal morphology reconstruction

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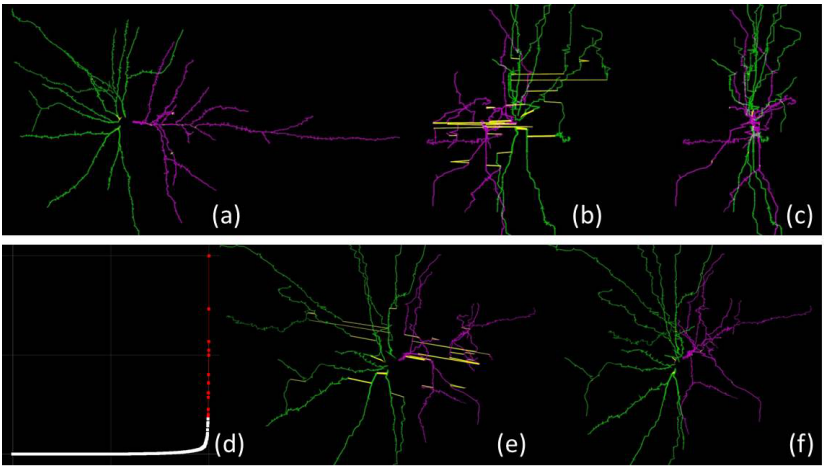
Many researchers share neuronal morphology files along with their publications or contribute the files as independent raw data to public repositories such as the NeuroMorpho project. These morphology files not only serve as important supplements for the original scientific contributions, but also are considered to be extraordinary sources for realistic neuronal morphology simulation. Since reconstructed model neurons are mostly traced manually from brain slices under a light microscopy using a computer tracing system such as Neurolucida system, topological errors are often created during the time-consuming reconstruction. In most cases, the error is a big jump along Z coordinates called 'Z-Jump' [Brown et al. 2011], which always happens between the initial point of one branch and the node point that connects two or more branches (an example is given in Figure 1). For instance, the data file corresponding to Neuromorpho.org ID:NMO_01056 appears normal at the view of X and Y coordinates (Figure 1(a), but many Z-Jumps become visible (marked as the yellow lines in Figure 1(b).) at the view of Y and Z coordinates. Obviously, such kind of morphology files cannot accurately represent the morphological properties of original neurons, and hence cannot directly be used for realistic neuronal morphology simulation. A correction of the error is necessary to recover the reconstruction files to normal morphologies of original neurons. For this need, we developed an automatic Z-Jump recover tool.

Since different researchers may be used to tracing neuronal branches with different distances between points in the morphology structure, a fixed threshold value to judge whether there is a Z-jump may not be appropriate. We proposed that the threshold value should be dynamic according to different reconstruction files. We rank the distances between two neighborhood sampled nodes. We assume 97.5% of the distances are in proper ranges (Let dn be the distance at the rank point of 97.5%). For the rest of the distances, if it equals to or is greater than 5 times of dn, then it is considered to be irregular distances (the red points in Figure 2(a) present the irregular distances in NMO_01056, and 14 distance values out of 3215 are irregular distances). For these irregular distances, we move the child node to the Z coordinate of the parent node, and the later connections along the same branch of the child node are moved accordingly. By using this method, the problem of Z-Jumps can be avoided (Figure 1(c) provides a neuronal morphology structure that is corrected from Figure 1(b) by the Z-Jumps recover tool developed in this study. Figure 2(b) and Figure 2(c) present the structure before and after recovery from another angle). We compare the identified Z-Jumps in NMO_01056 with the ones identified by the StdSwc tools developed by the NeuroMorpho project, 2 extra expert confirmed errors were identified (12 irregular distances were identified by StdSwc). If we further restrict the threshold to 3*dn, 10 extra Z-Jumps (with human judges) were identified.

Through automatic detections using the standards proposed above, we found that around 26.14% of the 10004 neuronal morphology files in Neuromorpho.org present the problem of Z-Jumps to varying degrees (covering 18 out of 22 species, except for C. Elegans, Turtle, Drosophila and Frog). All of the identified 2615 files were improved and reproduced using our developed method.



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D09 Ant-App-Database towards neural, behavioral research on deserts ants and approximate solar estimations

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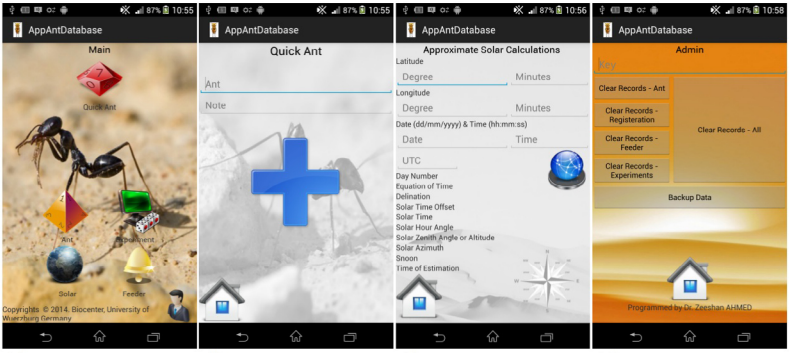
The neural, behavioral research of desert ants (Cataglyphis fortis) [1], [2] requires on field analysis of the nest search runs, feeding habits, path segmentations, positioning at different day times and polarized sun light's compass based celestial navigations [3] etc. Normally the experimentation is performed in the natural environmental conditions, which in return derive different kinds of information e.g. locations, feeders, geographical alignments, solar positions and timings etc. Due to the rise in temperature and unpredictable distribution of food at the fields, it is found to be complex and time consuming to perform such analytical and observatory studies without a comprehensive technological solution, which can help in quick and efficient way.

Meeting the technological objectives of this research, we took a step in the development of a new user friendly, embedded and biological database system i.e. Ant-App-Database; smart phone, tablet application towards the efficient experimental data manipulation and management (Fig. 1). Furthermore to have the approximate geographical measurements of the observer's locations, using different Astronomical Algorithms [4], [5], [6] recommended by the National Oceanic and Atmospheric Administration (NOAA), it estimates approximate Georgian Day Number, Decimal Day, Decimal Day of the Year, Fractional Year, Equation of the Time, Declination, Solar Time Offset, Solar Time Solar Zenith Angle, Solar Hour Angle, Solar Azimuth Angle and Solar noon.

In addition, a desktop application i.e. Dataplus; is developed towards the efficient experimental data extraction from the database (generated by the smart phone application) and conversion into the Microsoft Excel format (Fig. 2). Both smart phone and desktop applications have been developed following the newly proposed software development paradigm i.e. Butterfly [7], integrating formal Unified Modelling Language (UML) [8] perspectives and incorporating Human Computer Interaction (HCI) [9], [10] design patterns. This abstract/oral presentation is about to introduce and justify the usefulness of the newly proposed solution (first smart phone based application in the World), helpful for the observers in managing the experimental data including location, date, time, geographical measurements, feeders, registered and unregistered ants in a swift way. Moreover it's about to brief architected designs, implementation details, used technologies, pitfalls and future recommendations.

The presented applications (Ant-App-Database and Dataplus) are not only beneficial for the behavioral research on desert ants but can also be used for other related experiments on different insects.



(a) (b) (c) (d)

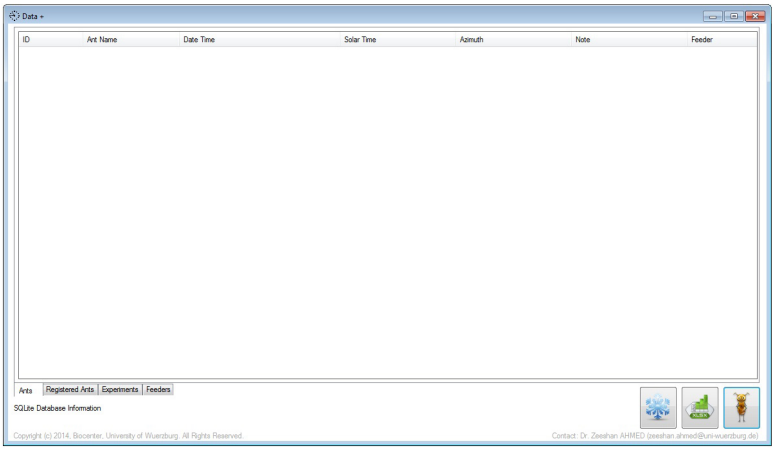


Figure Legends:

Fig. 1: Ant-App-Database; Graphical User Interface including following interfaces: Main (a), Quick Ant (b), Approximate Solar Calculations (c) and Admin (d).
Fig. 2: Dátaplus; Graphical User Interface.

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D11 SciCrunch: A cooperative and collaborative data and resource discovery platform for scientific communities

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Introduction
SciCrunch was designed to help communities of researchers create their own portals to provide access to resources, databases and tools of relevance to their research areas. A data portal that searches across hundreds of databases can be created in minutes. Communities can choose from our existing SciCrunch data sources and also add their own. SciCrunch was designed to break down the traditional types of portal silos created by different communities, so that communities can take advantage of work done by others and share their expertise as well. When a community brings in a data source, it becomes available to other communities, thus ensuring that valuable resources are shared by other communities who might need them. At the same time, individual communities can customize the way that these resources are presented to their constituents, to ensure that their user base is served. To ensure proper credit and to help share expertise, all resources are tagged by the communities that create them and those that access them.

Exploring Data
SciCrunch is one of the largest aggregations of scientific data and tools available on the Web. One can think of SciCrunch as a "PubMed" for tools and data. Just as you can search across all the biomedical literature through PubMed, regardless of journal, SciCrunch lets you search across hundreds of databases and millions of data records from a single interface. Such databases are considered part of the "hidden web" because their content is not easily accessed by search engines. SciCrunch enhances search with semantic technologies to ensure we bring you all the results. SciCrunch provides three primary searchable collections:

- SciCrunch Registry – is a curated catalog of thousands of research resources (data, tools, materials, services, organizations, core facilities), focusing on freely-accessible resources available to the scientific community. Each research resource is categorized by resource type and given a unique identifier.

- SciCrunch Data Federation – provides deep query across the contents of databases created and maintained by independent individuals and organizations. Each database

is aligned to the SciCrunch semantic framework, to allow users to browse the contents of these databases quickly and efficiently. Users are then taken to the source database for further exploration. SciCrunch deploys a unique data ingestion platform that makes it easy for database providers to make their resources available to SciCrunch. Using this technology, SciCrunch currently makes available over 200 independent databases, comprising ~400 million data records.

• SciCrunch Literature – provides a searchable index across literature via PubMed and full text articles from the Open Access literature.

SciCrunch Communities

SciCrunch currently supports a diverse collection of communities (Figure 1), each with their own data needs:

• CINERGI – focuses on constructing a community inventory and knowledge base on geoscience information resources to meet the challenge of finding resources across disciplines, assessing their fitness for use in specific research scenarios, and providing tools for integrating and re-using data from multiple domains. The project team envisions a comprehensive system linking geoscience resources, users, publications, usage information, and cyberinfrastructure components. This system would serve geoscientists across all domains to efficiently use existing and emerging resources for productive and transformative research.

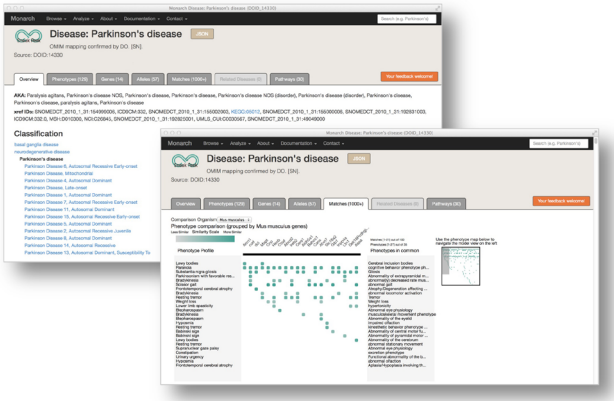
• Monarch Initiative (monarchinitiative.org; Figure 2) – provides tools that will use semantics and statistical models to support navigation through multi-scale spatial and temporal phenotypes across in vivo and in vitro model systems in the context of genetic and genomic data. These tools will provide basic, clinical, and translational science researchers, informaticists, and medical professionals with an integrated interface and set of discovery tools to reveal the genetic basis of disease, facilitate hypothesis generation, and identify novel candidate drug targets. The goal of the system is to promote true translational research, connecting clinicians with model systems and researchers who might shed light on related phenotypes, assays, or models.

• Neuroscience Information Framework (NIF) – is a biological search engine that allows students, educators, and researchers to navigate the Big Data landscape by searching the contents of data resources relevant to neuroscience - providing a platform that can be used to pull together information about the nervous system. Underlying the NIF system is the Neurolex knowledge base. Neurolex seeks to define the major concepts of neuroscience, e.g., brain regions, cell types, in a way that is understandable to a machine.

• NIDDK Information Network (dkNET) – serves the needs of basic and clinical investigators by providing seamless access to large pools of data relevant to the mission

of The National Institute of Diabetes, Digestive and Kidney Disease (NIDDK). The portal contains information about research resources such as antibodies, vectors and mouse strains, data, protocols, and literature.

• Research Identification Initiative (RII) – aims to promote research resource identification, discovery, and reuse. The RII portal offers a central location for obtaining and exploring Research Resource Identifiers (RRIDs) - persistent and unique identifiers for referencing a research resource. A critical goal of the RII is the widespread adoption of RRIDs to cite resources in the biomedical literature. RRIDs use established community identifiers where they exist, and are cross-referenced in our system where more than one identifier exists for a single resource.



D12 The BrainLiner platform for sharing and searching time-aligned neurophysiological data

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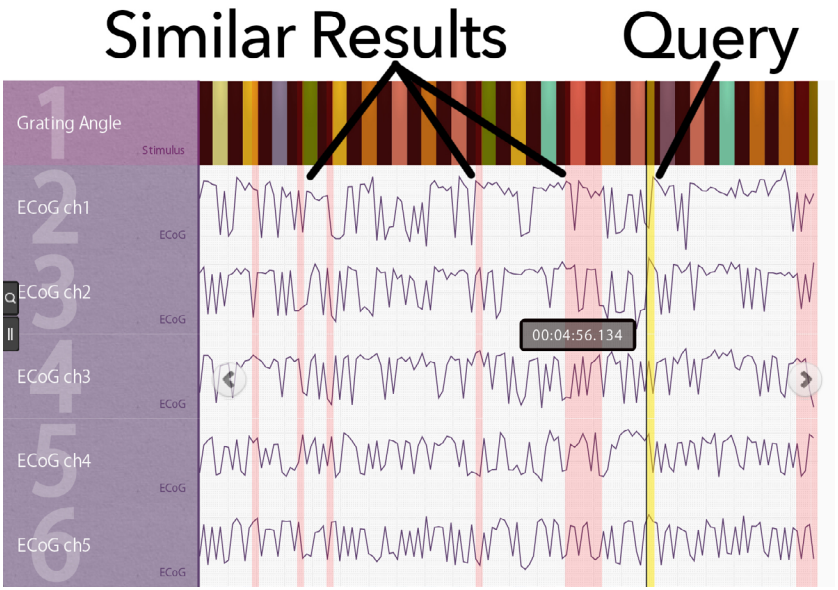
BrainLiner (brainliner.jp) is a platform for sharing time-aligned brain and behavioral data. BrainLiner and other databases support sharing brain activity data for the purposes of data re-use and scientific replication and verifiability. However, many other databases treat and store brain activity and behavioral data separately. For example, stimulus time course and motion capture are often stored in separate files from electrode data. This makes it cumbersome to analyze the neural representation of properties related to the task.

BrainLiner focuses on supporting contemporary data-driven neuroscience approaches, such as neural decoding, where the statistical relationship between brain activity and behavior can be used for practical applications such as uncovering the structure of information representation in the brain. As such, BrainLiner places equal emphasis on behavioral data as on brain activity data.

The data on BrainLiner are stored in a standardized file format. The explicit representation of brain activity and behavioral data that are time-aligned and represented in a standardized data format allows our platform to automatically process data in many ways. Users can preview our standardized file format from within a web browser, getting a glimpse at not only brain activity, but also information about the task or behavior of subjects. In addition, we can also perform more advanced analyses, such as data similarity search (Figure 1), directly in the browser.

Our data similarity search demonstrates the utility of using a common file format throughout a database. Our search method maps the similarity of time windows within a single data file. The search uses information about the modality of data to index only electrocorticography (ECoG) or electroencephalography (EEG) files. Indexed files are split into time windows and then the pairwise similarity between all time windows are calculated using an unsupervised method. This results in a large number of similarity scores. For efficiency, these values are then quantized by keeping only time windows that are correlated with p values of less than 0.05. Indices representing spans of similar time windows are then stored in a sparse index. This has the advantage of being able to respond to a user's query in a very short time frame.


Similar Results
Query
Grating Angle
Stimulus
ECoG ch1
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D13 Linked Neuron Data (LND): A platform for integrating and semantically linking neuroscience data and knowledge

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Linked Neuron Data (LND) is an effort and a Web-based platform for integrating and semantically linking Neuroscience data and knowledge from multiple scales and multiple data sources together to support comprehensive understanding of the brain. Currently LND integrates structured neuroscience knowledge from Allen Brain Atlas [Sunkin et al. 2013], NeuroLex [Larson and Martone 2013], NIF Ontology [Imam et al. 2012], NeuroMorpho [Ascoli et al. 2007], Mesh terms, etc. It also extracts declarative domain knowledge from unstructured sources such as PubMed abstracts, Neuroscience literatures and books and the extracted knowledge is represented as triples, such as < apical dendrite, part of, pyramidal neuron> (247,239 triples are extracted by using pattern based information extraction. Considering the quality of the extracted triples, current extractions focus on is-a, part-whole, synonyms relations, and attribute value pairs for specific entities, etc.). All the integrated and extracted knowledge are represented in RDF/OWL. Currently, Linked Neuron Data contains 2,567,178 semantic knowledge triples that describe various declarative knowledge on Neuroscience, including: (1) hierarchical organizations of the brain (with hierarchical brain regions, types of neurons in the specific region, etc. as shown in Figure 1); (2) links among different brain components from different species; (3) relationships among brain components, brain diseases and cognitive functions (including 25,497 triples, extracted from PubMed articles, and Wikipedia pages); (4) facts about brain components (e.g. location distributions, functions, and neurotransmitters of certain types of neurons).

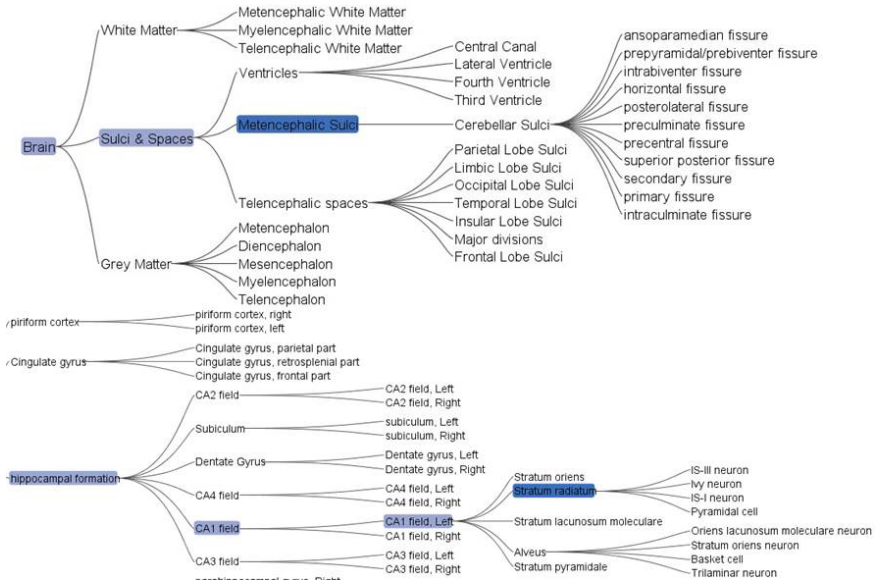
Compared to many other efforts (such as NeuroLex [Larson and Martone 2013], whose knowledge is mainly from experts manual contributions), most of the knowledge in Linked Neuron Data (LND) is integrated or automatically extracted from structured and unstructured data sources. And the focus of LND is on how to semantically link knowledge from different data sources together and how neuroscience researchers can benefit from the links and this neuroscience knowledgebase in general.

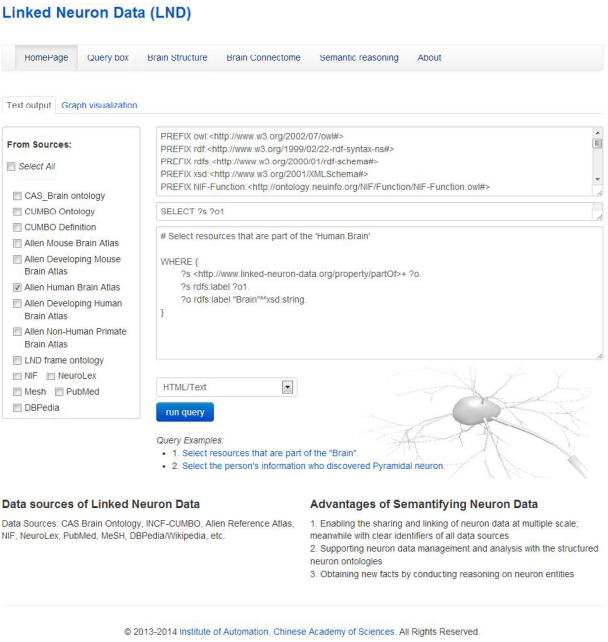
Links among different resources are automatically constructed by the step wise bag-of-words entity linking algorithm developed in our previous study for creating very large scale semantic knowledge bases [Zeng et al. 2013a, Zeng et al. 2013b]. Several efforts are made to ensure the quality of the entity linking process for LND. Firstly, we consider automatic direct mapping when different resources share the same term. Secondly, synonyms of different neuroscience domain terms are used to link these resources together. These pairs of synonyms are extracted from Wikipedia redirects (7,222,839 pairs in all, and 23,270 pairs contain neuroscience domain terms in the current LND knowledge base), Allen Brain Atlas (4,756 pairs), and NeuroLex (103,704 pairs), etc. For those who share the same term while

actually do not share the same meaning, we differentiate these resources through entity disambiguation process by using the tool developed in [Zeng et al. 2013a] (For example, currently there are 5 pages for the term "hippocampus" on Wikipedia. They refer to a type of animal, a brain region, a type of magical beast, etc. When linking knowledge about "hippocampus" from Wikipedia to Allen Brain Atlas, the program will automatically find the right "hippocampus" to be linked with). Currently, LND has already established 31,940 links among different knowledge sources (e.g. Links among domain terms from Allen Brain Atlas, NeuroLex and DBPedia/Wikipedia). 1322 entity disambiguation process were done, and the precision is 91.2%. All the entities that are semantically equal to each other are linked together by the owl:sameAs relation so that these knowledge can be used for semantic search and reasoning tasks over the Linked Neuron Data platform.

With the entity linking efforts, Neuroscience knowledge from different sources are connected together, and Neurosciences researchers can benefit from these links. For example, LND users can obtain 265 piece of knowledge about "hippocampus" from 6 sources (including Allen Brain Atlas, NIF Ontology, NeuroLex, CAS Brain Ontology, Neuromorpho and DBPedia). LND can also identify how many brain regions contain pyramidal neurons through the integration and linking of NeuroLex, Wikipedia, and Neuromorpho knowledge.

The Linked Neuron Data (LND) platform can be accessed through linked-neuron-data.org. Figure 2 provides a screen shot of the LND platform. The neuroscience knowledge in LND can be obtained by issuing SPARQL or keyword queries to the platform, and the query results can be downloaded directly or displayed on the LND Web interface.





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D14 Neuroinformatics infrastructure for interoperability of repositories developed by J-Node

Yoko Morii[1], Yoshihiro Okumura[1], Sadanori Kamakura[1], Yui Isono[1], Sawako Suenaga[1], Shiro Usui[1] and Yoko Yamaguchi[1]
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INCF National Node of Japan (J-Node for short) has been promoting both domestic and international neuroinformatics activities by providing neuroscience platforms (web databases) in individual research fields and infrastructures common to the platforms J-Node counted 13th platform this spring, on which one can find data-model-tool in individual fields, an environment for live simulation of models and tools, tutorial contents and so on. Most of these platforms are commonly developed and managed by utilizing XooNIps, a content management system developed at RIKEN BSI. J-Node portal is open at neuroinf.jp. J-Node now aims to further promote the utility beyond different research fields or repositories and to serve for comprehensive research interests in the brain science. Simulation platform for an instantaneous on-line use of mathematical models currently offers more than 250 models and tools including all models of ModelDB (SenseLab at Yale University). Recently, J-Node launched a cross-site searching system throughout databases on OAI-PMH based protocol. This allows you to find any data on J-Node's platforms from anywhere using metadata schema, Dublin Core, JuNii2, Gene Terms having title, creator, etc. So far, 12 repositories in J-Node with more than 60,000 contents and biomedical and genomic information in National Center for Biotechnology Information (NCBI) database are available through this system. In addition, the utility of the search system at individual J-Node Platforms and mutual link of relevant data among the platforms by using the common metadata format are under development. Thus, our approaches should accelerate collaboration with INCF, nodes and groups working on databases together and finally exchanging researcher's knowledge and outputs.

D15 The Flysim project – persistent simulation and real-time visualization of fruit fly whole-brain spiking neural network model

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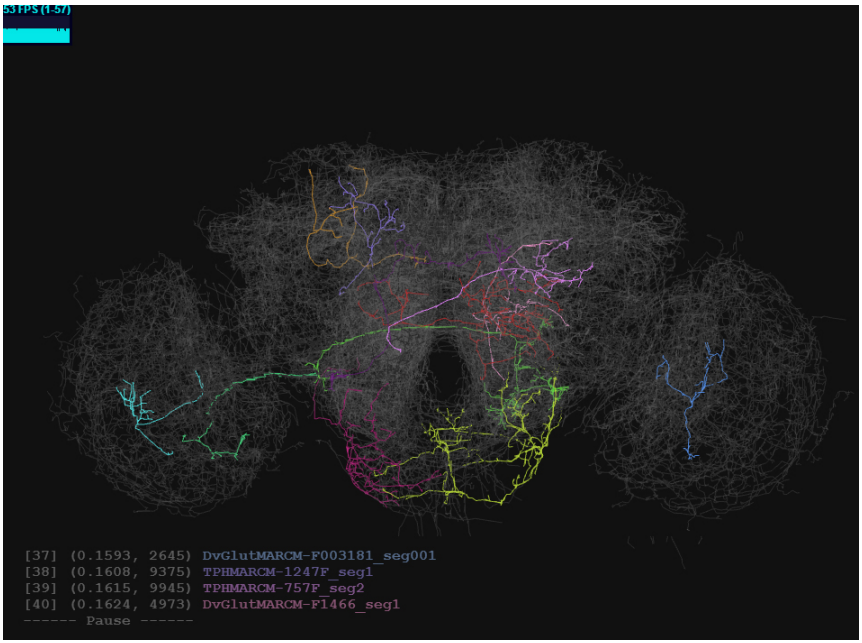
3. National Tsing Hua University, Brain Research Center, Hsinchu city, Taiwan

Computer simulations play an important role in testing hypotheses, integrating knowledge and providing predictions of neural circuit functions. While lots efforts have been put into simulating primate or rodent brains, fruit fly (Drosophila melanogaster) is becoming a promising model animal in computational neuroscience for its small brain size, complex cognitive behavior and abundant data from genes to circuits.

With the expectation that most neurons in Drosophila brain will be mapped out in the next few years, we propose the Flysim project with an aim to establish a data-driven neural network model of Drosophila. The project consists of four components: 1) analyzing neuronal data from Flycircuit (flycircuit.tw) (Chiang, et. al. Current Biology, 2011) database, 2) building a whole-brain spiking neural network model, 3) performing persistent neural network simulations and 4) visualizing the simulated brain activity in real time. To this end, we first developed computer algorithms to identify axonal and dendritic domain for each neuron in the database (the SPIN project)(Lee, et al. Neurinformatics, 2014), predicted potential synapses between neurons and constructed the brain-wide connectome. Next, we developed a highly flexible neural network simulator which is capable of receiving control comments online from remote users. Finally, we developed an interface to pass the simulated data to a webserver for live demonstration. Users can monitor the neural activity in a 3-D virtual fly brain (Figure 1) and issue control comments such as stimulus onset/offset in real time.

Currently, the Flysim simulator supports the leaky integrate-and-fire neuron model and ionotropic synapses including Ach, AMPA, NMDA and GABAA. For the sake of flexibility, we used a modular design for the system and the current CPU-based simulation may be replaced by a GPU-based system such as Neurokernel. We have built a "primitive" Drosophila brain network of ~22,000 neurons, which account for roughly 20% of the fly brain. Despite being at its early stage, this cellular-level brain network model allows us to study some of the fundamental properties of neural networks including balance of excitation and inhibition, critical behavior, long-term stability and plasticity.



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D16 Parametric Anatomical Modeling: A method for modeling the anatomical layout of neurons and their projections

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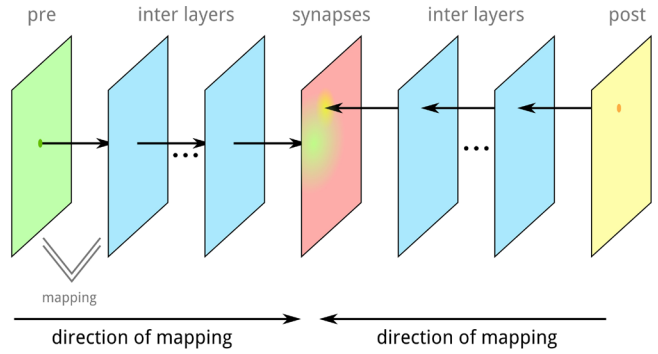
Biological neural networks are likely to be described by a low-dimensional parameter space. Those parameters include, for example, the 3d-shape of neuron layers, the neurons' spatial projection patterns, spiking dynamics and plasticity rules. Many studies generate artificial neural networks that match some of the properties of biological networks to study their computational properties. While spiking dynamics and plasticity rules can comparatively easily be expressed in a programming language and have been subject of extensive research, defining and investigating anatomically more realistic connection and latency properties for large-scale artificial neural networks remains a challenging task. In particular, a method is missing that allows to translate anatomical data from e.g. histological images and tracer studies into an encoding that can generate more realistic network architectures.

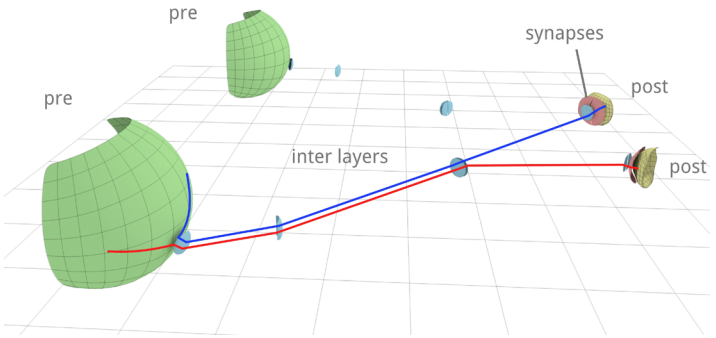
We present a new method, called Parametric Anatomical Modeling (PAM), to fill this gap. The basic idea behind PAM is that neural networks are computed based on neuronal, synaptic and intermediate layers, which are generated from anatomical data. Using a set of mapping techniques, complex connection patterns between those layers can be easily defined (fig. 1). For example, any location on one layer can be mapped on another layer based on euclidean distance, a normal vector or topological similarity. Connections between neurons are computed by mapping pre- and post-synaptic locations on a synaptic layer and applying connectivity kernels on the surface of the synaptic layer. A central feature of PAM is that distances between neurons (which may affect transmission delays) can be computed by combining spatial distances on the surface of layers and spatial distances between layers. Thereby, complex connection and distance patterns between layers can be expressed and be used as template for generating small-scale and large-scale network architectures. PAM is implemented as a Python tool and integrated in the 3d-modeling software Blender. We provide a set of add-ons and Python modules that amend the functionality of Blender to generate and relate anatomical layers to each other and to create neural networks for the network simulator NEST. These tools along with example files and video tutorials will be freely available.

On a 3d-model of the hippocampus and entorhinal cortex, we demonstrate the benefits of PAM and show how PAM can help to uncover the relationship between the form and function of the hippocampus. Models created by PAM can also serve as an educational tool to visualize the 3-d connectivity of brain regions. The low-dimensional, but yet biologically plausible, parameter space renders PAM particularly suitable for analysing allometric and evolutionary factors in networks and for modeling the complexity of real networks with comparatively little effort.



Connection
- List of layers
- Mapping for each consecutive list-pair
- Index of synaptic layer
- Connectivity kernels

Mapping
- Topological
- Euclidean
- Normal
- Random



D17 Lessons from a simple tool for neuroimaging data sharing

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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. At this point, the system is in place and working as specified. Users need only to start using the system, but we have not seen the system adopted as we anticipated. We not see this as a failure of the system, but rather as a form of progress in ongoing data sharing efforts: technical barriers have been removed, throwing into relief some of the social issues standing in the way of effective data sharing, and exposing these issues will allow us to better understand and focus on them. With "we can't share" out of the way, we can better attack "we won't share." And as further barriers are removed, we have in place an infrastructure for sharing and archiving. The client tools and access to the public image database are available at xnat.incf.org.

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D18 Neuroimaging resources, data and computation: NITRC revisited

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2. TCG Inc., Washington, USA

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, clinical neuroinformatics, imaging genomics, and computational neuroscience. 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 (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 software and data resources (655 to date), many relevant to imaging research, some identify themselves specific to cancer research such as TCIA and MITK Diffusion. NITRC-R averages monthly 21,000 visits and 76,000 pageviews. The NITRC-IR offers 4,764 subjects, and 4,779 MR Imaging Sessions searchable across nine 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.

D19 eScience infrastructure for running validated image analysis pipelines: How to best compare MRI scans from different medical centers

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2. Erasmus MC, Biomedical Imaging Group Rotterdam, Depts. Medical Informatics and Radiology, Rotterdam, Netherlands
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5. Radboudumc, Dept. of Geriatric Medicine/Radboud Alzheimer Centre, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Netherlands
6. Maastricht University, Dept. of Psychiatry and Neuropsychology/Alzheimer Center Limburg, Maastricht, Netherlands
7. VU University Medical Center, Dept. of Radiology and Nuclear Medicine, Neuroscience Campus Amsterdam, Amsterdam, Netherlands

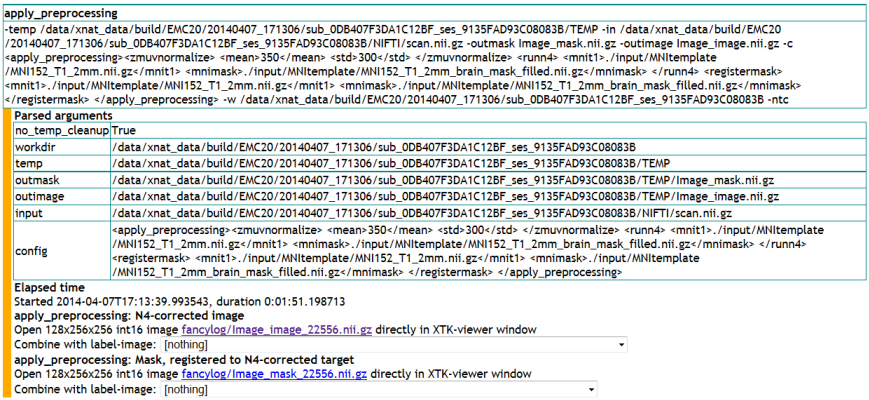
We recently introduced an eScience infrastructure for the secure sharing of neuroimaging data and running validated analysis pipelines on a high performance cloud [1]. We have populated this infrastructure with two thousand structural MR images from four Dutch medical centers. As a pilot project, we are segmenting the hippocampus for each of these images, thereby running into a number of practical issues. The most prominent question is whether the pipeline that we use, which has been tuned to perform optimally on data from a single MR scanner, can be directly applied to the four datasets, which differ in resolution, scanner type, and acquisition protocol. The most prominent step of the pipeline [2] is the registration of a set of twenty reference segmentations to the target scan in order to create a probabilistic atlas in target space. This is then combined with an intensity model, and the energy function is minimized via graph cuts. Ideally the pipeline would be able to accept new scans of unknown source, and use a standard set of manual segmentations for registration. We have however observed that the (nonlinear) registration performs worse when the source and target scans have dissimilar tissue intensity scales, which leads to an increased bias and variance of derived results such as the hippocampal volume.

An alternative approach is not to use a single set of manual segmentations for all data, but use separate segmentations for each cohort that is added to the platform. This introduces another type of bias when the manual segmentations have been carried out by different investigators using different criteria. We investigate whether the improved statistical power of combining cohorts outweighs the bias and variance introduced by the different scan parameters.

Two neuroinformatics tools are presented as components of the infrastructure:

1. A Java-based upload tool that takes care of client-side pseudomisation and subsequent upload to a central XNAT [3] server.

2. Fancylog (github.com/rbakker/fancylog), a Python-based logging system that presents, as the pipeline runs, all executed steps of the pipeline and their intermediate results in a dynamic webpage, as illustrated in Figure 1. It uses the XTK viewer [4] to display volumetric images in the browser.


[-] 4.1 apply_preprocessing

apply_preprocessing

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Parsed arguments

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outmask	/data/xnat_data/build/EMC20/20140407_171306/sub_0DB407F3DA1C12BF_ses_9135FAD93C08083B/TEMP/Image_mask.nii.gz
outimage	/data/xnat_data/build/EMC20/20140407_171306/sub_0DB407F3DA1C12BF_ses_9135FAD93C08083B/TEMP/Image_image.nii.gz
input	/data/xnat_data/build/EMC20/20140407_171306/sub_0DB407F3DA1C12BF_ses_9135FAD93C08083B/NIFTI/scan.nii.gz
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Elapsed time

Started 2014-04-07T17:13:39.993543, duration 0:01:51.198713

apply_preprocessing: N4-corrected image

Open 128x256x256 int16 image fancylog/Image_image_22556.nii.gz directly in XTK-viewer window

Combine with label-image: [nothing]

apply_preprocessing: Mask, registered to N4-corrected target

Open 128x256x256 int16 image fancylog/Image_mask_22556.nii.gz directly in XTK-viewer window

Combine with label-image: [nothing]

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Posters and demos are invited to stay up during the full meeting.
Presentation of posters is divided into two sessions.

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

Poster abstracts

Topics:

P01 Advanced Machine Learning for classification of EEG traits as Parkinson's biomarker

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2. Hopital du Sacre-Coeur, Montreal, Centre d'Études Avancées en Médecine du Sommeil, Montreal, Canada
3. Beth Israel Deaconess Medical Center and Harvard Medical School, Berenson-Allen Center for Noninvasive Brain Stimulation, Boston, MA, USA
4. Université de Montréal, Department of Psychiatry, Montréal, Canada

We aim to develop non-invasive, low-cost preclinical markers for synucleinopathies (Parkinson's Disease - PD or Dementia with Lewy Bodies - DLB) with impact on neuroprotection. In a first stage we have applied Machine Learning techniques to the analysis of the spontaneous, waking EEG of REM Sleep Behavior Disorder (RBD) patients. We know that patients with RBD may evolve towards PD and other synucleinopathies (i.e. DLB) providing a useful guide in the search for biomarkers. EEG has proven to be sensitive to brain alterations related to both RBD and PD patients, and it is known that patients with either RBD or de novo PD without obvious cognitive alterations show similar EEG/MEG alterations (mainly slowing of the EEG) while awake. In the work described herein we achieve the classification of patients according to their ultimate diagnosis, differentiating among different patient groups. We have analyzed EEG data from a study of RBD patients at the Center for Advanced Research in Sleep Medicine of Montréal. The EEG was recorded from 8 patients who years later evolved to PD, 8 patients who later evolved to LBD, 10 patients with RBD who did not convert, and 17 healthy controls. It is worth mentioning that 80% of the PD and DLB patients developed disease at a follow-up of 8 years. Support Vector Machines were applied to different feature types. Absolute Band Power features extracted each 4 seconds outperform the other ones. After non-parametric feature selection of the 5 most discriminative channel-band combinations, classification was applied. A procedure for performance estimation close to operational conditions, which is denoted as leave-pair-subjects-out, has been employed for evaluation of the implemented system. Excellent performance levels, AUC 93.75-99%, were obtained for all realized group comparisons. In conclusion, we believe that these results support the idea that classification of EEG shows great potential as a preclinical biomarker. Our results confirm the existent literature, where EEG slowing characterizes RBD and PD/DLB patients. Furthermore we have attained this characterization at the individual subject level for the first time by employing machine learning. Given that EEG was acquired 8 years before disease development in a majority of cases, we believe that the utilization of the developed system for conversion prognosis of synucleinopathies (PD or DLB) will have real impact on both early treatment and drug development.

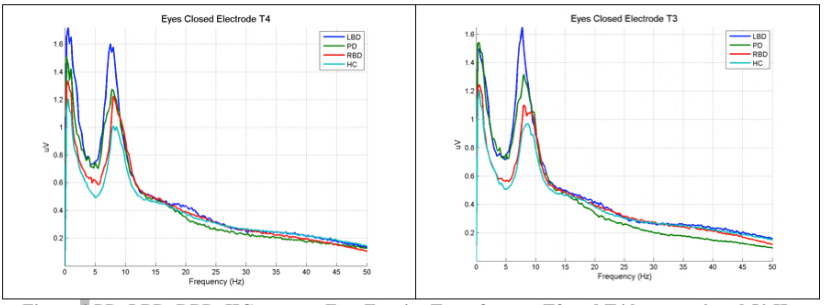


Figure 1 PD, LBD, RBD, HC average Fast Fourier Transform at T3 and T4 between 0 and 50 Hz.

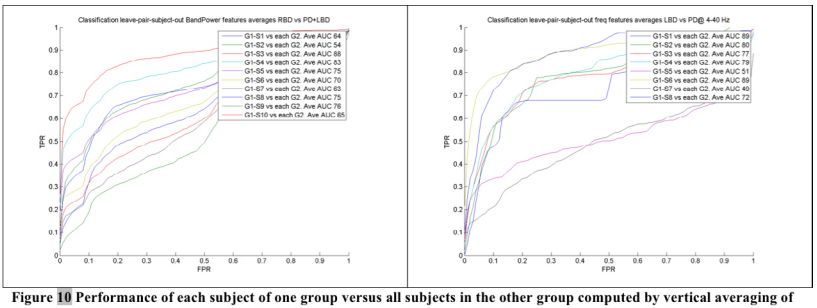
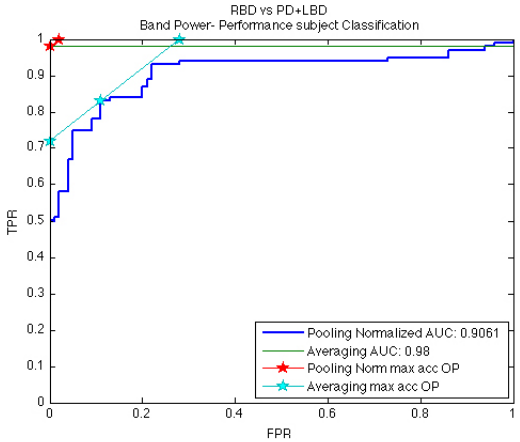


Figure 10 Performance of each subject of one group versus all subjects in the other group computed by vertical averaging of the ROC in epoch classification. Left: Band Power features in RBD vs. PD+LBD comparison. Right: FFT features in PD vs. LBD comparison.



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P02 A big-data approach to automated EEG labeling

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2. Temple University Hospital, Philadelphia, USA

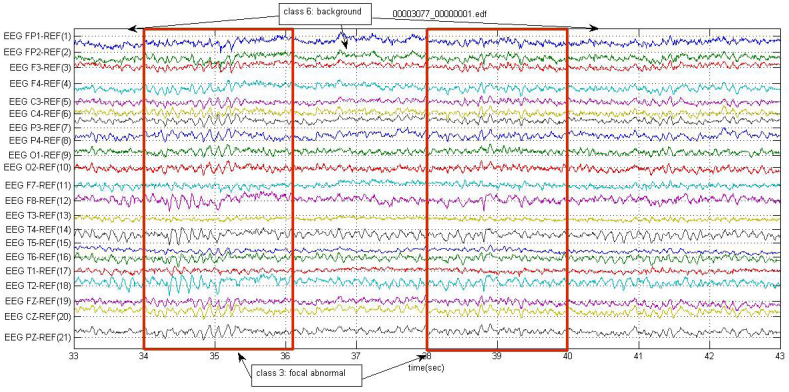
Electroencephalograms (EEGs) are valuable indicators of neural activity, both because of their non-invasive and inexpensive nature, and because a wealth of prior knowledge exists on their interpretation. Software for automatically reading EEGs has long been a focus of neuroinformatics research, since such a tool would be a boon to neuroscientists studying brain function as well as to neurologists who must manually scan hours of patient recordings. Prior research has relied either on heuristic rules for signal interpretation or on pattern recognition algorithms trained on insufficient datasets. Owing to the variability and complexity of neural function, both approaches are fundamentally limited, and resulting tools have failed to be transformative to both clinicians and researchers.

In response, we have created a new data-rich EEG resource by amassing archival clinical EEG data recorded Temple University Hospital over the past decade. The resulting data corpus (TUH-EEG) comprises some 22,000 EEG records from approximately 15,000 unique patients, and includes medical histories and clinical diagnoses along with the raw EEG traces. Data have been de-identified appropriately, and all work has been approved by the Temple University IRB.

The size and scope of the TUH-EEG dataset is enabling us to apply a new generation of machine learning technology based on deep learning. This technology automatically self-organizes knowledge in a data-driven manner and learns to emulate a physician's decision-making process. We are combining deep learning with unsupervised training so that detailed transcriptions of the data are not required. Performance of unsupervised training on vast amounts of data has recently been shown to approach or even exceed supervised training on much less data, giving rise to the notion of big data – learning from vast archives of noisy, poorly transcribed data. We have validated this approach on the CHB-MIT scalp EEG database and have achieved a 94% seizure detection rate, which compares favorably with state of the art on this task.

We are presently using unsupervised deep learning on the TUH-EEG corpus to train a system that can differentiate between six so-called signal primitives: (1) focal epileptiform, (2) general epileptiform, (3) focal abnormal, (4) general abnormal, (5) artifacts, (6) background. Once these primitives can be reliably detected, they can be used to assess the presence of higher-level phenomena specific to certain disease states or conditions. We are implementing an unsupervised training technique in which we iteratively annotate the data using the previous iteration of the technology. This is the approach we believe will be most promising for TUH-EEG since we do not have access to manually transcribed labels. It will not only demonstrate our ability to learn from data automatically, but also provide time

aligned marks for physicians to review. Preliminary results suggest a primitive sensitivity of 74% with a false alarm rate of 0.6/session; our goal for operational performance is 95% sensitivity.



P03 Model validation using the Mozaik framework

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One of the current challenges in computational neuroscience is not only to build high fidelity models of brain structures reflecting their biological complexity, but also to test them with as broad a range of measures and stimulation conditions as possible. The need to repetitively perform such tests on a model under development, and the increasing need to make such thorough comparisons between different models, can make manual operation of such testing schemes extremely time consuming and error prone, greatly decreasing productivity. This highlights the increasing need for automation of these processes. However, ad-hoc 'in-house' automation of such processes can itself take a significant amount of time and typically requires further work each time the specifications of the project change. The recently released Mozaik framework [1] formalizes the entire testing workflow using a general API, offering full automation of stimulation, data-collection and subsequent analysis and visualization of spiking neuronal network models, thus addressing both the automation of testing workflows and the generalization of such automation to a wide range of workflow types. Here we present a specific use-case of applying the Mozaik framework to incremental development of a detailed model of the thalamo-cortical loop, which is being continuously tested against a range of measures under several stimulation paradigms.

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P04 Self-sustained activity in cortical network models

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The resting state of the brain is characterized by absence of external stimuli and cognitive tasks [1]. In this state the cortex displays self-sustained activity characterized by irregular neuronal firing and collective oscillations covering a wide range of frequencies [2,3]. Since in the resting state the brain is essentially disconnected from the external world, the understanding of the mechanisms responsible for the existence of the self-sustained cortical activity patterns may give us insights on the brain's intrinsic functioning. In this work, we use computer simulations of cortical-like network models to attempt to contribute to this understanding. Our models have hierarchical and modular architecture constructed according to the top-down method of Wang et al. [4]. They are composed of excitatory (80% of total) and inhibitory (20% of total) neurons that belong to the five main electrophysiological cortical cell classes: regular spiking (RS), intrinsically bursting (IB), chattering (CH), fast spiking (FS) and neurons that produce low threshold spikes (LTS). Neurons from the former three classes are excitatory and neurons from the latter two classes are inhibitory [5]. The neurons were modeled by the Izhikevich model [6]. We adopted a conductance-based model [7] for the synaptic connections between neurons. When a presynaptic neuron fired, a fixed increment (Ge or Gi for an excitatory or an inhibitory synapse, respectively) was added to the corresponding synaptic conductance. Otherwise, the synaptic conductance decayed exponentially with a fixed time constant (Te or Ti for an excitatory or an inhibitory synapse, respectively). The excitatory cell population of our network models was composed of a mixture of up to two cell types: RS cells (always present at a given proportion of the excitatory cell population) and either CH or IB cells (at the remaining proportion of the excitatory population). The inhibitory cell population was composed of only one cell type, either FS or LTS. The network models were activated by injection of external current of variable amplitude to a variable fraction of the network neurons for a variable short time (initial conditions). After stimulus termination the network was left to evolve freely. The different activity patterns displayed by our models can be grouped into four major classes: 1) more or less constant population firing rate with strongly irregular individual firing that lasts until the end of the simulation (constant self-sustained activity); 2) large-scale oscillatory population firing rate, corresponding to different groups of neurons firing synchronously, that lasts until the end of the simulation (oscillatory self-sustained activity); 3) same behavior as in 2) but lasting only for some period (oscillatory non-self-sustained activity); and 4) fast population activity decay after termination of external input (decay). We studied the behavior of these four activity states in the (Ge, Gi) diagram for different modularity levels, network compositions and initial conditions. The area of the diagram corresponding to self-sustained activity is very fragmented and strongly dependent on network structure and initial conditions. Nevertheless, in all cases studied the area corresponding to self-sustained activity is mostly concentrated in the upper right

corner of the diagram and setting the inhibitory strength to zero allows no self-sustained activity. This means that self-sustained activity is more favored by stronger synapses than by weaker ones. Other factors that favor self-sustained activity in our models are number of modules in the network and network composition. The probability of having self-sustained activity increases with the number of modules in the network. Networks with two types of excitatory neurons (specially RS and CH) have more probability of having self-sustained activity than networks with only RS neurons. And LTS inhibitory neurons favor more self-sustained activity than FS inhibitory neurons. In conclusion, our work suggests that the properties of ongoing cortical activity depend on both the topology and the neuronal composition of the cortical network.

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P05 First neuronal connectomics challenge: From imaging to connectivity

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We have organized a challenge to reverse engineer the structure of neuronal networks from patterns of activity recorded with calcium fluorescence imaging. Unraveling the brain structure at the neuronal level at a large scale is an important step in brain science, with many ramifications in the comprehension of animal and human intelligence and learning capabilities, as well as understanding and curing neuronal diseases and injuries. However, uncovering the anatomy of the brain by disentangling the neural wiring with its very fine and intertwined dendrites and axons, making both local and far reaching synapses, is a very arduous task: traditional methods of axonal tracing are tedious, difficult, and time consuming. This challenge proposed to approach the problem from a different angle, by reconstructing the effective connectivity of a neuronal network from observations of neuronal activity of thousands of neurons, which can be obtained with state-of-the-art fluores- cence calcium imaging. To evaluate the effectiveness of proposed algorithms, we used data obtained with a realistic simulator of real neurons for which we have ground truth of the neuronal connections. We produced simulated calcium imaging data, taking into account a model of fluorescence and light scattering. The task of the participants was to reconstruct a network of 1000 neurons from time series of neuronal activities obtained with this model. Over 120 participants attended to the challenge (still running at the moment of submission at kaggle.com/c/connectomics), many of them largely outperforming the proposed benchmarks. We propose here a systematic and comparative analysis of some of the leading algorithmic solutions emerged from the challenge.

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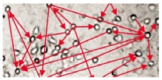

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1	↑3	Lukasz 8000 *	0.93679	68	Sun, 27 Apr 2014 15:53:07 (-0.5h)
2	↑3	Ildefons Magrans *	0.93658	16	Sat, 26 Apr 2014 22:03:02
3	↑18	Sium *	0.93637	16	Sun, 27 Apr 2014 05:24:33
4	↓3	Lejlot & Rafal	0.93618	78	Sat, 26 Apr 2014 06:13:22
5	↓2	AAAGV	0.93493	113	Sat, 26 Apr 2014 18:20:47
6	↑24	Alexander N & vopern	0.93453	5	Sat, 26 Apr 2014 18:10:45
7	↓5	Matthias Ossadnik	0.93433	42	Thu, 24 Apr 2014 21:19:21 (-24.3h)
8	↑7	gaucho81	0.92145	19	Sat, 26 Apr 2014 18:00:53
9	↑4	DJMN	0.92036	16	Wed, 23 Apr 2014 21:57:47
10	↑27	killertom	0.92017	7	Fri, 25 Apr 2014 07:22:03
11	↓5	Gideon & Alex	0.91752	36	Sat, 26 Apr 2014 16:05:02 (-21.7d)
12	↓5	Gábor S	0.91726	4	Wed, 09 Apr 2014 11:39:04
13	↓5	Sandro	0.91574	15	Wed, 23 Apr 2014 14:30:13 (-0.3h)
14	↓5	lnicalo	0.91520	8	Tue, 22 Apr 2014 22:01:29 (-18.2d)
15	↓5	Byron Galbraith	0.91466	9	Tue, 25 Mar 2014 20:58:59
16	new	camaroncina	0.91386	1	Mon, 28 Apr 2014 00:19:56
17	↓6	D.H.	0.91356	8	Tue, 15 Apr 2014 04:17:32 (-9.4d)
18	↓6	DanC	0.91328	11	Sat, 26 Apr 2014 16:17:03 (-20.8d)
19	↓5	Sali Mali	0.91210	4	Sat, 05 Apr 2014 11:41:18
20	↓2	Algoasaurus	0.91067	65	Sun, 27 Apr 2014 10:45:34
21	↓5	ULB MLG	0.90966	54	Sat, 26 Apr 2014 07:25:32 (-39.9d)
22	↓5	Felix_Flo	0.90801	1	Sat, 05 Apr 2014 18:51:29

P06 Linking population dynamics and high-level cognition: Ambiguity resolution in a neural sentence processing model

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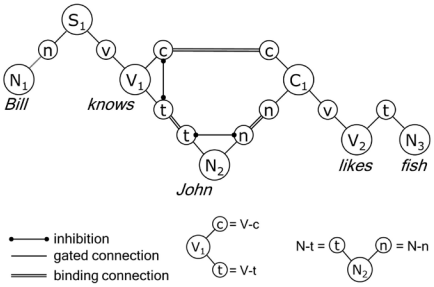
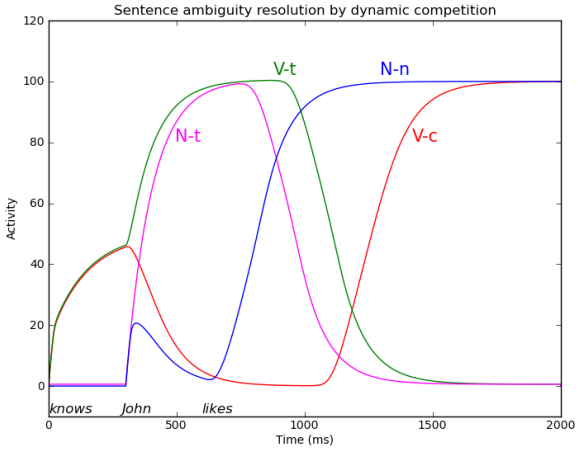
A dynamic interaction in our neural sentence model [1,2] can resolve an example of sentence ambiguity in line with human sentence processing. The ambiguity concerns the difference between Bill knows John (1) and Bill knows John likes fish (2). In (1) John is the theme (object) of knows, but in (2) knows has a complement (John likes fish) with John as subject. In online processing, humans can easily switch from John as theme of knows to John as subject in a complement of knows, which resolves the ambiguity between the roles of John and knows in (1) vs. (2). Figure 1 shows the representation of (1) and (2) in terms of the model [1,2]. Large circles are neural 'syntax assemblies' representing syntactic information, here sentence (S1), noun (N1, N2, N3), verb (V1, V2) and clause (C1). Small circles are subassemblies used for binding syntax assemblies. Connections between the syntax assemblies and subassemblies are gated, which controls the flow of activation in the sentence structure (initiated by external control signals). Binding is also achieved by gating, initiated by the co-activation of the assemblies involved. First, neural 'word assemblies' (not shown) bind to syntax assemblies of their type (e.g., knows to V1, John to N2). The syntax assemblies bind using their subassemblies of the same type. F1 shows how in (1) John can bind to knows as theme. Here, V1 and N2 activate their theme (t) subassemblies (V-t and N-t), because a control network [2] recognizes John as theme of knows and opens the gates to activate V-t and N-t. If no more words follow, this results in the representation of (1). But in (2), V-c and N-n have to bind to the complement clause C1 instead. Figure 2 shows the activation of V-t, N-t, V-c and N-n, implemented as neural populations with Wilson-Cowan dynamics. At 0 ms, knows activates V-t and V-c, anticipating a theme or complement. At 300 ms, N-t and N-n are activated as potential roles of John. Initially V-t and N-t start to bind and win the competition with V-c and N-n. At 600 ms, likes initiates the activation of clause C1 as complement, which starts to bind with N-n and V-c. This results in the competitions V-c with V-t and N-n with N-t. N-n and V-c win the competition, which results in the correct binding in (2) and overrides the binding V-t with N-t that would arise in (1). The dynamical resolution of a sentence ambiguity in line with human processing illustrates the possibility to implement aspects of high-level cognition in neuronal models based on population dynamics.





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P07 Collection of simulated data for validation of methods of analysis of extracellular potentials

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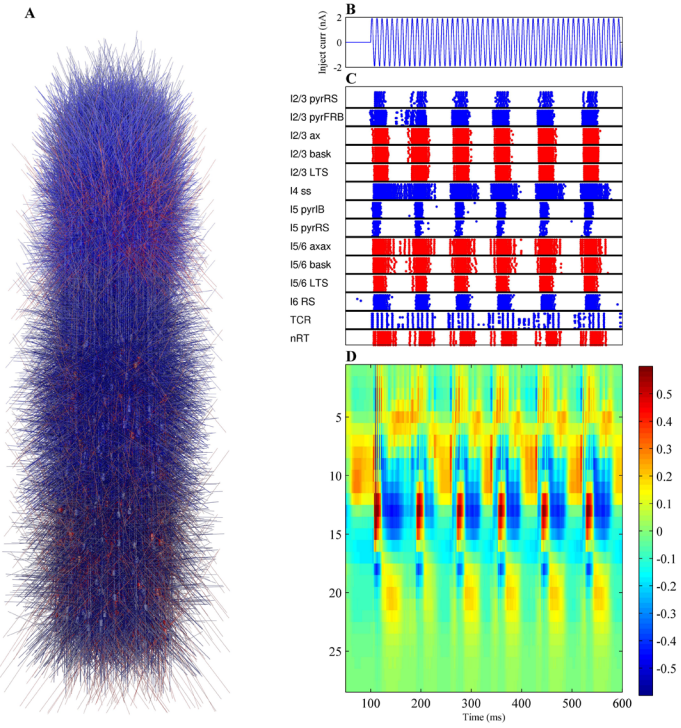
To test various methods of data analysis e.g. reconstruction of current source density (Potworowski et al. 2012), laminar population analysis (Einevoll et al. 2007) spike sorting algorithms etc. and to verify hypothesis concerning relationship between different aspects of recordings, e.g. local field potentials and synaptic currents we need realistic ground truth data. Generating such data requires plausible models of neural activity, access to high performance computers and time to prepare and run the simulations and process the output. To facilitate such tests and comparisons by the community we provide a rich collection of datasets including intracellular voltage traces; transmembrane currents; extracellular potential.

The data were generated in Neuron using the largest publicly available model of thalamocortical network (Traub et al. 2005). The model contains around 200 000 compartments in 3560 multicompartmental cells in 14 populations and was extended by adding 3-dimensional cell morphologies in NeuroML (Gleeson et al. 2007); distribution of cortical neurons in a cortical column; saving selected variables; providing additional stimuli.

The collection contains responses to oscillatory (12.5 Hz, 25 Hz, 50 Hz, 100 Hz, 200 Hz) or step input (2 ms) into thalamic cells. Since the datasets are large (e.g. voltage data from 600 ms of network activity takes more than 5 GB in binary format), more variables are provided for a simulation of 10% of the network.

Every dataset contains: voltage and sum of transmembrane currents in every segment every 0.1 ms; spike times; position of every segment; extracellular potential calculated on 28 electrodes. We also provide a script to calculate extracellular potential anywhere. For the simulation of the small network we further provided separate values of different transmembrane currents: GABA A, NMDA, AMPA, capacitive, passive, sodium, potassium, calcium, anomalous rectifier, two kinds of calcium low threshold T type currents (Traub et al. 2003, 2005) (not causing [Ca2+] influx) and other (e.g. steady bias and ectopic currents; Traub et al. 2005).

Fig 1: A) Cortical cells in the Traub's model. Blue: excitatory, red: inhibitory. B) Example input (100 Hz oscillatory injection) to thalamocortical relay cells C) Raster plot showing response to the stimulus in ten random cells from each population. D) Extracellular potential computed on 28 electrodes placed in the center of the column.



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P08 A neurorobotic approach of emotion: Implemented neurodynamics mediate a coupling between top-down abductive inference and bottom-up sensations

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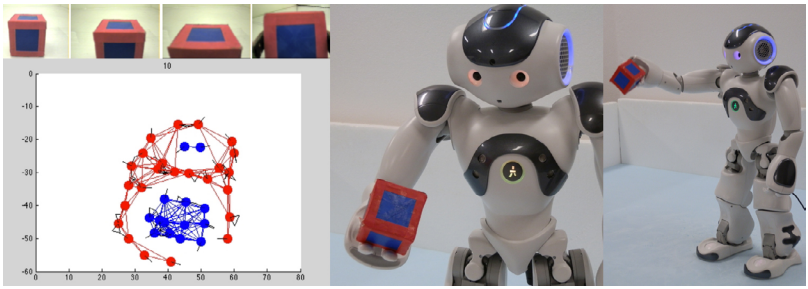
A simple extension of robotics hardly accomplishes the level of what a robot knows like an educated person and becomes skeptical about the own ability and counterpart's true intentions. It is designed in the range of interpreter or translator without any feeling. Neither they are disgusted with someone's attitude nor indignation swells inside. A lack of feeling or sensation. An abductive inference is considered to be necessary to be conscious what happens externally and internally [1, 2]. Computational models with oscillator synchronization mechanisms have proposed to explain the process phenomenologically as a potential neurodynamics [3, 4]. A synchronization mediates a coupling between top-down abduction and bottom-up possible interpretations based on sensory signals.

Recently, neurorobotic approaches to understand what the brain works are highlighted such as testable platforms for motor control and locomotion, reward systems and action selections, hippocampus and memory systems, and even for medical cares of autistic symptoms and Parkinson's disease [5, 6, 7]. We have proposed a phenomenological model of emotion [8] and extend it to a neural dynamics toward robotic implementations [9]. A non-linear oscillator dynamics can be applied to a top-down abduction by reading information of firing phases which differentiate distributed phases and a concentrated phase depending on the spatio-temporal context, called phase coding (Figure 1). In verification of a hypothesis of Damasio [1], which focuses on the difference between feeling and emotion, i.e. changes in physical and chemical state and its awareness, computational models with neurobiological background [2] remain within the framework to test an isolated system from environmental change and influences by the presence of others. Neurorobotic approaches offer a hybrid platform to take into consideration of combinatory effects involving real-time interactions with humans, and it may develop into an effective tool to investigate how our emotion comes from.



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P09 A working memory mechanism and strategy transition dynamics when solving SUDOKU puzzle

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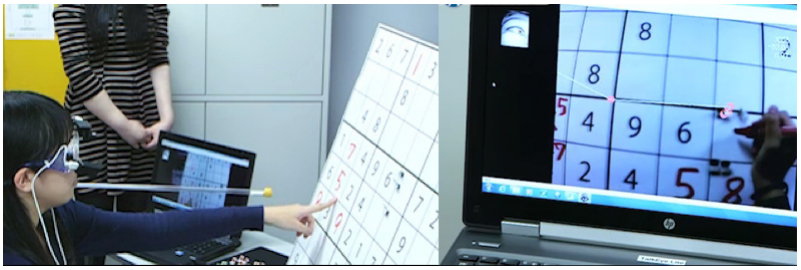
Sudoku is a popular puzzle to fill the right number in empty boxes of the nine-by-nine Sudoku grid with deductive (or sometime speculative) inference by cues of given numbers in some boxes, which restrict the degree of freedom in the final set and provide an unique solution for being a puzzle. Interestingly, the same puzzle can be formed as the four-by-four and sixteen-by-sixteen, yet people get excited at solving the nine-by-nine version. A plausible reason why is that the former one is too easy and the latter one is too difficult for humans to solve. The solving style varies from individual to individual and there are different preferences in transition between primitive solution strategies. According to Delahaye [1], professional solvers frequently use simple strategies called "only cell" (finding a cell which has no option except putting a specific number) and "forced cell" (a method of elimination), and systematically switch them to other complicated strategies such as simplifying the range of possibilities and try-and-error (including a hypothetical reasoning) at the moment to face a situation that only/forced cell strategies do not work properly as they felt.

In our experimental observation of amateurs with different experiences which may corresponds to levels of skills, subjects exhibit individual preferences on a tendency of transition between primitive strategies. Post-experimental interviews revealed that some person has a fixation for a specific number because of the one's most favorite number and the other changed the fixation in order. It suggests that try-and-error in Delahaye's sense is not equivalent to a random process with the probability density distribution defined by efficiency, or a confidence rating. Instead of the confidence, they rely on adherence. We discussed a possible neural dynamics for solving the puzzle [2], as a form of working memory mechanism with a spontaneous of working table related to the prefrontal-parietal network and an emotional judge provided by the hippocampal-amygdala-prefrontal network [4]. The present result partly supports our hypothesis.



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P10 Axonal and dendritic density field estimation from incomplete single-slice neuronal reconstructions

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Neuronal signal integration and information processing in cortical networks critically depend on the organization of synaptic connectivity. Synaptic connections between neurons can form when their axons and dendrites come in close proximity of each other. The spatial innervation of neuronal arborizations can also be described by their axonal and dendritic mass density fields. Recently we showed that population mean density fields, averaged over a number of neurons of a given cell type, can be used for estimating synaptic connectivity between neurons with overlapping axonal and dendritic density fields (Van Pelt et al., 2010; Van Pelt and Van Ooyen, 2013).

Deriving population mean density fields requires a sufficient number of experimentally reconstructed neurons. Much morphological data, made available via open-access databases, however, is derived from single slice neuronal reconstructions, which are generally incomplete because of cut branches.

Here, we describe a method to recover the lost mass, which is based on an estimation of the mass inside the slices and an extrapolation of the mass to the space outside the slices, assuming axial symmetry in the spatial distribution of neuronal mass. This 'completion method' has been validated using a set of neurons generated with our NETMORPH simulator. These neurons were artificially sliced and subsequently recovered by the completion method. Dependent on the slice thickness and the extent of the arbors orphan branches may occur (inside branches which have lost their outside parents), which are not anymore part of the contiguous structure of the sliced neuron. For 300 µ thick slices, however, the validation showed a full recovery of dendritic mass and an almost full recovery of axonal mass.

The completion method has been applied to three experimental data sets of reconstructed rat L2/3 pyramidal neurons. The recovery results showed that in 300 µm thick slices intracortical axons have lost by slicing about 50% of their mass and dendrites about 16% of their mass. The completion method can be applied to single slice reconstructions as long as axial symmetry can be assumed in the axonal and dendritic mass distribution. This opens the possibility to use the many cell-type specific reconstructions from open-access data bases for constructing, by completion, their population mean mass density fields and apply these fields in connectivity studies.

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P11 Combining spiking neuronal network model with presynaptic and astrocyte interface models

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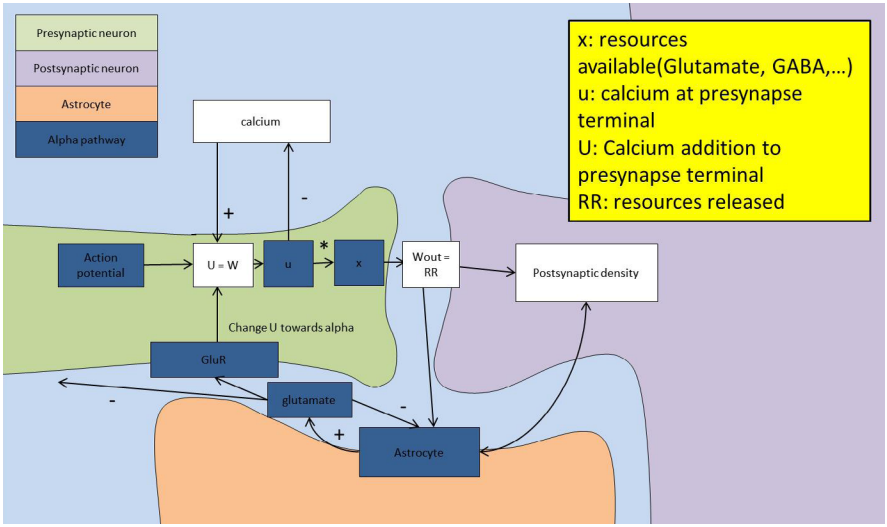
Astrocytes have gained an increased interest in neuroscience due to their ability to influence synaptic transmission through gliotransmitters. The effects of gliotransmitters are computationally modeled by various groups. However models integrating astrocytes and their effects in the network level are lacking. Here we introduce a simulation scheme of astrocyte control of single synapses extend that to its effects on neuronal network behavior. A version of Tsodyks-Markram presynaptic model is used as described by De Pittá et al. (2011) and astrocytic effects as described in the same paper. These effects are applied to spiking neuronal network INEX by Lenk (2011). The simulators are combined by modifying values of synaptic strengths (W) in the INEX model according to neurotransmitters released in presynaptic models attached to each synapse (see Figure 1). At an event of spike amount U calcium enters the presynaptic terminal and binds to vesicle sensors u. There is an amount of x neurotransmitter present in the presynapse at any given time. Amount of u*x resources are released. Glutamate affects the value U by modifying parameter alpha. Alpha describes the effect of presynaptic glutamate receptors to release probability. U is changed towards alpha depending on glutamate amounts released by astrocyte. INEX parameter W is used for initial U for each synapse and resources released (RR) as weight for spiking synapse. A linear relationship between neuro-transmitter amounts and their effect to axon hillock computation is assumed. Astrocytes release gliotransmitters according to presynaptic releases which they detect. Release of gliotransmitters follows very simplified calcium dynamics in astrocyte. As in many other models we assume that gliotransmission reduces the strength of the synapse. We simulated a small network with 100 neurons (80 excitatory and 20 inhibitory) with and without astrocyte effect on synapses. When astrocytes were present in the model every astrocyte was linked with single excitatory synapse. Inhibitory synapses had presynaptic dynamics but no astrocyte effect in both cases. Our results show that, in accordance with the theory, network with astrocytes and with high activity gets activity reduced according to astrocytic glutamate releases to single synapses. As astrocytic glutamate is taken up, the activity increases. As a result additional releases by astrocytes reduce the activity again. This leads to periodic bursting of network. In the network without astrocytes two types of behavior can be seen. Some neurons are spiking almost constantly while others follow in short bursts. These bursts are approximately 50% longer than bursts in the astrocytes including network. Thus our results show that astrocytes regulate network activity by regulating individual synapses. The astrocytic glutamate reduces activity and makes it more periodic by comparison. To conclude, we combined a spiking neuronal network model with presynaptic and astrocyte interface models and could observe reduction in the neuronal activity and periodic synchronous bursting when astrocytes were present.


Presynaptic neuron
Postsynaptic neuron
Astrocyte
Alpha pathway
calcium
x: resources available(Glutamate, GABA,...)
u: calcium at presynapse terminal
U: Calcium addition to presynapse terminal
RR: resources released
+
-
Action potential
U = W
u
*
x
Wout = RR
Postsynaptic density
Change U towards alpha
GluR
glutamate
-
-
+
Astrocyte

P12 Bifurcation analysis in a single-compartment Traub model for hardware based emulation

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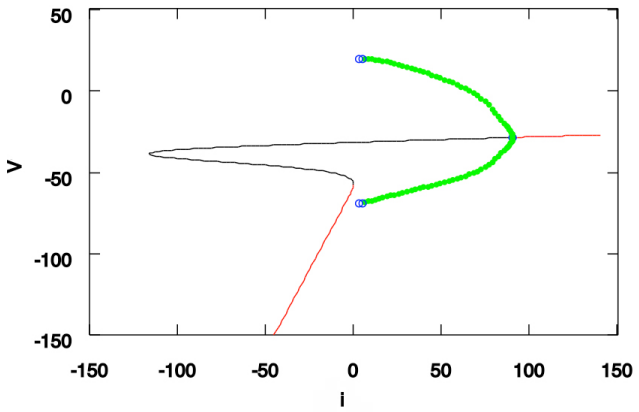
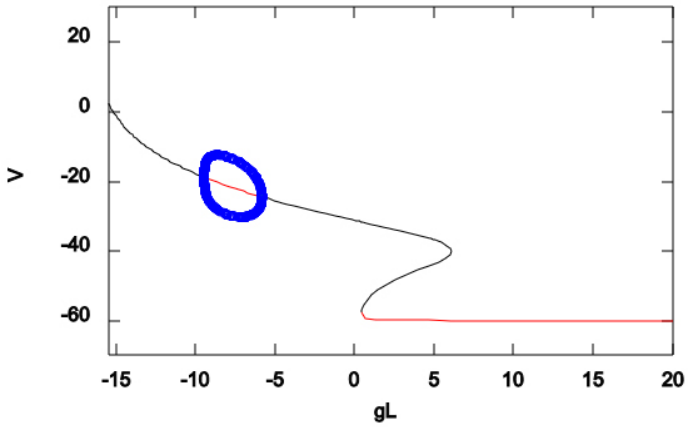
In this work we make a bifurcation analysis for a single compartment representation of Traub model, one of the most important conductance-based models. The analysis focuses in two principal parameters: current and leakage conductance. Study of stable and unstable solutions is explored; also Hopf-bifurcation and frequency interpretation when current varies are examined. This is the first analysis done that considers single-compartment version of a Traub model. This study allows having control of neuron dynamics and neuron response when these parameters change. Analyses like these are particularly important for several applications such as: tuning parameters in learning processes, neuron excitability tests, measure bursting properties of the neuron, among others. Finally a hardware implementation tests were developed to corroborate these results. The leakage conductance value was tuned in order the neuron remains at fixed value when it is at resting state. This parameter is the best option to change if does not want to compromise the dynamic of the original model. Through bifurcation analysis, it was detected one stable and one unstable solution (equilibrium points) for this model. A Hopf bifurcation was discovered at the point I = 90 mA, given to the current range [0 90]mA a set of stable periodic orbits with different action potentials amplitudes. The frequencies range for this periodic orbits are from 50 to 341 Hz.





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P13 Simulation of matured in vitro human neuronal cell networks

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Current state of the art in vitro neuronal systems apply cultured neuronal networks on multielectrode arrays (MEAs). With MEAs, neuronal cell networks also derived from human pluripotent stem cells (hPSC-NN) can be recorded. In the past, we built a phenomenological model called INEX (INhibitory-EXcitatory) that was used to simulate developing hPSC-NNs on MEAs. In this paper we propose a simulation of maturated hPSC-NNs by modifying our INEX model to simulate activity of matured hPSC-NN. We focus on synchronous bursts which are a main feature of mature neuronal activity patterns. The INEX model is based on an inhomogeneous Poisson process to simulate neurons which are active without external input or stimulus resembling our in-vitro MEA experiments. Each simulated neuron has either an inhibitory or an excitatory effect to its neighbors. The model consists of four parameter types: internal noise, exhibitory and inhibitory synaptic strength and a spike time history which ensures synchronous bursting of the neurons. These parameter types; are chosen in such a way that the resulting spike trains resemble spike trains of 2D MEA experiments with hPSCNNs with respect to spike and burst rate. A network with 1,000 neurons and 10 per cent connectivity was simulated.

For validation, we examined in vitro MEA recordings from nine relatively mature hPSC-NNs performed for approximately 300 seconds 27 to 39 days after plating. We calculated the median and quartiles of the spike and burst rate, the number of spikes per burst and the burst duration using the burst analysis tool by Kapucu et al. (2012) for both the simulated and the experimental data. Moreover, we used the detection method of synchronous burst events published by Raichmann and Ben-Jacob (2008). The results show that we can simulate typical spike and burst patterns as known from MEA experiments with maturated hPSC-NNs and in particular synchronous bursts. The validation showed that all calculated median values of the INEX data are within the lower and upper quartile of the MEA data. To conclude, the calculated features adapted from spikes and bursts show that matured hPSC-NNs as observed in MEA experiments can be modeled by the INEX model.

P14 The effect of longer range connections on neuronal network dynamics

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The dynamics of neuronal networks are often studied in neuronal cultures measured with microelectrode arrays. However, the spatial structure and the connections in the cultures are hard to determine and control. Thus, it is difficult to inspect, how different spatial structures in the networks affect the network behavior. In this study, we built computational model networks with different connection lengths and analyzed, how longer range connections affect the neuronal network behavior.

The model was based on INEX (Lenk 2011), a probabilistic neuronal network model with excitatory and inhibitory neurons. The topology model is demonstrated in Fig 1. Briefly, the neurons were scattered in 2D or 3D space and then connected inside a varying radius with a specific probability so that the resulting network was approximately 10 % connected. Linear delays were added to the connections: the greater the distance between the neurons, the longer the delay of the action potential. The maximum delays were 15 ms. The simulations were performed using the NEST simulator (Gewaltig and Diesmann 2007). The bursting statistics of the neurons were calculated using the Cumulative Moving Average method (Kapucu et al. 2012). The calculated statistics were the mean spike rate, burst rate, burst duration and number of spikes in burst. For the statistical analysis, 64 neurons were selected from each network, representing the electrodes in a standard in vitro multielectrode recording.

The statistics of the spiking and bursting behavior are presented in Fig 2. The effect of longer range connections was similar in 2D and 3D. The burst duration and number of spikes in burst increased remarkably and almost linearly as longer range connections were included in the network. This implies that the bursts die away fast in the networks with only short connections, when all the neighboring neurons have spiked. As the longer range connections are added, each neuron will get input also from more distant neurons and the bursts will last longer.

In 2D, also the spike and burst rate first increased slightly as the maximum connection length increased and then started to decrease again. The increase of the spike rate is most likely related to the increase of number of spikes in burst. The increase of the burst rate implies that the longer range connections turn individual spikes into bursts more likely than when there are only short connections in the network. After the initial increase, the spike and burst rates decrease slightly, as the connections become longer in both 2D and 3D. This decrease may arise from that the longer range connections make the networks more random. As a conclusion, the longer range connections make the bursts in a neuronal network longer, but do not greatly affect the number of spikes or bursts in the network.

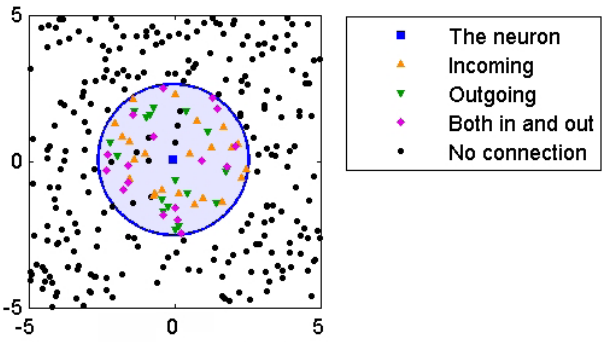

Fig. 1. A demonstration of the topology model. The in-coming and out-going connections and the range of connections of one neuron are shown. Note that not all neurons in the network are shown.

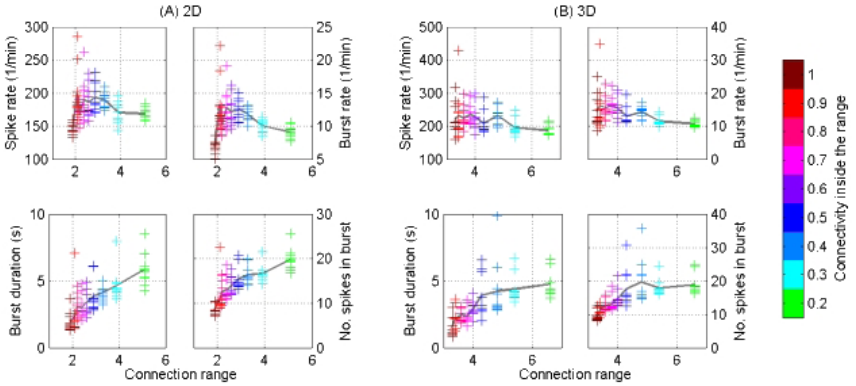

Fig.2 The spike and burst statistics of the (A) 2D and (B) 3D networks with different ranges for connections. Each mark corresponds to the median in one model network.

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P15 Computing local field potentials based on spiking cortical networks

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While recordings of extracellular potentials in neural tissue are commonly used for monitoring neural activity, interpretation of the low frequency part, the Local Field Potential (LFP), in terms of the underlying network activity, remains ambiguous. Several studies have shown that the LFP depends on the electrode position, extracellular volume conductor, neuronal morphology, synapse distributions and synaptic input correlations [1,2]. In order to relate spiking network dynamics to the LFP, we have developed a hybrid scheme that uses the spiking activity of a network of single-compartment leaky integrate-and-fire model neurons (implemented in NEST [3], Fig. 1a,b). This network provides synaptic input to populations of detailed multi-compartmental neuron model which in turn generate the LFP (implemented with LFPy [4] using NEURON [5], Fig. 1c,d). We here apply the methodology to a novel network model describing 1 mm2 of cat primary visual cortex with a total of 78000 cells spread across layer 2/3 to layer 6 with one excitatory and one inhibitory population per layer [6]. For the LFP model, sixteen cell types with passive membrane properties are used. The cell-type and layer-specific connectivity is specified on the basis of the connectivity of the spiking network model and further anatomical data [7]. Our results show that both spontaneous and stimulus-evoked LFPs depend critically on the underlying network state, i.e., whether the ongoing network state is synchronous or asynchronous. Moreover, we show that full-scale simulations, i.e., simulations including all cells in the network, are required to address the effect of network correlations on the LFP. Further, the hybrid scheme can be used to develop simplified proxies for LFP generation from simplified network models, and provides insight on the link between experimental measurements and the underlying network activity.

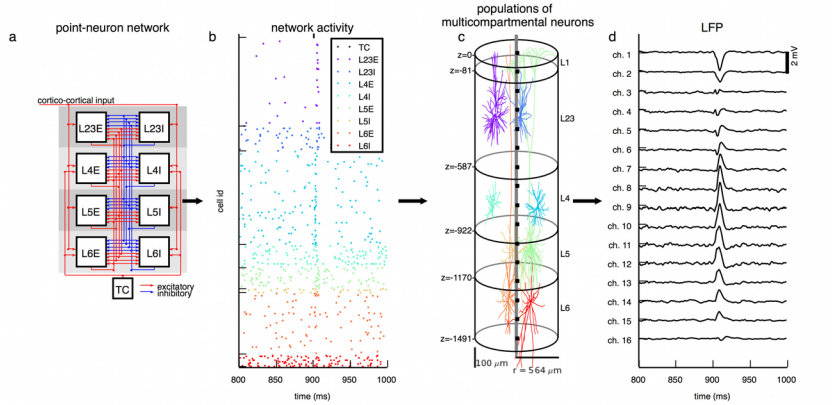

Figure 1: Schematic illustration of the hybrid scheme. Spiking activity generated in a layered spiking-neuron network simulation (panel a modified from [6], b where E and I denote excitatory and inhibitory populations) are in turn used as synapse activation times onto equivalent, but morphologically detailed populations of multi-compartment neuron models (c). The resulting trans-membrane currents of single cells allows e.g., superimposing the generated LFP contribution from each population (d).

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P16 Interneuron cell types differentially modulate gain in a multi-compartmental pyramidal cell model

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Recent experimental work has shown a differential effect of activation of different types of interneurons on input/output the gain of relationship of pyramidal cells, when tested either using current injection or using the presentation of sensory stimuli. These experiments support the hypothesis that interneuron activity plays a key role in the dynamic transmission of signals. On the local circuit level, interneuron activity could affect the input-output relation of local pyramidal cells in a subtractive or divisive way, or shift the dynamic range of the cell (Silver, 2010; Tiesinga et al., 2008).

In recent studies, contradictory results have been found concerning the effect on the gain of orientation-tuned pyramidal cells by two separate populations of interneurons, the somatostatin positive (SOM+) and parvalbumin positive (PV+) interneurons (Lee et al., 2012; Wilson et al., 2012). In Lee et al report results suggesting a divisive effect for SOM+ and a subtractive effect for PV+, whereas Wilson et al report results indicating the contrary. The reason these differences remain unclear. An explanation potentially involves differences in experimental protocols, resulting in differences in network state and pattern of synaptic background activation due to anesthesia and strength of optogenetic activation. The effects these differences have on the measured gain depends on the differences in morphology, axonal targets and intrinsic electrophysiological properties between the SOM+ and PV+ interneuron types.

Using a modelling approach, we examined the effects of interneuron activity on the gain of a layer 5 pyramidal cell. To this end, we adapted a multi-compartmental model of a layer 5 pyramidal neuron (Li et al., 2013) and assessed the significance of spatially and temporally patterned inputs for gain modulation. The model pyramidal cell received inhibitory inputs from SOM+ interneurons on the distal dendrite and/or inhibitory inputs from PV+ cells on the proximal dendrites and the soma, as well as excitatory synaptic inputs. Inputs were either timed randomly or locked to an oscillatory rhythm, since PV+ interneurons are known to play a key role in gamma rhythm generation, while SOM+ cells were considered to be locked to a slower rhythm.

We found that the effect of SOM mediated dendritic inhibition was different depending on whether the excitatory inputs arrived at the same location on the dendrite or at the soma and a different part of the dendritic tree. Taken together, these results show that testing gain changes via current injection at the soma might give potentially misleading results for the differential effects on gain of interneurons targeting different parts of a neuron's morphology.

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P17 Cortical cytoarchitecture and distance predict corticocortical connectivity

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Information processing in the brain is strongly constrained by anatomical connectivity. However, the principles governing the organization of corticocortical connections remain elusive. Here, we tested three models of relationships between the organization of cortical structure and features of connections linking 49 areas the cat cerebral cortex. Factors taken into account were areas' relative cytoarchitectonic differentiation (structural model), relative spatial position (distance model), and relative hierarchical position (hierarchical model). Cytoarchitectonic differentiation and spatial distance (themselves uncorrelated) correlated strongly with the presence or absence of interareal connections, whereas no correlation was found with relative hierarchical position. The two independent factors of structural type difference and spatial distance were integrated into a model of corticocortical connectivity which allowed us to predict the existence of connections in the data set with more than 85% accuracy at moderately conservative classification thresholds. Moreover, a strong correlation was observed between laminar projection patterns and cytoarchitectonic differentiation. Additionally, architectonic differentiation correlated with the absolute number of corticocortical connections formed by areas, and varied characteristically between different cortical subnetworks, including a module of hub areas. Thus, anatomical connectivity in the cat cerebral cortex can, to a large part, be explained by the two independent factors of relative cytoarchitectonic differentiation and spatial distance of brain regions. Hierarchical area rankings, by contrast, did not add explanatory value. As both the structural and distance model were originally formulated in the macaque monkey, their applicability in another mammalian species suggests a general principle of cortical organization.

P18 Growth and development of the postsynaptic active region of an excitatory glutemergic synapse: An integrated model

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In an excitatory dendrite, the genesis of a synapse begins with a dendritic filopodium making a tactile contact with a presynaptic bouton due to growth initiated by BDNF-TrkB mediated actin polymerisation in the filopodium. During its development, the postsynaptic spine head enlarges and the apical periphery becomes the site for synaptic activity. The assimilation of the postsynaptic density (PSD) in this site marks the begining of postsynaptic development, which subsequently develops to become the kernel of synaptic activity and provides a scaffolding that houses the receptors, CAMs and the various growth related protiens, the study of which is incipient. The morphology of PSD and the potentiation of an excitatory synapse have a relationship that is synergic in nature. Our petrinet based model aims to trace the genesis and the morphological modifications undergone by the PSD of the postsynaptic region of an excitatory glutemergic synapse, begining from the genesis of an excitatory synapse, through the various stages of its development. The chief signalling pathways include those triggered by NMDA and AMPA receptors, Trkb-BDNF, Integrin and Epherin and the ionotropic receptors that are the focus of our study are NMDA and AMPA where NMDA acts as a ligand gated ion channel for Ca2+ and AMPA for Na+. In our model, we have proposed a mechanism that controls the shape of the postsynaptic region of synaptic activity as a function of the positions of neuriligin (Nlg-1) molecules on the PSD platforms through a method of zonal actin polymerization (ZAP). Acoording to our hypothesis, the polymerization of actin occurs in individual "zones" beneath the PSD. The zones which underlie the Nlg-1 pillars or, are in their vicinity, have inhibitted growth due to excess opposing force offered by the PSD, in comparision with zones devoid of Nlg-1 influence. Depending upon the positions of the Nlg-1 molecules near the centre and/or at the ends of the PSD, a plethora of shapes starting from a convex spherical spine head to a concave cup-shaped one can be obtained. Furthermore, we intend to incorporate a system of retrograde signalling mediated the generation and release of retrograde messangers which is instigated by Ca2+ influx in the postsynapse. The activation of the PLC pathway by neurotrophins produces DAG from the lipids upon hydrolysis. DAG then generates the endocannabinoid receptor messengers upon interaction with Ca2+.

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P19 Workflow for integration and analysis of histological data in rodent brain Waxholm Space

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Identification and analysis of distribution of various cellular markers visualized in histological materials are fundamental to many experimental investigations in the rodent brain. Since investigations of distributed brain systems and manifestations of ageing and brain disease across the brain often require brain-wide analysis, technologies for efficient acquisition of large amounts of image data from individual brains are increasingly used. A major challenge in this context is the task of analyzing large amounts of high-resolution image data and identifying the anatomical regions and subregions in which the labelled cellular elements are observed. To this end, common reference frameworks are introduced, including brain atlases with standardized brain atlas space, such as the recently introduced volumetric Waxholm Space atlases developed for the mouse and rat brain (Hawrylycz et al., 2011; Papp et al., 2014). We here present a workflow aimed at providing 1) automatic, or semi-automatic identification of labeling in large series of microscopic section images acquired with robotic microscopes or slide scanners, 2) spatial anchoring of histological section images to the volumetric Waxholm Space atlases, and 3) atlas based analysis of the distribution of labelling. The work flow begins with histological section image data and ends with the analysis of data anchored to the Waxholm Space atlases. Automated analyses include image filtering to identify and quantify labelling, and assignment of spatial location parameters to determine where in the brain labelling is located. The workflow was tested using experimental material from recently published studies on brain-wide mapping of axonal connections in the rat and distribution of genetic markers in transgenic mouse models of neurodegenerative disease. High-resolution images of complete coronal, sagittal or horizontal sections were acquired using a slidescanning system. Image processing parameters were optimized on selected representative sections, and then applied to complete image series. Within a wide range of labeling densities, the automatic method provided reliable results and offered opportunities for efficient, standardized analysis of labeling distribution across the brain. The work flow presented, with the concepts and tools provided, allows efficient registration of section image data to a volumetric reference atlas and brain-wide analysis of histologically labelled cellular markers.

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P20 Growing the INCF Digital Atlasing Infrastructure

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Digital brain atlases are essential tools in neuroscience research. They function as references and analytical tools, and provide stable integration frameworks as a basis for investigations of normal and abnormal brain structure and function. Thus, the aim of the International Neuroinformatics Coordinating Facility (INCF, incf.org) Digital Atlasing Program (incf.org/programs/atlasing) has been using digital atlases as the basis of a framework for data sharing. We have created a prototype framework for this purpose, related recommendations, standards, and documentation to make the rapidly growing collection of multi-dimensional data of the rodent brain widely accessible and usable to the research community. The framework consists of a canonical atlas space (Waxholm Space, WHS) and a hub-based distributed INCF Digital Atlasing Infrastructure (DAI). The current framework is primarily for the adult C57BL/6J mouse, but we are in the process of expanding it to the rat.

Recently, work has revolved around creating greater access to DAI for neuroscientists via query tools (e.g. WIB, WHSlookup, the Atlasing Portal, and the atlasing wiki) and facilitating their ability to bring new data into this framework via registration tools (e.g. Jibber, JAWs, and high throughput 2D image registration tools), improving reliability and access to this data as well as certain components of the infrastructure (e.g. hardware, versioning and URIs, creating and updating registrations between key atlases including the new Allen Brain Atlas), and developing WHS for the rat (Wistar and Sprague-Dawley).

Tying 2D image registration workflows to DAI has been a main focus of the program, which crosses into areas dealing with metadata, provenance, and ontologies. Other supporting project areas include registration fiducials, standards, metadata, provenance, and data management and handling.

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.

For an overview and access to tools, visit the Atlasing Portal at incf-dev.crbs.ucsd.edu/atlasportal/catalog/main/home.page. For more information about Program activities and projects, visit the INCF wiki at wiki.incf.org/mediawiki/index.php/Digital_Brain_Atlasing. For access to the code repository, see code.google.com/p/incf-dai.

P21 Automated workflow for mapping tracer injection studies of the common marmoset into a reference template

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The goal of the study is to establish an automated workflow for mapping common marmoset connectivity data obtained from tracer injection studies into reference template space of a stereotaxic atlas [1, 2].

Nine marmosets were injected with fluorescent retrograde tracers in the dorsolateral prefrontal cortex. Retrograde tracers label the cell bodies of neurons that send projections to the injection site, thus providing a map of neuronal inputs. Due to the limited number of distinguishable tracers, building a map of connectivity requires the registration of multiple specimens to a common atlas. Furthermore, registration to a common coordinate system will allow purely spatially based comparisons of connectivity unlike the traditional method relying on prior assignment of data to discrete anatomical structures.

Several steps are required to map the data obtained from a single specimen into the atlas space. During the initial stage, the locations of stained cells marked on the fluorescence sections are transferred to the neighboring Nissl sections. Afterwards, the Nissl stained sections are stacked and reconstructed into volumetric form. The reconstruction is initially performed with affine transformations followed by deformable warping. The latter step removes section specific distortions and allows for more reliable subsequent deformable mapping [3] into the atlas space. The process yields a set of transformations which are then applied to the actual cells locations. In the final step the individual cells are assigned to a particular brain structure based on the atlas parcellation. The described process will be conducted for nine test cases and will result in a database of the cell's coordinates in the atlas space.

The reliability of the workflow will be assessed by comparing the number of the cells in each cortical area indicated by the automated approach with the count determined manually by an anatomist. Once established, the workflow will allow the processing of the remaining cases to produce a spatially defined connectivity map of the marmoset cortex, independent of anatomical parcellation scheme [4]. Furthermore, this map can be used as a gold standard in DTI validation studies.

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P22 Registration of serial two-photon data to rodent brain Waxholm Space

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Serial two-photon tomography (STPT) is a novel method combining vibratome sectioning with two-photon block-face imaging to produce volumetric representation of fluorescent markers at cellular resolution across entire organs, such as the mouse or rat brain (Ragan et al., 2012). Performing brain-wide analysis of the distribution of the visualized cellular objects and integration of large data sets across individual specimens require the use of efficient and automatized neuroinformatics pipelines. This work presents a procedure to register STPT data to the recently introduced Waxholm Space atlases developed for the mouse and rat brain (Hawrylycz et al., 2011; Papp et al., 2014). With the use of these digital atlas resources, available through the INCF Software Center, STPT data can be integrated in standardized 3-D space. The proposed pipeline takes as input series of high-resolution STPT images (0.82 μm^2) capturing tissue (auto)fluorescence. These series of optical section images are spaced without gap at regular intervals (50 µm) across entire C57/Bl6 mouse or Sprague Dawley rat brains. Each slice is independently corrected for uneven illumination and contrast adjusted to optimize structural contrast of STPT data. Volumetric data are then generated by combining these slices and resampling the voxels to 25 μm^3. A synthetic registration target volume, matching the signal intensity distributions of the STPT volume, was derived from the mouse and rat Waxholm Space templates. STPT volumes are warped to the synthetic target volume using a multi-step parametric registration procedure including rigid, affine and non-linear transformations. The spatial accuracy of the full procedure was evaluated by comparing a collection of selected anatomical reference structures, manually defined in the STPT volumes with corresponding landmarks defined in the mouse and rat Waxholm Space MRI templates. This procedure thus allows efficient registration of STPT autofluorescence images to mouse and rat Waxholm Space and represents one of several new digital atlasing approaches for anatomical analysis and data integration in rodent brain models.

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P23 Can we hear the shape of a neuron? Cell type classification in high density multi-electrode recordings

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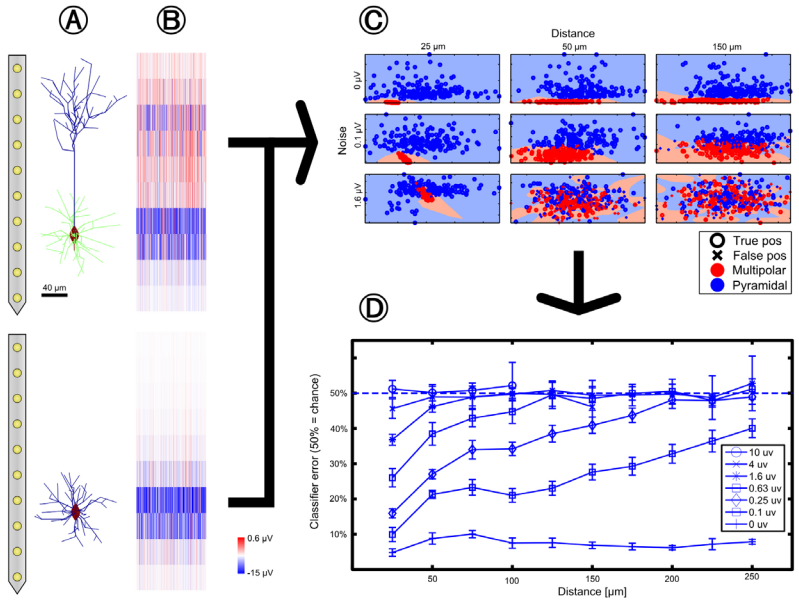
There is a trend toward the use of in vivo electrode probes with hundreds or even thousands of contact sites. The contact pitch (<50 µm) is much smaller than the spatial extent of a single neuron (~1 mm); thus, the extracellular potential (EP) generated by a single cell can be detected on many sites simultaneously [1]. Morphology of the cell determines the spatial profile of the EP, because most compartments of the cell support passive or active transmembrane currents [2]. We hypothesize that morphological characteristics of the neuron (cell type) can be inferred by inspecting this profile, where existing classification approaches rely exclusively on temporal information from a single electrode contact.

We set up a software pipeline consisting of a forward model and classifier. Neurons with randomized morphologies were generated [3] according to two templates: pyramidal and multipolar (Fig. 1A). The model neurons had a passive membrane together with active Hodgkin-Huxley channels in the soma only. Cells received balanced excitatory and inhibitory synaptic inputs that were uniformly distributed along the dendritic tree. Extracellular potentials were calculated using Poisson's equation for currents under the assumption of an unbounded, homogeneously resistive extracellular medium [2][4]. The multiunit activity (MUA) was obtained by acausally band-pass filtering the EP between 0.3 and 3 kHz, after which the spatial profile at the peak value of the MUA was extracted (Fig. 1B). The activity of all other active cells in the area surrounding the electrode was modeled as additive white Gaussian noise, of which the standard deviation was varied. Sample profiles were concatenated and fed into an SVM classifier after pre-processing (Fig. 1C). Reported values (Fig. 1D) were obtained using 50/50 cross-validation and for SVM hyperparameter values optimized to minimize test error.

In the absence of noise, morphological classes can be discriminated with a reliability of more than 90% for neurons at distances from the electrode up to 250 µm. Increasing noise amplitude pushed the classifier performance toward chance level, both decreasing in accuracy at close distances and restricting successful classification to a smaller range of distances between cell and electrode. A notable increase in classification error occurred at the boundary of the dendritic tree, corresponding to the boundary between the near and far electric field.

We conclude that within the context of this model, classification of gross neuronal morphology based on the EP spatial profile is feasible. Proximity of the recording sites to the dendritic tree is not strictly necessary, as the far-field component could also be used successfully for classification. Real-world benchmarking of the classifier could benefit from experimental data with a known ground truth, for instance obtained using cell type-specific optogenetic activation.



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P24 Low-frequency phase-locking of selective human medial temporal lobe neurons to the local field potential of contralateral lateral prefrontal cortex during visual stimulation

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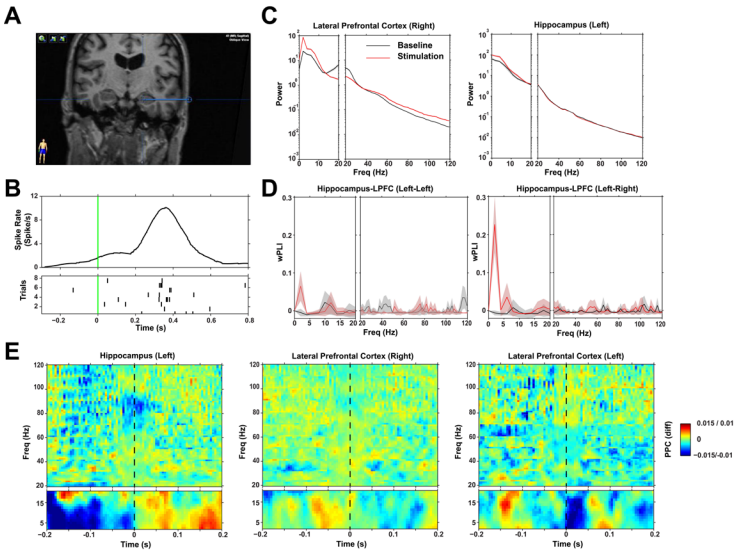
Human medial temporal lobe (MTL) neurons show selective and invariant responses to complex visual stimulation [1], but it is yet unknown whether this activity is supported by a coordinated response of a distributed brain network [2]. To inquire this, we recorded single-neuron and local field potential (LFP) activity during two sessions in eight epilepsy patients implanted with electrodes for presurgical focus localization, in the MTL and lateral prefrontal cortex (LPFC) in both hemispheres (Fig 1A). Patients passively observed pictures of celebrities and relatives for 1 s (stimulation) with interleaved pauses of 0.5 s (baseline) between pictures. Every picture was presented 8 times during a session. Here, we presented preliminary data for 1 patient. We observed 3 MTL neurons (medial left hippocampus [HPC]) with selective responses to stimulation (Fig 1B). The LFP in HPC and LPFC areas revealed an increase of power in a low-frequency band during the stimulation condition, together with a decrease of the beta-band range (Fig 1C). We therefore analyzed interareal connectivity between these regions using the weighted phase-lag index (wPLI), a metric with reduced sensitivity to sample bias and volume conduction effects [3]. We observed a significant increase of wPLI during stimulation in the delta-theta range between HPC and LPFC (Fig 1D). Interestingly, the left HPC connected preferentially to the contralateral LPFC. Finally, we asked whether the observed selective-to-stimulation MTL spikes were phase-locked with the LFP in these areas. We calculated the difference in the pairwise phase consistency (PPC) metric [4] between selective and non-selective spikes and the LFP of the recorded areas. A low-frequency PPC increase in the right LPFC, 0.05 s previous to the MTL spike, was followed by an increase in HPC low-frequency PPC after the spike occurrence, and a decrease in phase-locking with the ipsilateral LPFC (Fig 1E). These results suggest the activation of a low-frequency band network probably initiated at the contralateral LPFC, which may support selective activity of MTL neurons during stimulation.



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P25 Towards a common format for storing electrophysiology data

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The need for common data formats for neuroscience data is becoming increasingly important because new projects and technologies are greatly enlarging the volume of data to be shared among laboratories and researchers. The focus here is a unified data format for cellular-based, neurophysiology data, including intra- and extra-cellular voltage recordings as well as optical physiology data (i.e., cellular imaging) and include complex metadata related to stimuli and behavior. To define basic requirements for a common data format, use cases from a multitude of laboratories must be considered. This has been done over the last few years by the Electrophysiology Task Force (Teeters et. al. 2013) of the INCF Program on Standards for Data Sharing. The first part of this poster will summarize the comprehensive document worked out by the Task Force. Specifically, the document describes the different types of data and metadata that must be stored at a minimum to represent electrophysiology data, including relationships between the data types, etc. To meet the urgent need of storing existing and currently produced data, the Kavli foundation has organized the initiative "Neurodata without Borders - Cellular Neurophysiology (NWB-CN)" (Reardon, S., 2014), an ambitious one-year project to produce a common data format accommodating use cases of four large experimental labs/institutions: the Allen Brain Institute, Janelia Farm and two big labs at NYU and Caltech. Although focusing on a limited set of use cases, the project's goal is to use best existing practices, like the Task Force recommendations, and develop products that will serve the broader community. The NWB-CN project started in May 2014 and has three stages, each scheduled to last four months. The first stage, to be completed by the time of the 2014 INCF Congress, is to gather example data sets and make them available at CRCNS.org. Stage 2, starting at the time of the 2014 INCF Congress, will invite proposals from data model designers, vendors of data formats, and developers to propose formats for storing data based on the example data sets; and to select a common format. Stage 3 is to develop software to implement and use the common format. The second part of this poster will describe the particular use cases in the NWB-CN project and provide information on how to propose data models and data formats to the project.

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P26 Analysis of muscle fatigue progression in biceps brachii using surface electromyography signals and wavelet packet entropies

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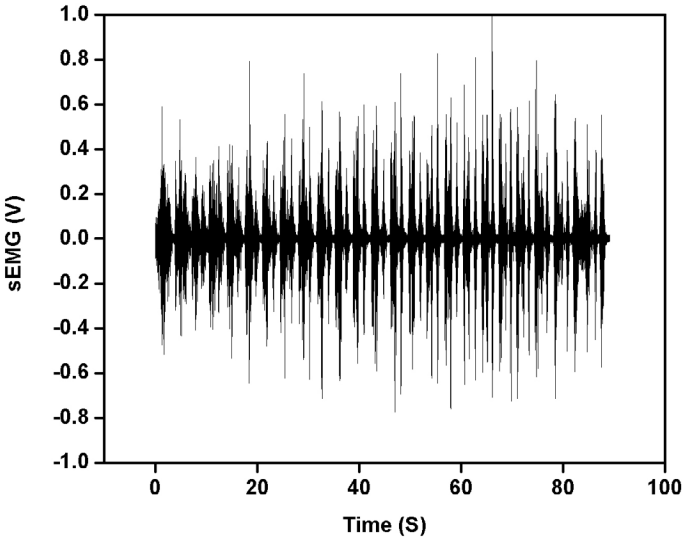
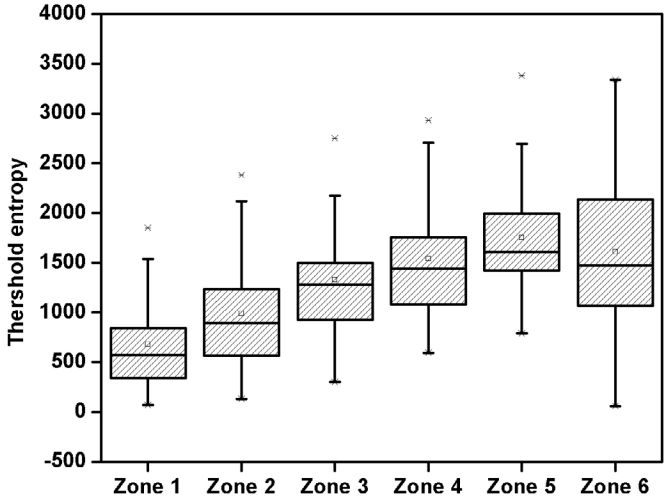
Muscle fatigue is a neuromuscular condition where muscles fail to generate the expected or required force to perform the task continuously. It is associated with both central and peripheral nervous systems. This condition can also be caused due to neuromuscular disorders such as Parkinson's disease, Carcinoma, Facioscapulohumeral dystrophy, Myotonic dystrophy and Hereditary motor and sensory neuropathy type I.

Surface electromyography (sEMG) is a non-invasive technique, which records the electrical activity of neuromuscular system. It is a complex, nonstationary and multicomponent signal. Most of the real life activities such as cyclic exercise and walking are based on dynamic contraction of muscles. Degree of nonstationarity is increased in dynamic contractions due to recruitment and de-recruitment of motor units, movement of innervations zones with respect to electrode and changes in muscle fiber length, firing rate and conduction velocity. The sEMG signals are often analyzed in the time domain, frequency domain and time-frequency domain. Although several methods of signal analyses are reported in the literature, the analysis of fatigue progression still remains a challenging task.

In this work, an attempt has been made to analyze progression of fatigue in biceps brachii muscle using surface EMG signals and wavelet packet entropies. The sEMG signals are recorded from biceps brachii of fifty healthy volunteers under well defined protocol and are preprocessed. The preprocessed signals are divided into six equal epochs. Further, these signals are subjected to wavelet packet transform. The entropies such as Shannon, threshold, norm, sure and log energy are extracted from the wavelet packet coefficients. The results show that Shannon, threshold and norm entropies are found to be distinct in all zones. Also the seperability of these entropies are appreciable between zone 1 and zone 6 which corresponds to non-fatigue and fatigue zone respectively. The t-test performed gives a p-value less than 0.0001 implying that the features are extremely significant. The demographics of subjects, representative sEMG signals and threshold entropy for all zones are shown below.


sEMG (V)
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
0
20
40
60
80
100
Time (S)


Thershold entropy
4000
3500
3000
2500
2000
1500
1000
500
0
-500
Zone 1
Zone 2
Zone 3
Zone 4
Zone 5
Zone 6

P27 INCF workshop report: New perspectives on workflows and data management for the analysis of electrophysiological data

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Breakthroughs in recording technologies and analysis approaches have led to unprecedented levels of complexity in electrophysiological experiments. The ability to perform massively parallel recordings from hundreds of neurons in the brain paired with a strong interest in complex, natural stimulation and behavioral paradigms, results in a surge of intricately interwoven incoming data that require to be analyzed with sophisticated methods. These factors pose a challenge for researchers who, over the course of years, are confronted with planning of the analysis, organization of workflows in larger teams, programming of software, and bookkeeping of the results obtained by constantly evolving analysis methods. The complexity of electrophysiological research has reached a level where a well-structured data analysis workflow has become a necessity. The INCF Program on Standards for Data Sharing supported the organization of a 2-day workshop to provide a discussion platform for researchers and developers who work on components that are instrumental in such workflows. The workshop focused on three major issues related to workflows in electrophysiology: (i) data structures and software libraries that enable interfacing of data from various sources and integration of methods for data manipulation and analysis, (ii) documentation and provenance tracking solutions to support reproducible analysis processes able to cope with the required levels of flexibility and data size, and (iii) workflow management systems that allow automatic and extensible processing of complex analysis workflows, in particular on high performance computers. In addition, experimental neuroscientists reported on workflow related needs from the user's perspective.

In this presentation, we summarize the existing approaches for data structures/software libraries, documentation/provenance, workflow management systems, and supercomputing that were highlighted during the workshop, and discuss how these are related from the perspective of the workflow. We point out the challenges identified by the participants for workflows and data management in electrophysiology. Finally, we present the conclusions of the workshop which were formulated as a set of recommendations for the INCF how to improve the workflow/data management situation based on INCF's activities within this domain.

P28 Describing neurophysiology data and metadata with OEN, the Ontology for Experimental Neurophysiology

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One of the major issues in Neurophysiology is the large diversity of data formats used to store both raw data and the associated metadata. The INCF Program on Standards for Data Sharing with the Task Force on electrophysiology (incf.org/programs/datasharing/electrophysiology-task-force) is concerned with developing data formats and metadata standards to alleviate this situation. However, existing ontological resources continue to lack terms for accurately and unambiguously annotating the breadth of electrophysiological data. With the development of different resources for sharing this particular type of data, the community needs controlled vocabularies to standardize the descriptions of the different types of recording paradigms, parameters and experimental procedures. Thus we have started developing the Ontology for Experimental Neurophysiology (OEN, github.com/G-Node/OEN). Because electrophysiology as a field is heterogeneous and the corresponding scope of the ontology considerable, the development of the OEN has been separated along two main branches: a branch considering devices and methods, and a branch considering neurophysiological concepts.

Building a terminology describing neurophysiological concepts (e.g. action potential, synaptic plasticity, afterhyperpolarisation potential,...) is difficult as these concepts legitimately belong to more than one ontology branch. This ontological entailments, i.e., what is allowed as a property of the term, will be different depending on the ontology branch increasing the complexity of the knowledge model. To address this difficulty we have devised a strategy using web-based surveys and detailed literature analyses to study how these terms are used by the community while ensuring that they are immediately usable in affiliated projects by importing terms related to Neurophysiological concepts into NeuroLex (neurolex.org).

The development of the device/method branch is use-case driven with the first aims of precisely describing specific lab devices and methods, annotating the EEGbase database (eegdatabase.kiv.zcu.cz), and enriching odML descriptions (g-node.org/odml/terminologies) with structured semantic information. In order to maximize the interoperability of the OEN device/method branch, terms for electrophysiological methods, tools and parameters gathered from various sources (EEGBase, odML terminologies, Neurolex,…) are mapped with existing ontologies related to experiments or investigation, including OBI (obi-ontology.org), NEMO (purl.bioontology.org/ontology/NEMO) and ERO (code.google.com/p/eagle-i/wiki/Documentation), The terms already defined in these ontologies are incorporated in OEN using the MIREOT approach (Courtot et al., 2011). The various terms composing the OEN device/method branch are contained in a dedicated terminology which will be used to build formal models describing necessary complex concepts such as experiment setups, acquisition system settings, workflows, etc.

Thus, the OEN is a comprehensive basis to build common knowledge models to enrich existing neurophysiological resources.

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P29 File format and library for neuroscience data and metadata

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Growing complexity of experiments and amount of acquired data in the field of neuroscience and electrophysiology pose increasing demands on data and metadata management. File formats that can represent and persist such information play a key role in this process. Existing file formats are often highly domain specific and typically designed for efficiency with respect to certain kinds of data, such as time series or image data, or specific recording software or devices. The fact that many formats are only accessible via proprietary software imposes further limitations. Moreover many existing formats only have limited support for metadata annotations. A common, open and standardized file format that is versatile enough to represent various kinds of data together with metadata has the potential to increase community-based tool development as well as data sharing among different labs. Here we present such a file format: it is based on a well defined data model which can be used to represent data and metadata in various backends. In order to specify a concrete file format, we used the model to create a schema for HDF5 files (hdfgroup.org/HDF5). The data model is able to represent and describe multidimensional data. It supports storing time series, spike trains, image and image stack data and various other kinds of data. It further allows the definition of points and regions of interest which can represent for example events or data segments. All data elements can be annotated with additional metadata using the odML data model (Grewe et al. 2011), which is an intrinsic part of the model specification. The data model is designed for being as flexible as possible but still expressive enough to provide the information, including units, sampling rates and labels, that is necessary to create a plot from the data without human interaction. The data model by design is not domain specific, but supports type annotation, providing the means to represent data in the generic model as domain specific entities. Due to its flexible design the data model is compatible with many other formats and able to represent data from NEO (neuralensemble.org/neo) or Neuroshare (neuroshare.org) files. In the HDF5 format, the data model is represented in a rather flat hierarchy. A file consists of 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 developed 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 g-node.org/nix.

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P30 A wiring diagram of protocerebral bridge for visual information processing in the drosophila brain

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A major challenge in neuroscience is to understand how a physical wiring network relays information flow from sensory input to behavioral output in a complex brain. The protocerebral bridge (PB) is a major part of the insect central complex, a pre-motor center analogous to the human basal ganglia. By deconstructing the adult Drosophila PB network into hundreds of single neurons and reconstructing them into a common 3D framework, we have constructed a comprehensive map of PB circuits with labeled polarity and predicted directions of information flow. Our analysis reveals a highly ordered information processing system that involves directed information flow among CX subunits through 194 distinct PB neuron types. This system follows several highly-ordered wiring principles indicating multiple levels of mirror, convergence, divergence, reverberation and parallel signal propagation within the CX. This layout of PB neuronal circuitry provides some clues as to how visual sensory cues are processed in the fly's brain to drive proper locomotor output.

P31 Adjusted Brain Measure (ABM): A simple, relative measure of brain status

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Several measurements can be taken from a brain using various technologies, including magnetic resonance (MR), magnetoencephalography, electroencephalography, positron emission tomography, and others. In addition, several further measurements can be taken within these modalities. For example, within the MR technology, one can do structural imaging, diffusion weighted imaging, fMRI, spectroscopy, etc. Typically, the values for these measurements are reported as individual values (for a particular brain) or as summary statistics (e.g. mean and standard deviation) for a group of brains. Here we show how these diverse measurements can be adjusted to yield a single, composite measure (Adjusted Brain Measure, ABM) that can serve for ranking individual brains within a population. We calculate ABM by taking into account deviations from the norm (50th percentile) of individual measurements as well as the variability among these deviations. ABM has the following useful properties: (a) it is dimensionless and robust; (b) it can be calculated easily and quickly from small or very large sets of K measurements ($2 \leq K < \infty$); and (c) it tends to zero for a set of measurements that are close to the norm in the study population and, hence, it can serve as a screening tool to identify brains deviating from the norm at a chosen threshold. The procedure by which ABM is obtained is fairly general and can be applied to other, very diverse fields where a distillation of multivariate data to a single index may be desired (e.g. cognitive assessments, general medical tests, environmental variables, socioeconomic applications, etc.).

P32 Parallel confidence-weighted classification of large-scale, multimodal neural data on MapReduce

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Existing neuroimaging technologies, such as magnetic resonance imaging and magnetoencephalography, continue to produce large, complex, high-dimensional data for numerous psychological disorders and neurological diseases. To identify these disorders/diseases from neural data, researchers typically apply one classification algorithm or compare multiple classification algorithms. By linking multiple classifiers (e.g. k-Nearest Neighbors, Naïve Bayesian, Decision Tree, k-Means, Support Vector Machines, Expectation-Maximization, etc.), the collective performance of the various algorithms can be exploited to yield consistent overall classification performance. Here we introduce the linked-classifier, which processes weighted inputs of several classifiers to yield a final, confidence-based classification outcome. Now, the application of multiple classification algorithms on large-scale data creates both memory and time constraints on standard, stand-alone computers. We overcome this problem by implementing our analysis within a MapReduce framework (see Figure 1) running in a computer cluster. The MapReduce framework is a computing paradigm that simplifies data demanding parallel computation. Thus, by taking advantage of this framework and the speed of its implementation, the multi-linked classifier functions run fast allowing for efficient robust classifications.

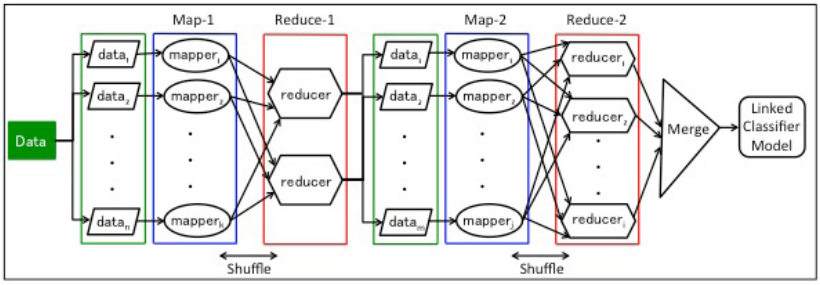

Figure 1. Pseudo-architecture for linked classifier

P33 Developing and using the data models for neuroimaging: The NIDASH Working Group

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18. Sage Bionetworks, Seattle, USA
19. Washington University, St. Louis, USA
20. Centre National de la Recherche Scientifique, Sophia Antipolis, France
21. University of Texas, Austin, USA
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Introduction

In neuroimaging, data sharing remains an exception [1]. While publishing a paper in many disciplines requires that data be made public, in human brain imaging there is no community standard for data sharing. However, the neuroimaging community increasingly recognizes sharing raw and processed data is critical for reproducible research, enabling meta-analyses and allowing for serendipitous discoveries.

In light of this challenge, two working groups focused on this mission joined to support the development of standards and tools that will have a community-wide impact on the prevalence of neuroimaging data data sharing: (1) the Biomedical Informatics Research Network Derived Data Working Group (BIRN-DDWG) [10], and (2) the Neuroimaging Task Force formed by the International Neuroinformatics Coordinating Facility's (INCF) Program on Standards for Data Sharing [9]. We report here on their common work to facilitate the sharing of many aspects of neuroimaging data and analyses.

Methods

The NIDASH Data Model Working Group (NI-DMWG) is composed of members of the BIRN-DDWG and the INCF Neuroimaging TF (incf.org). It holds weekly calls with participating members from the international community as well as several INCF-hosted yearly meetings. The TF wiki [11] is the primary resource for disseminating information and contains weekly minutes, publications, and links to products. NIDASH code is available on the "NI-" GitHub repository (github.com/ni). The Google Group incf-datasharing [12] hosts an email list on data sharing issues, reaching out to a wider community. The NIDASH-TF meets several times a year to review progress on projects (eg [16]) that will make data sharing easier and fruitful for the scientific community.

Results & Discussion

The NI-DMWG has developed DICOM [6,7] and neuroimaging [2,7] terminologies, and the NIDASH Data Model (NI-DM) [2,5]. NI-DM is a neuroimaging-specific extension of the PROV Data Model (PROV-DM; [11]) to facilitate sharing of semantically meaningful neuroimaging provenance and derived data. Using these tools, we have developed novel applications to demonstrate federating data across relational databases and spreadsheets [4], visualizing FreeSurfer segmentations [13] across a large cohort [3], and modeling SPM statistical results [8]. Further, we have begun development of detailed specifications of the core NI-DM standard and "object models" specifying the recommended minimal set of entities, agents, and activities to describe datasets, workflows, and derived data. A first version of the SPM statistical analysis object model specification [14] and examples [15] are available online. We have also developed a website for sharing raw statistical maps (NeuroVault.org) which will use NI-DM.

The INCF-TF meetings have encouraged adoption of these resources in various outside projects. We are linking this work with projects that are providing and hosting data, developing lexicons, and generating derived data for different purposes (e.g. data mining). The group includes developers and is in close contact with projects that plan to use these resources, or may do so in the future (e.g., Neurosynth, Neurovault, Brainspell), as well as with developers of integration platforms (e.g. NeuroDebian).

Conclusions

The immediate goals of the NIDASH DM working group are to 1) refine existing terminologies and object models, 2) continue working with software developers to incorporate NI-DM

into their software, 3) create similar models for related tools (e.g., FSL, AFNI) so that common aspects across software packages can be identified, and 4) facilitate broad and expanded use of the NI-DM standard for data querying and data exchange, fostering applications such as meta-analyses.

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P34 Neuroscience Simulation Data Format (NSDF): HDF-based format for large simulation datasets

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With growing importance of simulations in the field of Neuroscience, storage and management of data from in silico experiments has become a common challenge. As size and complexity of computational models keep increasing with hardware capabilities, the amount of generated data is becoming prohibitively large for text based formats like csv (Comma Separated Values). In absence of any efficient standard format, individuals and groups often create ad hoc formats and develop analysis tools around them. This hampers reuse of code and sharing of data. The same problem with model description is being addressed through several community standards (CellML, NeuroML, NineML, SBML). In a different approach, the neo library (Garcia et al., 2013) tries to address these problems for electrophysiology data. However, currently there is no functional solution for sharing simulation data. Such an open standard for simulations will facilitate sharing and development of analysis and visualization tools. Moreover, with the requirement of data sharing for publication in many journals (PLOS, Science, Nature), a common data format will also help in the review and verification process in computational neuroscience research. Here, we propose a format for storage and sharing of data from simulation experiments in computational neuroscience. This format is based on HDF5, which is a flexible, portable, and efficient file format for very large datasets. HDF5 is used in a wide range of scientific domains with diverse requirements (Klein et al., 2007; de Buyl et al., 2014).

Neuroscience simulations are performed in wide spatial and temporal scales, with varying complexity. We have developed a Neuroscience simulation data format (NSDF) for data that span the range from point processes to detailed compartmental models and networks as can be seen in typical use cases in Table 1. For efficient storage and retrieval, we propose saving data in 2D arrays whenever possible, organized as in Figure 1. The proposed format also incorporates data structures for storing morphology, connectivity information and other HDF5 attributes for storing metadata. We have utilized this format in tools for data visualization and analysis. We also used it to share a collection of open data from simulations of thalamocortical loop (Głąbska et al., 2014).

Figure 1: Structure of NSDF file: uniformly sampled data from each population of sources (neurons, compartments, etc) are stored in 2D datasets under the same group. The first dimension of the dataset is mapped to a dimension scale containing the source IDs. The second dimension is mapped to a dimension scale containing the sampling times. Spike-times from each population are stored as 1D datasets, one per source. The sources are mapped to the datasets by a mapping-dataset for each population. Same applies to nonuniformly sampled continuous data, but these are mapped to time dimension scales corresponding to the sampling times.

Table 1 : Example use cases

```
Pyramidal.h5
|
|___ data
|    |___ uniform
|    |         |___ population1
|    |         |         |
|    |         |         |___Vm[c1..c100, t1..t1000]
|    |         |         |___Ik[c1..c100, T1..T10000]
|    |
|    |___ events
|    |         |___ population1
|    |         |         |
|    |         |         |___ spike
|    |         |                   |___ spikes_cell1
|    |         |                   |___ spikes_...
|    |         |                   |___ spikes_cell100
|    |
|    |__ nonuniform
|
|___ map
|    |___ time
|    |    |___ t[t1..t1000]
|    |    |___ T[T1..T10000]
|    |
|    |___ uniform
|    |         |___ population1
|    |         |         |
|    |         |         |___ cells[c1_name..c100_name]
|    |
|    |___ events
|         |___ population1
|                   |___ spike[cell1->spikes_cell1
|                                  ..
|                              cell100->spikes_cell1100]
|
|___ model
     |___ morphology ...
     |___ morphology_names ...
```

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P35 Handling complex metadata in neurophysiological experiments

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Technological progress in neuroscience allows to record from tens to hundreds of neurons simultaneously, both in vitro and in vivo, using various recording techniques and stimulation methods. In addition, recordings can be performed under more or less natural conditions in (almost) freely behaving animals. To disentangle the relationship between behavior and neuronal activity, it is necessary to document animal training, experimental procedures, and details of the setup along with the recorded neuronal and behavioral data. In consequence, electrophysiological experiments become increasingly complex. Given these various sources of complexity, the availability of all experimental metadata is of extreme relevance for reproducible data analysis and correct interpretation of results.

In order to provide metadata in an organized, human- and machine-readable way, an XML based file format, odML (open metadata Markup Language), was proposed [1]. We here demonstrate the usefulness of odML for data handling and analysis in the context of a complex behavioral experiment with neuronal recordings from a large number of electrodes delivering massively parallel spike and LFP data [2]. We illustrate the conceptual design of an odML metadata structure and offer templates to facilitate the usage of odML in different laboratories and experimental contexts. In addition, we demonstrate hands-on the advantages of using odML to screen large numbers of data sets according to selection criteria relevant for subsequent analyses. Well organized metadata management is a key component to guarantee reproducibility of experiments and to track provenance of performed analyses.

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P36 ApiNATOMY: The generation of interactive circuitboard schematics of multiscale neuroscientific knowledge

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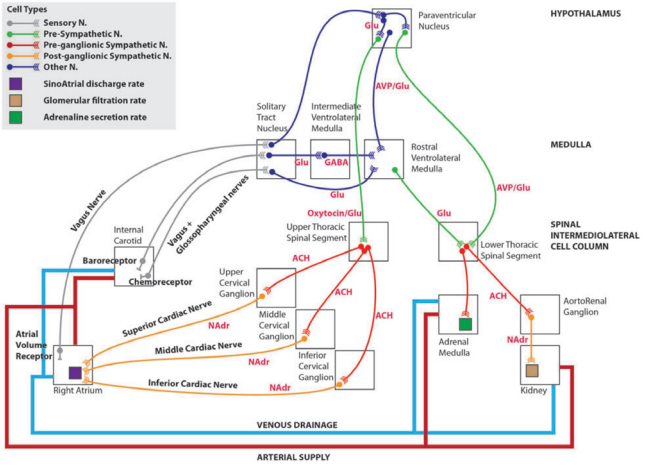
The field of connectomics, which aims to unravel the circuitry of the nervous system, has experienced a recent surge in the effort to collect "connectomes" across scales. In view of this surge, data on the microcircuitry, mesocircuitry and macrocircuitry of brains across multiple species will continue to accrue rapidly in future. These "wiring diagrams" will establish the blueprint through which nervous systems mediate their functions. Although the techniques for acquiring connectional data across these scales are producing the raw complex data, the informatics and analytics framework for representation and visualization of these data still lag considerably. In response to this lag, systems biology efforts have yielded a broad array of tools for visualizing networks, but most of these tools do little to help understand and compare networks or their spatial organization. Brain architecture at all scales represent networks constrained, shaped by anatomy, yet network visualization tools do not respect spatial constraints. Most tools are random in their renderings such that the position of nodes changes every time a manipulation is made, making it very difficult to interpret and compare network visualizations. In this work, we present some of our early results in developing the ApiNATOMY toolkit in response to knowledge management requirements from the neuroscientific field. Our approach allows for the consistent diagrammatic rendering of circuitry data, regardless of the scale, modality or species of acquisition (e.g. see Fig1). Through ApiNATOMY, the basic circuits utilized by the nervous system to mediate behavior can be revealed, compared and linked to actual data. In practice, ApiNATOMY provides:

- simplified, interpretable multiscale views of networks and circuits so that they can be compared across species;
- a grounding in the anatomy of the body in general, and nervous system in particular;
- a scripting language that allows the production of "smart" figures and diagrams;
- an interface between data and modeling platforms;
- an interface that works on tablets and mobile devices.

Our goal is to support the development of a "blueprint" of neuronal circuitry that applies to all scales and species through integration with the Neuroscience Information Framework. In addition, ApiNATOMY circuitboard schematics will be used to collaboratively create stylized renderings of connectivity of different types among neuroanatomical structures.



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P37 Usability and functionality of NeuroML description language evaluated using three distinct spiking neuron models

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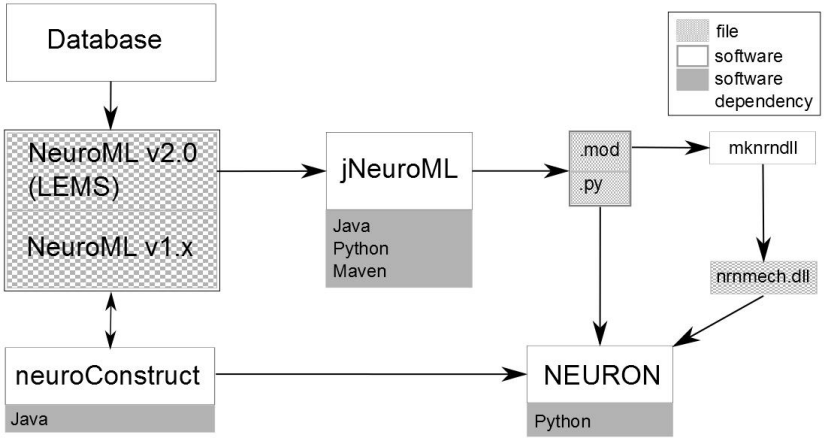
Computational models are increasingly used in the exploration and interpretation of complex phenomena of the brain and peripheral nervous system. The growing number of molecular, cellular and multiscale neural network models creates a need for straightforward transfer methods of models between simulators. This is accomplished with standard languages for simulator-independent model description, such as the Neural Open Markup Language (NeuroML) [1, 2] and NineML [3]. Description languages are expected to ease model sharing and facilitate the replication of results across different simulators. It is therefore of great interest to test the interoperability between model description languages and neural simulators, employing use cases that are commonly in the computational neuroscience community.

In this study, version 2.0 of the XML based NeuroML was studied and evaluated using a Windows operating system. Additionally, other description languages in neuroinformatics were examined and qualitatively compared to NeuroML. NeuroML implementations of the Hindmarsh-Rose [5], Izhikevich [6], and FitzHugh-Nagumo [7] spiking neuron models were analyzed and their conversion to the format used by the popular neural simulator NEURON [4] was performed. The entire conversion process is illustrated in Figure 1. Finally, a comparison of the models to corresponding reference implementations in the Matlab numerical computing environment was done.

Although some features were found to be malfunctioning when converting the models into the NEURON simulator format, the results demonstrate the power and ease of use of the latest version of NeuroML. Both the regular and chaotically behaving Hindmarsh-Rose models were transferred perfectly, with simulation results matching the reference implementation, while other models encountered some complications in the conversion process that could not be easily resolved. The usability of the tools was found relatively straightforward for a computer-oriented user; however, a biologically-trained person may have difficulties in using the tools.

This work is one of the few studies to quantitatively evaluate the performance, usability and functionality of NeuroML in the context of spiking neuron models. The present study showed the potential of the NeuroML description language in transferring models of neural systems between simulators, while also recognizing the need for an ecosystem of standard languages in the field of neuroscience. Eventually, standard languages will allow for faster and wider development of modeling and simulation software, leading to graphical tools that are accessible from all fields of neuroscience.



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P38 Pypet: A python toolkit for simulations and numerical experiments

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"Pypet" (python parameter exploration toolkit [1]) is a new multi-platform python toolkit for management of simulations and storage of numerical data. Exploring or sampling the space of model parameters is one key aspect of simulations or numerical experiments. pypet was especially designed to allow easy and arbitrary sampling of trajectories through a parameter space beyond simple grid searches. For instance, pypet could be used to manage the exploration of different neuron models in a python neural network simulation. Simulation parameters as well as the obtained results are collected by pypet and stored in the widely used HDF5 file format [2]. Furthermore, pypet provides an environment with various features. For example, among these are multiprocessing for fast parallel simulations, dynamic loading of data, integration of Git version control, and merging of results from several simulations. A rich set of data formats is supported encompassing native python types, Numpy and Scipy data, pandas DataFrames [3] as well as data from the BRIAN neural network simulator [4]. Moreover, the toolkit is easily extendible to allow the user to add customized data formats. pypet is a very flexible tool and suited for short python scripts as well as large scale projects in computational neuroscience and other disciplines that involve simulations and numerical experiments.

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P39 Extending provenance information in CBRAIN to address reproducibility issues across computing platforms

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Context
Neuroimaging tools are prone to reproducibility issues across computing platforms due to the propagation of numerical errors along pipelines (Gronenschild, et al., 2012). When different computing systems are used in the same study, these issues may alter the results and even generate false positives. We are designing a system to identify and mitigate reproducibility issues in experiments executed on distributed computing platforms. This system will extend the provenance information available in the CBRAIN web platform (Sherif, et al., 2014) with system-level monitoring information captured by the Kickstart tool (Deelman, et al., 2006).

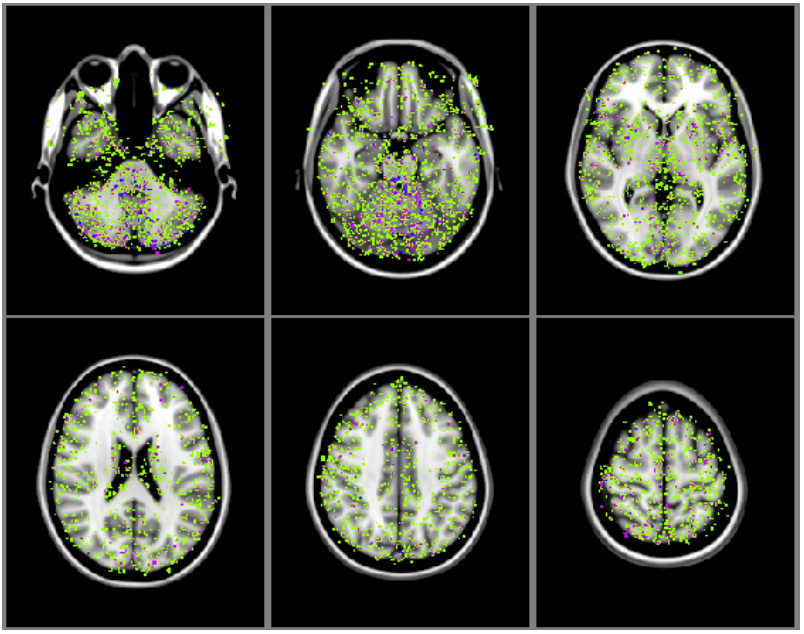
Method
We processed the 150-subject ICBM dataset (Mazziotta et al., 2001) with 3 pipelines: (i) brain tissue segmentation using FSL FAST (Zhang, et al., 2001) (ii) subcortical structure segmentation with FSL FIRST (Patenaude, et al., 2011) (iii) cortical thickness estimation with Freesurfer (Fischl and Dale, 2000). We used FSL 5.0 (build 506) to compare results obtained on two clusters running Linux CentOS 5 and Fedora 20 respectively. We used Freesurfer 5.3.0 and compared the results obtained with CentOS 4 and CentOS 6 x86_64 builds, executed on the Linux Fedora 20 cluster. Results: Brain tissue segmentations computed in FSL on CentOS5 vs. Fedora 20 have a Dice coefficient higher than 0.999 for grey matter, white matter, and CSF. Numerical differences result in discrete noise-like segmentation errors mostly located at the tissue interfaces (see Figure 1). Using ltrace (ltrace.org), we identified that these differences are due to different implementations of the exponential function (expf) between CentOS 5 (glibc 2.5) and Fedora 20 (glibc 2.18). Subcortical structure segmentations computed on CentOS5 vs. Fedora 20 have a Dice coefficient ranging from 0.59 to 1 (see Figure 2). Cortical thickness difference maps thresholded with random field theory (RFT) show significant differences between CentOS4 and CentOS6 Freesurfer builds for $p<0.05$ and $p<0.01$ (see Figure 3).

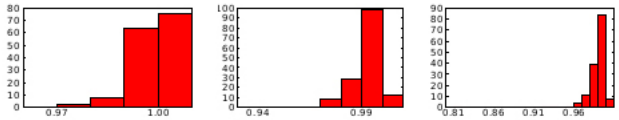
Discussion
Different computing platforms may produce substantially different results in neuroimaging pipelines. Therefore it is legitimate to avoid using multiple computing platforms in a study. However, this drastically reduces the amount of available computing resources, which slows down experiments. Our provenance-based system will help identify the maximal set of resources that can be used in a study without altering its results.

Figure 1: Sum of binarized differences between brain tissue segmentations of the 150 ICBM subjects with FSL FAST on Linux CentOS 5 vs. Linux Fedora 20. From top to bottom and left to right: z=33,53,73,93,113.

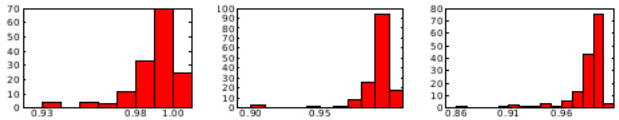
Figure 2: Histograms of DICE coefficients between segmentations obtained on CentOS5 vs. Fedora 20 with FSL FIRST. mu: mean; sigma: standard deviation.

Figure 3: Comparison of cortical thickness maps between CentOS4 and CentOS6 Freesurfer builds. Top row: CentOS6 vs CentOS4; bottom row: CentOS4 vs. CentOS6. From left to right, column (1): t statistics; columns (2)-(4): random field theory (RFT) maps thresholded at $p<0.05$, $p<0.01$ and $p<0.001$, respectively.

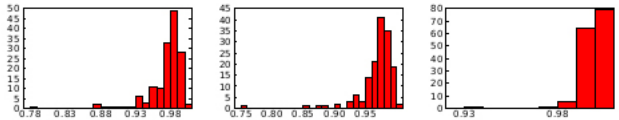




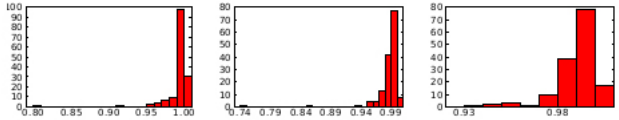
(a) Left-Thalamus-Proper μ=0.99, σ=0.01 (b) Left-Caudate μ=0.99, σ=0.01 (c) Left-Putamen μ=0.98, σ=0.02



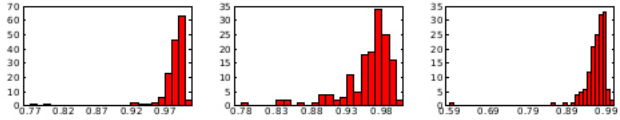
(d) Left-Pallidum μ=0.98, σ=0.01 (e) Brain-Stem / 4th Ventricle μ=0.99, σ=0.01 (f) Left-Hippocampus μ=0.98, σ=0.02



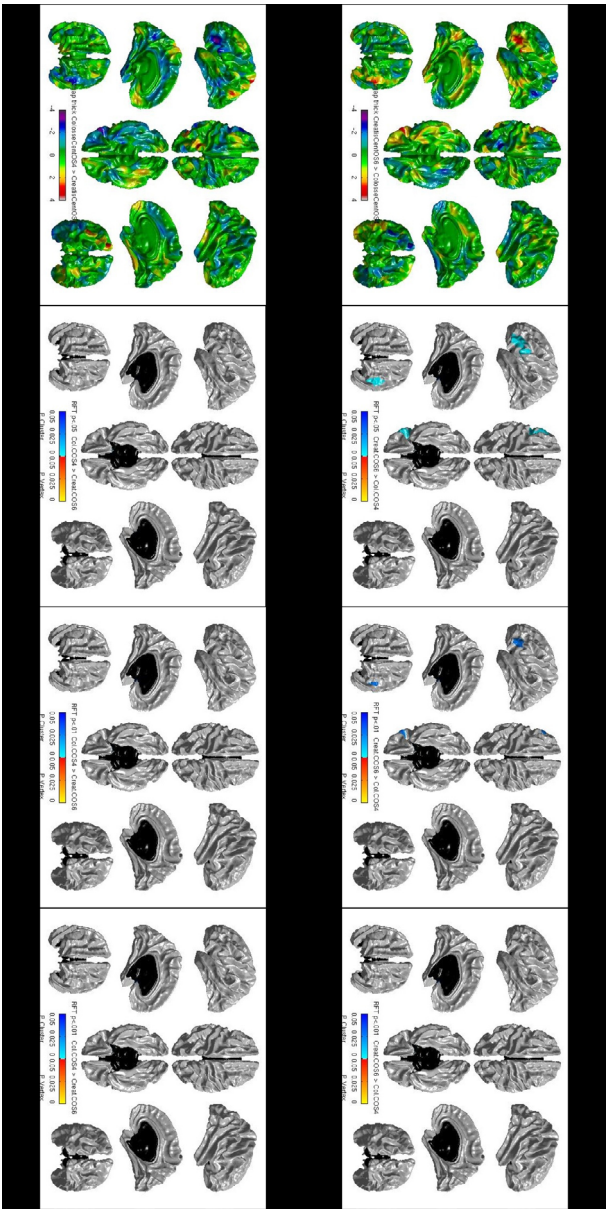
(g) Left-Amygdala μ=0.97, σ=0.03 (h) Left-Accumbens-area μ=0.96, σ=0.02 (i) Right-Thalamus-Proper μ=0.99, σ=0.01



(j) Right-Caudate μ=0.99, σ=0.02 (k) Right-Putamen μ=0.98, σ=0.03 (l) Right-Pallidum μ=0.99, σ=0.01



(m) Right-Hippocampus μ=0.98, σ=0.03 (n) Right-Amygdala μ=0.95, σ=0.04 (o) Right-Accumbens-area μ=0.96, σ=0.04



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P40 Predicting targets and signaling pathways of steroid hormones using the Allen Brain Atlas

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Steroid hormones have strong modulatory effects on cognitive function, mood and physiological regulation in the brain. Their effects are highly cell type dependent, and mediated via steroid receptors which are part of the superfamily of nuclear receptors (NRs) and act mainly as transcription factors. These effects are mediated by specific target genes and depend on cellular signaling partners, such as cell/tissue type-specific co-regulators [1, 2]. Even if these co-regulators are known for a number of well-studied brain regions [3], targets, mediators and in fact responsive brain areas remain unknown for most steroid effects on the brain.

The Allen Mouse Brain Atlas (ABA) (mouse.brain-map.org) provides genome-wide cellular-resolution in situ hybridization (ISH) gene expression map of the adult mouse brain [4]. This high resolution data allows the study of the effects of co-regulators on steroid receptors activity, by analyzing the co-localization of the receptors and co-regulators in different brain nuclei.

We used a data-driven approach to analyze the spatial co-expression patterns between each gene in the mouse genome and estrogen receptor alfa (Esr1, NR3a1). We find that a set of 15 genes which were shown to have sexually dimorphic gene expression patterns in the mouse brain [5] is significantly co-expressed with Esr1 in sexually important brain regions, such as the hypothalamus. We have also found that the top Esr1-co-expressed genes are enriched for known estrogen response element sequences.

The proposed method provides an immediately testable a set of candidate Esr1 targets and signaling partners with a role in sexual behavior. After validation, the candidate set of targets and signaling partners could allow selective targeting of brain regions. Knowledge on brain region specific target genes will greatly facilitate our understanding of the way in which steroid hormones affect so many aspects of the central nervous system (CNS) function, and will in fact lead to the prediction of unrecognized effects of steroids on the nervous system. While the approach is applicable to all nuclear receptors in the brain Esr1 based on available sources and tools to validate our predictions.

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P41 Classification of cortical areas using gene expression profiles

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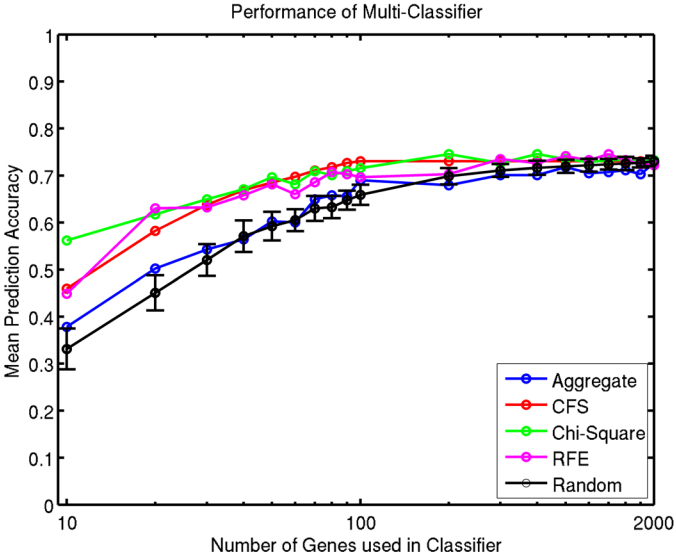
Brain atlases depict the parcellation of neural tissue into a set of spatially contiguous regions with distinct attributes. These "maps" traditionally reflect macroscopic anatomical or cytoarchitectural features and are only distantly connected to the proteins and molecules expressed in those areas. The Allen Brain Atlas (ABA) provides a collection of neuroanatomically-linked transcriptomic data collected with high spatial resolution at genome-scale. Determining the extent to which gene expression profiles differentiate the brain areas depicted in classical brain atlases begins to form a bridge between molecular anatomy and anatomical and functional brain organization. Several previous studies using the mouse ABA have demonstrated clustering of gene expression profiles that largely respect anatomical region boundaries (e.g., Lein et al., 2007; Bohland et al., 2010; Ko et al., 2013). Within the cortex, such clusters tend to follow laminar boundaries (e.g., Belgard et al., 2011), but some evidence supports more limited differential expression across cortical areas (e.g., Ng et al., 2009; Bohland et al., 2010).

Here we studied cortical expression profiles from the ABA using grid-based expression data (200 micron) registered to a 3D template. We used feature selection methods to choose most informative genes, and coupled these methods with support vector machines to learn relationships between normalized gene expression profiles and cortical region labels. We demonstrate results for classifiers trained to discriminate pairs of areas, which can achieve near 100% accuracy, and multi-class models that must classify any sample into one of 18 cortical regions. Using surprisingly few genes, a sample can be classified with > 70% accuracy. Feature selection methods achieve small but consistent improvements relative to random gene selection. To test whether classification accuracy is due to spatial autocorrelation independent of region boundaries, performance of classifiers trained on the reference atlas was compared to classifiers trained on random spatial parcellations of the cortex, constrained to match the distribution of region sizes in the reference atlas. While the latter achieved surprising accuracy, performance on the reference atlas was consistently better. Our results show that, while gene expression is relatively homogenous across the cortex, there are consistent transcriptomic differences that may underlie specialization of these regions.



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P42 Novel genes located in the co-expression networks detected with Transcriptome Tomography

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Detection of gene expression-anatomy association is crucial for understanding functions, in particular, of novel coding and non-coding genes. We have invented a framework for comprehensive gene expression density mapping on the whole three dimensional (3D) anatomical context, Transcriptome Tomography (ref.1): here, the methodology is shown in Movie 1. Measured expression densities are usable directly for gene-by-gene correlation analysis of co-expression, and then we have developed a novel bioinformatics framework for comprehensively assessing co-expression patterns that are latent within expression maps (paper in revision). Co-expression search using almost all genes expressed in the adult mouse brain can be done on our website: ViBrism-DB (Figure 1). In this presentation we would focus on previously uncharacterized mouse-specific genes that were co-expressed with genes encoding transcription factors and related molecules. The combinatorial expression of these genes associated with a discrete cell lineage of developmental stages seems to occur in the adult brain and the previously uncharacterized non-coding genes were located in a co-expression network position linking the combinations. This linkage suggests characteristics of these genes that coordinate multiple gene groups and create mouse-specific designs of neurogenesis.

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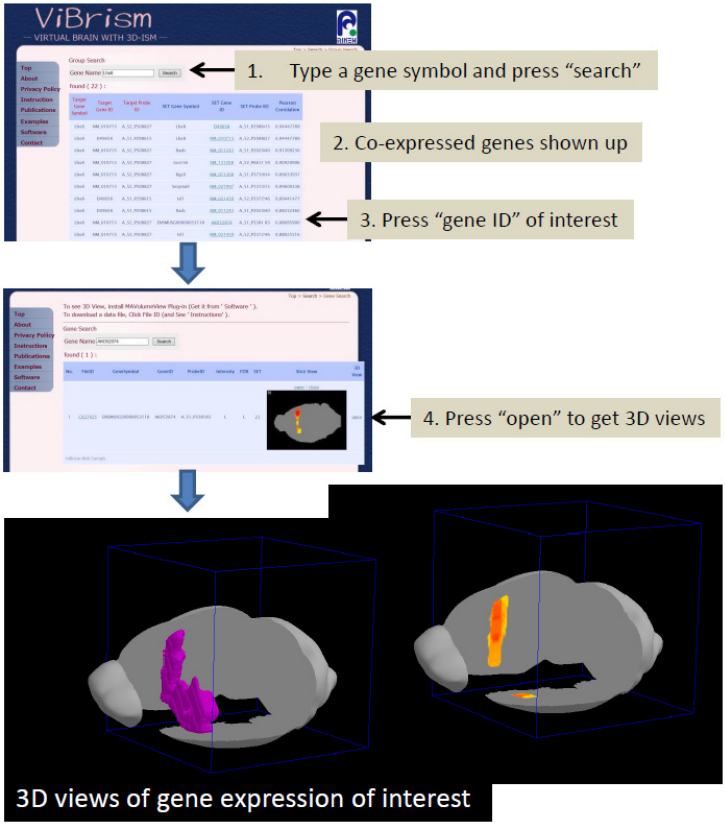
ViBrism
VIRTUAL BRAIN WITH 3D-ISM
1. Type a gene symbol and press “search”
2. Co-expressed genes shown up
3. Press “gene ID” of interest
4. Press “open” to get 3D views
3D views of gene expression of interest

P43 Brain-CODE: A large-scale neuroinformatics platform for deep and broad data

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The Ontario Brain Institute (OBI) funds over 35 institutions in the province of Ontario that collaborate to form disorder based programs centered on clinical, molecular, and imaging research in neuroscience. These programs which span across multiple institutions include epilepsy, cerebral palsy, neurodevelopmental disorders (for example Autism and ADHD), neurodegeneration (for example Parkinson's, Alzheimer's, and ALS), and depression – known collectively as the Integrated Discovery Programs (ID programs). The quality, depth, and diversity of the studies undertaken by these programs and therefore the resulting datasets, represent a significant big data opportunity for neuroscience. To make optimal use of the rich research data collected by the ID programs, OBI is implementing a unique large-scale informatics platform where data streams from each of the programs are being standardized and assimilated, allowing analyses within and across disease states. This web based platform is called Brain-CODE. OBI is working with other stakeholders – and leveraging existing infrastructure where possible – to establish and manage this cutting-edge platform.

Core Functionalities
The five core platform functionalities of Brain-CODE are data capture, data federation, data integration, collaborative data sharing, and secure data analysis. Each of these functionalities is being developed with careful consideration through learning from existing platforms, technologies, expertise, and working closely with researchers – the end users. We briefly outline the current efforts undertaken to address each.

Data Capture Applications
From an informatics perspective, data capture is the process of provisioning software data capture tools that enable researchers or study subjects to enter data via familiar and functionally complete applications, as well as automated data capture from basic science data technology or imaging devices. This is accomplished, in Brain-CODE using a Privacy by Design approach [1] with high security standards, policies, and data protection technology that enable data producers to transfer and store data including personal health information (PHI) of study subjects. In addition, third party data users, only access de-identified data sets which protect the study subjects from being re-identified.

Currently, OBI is leveraging a number of data capture software for researchers including REDCap [2] and Open Clinica [3] for clinical data, BASE for molecular and genomics data, and SPReD [4] for imaging data that is based on XNAT [5]. In addition, the Brain-CODE development team, led by the InDOC consortium [6], has developed custom tools for subject profile data entry known as the 'Subject Registry'. In addition there is an integration

layer built in to integrate the data from the multiple applications. Together, these tools provide a rich set of capabilities for the design of 'electronic Case Report Forms' (eCRFs) and administration of clinical instruments.

Integration

The diversity of data being captured in Brain-CODE requires the adoption of powerful data integration tools. To date, the Brain-CODE team has identified a number of open and proprietary tools that can work complementarily for this purpose including BioMart [7] and IBM InfoSphere [8]. We continue to work on the evaluation and identification of high performance tools that will connect to the diverse set of data and manage the user access to these data in Brain-CODE.

Federation

To facilitate the sharing of data and the analysis of data across neurological diseases and data types, two important steps have been taken and standardized across all OBI participating institutions. First, all subjects have their unique provincial health card identification number stored in an encrypted format on Brain-CODE. This will allow the linking of research data for a single subject from other studies or from other federated platforms and provide data scientists and researchers with the ability to gain a much greater understanding of the health condition and history of their subjects. This encryption is performed within the user's web browser, and the original number never leaves the research site; only the ciphertext is transmitted and stored in the Subject Registry. Furthermore, the private key required for decryption is maintained by a third-party and is not known to Brain-CODE. The encryption algorithm developed by the Electronic Health Information Laboratory (EHIL) who are members of the InDOC consortium, has a particular homomorphic property which allows mathematical operations and comparisons to be applied to the encrypted data itself, i.e. without the need for decryption. These encryption capabilities can be applied to other sensitive data stored in Brain-CODE and not only provide robust safeguards against re-identification, they also enable secure data integration. For example, data stored in Brain-CODE can be securely linked with administrative health databases maintained by the Institute for Clinical and Evaluative Sciences (ICES) using encrypted health card numbers. Encrypted deterministic or probabilistic linkages can also be performed with other data repositories (Ontario Health Study, NIH health databases, etc.) without requiring either party to disclose PHI. Other algorithms developed by EHIL are used to determine the risk of reidentification for particular datasets requested by researchers.

Standardization and Common Data Elements

Second, Common Data Elements (CDEs) have been identified using a Delphi consensus process [9] with researchers across the participating institutions. Demographic and clinical instruments that each study will be using have been selected through this process [10]. These CDEs have been based on existing international standards from NINDS [11] and CDISC [12], which will enable the wide ranging datasets in disease type and modality to be compared more effectively resulting in vastly enhanced analytical value. In addition, OBI is

actively engaged with researchers in similar efforts to establish imaging and '-omics' data standards. These important efforts will further empower the formation of new hypotheses and discoveries for patient centered care.

Other rich data collection initiatives and services exist across Ontario, Canada, and internationally with which Brain-CODE has a potential to establish partnerships for data linking and sharing. These federation efforts are currently underway in the form of early pilot studies and data transfer using high security protocols. As these efforts take shape, the potential to link administrative health information data or other rich research data for individual patients or across populations will become possible. These federation efforts will enable unprecedented scientific insight into patient health, comorbidities, longitudinal medical profiling, and a deeper understanding of the causal mechanisms behind neurological diseases.

Data Sharing and Analytics

Finally, the Brain-CODE team has recently entered a new design cycle of the Portal functionality and building the analytics capacity of the platform. Importantly, considerations with respect to the diversity of skillsets of the portal users is taken into account in combination with the wide variety of data types that are being collected on the platform. Specialized data analysis tools will be integrated in the initial phase to address clinical, imaging, genomic and proteomic data analysis. Powerful visualization tools for 'Visual Analytics' will also be evaluated and integrated into the platform to facilitate quick and intuitive investigation into the rich datasets. To promote the development and integration of powerful combined data analysis software, a developer workspace will be implemented in order to enable and attract data science and analytics talent to de-identified, yet rich, sets of data, carefully selected to address novel challenges in 'deep and broad' data analysis. This developer space could not only provide access to research data but also computational resources and technology via web applications and APIs. This developer space approach should help promote interest and the creation of new algorithms and tools for greater discovery in the growing data environment of Brain-CODE.

The collaboration and analytics capacity of Brain-CODE will grow as researchers embrace the potential of sharing their data and with the crucial collaboration of data partners, technology partners, and the training of expertise in data management and analysis. With OBI's commitment to empower researchers and data scientist in this process of discovery, genuinely rich opportunities are becoming possible for advanced discovery and patient care in the 21st century.

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P44 The CARMEN data sharing portal project: What have we learned?

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The UK CARMEN project represents one of the first major efforts at sharing electrophysiological datasets, and the techniques for processing them, using a portal. It started in 2006 (with the late Professor Colin Ingram as Principal Investigator), with funding from the UK EPSRC, and this was followed on with funding from the UK BBSRC. It has been providing a gradually improving service for about five years, starting from the capability or sharing data, and adding services, and workflows. It has its own internal data format, Neural Data Format: by converting proprietary dataset types to this format using a service, we enable services and workflows that process this format to be applicable to datasets originating from many different types of recording platforms.

Given the experience that we have gained from running this service, what have we learned? What would we do differently if we were to start again? Is there still interest in this type of capability, or has the world moved onwards? We recently put out a questionnaire to all registered users of CARMEN, and we have now some feedback from registered users, and (perhaps equally importantly) from people who registered and did not end up using the system.

In general, the use of the system for secure data sharing and exchange seems to have been the most popular. Certainly, in the design of the system, we were very aware that geographically distributed neuroinformaticians and neuroscientists wanted to share their datasets, and to be able to do so in a way that was secure. This seems to have been one of the successes of the system. Yet had we only wanted to do that, we could have put together a much simpler system altogether! Certainly, it is the case that some users have used the system in a much more powerful way, as evidenced by the recent paper [Eglen et al 2014]. But such types of users have been relatively few. What is it that has put users off from more sophisticated interaction with what is in essence a platform that could be used for extended analysis and sharing of data from many different laboratories?

One issue has been speed of access. Although the network at the server end is fast, many users do not have such fast access from their laboratories. The result is that uploading large datasets (and indeed downloading them as well) can be slow. There is little that the CARMEN staff can really do to help here, because the problem lies at the users end, and is not under the control of CARMEN itself.

Many users complained that the use of the services and workflows was difficult. They reported that it was difficult to work out exactly how to use them, and even to find out exactly what services were available precisely. This is a bit disappointing: a great deal of time was spent in trying to make services usable, and in enabling effective search techniques, and providing information on these services within the system. But perhaps the system is complex to use, and many users, more used to expensively developed sites that were easier to use, did not spend the time really finding out what could be done. That said, it is clear that running services was relatively complex, and further, that running multiple services (and workflows) was really quite difficult to organise. There does seem to be some agreement that using CARMEN services and workflows for cross-dataset analysis (i.e. on datasets from a number of sources) is of interest, however, very little data on CARMEN has been made public, so unless users have direct access to datasets that they can then upload, this type of activity has been difficult.

Some users simply did not like the concept: they wanted something that was decentralised, and could use many local machines. Some wanted a more professionally designed "look and feel" as well. For the first of these, the issue of dataset size is problematic - indeed, that was the reason for the basic design, with the concept of bringing the processing to the data, rather than the other way around. For the second, we too would have liked to employ more professional designers, but the budget did not stretch that far. Another suggestion is direct integration on to the systems that the neurophysiologists are already using. This would be a great idea, but there are many such systems (although integrating it on to Matlab, which is often used for initial data analysis would be a possibility).

In addition, the CARMEN project has been running at a time of rapid technological change within the Internet. Much of the user-facing processing was designed initially to use Java applets, because in that way we could provide systems that enabled uploading and downloading in a secure and effective fashion. But times have moved on, and one would now expect to use a mixture of HTML5 and JavaScript for these types of purposes.

The datasets are very complex, particularly when one includes the multiplicity of data types in electrophysiological datasets (simple time series, excerpted sections, spikes, etc., plus the metadata that describes the representation, and the experiments that produced the dataset). Neural Data Format (NDF) caters for these. At the time that the NDF was designed, HDF5 was not really able to work with data in the way that we desired. This is no longer the case, and were we to redesign NDF, we would now use an HDF5 based format. This would be a major task, but we can get around the issues by creating services to translate between HDF5 and NDF. It is worth noting that HDF5 alone does not solve the problem. Indeed one of the INCF Task Forces has been developing an HDF5 format for this type of application, and this work is only now nearing completion. Another aspect of technological change lies in data display. When CARMEN started, there was no straightforward way of enabling complex data display in a browser (short of a very complex Java applet). As a result, we used a proprietary piece of software for data display. Now, however, thanks to the large expansion in the capabilities of JavaScript, this is no longer the case.

Reading over the users comments, it appears that CARMEN, or a portal like it, remains a popular idea: however, it needs to be easy to use, both for upload/download and for running services and workflows. Documentation needs to be better, and easy to find (perhaps easy to find is critically important here). We are planning a new project proposal, and we will be taking these issues into account.

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P45 Interoperability between multilevel modeling platform PhysioDesigner and databases in Physiome.jp and Dynamic Brain Platform through Garuda platform

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In recent times, accumulation of considerable amounts of experimental data about various levels of physiological functions, from the level of protein to the body overall, accelerated growth of mathematical models in size and complexity. To develop detailed physiological models, a systematic supportive framework which can facilitate effective sharing and reuse of existing models is essential. It is important that such a supportive framework includes two components. One is model databases and the other is a system to assist modeling process.

The PhysioDesigner is a software platform available at physiodesigner.org that provides graphical support for the construction of mathematical models by explicitly expressing multiple hierarchies in physiological systems. In PhysioDesigner, structure and functions seen in physiology are managed as modules, and a model is constructed by defining relationships between the individual modules. Each module is quantitatively characterized by defining dynamics and constants. Models built on PhysioDesigner are written in Physiological Hierarchy Markup Language (PHML), a descriptive language designed to represent hierarchical structure and functional network of modules.

PhysioDesigner can interoperate with databases opened in the internet through database client applications supporting Garuda alliance (garuda-alliance.org), which mediates communication among applications. So far we have developed two client applications for databases in Physiome.jp and in Dynamic Brain Platform.

A portal site Physiome.jp was established in 2007 to release applications and databases supporting construction of physiological multilevel large-scale models. The portal is available at physiome.jp. In Physiome.jp, three kinds of databases are open to the public, which include a database of mathematical models written in PHML, and databases containing morphology and time series data.

Dynamic Brain Platform (DBPF) is one of neuroinformatics platforms promoted by the INCF Japan Node, in which there is a database including mathematical models of physiological functions, as well as other information, such as commentaries. It is accessible at dynamicbrain.neuroinf.jp.

To effectively utilize these data in the databases, client applications complying with Garuda alliance has been developed. The clients can seamlessly bridge information in the databases to tools, such as the modeling platform PhysioDesigner. The linkage can also be expanded to any other tools complying also with Garuda alliance. The seamless linkage between the databases and tools will greatly enhance usability of those data and promote development of models.

P46 A parallel programming model of local processing units in the fruit fly brain

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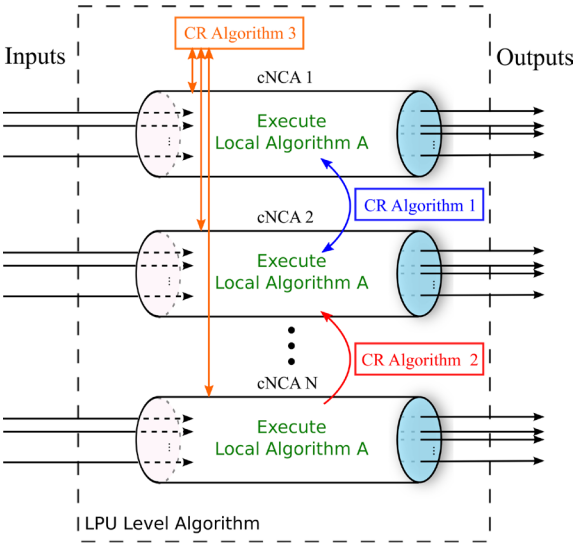
The fruit fly's brain can be subdivided into some 41 neural circuit modules called Local Processing Units (LPUs) [1]. Extensive local processing is achieved by spatially restricted local neurons in the LPUs. Yet little is known about the I/O transformations taking place in LPUs. To identify these transformations, it is necessary to determine the algorithms describing each LPU and the underlying circuit level implementation of these algorithms. Towards that end, we propose here a parallel programming model for exploration of high level LPU algorithms that takes into account existing anatomical observations of the underlying neuronal circuits of the fly brain neuropils. The programing model comprises canonical neural circuit abstractions (cNCAs) and composition rules (CRs) among them [2] (see Figure 1).

cNCAs are fundamental computational units in many LPUs. For example, cartridges and columns are cNCAs in the lamina and medulla LPUs, respectively, of the early visual system, and channels are cNCAs in the antennal lobe of the early olfactory system. Each LPU comprises tens, if not hundreds of its respective cNCAs. The cNCAs, by themselves, implement a particular algorithm that performs local computations. Such an algorithm may utilize multiple neurons that each perform, in turn, elementary operations. They are executed in all cNCAs independently and in parallel. Our focus on using cNCA rather than individual neurons as computational units highlights the preeminence of circuit building blocks underlying neural computation over elementary neuronal operations. It is instructive to compare cNCAs with threads that are widely used in parallel programming models of computer programming.

cNCAs alone can only realize a limited set of overall algorithms due to their independence. In our programming model, communication among cNCAs can be achieved by defining composition rules. CRs are global algorithms that are performed asynchronously and are implemented by a few neurons. By enabling interaction among cNCAs, the CRs facilitate the design of algorithms that can use locally processed information to achieve computation on different spatial brain scales. For example, spatially restricted information that is individually processed by cNCAs can be compared using CRs to implement motion detection algorithms in which computation between spatially displaced visual areas is essential. Thus, CRs are critical for the diversity and functionality of algorithms that can be realized using the programming model proposed here.

The LPU parallel programming model identifies the objects that are necessary in algorithmic I/O design of the neural circuit architecture. It is important then to explore the appropriate transformations that can be efficiently implemented under this model. We

demonstrate that the proposed programming model can be applied to a range of sensory LPUs, including those in vision and in olfaction. Furthermore, the neural implementation can flexibly and efficiently be implemented for a range of algorithms that process different sensory inputs. Thus, designing such a programming model facilitates not only the understanding of I/O relationships but also the design of new I/O behaviors for LPUs including odorant preprocessing in early olfaction and motion detection in early vision. Finally, we will demonstrate the compatibility of the designed LPUs in the context of Neurokernel architecture [3, 4, 5].



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P47 Neuroarch: A graph-based platform for constructing and querying models of the fruit fly brain architecture

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The fruit fly Drosophila melanogaster is an excellent model organism for reverse engineering information processing in biological brains due to its capacity for complex nonreactive behavior mediated by a brain containing a relatively small number of computational components. An increasingly powerful toolbox of genetic and electrophysiological techniques enables researchers to experimentally relate the fly's behavior to its brain structure. Efforts to fully map the fly's connectome have identified fewer than 50 distinct functional units in its brain, most of which are characterized by unique populations of local neurons [1, 2, 3]. The increasing volume of available biological data regarding the structure of these local processing units (LPUs) and the connectivity tracts between them must be leveraged in the design of in silico fly brain models.

Successfully modeling the fly brain requires integration and execution of LPU and tract models developed independently by multiple researchers [4, 5]. Software that enables such integration must also afford researchers the freedom to specify the parameters of LPU models that may employ disparate internal designs. Ongoing efforts to obtain increasingly accurate data regarding the fly's brain structure also demand that such software be sufficiently flexible to facilitate revision of the models in a straightforward manner even if completely new components must be added. Existing tools for structured specification of neural models [6] provide limited means for querying model data required by emulation engines responsible for efficient model execution. Moreover, changes to an LPU model's internal design may complicate its reimplementation by requiring that support for accessing new design elements be retrofitted into representations of the existing model.

To address the above concerns, we have developed a Python package called Neuroarch for representation and storage of LPU-based models of the fly brain. It provides researchers and software applications with a common interface for defining, querying, and manipulating integrated model data. Neuroarch's representation of the fly's brain distinguishes between the connectivity architecture linking its LPUs and the design of the individual LPUs identified in [3]; the former is modeled as graphs of communication ports exposed by each LPU and the connections between them while the latter comprises graphs of the internal modeling elements required by specific LPU models. Neuroarch's flexibility stems from its storage of all modeling elements comprised by the connectivity architecture and different LPU designs (including synaptic model instances) as graph nodes; edges are exclusively used to represent relation- ships between modeling elements. Neuroarch stores all model data in a graph database to accelerate those queries typically performed to determine which modeling elements must be updated simultaneously during model execution.

Both LPU design and inter-LPU connectivity model data is exclusively accessed through Neuroarch's object-relational mapping (ORM) of modeling elements to their internal database representations. A key feature of this ORM is its support for multimodal views of query results over stored model data that may be passed as operands to other graph operations. This enables model data to be accessed or modified either as a subgraph (to facilitate graph-based queries) or a tensor (to facilitate tabular or relational queries). Neuroarch's I/O layer extends and invokes the ORM to load model data expressed in several specification formats such as CSV, GEXF, and NeuroML. Models may also be constructed from basic circuit motifs (specified either as small graphs or tensors) using Neuroarch's graph composition operators.

We have used Neuroarch to drive fly brain emulations of a prototype multisensory coincidence detection system that integrates 4 independently developed LPUs in the fly vision and olfactory systems executed using the Neurokernel framework [4, 7]; model data for some of these LPUs is explicitly specified, while the remaining LPUs are constructed using Neuroarch's graph operators to compose canonical circuits identified in those LPUs [8].

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P48 On-line integration of multiple neural network and musculoskeletal models

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We are building a large-scale spiking neuron model of the thalamo-cortico-basal ganglia circuit with the aim of understanding its normal functions and the mechanisms underlying Parkinsonian symptoms, such as tremor. For this purpose, we need to combine multiple models incorporating the basal ganglia, the thalamus, the motor cortex, the spinal cord, and the musculoskeletal system. The minimum size models total 120k model neurons, though larger-scale versions need at least 1.8M neurons; this requires a large amount of computational power as well as the software infrastructure to connect them.

Models are often developed using different tools at separate locations. We need a system that supports distributed development and concurrent execution with efficient communication on parallel computers, so we use the MUSIC library, developed by INCF. It interconnects spiking neuron-level simulators on workstations and massive parallel systems, and comes with a C/C++ API and bindings to common simulators.

The Parkinsonian tremor is thought to originate in the basal ganglia through GPe and STN interaction, where inhibitory rebound causes rhythmic bursting. The oscillation is transmitted through thalamus and the cortical pyramidal tract neurons to spinal motor neuron pools that drives an opposing pairs of model muscles with Ia spindle feedback.

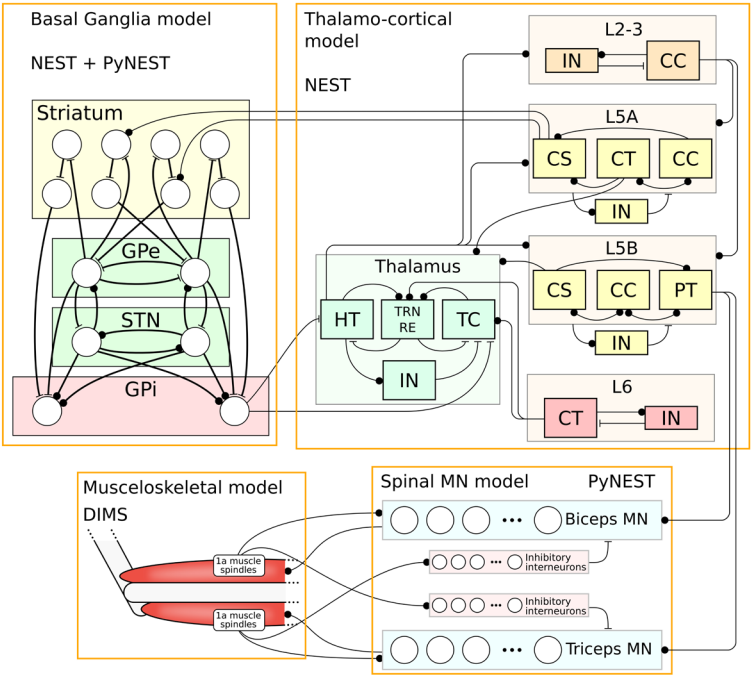
Connecting separate models has several benefits:

I) Each model is independent from the others, so we can use different simulators or separate versions with different built-in models or features as needed.

II) Model development is cleanly separated, and the interconnection structure provides a well-defined model API. Project members can work independently. Intermodel connection issues become clear at an early stage, and the integration work can happen in parallel with model development.

The cortical models are not yet tuned to produce realistic output and inputs to cortical layer 2/3 and the striatal direct pathways happen through preset Poisson sources. The motor neuron network lacks spindle II inputs and spinal networks, and there is no feedback to the CNS from the motor level. These are all issues we need to address in order to reproduce Parkinsonian tremor down to the motor level.

We are nevertheless already able to integrate them and let the integration work guide further model development. We show the current model architecture and performance figures for the interconnected system compared to the separate models



P49 Efficient generation of large-scale neural connectivity matrices using machine-learning techniques

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The Human brain project (HBP) aims to simulate a human brain in its entirety, for which the specific neuron-to-neuron connectivity is the key element. This connectivity needs to be generated quickly and in a computationally efficient way, which precludes simulating the entire development of the brain. The connectivity should be constrained by the data available, which is limited in size, has incomplete coverage of different brain areas and is heterogeneous because it derives from the use of different experimental techniques. A commonly used method is to generate the morphology of neurons in the sending (presynaptic) and receiving (postsynaptic) area and use Peters' principle to translate the occurrences of close appositions of axonal and dendritic branches into synapses. Here we introduce a faster method that does not require the entire morphology to be generated for each neuron, rather it is based on a smooth density for each neuron of the presynaptic (boutons) and postsynaptic elements (spines), representing the average axonal and dendritic morphology of its cell class. Because synapses are post-hoc assigned to the appropriate axonal and dendritic branch, this method can be used to match the experimentally measured branch distributions for synapse locations.

The key problem addressed here is translating these densities for a given voxel into actual elements. For this we have explored two methods. First, by considering it a problem of sparsifying voxel densities into zero and nonzero values, which can be solved by using the LASSO method with an appropriately weight for the sparsifying term. Second, by using an Ising model, where 1 means there is an element present in the voxel and 0 means there is not. The Ising model objective function was chosen to obtain (1) the desired spatial density profile, (2) the corresponding number of elements and (3) to increase the probability of elements at neighboring locations (necessary to reduce the length of the implied axon morphology). In our first simulations, the Ising model performed better than the LASSO approach. The connectivity matrix so generated had a log-normal degree distribution, with a mean and width that can be controlled by a few parameters.

Taken together our preliminary results indicate that this approach is a feasible way to generate large-scale connectivity matrices.

P50 Methods for co-simulation of multi-scale models

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In multi-scale models, multiple scales, and even physical formalisms, are used in a single model [1] while simulation tools in computational neuroscience are usually specialized for a single scale and formalism [2, 3, 4]. One possibility when solving such models is to use a co-simulation methodology. Co-simulation allows model components to be simulated by different tools, running simultaneously while exchanging data. However, a naive coupling of numerical methods for different models may lead to unexpected numerical problems going far beyond those which could be expected from the individual components.

With the ultimate goal of extending the MUSIC API [5] for multi-scale modeling through co-simulation by integration of numerical solvers, we have examined ways of moving beyond trial-and-error and ad-hoc methods [6, 7] when coupling solvers. We show techniques for how synchronization in bi-directional communication as well as error control [8] can be achieved in a framework motivated by waveform relaxation methods.

We apply these techniques when simulating a reduced MAPK model [6] in a spine in the context of the electrical activity of the whole neuron. The model exhibits bistability. It switches from the inactive to the active stable state after current injection to the soma. In our model, the stimulus of 0.09 nA causes a Ca2+ elevation of 1 uM in the spine during the stimulation period of 5 s. This condition is sufficient to switch on P-MAPK and phosphorylate potassium channels. The electrical part of the model is formulated using Hodgkin-Huxley formalism while biochemistry is formulated by the reaction-rate equations. This model gives us a stiff problem with a coupling strength varying along the integration.

We compare different techniques for achieving a balance between efficiency of coupling and accuracy of integration. This analysis will be used to set up the requirements for a generic API to perform co-simulation and, in particular, identify the signals which need to be propagated by a multi-scale API.

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P51 MUSIC - a tool for co-simulation of neuronal network models. Current status and future development

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MUSIC [1] is a tool for co-simulation. It provides a communication API which allows neuronal simulators and other tools to ship data between each other on-line during simulation. It supports simulations in a supercomputer cluster or on a desktop. MUSIC enables the construction of simulations encompassing multiple tools and combining model components written for different simulators. MUSIC is compatible with common MPI implementations such as OpenMPI and MPICH and is known to run on a variety of machines such as IBM BG/Q, Cray XC30 and the Japan K computer. It has been used on up to 32 K processors. Here, we give an update on the status of the latest MUSIC release which includes a new scheduler and support for multiple communication algorithms. MUSIC has also been extended to allow for simultaneous use of different communication layers, e.g. combining MPI-based communication with communication over UDP. This is useful when connecting simulations to external equipment. New Python bindings enables MUSIC-connected Python scripts. Another development is integration with PyNN [2], which is a simulator-independent language for building neuronal network models. PyNN release 0.8 includes a MUSIC interface enabling scripting of MUSIC co-simulations in PyNN. MUSIC has been benchmarked on multiple architectures. This includes benchmarks with artificial neurons, focusing on communication performance, and simulations of a cortical network using the NEST simulator [3]. We present some of these results and discuss strengths, shortcomings and potential future improvements. The next development steps are outlined, including a test suite, continuous integration, a multi-scale API and opening up the MUSIC project for collaborative development, with the aim of turning MUSIC into a community-based open source software project.

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P52 Do gold standards remain gold standards when compiling a large number of published tract-tracing studies into a connectivity database?

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Tract-tracing experiments are considered the gold standard when it comes to revealing structural connectivity in the brain. They provide a direct measurement of the axonal tracts of the neuron(s) with axons that start or terminate close to the injection site. Rapid developments in tracing techniques have resulted in a large body of literature, in which each publication describes a few experiments with a given protocol, species and brain atlas. For mouse, several large scale studies are under way in which brain-wide connectivity is measured with an automated tracing and analysis workflow. For ethical reasons however, such initiatives are unlikely to be applied to large mammals. The alternative is to rely on databases which combine findings from individual publications. We focus on a prime example of such a database: the CoCoMac collation of Macaque connectivity. Can the very diverse set of experimental protocols and nomenclatures be combined into a reliable wiring diagram of the brain? To study this, we built a new online platform for CoCoMac (cocomac.g-node.org) [1] with two essential components: (1) a custom wiring diagram builder, in which every detail of the included tracing experiment can be specified; and (2) a graphical nomenclature consistency tool, in which conflicting naming schemes can be resolved interactively. In this talk I will show that small errors in relating brain regions across atlases can have a detrimental effect on the resulting wiring diagram. With the consistent nomenclature, we continue to show different views of the connectivity matrix, such as retrograde vs. anterograde, intralateral vs. contralateral and with and without certain types of tracer. Finally we study the variability of the matrix by leaving out random subsets of tracing data. This variability predicts the effect of adding new data to CoCoMac, and indicates which brain regions require special attention.

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P53 Segmentation and shape analysis of Corpus Callosum (CC) in alzheimer brain MR images using improved variational level set method and phase congruency map

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Alzheimer's Disease (AD) is a neurological disorder and common form dementia that causes memory impairment problems in patients. AD leads to atrophy of gray and white matter structures and results in tissue loss. World Alzheimer report informs that an estimated population of 35.6 million people around the world suffers from this neurological disorder. Magnetic Resonance (MR) imaging is an useful non-invasive imaging modality which is highly useful in reflecting the brain pathology and different stages of AD. Corpus Callosum (CC) is the largest white matter structure that connects the left and right cerebral hemispheres. It is also responsible for integrating the sensory, motor and cognitive functions of brain. Manifestation of AD also results in the shrinkage of CC. Segmentation and feature extraction are essential in the shape analysis of CC. Level set methods are dynamic curves or surfaces that undergo iterative evolution to track the complex topological structures. The diffusion rate equation used in the level set function avoids the complex re-initialization problem and provides numerical stability. Local phase information extracted form an image provides maximum information in representing the lines and edges than the intensity values. Phase Congruency (PC) map obtained from an image can be used as an edge indicator in the level set evolution. In this work, T1-weighted sagittal view MR images are obtained from open access series of imaging studies, a public domain database. Image acquisition has been done using 1.5-T Vision scanner in both the men and women subjects. Images (Normal=20 and AD=20) are subjected to Phase Based Improved Variational Level Set Method (PBIVLSM) to segment CC. PC map extracted from the image is used as edge stopping criterion in the level set function. Geometric features are extracted from the segmented CC and analyzed graphically. Results show that PBIVLSM is able to segment CC in both the normal and AD subjects. The edge map obtained using PC is found to have continuous and high contrast edges in all the images. The extracted geometric features such as major axis and minor axis shows appreciable demarcation between the normal and AD images with the percentage difference of 4.85% and 11.19% respectively. Since shape analysis of CC is essential in the diagnosis of AD, this study seems to be clinically useful.

P54 A new automatic multi seed analysis for fMRI resting state data in animal model: Comparison to ICA

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Resting state connectivity is increasingly being studied in healthy and diseased brains in humans and animals. There are two major processing techniques to estimate functional connectivity of the resting brain. The first one is the independent components analysis (ICA), which divides temporal brain signals in different independent sources, or components. ICA is data-driven and thus allows data analysis without prior knowledge or subjective researcher interference. However, ICA results are hard to interpret and further quantitative characterization is difficult. The second method is hypothesis driven and includes manually defined regions of interest (ROIs) i.e. seed regions. The time series of each seed region is correlated with the time profile of each voxel resulting in a seed region specific correlation map. Obviously, the seed region approach relies on priori hypotheses and therefore might lack important information not addressed by the researcher. Additionally, the seed regions are subjected to reproducibility problems due to manual placing. Therefore, we present in this study a new automatic method based on the seed region approach which overcomes these flaws. Experiments were performed on 13 male rats anesthetized with isoflurane. BOLD fMRI scans were performed on a 4.7 T BioSpec MR (BRUKER, Germany) with a T2*-weighted gradient echo EPI sequence (22 axial slices, 64 x 64 matrix, TR= 2000 ms, TEef= 24.4 ms, in-plane resolution 391 x 391 µm, slice thickness 1000 µm). Functional data were analyzed using MagnAn (custom IDL program). After spatial smoothing (Gauss, FWHM 3px) resting BOLD signal time courses were low-pass filtered at 0.1 Hz and corrected for global signal fluctuations by linear regression using the global mean as regressor. A 15 component ICA was performed on each animal separately and subsequently averaged using self-organizing group-level ICA provided by BrainVoyager QX 2.8. For our new automatic multi seed correlation method in each rat brain 179 separate brain structures were defined by registering a 3D atlas (derived from Paxinos & Watson, 2007) to each dataset. Next, the seed regions were determined automatically in the center of mass of each of these brain structure. For each seed region the correlation values were averaged over each brain structure, subsequently resulting in a 179 x 179 asymmetric correlation matrix. The matrices were averaged across animals . The binarized ($r > 0.5$) average correlation matrix was translated into a (pseudo)directed network graph and further analyzed using sophisticated graph theorical measures. To validate these graphs against the standard ICA procedure we calculated Blondel communities and compared these communities to ICA components. After eliminating noise components 5 ICs representing different cortical and subcortical network fit well to the network communities (Fig. 1). Thus, our method is validated and can be used as a new approach to compare and characterize resting state networks from a novel perspective.

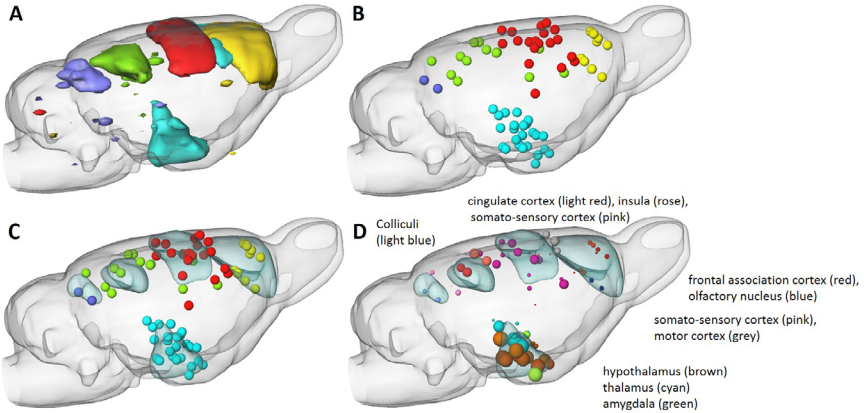

Fig 1: A: Grouplevel ICA Components No. 3 to 7 out of 15. B: Corresponding networks communities obtained with our new automatic multi- seed region approach, connection strength thresholded at r > 0.05. C: Overlay of ICA's and communities. D: as C but nodes colored according to our brainstructure atlas and node size codes graphtheoretical parameter outdegree.

P55 Detailed shape analysis of brains with Alzheimer's disease

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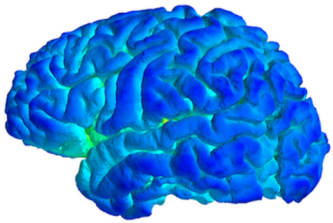
This work constitutes the most detailed shape analysis of MR images of brains with Alzheimer's disease ever conducted. The Mindboggle software (mindboggle.info) extracts features such as labeled regions (Klein, 2012), sulci, and fundi, and computes a variety of shape measures that include mean curvature, geodesic depth, travel depth (Giard, 2011), surface area, volume, different measures of cortical thickness, Laplace Beltrami spectra (Reuter, 2006), and Zernike moments. The outputs of Mindboggle (see mindboggle.info/users/README.html) include tables containing statistical measures computed on the distribution of each shape measure for each feature. We will construct and analyze these tables for healthy controls and patients with Alzheimer's disease or mild cognitive impairment from two data sets with hundreds of participants: ADNI (Jack, 2008) and AddNeuroMed (Simmons, 2009). We will present shape variation and covariation of shape measures across all brain regions in the two data sets.



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P56 Altered brain functional connectivity in patients with benign childhood epilepsy

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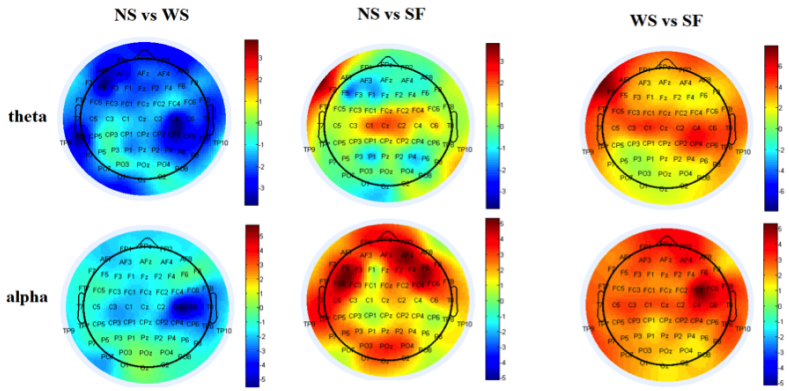
Alteration of functional connectivity may be a key feature for better understanding the pathology of epilepsy. In this study, we investigated how the dynamics of the healthy brain differ from the state of the brain of patients with benign childhood epilepsy during the resting state. To address this issue, we used resting state EEG to characterize functional brain connectivity in controls and epileptic patients. Using imaginary coherence and graph metrics, we found significant differences in functional connectivity between the control and epileptic groups within the theta (4-8 Hz) and alpha (9-13 Hz) bands. In particular, significant differences in functional connectivity and clustering coefficients were observed between epileptic patients and controls within different frequency bands. In the presence of interictal epileptiform discharges (IEDs), epileptic patients demonstrated significant increases in alpha coherence in the epileptogenic zone. However, patients showed lower alpha coherence in the frontal region in comparison with controls when EEG contained no IEDs. Similarly, the clustering coefficient decreased significantly in alpha band for epileptic patients in the absence of IED in comparison with normal subjects. These findings show altered resting state brain dynamics and functional connectivity in patients with benign childhood epilepsy in a frequency dependent manner.



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P57 A cortical-inspired multi-orientation geometry model for retinal image analysis

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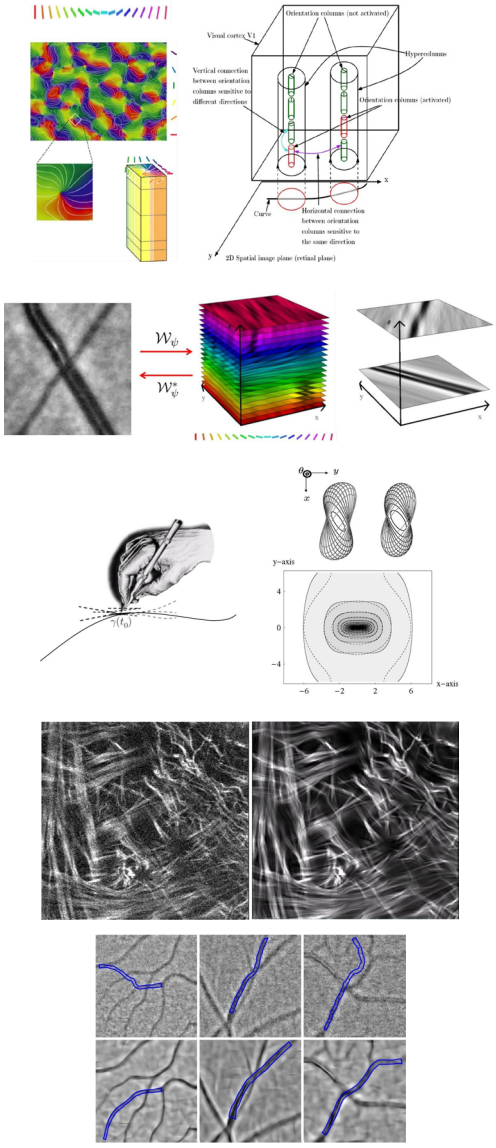
Hubel and Wiesel [1] discovered that the primary visual cells in cat's striate cortex have a strong directional preference, which relates to the orientation-selective property of the receptive fields in V1. See Figure 1, a so-called cortical hypercolum can be interpreted as a "visual pixel", neatly decomposed into a complete set of orientations. Motivated by the orientation-selective cells, so-called orientation scores are constructed by lifting all elongated structures (in 2D images) along an extra orientation dimension [2], see Figure 2. Similar to the perceptual organization of orientation in the visual cortex, a 2D orientation score is an object that maps each 2D position and orientation angle (x,y,θ) to a complex scalar. So the original 2D image domain can be extended to the score domain. A great advantage is that it can deal with multiple orientations per position, and the extra dimension enables new techniques for e.g. geometric reasoning and crossing preserving enhancement.

Since we do not want to tamper data-evidence before subsequent image processing operations take place, invertibility of our transformation between image and score is key in our multi-orientation mathematical modeling. We can now disentangle the elongated structures involved in a crossing session for a crossing preserving flow. Based on the invertible orientation score framework, Bekkers et al. [3] developed a fully automatic multi-orientation vessel tracking algorithm which outperforms other state-of-the-art tracking/detection algorithms.

Moreover, synaptic physiological studies of horizontal pathways in cats' striate cortex show that neurons with aligned receptive field sites excite each other [4]. Therefore, the visual system not only constructs the aforementioned score of local orientations, but also accounts for context and alignment by excitation and inhibition a priori, which can be modeled by left-invariant PDE's and ODE's for contour enhancement and contour completion directly on the score [5-8]. Figure 3 shows the stochastic contour enhancement kernel of linear left-invariant diffusion, which is obtained based on the modeling of Brownian motion in the Euclidean rotation-translation group (SE(2)).

In Figure 4 we see that by applying left-invariant diffusion on the invertible orientation score of a 2D image, the elongated structures can be excellently enhanced without destroying the separated crossing parts in the score domain. Therefore, this step is necessary as a pre-enhancing step for the subsequent tracking/detection. As a proof of concept, we show

examples of tracking on left-invariantly diffused invertible orientation scores on cases in retinal image vessel tracking where standard ETOS-tracking [3] without left-invariant diffusion fails, see Figure 5.



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P58 Separation of patients with schizophrenia and bipolar disorder based on MRI scans: Can machine learning aid in clinical diagnosis?

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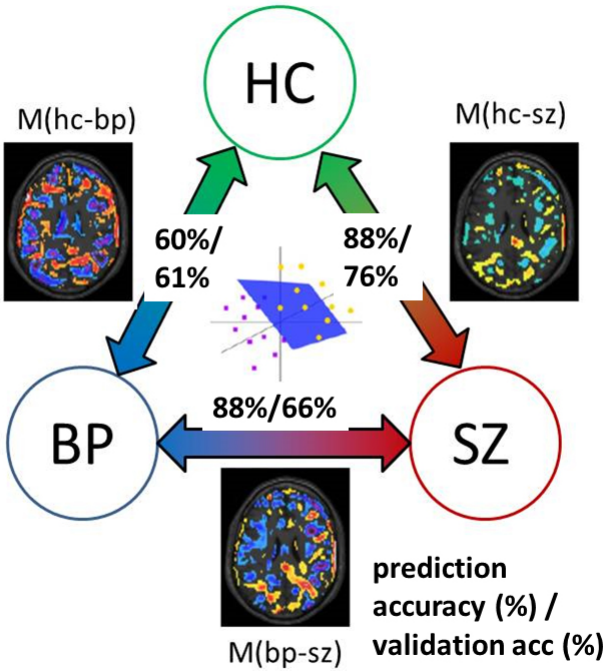
Background
The question of whether brain changes in schizophrenia and bipolar disorder are similar is not only relevant regarding their possible genetic and biological overlap; it also has clinical and diagnostic implications. Here we address the issue of whether structural MRI brain scans can be used to differentiate the two disorders. In a recent study we built a structural-MRI-based schizophrenia classification model and tested its predictive capacity in an independent test sample [1]. Using two large data sets, we confirmed the feasibility to use structural MRI for individualized prediction whether a subject is a schizophrenia patient or a healthy control, with an accuracy of 70.4%. Although scientifically interesting, the clinical use is limited: these classification models become really useful if they can predict a subject's future status, or its current status if this cannot be determined by other means.

Methods
Structural magnetic resonance 1.5 T whole brain images of 66 patients with schizophrenia, 66 with bipolar disorder, and 66 healthy controls were segmented and further processed to create gray matter density (GMD) maps, reflecting local gray matter tissue presence [2]. These GMD maps were used to train linear Support Vector Machines (SVM) [3]) to separate the three groups (Fig. 1). The validity, or generalizibility, of the models was first tested by leave-one-out cross-validation. Secondly, the models were applied without change to an independent data set acquired on a 3 T scanner that included 46 schizophrenia patients, 47 patients with bipolar disorder and 43 healthy control subjects.

Results
Schizophrenia patients could be correctly classified versus healthy subjects with an accuracy of 90%; they could be differentiated from bipolar patient with the same level of accuracy, i.e. also 88%. The model separating bipolar patients from healthy control subjects performed worse: 67% of the healthy subjects were correctly classified and only 53% of the bipolar patients (Fig. 1). Application of the 1.5 T models on the 3 T validation set yielded average classification accuracies of 76% (healthy vs schizophrenia), 66% (bipolar vs schizophrenia) and 61% (healthy vs bipolar).

Conclusion
We demonstrated the feasibility to use structural MRI for individualized prediction whether a subject is a schizophrenia patient or not, with an accuracy of 88%. In an independent validation set acquired on a scanner with different field strength the unaltered models performed significantly above chance level, with accuracies of 76% (schizophrenia vs

healthy) and 66% (schizophrenia vs bipolar). While the use of MRI to separate schizophrenia patients from healthy subjects has limited clinical value, the accurate separation of schizophrenia patients from bipolar patients could become a diagnostic aid for psychiatrists. The results also indicate that the gray matter pathology differs between schizophrenia and bipolar disorder to such an extent that they can be reliably differentiated using machine learning paradigms.



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P59 Segmentation and analysis of sub-cortical regions of autistic MR brain images using Gaussian distribution model based reaction diffusion multi-phase level sets and geometric feature

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Autism is a neurodevelopmental disorder characterized by cognitive dysfunctions such as communication defects, poor social interactions and repetitive behaviours. It affects widely distributed cortical regions and shows extensive reduction in subcortical regions such as corpus callosum, brain stem and cerebellum. Magnetic resonance (MR) imaging is a non-invasive method, which provides information about the anatomy of sub-cortical regions. In the T1-weighted mid-sagittal MR brain images, corpus callosum has the appearance of broad arched band with bright pixel intensity. The brain stem and cerebellum appear as a mixture of white and gray pixels.

In this work, the subcortical regions of control and autistic skull stripped MR brain images are segmented using Gaussian Distribution Model (GDM) based reaction diffusion multiphase level set method. The images considered for this analysis are obtained from autism brain imaging data exchange. In the multiphase level set, GDM is used as the intensity discriminator. The reaction diffusion is used to regularize the level set function. The curve is driven by a new Heaviside and Dirac functions to reach accurate boundaries. The level set function with two contours is used for the segmentation of sub-cortical regions. The results are validated with ground truth using Jaccard and Dice similarity measures. The geometric feature area is calculated from the cortical and subcortical regions. The results show that the GDM based reaction diffusion multiphase level set method is able to segment the regions. The level set method with two contours employed in this paper segments the brain into three regions. One of the contours in level set function extracts the high intensity pixels and the other extracts the low intensity pixels. From these images the desired sub-cortical regions such as corpus callosum, brain stem and cerebellum are labelled and separated from the undesired regions. The similarity measures calculated between segmented images and ground truth gives the values greater than 0.85. The geometric feature area calculated from the cortical and subcortical regions gives distinct variation ($p<0.0001$) between control and autistic images. As the geometric feature area extracted from cortical and sub-cortical regions are associated with brain dysfunction, this study helps to improve the diagnostic relevance of autistic subjects.

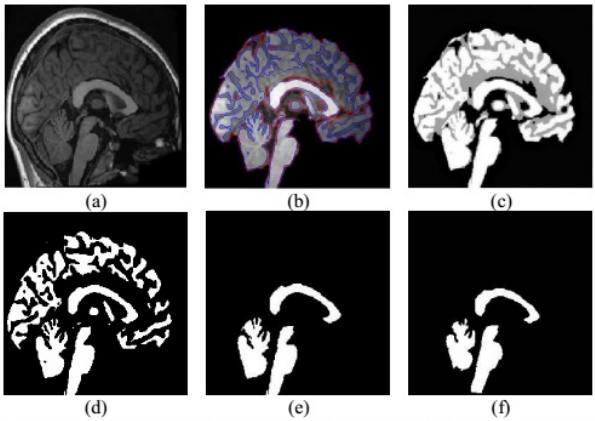

Figure 1 (a) T1 weighted autistic image (b) Final contour evolved in skull stripped image (c) Segmented regions (d) High intensity regions (e) Extracted brain sub-cortical regions and (f) Ground truth

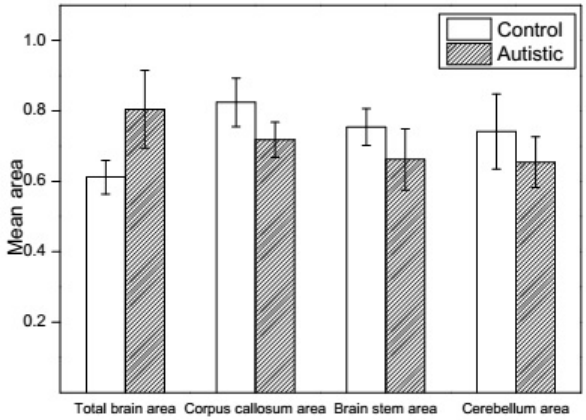

Figure 2 Bar plot of mean and standard deviation of geometric feature area calculated from whole brain, corpus callosum, brain stem and cerebellum

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P60 Understanding programmers' brains with fMRI

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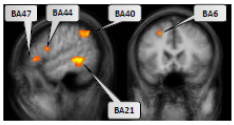
The human factor plays an important role in software engineering, because humans design, implement, and maintain software. One of the most important cognitive processes is program comprehension, because programmers spend most of their time with understanding source code [3,4,5]. However, despite of more than 30 years of research, we still have no clear understanding of the relevant processes during comprehending source code. To gain a deeper understanding of program comprehension, we measured it by using functional magnetic resonance imaging (fMRI) [2] since fMRI has proved successful to study comparatively complex cognitive processes in detail. Our hope is that in the process of understanding developer's cognition, we can create a platform for sharing how these complex processes map onto other studies of cognition, and even incorporate ideas for organizing software into models of cognitive processes.

In our study, we designed several short source-code snippets and asked computer-science students to determine the output if the source code would be executed (see Fig. 2 or project's website (tinyurl.com/ProgramComprehensionAndfMRI) for examples). As control condition, we let participants locate syntax errors that did not require understanding the source code (Fig. 3). After testing and refining the source-code snippets in behavioral pilot studies [1], we carried out the measurements with 17 participants on a 3~Tesla scanner. For fMRI, we acquired 985 functional volumes in 32 minutes and 50 seconds using standard echo planar imaging (EPI) sequence with whole brain coverage at an isotropic resolution of 3 mm. Functional data were analyzed in BrainVoyager employing a random effects GLM contrasting the program comprehension condition against the syntax condition.

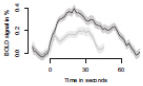
We found Brodmann areas 6, 21, 40, 44, and 47 are activated during program comprehension (Fig. 1). These areas are related to language processing, working memory, and problem solving, which is in line with the current understanding of program comprehension. The results of our study suggest that fMRI is promising to give us a more detailed understanding of program comprehension. Over the next years, we hope that more researchers will adopt our idea. By raising the awareness of how fMRI can be applied to software-engineering research, we also hope that more software engineers will contribute to develop more powerful fMRI paradigms. In the long run, we will gain a better understanding of the neural basis of designing, implementing, and maintaining software, which may in turn help to optimize tools or programming languages.

Additionally, our research will have a broad impact on education, so that training beginning programmers can be improved considerably. Despite intensive research (e.g., Technical Symposium on Computer Science Education, Innovation and Technology in Computer Science Education), it is still rather unclear how and why students struggle with learning programming. With a detailed understanding of the cognitive processes that underlie a developers' every-day task, we might find the right recipe to teach any student to become an excellent software developer (e.g., by including training language skills, since our study showed a close relationship to language processing).

As next steps, we will conduct more such experiments. To support replication and help other software-engineering researchers adopt fMRI for their research, we will make all data publicly available. Eventually, we hope to find answers to heatedly discussed questions, such as "How should we teach programming?" or "What makes a programmer excellent?".

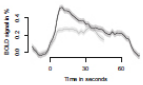


BA 6: Middle frontal gyrus
(Talairach coord.: -26, 17, 52; cluster size: 1279)



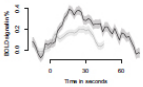
Attention
Division of attention
Language
Silent word reading
Working memory
Verbal/numeric
Problem solving

BA 21: Middle temporal gyrus
(Talairach coord.: -55, -39, -2; cluster size: 4746)



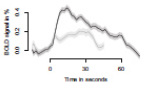
Semantic memory retrieval
Categorization

BA 40: Inferior parietal lobule
(Talairach coord.: -51, -49, 41; cluster size: 3368)



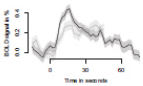
Working memory
Verbal/numeric
Problem solving

BA 44: Inferior frontal gyrus
(Talairach coord.: -50, 11, 16; cluster size: 698)



Working memory
Verbal/numeric

BA 47: Inferior frontal gyrus
(Talairach coord.: -52, 31, 0; cluster size: 546)



Language
Silent word reading
Working memory
Problem solving

Figure 1: Observed activation pattern for program comprehension and time courses of the BOLD response for each cluster. The gray area around the time courses depicts the standard deviation based on the participants. BA: Brodmann area.

```
1 public static void main(String[] args) {
2   String word = "Hello";
3   String result = new String();
4
5   for (int j = word.length() - 1; j >= 0; j--)
6     result = result + word.charAt(j);
7
8   System.out.println(result);
9 }
```

Figure 2: Source code for one comprehension task with expected output ‘olleH‘.

```
1 public static void main(String[] ) {
2   String word = "Hello';
3   String result = new String();
4
5   for (int j = word.length() - 1; j >= 0; j--)
6     result = result + word.charAt(j);
7
8   System.out.println{result);
9 }
```

Figure 3: Source code for a syntax task with errors in Line 1, 2, and 8.

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P61 Segmentation and analysis of hippocampus and ventricle in Alzheimer's brain MR images using Minkowski weighted K-means clustering and its ratiometric index

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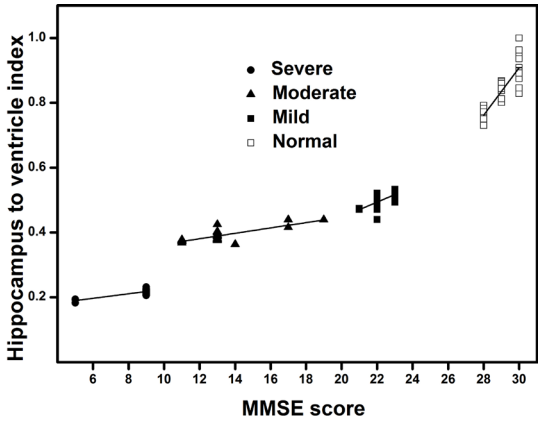
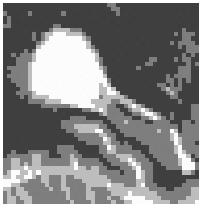
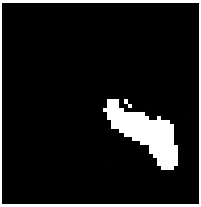
Alzheimer's disease (AD) is the common form of dementia, affecting over 24 million people worldwide with characteristic pathology of plaques and neurofibrillary tangles. This is accompanied by hippocampal atrophy and ventricular enlargement. Although AD and mild cognitive impairment (MCI) are commonly diagnosed using sets of clinical criteria, MRI findings aid the clinical diagnosis and predict clinical progression. Ventricles are located at the centre of the brain and appear dark in T1-weighted MRI scans.The hippocampus appears to be small and has regional appearance similar to its neighbouring structures. In this work, segmentation of both the hippocampus and the ventricle are carried out by Minkowski weighted K-means clustering method. The normal (30) and abnormal (30 mild, 30 moderate and 30 severe) images considered in this work are obtained from MIRIAD database. Initially, the ROI is selected from original T1 sagittal image. This multiobject segmentation approach extends the K-Means criterion using Minkowski metric as a distance measure. This formulation also uses weight updating computations. Here, four initial centroids are selected for clustering from the histogram of the image.The exponent of the Minkowksi distance measure is chosen to be 6. From the clustered output, the ventricle and hippocampus are extracted using morphology operations. The segmented images are quantified using Minkowski features which captures the topology changes. These features are calculated for hippocampus and the ventricles of different normal and abnormal images and analysed.The prominent feature is correlated with the Mini-Mental State Examination (MMSE) score. Results show that Minkowski metric weighted K-Means method is able to delineate the boundary of the hippocampus and ventricle from normal and abnormal conditions.The accuracy of segmentation is high (81%). It is observed that the Minkowski area of segmented hippocampus and ventricle provide significant discrimination of normal and abnormal subjects. The ratio of hippocampus to ventricle area helps in better discrimination of severity in pathology conditions. Its correlation with MMSE is observed to be very high for normal (R=0.87) subjects. The correlation is found to be moderately high for mild (R=0.70), moderate(R=0.72) and severe (R=0.84) Alzheimer subjects. Hence this ratiometric index which takes into account of atrophy of hippocampus and the enlargement of ventricle could be used for the study of progression in neurodegenerative disorder such as AD.







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P62 Visualization of synchronized stereoencephalographic recordings in a 3D smart image to aid presurgical evaluation of epilepsy

Stephan Meesters[1], Pauly Ossenblok[1], Louis Wagner[1], Petra van Houdt[1], Albert Colon[1], Olaf Schijns[2] and Andrea Fuster[3]
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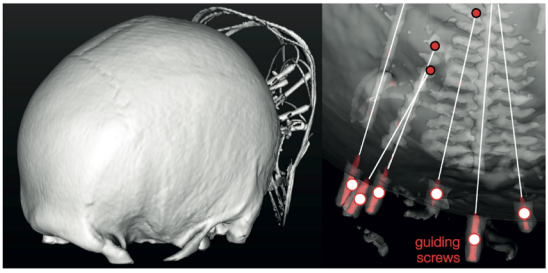
2. Maastricht University Medical Center, Neurosurgery, Maastricht, Netherlands
3. Eindhoven University of Technology, Department of Biomedical Engineering, Eindhoven, Netherlands

Rationale
Stereoelectroencephalography (SEEG) provides insight in the spatiotemporal dynamics of seizures by implanting depth electrodes in the brain regions assumed to play a role in onset and early propagation of seizures. Knowledge of the regions of epileptiform activity can aid physicians in surgical planning, which can be identified with a nonlinear association analysis [1]. To provide a clear visualization and make the results of depth electrode EEG (iEEG) analysis clinically applicable and accessible to physicians, depth electrode navigation software has been developed.

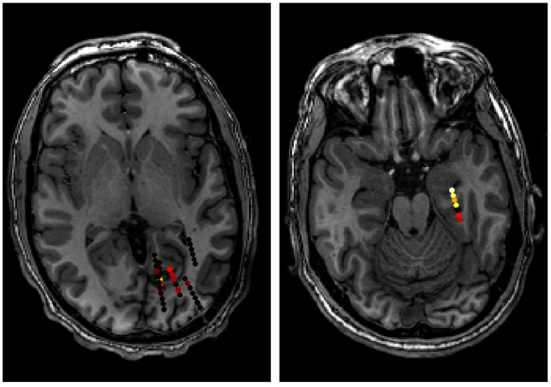
Materials and methods
Automatic detection of depth electrodes in computed tomography (CT) scans is a key feature of the software. The initial step is the detection of guiding screws, fixed to the skull, that are used to guide and hold the intracerebral electrodes. The guiding screws are cylinderical structures which can be extracted using the Frangi-vesselness filter [2]. The principal axes of inertia are computed for those structures which provides an initial location and orientation from which the entire electrode can be detected, as illustrated in Figure 1. The CT data is sampled along the found orientation and a scoring method is applied to find a suitable end point. Visualization combines the result of depth electrode detection with a skull rendering in the 3D viewport and with pre or post-operative MRI in the 2D viewport. Analysis of iEEG is performed by computing the nonlinear association strength functions for each electrode contact. A General Linear Model to correlate the association strength functions and epileptic discharges visualizes the activation pattern of these discharges [1].

Results
Each patient (N=6) was implanted with several platinum depth electrodes (DIXI medical, Besancon, France). Results show that 90% of electrodes were recognised, in which 15% needed further manual refinement of the tip. Pre-processing time takes 5 minutes by average. Depth electrode detection takes 1 minute, following by up to 5 minutes for manual corrections. Results of iEEG analysis done in a previous study by Van Houdt et al [1] are displayed as dots on an axial anatomical image, as shown in Figure 2, which for this patient indicates an epileptic active region in the hippocampus.



(a)

Figure 1: Skull including electrode wiring (left). Detection of guiding screws, orientation and estimated end points (right).



(a) (b)

Figure 2: Results of iEEG analysis reveiling high significant correlation patterns in the hippocampus (b) when compared to the occipital lobe (a).

Conclusion

Software has been developed for the automatic detection and visualization of depth electrodes. The algorithms employed are considered suitable for detecting stimulation electrodes as well, commonly used in deep brain stimulation (DBS). Future work will focus on the improvement and integration of iEEG analysis within the software that enables to visualize the activation

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2. A. Frangi and W. Niessen, "Multiscale vessel enhancement filtering," Medical Image Computing and Computer-Assisted Intervention - MICCAI'98, 1998. maps as shown in Figure 2 in relation to the dynamics of the epileptic discharges.

P63 The dependency of parietal activation on visuospacial operation performance in the elderly – an event-related fMRI study

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2. Kobe University, Electrical and Electronic Engineering, Kobe, Japan

It has been proposed that physical exercises can assist cognitive recovery in the elderly [1], however, their effectiveness has been controversial [2]. The backgrounds of this discrepancy may be heterogeneity of the populations studied and various exercise protocols employed. In order to clarify the conditions to predict validity of physical exercises, it is desirable to establish a method to classify the subjects based on their cognitive and physiological status. For this evaluation, the neuronal basis of the tasks used in the exercises should be clarified. We investigated the availability of a virtual performance task designed from exercises for the elderly as a model to test age-related changes in brain function. Twenty-four elderly (over 60, 12 females) and 24 non-elderly (20 - 54, 12 females) healthy volunteers participated in an event-related fMRI experiment simulating the visuo-motor transformation of bean transfer test (BTT), one of the physical test batteries for elderly [3]. Functional data were obtained by using a 3T-MR scanner (TR = 3000 ms, TE = 30 ms, 39 axial slices, 3 mm thick, 0.75 mm gap, matrix = 64 x 64, FOV = 192 mm, BW = 1420 Hz/Px, 128 volumes), and the reaction time in each trial were recorded at 6 points by synchronizing to the TTL signal from the MR scanner. The functional images were processed using SPM8. It was indicated that the activations representing the whole trial of virtual BTT (VBTT) were contributed by different steps in each age group. In young subjects, major activations were detected at CP0 (bean appearance), CP1 (start clipping) and CP4 (finish transferring), while they were detected at CP0 and CP2 (finish clipping) in the elderly subjects. Activations in the left BA 3, 5, 6, 40, 43 and the right BA7 were significantly augmented in the elderly group at CP2 (FEW, $p< 0.05$). Within the elderly subjects, further activations in the left BA5 and right BA7 were augmented in the higher bean clipping performance group (12 subjects, FDR, $p< 0.001$) at CP2. However, no augmentation of brain activations was detected in the higher bean transfer performance group in contrast to the lower performance group at CP2, 3 (start transfer) or 4. The activations were not significantly different between the two age groups when the contrasts obtained from the whole trial were compared. By using partitioning analysis employing accurate response times for each step of VBTT, differential activations characteristic to the two age groups could be extracted. In conclusion, it was suggested that the relationship between performance of visuo-spatial operation and parietal activation may be a potential indicator of functional compensation capability in the elderly depending on further neuronal recruitment.

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P64 A two-stage approach to estimating voxel-specific encoding models improves prediction of hemodynamic responses to natural images

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Unsupervised feature learning has become an alternative approach to descriptive and explanatory modeling of single voxel responses to natural images in functional magnetic resonance imaging. In this approach, features are first learned from low-resolution and small natural image patches since learning generally requires a large amount of memory and computation power. Features are then nonlinearly extracted from stimuli and finally linearly regressed on stimulus-evoked single voxel responses. While this approach was recently shown to improve prediction of human brain activity in response to natural images, it has two problems. First, features that are learned from low-resolution and small natural image patches might not be adapted to statistical regularities that alter single voxel responses. Second, features that are extracted from stimulus regions that are outside single voxel receptive fields might be notoriously redundant, and overfitting might occur. In this study, we introduce a two-stage approach to solve these problems. In the first stage, a general encoding model is estimated and used to simulate single voxel responses to point stimuli. Single voxel receptive fields are estimated by fitting two-dimensional Gaussian functions to simulated single voxel responses. In the second stage, new voxel-specific encoding models are estimated as follows: For each voxel, features are (i) learned from high-resolution natural image patches that are of the same size as its estimated receptive field, (ii) nonlinearly extracted from stimulus regions that are within its estimated receptive field and (iii) linearly regressed on its stimulus-evoked responses. Concretely, features are learned using sparse coding, nonlinearly extracted using convolution and compressive nonlinearity, and linearly regressed using ridge regression. Note that different features are learned for each voxel. We validate the two-stage approach by predicting single voxel responses to natural images and identifying natural images from stimulus-evoked multiple voxel responses. We show that encoding and decoding performance of the voxel-specific encoding models is significantly higher than that of the general encoding model. These results demonstrate that the two-stage approach improves modeling of single voxel responses to natural images in functional magnetic resonance imaging.

P65 Sparse tomographic reconstruction of brain tissue from serial section electron microscopy

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High throughput imaging of large volumes of brain tissue at synaptic level has the potential to transform the acquired anatomical maps into the realm of Neuroinformatics. This, however, poses a substantial challenge to imaging technologies due to the requirement of both high resolution and large spatial scale. Various types of volume Electron Microscopy (EM) methods have been proposed in recent years for neural circuit reconstruction [1]. While these methods differ in terms of the utilized type of EM and sectioning technique, they are commonly limited in the resolution in the depth direction due to the involved mechanical cutting process. Low depth resolution could significantly reduce the ability to reliably identify different subcellular structures that may play an important role in structural plasticity of neuron connections. Although Electron Tomography (ET) can be applied together with serial section EM methods [2, 3] to computationally improve the depth resolution, it typically requires tens to hundreds of EM images acquired from series of tilt angles in order to generate a satisfactory reconstruction. This severely limits the throughput and exposes the sample with excessive electron-dose causing sample damage.

In this work, we show that a reasonable tomographic reconstruction can be achieved using limited data from a small number of projection images. By exploring the information from reconstructions of adjacent sections of the sample and the fact that these sections together form a continuous large area of brain tissue with sparse boundaries, multiple sections are reconstructed simultaneously together as a single reconstruction using iterative reconstruction techniques. This approach helps reduce ambiguities raised by the limited number of projections and the missing wedge, and guides the reconstruction algorithm toward a reasonable numerical solution using only a few projection images. The figure below demonstrates the performances of the reconstruction using the proposed technique. In total 30 of the 100nm sections are reconstructed together with only 5 projection images (range from -70 to 70 degree) for each section. The results show that significant greater depth resolution is achieved for the complete reconstruction comparing to the original 100nm depth resolution. The yellow box highlights the results in a smaller region indicating the image quality of the numerical reconstruction. Furthermore, the reconstructed cross-sections appear to be free of distortion and highly continuous among adjacent sections. The proposed technique has the potential to improve both resolution and throughput of 3D reconstruction, and to provide high quality volume information of brain tissue for better understanding of the relation between functions of the nervous system and the underlying neuronal circuits.

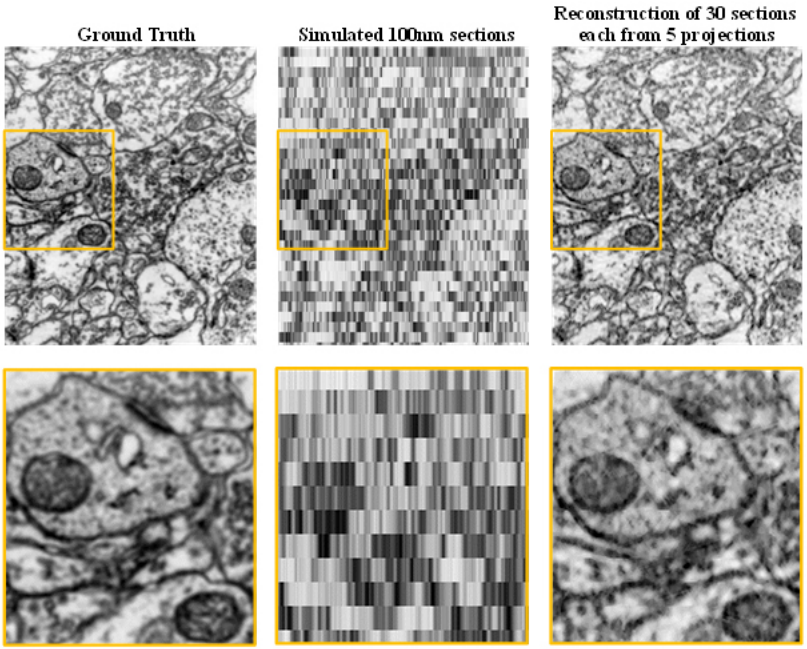

Figure. Cross-section of tomography reconstruction of brain tissue from limited data. Projections of sections from 5 tilt angles (-70 to 70 degree) are used to reconstruct 30 of the 100nm serial sections. Image courtesy to the OPEN CONNECTOME PROJECT [4].

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P66 Mapping cognitive ontologies to and from the brain

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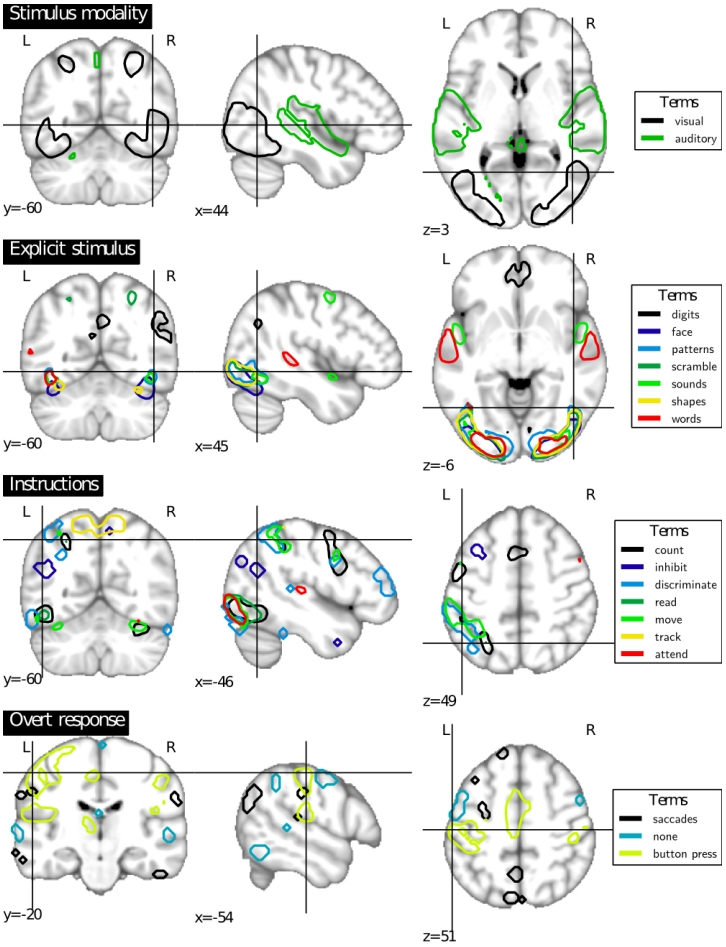
Introduction
Large-scale mapping of cognitive brain functions using fMRI relies on the accumulation of individual studies. fMRI meta-analyses combine several studies and open the opportunity to invert the statistical inference of individual studies standard analysis [2]. Our goal is to find a bidirectional link between brain activity patterns and cognitive functions. To that end, we propose a methodology that leverages the Cognitive Paradigm Ontology (CogPO) [5] to perform image-based meta analyses. We use two models: forward inference to find regions activated for a given label, and reverse inference to find regions predictive of a given label.

Method
In order to find correspondences between studies, we choose to use activation maps and label them with terms drawn from CogPO. CogPO describes paradigms by defining categories of terms such as the explicit stimulus, or the instructions. Those terms are likely to be shared across studies regardless of the original topic of the study. In this work, we use 19 studies, mainly from OpenfMRI [3], comprising 131 different conditions and labeled with 19 terms. Forward inference: we use the standard fMRI analysis framework and, for each voxel of the subject-level activation maps, tests its significance relative to a term using a General Linear Model. The design matrix models the presence of the terms. Reverse inference: We use a One-vs-All (OvA) approach to predict the presence of CogPO terms. The classifiers are trained within a leave-one-study-out or leave-one-laboratory-out cross validation scheme. Predicting terms on new experiments ensures we are not building a study detector.

Results
Forward inference: The resulting regions (Figure 1) lack functional specificity, but are relevant to the corresponding terms. Reverse inference: The prediction problem is highly multi-class and imbalanced, as seen in the long-tailed distribution of the terms representation (Figure 2). Figure 2 also shows the corresponding precision and recall scores of several classifiers, as well as the chance levels for both cross validations.

Conclusion
We present a methodology to accumulate knowledge across studies. We use ontology terms to find commonalities between studies and a careful cross validation to avoid learning idiosyncrasies. The main remaining roadblock is the class imbalance problem, which goes together with a lack of data in general. This is a known egg and chicken problem, as few datasets are available online, few meta-analysis methods are developed and further limit the incentive for sharing new data [1, 4]. In the future, we plan to apply this methodology to more datasets, and extend it to make zero-shot learning of tasks.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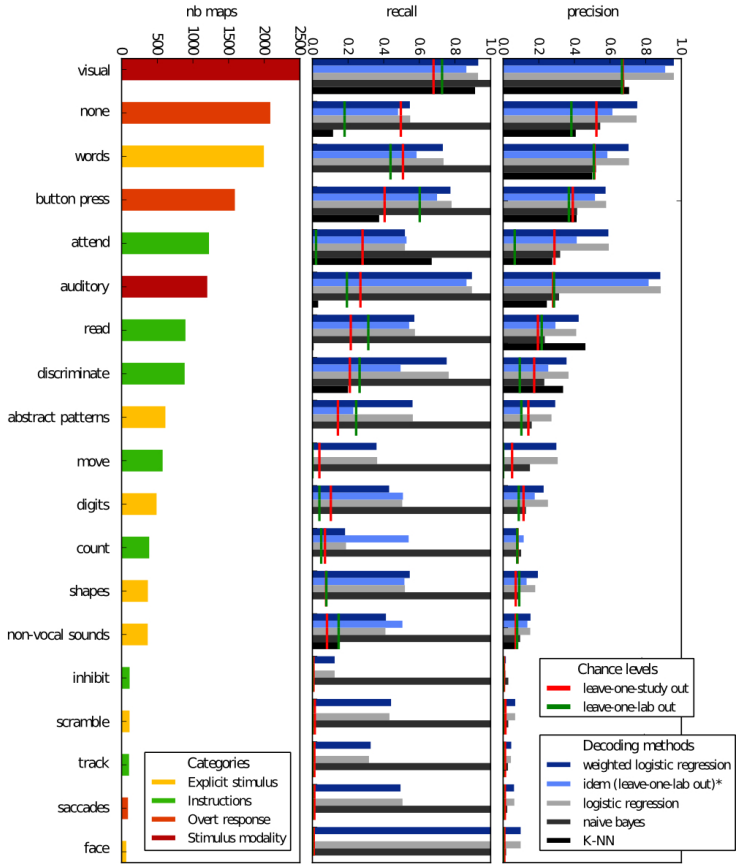

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