Neuroinformatics

INCF Canadian Neuroinformatics Workshop

A Satellite Symposium of the CAN 2012 Meeting



May 24th, 2012
Vancouver, BC. Canada

incf

INCF Canadian Neuroinformatics Workshop

A satellite symposium of the CAN 2012 meeting

Date and Location

Thursday May 24th, 2012, Sheraton Wall Centre, Vancouver, British Columbia

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Scientific Organiser

INCF

NeuroDevNet

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Acknowledgements

INCF would like to thank Paul Pavlidis and Elodie Portales-Casamar for their invaluable work helping organize this workshop. With them, our combined thanks extend to Dan Goldowitz for his superb support of this workshop and connecting us with people, especially the CAN2012 organisers, to whom we also extend great thanks for allowing this workshop to become an official satellite meeting to the CAN2012 meeting and promoting it on the CAN web site. We would also like to thank members of the Program Committee for arranging such an excellent scientific program.

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Information about the Hosts

INCF

The International Neuroinformatics Coordinating Facility (INCF) was launched in 2005, following a proposal from the Global Science Forum of the OECD to establish an international collaborative informatics infrastructure for neuroscience, and currently has 16 member countries across North America, Europe and Asia. INCF establishes and operates scientific programs to develop standards for neuroscience data sharing, analysis, modeling and simulation while coordinating an informatics infrastructure designed to enable the integration of neuroscience knowledge worldwide and catalyze insights into brain function in health and disease. Please see www.incf.org for more information.

NeuroDevNet

NeuroDevNet, a Canadian Network of Centres of Excellence (NCE), is dedicated to helping children overcome neurodevelopmental disorders. Network investigators seek to understand the causes of neurological deficits, and to transfer this knowledge to health care professionals, policy makers, and communities of interest. NeuroDevNet works with its partners in academia, the community, not-for-profit sector, industry, and government, and across traditional disciplinary boundaries and sectors, to ensure generated knowledge is translated into tangible diagnostic, preventative, therapeutic, social, economic, and health benefits for all. Please see www.neurodevnet.ca for more information.

Program Committee

- Co-Chair: Paul Pavlidis, Scientific Director, NeuroDevNet Neuroinformatics Core
- Co-Chair: Linda Lanyon, Head of Programs, INCF
- Dan Goldowitz, Scientific Director, NeuroDevNet
- Elodie Portales-Casamar, NeuroDevNet Neuroinformatics Core Manager
- Alan Evans, Professor, McGill University; Director, Montreal Consortium for Brain Imaging Research



Speakers, left to right: Maryann Martone, Rob Williams, Linda Lanyon, Alan Evans, Paul Pavlidis, Dan Goldowitz, Sean Hill, Gunnar Blohm, Ibolja Cernak, Matthijs van der Meet, Stephen Strother, John Tsotsos, Elodie Portales - Casamar and Christian Beaulieu.

Executive Summary

On Thursday 24th May 2012, the International Neuroinformatics Coordinating Facility (INCF) and NeuroDevNet jointly hosted a satellite workshop at the Canadian Association for Neuroscience annual meeting in Vancouver, Canada, on the theme of Canadian Neuroinformatics. The aim of the workshop was to help build the Canada neuroinformatics community, enabling Canadian scientists from diverse neuroinformatics-related fields to gather, exchange knowledge and discuss whether there was community desire for Canada to join the INCF.

The workshop comprised a rich scientific agenda, which displayed the diversity and strength of Canadian neuroinformatics research, and concluded with a discussion about Canada's future involvement with INCF. Scientists at the meeting were very supportive of the idea of Canada joining INCF and produced a next steps action plan to build the neuroinformatics community in Canada in preparation for it forming an INCF National Node. Subsequent to the meeting, the community-building plan has been largely put into action and momentum within the community continues to build.

Background and Meeting Outline

On Thursday 24th May 2012, the International Neuroinformatics Coordinating Facility (INCF) and NeuroDevNet jointly hosted a satellite workshop at the 6th Annual Canadian Association for Neuroscience meeting in Vancouver, Canada, on the theme of Canadian Neuroinformatics. The agenda is given in the appendix. The aim of the workshop was to help build the Canada neuroinformatics community, enabling Canadian scientists from diverse neuroinformatics-related fields to gather, exchange knowledge and discuss whether there is community desire for Canada to join the INCF. More than 60 participants attended the workshop.

Over the past few years several scientists in Canada have expressed interest in the country becoming more closely involved with INCF. There are obvious synergies between neuroinformatics work in Canada and the aims of INCF. With USA and most major European countries forming National Nodes of the INCF, a Canadian Node seems to be an obvious and desirable goal. In partnership with NeuroDevNet, INCF sought to facilitate this meeting in order to bring scientists together to discuss whether and how this goal should be attained, as well as promote a scientifically rich agenda of neuroinformatics presentations.

The scientific part of the agenda, which is described in the next section, displayed the diversity and strength of Canadian research in neuroinformatics-related fields. A broad range of speakers reflecting many neuroscientific domains and Canadian Provinces participated. Lunch and coffee breaks provided opportunities for networking and for Canadian scientists to talk with three representatives of the INCF USA Node and three members of the INCF Secretariat about INCF Programs and activities. Representation from the USA included two chairs of Oversight Committees for INCF's programs (Drs Maryann Martone and Robert Williams) and a graduate student member (Nolan Nichols) of one of INCF's Task Forces. The student representative talked to Canadian graduate students about benefits of being involved with INCF as a junior researchers and how it has enabled him to work with senior scientists from around the world. The meeting concluded with a discussion about Canada's future involvement with INCF. Scientists at the meeting were very supportive of the idea of Canada joining INCF and produced a next steps action plan to build the neuroinformatics community in Canada in preparation for it forming an INCF National Node. Since the meeting the initial actions to facilitate communication within the community have been taken and the community is rapidly growing in strength and cohesion.

Voices of the Community

Stephen Strother



"INCF membership will allow Canadian researchers to take a more active role in coordinated development of international standards and tools in neuroinformatics. This is likely to result in cost savings by helping to avoid a lot of uncoordinated and duplicated development of tools and standards designed to facilitate Canadian neuroscience research. The sooner Canada contributes to, adopts and can access the rapidly developing neuroscience standards, tools and data sources around the world for which INCF acts as a portal and clearing house the faster Canadian neuroscience research is likely to progress."

Scientific Program

Introduction and welcome

Paul Pavlidis, Scientific Director, NeuroDevNet Neuroinformatics Core

1. Session 1: International Neuroinformatics Coordinating Facility

Chair: Linda Lanyon

Sean Hill, INCF Executive Director, INCF Secretariat, Karolinska Institute, Stockholm

Role of INCF: Toward a Global Collaborative Infrastructure for Neuroscience

The International Neuroinformatics Coordinating Facility (INCF) was launched in 2005, following the proposal by the Global Science Forum of the Organization for Economic Cooperation and Development (OECD) to create an organization to coordinate an open international infrastructure and integrate heterogeneous neuroscience data and knowledge bases and enable new insights from analysis, modeling and simulation. Here we present the INCF multi-phase strategy to deploy such an infrastructure with specific capabilities and milestones. The first phase would establish a globally federated dataspace with searchable metadata. The second phase would develop an object-based data integration layer employing web services to ensure the unique identification of all data through ontologies and spatial coordinates, while using data models to access diverse data formats through standard interfaces. The third phase would establish standard workflow management for analysis, visualization, modeling and simulation



can then be built on top of the data integration layer. The development of portal interfaces will be critical to provide interactive user access to data, analyses and simulation results. This infrastructure should facilitate international sharing, publication and integration of neuroscience data across multiple levels and scales.

INCF US Node scientific activities:

Maryann E. Martone, Neuroscience Information Framework, University of California, San Diego, La Jolla, CA, USA. INCF Oversight Committee Chair – Program on Ontologies of Neural Structures

Navigating the Neuroscience Data Landscape

The number of available neuroscience resources (databases, tools, materials and networks) available via the web continues to expand, particularly in light of newly implemented data sharing policies required by funding agencies and journals. However, the nature of dense, multi-faceted neuroscience data and the design of classic search engine systems continues to make efficient, reliable, and relevant discovery of such resources challenging. This challenge is especially pertinent for online databases, whose dynamic content is largely opaque to contemporary search engines and which are developed using a myriad of platforms, data models and terminologies. The Neuroscience Information Framework (NIF; http://neuinfo.org) was initiated to address the problem of finding and utilizing neuroscience-relevant resources. The NIF project is one of several large US-based neuroinformatics projects that comprise the US Node network of the INCF. The NIF portal has been available since 2008, during which time NIF has been surveying the resource landscape for the neurosciences, identifying relevant resources and working to make them easily discoverable by the neuroscience community. The NIF portal, and associated Neurolex Wiki, currently comprises the largest source of neuroscience-relevant information on the web, currently searching simultaneously over 180 independent databases, the biomedical literature and a resource catalog containing over 5000 resources characterized by resource type and keywords. In this presentation, I provide a survey of the resource landscape for neuroscience: what types of resources are available, how many there are, what they contain and, most importantly, ways in which these resources can be utilized by the research community to advance neuroscience research. I will highlight how the NIF project has worked within the context of the INCF to help develop standards and tools for information integration for the neurosciences, particularly the Program on Ontologies for Neural Structures (PONS).

Rob Williams, Department of Anatomy and Neurobiology and Center for Integrative and Translational Genomics, University of Tennessee Health Science Center, Memphis, TN, USA. INCF Oversight Committee Chair – Digital Brain Atlasing Program

Atlases, Genomes & Genetics: An International Tool Set to Help Understand Brain Function



Rob Williams

Atlases are frameworks for genomics and genetics that have the potential to enable efficient exploration for hypothesis generation, comparative analysis, and direct hypothesis testing. To harness this potential, the INCF Program on Digital Atlasing has developed a coordinate-based reference space—the Waxholm Space—and supporting web services to translate between different mouse atlases and simultaneously integrate different types of data. I will present a general overview of the INCF Program on Digital Atlasing as well as an overview of three different genomic and genetics resources, GEMMA, GeneMania, and GeneNetwork, for mouse and humans populations that are currently available. I will also discuss efficient systems neurogenetics and reciprocal translation between mouse and human populations.

2. Session 2A: Neuroinformatics in Canada - Neuroimaging

Chair: Paul Pavlidis

Alan Evans, Montreal Neurological Institute (MNI), McGill University, Montreal

CBRAIN: A Global HPC Portal for Brain Imaging Research

The MNI group can contribute the following technologies and human resources to INCF activity:

TECHNOLOGY

LORIS Web Database

LORIS is a web-enabled multi-site database system for storage and querying of imaging/behavioural/clinical/genetic data (Das et al., 2012). Originally developed for the longitudinal NIH MRI Study of Normal Brain Development (Evans et al., 2006), LORIS is used for numerous international multi-site studies of abnormal development (e.g. IBIS autism network in US, NeuroDevNet in Canada) and neurodegeneration (e.g. Innomed/AddNeuroMed, NeuGrid networks in Europe).

LORIS has three main capabilities – in addition to being (i) a data repository, it is also (ii) a project management environment for continuous oversight and coordination of multi-site data collection, and (iii) a portal to fully-automated image analysis pipelines (e.g. fMRI, MRI, PET) and statistical packages (e.g. MNITools, SPM, FSL, AFNI).

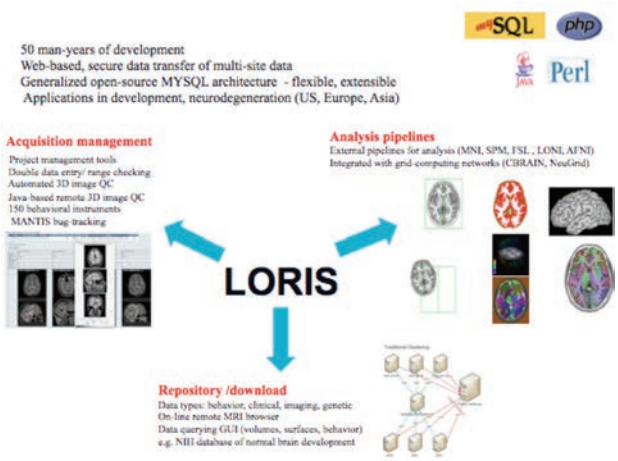


Figure 1: LORIS Web Database has 3-fold functionality

Pipeline Analysis

The CIVET pipeline is widely used for structural MRI analysis, incorporating algorithms for intensity normalization (N3, Sled et al. 1998), spatial normalization (ANIMAL. Collins et al., 1994, 1995), cortical thickness/area analysis (CLASP, MaDonald et al., 2000; Kim et al., 2005; Lee et al., 2006). The CIVET pipeline has been extensively employed for analysis of pediatric data over the past decade, as illustrated by the non-exhaustive list below.

- Normal development (Lerch et al. 2006 ; Shaw et al. 2006, 2008 ; Lenroot et al., 2007 ; Lyttelton et al., 2007, 2009 ; Im et al., 2008 ; Hyde et al. 2009 ; Ducharme et al., 2011, 2012 ; Ganjavi et al., 2011 ; Karama et al., 2009,2011 ; Khundrakpam et al., 2012 ; Nguyen et al., 2012)
- Developmental disorders (Gogtay et al. 2004, 2007 ; Chung et al. 2005 ; Shaw et al. 2006, 2007b, 2009 ; Giedd et al., 2007 ; Meguid et al., 2009 ; Webster et al., 2006, 2008 ; Fahim et al., 2012)



Alan Evans

- Imaging genetics (Shaw et al. 2007ac, 2009 ; Lenroot et al. 2009 ; Hulshoff-Pol et al., 2006ab ; Peper et al., 2009)
- Cortical morphology covariance (Lerch et al., 2006 ; Gong et al. 2009, 2012 ; Khundrakpam et al., 2012)

The fMRI NIAK pipeline incorporates functional connectivity analysis (BASC ; Bellec et al., 2011) and statistical analysis (fMRIstat, Surfsat, ; Worsley et al., 1996). Correlation-based connectivity analysis is also provided, either vertexwise and seed-based (MACACC) or as an ROI-based graph theoretical approach (GRETNA)

CBRAIN

LORIS and CIVET are deployed as part of a CANARIE-funded Network-Enabled Platform (NEP) project, dubbed CBRAIN, that links brain imaging research centres to high-performance computing (HPC) resources CBRAIN (www.cbrain.mcgill.ca) is a lightweight and flexible portal for integrating distributed data and compute resources. As well as the 100,000 processors available within Canada, CBRAIN has been successfully expanded to include international sites in Europe, Latin America, US and the Pacific Rim, most notably incorporating national HPC facilities in Germany (Juelich) and S. Korea (KISTI). As of Dec 2011, the CBRAIN network included 41 user groups in 11 countries.

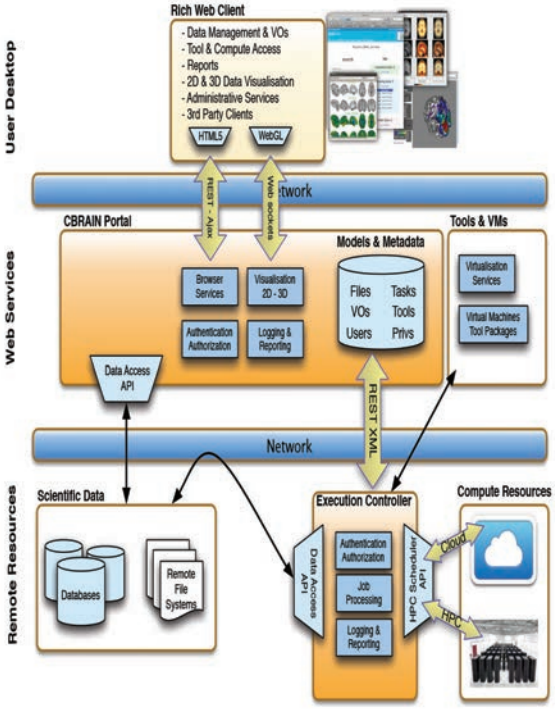


Figure 2: The CBRAIN portal removes complexity of interacting with HPC facilities.

Visualization

BrainBrowser (www.cbrain.mcgill.ca) is a WebGL-mediated web browser for interactive exploration of 3D surface-based data (e.g. output of Surfstat). It can be used to manipulate structural or functional surface maps.

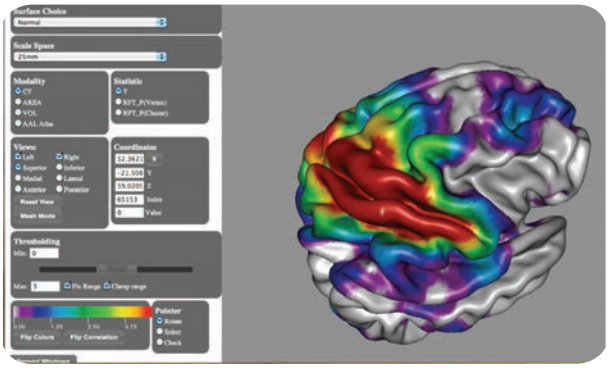


Figure 3: BrainBrowser allows interactive exploration of surface-based data, either structural or functional.

Atelier3D (or A3D) is a 3D interactive viewer for exploration of large datasets such as the Big Brain (see below) which is approximately 1 Terabyte in size. A3D uses a hierarchical block decomposition of the volume to allow rapid multiplanar and oblique cuts through the volume.

The Big Brain

Originally collected by Katrin Amunts' group in Juelich, this dataset consists of 7404 serial coronal sections of 20 µm thickness, Merker-stained for high contrast between cell bodies and neuropil. Each section was digitized with a flat-bed scanner at 10 µm resolution (11K x 13K). After extensive processing by Evans' group to remove distortions, rips/tears, optical imbalance etc., all sections have been reconstituted into a 3D volumetric dataset with 20 µm isotropic resolution. Advanced visualization tools allow for real-time arbitrary oblique sectioning and exploration of this 1 Terabyte dataset (~125,000 larger than a typical MRI volume).

We propose to develop this dataset as a reference template that will facilitate the integration of information at different spatial scales. We propose to develop the tools for handling the Big Brain (i) non-linear spatial normalization into stereotaxic space, a non-trivial challenge given the different intensity distribution between the Merker-stain and the intensity distribution of the target MRI volume, (ii) gross morphometric analysis: e.g. multivariate tissue-classification, volume-of-interest segmentation and cortical surface extraction, (iii) fine morphometric analysis: e.g. cortical thickness, cortical layering, cerebellar folial morphometry.

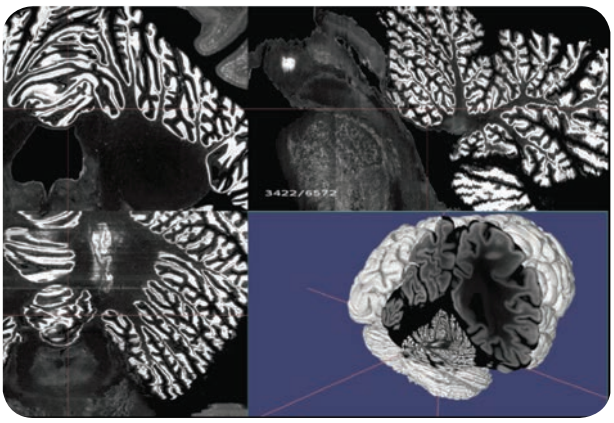


Figure 4: The Big Brain, showing orthogonal sections through cerebellum (original sections in top left) and a 3D context for the three section planes in A3D (bottom right).

HUMAN RESOURCES

The CBRAIN team in Montreal consists of 10 IT professionals with extensive experience in coding (C++, Java, Python etc.), web services, databasing, pipeline processing and workflow management. CBRAIN is designed to provide a national IT platform for brain research. In addition to CBRAIN, the MNI group contains some 20-30 programmers/trainees with experience in all forms of brain image analysis. We believe that this community would be a major node for INCF, at both national and international levels. The CBRAIN are already tightly coupled with CANARIE and Compute Canada and INCF is a natural fit for CBRAIN. Within INCF, the MNI could participate in the building of an international IT infrastructure, making available CBRAIN technology. For instance, Dr. Evans' group is the only Canadian participant in the Human Brain Project (Markram, Frackowiak). We already collaborate on specific international projects that can make use of the CBRAIN infrastructure, such as the Big Brain project with Katrin Amunts/Karl Zilles in Juelich and the NeuGrid/OutGrid network (Frisoni et al., 2011). We believe that the extensive CBRAIN international links in India, Korea, China, Latin America would be a major contribution to INCF growth. In order to further develop these ideas, we propose to host an INCF delegation at the MNI in Summer 2012, following HBM in Beijing, with the purpose of exploring synergies at both technical and scientific levels.

Todd S Woodward, University of British Columbia, Vancouver, BC

Constrained PCA for Relating Deconvolved fMRI Signal to Experimental Conditions



Tood Woodward

Introduction

A number of challenges face connectivity-based, data driven (exploratory) analyses of fMRI data. One challenge is to isolate the neural networks involved in the execution of the experimental task. A second is how to do this without imposing strong assumptions about the shape of the hemodynamic response associated with the task. A third is identification of a method for determining whether or not a neural network is reliable. A fourth is to statistically compare activation in these neural networks across experimental conditions, and across groups. A fifth is to identify the percentage

of variance in the fMRI signal accounted for by stimulus presentation, and by each neural network separately. Constrained Principal Component Analysis for fMRI data (fMRI-CPCA; Woodward et al., 2006; Woodward et al. in press; Metzak et al., 2012) provides solutions to these challenges. This software is freely available from the NITRC web site for neuroimaging tools (www.nitrc.org/projects/fmricpca).

Methods

Isolation of neural networks involved in execution of the experimental task is achieved by using regression to determine BOLD signal variance that is predictable from the stimulus timing. A hemodynamic-response-shape-free finite impulse response (FIR) model is used as predictor variates in this multivariate multiple regression. The reliability of the networks are determined by producing subject-, condition- and timepoint-specific FIR models, with the involvement of each neural network in each combination quantified by a single number (predictor weight). Analyzing these predictor weights using a traditional ANOVA allows significance testing (on the peristimulus time factor) to determine whether or not the component is reliable. ANOVA interactions with condition or group indicate whether the HDR shape depends on condition and/or group. Oblique rotation can be applied, providing temporal correlations between component scores. Finally, the percentage of BOLD signal variance accounted for by the multivariate multiple regression (i.e., by stimulus presentation) is readily available, as are the percentages of variance accounted for by each component.

The simplest application of CPCA involves preparation of two matrices. The first contains columns of normalized and smoothed subject-mean-centered activations for all voxels over all scans: Z. The second, G, contains the FIR model of the expected BOLD response to the timing of stimulus presentations. Multivariate multiple regression is then carried out:

$$Z = GC + E \quad (1)$$

Where $C = (G'G)^{-1}G'Z$

The predicted scores from this multivariate multiple regression (GC) are then submitted to singular value decomposition (SVD), and this produces the component scores (TRs) and component loading (voxels).

$$UDV' = GC \quad (2)$$

The component loadings in V can be (optionally) rotated, thresholded and displayed on a brain image. All statistical testing is carried out at the random effects level on the matrix P (predictor weights), where

$$U = G*P.$$

Results

The following fMRI-CPCA analysis results are from a working memory experiment investigating schizophrenia using the Sternberg paradigm, whereby 2, 4, 6 or 8 letters were encoded during a 4 second display, and maintained in short term memory for 6 seconds, at which time 1 letter was displayed and subjects were required to indicate whether or not they had previously viewed that letter. The fMRI-CPCA analysis resulted in a 3-component solution (see Figure 5). The results suggest that working memory capacity is reached sooner for schizophrenia patients as the overt levels of working memory load increase, evident in Components 2 and 3.

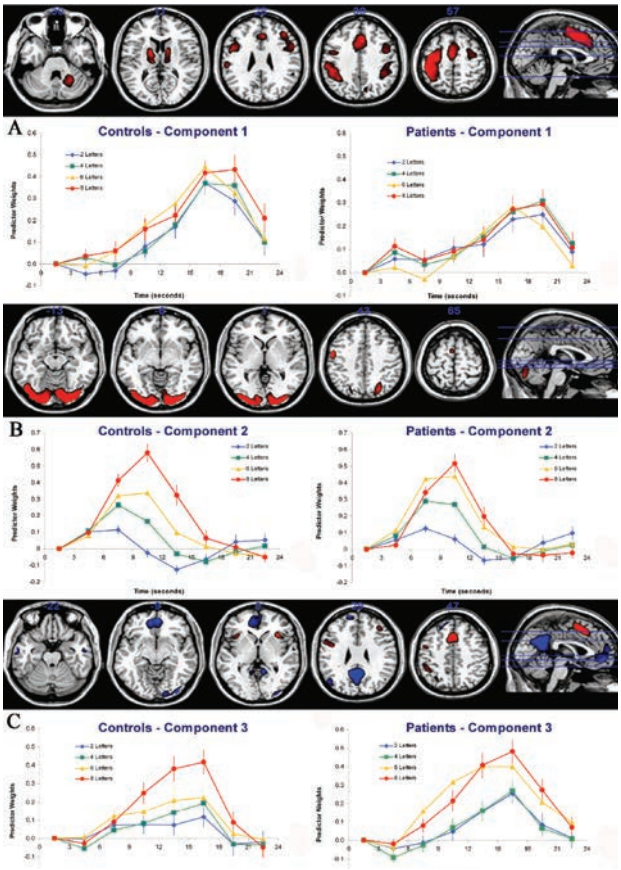


Figure 5: The dominant 5% of component loadings from each extracted component (rotated V) image displayed on a structural brain image template. (A) Component 1 image with positive component loadings displayed in red (min = 0.26, max = 0.34). No negative

component loadings passed this threshold. Axial slices are located at the following MNI z-axis coordinates: -30, 11, 28, 38, 57. (B) Component 2 image with positive component loadings displayed in red (min = 0.21, max = 0.35). No negative component loadings passed this threshold. Axial slices are located at the following MNI z-axis coordinates: -13, -6, 1, 43, 65. Error bars are standard errors. (C). Component 3 image with negative component loadings displayed in blue and positive component loadings displayed in red (min = |0.14|, max = |0.23|). Axial slices are located at the following MNI z-axis coordinates: -22, -9, 0, 29, 47. For each component, the mean FIR-based plot of predictor weights for healthy controls and schizophrenia patients are plotted as a function of peristimulus time and are located beneath the functional brain image for the respective component. Error bars are standard errors. Previously published in Metzak et al., 2012.

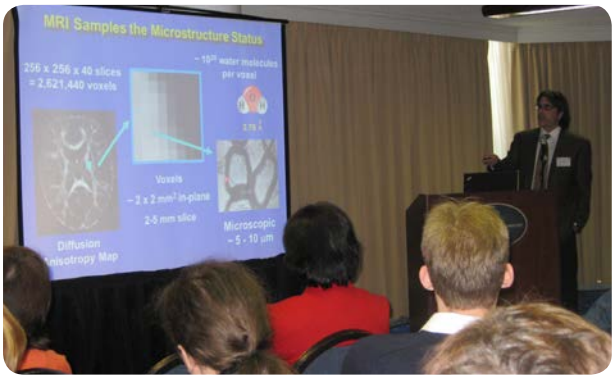
Conclusions

This FIR-CPCA analysis software provides a method for assessing functional connectivity between neural regions engaged by a verbal delayed recognition task. This approach allowed (1) determination of multiple functional networks involved in working memory, (2) estimation of the pattern of BOLD changes associated with each functional network over peristimulus time points, and (3) a statistical test of the degree to which experimental manipulations (in this case working memory load and group) affects each functional network. The ability to visualize the pattern of activity of a correlated network over time, and its sensitivity to experimental manipulations, is suited particularly to investigation of multiple-stage cognitive tasks.

Christian Beaulieu, University of Alberta, Edmonton, AB

The Power and Perils of the Diversity of Quantitative Structural Brain Imaging in Clinical Studies

Imaging of the brain non-invasively, by such methods as magnetic resonance imaging (MRI), is an essential part of modern neuroscience for investigating the underlying brain abnormalities associated with neurological and psychiatric disease. Clinical MRI relies on qualitative viewing of evident lesions and anomalies to aid in diagnosis; however, quantitative measurements highlight brain differences not apparent by qualitative analysis. Further, many more types of images with complementary contrasts are acquired in a research setting and yield novel physiological/microstructural information otherwise not attainable. These include measurements of white matter wiring and myelination, iron deposition, cortical function and thickness, blood vessels, perfusion, and metabolism. Modern day protocols thus generate an enormous amount of raw data which then is post-processed to generate numerous quantitative parametric maps that require regional brain analysis. This "shot-gun" approach is more readily achieved at high static magnetic fields due to greater signal and is attractive to researchers to eek the most of expensive scanner time and to provide a comprehensive view of the status of the brain in a given patient. The ultimate goal is to determine which, if any, of the methods provide the most diagnostic and prognostic information that is clinically relevant and ought to be incorporated into clinical MRI protocols of that patent group. However, protocols for the same type of scan vary from site-to-site, even with the same scanner model, which result in different quantitative metrics that complicate the amalgamation or comparison of data between studies.



Christian Beaulieu

This is not surprising as there is no "one size fits all" MRI protocol. Further, the data overload is evident in that even a rather simple protocol, as that used by the NeuroDevNet Fetal Alcohol Spectrum Disorders demonstration project, acquires 7348 brain slice images in 22 minutes (T2, FLAIR, DTI, T1, resting state fMRI). The analysis of the numerous brain regions, particularly in ever more common large population studies, becomes problematic necessitating more automated

Voices of the Community

Gunnar Blohm



"I see value in INCF membership for several reasons. (1) being part of an international organization that promotes computational neuroscience nationally and internationally could lead to more and better funding opportunities. (2) access and contributions to training highly qualified personnel and students. (3) a better organization and coordination of computational neuroscience within Canada."

pipelines that make a number of assumptions that may compromise the accuracy and rely on extensive computing resources. In most cases, there are multiple software packages and strategies to analyze each data set, each with their advantages and disadvantages. In summary, modern imaging is capable of providing a wealth of key information from the human brain and provides insights not achievable in any other way, yet the vast range of contrasts, acquisition protocols, and post-processing options is both a blessing and a curse.

Stephen Strother, Universtiy of Toronto, Baycrest, Toronto, ON

Ontario Experience with the XNAT-based Stroke Patient Research Recovery Database



Stephen Stroher

We have 4 years' experience with a multi-centre neuroinformatics infrastructure designed to support the Heart and Stroke Foundation Centre for Stroke Recovery (CSR) in Ontario. CSR is a unique 10-year old virtual centre encompassing a three-site collaboration between the University of Ottawa, Sunnybrook Health Sciences Centre and Baycrest in Toronto (http://heartandstroke-centrestrokerecovery.ca/). The Stroke Prevention and Recovery Research Database (SPReD) is a centre-wide platform spanning the multiple CSR sites in two cities. SPReD is based on the Extensible Neuroimaging Archive Toolkit (XNAT), an open-source imaging informatics platform developed at Washington University (www.xnat.org). Initiated in 2008 SPReD is a multisite, platform initiative that contains extensible demographic, behavioural, clinical, genetic and imaging modules. Design goals for SPReD included: 1) flexible integration of existing and local front-end databases (e.g., MySQL, Access) and web-based data entry (e.g., RedCAP); 2) integration of common data across independent studies where possible with ongoing, bottom-up "common data element" (CDE) program; 3) a flexible security model controlled by principal investigators who own and have legal responsibility for project data; 4) highly secure subject ID vault for management and matching of subjects' identified data; 5) federated Advanced SPReD Query (ASQ) tool allowing existence of limited through extensive data to be obtained on CSR projects within regulatory requirements across multiple SPReD sites; 6) automated launching and reintegration of processed neuroimaging data with provenance using image processing pipeline managers (e.g., LONI pipeline) and high performance computing infrastructure accessed through the CBRAIN portal (https://cbrain.mcgill.ca/research/ace-lab).

3. Session 2B: Neuroinformatics in Canada - Computational Modelling

Chair: Linda Lanyon

John K. Tsotsos, Department of Computer Science & Engineering and Centre for Vision Research, York University, Toronto, ON

Attending via Selective Tuning: From Computational First Principles to Predictions and Experiment

The goal of the Selective Tuning model is to understand attentive visual processes. By contrast with other models, it is not based on nor does it easily account for quantitative performance data (as do Sperling et al. or Bundesen) and is a 'first principles' theory exactly in the Marr sense. The model exhibits explanations and predictions across levels of abstraction - neural, systems, behavior - and the predictions have strong supporting evidence. It is fully implemented to function from image acquisition to behavioral output (in a computer vision sense). The major conclusion is that attention controls how the visual cortex is used in any given task. The research also shows how it is possible to derive a theory from first principles (without training or fitting data) using the language of computation with strong explanatory and predictive power.

G**unnar Blohm,** Computational Sensorimotor Neuroscience Lab, Queen's University, Kingston, ON

Theoretical Bridges between Behaviour and Neurophysiology in Sensory-motor Function

After introducing the computational neuroscience group at Queen's University, I presented the research questions my lab tries to answer. As an example, I elucidated my multi-disciplinary research approach in the field of sensory-motor transformations. To get an in-depth understanding about how single neuron properties lead to behaviour, we use analytical models, numerical simulations, behavioural experiments, brain imaging and patient work. I believe that computational modelling is a crucial component of efficient and hypothesis-driven scientific work.



Gunnar Blohm

Matthijs van der Meer, Department of Biology and Centre for Theoretical Neuroscience, University of Waterloo, ON

Model-based Prediction in the Rodent Hippocampus

The hippocampus is a brain structure most famously associated with episodic memory -- the ability to recall what happened on our 18th birthday, or where we parked our car this morning. By recording from large ensembles of neurons in the rat hippocampus, we can ask how neural activity during experience relates to subsequent memory and behavioral choice informed by that memory. Decoding these neural ensembles reveals that the hippocampus compresses ongoing experience into repeating sequences, which can "look ahead" or "look behind" the animal as required. Furthermore, subsequent recall is not limited to literal "replay" of experience but includes, for instance, sequences not previously experienced. Finally, neurons in the ventral striatum, a reward-related brain structure



Matthijs van der Meer

that receives inputs from the hippocampus, participate in these hippocampal timing phenomena. Simulations using spike timing-based learning rules show that hippocampal compression of ongoing experience facilitates the rapid association of places and rewards. Taken together, these observations contribute to a mechanistic theory of how hippocampal memories form a predictive world model useful for, say, taking a shortcut directly to your car in the parking lot.

4. Session 2C: Neuroinformatics in Canada - Clinical Neuroinformatics

Chair: Paul Pavlidis

Ibolja Cernak, University of Alberta, Edmonton, AB

Military Relevant Traumatic Brain Injury Research - Challenges and Opportunities

Based on the U.S. Defense and Veterans Brain Injury Center analysis, close to 250,000 U.S. military service members had a diagnosis of traumatic brain injury in the period of 2001–2012. The overwhelming distribution of mild traumatic brain injury was caused by blast. Because many servicemen with potential brain damage remain undiagnosed or have delayed diagnosis, this number could be potentially higher. Neurological consequences of blast exposure(s) and related



Ibolja Cernak

psychological impairments have been recognized as significant health problems among Canadian Forces (CF) military personnel and veterans also. Blast-induced neurotrauma (BINT) is caused by a complex physical environment generated by an explosion and diverse effects of the resulting blast. While the majority of current studies focuses on direct blast-head interaction, the role of multi-organ response in BINT is underestimated. Potential mechanisms by which blasts cause brain injury include: (1) direct interaction with the head through direct passage of the blast wave through the skull and/or causing acceleration and/or rotation of the head and (2) transfer of kinetic energy from the blast wave through large blood vessels in the abdomen and chest to the central nervous system; namely, as the front of the blast overpressure interacts with the

body surface and compresses the abdomen and chest, it transfers its kinetic energy to the body's fluid phase. The resulting hydraulic interaction initiates oscillating waves that traverse the body at about the speed of sound in water and deliver the kinetic energy of the blast wave to the brain. Once delivered, that kinetic energy causes both morphological and functional damage to distinct brain structures. The two potential ways of interaction do not exclude each other. Most recent experimental data suggest both the importance of the blast's direct interaction with the head, and the role of the whole-body involvement and consequent shockwave-induced vascular load in the pathogenesis of BINT. Thus, BINT is caused by multiple, interwoven mechanisms of systemic, local, and cerebral responses to blast exposure, often interacting with the body simultaneously. Recent experimental and clinical results clearly demonstrated the importance of the blast–body interaction as well as the decisive role of autonomous nervous–neuroendocrine–immune systems interaction in the pathogenesis of BINT suggesting that shielding the head alone without preventing the coupling of the blast wave with the torso and subsequent energy transfer inside the body would not provide efficient protection from BINT. New protective materials and strategies are needed to achieve an effective protection from blast effects.

Recent studies involving CF personnel estimated that 10–15% of deployed military forces will become stress casualties. However, many deployed military personnel never leave the relative safety of a base camp where they are employed in logistical support, while other combat support soldiers regularly experience the hardship of the combat area even though their primary role does not include engagement with the enemy. Hence, there is a possibility that the numbers within the combat units are actually higher, probably in the range of 30%. Our new clinical research project using a personalized medicine approached aims to answer the question what makes 70% of soldiers resilient toward BINT and related long-term neurological deficits; post-traumatic stress disorder (PTSD); major depressive disorder (MDD); or other stress-related symptoms when they too have been exposed to stressful events? We will utilize state-of-the-art knowledge that measures the influence of the environment on functional integrity and the capacity of the individual to respond to BINT, ability to compensate and/or repair the injury-induced deficits, and the likelihood of responding positively to treatments. The measurements will provide a biological, objectively quantifiable anchor for subjective feelings and self-reported information. The information gained will also provide insight into the progress of the disease (BINT), its co-morbidities (PTSD or MDD), and the efficacy (positive, negative, or status-quo) of treatment-induced effects. All collected data will be entered in a machine learning system to utilize the data sets and identify linear and/or highly complex, non-linear relationships between biological and functional performance measures to reach predictive ability.



Elodie Portales-Casamar and Paul Pavlidis

5. 2D: Neuroinformatics in Canada - Neurogenomics

Chair: Linda Lanyon

Paul Pavlidis, Associate Professor of Psychiatry / Centre for High-throughput Biology. Scientific Director, NeuroDevNet Neuroinformatics Core

Neurogenomics and Knowledgebases

The neuroinformatics-related research in my lab is centred on the analysis of neurogenomics data and the development of relevant algorithms, tools and knowledgebases. First I presented Gemma, our database system for functional genomics data meta-analysis (http://www.chibi.ubc.ca/Gemma), and a motivating case study of a meta-analysis of gene expression patterns in the postmortem human brain in schizophrenia. I described Neurocarta, a database of gene-phenotype relationships initially focused on neurodevelopmental disorders, and touch on challenges in the interpretation of gene function using gene networks. I then described ongoing work to develop a novel database of anatomical neural connectivity using text mining approaches. I presented an application of such knowledgebases to the interpretation of gene expression patterns in the rodent brain.

Dan Goldowitz, Centre for Molecular Medicine and Therapeutics, University of British Columbia. Scientific Director, NeuroDevNet



Lions Gate Bridge, Vancouver, Canada

The Intersection of Biology and Informatics for Insights into the Regulation of Genes in Cerebellar Development

With the technology available to query the whole transcriptome of a single cell or tissue, it falls to bioinformatics to help process the data to make sense of gene to gene interactions and the regulatory networks that drive biological processes. However, single snapshots of the transcriptome are an impoverished way to find meaningful gene interactions. In our work, we have utilized a simple neuronal structure, the cerebellum, and sampled the transcriptome of the whole cerebellum in the C57BL/6J mouse at 24-hour periods over embryonic development and then over 3 day periods during the first week of postnatal life. These data have been normalized and subjected to three bioinformatic algorithms to gain an appreciation of the genes and gene networks that may be key to specific processes of cerebellar development. The project is called Cerebellar Gene Regulation in Time and Space (CbGRiTS) and is available to developmental biologists and neuroscientists to explore the role of genes in brain development and to algorithm developers to apply their special informatic analyses to the dataset. To enhance exploration of the data we have linkouts to the major, online in situ hybridization databases (Allen Brain and GenePaint), a graph function, and a gene saving function to accumulate results from searches. We also have included data from the DBA/2J mouse as a complementary dataset to the B6 mouse and three mutants that target the cerebellar granule cell. We see CbGRiTS as a community resource to apply informatic tools to explore this rich time-series data an develop hypotheses concerning gene regulatory networks in brain development.

Discussion about Canada´s Future Involvement with INCF

Chair: Linda Lanyon

Following the scientific agenda, the meeting concluded with a discussion about strategies for forming an INCF National Node, and the benefits of having such a Node in Canada. Discussion began with the question of whether the scientists present saw a benefit in Canada joining INCF, what could INCF offer Canada and what could Canadian researchers contribute to INCF's programs & infrastructure.

Participants were highly enthusiastic about Canada's contribution to collaborative international neuroinformatics: Canada is big enough to have an international impact and small enough to collaborate easily. There exists a strong alignment between Canadian neuroinformatics efforts and the aims and work of the INCF. In addition, Canadian research could extend the current domains within the INCF community. Canada has a very strong neuroethics core that could contribute greatly in steering this theme within INCF's current and future Programs. By being a part of an INCF Node and involved in INCF's Program, Canadian researchers would be able to foster collaborations with people and projects across the INCF network.

Voices of the Community

Jill Kowalchuk, Interim Executive Director, Compute Canada - Calcul Canada



"Compute Canada - Calcul Canada is eager to work with the Canadian neuroinformatics community and INCF to support the creation of a national node in the INCF network. Our role is to provide infrastructure and support for exactly the types of research which were presented at the workshop. We already have a good working relationship with CBRAIN and with individual neuroinformatics researchers in Canada. We also have experience in supporting international collaborations of this nature and are happy to help however we can."

INCF membership would increase training opportunities in the field: there is currently no course in neuroinformatics in Canada. Junior Canadian researchers participating in INCF's task forces would have the opportunity to work alongside senior researchers from other countries.

The addition of a Canadian Node to the INCF network would align parallel efforts, avoid duplication of work and allow Canada to more fully contribute to emerging international standards within the field. Clinical standards, for example, will be worked out internationally over the next few years: Canada will miss out on participation in standards setting is it waits too long to join. Importantly, being an INCF Node and having representation on the INCF Board of Directors would allow Canada to play a leading role in setting the agenda for international neuroinformatics. The workshop participants defined themselves as a group of Canadians who wanted to pursue this adventure.

The only challenge in Canada achieving INCF membership was seen to be obtaining the funding for the membership fee. In-kind contributions cannot be accepted so it would be necessary to raise the money from funding agencies. Participants highlighted the necessity to demonstrate to funding agencies how the money would be returned to Canada. INCF can provide a list of benefits of membership (and has since done so when requested by an agency) but does not pay money to its National Nodes. However, INCF membership can be used to raise funding for Node activities, as has been done by the United Kingdom Node.

Suitable funding agencies are CIHR, NSERC and CANARIE. Compute Canada - Calcul Canada is also very relevant: though they cannot provide money, they could help later to provide computing resources, possibly in collaboration with CANARIE. Brain Canada has an infrastructure program that is an excellent fit for this field but their funding model provides money that must stay within the country: this could be a source of funding for Node activities.

1. Next Steps Action Plan

In order to help establish a stronger cohesive Canadian Neuroinformatics Community, the participants determined that following are required:

1. We need a registry:

    a. The community needs an email list where neuroinformatics announcements can be made and people can connect.

    b. The community needs an web presence (wiki) where dialogue and ideas can be exchanged

2. We need to bring more people on board:

    a. Launch a campaign to reach everyone who would be interested (universities with relevant programs).

    b. Band together under a name.

    c. Write letters to scientists.

    d. A follow-up workshop could be integrated into a NeuroDevNet event or next year's CAN meeting.

    e. Could CAN help through their membership to connect us to the community?

3. We should use the US as an example of the value of being part of INCF.

4. A small group should get together and write a white paper:

    a. Paul Pavlidis was identified as the potential lead for the Node.

    b. A committee needs to be organized that includes all disciplines and provinces. Many people volunteered:

        - Modeling: Gunnar Blohm
        - Clinical: Steven Strother
        - Neuroethics: Nina di Pietro
        - Neuroimaging: Alan Evans

5. It would be helpful to get feedback from INCF regarding what seems interesting to the international community from Canada's research profile.

6. We need to better define neuroinformatics to communicate with the community: INCF is working on this to reach a broader audience.

7. INCF will write the workshop report and this will be used in subsequent interactions with funding agencies.

2. Subsequent Activities

Following the positive response from the Canadian neuroinformatics community at the workshop, the momentum within the community has persisted and a number of activities have taken place:

The meeting helped foster the emergence of a Canadian Neuroinformatics Steering Committee (www.neuroinfocomp.ca/committee) which is currently working to improve the visibility of the field and help develop new funding and training opportunities. The current members of the Canadian Neuroinformatics Steering Committee are (alphabetical order):

- Gunnar Blohm, Queen's University, Kingston, ON
- Maurice Chacron, McGill University, Montreal, QC
- Chris Eliasmith, Centre for Theoretical Neuroscience, University of Waterloo, ON
- Alan Evans, Montreal Neurological Institute, McGill University, Montreal, QC
- Paul Pavlidis, Centre for High-throughput Biology, University of British Columbia, Vancouver, BC
- Stephen Strother, Baycrest, University of Toronto, ON
- Thomas Trappenberg, Dalhousie University, Halifax, NS

The development of the Canadian Neuroinformatics and Computational Neuroscience (CNCN) web site: www.neuroinfocomp.ca/ is the first initiative arising from this committee and will be the central point where future initiatives will be announced and released. INCF collaborated in the design of the logo for this site. The web site is a portal for communication with the community and its goal is to enhance the visibility and impact of neuroinformatics and computational neuroscience in Canada. The portal facilitates the sharing of knowledge and encourages knowledge transfer through commonly organized events, mailing lists and open-access teaching and research resources. The hope is that new collaborations and scientific coordination will be encouraged, leading to more efficient knowledge advancement and transfer. The site contains links to events, people, research, training and other resources. From the site, people can subscribe to an email list which is used for community announcements. After being in existence for one month, with no large-scale solicitation, more than 50 registrants representing ~20 universities and institutions in 5 provinces joined the Directory on this site. More are expected to join as the CNCN initiative becomes more widely known and promoted. The CNCN public directory of people can be found here: www.neuroinfocomp.ca/people.

Concentrations of expertise in neuroinformatics in Canada have been identified in the following sites:

- Centre for Vision Research (York)
- Centre for Theoretical Neuroscience (Waterloo)
- NeuroDevNet NCE Neuroinformatics Core (UBC)
- Montreal Neurological Institute (McGill)
- Rotman Research Institute at Baycrest (Toronto)
- Centre of Neuroscience Studies (Queen's)
- Canadian centre for behavioral neuroscience (Lethbridge)
- Centre for Neural Dynamics (Ottawa)

INCF has supported the community in these efforts by providing information and meeting with funding agencies. The INCF Secretariat remains ready to help and assist the Canadian community in any way as it prepares to form itself into an INCF Node.

Voices of the Community

Matthijs van der Meer

Thank you very much for making the INCF workshop such a success, and for bringing the INCF to Canada. I'm very excited by the prospect of a Canadian node - I feel the time is right for a coordinated effort to make informatics more accessible to Canadian neuroscience, and provide an avenue for Canadian neuroscience to contribute to projects with global reach.… The large datasets generated by my lab offer rich potential for computationally intensive analysis and integration with large scale models. Many neuroinformatics challenges and opportunities arise from this approach, and are shared by a significant number of labs in the field. I can see several ways in which a Canadian INCF node would be valuable: maximizing the impact of data and other lab deliverables, benefiting from training and networks, facilitating awareness, contacts and advocacy, avoiding duplication of effort through international coordination and bringing a Canadian voice at the table where global initiatives are shaped …I have many friends and colleagues who are also interested in organizing Canadian neuroinformatics/computational neuroscience, so I hope an avenue to engage them can be created soon."



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Totem poles at Stanley Park, Vancouver, Canada

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Program

May 24th
Sheraton Wall Centre

9:00 am
Dr. Paul Pavlidis, Scientific Director, NeuroDevNet Neuroinformatics Core
Introduction and Welcome

Session 1: International Neuroinformatics Coordinating Facility INCF

9:15 am
Dr. Sean Hill, INCF Executive Director, Karolinska Institute, Stockholm
Role of INCF: Toward a Global Collaborative Infrastructure for Neuroscience

9:55 am
Dr. Maryann Martone, UCSD, La Jolla, CA
Navigating the Neuroscience Data Landscape

10:25 am
Dr. Rob Williams, Department of Anatomy and Neurobiology and Center for Integrative and Translational Genomics, UTHSC, Memphis, TN, USA
Atlases, Genomes, and Genetics: An International Tool Set to Help Understand Brain Function

10:55 - 11:10 am
Coffee break

Session 2A: Neuroinformatics in Canada - Neuroimaging

11:10 am - 12:35 pm
Dr. Alan Evans, MNI, McGill, Montreal, QC
CBRAIN: A Global HPC Portal for Brain Imaging Research
Dr. Todd Woodward, UBC, Vancouver, BC
Relating Functional Networks to Experimental Conditions: CPCA for fMRI and MEG Data
Dr. Christian Beaulieu, U. of Alberta, Edmonton, AB
The Power and Perils of the Diversity of Quantitative Structural Brain Imaging in Clinical Studies
Dr. Stephen Strother, Baycrest, U. of Toronto, Toronto, ON
Ontario Experience with the XNAT-based Stroke Patient Research Recovery Database

12:35 - 1:35 pm
Lunch (provided in Sheraton)

Session 2B: Neuroinformatics in Canada - Computational Modelling

1:35 - 2:40 pm
Dr. John Tsotsos, Computer Science & Engineering and Centre for Vision Research, York U., Toronto, ON
Attending via Selective Tuning: From Computational First Principles to Predictions and Experiment
Dr. Gunnar Blohm, Queen's U., Kingston, ON
Theoretical Bridges between Behaviour and Neurophysiology in Sensory-motor Function
Dr. Matthijs van der Meer, CTN, U. Waterloo, ON
Model-based Prediction in the Rodent Hippocampus

Session 2C: Neuroinformatics in Canada - Clinical Neuroinformatics

2:40 - 3:00 pm
Dr. Ibolja Cernak, U. of Alberta, Edmonton, AB
Military Relevant Traumatic Brain Injury Research - Challenges and Opportunities

3:00 - 3:20 pm
Coffee break

Session 2D: Neuroinformatics in Canada - Neurogenomics

3:20 - 4:00 pm
Dr. Paul Pavlidis, CHiBi, UBC, Vancouver, BC
Neurogenomics and Knowledgebases
Dr. Dan Goldowitz, CMMT, UBC, Vancouver, BC
The Intersection of Biology and Informatics for Insights into the Regulation of Genes in Cerebellar Development

4:00 pm Discussion
Discussion about the strategies for forming an INCF national node, and the benefits of having such a node in Canada

7:00 pm
Dinner (invitation only)

INCF Canadian

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