

# Final Report for the SAMSI Program on Challenges in Computational Neuroscience (2015–2016)

Directorate Liaison: Thomas Witelski

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## Summary

The Program on Challenges in Computational Neuroscience was a year-long research program taking place at SAMSI in 2015-2016. It brought together a wide array of researchers in mathematics, statistics, neuroscience and biostatistics to advance current questions in neuroimaging of activity in the brain, modeling of networks of neurons, and other related areas. This report gives an overview of the participants, the working groups and the workshops organized as part of this program.

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# 1 Overview

Neuroscience is a field that is accumulating exponentially growing volumes of data on specific aspects of the healthy and diseased brain, in different species, and at different ages. Brain theory, modeling, and statistics will be essential to turn this data into better understanding of the brain.

The Challenges in Computational Neuroscience (CCNS) program was targeted to develop mathematical and statistical methods in neuroscience to meet this critical need. Key problems include understanding the mechanisms that bridge multiple spatial and temporal scales, linking the activity of individual components (e.g., molecular biology, genetics, and neuron networks) and their interactions to the overall complex dynamic behavior of the brain and nervous system.

The CCNS program brought together researchers that could address the underlying methodological, theoretical, and computational challenges. Probability and statistics, dynamical systems, geometry, and computer science will be combined with respect to theory and in applications. Researchers in neuroscience, biomedical engineering, computer science, applied mathematics, and statistics were encouraged to apply to the program.

## 1.1 Research workshops and focal activities

The CCNS program has highlighted by several meetings that brought together leading researchers to discuss important issues in neuroscience. Details on each workshop will be given in Section 2:

1. Program Planning Workshop, August 4, 2014
2. Opening Workshop, August 17-21, 2015
3. Workshop on Challenges in Linking Statistical and Mathematical Neuroscience, October 14-15, 2015
4. Neuromuscular Control and Collective Behavior Workshop, January 13-15, 2016
5. Workshop on Mathematical and Statistical Challenges in Neuroimaging Data Analysis, January 31-February 5, 2016
6. Workshop on Optical Imaging Data Analysis, February 1-2, 2016
7. Workshop on Mathematics of Neural Networks and Neural Codes, March 9-11, 2016
8. Workshop on Challenges in Functional Connectivity Modeling and Analysis, April 8-10, 2016
9. Transition Workshop, May 4-6, 2016

## 1.2 Working groups

There were eleven working groups focusing on different research problems within the scope of the program. The working groups commenced meetings starting at the Opening Workshop in the fall. The leaders of the groups are given below. Details on the ongoing activities of each of the working groups are given in Section 3:

1. Clinical brain imaging  
Ciprian Crainiceanu (Johns Hopkins University)

2. Computational approaches to large-scale inverse problems with applications to neuroscience  
Arvind Saibaba (North Carolina State University)
3. Understanding neuromechanical processes in locomotion with physical modeling and network analysis  
Laura Miller (University of North Carolina), Katie Newhall (University of North Carolina)
4. Mathematical and statistical approaches to modeling brain networks: circuits and systems  
Rob Kass (Carnegie Mellon University), Uri Eden (Boston University), Mark Kramer (Boston University)
5. Theory of neural networks: structure and dynamics  
Carina Curto (Pennsylvania State University), Brent Doiron (University of Pittsburgh), Chris Hillar (University of California San Francisco and University of California Berkeley)
6. Acquisition, reconstruction, and processing of MRI data  
Daniel Rowe (Marquette University)
7. Imaging genetics  
Hongtu Zhu (University of North Carolina)
8. Structural connectivity  
David Dunson (Duke University), Hongtu Zhu (University of North Carolina)
9. Functional imaging methods and functional connectivity  
Hernando Ombao (University of California-Irvine), John Aston (University of Cambridge)
10. Big data integration in neuroimaging  
Martin Lindquist (Johns Hopkins University), Timothy Johnson (University of Michigan)
11. Analysis of optical imaging data  
Mark Reimers (Michigan State University)

### 1.3 Educational activities

The undergraduate and graduate educational activities connected with the CCNS program will be described in Section 4:

1. Computational Neuroscience Summer School, July 27-31, 2015
2. Undergraduate workshop, October 19-20, 2015
3. Graduate Courses:
  - (a) Fall 2015 Course: Statistical Methods for Neuroimaging Data Analysis
  - (b) Spring 2016 Course: Mathematics of Neural Networks and Neural Codes

### 1.4 Program leaders

The main organizer of the program was Professor Hongtu Zhu (previously at University of North Carolina, now University of Texas MD Anderson Cancer Center). He was pivotal in bringing together other important researchers in computational neuroscience to develop the program. Zhu had previously organized a summer program on Neuroimaging Data Analysis at SAMSI in June 4-14, 2013.

The national program leaders for the CCNS program were:

- Ciprian Crainiceanu (Johns Hopkins University)
- Carina Curto (Pennsylvania State University)
- Bard Ermentrout (University of Pittsburgh)
- Timothy Johnson (University of Michigan)
- Robert Kass (Carnegie Mellon University)

- Thomas Nichols (University of Warwick, United Kingdom)
- Liam Paninski (Columbia University)
- Daniel Rowe (Marquette University)
- Victor Solo (University of New South Wales, Australia)
- Anuj Srivastava (Florida State University)
- Bin Yu (University of California, Berkeley)

Additionally, the committee of Local Scientific Coordinators was:

- David Dunson (Duke University)
- J. S. Marron (University of North Carolina)
- Ezra Miller (Duke University)
- Haipeng Shen (University of North Carolina)
- Rui Song (North Carolina State University)
- Hongtu Zhu (University of North Carolina)

The SAMSI Directorate Liaison for the program was Thomas Witelski (Duke University).

## 1.5 Postdoctoral associates

Four postdoctoral associates were hired in 2015 for the program:

1. Adam Jaeger (2015 Ph.D. University of Georgia) Scientific mentor: Ezra Miller, Duke University, Statistics
2. Benjamin Risk (2015 Ph.D. Cornell University) Scientific Mentor: Hongtu Zhu, University of North Carolina, Biostatistics
3. Sarah Vallelian (2015 Ph.D. University of Texas at Austin) Scientific Mentor: Arvind Saibaba, North Carolina State University, Mathematics
4. Zhengwu Zhang (2015 Ph.D. Florida State University) Scientific Mentors: Hongtu Zhu, University of North Carolina, Biostatistics and David Dunson, Duke University, Statistics

## 1.6 Visitors

There were a number of long term visitors for the program:

- D. Andrew Brown (Clemson)
- Ciprian Crainiceanu (Johns Hopkins University)
- Ivor Cribben (University of Alberta)
- Carina Curto (Pennsylvania State University)
- Subharup Guha (University of Missouri)
- Chris Hillar (University of California Berkeley)
- Vladimir Itskov (Pennsylvania State University)
- Bei Jiang (Columbia University)
- Linglong Kong (University of Alberta)
- Michael Lavine (University of Massachusetts-Amherst)
- Xi Luo (Brown University)

- Vic Patrangenaru (Florida State University)
- Lingyun Qiu (University of Minnesota)
- Daniel Rowe (Marquette University)
- Huiyan Sang (Texas A&M University)
- Jianqing Shi (Newcastle University)
- Ramon Vera (Pennsylvania State University)
- Xiao Wang (Purdue University)
- Wei Wu (Florida State University)
- Yihong Zhao (New York University)
- Hongxiao Zhu (Virginia Polytechnic Institute)

## 1.7 Faculty fellows

The faculty from SAMSI's three parent Universities (Duke, UNC and NCSU) serving on the Local Scientific Committee or as Faculty Fellows constituted important core groups in the CCNS program. They were involved in many program activities including several working groups and mentoring postdocs and graduate students.

- Katherine Heller (Duke University, Statistics)
- Ezra Miller (Duke University, Mathematics/Statistics)
- Laura Miller (University of North Carolina, Mathematics)
- Katie Newhall (University of North Carolina, Mathematics)
- Rui Song (North Carolina State University, Statistics)
- Kai Zhang (University of North Carolina, Statistics)
- Hongtu Zhu (University of North Carolina, Biostatistics)

## 1.8 Graduate students

The following students were SAMSI graduate fellows in the CCNS program from the Triangle Universities:

- Darryl Wade (Duke University, Mathematics)
- Jieren Xu (Duke University, Mathematics)
- Chengchun Shi (North Carolina State University, Statistics)
- Yang Yu (University of North Carolina, Statistics)
- Julia Samson (University of North Carolina, Biology)
- Qunqun Yu (University of North Carolina, Statistics)

Additionally, Mary Kociuba (Marquette University, Math) was a long-term visiting graduate student for the whole year. She was doing research toward her thesis, supervised by Daniel Rowe. Similarly Simeng Qu (Purdue University) was a visiting graduate student in Fall 2015, working with her advisor Xiao Wang.

## 2 Research workshops

### 2.1 Program planning workshop

There was a meeting to plan the activities of the SAMSI program among many leading researchers in statistical neuroscience. The planning workshop was held at the 2014 Joint Statistical Meetings, in Boston on August 4, 2014.

In the meeting, key points for discussion were the scientific approaches and goals for the programs:

1. Organizing principles: there are two fundamental modeling approaches in the field
  - (a) Top-down: Data-driven studies that are characterized by statistical analysis, data processing and modeling working with real data sets from various measurement modalities (MRI, EEG, ...).
  - (b) Bottom-up: Modeling of neuroscience system in terms of fundamental elements including differential equation models for neuron spiking activity, physiology of individual neurons, and network theory.

And finally, the program should seek to integrate these approaches to generate better connectivity between groups and better awareness of remaining fundamental challenges in neuroscience.

2. Specific aims for the program:
  - (a) Training the next-generation of statisticians on computational neuroscience.
  - (b) Enhancing collaborations among statisticians, mathematicians with neuroscientists.
  - (c) Developing productive research working groups that generate conference talks, research papers, grant proposals, and survey/overview articles/book chapters.
  - (d) Making progress on clarifying the big questions in current neuroscience, with the involvement of real neuroscientists.

The attendees at planning meeting were: Hongtu Zhu, E. Brown, B. Caffo, C. Crainiceanu, T. Johnson, R. Kass, M. Lindquist, H. Ombao, T. Ogden, D. Rowe, V. Solo, R. Song, J.L. Wang, B. Yu, and representing SAMSI were Richard Smith and Thomas Witelski.

### 2.2 Opening Workshop

The Opening Workshop for the CCNS program was held on August 17-21, 2015 at the Hamner Conference Center, Research Triangle Park, North Carolina.

The Workshop provided an overview of the core topics in the CCNS program with particular attention to the development of methodological, theoretical, and computational treatments of high-dimensional mathematical and statistical models with applications in computational neuroscience.

On Monday, August 17 there were five overview lectures by leading researchers in computational neuroscience. From Tuesday to Thursday, invited speakers addressed additional issues associated with spike train data analysis, big data, the NIH BRAIN initiative, imaging genetics, and neuroimaging data analysis. A poster session and reception took place on Tuesday, August 18.

On Thursday August 20, Working Groups were introduced, centering on problems and research directions identified in the Workshop. These groups will meet weekly over the course of the program, with the initial meetings held on Friday August 21.

### 2.3 Workshop on Challenges in Linking Statistical and Mathematical Neuroscience

This workshop was held at Boston University on October 14-15, 2015 and was organized by Mark Kramer, Uri Eden, and Rob Kass.

The primary aim of this workshop was to identify areas of overlap, and potential synergies, in mathematical and statistical modeling in order to advance approaches that combine mathematical, computational, and statistical reasoning in neuroscience. Rapidly evolving technologies now permit the acquisition, storage, and analysis of vast spatiotemporal data sets of observations of the brain's activity which consists of extremely complicated dynamics propagating within the complex anatomy of the brain. To understand this data, modeling approaches that mathematically express scientific knowledge and rigorously connect the observed activity with non-obvious statistical and biological features are required.

This workshop was the focal activity of the working group on Mathematical and Statistical Approaches to Modeling Brain Networks.

## **2.4 Neuromuscular Control and Collective Behavior Workshop**

This workshop was held at SAMSI on January 13-15, 2016 and was organized by Katie Newhall and Laura Miller.

In most animals, the nervous system is a fundamental component of actuating movement. Swimming, flying, and maneuvering requires sensing the environment and controlling the movement accordingly. The goal of this workshop was to develop a preliminary model of the activation of muscles by motor neurons and the resulting effect on locomotion.

In general, the strength of the muscular response is proportional to the frequency of action potentials conducted along motor neurons combined with the fraction of motor neurons that are entrained to activate individual muscle fibers. The mapping of motor neuron signal to muscle response can vary greatly across organisms and between muscle types. The details of this mapping, particularly in terms of the dynamical response, will be a focus of the modeling efforts.

This workshop was a focal activity of the working group on Neuromechanical processes.

## **2.5 Workshop on Mathematical and Statistical Challenges in Neuroimaging Data Analysis**

The CCNS program co-sponsored a closely related 5-day workshop that was held at the Banff International Research Station: Mathematical and Statistical Challenges in Neuroimaging Data Analysis (16w5036) on January 31-February 5, 2016. The organizers of the workshop were Brian Caffo (Johns Hopkins University), Farouk Nathoo (University of Victoria), Hongtu Zhu, Linglong Kong, and Todd Ogden (Columbia University).

SAMSI supported the travel of several US participants to take part in the workshop. This included two SAMSI postdocs (Risk and Zhang), two graduate students, and five other junior faculty.

## **2.6 Workshop on Optical Imaging Data Analysis**

This workshop was held at SAMSI on February 1-2, 2016 and was organized by Casey Diekman (NJIT), Michael Lavine and Mark Reimers.

This workshop was aimed to introduce many statisticians to optical imaging data and present the major issues at present and expected in the near future. Optical imaging is widely considered the most promising technology to achieve the aims of the BRAIN initiative. New indicators of neural activity are being developed every year, and imaging technology improves continually. These data will revolutionize neuroscience, just as microarrays revolutionized genomics, and should be similarly fruitful as a stimulus to innovation in statistics. Nevertheless there are almost no statisticians currently working with these data, both because these data are unfamiliar and are harder to access.

The objectives were to introduce statisticians to the characteristics of optical technologies and to the kinds of statistical questions that are pressing now and may be appearing in the near future and to stimulate discussion about promising approaches to the largely unsolved statistical challenges of the new high-throughput optical data.

This workshop was a major activity of the working group on optical imaging.

## 2.7 Workshop on Mathematics of Neural Networks and Neural Codes

This workshop was held at SAMSI on March 9-11, 2016 and was organized by Carina Curto, Brent Doiron (University of Pittsburgh), Chris Hillar, and Vladimir Itskov.

This workshop featured a full day of talks, targeting specific areas in the theory of neural networks and neural codes that are currently active areas of research. The second and third days focused on research sessions to further collaboration among the participants.

On the networks side, the focus is on training and fitting various types of networks (discrete models, rate models, spiking models) to produce dynamic activity patterns. This necessitates both a deep understanding of the dynamics of the networks in question, as well as state-of-the-art fitting techniques. Recent theoretical advances have led to an improved understanding of the dynamics of threshold-linear network, spiking networks with embedded cell assemblies, and pattern storage in Hopfield networks. Data sets for training these networks consist of synthetic spiking data, generated by spiking networks where we can control the “ground truth,” and real spiking data from electrophysiological recordings.

On the neural coding side, the emphasis is on the further development of topological and algebraic methods for analyzing neural activity from simultaneous recordings of neurons. This activity can be pre-processed to obtain neural correlations and neural codes. Many mathematical questions arise when trying to understand how important features of correlation or coding structure can be extracted from these data. The workshop considered recent advances with participants, and built on existing research collaborations.

This workshop was the focal activity of the working group on the theory of neural networks.

## 2.8 Workshop on Challenges in Functional Connectivity: Modeling and Analysis

This workshop was held on April 8-10, 2016 at the Hamner Conference Center, Research Triangle Park, North Carolina. It was organized by Hernando Ombao, Daniel Rowe, Marina Vannucci (Rice University), and Ting-ting Zhang (University of Virginia).

In this workshop, there were lectures by experts who introduced to mathematicians and statisticians the substantive issues on characterizing and modeling connectivity, both structural and neuronal, using various data modalities that capture different facets of brain anatomy and functionality. There were invited talks from different experts in the area of space-time modeling to discuss state-of-the-art modeling approaches and their limitations; and to identify new lines of research that are motivated by the current neuroscientific problems. Finally, representatives from both NIH and NSF will provided information on existing funding opportunities and future directions of these two institutions. A panel shared their ideas about how to improve the presentation and organization of proposals.

This workshop was a major activity of the working group on functional connectivity.

## 2.9 Transition Workshop

This workshop was held at SAMSI on May 4-6, 2016 and was organized by Hongtu Zhu.

The transition workshop for the Computational Neuroscience program was an opportunity for the active working groups in the program to exchange results and share their perspectives on common issues. This workshop focused on the research progress that has been made in connection with the many areas spanned by the CCNS program. Sessions of talks were dedicated to each working group will feature presentations by active members. The workshop also sought to facilitate planning for continuing collaborations on further research questions to extend beyond the period of the CCNS program.

One notable follow-on activity is a special issue of the journal *Statistics in Bioscience* dedicated to the CCNS program. The issue, to be titled “*Challenges in Computational Neuroscience*” has guest editors Hongtu Zhu, Martin Lindquist, Timothy Johnson.



## 3 Working Groups

Each working group provided a summary of its activities during the CCNS program.

### 3.1 Clinical Neuroimaging

This research group is focused on clinical brain imaging with specific focus on structural magnetic resonance imaging (MRI) and computed tomography (CT) with application to the diseased brain. The first goal was to familiarize students with available tools for data analysis using a one-week training course. The second goal was to introduce students and researchers to several data sets and scientific problems of high interest in clinical research. We have focused on multiple sclerosis (MS) and stroke. Projects the group has worked on include:

1. Stroke and MS lesion segmentation using multiple MRI sequences and CT;
2. Dynamics of lesions over time;
3. Association between lesion size and localization and clinical outcomes;
4. Spatio-temporal modeling of lesion processes;
5. Pre-processing steps for the diseased brain including spatial and intensity normalization and bias correction;
6. Lesion mapping on a standard template after registration.

The group had a weekly meeting every Thursday from 11:30am-12:30pm and meetings were conducted using Dr. Crainiceanu's GotoMeeting account. This allowed everybody to participate and provided one the best resources for education, communication, and dissemination of results within the research group. The research group continues to meet weekly and a core group of researchers is working on the same themes in various subgroups.

Sources of data for the working group included: the ISLES Challenge data<sup>1</sup>, ADNI data<sup>2</sup>, OSIRIX public data<sup>3</sup>, and NIH MS-MRI data sets (not public).

A number of papers were published in connection with the working group's activities:

1. Removing inter-subject technical variability in magnetic resonance imaging studies. Fortin JP, Sweeney EM, Muschelli J, Crainiceanu CM, Shinohara RT; Alzheimer's Disease Neuroimaging Initiative. *Neuroimage*. 2016 May 15;132:198-212.  
doi: 10.1016/j.neuroimage.2016.02.036. Epub 2016 Feb 23
2. Fast Covariance Estimation for High-dimensional Functional Data. Xiao L, Zipunnikov V, Ruppert D, Crainiceanu C. *Stat Comput*. 2016 Jan 1;26(1):409-421. Epub 2014 Jun 27.
3. Relating multi-sequence longitudinal intensity profiles and clinical covariates in incident multiple sclerosis lesions. Sweeney EM, Shinohara RT, Dewey BE, Schindler MK, Muschelli J, Reich DS, Crainiceanu CM, Eloyan A. *Neuroimage Clin*. 2015 Nov 11;10:1-17.  
doi: 10.1016/j.nicl.2015.10.013. eCollection 2016.
4. Quantitative Intracerebral Hemorrhage Localization. Muschelli J, Ullman NL, Sweeney EM, Eloyan A, Martin N, Vespa P, Hanley DF, Crainiceanu CM. *Stroke*. 2015 Nov;46(11):3270-3.  
doi: 10.1161/STROKEAHA.115.010369. Epub 2015 Oct 8.
5. Validated automatic brain extraction of head CT images. Muschelli J, Ullman NL, Mould WA, Vespa P, Hanley DF, Crainiceanu CM. *Neuroimage*. 2015 Jul 1;114:379-85.  
doi: 10.1016/j.neuroimage.2015.03.074. Epub 2015 Apr 7.

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<sup>1</sup><http://www.isles-challenge.org/>

<sup>2</sup><http://adni.loni.usc.edu/>

<sup>3</sup><http://www.osirix-viewer.com/datasets/>

6. Reproducibility and bias in healthy brain segmentation: Comparison of Two Popular Neuroimaging Platforms. D.L. Tudorascu, H.T. Karim, J. Maronge, L. Alhilali, S. Fakhran, H.J. Aizenstein, J. Muschelli, C. Crainiceanu, *Frontiers in Neuroscience*. 2016; 10; 503.  
doi: 10.3389/fnins.2016.00503.

Submitted and in preparation:

- D. B. Woodard, R. B. Falafala, and C. Crainiceanu. Model-based image segmentation via Monte Carlo EM, with application to DCE-MRI.

and book chapters (refereed):

1. A Tutorial for Multisequence Clinical Structural Brain Imaging. In *The Handbook for Neuroimaging Data Analysis*. E. Sweeney, A. Eloyan, R.T. Shinohara, C. Crainiceanu.
2. Modeling change in the brain: methods for cross-sectional and longitudinal data. In *The Handbook for Neuroimaging Data Analysis*. P.T. Reiss, W. Thompson, C. Crainiceanu

Other products:

1. More than 25 presentations at various conferences including ENAR 2016, JSM 2016, SAMSI and Statistics in Imaging Conferences, including:
  - Statistical Methods in Imaging, May 28-29, 2015, University of Michigan<sup>4</sup>
  - Annual Imaging Statistics Conference June 1st - 3rd, 2016, University of Colorado Anschutz Medical Campus - Aurora, Colorado<sup>5</sup>
  - Challenges and Advances on Big Data in Neuroimaging, August 25 - 26, 2016, Cleveland Clinic<sup>6</sup>
2. Many R packages have been developed and the members of the group are now leading the formation of Neuroconductor, the largest repository of R packages for analysis of Neuroimaging data.
3. Grant proposals: The SAMSI work has made possible a funded NIH R21 grant: R21NS093349: Spatiotemporal Modeling of MRI Grain Lesion Trajectories of Biomarker Discovery and the submission of the NIH RO1 grant Statistical methods for longitudinal multivariate neuroimaging biomarkers  
At least 3 other RO1 grants are in various stages of development and will be submitted for possible funding to NIH.

Working group participants:

- WG leader: Ciprian Crainiceanu
- WG coordinator: Sarah Vallelian
- Postdocs: Jacek Urbanek, Benjamin Risk, Zhengwu Zhang
- Other active members: John Aston, Andrew Brown, Anis Davoudi, John Daye, Sathish Deevi, Tanujit Dey, Michele Guindani, Jaroslaw Harezlak, Katherine Heller, Duy Hoang Thai, Sandra Hurtado Rua, Chin-Yueh Liu, Xi Luo, Michelle Miranda, Thomas Nichols, So Young Park, Joerg Polzehl, Jordan Rodu, Huiyan Sang, Rui Song, Karsten Tabelow, Shahin Tavakoli, Xiaofeng Wang, Zhiyuan Xu, Yu Yue, Fengqing Zhang, Lingsong Zhang, Yuping Zhang, Yi Zhao, Yihong Zhao, Russell Shinohara, Dana Tudorascu, Jean Pierre Fortin, Elizabeth Sweeney, John Muschelli, Ji Soo Kim, Gina Norato, Kristin Lin

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<sup>4</sup>[http://sph.umich.edu/biostat/events/imaging\\_workshop.html](http://sph.umich.edu/biostat/events/imaging_workshop.html)

<sup>5</sup> <http://www.ucdenver.edu/academics/colleges/PublicHealth/Academics/departments/Biostatistics/Imaging-Conference/Pages/default.aspx>

<sup>6</sup> <http://www.bio.ri.ccf.org/bigdata/>

## 3.2 Computational Inverse Problems with applications in Neuroscience

Accurate imaging of the human brain is important for many applications in neuroscience, such as understanding structural and functional connectivity and diagnosing brain disorders. Several imaging modalities such as EEG, MEG, X-ray tomography can be mathematically described as an ill-posed inverse problem. The goal of this working group is to derive fast and efficient algorithms to reconstruct images from the data and also to quantify the resulting uncertainty associated with the reconstructions.

### 1. Multispectral photoacoustic tomography

Photoacoustic tomography is an imaging modality that combines a rich optical contrast with the resolution of ultrasound tomography. Data can be collected using incident light, excited at several different wavelengths, on the tissue region of interest. Collecting data at many wavelengths is beneficial in the reconstruction, since it reduces the ill-posedness and can reconstruct oxygenated saturation which is informative of activation. However, this makes the computational problem much more challenging. To speed up the inversion, we will use a surrogate model, based on Proper Orthogonal Decomposition, which is easier to evaluate but still preserves several important features of the full order model. The benefits of the proposed methods will be demonstrated on challenging synthetic model problems.

**Active members:** Sarah Vallélian, Arvind K. Saibaba

### 2. Efficient linear solvers for Bayesian inverse problems

We develop a generalized hybrid iterative approach for computing solutions to large-scale Bayesian inverse problems. The main features of our algorithm are the solvers is that it efficient in that the main costs per iteration are matrix-vector multiplications (and not inverses and square-roots), and automatic that regularization parameters and stopping criteria can be determined during the iterative process. We provide insight into the convergence of the algorithm by interpreting the iterates as a filtered Generalized SVD, and provide connections to other related solvers. The generalized hybrid approach is ideal for large-scale problems where covariance kernels are defined on irregular grids or are only available via matrix-vector multiplication, e.g., those from the Matérn class. Numerical examples from image processing (super-resolution for MRI images) demonstrate the effectiveness of the described approaches.

**Active members:** Julianne Chung, Arvind K. Saibaba

### 3. Efficient sampling methods for Bayesian Inverse Problems

In the Bayesian approach to inverse problems, computing functions of the posterior distribution is useful to quantify uncertainty in the parameter reconstructions. Sampling posterior distributions corresponding to high dimensional input spaces is one of the big open problems in the area of uncertainty quantification. Another challenge is to estimate the noise level and regularization parameters that govern the relative importance between the data misfit part of the likelihood and the regularization parameter. We adopt a Hierarchical Bayesian approach and propose a fast way to accelerate Markov Chain Monte Carlo sampler. We demonstrate the benefits of our sampling methods on application including EEG imaging with a realistic head model and CT imaging.

**Active members:** Andrew Brown, Arvind K. Saibaba, Sarah Vallélian.

### 4. Simultaneous Segmentation and Deconvolution

Given a noisy and blurred piecewise smooth signal, e.g. brain imaging, image reconstruction tries to recover the true underlying signal. Image segmentation (based on the Mumford and Shah model) turns a piecewise smooth signal into a piecewise constant, e.g., clustering brain tissue into white and gray matter. In this work, we simultaneously address two issues, image segmentation and deconvolution, using approximation theory in function space. This is mathematically expressed as a constrained non-convex minimization problem in the Banach space (in the discrete setting) and is tackled using convex relaxation. A piecewise smooth component is measured by the  $\ell_1$  norm of its directional mean curvature which can reduce the so-called “stair-case effect.” Both theoretical results and demonstrations on images of relevance to neuroscience will be discussed.

**Active members:** Duy Hoang Thai, David Banks, Lucas Mentch

## 5. Generating Realistic Random Correlation Structures

There are two different proposed manuscripts as part of this Working Group. The first manuscript offers several simple computational algorithms for generating random entries of the Cholesky factor of a correlation matrix. Utilizing the inner order of  $[0, 1]$  Schur-complements required for the generation of a positive definite correlation matrix. The second manuscript revisits the famous Tikhonov regularization problem (a.k.a. Ridge Regression) through the explicit representation of the semi-partial covariance coefficients given by Cholesky factor. One of the main results is the obtaining of a mathematical justification for using a more sensitive novel version of diagonal Tikhonov matrix, suggested as an elegant new solution for preserving the positive-definiteness of the inverted  $X^T X$  matrix.

**Active members:** Vered Madar

## Presentations and mini-symposia

1. A.K. Saibaba and J. Chung, “Fast Iterative Methods for Bayesian Inverse Problems.” Copper Mountain Conference on Iterative Methods, March 2016.
2. Transition Workshop, SAMSI, May 2016.
  - J. Chung, “Computational Methods for Large-Scale Inverse Problems.”
  - S. Vallélian, “Reduced Order Modeling in Photoacoustic Tomography.”
  - A. Brown, “Efficient Markov Chain Monte Carlo Methods for Hierarchical Bayesian Inverse Problems.”
  - D.H. Thai, “Simultaneous Image Segmentation and Deconvolution.”
3. Minisymposium at the SIAM Conference on Imaging Sciences (2016) Albuquerque, New Mexico, (May 23-26, 2016): “Inverse Problems in Neuroscience”, organized by Sarah Vallélian and Arvind K. Saibaba.
  - “Reduced order modeling in Photoacoustic Tomography” Sarah Vallélian and Arvind K. Saibaba.
  - “Nonlinear Quantitative Photoacoustic Tomography with Two-Photon Absorption” Kui Ren, Rongting Zhang.
  - “A hierarchical Krylov–Bayes iterative inverse solver for MEG with physiological preconditioning” D Calvetti, A Pascarella, F Pitolli, E Somersalo, B Vantaggi.
  - “On Preconditioning Newton Method for Constrained Optimization Problems” Amir Gholaminejad, George Biros.
4. Julianne Chung and Arvind K. Saibaba, “Generalized Hybrid Iterative Methods for Large-Scale Bayesian Inverse Problems” SIAM Conference on Imaging Sciences, May 2016.
5. D.H. Thai, “Multiphase Segmentation For Simultaneously Homogeneous + Textural Images” Poster Presentation, SIAM Conference on Imaging Sciences, May 2016.

## Other products in progress

1. Julianne Chung and Arvind K. Saibaba, “Generalized Hybrid Iterative Methods for Large-Scale Bayesian Inverse Problems,” *Submitted* to SIAM Journal on Scientific Computing, Copper Mountain special issue.
2. Andrew Brown, Arvind K. Saibaba, Sarah Vallélian. “Efficient Markov Chain Monte Carlo Methods for Hierarchical Bayesian Inverse Problems.” *In preparation.*
3. D.H. Thai. “Simultaneously Two-phase Segmentation and Deconvolution for Piecewise Smooth Image.” *In Preparation.*

4. V. Madar, “Generating Realistic Random Correlation Structures: A New Simpler Algebraic Framework for Generating Correlated Random Variables.” *In preparation*.
5. V. Madar, “Revising Tikhonov regularization through the closed-form representation of Cholesky factor.” *In preparation*.

### Main WG participants

- WG leader: Arvind K. Saibaba (NCSU).
- WG coordinator: Sarah Vallélian (SAMSI).
- Post-docs: Sarah Vallélian (SAMSI), Duy Hoang Thai (SAMSI).
- Graduate Students: None.
- Other active members: Prof. Andrew Brown (Clemson), Dr. Vered Madar (UNC).

## 3.3 Neuromechanical Processes

Swimming, flying, and maneuvering requires sensing the environment and controlling the movement accordingly. In most animals, the nervous system is a fundamental component of actuating movement. The goal of this working group is to develop a preliminary model of the activation of muscle by motor neurons and the resulting effect on locomotion. In general, the strength of the muscular response is proportional to the frequency of action potentials conducted along motor neurons combined with the fraction of motor neurons that are entrained to activate individual muscle fibers. The mapping of motor neuron signal to muscle response can vary greatly across organisms and between muscle types. The details of this mapping, particularly in terms of the dynamical response, will be a focus of the modeling efforts.

Existing state-of-the-art models lack integration across components necessary to accurately model insect locomotion. For example, the SLIP (spring-loaded inverted pendulum) walking model describes the motion of the animal’s center of mass connected to an inverted pendulum with variable length controlled by a linear spring. The dynamics are completely controlled by gravity (Hamilton-Jacobi equations), yielding unrealistic time dynamics. Recently, we discussed modifications to this SLIP model that mimic muscle control of the leg angle, as walking is different from falling under gravity. This model has the potential to match experimental data from Bhandawat’s Lab and collaborators at Duke.

Another example is the connection between neuronal firing models and Hill muscle model which describes the force a muscle can produce when contracting its length at a given velocity. Although action potentials may be described as an all-or-nothing response, the strength of muscle contraction is not. Current models assume the muscle is either fully activated or not activated and do not account for partial activation. The magnitude of contraction is controlled by the frequency of action potentials generated by motor neurons and the number of muscle fibers that are activated. We recently discussed a detailed model of acetylcholine release and breakdown, its effect on Calcium release from the sarcoplasmic reticulum, and the binding and unbinding of this Calcium to tropomyosin, which in turn controls the contraction of a muscle sarcomere. This detailed model has the potential to shed light on a reduction relating action potentials in motor neurons to force generated by muscle contraction; a key ingredient for a future large-scale, multi-limb model.

In the Fall semester, the group held weekly tutorials to share knowledge and ideas on neuron and muscle biology, as well as modeling among group members. Topics included: current research in insect locomotion, Lagrangian formulation of the dynamics of legged locomotion, Hodgkin-Huxley and integrate-and-fire simulations, fluid dynamics, muscle models, biology of muscle activation, and Hill muscle models.

In the Spring semester, the group focused in on two specific problems: insect locomotion and nerve-muscle mechanics. For both problems, subgroups set out to work on models (aSLIP model for insect walking and neuromechanical model of calcium release in muscles). Weekly meetings were held to keep track of our progress and to discuss group goals.

A detailed meeting schedule is given below:

- *Aug. 21-31*: Laura Miller and Katie Newhall began uploading overview papers, links, and simulation code. Group members began reviewing the posted materials.

- *Sept. 1*: First group meeting.
- *Sept. 8*: Group discussion on readings. Tutorial on neuron biology by Michael Senter and tutorial on Hodgkin-Huxley and integrate-and-fire neuron models by Yuan.
- *Sept. 15*: Group discussion on readings. Tutorial on muscle biology by Julia Samson and tutorial on Hill muscle models by Laura.
- *Sept. 22*: Group discussion on readings. Tutorial on muscle models by Laura Miller.
- *Sept. 29*: Group discussion on readings. Continuing the tutorial on muscle models, and tutorial on biology of muscle activation by Laura Miller.
- *Oct. 6*: Set working group “goals and outcomes” to submit to SAMSI. Tutorial on fluid dynamics by Katie Newhall.
- *Oct. 13*: Tutorial and demonstration of Hodgkin-Huxley and integrate-and-fire simulations by Katie Newhall.
- *Oct. 20*: Tutorial on Lagrangian formulation of the dynamics of legged locomotion by Tirtho Biswas and Vikas Bhandawat.
- *Oct. 27*: Tutorial and presentation on current research in insect locomotion (fruit flies walking) by Tirtho Biswas and Vikas Bhandawat.
- *Nov. 10*: More on muscle activation by Laura Miller. Assigned tasks for next group meeting. Papers on integrated models uploaded by Laura Miller to be read & discussed at next meeting.
- *Dec. 1*: Group discussion on readings led by Alex Hoover and report by group members on action items from November 10. Literature on invertebrate muscle and calcium dynamics uploaded by Laura Miller.
- *Jan. 13-15*: Group workshop at SAMSI, details below and full report available<sup>7</sup>
- *Feb. 2*: Review of the video of Boyce Griffith’s lecture at UNC on detailed neuromechanics models.
- *Feb. 9*: Presentations on research progress by Tirtho Biswas and Michael Senter.
- *Feb. 16*: Review of Tirtho Biswas’s notes on connecting the Hill model to COM templates posted.
- *Feb. 23*: Worked on goals for the rest of the semester.
- *Mar. 1*: Short updates by Laura Miller, Jennifer Kile, Michael Senter and Sarah Vallelia. Posted discussion list for next meeting.
- *Mar. 8*: Posted action items for next meeting.
- *Mar. 22*: Presentation on research progress on their aSLIP template by Tirtho Biswas and Vikas Bhandawat. Group review of their article draft. Discussing the direction for the calcium model project.
- *Mar. 29*: Presentation on research progress on models for jellyfish swimming by Alex Hoover. Continuing discussions for the calcium model project via email.
- *Apr. 5*: Discussed our plans for the closing workshop. Julia Samson presented some figures from the calcium book.
- *Apr. 12*: Laura distributed Nature paper on lobsters including neural recordings and temporally resolved force data. Sarah Vallelia and Julia Samson discussed writing the introduction for the calcium paper.
- *Apr. 19*: Katie Newhall and Jennifer Kile discussed further simulations for the calcium paper.
- *May 3*: Discussed the group presentations at the Transition workshop and moving forward with research in the summer.

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<sup>7</sup><https://docs.google.com/document/d/1oJ0n3JN2sycbAX6Rasi3yyTscfWLEBEMUaf0o4MTa7I/edit>

Papers that have either been written or are in preparation:

We plan to submit two papers to the Bulletin of Mathematical Biology and Journal of Theoretical Biology or Current Biology:

- Vikas Bhandawat, Tirtho Biswas, Sarah Vallelia. “Integration of a walking template with muscles for walking in *Drosophila*.”
- Katherine Newhall, Julia Samson, Sarah Vallelia, Michael Senter, Yuan Gao, Jennifer Kile, Laura Miller. “A mathematical model for integrating spike trains with intracellular calcium release and the resulting generation of muscular force.”

Other products and notable activities of the working group:

- Organized minisymposium “Neuromechanical Modeling of Invertebrates” for SIAM Conference on the Life Sciences in Boston in July 2016. Talks include:
  - “Spike Trains to Force Generation” by Katie Newhall,
  - “Neural Control of Leg Movements in *Drosophila*” by Vikas Bhandawat,
  - “Towards a Biomechanical Template for Slow Walking” by Tirtho Biswas,
  - “Neuromechanical Control of Jellyfish Turning” by Grace McLaughlin
- Developed MATH 892 Neuromechanics Module, a 5 week module course for graduate students as part of an initiative to integrate modeling, data and statistics at UNC between multiple departments. Many of the lectures were built from the tutorials first presented in the working group. There were 9 registered students and a number of auditing students from math and biology.
- *January 13*: Neural anatomy and function, basic mathematical models of action potentials and neural networks (Hodgkin Huxley, Integrate and Fire)  
Handouts: Introductory material on the biology of neurons and data available.  
Peskin and Hoppensteadt chapters on Hodgkin Huxley and Muscle Mechanics, Miller and Levy chapters on muscles and neurobiology.  
Lecture Based Tutorials: Dr. Newhall
- *January 20*: Muscle anatomy and macroscopic behavior of muscles (force-velocity, length tension, three-element Hill model), data analysis of locomotion, neuromuscular diseases.  
Software: Biomechanical Toolkit, <https://code.google.com/p/b-tk/#Documentation>  
Sample data: <https://www.c3d.org/sampledata.html>  
Reading: Arnaud Barrea, Stephane Armand (2014). Biomechanical ToolKit: Open-source framework to visualize and process biomechanical data. Computer Methods and Programs in Biomedicine, 114: 80–87.  
Introductory material on the biology of muscle. Short lecture and hands-on simulations: Laura Miller
- *January 27*: Muscle activation by neurons, cellular processes within the muscle, multiple spike train data analysis  
Handouts: Miller and Levy chapter on muscle activation, paper by Emery Brown et al. on “Multiple neural spike train data analysis: state-of-the-art and future challenges,” related papers.  
Readings on calcium dynamics in muscle cells.  
Lecture Based Tutorials: Katie Newhall and Laura Miller
- *February 3*: Active contraction models for muscle and IBAMR  
Software: <https://github.com/IBAMR/IBAMR>, An adaptive and distributed-memory parallel implementation of the immersed boundary (IB) method  
Lecture Based Tutorial and hands-on simulations: Boyce Griffith
- *February 10*: Guest speakers on neuromuscular disease and neuromechanics, Student project presentations

- Held 3 day Workshop on Neuromechanics at SAMSI:
  - *Wednesday, January 13*: Informal talks were given on three aspects of the project: insect walking, muscle mechanics, and neurobiology. These talks were followed by a group discussion on where the working group should go from here.
 

Bhandawat and Biswas reported on their modifications to the peg-leg/SLIP model of insect walking (P. Holmes et al 2006) to better fit the time course of experimental fruit fly data.

Newhall led a discussion on the Hodgkin Huxley neuron model. In the discussion that followed, the group determined that only spike train models are required to force a model of calcium dynamics inside the muscle fiber.

Miller reviewed the 2010 T. L. Williams paper and its model of intracellular calcium dynamics. In the discussion that followed, the group brainstormed ideas on how to replace the stimulus term with a parameter that depends on the time course of spike trains.

After the talks, the group discussed the possibility of performing experiments on grasshoppers and/or fruit flies to determine the force generated when the motor neuron is stimulated.

There was also a discussion on how invertebrate muscle is substantially different from vertebrate muscle. The group collectively performed a literature search for papers that would provide alternative models and parameter values. Some of the main results of the literature review were a collection of papers with very detailed models of human skeletal muscle and data and models for locust muscle.
  - *Thursday, January 14*: The focus of this day of the workshop was to flush out the details of a model for intracellular calcium dynamics and the generation of force. A second goal was to work out the preliminary details of a model for insect walking with simplified muscles.
 

In the morning, the group collectively edited a MATLAB code to reproduce calcium and force dynamics in the Williams 2010 paper. In addition, the group analytically determined a steady state solution and numerically reproduced that steady state solution. Also, figures were generated that qualitatively reproduced results in the Williams paper (note there are some remaining questions on parameter selection).

In the afternoon, the group discussed two different geometries for adding two effective muscle fibers to the SLIP model of insect walking.

During the day, Miller and Newhall set up collaborative tools for the group such as GitHub, Drop-Box, and ShareLaTeX. Templates were made for writing at least two papers on the calcium-spike train dynamics model and the insect walking model with muscles.

The group submitted a minisymposium proposal to SIAM Life Sciences 2016 Conference in Boston, MA. The minisymposium will be on neuromechanics with four speakers from the workshop.
  - *Friday, January 15*: The group met in the morning on the final day of the workshop. The goal of the day was to wrap up modeling ideas, write down the outcomes and models generated during the workshop, and make a schedule of goals going forward.
 

Miller updated the Sakai site with relevant papers for group members to read based on the previous days' discussions on Integrated Models and Invertebrates.

Miller led a modeling discussion to solidify possible approaches to connect spike trains inputs to Calcium and force dynamics.
- Boyce Griffith and Laura Miller to submit a grant proposal NSF's call for proposals on Innovative Computational Infrastructure for Understanding the Brain (nsf16076). The proposal focused on developing neuromechanical modules to integrate into the Immersed Boundary with Adaptive Mesh Refinement (IBAMR) software library. This infrastructure can be used to pose questions on how muscle is activated in model organisms as they swim or fly.
- Katie Newhall wrote a letter of intent for the Beckman Young Investigators that was based upon the main ideas explored in this working group. Title: Integrated Neurological Modeling of Locomotion. The grant was not invited for submission as a full proposal.

Working group participants:



- WG leaders: Katie Newhall (UNC), Laura Miller (UNC)
- WG coordinator: Sarah Vellelian (SAMSI)
- Post-docs: Sarah Vellelian (SAMSI), Alex Hoover (Tulane University)
- Graduate Students: Yuan Gao (UNC), Julia Samson (UNC), Michael Senter (UNC), Jennifer Kile (RPI)
- Undergraduates: Nathan Taylor (UNC)
- Other Faculty: Tirtho Biswas (Loyola University, New Orleans), Boyce Griffith (UNC), Vikas Bhandawat (Duke University)

### 3.4 Mathematical and Statistical Approaches to Modeling Brain Networks: circuits and systems

Initially, the Working Group met virtually (via Webex) twice per month. Prof. Eden hosted these biweekly webinars. The focus of the discussions was how to build links between mathematical and statistical modeling. To that end, participants analyzed a spike train data set provided by Dr. Fernando Fernandez using mathematical modeling and statistical modeling tools. Doing so, the participants learned to communicate between these different modeling classes.

Following the workshop in October (see below), a subset of Working Group participants has been drafting a review article that summarizes the links between mathematics, statistics, and neuroscience. This article has been accepted publication:

- Computational Neuroscience: Mathematical and Statistical Perspectives, Annual Review of Statistics and Its Application Vol. 5: (Volume publication date: March 2018) by Robert E. Kass, Shun-ichi Amari, Kensuke Arai, Emery N. Brown, Casey O. Diekman, Markus Diesmann, Brent Doiron, Uri Eden, Adrienne Fairhall, Grant M. Fiddymment, Tomoki Fukai, Sonja Grun, Matthew T. Harrison, Moritz Helias, Hiroyuki Nakahara, Jun-nosuke Teramae, Peter J. Thomas, Mark Reimers, Jordan Rodu, Horacio G. Rotstein, Eric Shea-Brown, Hideaki Shimazaki, Shigeru Shinomoto, Byron M. Yu, Mark A. Kramer  
<https://doi.org/10.1146/annurev-statistics-041715-033733>

4. Other products of the working group, such as software or conference presentations.

We held a workshop at Boston University, Boston, MA, on October 14-15, 2015. This workshop was part of a year-long program in 2015-2016 focused on Challenges in Computational Neuroscience, which was run by SAMSI. At the Boston workshop we identified areas of overlap, and potential synergies, in mathematical and statistical modeling to advance our understanding of neuronal data. A particular goal was for participants to form groups who might work together in some productive way. We brought together a small group of researchers with expertise in statistics, mathematics, computational modeling, and neuronal data - and with motivation to bridge the gaps between these separate fields. The workshop began with a series of brief presentations that aimed to expose open problems. Participants then broke into groups to work on specific topics, and reconvened to assess progress and plan future activities. The workshop discussions were extremely helpful: we are now writing a collaborative review paper that outlines the perspectives, languages, and approaches of the two different disciplines in their shared effort to understand neuronal data.

Working group participants:

- WG leaders: Rob Kass (Carnegie Mellon University), Uri Eden (Boston University), Mark Kramer (Boston University)
- WG coordinator: Adam Jaeger (SAMSI)
- Postdocs: Adam Jaeger (SAMSI)

- Other active members: Matt Harrison (Brown), Shigaru Shinomoto (Kyoto U), Hiro Nakahara (RIKEN), Byron Yu (CMU), Kyle Lepage (Allen Brain Institute), Brent Doiron (Pitt), Valerie Ventura (CMU), Adrienne Fairhall (University of Washington), Sonja Gruen (Research Center Julich), Markus Diesmann (Bernstein Center Freiburg), Peter Thomas (Case Western Reserve), Mark Reimers (Mich State), Horacio Rotstein (NJIT), Casey Diekman (NJIT), Ken Arai (Boston), Nancy Kopell (Boston), Mark Reimers (Michigan State), Eric Shea-Brown (University of Washington), Jordan Rodu (CMU), Fernando Fernandez (Boston).

### 3.5 Theory of neural networks: structure and dynamics

This working group was focused on developing theoretical tools to address neuroscience problems arising in network theory and neural coding. The members were all at the intersection of neuroscience and mathematics.

On the networks side, the focus was on dynamics of threshold-linear networks, spiking networks with embedded cell assemblies, and pattern storage in Hopfield networks. WG research activities included:

- (i) mathematical analysis of network dynamics,
- (ii) computational experiments and software development, and
- (iii) testing various heuristics for fitting networks to real and synthetic data, as well as for predicting emergent dynamics from network structure.

On the neural coding side, the emphasis was on the further development of topological and algebraic methods for analyzing neural activity from simultaneous recordings of neurons. This activity data can be pre-processed to obtain neural correlations and neural codes. WG research addressed a variety of mathematical questions that arise when trying to understand how important features of correlation or coding structure can be extracted from these data.

In Fall 2015 we held weekly WG meetings via WebEx, which initially consisted of talks/lectures designed to build a common background among WG members. This was an exploratory phase, and the WG leaders also held separate meetings to discuss possible projects.

In Spring 2016, several members of the WG were in residence at SAMSI for extended periods. This enabled more focused and in-person meetings among subgroups. We also held a 3-day workshop in early March, which was very successful and brought most of the WG participants to SAMSI. In addition, several participants stayed 1-3 weeks beyond the workshop period, to continue working on joint research projects. Frequent meetings among subgroups of the WG continued throughout the Spring semester, and over the summer.

Papers written or in preparation:

1. K. Morrison, A. Degeratu, V. Itskov, C. Curto. Diversity of emergent dynamics in competitive threshold-linear networks: a preliminary report. This is a preprint that was posted on arXiv.org in May 2016, and was written during Spring 2016 with much input from WG activities. It is being revised so that it can be submitted to a (high-profile) journal. (arXiv preprint arXiv:1605.04463 (2016))
2. C. Curto. “What can topology tell us about the neural code?” *Bulletin of the American Mathematical Society* 54 (1), 63-78 (2017). (doi: 10.1090/bull/1554)  
This paper was written in Fall 2015, and was influenced by the WG.
3. J. Cruz, C. Giusti, V. Itskov, B. Kronholm. “On open and closed convex codes.”  
This paper was in progress throughout the WG year, and J. Cruz was picked up as a co-author directly as a result of his involvement in the WG. (arXiv preprint arXiv:1609.03502 (2016))
4. C. Curto, R. Vera. “The Leray dimension of a convex code.”  
This paper is in preparation, and was primarily written in Spring 2016 while both CC and RV were in residence at SAMSI. (arXiv preprint arXiv:1612.07797 (2016))

5. C. Parmelee, K. Morrison, C. Curto. “Predicting sequences of activation in small threshold-linear networks.” In preparation. Most of the research was conducted as part of the yearlong WG activities.
6. Charles J. Garfinkle and Christopher J. Hillar. “Sparse coding is stable.” In preparation.

Other products:

- Software:
  - Software for running network simulations with the CTLN model was developed by C. Curto and K. Morrison, and posted on GitHub. <https://github.com/nebneuron/CTLN>
  - Software for computations with simplicial complexes was developed by V. Itskov and his graduate students, and posted on GitHub. <https://github.com/nebneuron/Simplicial>
  - The Clique Topology package developed by C. Giusti, C. Curto, and V. Itskov was updated in Fall 2016, for use with the SAMSI WG. It can also be found on GitHub. <https://github.com/nebneuron/cliique-top>
  - The HDNET package developed by C. Hillar and F. Effenberger was updated for use with the SAMSI WG. It is available at: <https://github.com/team-hdnet/hdnet>
- Grant proposals:
  - NIH Brain Initiative RFA-EB-15-006 Theories, Models and Methods. C. Curto (lead PI) and K. Morrison submitted an application to this R01 grant program in October 2015, as part of the WG activities. We received notification from NIH on Aug 15, 2016 that our grant has been recommended for funding. NIH R01 EB022862 (C. Curto lead PI; K. Morrison co-I; \$1,134,009; BRAIN Initiative grant) Emergent dynamics from network connectivity: a minimal model, 2016-2019.
  - C. Curto applied for a McDonnell Foundation JSMF Scholar Award in Studying Complex Systems in March 2016, while in residence at SAMSI. Unfortunately, it was not recommended for funding.
- New collaborations: Many new collaborations were initiated as part of the SAMSI WG, and were intensified during the March workshop. The following collaborations do not yet have specific papers to show, but remain active and have the potential to generate interesting publications over the next few years.
  - Charles J. Garfinkle and Christopher J. Hillar. “Sparse coding is stable.” In preparation.
  - C. Hillar, V. Itskov, F. Effenberger. “Topological data analysis of Hopfield networks and ripple sequences.”
  - S. Marzen, K. Morrison, C. Curto. “Information-theoretic analysis of convex codes.”
  - C. Curto, C. Hillar. “Fitting CTLN networks”
  - S. Kadir, V. Itskov, C. Curto. “Topological analysis of visual cortex data”
  - D. Rolnick, C. Curto. “Proving the existence of limit cycles in the CTLN model”
  - B. Doiron, C. Hillar, C. Huang. “Fitting Hopfield matrices to spiking cortical networks”

Working group participants:

- WG leaders/organizers: Carina Curto (Penn State), Brent Doiron (University of Pittsburgh), Chris Hillar (University of California San Francisco and UC-Berkeley)
- WG coordinator: Adam Jaeger (SAMSI)
- Post-docs: Zvi Rosen (Penn State/U Penn), Ramon Vera (Penn State), Nora Youngs (Harvey Mudd), Chengcheng Huang (Pittsburgh), Chad Giusti (U Penn), Ngoc Tran (Max Planck, Germany), Felix Effenberger (Max Planck, Germany), Shabnam Kadir (University College London), Adam Jaeger (SAMSI)

- Graduate students: Aubrey Thompson (Pittsburgh), Alex Kunin (Penn State), Min Chun Wu (Penn State), Caitlyn Parmelee (University of Nebraska-Lincoln), Joshua Cruz (Duke), David Rolnick (MIT), Sarah Marzen (Berkeley), Sara Kalisnik (Stanford), Greg Henselman (U Penn), Charles Garfinkle (UC Berkeley)
- Other faculty: Vladimir Itskov (Penn State), Katie Morrison (Penn State/University of Northern Colorado), Horacio Rostein (NJIT)

### 3.6 Acquisition, reconstruction and processing of MRI data

In fMRI and fcMRI, many reconstruction and processing steps are performed on data and a large portion of the data is omitted from analysis. The measurements taken by the scanner are not voxel values. The actual measurements taken by the scanner are to a good approximation, an array of complex-valued (real and imaginary) spatial frequencies. This array of spatial frequency measurements are two-dimensional inverse Fourier transforms reconstructed into an image. The resulting image is complex-valued but generally converted into a magnitude-only image. Image processing is performed before and after this inverse Fourier transform reconstruction process. There are statistical effects from performing the reconstruction and processing that change the voxels mean, variance, and correlation structure.

One product from this working group was a chapter titled “*Image Reconstruction in Functional MRI*” by Daniel Rowe to be published in the *Handbook of Neuroimaging Data Analysis* (editors H. Ombao, M. Lindquist, W. Thompson, J. Aston), published in late 2016 by Chapman & Hall/CRC Press (ISBN 9781482220971). This book chapter outlined and described the fundamentals of fMRI image reconstruction and image processing along with their effects. This work was presented at the CCNS Transition Workshop in May 2016 in a talk titled “*A Gentle Introduction to Image Processing and Reconstruction in fMRI*”. This was a great lead-in to the reconstruction and processing working group.

In the reconstruction and processing working group, the main topics we discussed were what are called Accelerated MR Imaging. The main idea in accelerated imaging is to measure less  $k$ -space data and reduce scan time so that the time between successive volume images is reduced. However, one consequence of measuring less data is that images are aliased. There are two main approaches to accelerated MR imaging. The first approach named SENSE operates in image space. SENSE reconstructs aliased images from less  $k$ -space data, then uses images from fully measured  $k$ -space data to account for the missing image information. The second approach named GRAPPA operates in  $k$ -space. GRAPPA aims to interpolate the missing  $k$ -space data before the images are reconstructed. SENSE and GRAPPA were traditionally applied within each image but more recently are being applied through slices. There are limitations on how much the images can be accelerated within a slice and thus through slice acceleration has definite advantages. However, there is no free lunch when less data is measured. When less data is measured and the traditional SENSE or GRAPPA image reconstruction techniques are applied within a slice, it has been shown that artificial correlation is induced either through the folds. Since the same basic techniques are being applied through slice, it is logical that artificial correlations would also be induced through the slices.

Presentations stemming from WG research:

1. Daniel Rowe, “*A Gentle Introduction to Image Processing and Reconstruction in fMRI*”, CCNS Transition Workshop, SAMSI, May 2016.
2. Daniel Rowe, “*Statistical Analysis of Image Reconstructed Fully-Sampled and Sub-Sampled fMRI Data*”, Mathematical and Statistical Challenges in Neuroimaging Data Analysis Workshop, Banff International Research Station, Banff, Alberta, Canada, February 2016.  
Preliminary theoretical results on SENSE image acceleration through slices.
3. Daniel Rowe, “*The Current State of Image Processing and Reconstruction with Future Directions*”, CCNS transition workshop, SAMSI, May 2016.
4. Daniel Rowe, “*SENSE-Induced Correlation in Simultaneous Multi-Slice fMRI*” American Statistical Association Section on Imaging, Joint Statistical Meetings in Chicago, August 2016.

There are plans to continue this work and submit it for publication.

5. Benjamin Risk, “*Examination of Artifacts from Multiband Imaging*”, CCNS Transition Workshop, SAMSI, May 2016.

Rowe and Risk worked on theoretical quantification and empirical assessment of through-slice correlation from GRAPPA. This is extremely important because the Human Connectome Project uses through-plane GRAPPA to acquire images for fMRI. Risk found that artificial correlations induced through-plane from GRAPPA reconstruction are not of biological origin.

6. Mary Kociuba, “*A Method to Mitigate Inter-slice Signal Leakage in SMS-fMRI*”, CCNS Transition Workshop, May 2016.

Kociuba worked on techniques to mitigate induced through slice correlation in SENSE type image reconstructions. This work was part of her dissertation that she successfully defended in summer 2016 under the direction of Rowe at Marquette University. There are plans to submit this work for publication. Kociuba started a postdoc in the Biomedical Image Computing Group in the Department of Pediatrics at the University of Washington in Fall 2016.

Working group participants:

1. WG leader: Daniel Rowe
2. Postdoc: Benjamin Risk
3. Graduate student: Mary Kociuba

### 3.7 Imaging Genetics

Despite the numerous successes of genome-wide association (GWA) studies, it remains extremely challenging to unravel the genetic basis of most mental and neurodegenerative illnesses because each genetic variant may only have a small contribution to disease outcome and such genetic basis can be very heterogeneous. With modern techniques, it is possible to collect big data from multiple resources in order to better identify and characterize genetic variants that are associated with a specific disease outcome through some intermediate traits, such as imaging measures. In particular, neuroimaging data as the best candidates of such intermediate traits have been/are being widely collected besides genetic and clinical data in connectome genetics. However, there is a severe lack of powerful statistical and computational methods in fully exploiting big imaging and genetic data in order to disentangle the genetic basis of common mental and neurodegenerative diseases.

Sources of data for the working group’s activities included the Human Connectome Project and the Philadelphia Neurodevelopmental Cohort. Graduate students (all from UNC) in the group each worked on projects using this data:

- Jingwen Zhang: GWAS method for correlating white matter bundles with SNP data.
- Yang Yu: GWAS method for correlating white matter bundles with SNP data
- Chao Huang: GWAS method for correlating functional data with SNP data
- Jasmine Yang: GWAS method for correlating functional connectivity matrices with SNP data
- Eunjee Lee: GWAS method for correlating functional connectivity matrices with SNP data

The WG had an active schedule of meetings with presentations on research topics or presentations of progress on projects:

- *Aug. 26*: Hongtu Zhu (University of North Carolina), Working Group Introduction and Schedule
- *Sept. 2*: Hongtu Zhu (University of North Carolina), Brief Introduction of the PNC data
- *Sept. 16*: Steve Marron (University of North Carolina), TCGA Lobular Freeze Data Analysis

- *Sept. 23*: Subharup Guha (University of Missouri), Nonparametric Variable Selection, Clustering and Prediction for High-Dimensional Regression

The development of parsimonious models for reliable inference and prediction of responses in high-dimensional regression settings is often challenging due to relatively small sample sizes and the presence of complex interaction patterns between a large number of covariates. We propose an efficient, non-parametric framework for simultaneous variable selection, clustering and prediction in high-throughput regression settings with continuous or discrete outcomes, called VariScan. The VariScan model utilizes the sparsity induced by Poisson-Dirichlet processes (PDPs) to group the covariates into lower-dimensional latent clusters consisting of covariates with similar patterns among the samples. The data are permitted to direct the choice of a suitable cluster allocation scheme, choosing between PDPs and their special case, a Dirichlet process. Subsequently, the latent clusters are used to build a nonlinear prediction model for the responses using an adaptive mixture of linear and nonlinear elements, thus achieving a balance between model parsimony and flexibility. We investigate theoretical properties of the VariScan procedure that differentiate the allocations patterns of PDPs and Dirichlet processes both in terms of the number and relative sizes of their clusters. Additional theoretical results guarantee the high accuracy of the model-based clustering procedure, and establish model selection and prediction consistency. Through simulation studies and analyses of benchmark data sets, we demonstrate the reliability of VariScan's clustering mechanism and show that the technique compares favorably to, and often outperforms, existing methodologies in terms of the prediction accuracies of the subject-specific responses.

- *Sept. 30*: Jingwen Zhang (University of North Carolina), Genetic Data of PNC dataset
- *Oct. 14*: Jianhua Hu (MD Anderson Center, University of Texas), Integration of multi-platform omics data
- *Oct. 28*: Hongtu Zhu (University of North Carolina)
- *Nov. 11*: Yang Yu (University of North Carolina), Preliminary DTI GWAS results.
- *Nov. 18*: Xiao Wang (Purdue University), A Brief Introduction to Big Data and Apache Spark  
Abstract: In this talk, I will first briefly introduce the challenges of statistical computing for big data. I will then present a modern big data platform called Apache Spark. The Spark history, installation, and simple operations will be illustrated.
- *Dec. 2*: Kaixian Yu (Florida State University), Bayesian network structure learning with a sequential Monte Carlo method

A Bayesian network is a graphical representation of a joint distribution that encodes the conditional dependencies and independencies among the variables. We proposed a novel three-stage BN structure learning method, called GRASP (GRowth-based Approach with Staged Pruning). In the first stage, a new skeleton (undirected edges) discovery method, double filtering (DF), was designed. Compared to existing methods, DF requires smaller sample sizes to achieve similar statistical power. Based on the skeleton estimated in the first step, we proposed a sequential Monte Carlo (SMC) method to sample the edges and their directions to optimize a BIC-based score. SMC method has less tendency to be trapped in local optima, and the computation is easily parallelizable. On the third stage, we reclaim the edges that may be missed from previous stages. We obtained satisfactory results from simulation study and applied the method to infer gene regulatory networks from real experimental data.

- *Jan. 6*: Jingwen Zhang (University of North Carolina), Meta-Analysis of Genome-Wide Association Studies: A Practical Guide

Meta-analysis is an effective approach to combining summary statistics across multiple studies. This approach has been widely used in recent genome-wide association studies (GWAS) and next-generation sequencing (NGS) studies. As a result, numerous disease susceptibility loci, which cannot be found in a single GWAS, have been identified through the meta-analysis of multiple studies. We give an overview how meta-analysis techniques can be used in consortium projects and provide guidance for future studies.

- *Jan. 13:* Yue Wang (University of North Carolina), Methods of integrating data to uncover genotype-phenotype interactions  
Recent technological advances have expanded the breadth of available omic data, from whole-genome sequencing data, to extensive transcriptomic, methylomic and metabolomic data. A key goal of analyses of these data is the identification of effective models that predict phenotypic traits and outcomes, elucidating important biomarkers and generating important insights into the genetic underpinnings of the heritability of complex traits. There is still a need for powerful and advanced analysis strategies to fully harness the utility of these comprehensive high-throughput data, identifying true associations and reducing the number of false associations. In this Review, we explore the emerging approaches for data integration including meta-dimensional and multi-staged analyses which aim to deepen our understanding of the role of genetics and genomics in complex outcomes. With the use and further development of these approaches, an improved understanding of the relationship between genomic variation and human phenotypes may be revealed.
- *Jan. 27:* Junghi Kim (University of Minnesota), Adaptive testing for multi-trait and multi-SNP associations with GWAS and sequencing data  
We study the problem of testing for single marker-multiple phenotype associations based on genome-wide association study (GWAS) summary statistics without access to individual-level genotype and phenotype data. For most published GWASs, because obtaining summary data is substantially easier than accessing individual-level phenotype and genotype data, while often multiple correlated traits have been collected, the problem studied here has become increasingly important. We propose a powerful adaptive test and compare its performance with some existing tests. We illustrate its applications to analyses of a meta-analyzed GWAS dataset with three blood lipid traits and another with sex-stratified anthropometric traits, and further demonstrate its potential power gain over some existing methods through realistic simulation studies. We start from the situation with only one set of (possibly meta-analyzed) genome-wide summary statistics, then extend the method to meta-analysis of multiple sets of genome-wide summary statistics, each from one GWAS. We expect the proposed test to be useful in practice as more powerful than or complementary to existing methods.
- *Feb. 10:* Jasmin Yang (University of North Carolina), Preprocessing and GWAS on PNC Behavioral Data
- *Mar. 1:* Jasmin Yang (University of North Carolina), Update on preprocessing and GWAS on PNC Behavioral Data
- *Mar. 23:* Ziliang Zhu (University of North Carolina), Preprocessing and GWAS Analysis of PNC Resting State fMRI Data
- *Mar. 30:* Jingwen Zhang (University of North Carolina), Genetic imputation of PNC dataset

Mr. Chao Huang and Ms. Jingwen Zhang also presented their preliminary results in the workshop on “Mathematical and Statistical Challenges in Neuroimaging Data Analysis” at Banff, Canada, February 2016.

Working group participants:

- WG leader: Hongtu Zhu
- WG coordinator: Zhengwu Zhang
- Post-docs: Zhengwu Zhang, Jin Yian
- Graduate Students: Jingwen Zhang, Yang Yu, Chao Huang, Jasmine Yang, Eunjee Lee
- Other active members: Steven Marron, Pan Wei, Xi Luo, Hongxiao Zhu, Rui Song, Thierry Chekouo, Guanhua Chen, John Daye, Shanshan Ding, XiangNan Feng, Habib Ganjgahi, Jinko Graham, Subha Guha, Jianhua Hu, Peng Huang, Bei Jiang, Junghi Kim, Mary Kociuba, Dehan Kong, II-Youp Kwak, Eunjee Lee, Yimei Li, Chien Wei Lin, M. Henry Linder, Vered Madar, Zhengqing Ouyang, Ah Yeon Park, Simeng Qu, Benjamin Risk, Huiyan Sang, Rui Song, Faezeh Tamimi, Wei Tu, Michelle Wang,

Yichao Wu, Jieren Xu, Zhiyuan Xu, Lingzhou Xue, Fengqing Zhang, Kai Zhang, Lingsong Zhang, Xiaoke Zhang, Xin Zhang, Yuping Zhang, Yi zhao, Yihong Zhao, Yize Zhao, Yihui Zhou, Wensheng Zhu, Ziliang Zhu.

### 3.8 Structural Connectivity

There has been greatly increasing interest in better measuring the structural connection network (connectome) in the brain, and in relating variability in this network to human cognitive traits and neuropsychiatric disorders. Currently human connectomes are estimated by a multistage pipeline relying on diffusion tensor imaging and structural imaging. This relies on the diffusion properties of water molecules in the white and grey matter tracts in the brain to obtain a 'fiber' map describing the locations of the grey matter tracts along which most of the electrical activity in the brain occurs. The fiber network is estimated via computer imaging algorithms, and it is unclear how reliable this estimation is. In addition, there are many challenges that arise in studying variability in the fiber network, ranging from a lack of statistical models for characterizing the population distribution of such a complex object, to alignment problems across different individual's brains, to questions of scale (should we study variability on a fine or coarse scale?) to computational intractability given the vast size. This working group will bring together individuals having a variety of perspectives ranging from mathematicians with an interest in geometric data analysis to computer scientists (theoretical and applied) interested in graph problems to high-dimensional data statisticians. The focus will be on solving the array of problems that arise in developing a scalable and reliable approach for statistical inference in brain connectome data.

Some of the notable projects in the working group were carried out by postdocs and graduate students:

- Zhengwu Zhang (SAMSI): Robust brain structural connectivity analysis using HCP data  
The connection structure in an individual's brain plays a fundamental role in how the mind responds to everyday tasks and life's challenges. Modern imaging technology such as diffusion MRI (dMRI) makes it easy to peer into an individual's brain and collect valuable data to infer the structural connectivity. The difficulty for current statistical analysis of such data is to extract precise and robust connectivity networks from the brain. We will develop a state-of-the-art data processing pipeline to reliably construct structural connectivity from dMRI, including streamline extraction, adaptive streamline compression, and robust connectivity matrix construction. We will also discuss some potential statistical analyses to the extracted data.
- Jingwen Zhang (UNC): HPRM: Hierarchical Principal Regression Model of Diffusion Tensor Bundle Statistics  
In a typical diffusion tensor Imaging (DTI) study, diffusion properties are observed among multiple fiber bundles to understand the association between neurodevelopment and clinical variables, such as age, gender, biomarkers, etc. Most research focuses on individual tracts or use summary statistics to jointly study a group of tracts, which usually ignores the global and individual functional structures. To address this problem, we propose a hierarchical functional principal regression model, consisting of three components: (i) a multidimensional Gaussian process model to characterize functional data, (ii) a latent factor model to jointly analyze multiple fiber bundles and to capture common effect shared among tracts, and (iii) a multivariate regression model study tract-specific effect. A multilevel estimation procedure is proposed and a global statistic is introduced to test hypothesis of interest. Simulation is conducted to evaluate the performance of HPRM in estimating shared effect and individual effect. We also applied HPRM to a genome-wide association study (GWAS) of one-year twins to explore important genetic markers in brain development among young children.

Sources of data for the working group's activities included the Human Connectome Project and the UNC-CH Neonate brain development project.

The working group had an active schedule of meetings with presentations on research topics or presentations of progress on projects:

- *Aug. 26*: Hongtu Zhu (University of North Carolina), Working group introduction and schedule



- *Sept. 1:* Zhengwu Zhang (SAMSI), Human Connectome Overview
- *Sept. 15:* Luda Sakhanenko (Michigan State University), Global rate optimality in a model for Diffusion Tensor Imaging
- *Sept. 29:* Jian Chen (NIH), Computational Diffusion MRI: Acquisition and Reconstruction
- *Oct. 13:* Zhengwu Zhang (SAMSI), Recent progress on structural connectivity extraction from HCP data
- *Oct. 27:* Lu Wang (Duke University), Bayes modeling of brain networks  
 Replicated network data are available in many research fields. In connectomic applications, interconnections among brain regions are collected from each patient, with interest focusing on studying common structures and individual differences in the architecture of interconnections in the brain. Current methods study shared connectivity patterns or reduce network data to summary statistics prior to statistical analysis, while we propose a fully generative Bayesian nonparametric approach for modeling the population distribution of network-valued data. The joint distribution of the edges follows a multivariate Bernoulli distribution, with transformed edge probability vectors expressed as the sum of a shared similarity vector and a class-specific deviation modeled via flexible mixtures of low-rank factorization exploiting the network structure. The formulation is provably flexible, leads to a simple Gibbs sampler, and provides a framework for clustering network-valued data, while adaptively shrinking towards lower dimensional representations. We discuss theoretical properties and illustrate the performance in simulations and application to human brain networks.
- *Nov. 10:* Raymond Wang (Iowa State University)  
 Diffusion magnetic resonance imaging is an imaging technology designed to probe anatomical architectures of biological samples in an in vivo and non-invasive manner through measuring water diffusion. The contribution of this work is threefold. First it proposes a new method to identify and estimate multiple diffusion directions within a voxel through a new and identifiable parametrization of the widely used multi-tensor model. Unlike many existing methods, this method focuses on the estimation of diffusion directions rather than the diffusion tensors. Second, this work proposes a novel direction smoothing method which greatly improves direction estimation in regions with crossing fibers. This smoothing method is shown to have excellent theoretical and empirical properties. Lastly, this work develops a fiber tracking algorithm that can handle multiple directions within a voxel. The overall methodology is illustrated with simulated data and a data set collected for the study of Alzheimer's disease by the Alzheimer's Disease Neuroimaging Initiative (ADNI).
- *Dec. 8:* Joerg Polzehl (Weierstrass Institute for Applied Analysis and Stochastics, Berlin), Analyzing dMRI data: Consequences of low SNR  
 The talk focuses on statistical properties of measured MR signals and attempts to illustrate consequences of ignoring low SNR in the analysis. I'll shortly discuss issues in MR acquisition, image reconstruction and preprocessing. I'll propose a method for noise quantification in MR images. I'll show how Bias occurs in estimated characteristics in diffusion MR data and show how this can be avoided by adequate modeling. Findings will be illustrated using simulations and data from the Human Connectome Project.
- *Jan. 5:* Zhengwu Zhang (SAMSI), Metric-Based Registration and Analysis of Functional Data  
 In this talk, I will introduce a comprehensive framework for a joint registration and analysis of functional data. The term functional data is used here very generally as it encompasses a variety of situations including real-valued functions, Euclidean curves, and trajectories on nonlinear manifolds. This framework uses the Fisher-Rao Riemannian metric to derive a proper distance on the quotient space of functions modulo the time-warping group. A convenient square-root velocity function (SRVF) representation transforms the Fisher-Rao metric into the standard L2 metric, simplifying the computations. This distance is then used to define a Karcher mean template. Individual functions are aligned by warping them to the Karcher mean template. The advantages of this framework are demonstrated using both simulated and real data from different application domains.

- *Feb. 10*: Jing Zhang (Georgia State University), Inferring Functional Interaction and Transition Patterns via Dynamic Bayesian Variable Partition Model  
Multivariate connectivity and functional dynamics have been of wide interest in the neuroimaging field, and a variety of methods have been developed to study functional interactions and dynamics. In contrast, the temporal dynamic transitions of multivariate functional interactions among brain networks, in particular, in resting state, have been much less explored. This article presents a novel dynamic Bayesian variable partition model (DBVPM) that simultaneously considers and models multivariate functional interactions and their dynamics via a unified Bayesian framework. The basic idea is to detect the temporal boundaries of piecewise quasi-stable functional interaction patterns, which are then modeled by representative signature patterns and whose temporal transitions are characterized by finite-state transition machines. Results on both simulated and experimental datasets demonstrated the effectiveness and accuracy of the DBVPM in dividing temporally transiting functional interaction patterns. The application of DBVPM on a post-traumatic stress disorder (PTSD) dataset revealed substantially different multivariate functional interaction signatures and temporal transitions in the default mode and emotion networks of PTSD patients, in comparison with those in healthy controls. This result demonstrated the utility of DBVPM in elucidating salient features that cannot be revealed by static pair-wise functional connectivity analysis.
- *Feb. 24*: Xi Luo (Brown University), Graph Models for Brain Connectivity: Algebraic (Non-likelihood) Methods
- *Mar. 15*: Sean L. Simpson (Wake Forest School of Medicine), Disentangling Brain Graphs: A Note on the Conflation of Network and Connectivity Analyses

Dr. Zhengwu Zhang and Miss Jingwen Zhang also presented their preliminary results in the workshop on “Mathematical and Statistical Challenges in Neuroimaging Data Analysis” in Banff, Canada, February 2016.

Working group participants:

- WG leaders: David Dunson (Duke) and Hongtu Zhu (UNC)
- WG coordinator: Zhengwu Zhang
- Post-docs: Zhengwu Zhang, Jin Yian
- Graduate Students: Chao Huang, Yu Yang, Jingwen Zhang
- Other active members: Anuj Srivastava, Pan Wei, Jian Cheng (NIH), Maxime Descoteaux, John Daye, Paromit Dubey, Raymond Falk, Junhan Fang, Habib Ganjgahi, Shobo Han, Jaroslaw Harezlak, Chao Huang, Bei Jiang, Junghi Kim, Dehan Kong, Linglong Kong, Suprateek Kundu, Sebastian Kurtek, Eunjee Lee, Yimei Li, Chin-Yueh Liu, Xi Luo, Ezra Miller, Gabriel Ocker, Zhengqing Ouyang, Subhadip Pal, Joerg Polzehl, Huiyan Sang, Christof Seiler, Karsten Tabelow, Faezeh Tamimi, Shahin, Tavakoli, Wei Tu, Darryl Wade, Jane-Ling Wang, Lu Wang, Michelle Wang, Ye Wang, Raymond Wang, Chong Wu, Jieren Xu, Lingzhou Xue, Fengqing Zhang, Jingwen Zhang, Yuping Zhang, Yihong Zhao, Yize Zhao, Yihui Zhou, Ziliang Zhu.

### 3.9 Functional connectivity

This working group is intended to complement the other CCNS working groups that focus on other data modalities: spike train, structural and functional magnetic resonance imaging. The focus of this working group is on modeling electroencephalograms which, among the different modalities, is least invasive, least expensive to collect and has excellent temporal resolution (and thus can capture dynamics in brain process). The main goals of the working group were:

1. To provide a forum for discussing and learning state-of-the-art methods for analyzing electroencephalograms and data from several imaging modalities.

2. To provide a forum for identifying open lines of statistical, mathematical and computing research as related to modeling EEG and multi-modal imaging data

The highlight of the group's activities was organizing a major workshop in April 2016:

Challenges in Modeling Dependence in High Dimensional Space-Time Stochastic Processes With Applications to Multi-modal Brain Connectivity

Workshop Organizing Committee: Hernando Ombao (University of California, Irvine), Daniel Rowe (Marquette University), Marina Vannucci (Rice University), Ting-ting Zhang (University of Virginia)

The workshop was attended by roughly 45 mathematicians, statisticians and computer scientists at all career levels: PhD students, post-doctoral researchers, faculty at the assistant, associate and full professor levels. In the workshop, neuroscience experts who will give introductory lectures on basic physiology and anatomy. These lectures introduced mathematicians and statisticians on the substantive issues on characterizing and modeling connectivity, both structural and neuronal, using various data modalities that capture different facets of brain anatomy and functionality such as structural MRI, neuronal spike train, local field potential, electroencephalograms and functional MRI. These were all essential to developing novel statistical and mathematical models, tools and algorithms that are meaningful in the sense that the models have solid physiological basis.

The workshop presented a unique opportunity to bring together in one place several of the leading researchers in the area. Different experts in the area of space-time modeling discussed state-of-the-art modeling approaches and their limitations; and identified new lines of research that are motivated by the current neuroscientific problems.

During the workshop, representatives from both NIH and NSF who provided information on existing opportunities and future directions of these two institutions. The panel also discussed the actual review process and shared their own ideas about how to improve the presentation and organization of the proposals.

Working group participants:

- WG leaders: Hernando Ombao (University of California, Irvine) John Aston (Cambridge University)
- WG coordinator: Benjamin Risk

### 3.10 Big Data Integration in Neuroimaging

Many large-scale neuroimaging data sets are becoming publicly available, including ADNI, HCP, UK Biobank, PING, PNC, among others. In the coming years the ability to efficiently utilize these data sets will become increasingly important. This working group focused on these issues, including the need to develop efficient, both statistically and computationally, methods to analyze these data; how to use these large databases of images to help inform on a new study.; and how to efficiently integrate these disparate data sets into a large analysis and to do so efficiently.

The working group met on a roughly bi-weekly basis on Wednesday afternoons at 3pm. Early meetings were centered around brainstorming about topics to work on and datasets to utilize. We ultimately decided to focus our efforts on data from the Human Connectome Project (HCP) database.<sup>8</sup> Many of the WG members did not have much experience with imaging data, and the HCP website has preprocessed data available, making the startup costs less daunting. This included:

- Overview of large-scale neuroimaging data sets that are publicly available, including ADNI, HCP, UK Biobank, PING, PNC, among others.
- Overview of the types of data sets available the Human Connectome Project (HCP) database, including a discussion of resting-state and task-based fMRI. How of download and view data obtained from the HCP database.

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<sup>8</sup> <http://www.humanconnectome.org>

Later meetings were generally centered around a talk given by an invited speaker, followed by discussion. This covered important questions in neuroimaging data analysis and research topics in neuroimaging. These included Bayesian models in neuroimaging, spatio-temporal models, and the study of brain dynamics.

One notable project carried out in the group was by Qunqun Yu, SAMSI graduate fellow working with Steve Marron. She performed a Joint and Individual Variation Explained (JIVE) analysis on the HCP data sets.

Presentations in working group's meetings:

- *Sep. 30*: Wei Tu, A Brief Review of Resting-state fMRI in HCP
- *Oct. 14*: Hongxiao Zhu, HCP data: task-fMRI and individual differences in behavior
- *Oct. 21*: Ben Risk, On the HCP Workbench
- *Nov. 4*: Amanda Mejia, Resting-state fMRI and GICA in the Human Connectome Project
- *Feb. 10*: Daniele Durante, Bayesian Inference for Group Differences in Brain Networks
- *Feb. 24*: Qunqun Yu, JIVE Integration of HCP Data
- *Mar. 2*: Lu Wang, Bayesian Network Response Regression
- *Mar. 16*: Jian Kang, Scalar-on-Image Regression via the Soft-Thresholded Gaussian Process
- *Mar. 30*: Ivor Cribben, A spectral clustering change point method for estimating whole brain dynamics
- *Apr. 13*: Ben Risk, A spatiotemporal mixed model for multi-subject task fMRI via method of moments

Working group participants:

- WG leaders: Martin A. Lindquist (Johns Hopkins University), Timothy D. Johnson (University of Michigan)
- WG coordinators: Yize Zhou (SAMSI), Ben Risk (SAMSI)
- Postdocs: Yize Zhou (SAMSI), Ben Risk (SAMSI), Michelle Miranda (University of North Carolina)
- Graduate Students: Cui Guo (University of Michigan), Amand Mejia (Johns Hopkins University), Wei Tu (University of Alberta), QunQun Yu (University of North Carolina)
- Other active members: Linglong Kong (University of Alberta), Steve Marron (University of North Carolina), Xi Rossi Luo (Brown University), Hongxiao Zhu (Virginia Tech University), Ryan Yue (CUNY), Ray Falk, Rui Song (NCSU) Yihong Zhao, Chengchun Shi (NCSU), Simeng Qu, Chujui Chen, Huiyan Sang, Sathish Deevi

### 3.11 Optical Imaging

This working group met (virtually) by WebEx most Wednesdays at 2pm Eastern time from the first week of September 2015 until early June 2016, and one sub-group has continued to meet alternate weeks during summer 2016. Most meetings lasted 70-90 minutes. During the Fall semester most sessions aimed to educate ourselves about the technology, the pre-processing issues, and some statistical methods we might use. Some guest speakers contributed. During the Winter/Spring semester, we held a workshop at SAMSI, and continued to meet virtually. After the workshop sub-groups began to focus more on specific problems such as pre-processing for wide-field voltage data, for calcium imaging data, and to investigate stability and consistency of activity patterns from calcium imaging data. We had several virtual talks by leaders in the field over WebEx. Eftychios Pnevmatikakis (Simons Foundation) discussed his new statistical methods (which appeared a few months later in *Neuron*) for identifying cells in two-photon imaging data with the group for over an hour.

We conducted a two-day workshop at SAMSI in February 2016, which was attended by about fifteen of our regular participants, some ad-hoc participants, and several invited guests - experimentalists who generated large optical imaging data sets:

1. Bruce McNaughton (UC Irvine), Neuroscience Questions Opened up by Optical Imaging
2. Yiyang Gong (Duke), Spike detection with engineered optical voltage sensors
3. Matthew Valley (Allen Institute for Brain Science), Strategies for large-scale calcium imaging in the mouse brain
4. Dieter Jaeger (Emory University), Voltage sensitive protein imaging for the analysis of sensory-motor integration: Signal preprocessing and artifact removal.

We also had presentations by several (about half of all) people who had published methods for optical image data analysis:

1. Eftychios Pnevmatikakis (Simons Foundation), Simultaneous denoising, deconvolution, and demixing of calcium imaging data
2. Alexandre Reynaud (McGill University), Linear model decomposition for voltage-sensitive dye imaging signals
3. Jason Wittenbach (HHMI Janelia Farm), Challenges and Opportunities in Scalable Analysis of Neural Imaging Data
4. Yu Hu (Harvard University), Brain-wide mapping of functional neuron groups in larval zebrafish

We also had presentations by seven people who had worked on different aspects of data within the SAMSI group.

In other activities, a sub-group (mostly Michigan State contributors and Michael Lavine) has made considerable progress on pre-processing wide-field voltage imaging data. From this work we anticipate several publications will be submitted. Another sub-group (Mark Reimers, Jinghao Lu, Valentina Staneva, Michael Lavine) has made some headway on finely characterizing population activity in relation to sensory experience using a public calcium imaging data set (the original publication crudely characterized only single cell responses). We anticipate submissions for publication in 2017.

Working group participants:

- WG leader: Mark Reimers (Michigan State U)
- Active working group members: Michael Lavine (U Mass Amherst), Valentina Staneva (University of Washington)
- Graduate students: Pengcheng Zhou (Carnegie Mellon University), Jinghao Lu (Duke)
- Other participants: Yuying Xie (Michigan State U), Jordan Rodu (Carnegie Mellon University), Casey Diekman (NJIT), Eftychios Pnevmatikakis (Simons Foundation), Ping-Shou Zhong (Michigan State U), Grace Hong (Michigan State U), Ming Yan (Michigan State U)

## 4 Educational Activities

### 4.1 Summer School

A summer school on Computational Neuroscience was held at The Solution Center, Durham, NC on July 27-31, 2015. This 5-day program was organized by Hongtu Zhu and featured instructors teaching short courses on five major research topics in computational neuroscience:

1. *Neural Spike Train Analysis*, Uri Eden (Boston University) and Mark A. Kramer (Boston University). Lecture topics included point processes and generalized linear models for spike trains and biophysical models.

2. *Compressed Sensing for Signal Processing*, Justin Romberg (Georgia Tech).  
Lecture topics included mathematical fundamentals of compressive sensing, low rank matrix recovery, basics of optimization, sparse representations, sparse embeddings and  $L_1$  minimizations and applications to dynamic reconstruction.
3. *Functional Data Analysis for Medical Imaging Data*, Hans-Georg Muller (University of California, Davis) and Jane-Ling Wang (University of California, Davis).
4. *Shape Analysis and Diffeomorphisms for Medical Imaging Data*, Laurent Younes (Johns Hopkins University).
5. *Big-biomedical Data Integration and Analysis*, Jeffrey S. Morris (MD Anderson Cancer Center, University of Texas), Yu-Ping Wang (Tulane University) and Hongtu Zhu (University of North Carolina).  
The final series of lectures focused on biomedical applications:
  - *Functional Regression Methods for Integration of Big Biomedical Imaging Data*, Morris
  - *Big Data Integration in Biomedical Studies*, Zhu
  - *Integration of brain imaging, genomics, networks and biological knowledge*, Wang.

The instructors gave in-depth overviews of each topic followed by problem/discussion sessions. Software packages were introduced to students with datasets to carry out some simple data analysis.

This summer school was targeted for graduate students, postdocs, and junior faculty from neuroscience, biomedical engineering, radiology, statistics, and applied mathematics and had over 100 participants.

## 4.2 Undergraduate workshop

A workshop for undergraduate students connecting with the CCNS program was held on October 19-20, 2015. The workshop was organized by SAMSI Deputy Director Sujit Ghosh and was attended by more than thirty students from across the country. The workshop was composed of a number of presentations, discussions and hands-on activities:

1. *A Tutorial for Clinical Brain Imaging*, Ciprian Crainiceanu.
2. *A Primer on Diffusion Tensor Imaging Study of Multiple Sclerosis*, Ana-Maria Staicu (North Carolina State University).
3. *Overview of the Research Lab and Tour of Facilities at Kafui Dzirasa's Laboratory for Psychiatric Neuroengineering (Neurobiology Department, Duke University School of Medicine)*, Stephan Mague (Duke University).
4. *A Tutorial on Image Reconstruction using Discrete Fourier Transformation with R demos*, Benjamin Risk (SAMSI).
5. *A Tutorial on Computed Tomography with MATLAB/Python demos*, Sarah Vallelian (SAMSI).
6. *Panel Discussion: Careers in Mathematical Sciences*, SAMSI Graduate students and Postdoctoral fellows – Adam Jaeger, Lucas Mentch, and Zhengwu Zhang (SAMSI)
7. *Mathematical Models for Muscle Activation*, Laura Miller
8. *Topology for Statistical Analysis of Brain Artery Images*, Ezra Miller

### 4.3 Graduate Courses

Two graduate special topics courses were taught at SAMSI in connection with the CCNS program. They were attended by visitors to the program and by students from Duke, University of North Carolina and North Carolina State University:

1. Fall 2015 Course: *Statistical Methods for Neuroimaging Data Analysis*, Hongtu Zhu (University of North Carolina)
2. Spring 2016 Course: *Mathematics of Neural Networks and Neural Codes*, Carina Curto (Pennsylvania State University)

## APPENDIX: WORKSHOP SCHEDULES FOR THE CCNS PROGRAM

### 2015-16 Program on Challenges in Computational Neuroscience (CCNS) Opening Workshop: August 17 – 21, 2015

#### Schedule:

**Monday, August 17<sup>th</sup>**

*Hamner Conference Center Auditorium*

- 8:00-8:30      Registration
- 8:30-8:45      Introduction and Welcome – **Richard Smith**, SAMSI
- 8:45-10:00     **Rob Kass**, Carnegie Mellon University  
*“A Statistical Perspective on Spike Train Analysis, and Possible  
Connections with Modeling”*
- 10:00-10:10    Break
- 10:10-11:25    **Kenneth Miller**, Columbia University  
*“Modeling Neural Circuits”*
- 11:25-12:40    **Emery Brown**, Harvard/MIT  
*“Neuroscience. A Broad and Open Frontier for Statistics”*
- 12:40-1:40     Lunch (Galleria)
- 1:40-2:00      **Thomas Witelski**, SAMSI  
*“Working Groups at SAMSI”*
- 2:00-3:15      **Martin Lindquist**, Johns Hopkins University  
*“Principles of Functional Neuroimaging”*
- 3:15-3:25      Break
- 3:25-4:40      **Maxime Descoteaux**, Universite de Sherbrooke  
*“Diffusion MRI Tractography and Connectomics: problems and  
challenges”*
- 4:40-5:00      Discussion

**Tuesday, August 18<sup>th</sup>**

*Hamner Conference Center Auditorium*

- 8:00-8:30      Registration and Announcements



- 8:30-9:30      **Edward Boyden, MIT**  
*“Tools for Mapping Brain Computations”*
- 9:30-10:30    **Markus Diesmann, Juelich Research Centre**  
*“Brain-Scale Simulations at Cellular and Synaptic Resolution: Necessity and Feasibility”*
- 10:30-11:00    Break
- 11:00-12:00    **Uri Eden, Boston University**  
*“Estimating Neural Dynamics using Point Process Models”*
- 12:00-1:00     Lunch (Galleria)
- 1:00-1:20      **Brent Doiron, University of Pittsburgh**
- 1:20-2:20      Introduction to the Theoretical Neural Networks Working Group
- 2:20-3:20      **Friedrich Sommer, University of California, Berkeley**  
*“Understanding the Functions of Oscillatory LFP”*
- 3:20-3:40      Break
- 3:40-5:00      Panel Discussion:  
**Sonja Gruen, Juelich Research Centre**  
**Eric Shea-Brown, University of Washington**  
**Matthew Harrison, Brown University**  
**Brent Doiron, University of Pittsburgh**
- 5:00-7:00      Poster Session/Reception  
(The board dimensions are 4 ft. wide by 3 ft. high. They are tri-fold with each side being 1 ft. wide and the center 2 ft. wide. Please make sure your poster fits the board. The boards can accommodate up to 16 pages of paper measuring 8.5 inches by 11 inches.)

**Wednesday, August 19<sup>th</sup>**  
*Hamner Conference Center Auditorium*

- 8:15-8:30      Announcements
- 8:30-9:30      **Stephanie Jones, Brown University**  
*“Biophysically Principled Computational Modeling of Human MEG/EEG Signals to Link Mechanism to Function”*
- 9:30-10:30    **Wei Ji Ma, New York University**

*“The Inevitability of Probability: Near-Optimal Probabilistic Inference in Generic Neural Networks Trained with Non-Probabilistic Feedback”*

10:30-11:00 Break

11:00-11:20 Introduction to the Inverse Problems Working Group

11:20-12:20 **Greg Farber**, NIH/NIMH  
*“The BRAIN Initiative, NIH, and Support for Computational Neuroscience”*

12:20-1:20 Lunch (Galleria)

Lunch Panel Discussion - Optional (Dogwood Room)  
**Wei Ji Ma**, New York University  
*“Growing Up in Science”*

1:20-2:20 **Daniel Rowe**, Marquette University

2:20-3:20 **Ruben Gur**, University of Pennsylvania  
*“Multimodal Neuroimaging and Behavioral Phenotyping in a Genomic Neurodevelopmental Context”*

3:20-3:50 Break

3:50-4:50 **Raquel Gur**, University of Pennsylvania  
*“Integration of Neuroimaging and Behavioral Phenotypes in Informative Populations: the clinical neuroscience perspective”*

**Thursday, August 20<sup>th</sup>**

*Hamner Conference Center Auditorium*

8:15-8:30 Announcements

8:30-9:30 **Polina Golland**, MIT  
*“From Pixels to Brain Networks: Modeling Brain Connectivity and Its Changes in Disease”*

9:30-10:30 **Michael Miller**, Johns Hopkins University  
*“Neuroinformatics and the Complexity of the Brain at the Imm Morphome Scale”*

10:30-11:00 Break

11:00-12:00 **Peter Bandettini**, NIMH

*“New fMRI Observations at an Individual Level Using Novel Acquisition, Paradigm, and Processing Approaches”*

12:00-1:00 Lunch (Galleria)

1:00-2:00 **James Haxby**, Dartmouth  
*“A Common Model of Representational Spaces in Human Cortex”.*

2:00-2:30 Break

2:30-3:30 Discussion: *“Working Groups”*

**Friday, August 21<sup>st</sup>**

*Hamner Conference Center Auditorium*

8:45-9:00 Announcements

9:00-10:00 **Thomas Nichols**, (Warwick)  
*“Two Wildly Different Approaches to Brain Connectivity in fMRI”*

10:00-12:00 Initial Working Group Meetings

12:00 Adjourn and Box Lunch (Galleria)

**2015-16 Program on Challenges in Computational Neuroscience (CCNS): Challenges In Linking Statistical & Mathematical Neuroscience: October 14 – 14, 2015 (Boston)**

**Schedule:**

**Wednesday, October 14, 2015**

University of Boston

8:30 - 9 Breakfast at Hariri Institute (111 Cummington Mall, Boston, MA)

9-9:15 Introduction and goals for Day 1  
(Uri Eden and Rob Kass)

9:15-12:30 Presentation of Research Paradigms: Retrospective view  
(Uri Eden, Rob Kass and Mark Kramer)

10:30-11 Coffee break

12:30-1:30 Lunch

1:30-1:45 Summary of morning discussion and afternoon agenda

1:45-3:00 Research Paradigms: Prospective view

- 3-3:30 Coffee break
- 3:30-5 Summary of Day 1 and Plans for Day 2
- 6-8 Working Dinner (continued discussion)

**Thursday, October 15, 2015**

University of Boston

- 8:30-9 Breakfast at Hariri Institute
- 9-9:15 Outline goals for today Day 2
- 9:15-12 Group discussions
- 10:30-11 Coffee break
- 12-1 Lunch at Hariri Institute
- 1-2 Review of the working document
- 2 - 3 Discussion of future plans.  
(meeting ends)

**2015-16 Education & Outreach Program: Undergraduate Workshop: October 19 – 20, 2015**

**Schedule:**

**Monday, October 19, 2015**

**SAMSI, Room 150**

- 8:15-8:30 Shuttle to SAMSI (meet in hotel lobby)
- 8:30-9:00 Registration (**Zhengwu Zhang** and **Karem Jackson**, SAMSI)
- 9:00-9:15 **Sujit Ghosh**, SAMSI/NCSU and **Jamie Nunnally**, SAMSI/NISS  
*Welcome and Introduction*
- 9:15-10:30 **Ciprian Crainiceanu**, Johns Hopkins University  
*A Tutorial for Clinical Brain Imaging*
- 10:30-11:45 **Ana-Maria Staicu**, NC State University  
*A Primer on Diffusion Tensor Imaging Study of Multiple Sclerosis*

- 11:45-12:30 Group Photo and Lunch at SAMSI
- 12:30-12:45 Shuttle to Dzirasa's Lab (Meet in Parking lot)
- 12:45-2:00 **Stephan Mague**, Center for Neuroimaging, Duke Univ.  
*Overview of the Research Lab and Tour of Facilities*
- 2:00-2:15 Shuttle back to SAMSI (meet in Lab's reception)
- 2:15-3:15 **Benjamin Risk**, SAMSI  
*A Tutorial on Image Reconstruction using Discrete Fourier Transformation (with R demos)*
- 3:15-3:30 Break
- 3:30-4:30 **Sarah Vellelian**, SAMSI  
*A Tutorial on Computed Tomography (with Matlab/Python demos)*
- 4:30-4:45 Break and Move to NISS Room 104
- 4:45-5:30 SAMSI Graduate Students and Postdoctoral Fellows  
Moderators: **Adam Jaeger**, **Lucas Mentch** and **Zhengwu Zhang**, SAMSI  
*Panel Discussion: Career in Mathematical Sciences*
- 5:30-6:45 Meet with SAMSI Members and Dinner at SAMSI
- 7:00+ Shuttle to the Hotel

**Tuesday, October 20, 2015**  
**SAMSI, Room 150**

- 8:15-8:30 Shuttle to SAMSI (Check out and meet in hotel lobby)
- 9:00-9:15 Recap: **Sujit Ghosh**, SAMSI, NCSU
- 9:15-10:30 **Laura Miller**, UNC-CH  
*Mathematical Models for Muscle Activation*
- 10:30-11:45 **Ezra Miller**, Duke University  
*Topology for Statistical Analysis of Brain Artery Images*
- 11:45-12:00p Submit Evaluation Forms and Adjourn
- 12:00p+ Box Lunch and Shuttle to RDU Airport

**2015-16 Program on Challenges in Computational Neuroscience (CCNS): Neuromuscular Control and Collective Behavior: January 13-15, 2016**

**Schedule:**

**Wednesday January 13th**  
**SAMSI**

- 8:45-9:00 Opening Remarks: **Laura Miller** (UNC-Chapel Hill)
- 9:00-9:30 Opening Discussion

- 9:30-10:30      **Tirtho Biswas** (Loyola University, New Orleans) and **Vikas Bhandawat** (Duke University)  
*Progress report on models of insect walking with data validation*
- 10:30-10:45      Break
- 10:45-11:30      **Laura Miller** (UNC-Chapel Hill)  
*Progress report on muscle activation*
- 11:30-12:00      Group Discussion
- 12:00-1:30      Lunch (SAMSI 2nd Floor Lounge)
- 1:30-2:30      **Katie Newhall** (UNC-Chapel Hill)  
*Progress report on modeling motor neurons*
- 2:30-4:00      Group discussion on an integrative model of insect walking
- 4:30-7:00      UNC Chapman Hall 435 – Neuromechanics Module Lecture 1
- 7:00              Informal group dinner at local restaurant

**Thursday January 14<sup>th</sup>**  
**SAMSI**

- 8:45-9:00      Announcements: **Laura Miller** (UNC-Chapel Hill)
- 9:00-10:15      **Laura Miller** (UNC-Chapel Hill)  
*Discussion on goals / timeline for working group projects*
- 10:15-10:30      Break
- 10:30-12:00      Breakout session, subgroup research meetings – SAMSI Room 150, SAMSI Room 219, NISS Room 104  
(insect walking, translating spike trains to muscle activation, muscle models)
- 12:00-1:30      Lunch (SAMSI 2nd Floor Lounge)
- 1:30-3:00      Continue subgroup research meetings
- 3:00-3:30      Break
- 3:30-5:00      Subgroup reports and discussion

5:00 Shuttle departs

**Friday, January 15th**

*SAMSI*

8:45-9:00 Announcements: **Laura Miller** (UNC-CH)

9:00-10:15 Group work on integrative model of insect walking

10:15-10:30 Break

10:30-12:00 Path forward

12:00 Adjourn and Box Lunch

**2015-16 Program on Challenges in Computational Neuroscience (CCNS): Mathematical and Statistical Challenges in Neuroimaging Data Analysis (16w5036) BANNF/BIRS: January 31 – February 5, 2016**

**Schedule:**

**Sunday, January 31**

16:00 - Check-in begins at 16:00 on Sunday and is open 24 hours (Front Desk - Professional Development Centre)

17:30 - [Dinner ↓](#) (Vistas Dining Room)

19:30 - Informal gathering (Corbett Hall Lounge (CH 2110))

**Monday, February 1**

07:00 - [Breakfast ↓](#) (Vistas Dining Room)

08:45 - Introduction and Welcome by BIRS Station Manager (TCPL 201)

09:00 - Hongtu Zhu: Workshop Opening (TCPL 201)

09:10 - Morning Session I, Chair: Xi Luo (TCPL 201)

09:10 - [Ying Guo: Exploring the brain connectivity: questions, challenges and recent findings ↓](#) (TCPL 201)

09:35 - [Hernando Ombao: A Unified Modeling Framework for State-Related Changes in High Dimensional Effective Brain Connectivity ↓](#) (TCPL 201)

10:00 - Floor Discussion (TCPL 201)

10:10 - Coffee Break (TCPL Foyer)  
10:30 -  
10:30 - Morning Session II Chair: Timothy Johnson (TCPL 201)  
11:30 -  
10:30 - [Jian Kang: Bayesian feature screening for big neuroimaging data via massively parallel computing ↓](#) (TCPL 201)  
10:55 -  
10:55 - [Moo Chung: Learning Large-Scale Brain Networks for Twin fMRI ↓](#) (TCPL 201)  
11:20 -  
11:20 - Floor Discussion (TCPL 201)  
11:30 -  
11:30 - Lunch (Vistas Dining Room)  
13:00 -  
13:00 - [Guided Tour of The Banff Centre ↓](#) (Corbett Hall Lounge (CH 2110))  
13:50 -  
13:50 - [Group Photo ↓](#) (TCPL Foyer)  
14:00 -  
14:00 - Afternoon Session I Chair: Jian Kang (TCPL 201)  
15:00 -  
14:00 - [Joerg Polzehl: Modeling high resolution MRI: Statistical issues ↓](#) (TCPL 201)  
14:25 -  
14:25 - [Bei Jiang: Modeling Placebo Response using EEG data through a Hierarchical Reduced Rank Model ↓](#) (TCPL 201)  
14:50 -  
14:50 - Floor Discussion (TCPL 201)  
15:00 -  
15:00 - Coffee Break (TCPL Foyer)  
15:30 -  
15:30 - Afternoon Session II Chair: Farouk Nathoo (TCPL 201)  
16:30 -  
15:30 - [Daniel Rowe: Statistical Analysis of Image Reconstructed Fully-Sampled and Sub-Sampled fMRI Data ↓](#) (TCPL 201)  
15:55 -  
15:55 - [Stephen Strother: Metrics for evaluating functional neuroimaging processing pipelines ↓](#) (TCPL 201)  
16:20 -  
16:20 - Floor Discussion (TCPL 201)  
16:30 -  
16:30 - Afternoon Session III Chair: Ying Guo (TCPL 201)  
17:30 -  
16:30 - [Vikas Singh: A multi-resolution scheme for analysis of brain connectivity networks ↓](#) (TCPL 201)  
16:55 -  
16:55 - [Jie Peng: Fiber orientation distribution function estimation by spherical needlets ↓](#) (TCPL 201)  
17:20 -  
17:20 - Floor Discussion (TCPL 201)  
17:30 -



17:30 - [Dinner ↓](#) (Vistas Dining Room)  
19:30

## **Tuesday, February 2**

07:00 - Breakfast (Vistas Dining Room)  
09:00

09:00 - Morning Session I Chair: Wei Pan (TCPL 201)  
10:00

09:00 - [Farouk Nathoo: A Bayesian Group-Sparse Multi-Task Regression Model for Imaging Genomics ↓](#) (TCPL 201)  
09:25

09:25 - [Michele Guindani: Bayesian predictive modeling for imaging genetics with application to schizophrenia ↓](#) (TCPL 201)  
09:50

09:50 - Floor Discussion (TCPL-201)  
10:00

10:00 - Coffee Break (TCPL Foyer)  
10:30

10:30 - Morning Session II Chair: Lexin Li (TCPL 201)  
11:30

10:30 - [Bin Nan: Tuning parameter selection for voxel-wise brain connectivity estimation via low dimensional submatrices ↓](#) (TCPL 201)  
10:55

10:55 - [Xi Luo: Network of Networks: A Large Scale Graphical Model for Whole Brain Networks Using fMRI ↓](#) (TCPL 201)  
11:20

11:20 - Floor Discussion (TCPL 201)  
11:30

11:30 - Lunch (Vistas Dining Room)  
13:30

13:30 - Afternoon Session I Chair: Chao Huang (TCPL 201)  
15:00

13:30 - [Jingwen Zhang: HPRM: Hierarchical Principal Regression Model of Diffusion Tensor Bundle Statistics ↓](#) (TCPL 201)  
13:45

13:45 - [Zhengwu Zhang: Robust brain structural connectivity analysis using HCP data ↓](#) (TCPL 201)  
14:00

14:00 - [Wei Tu: Non-local Fuzzy C-Means Clustering with Application to Automatic Brain Hematoma Edema Segmentation using CT ↓](#) (TCPL 201)  
14:15

14:15 - [Benjamin Risk: Large covariance estimation for spatial functional data with an application to twin studies ↓](#) (TCPL 201)  
14:30

14:30 - [John Muschelli: Neuroimaging in R: fslr and Other R Packages ↓](#) (TCPL 201)  
14:50

14:50 - Floor Discussion (TCPL 201)  
15:00

15:00 - Coffee Break (TCPL Foyer)  
15:30

- 15:30 - Afternoon Session II Chair: Hongtu Zhu (TCPL 201)  
 17:30 -  
 15:30 - [Roundtable Discussion: John Aston, Martin Lindquist, Hernando Ombao, Joerg Polzehl, Hongtu Zhu](#) ↓ (TCPL 201)  
 17:30 -  
 17:30 - Dinner (Vistas Dining Room)  
 19:30 -

### Wednesday, February 3

- 07:00 - Breakfast (Vistas Dining Room)  
 09:00 -  
 09:00 - Morning Session I Chair: Hongtu Zhu (TCPL 201)  
 10:00 -  
 09:00 - [John Aston: Functional Data, Covariances and FPCAs of brain data](#) ↓ (TCPL 201)  
 09:25 -  
 09:25 - [Jeffrey Morris: Spatial Functional Models for Event-Related Potential Data, with Application to Smoking Cessation Study](#) ↓ (TCPL 201)  
 09:50 -  
 09:50 - Floor Discussion (TCPL 201)  
 10:00 -  
 10:00 - Coffee Break (TCPL Foyer)  
 10:30 -  
 10:30 - Morning Session II Chair: Todd Ogden (TCPL 201)  
 11:30 -  
 10:30 - [Jianhua Hu: Analysis of spatially correlated functional data in tissue perfusion imaging](#) ↓ (TCPL 201)  
 10:55 -  
 10:55 - [Brian Hobbs: Recent advances in cancer imaging](#) ↓ (TCPL 201)  
 11:20 -  
 11:20 - Floor Discussion (TCPL 201)  
 11:30 -  
 11:30 - Lunch (Vistas Dining Room)  
 13:30 -  
 13:30 - Free Afternoon (Banff National Park)  
 17:30 -  
 17:30 - Dinner (Vistas Dining Room)  
 19:30 -

### Thursday, February 4

- 07:00 - Breakfast (Vistas Dining Room)  
 09:00 -  
 09:00 - Morning Session I Chair: Bei Jiang (TCPL 201)  
 10:00 -  
 09:00 - [Lexin Li: Estimation and Inference for Brain Connectivity Analysis](#) ↓ (TCPL 201)  
 09:25 -  
 09:25 - [Shuo Chen: Population level differentially expressed brain connectivity network detection and inferences](#) ↓ (TCPL 201)  
 09:50 -

- 09:50 - Floor Discussion (TCPL 201)  
10:00
- 10:00 - Coffee Break (TCPL Foyer)  
10:30
- 10:30 - Morning Session II Chair: John Aston (TCPL 201)  
11:30
- 10:30 - [Xiao Wang: Optimal Estimation for Quantile Regression with Functional Response](#) ↓  
10:55 (TCPL 201)
- 10:55 - [Yimei Li: SGPP: Spatial Gaussian Predictive Process Models for Neuroimaging Data](#)  
11:20 ↓ (TCPL 201)
- 11:30 - Lunch (Vistas Dining Room)  
13:30
- 13:30 - Afternoon Session I Chair: Xiao Wang (TCPL 201)  
15:00
- 13:30 - [Marina Vannucci: A Bayesian modeling approach of multiple-subject fMRI data](#) ↓  
13:55 (TCPL 201)
- 13:55 - [Todd Ogden: Functional and imaging data in precision medicine](#) ↓ (TCPL 201)  
14:20
- 14:20 - [Anuj Srivastava: Elastic Functional Data Analysis for Modeling Shapes of Anatomical Structures](#) ↓ (TCPL 201)  
14:45
- 14:45 - Floor Discussion (TCPL 201)  
15:00
- 15:00 - Coffee Break (TCPL Foyer)  
15:30
- 15:30 - Afternoon Session II Chair: Martin Linqvist (TCPL 201)  
16:30
- 15:30 - [Wei Pan: Testing for group differences in brain functional connectivity](#) ↓ (TCPL 201)  
15:55
- 15:55 - [Russell Shinohara: Two-Sample Tests for Connectomes using Distance Statistics](#) ↓  
16:20 (TCPL 201)
- 16:20 - Floor Discussion (TCPL 201)  
16:30
- 16:30 - [Tingting Zhang: Bayesian Inference of High-Dimensional, Cluster-Structured Ordinary Differential Equation Models with Applications to Brain Networks](#) ↓ (TCPL  
16:55 201)
- 16:55 - [Martin Linqvist: Dynamic Connectivity: Pitfalls and Promises](#) ↓ (TCPL 201)  
17:20
- 17:20 - Floor Discussion (TCPL 201)  
17:30
- 17:30 - Dinner (Vistas Dining Room)  
19:30

**Friday, February 5**

- 07:00 - Breakfast (Vistas Dining Room)  
09:00 - Morning Session I Chair: Yimei Li (TCPL 201)  
10:00 -  
09:00 - [Ivor Cribben: Temporal autocorrelation and between-subject heterogeneity in resting-state functional connectivity ↓](#) (TCPL 201)  
09:25 -  
09:25 - [Dana Cobzas: Sparse Classification for Significant Anatomy Detection in a Group Study ↓](#) (TCPL 201)  
09:50 -  
09:50 - Floor Discussion (TCPL 201)  
10:00 -  
10:00 - Coffee Break (TCPL Foyer)  
10:30 -  
10:30 - Morning Session II Chair: Yihong Zhao (TCPL 201)  
11:30 -  
10:30 - [Giseon Heo: Persistent homology: an approach for high dimensional data analysis ↓](#) (TCPL 201)  
10:55 -  
10:55 - [Matthew Brown: Opening the analysis black box: Improving robustness and interpretation ↓](#) (TCPL 201)  
11:20 -  
11:20 - Floor Discussion (TCPL 201)  
11:30 -  
11:30 - [Checkout by Noon ↓](#) (Front Desk - Professional Development Centre)  
12:00 -  
12:00 - Lunch from 11:30 to 13:30 (Vistas Dining Room)  
13:30 -

**2015-16 Program on Challenges in Computational Neuroscience (CCNS): Workshop on Optical Imaging Data Analysis: February 1-2, 2016**

**Schedule:**

**Monday February 1<sup>st</sup>**

*SAMSI*

- 9:00-9:15                      Opening Remarks: **Mark Reimers**, Michigan State University
- 9:15-10:00                     KeyNote: **Bruce McNaughton**, University of California, Irvine  
  “*Neuroscience Questions Opened up by Optical Imaging*”
- 10:00-10:40                    Session 1: Optical Technologies and Experiments  
**Yiyang Gong**, Duke University
- 10:40-11:00                    Break
- 11:00 – 12:30                   Session 1: Optical Technologies and Experiments (continued)  
**Matthew Valley**, Allen Institute for Brain Science  
**Dieter Jaeger**, Emory University

12:30 – 1:30	Lunch
1:30 – 3:00	<p>Session 2: Pre-processing Issues</p> <p>Part I: Calcium Imaging  <b>Eftychios Pnevmatikakis</b>, Simons Foundation</p> <p>Brief Reports and Issues:  <b>Michael Lavine</b>, University of Massachusetts, Amherst  <b>Valentina Staneva</b>, University of Washington  <b>Pengcheng Zhou</b>, Carnegie Mellon University</p> <p>Discussion of Outstanding Issues</p>
3:00-3:20	Break
3:20 – 5:00	<p>Session 2: Pre-processing Issues (continued)</p> <p>Part II: Voltage Imaging  <b>Alexandre Reynaud</b>, McGill University</p> <p>Brief Reports and Issues:  <b>Ming Yan</b>, Michigan State University  <b>Mark Reimers</b>, Michigan State University</p>
5:00 – 5:30	Working Groups
5:30- 7:00	Reception (2 <sup>nd</sup> Fl Commons) and Software Tutorials (Room 150)

**Tuesday Febraury 2<sup>nd</sup>**  
*SAMSI*

9:00 – 10:15	<p>Session 3: Handling Big Data  <b>Jason Wittenbach</b>, HHMI Janelia Farm</p> <p>Brief Reports and Issues:  <b>Ming Yan</b>, Michigan State University</p>
10:15-10:45	Break
10:45 – 12:15	<p>Session 4: Network and Connectivity Analysis  <b>Yu Hu</b>, Harvard University</p> <p>Brief Reports and Issues:  <b>Yuying Xie</b>, Michigan State University  <b>Mark Reimers</b>, Michigan State University</p>
12:15 – 1:15	Lunch

1:15 – 2:45                      Session 5: Dimension Reduction and State-Space Dynamics

Brief Reports and Issues:

**Kathleen Champion**, University of Washington

**Mark Reimers**, Michigan State University

**Casey Diekman**, New Jersey Institute of Technology

**Grace Hong**, Michigan State University

2:45                                      Break

3:00                                      Wrap-up Discussion

**2015-16 Program on Challenges in Computational Neuroscience (CCNS): Workshop on Neural Networks & Neural Codes: March 9 – 11, 2016**

**Schedule:**

**Wednesday March 9<sup>th</sup>**

*SAMSI*

9:00-9:15                              Registration

9:15-9:30                              Opening Remarks

Morning session - Recurrent Neural Networks

9:30-10:00                              **Chris Hillar**, University of California, SF and Berkeley  
*Overview of Network Models (Discrete, Rate, Spiking)*

10-11:00                                **Carina Curto**, Pennsylvania State University  
*Emergent Dynamics from Network Connectivity: A Minimal Model*

11-11:30                                **Chengcheng Huang**, University of Pittsburgh  
*Attentional Effects on Within-area and Between-areas Noise Correlations*

11:30-12:00                              **Aubrey Thompson**, University of Pittsburgh  
*Neural Coding in Metastable Cortical Dynamics*

12:00                                      **Chris Hillar**, University of California, SF and Berkeley  
*Fitting Recurrent Networks*

1:00-2:30                                Lunch

Afternoon session - Algebra and Topology of Neural Codes

2:30-3:00                                **Carina Curto**, Pennsylvania State University  
*Overview of Topology in Neuroscience*

- 3:00-4:00            **Chad Guisti**, University of Pennsylvania  
*Topological Analysis of Neural Correlations*
- 4:00-5:00            **Vladimir Itskov**, Pennsylvania State University  
*Convexity and Combinatorial Topology of Neural Codes*
- 5:00-6:00            **Nora Youngs**, Harvey Mudd College  
*Algebraic Analysis of Neural Codes Using the Neural Ring*

**Thursday March 10<sup>th</sup>**

- 9:30-10:30           Discussion of Network-related Research Projects  
(led by Carina Curto, Chris Hillar)
- 10:30-1:00           Collaborative Research Time
- 1:00-2:00            Lunch
- 2:00-3:00            Discussion of Topology-Related Research Projected  
(led by Vladimir Itskov)
- 3:00-5:30            Collaborative Research Time

**Friday March 11<sup>th</sup>**

- 9:30-12:00           Research Sessions
- 12:00-1:00           Lunch
- 1:00-3:00            Collaborative Research Time
- 3:00                    Workshop Adjourns

**2015-16 Program on Challenges in Computational Neuroscience (CCNS): Challenges  
In Functional Connectivity Modeling and Analysis: April 8-10, 2016**

**Schedule:**

**Friday, April 8<sup>th</sup>**

Hamner Conference Center

- 8:00                    Shuttle to Hamner Conference Center
- 8:30– 9:00            Welcome by SAMSI Associate Director: **Thomas Witelski**  
Introduction to CCNS Program: **Daniel Rowe** (Marquette University)  
Overview of the Aims of the Workshop: **Hernando Ombao** (University of California,  
Irvine)

9:00 –10:15	<b>David Moorman</b> (University of Massachusetts, Amherst) <b>Lecture:</b> <i>Neurophysiology and Behavior: Spike Trains and Fields</i>
10:15– 10:45	Break
10:45–12:00	<b>Ramesh Srinivasan</b> (Univ California, Irvine) <b>Lecture:</b> <i>Functional Connectivity and the Neurophysics of EEG</i>
12:00–1:15	Lunch
1:15–2:15	<b>Paul Laurenti</b> (Wake Forest University) <b>Lecture:</b> <i>Interdependence and Brain Networks</i>
2:15–2:45	Break
2:45–3:45	<b>Stefano Castruccio</b> (Newcastle University, UK) <b>Lecture:</b> <i>Overview of Spatial Statistics with Applications to fMRI</i>
3:45–4:15	Break
4:15–5:15	<b>Joke Durnez</b> (Stanford University) <b>Lecture:</b> <i>Power and Sample Size Calculations in fMRI</i>
5:45–8:00	Dinner and Informal Discussions on Grants Opportunities and Grant Writing <b>Alicia Carriquiry</b> (Iowa State University) <b>Nandini Kannan</b> (NSF Program Director) <b>Michael Kosorok</b> (University of North Carolina) <b>David Stoffer</b> (University of Pittsburgh)
8:00	Shuttle departs to hotel

**Saturday, April 9th**

Hamner Conference Center

9:00	Shuttle to Hamner Conference Center
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9:30–10:30	<p><b>Integrative Methods for Neuroimaging Data</b> Organizer: <b>Marina Vannucci</b> (Rice University)</p> <p><b>Vince Calhoun</b> (University of New Mexico) <i>Approaches to Multi-Model Fusion of Brain Imaging Data</i></p> <p><b>Rajarshi Guhaniyogi</b> (University of California, Santa Cruz) <i>Bayesian Tensor Regression: A Scalable Bayesian Framework for Neuroimaging Data</i></p>
10:30–11:00	Break
11:00–12:30	<p><b>Integrative Methods for Neuroimaging Data (Continued)</b></p> <p><b>Dubois Bowman</b> (Columbia University) <i>Integrative Methods for Functional and Structural Connectivity</i></p> <p><b>Michele Guindani</b> (MD Anderson) <i>Integrative Bayesian Modeling Approaches to Imaging Genetics</i></p> <p>Discussion</p>
12:30–2:00	Lunch and Poster Session
2:00–3:00	<p><b>fMRI Connectivity</b> Organizer: <b>Ting-ting Zhang</b> (University of Virginia)</p> <p><b>Jane-Ling Wang</b> (University of California, Davis) <i>A New Measure of Synchronization to Quantify Brain Connectivity</i></p> <p><b>Ani Eloyan</b> (Brown University) <i>Functional Connectivity in Autism via Independent Component Analysis</i></p>
3:00–3:30	Break
3:30–5:00	<p><b>fMRI Connectivity (Continued)</b></p> <p><b>Mary Kociuba</b> (Marquette University) <i>Complex-Valued Time-Series Correlation in the Frequency Domain Increases Sensitivity in FMRI Analysis</i></p> <p><b>Martin Lindquist</b> (Johns Hopkins University) <i>Dynamic Connectivity: Pitfalls and Promises</i></p> <p>Discussion</p>
5:00–6:00	Break

**2015-16 Program on Challenges in Computational Neuroscience (CCNS): Transition  
Workshop: May 4-6, 2016**

**Schedule:**

**Wednesday, May 4th**

SAMSI Room 150

- 8:15 Shuttle
- 8:45– 9:00 Opening Remarks by SAMSI Associate Director: **Thomas Witelski**  
Neuromechanics
- 9:00 –9:30 **Laura Miller**, UNC and **Katie Newhall**, UNC  
*Modeling the Muscular Response to Motor Neuron Spike-Trains*
- 9:30-10:00 **Tirthabir Biswas**, Loyola  
*A New Template for Walking*
- 10:00-10:30 **Alexander Hoover**, Tulane  
*Neuromuscular Control of Jellyfish Turning*
- 10:30– 11:00 Break
- 11:00–11:30 Big Data Integration, Part 1  
**Hernando Ombao**, UC Irvine  
*The Future Outlook in EEG Analysis*
- 11:30-11:45 Discussion
- 11:45–1:15 Lunch
- 1:15-1:45 Big Data Integration, Part 2  
**Xi Luo**, Brown  
*Estimating Brain Pathway Effects Using Large-scale Multilevel Models*
- 1:45–2:15 **Qunqun Yu**, UNC  
*Joint and Individual Variation Explained (JIVE) Integration of HCP Data*
- 2:15-2:45 **Amanda Mejia**, Johns Hopkins  
*PCA Leverage: Outlier Detection for High-Dimensional fMRI Data*
- 2:45-3:00 Discussion
- 3:00-3:30 Break
- 3:30-4:30 Optical Imaging  
**Mark Reimers**, Michigan State  
*Issues in Data Analysis for Optical Imaging*
- 4:30-5:00 Discussion
- 5:00 Shuttle departs to hotel

**Thursday, May 5th**

SAMSI Room 150

8:30 Shuttle  
Inverse Problems

9:00–9:30 **Julianne Chung**, Virginia Tech  
*Computational Methods for Large-Scale Inverse Problems*

9:30–9:50 **Sarah Vallelian**, SAMSI  
*Reduced Order Modeling in Photoacoustic Tomography*

9:50–10:10 **Andrew Brown**, Clemson  
*Efficient Markov Chain Monte Carlo Methods for Hierarchical Bayesian Inverse Problems*

10:10–10:30 **Hoang Duy Thai**, SAMSI  
*Simultaneous Image Segmentation and Deconvolution*

10:30–11:00 Break  
MRI Processing Part 1

11:00–11:10 **Daniel Rowe Marquette**  
*A Gentle Introduction to Image Processing and Reconstruction in fMRI*

11:10–11:40 **Iain Bruce**, Duke  
*Quantifying Correlations Artificially Induced in fMRI Data by the SENSE pMRI Model*

11:40–12:10 **Benjamin Risk**, SAMSI  
*Examination of Artifacts from Multiband Imaging*

12:10–1:30 Lunch  
MRI Processing Part 2

1:30–2:00 **Mary Kociuba**, Marquette  
*A Method to Mitigate Inter-slice Signal Leakage in SMS-fMRI*

2:00–2:20 **Adam Jaeger**, SAMSI  
*Topology and fMRI Data*

2:20–2:30 **Daniel Rowe Marquette**  
*The Current State of Image Processing and Reconstruction with Future Directions*

2:30–3:00 Break  
Structural Connectivity

3:00–3:30 **Sean Simpson**, Wake Forest School of Medicine  
*Disentangling Brain Graphs: the Conflation of Network and Connectivity Analyses*

3:30–4:00 **Jian Cheng**, NIH  
*Mapping Tissue Microstructure using Spherical Polar Fourier Diffusion MRI*

4:00–4:30 **Zhengwu Zhang**, SAMSI  
*Robust Human Brain Structural Connectivity Analysis*

4:30–5:00 **Lu Wang**, Duke  
*Bayesian Network-Response Regression*

5:00–7:00 Poster Session and Reception

7:00 Shuttle departs to hotel

**Friday, May 6th**

SAMSI Room 150

8:30 Shuttle  
Imaging Genetics

9:00-9:30 **Michele Guindani**, MD Anderson  
*Integrative Bayesian Modeling Approaches to Imaging Genetics*

9:30-10:00 **Yihong Zhao**, NYU  
*Imaging Genetics toward Mechanistic Understanding of Psychiatric Disorders*

10:00-10:30 Break

10:30-11:00 **Chintan Mehta**, Yale  
*Identifying Genetic Variants for Learning Ability with Neuroimaging*

11:00-11:30 **Jasmine Yang**, UNC  
*Imaging Genetic Analysis for PNC Behavioral Data*

11:30-12:00 **Hongtu Zhu**, UNC

12:00 Closing Remarks and Box Lunch

1:00 Shuttle to RDU Airport