

# Workshop on Medical Image Analysis

Biotechnology Center Auditorium, 425 Henry Mall

University of Wisconsin-Madison

May 21, 2013 10:00AM-5:00PM

## 10:00-11:00AM Cell Imaging

Multidimensional Image Informatics in Live Cell Imaging

*Kevin W. Eliceiri, Ph.D., Laboratory for Optical and Computational Instrumentation (LOCI)*

Computational Analysis Methods for Collagen Image Based Assays

*Jeremy Bredfeldt, Laboratory for Optical and Computational Instrumentation (LOCI)*

## 11:00AM-12:30PM Laplace Eigenfunction Methods for Medical Images

A Wavelets Based Schemes for Group-wise Differential Analysis of Networks & Connectivity  
Meshes in Neuroimaging

*Vikas Singh, Ph.D., Department of Biostatistics and Medical Informatics*

Hyperspherical Harmonics and their Application to Medical Imaging

*Ameer Pasha Hosseinbor, Department of Medical Physics, Waisman Laboratory for Brain Imaging and Behavior*

Twin Effects on Amygdala and Hippocampus Shapes via Heat Kernel Regression on Manifolds

*Moo K. Chung, Ph.D., Department of Biostatistics and Medical Informatics*

## 2:00-3:00PM Methods for Alzheimer's Disease

Brain Morphological Shape Markers for Alzheimer's Disease and Vascular Dementia

*Anqi Qiu, Ph.D., Department of Bioengineering, National University of Singapore*

Analyzing Neuroimaging Data via In-Situ Statistics

*Michael H. Coen, Ph.D., Department of Biostatistics and Medical Informatics*

## 3:00-5:00PM fMRI Analysis

Processing Choices in Resting-state Functional Magnetic Resonance Imaging

*Rasmus M. Birn, Ph.D., Department of Psychiatry and Medical Physics*

Using the G-factor and SENSE Induced Correlations for Optimizing fcMRI Study Specific RF  
Coil Design

*Iain P. Bruce, Marquette University*

A Statistical fMRI Model for Differential  $T_2^*$  Contrast Incorporating  $T_1$  and  $T_2^*$  of Gray Matter

*M. Muge Karaman, Marquette University*

A Temporal Frequency Description of the Spatial Correlation Between Voxels in fMRI Due to  
Spatial Processing

*Mary Kociuba, Marquette University*

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for additional information.

# Program

**Kevin Eliceiri, Director, Laboratory for Optical and Computational Instrumentation (LOCI)**

## *Multidimensional Image Informatics in Live Cell Imaging*

Light microscopy is providing key insights into cellular dynamics of normal and disease processes, a task being greatly facilitated by technical developments in optical probes and instrumentation. Fluorescent protein reporters allow virtually any protein to be labeled and thereby visualized in a cell, tissue or organism. Along with these developments in fluorescence probe technology, new optical techniques such as Fluorescence Resonance Energy Transfer (FRET), Multiphoton Laser Scanning Microscopy (MPLSM), Second Harmonic Generation (SHG) imaging and Fluorescence Lifetime Imaging (FLIM), are revealing how individual cellular components are assembled into cytoplasmic machinery, and how this machinery functions. Our central aim is to develop hardware and software strategies for extracting all the data possible from the weak fluorescence signals that are typically obtained when observing living specimens. This involves the development and application of algorithms and software for acquisition, analysis and visualization including noise reduction, feature extraction, exponential curve fitting, spectral unmixing, user guided segmentation, image compression and 3D visualization approaches. Much of this work is under the umbrella of our ImageJ2 software development to offer practical tools for developers and end user alike for the analysis of microscopy image data.

**Jeremy Bredfeldt, Laboratory for Optical and Computational Instrumentation (LOCI)**

## *Computational Analysis Methods for Collagen Image Based Assays*

Collagen reorganization at the tumor stromal boundary is an important step in the metastatic progression of cancer cells. Therefore, techniques that can characterize this reorganization at the cellular level have significant research and diagnostic value. At LOCI, we use second harmonic generation (SHG) imaging to produce cell resolution, high contrast images of collagen. SHG images of collagen pose significant challenges to quantitative analysis. For example, to assess changes in the collagen morphology, we are interested in features including, but not limited to, collagen fiber angle, fiber number, or fiber length. Our image analysis methods currently include grey level statistics, Fourier, wavelet and curvelet transforms, and a fiber tracking algorithm. However, we still have difficulty extracting features with high precision. In addition, it is often desirable to analyze collagen with respect to other cellular or extracellular components. To achieve this, we combine other modalities with SHG imaging such as bright field or fluorescence microscopy. This introduces many new challenges such as registration between SHG and bright field images or segmentation algorithms and analysis of collagen fiber characteristics with respect to morphology of these segmented structures. Although our techniques have achieved some success against these challenges, improvements are necessary at each step to produce reliable collagen image based assays.

**Vikas Singh, Dept. of Biostatistics and Medical Informatics**

***A Wavelets Based Schemes for Group-wise Differential Analysis of Networks and Connectivity Meshes in Neuroimaging***

Many statistical analysis problems in Neuroimaging involve data represented as a shape mesh or network, for example, cortical surface meshes and brain connectivity networks derived from functional and diffusion MR images respectively. Identifying significant differences across clinically disparate groups is an important step in various neuroscience studies. In this talk, I will describe some of our ongoing work in adapting results from harmonic analysis to facilitate the above analysis task. In particular, I will discuss how shape descriptors and filtering schemes based on non-Euclidean Wavelets can give improvements when performing tests involving cortical surface thickness data and white matter connectivity networks. Briefly, I will also cover applications to perceptually meaningful shape segmentation and surface registration. This is joint work with Moo K. Chung, Charles Hatt, Sterling C. Johnson, Won Hwa Kim, Alex Leow, and Deepti Pachauri.

**Ameer Pasha Hosseinbor, Department of Medical Physics**

***Hyperspherical Harmonics and their Application to Medical Imaging***

The hyperspherical harmonics (HSH) are the multidimensional analogues of the 3D spherical harmonics, and their physical application has been mainly limited to quantum chemistry to solve the Schrodinger equation for hydrogen-like species. In this talk, we discuss the utility of the HSH to medical imaging applications by extending their use to shape analysis and computational diffusion magnetic resonance imaging (MRI). First, we formulate a 4D HSH-based parameterization for multiple, disconnected objects (i.e. anatomical structures with changing topology), which we term HyperSPHARM, and present results on brain subcortical structures. Lastly, we use the 4D HSH to model the diffusion MRI signal in the brain, thereby developing a 4D hyperspherical interpretation of the diffusion signal-space. In both these medical imaging applications, the incorporation of a 4th dimension substantially reduces the number of fitting parameters needed to get an accurate reconstruction.

**Moo K. Chung, Department of Biostatistics and Medical Informatics**

***Twin Effects on Amygdala and Hippocampus Shapes via Heat Kernel Regression on Manifolds***

The differential correlations of monozygotic (MZ) and dizygotic (DZ) twin pairs against the normal population provide a natural way of disentangling genetic contribution from other factors in twin studies. We will determine the contribution of twin effects on amygdala and hippocampus surface shapes obtained from MRI. As a way to smooth out noisy deformation fields along the subcortical manifolds, heat kernel regression using the eigenfunctions of the Laplace-Beltrami operator is applied. MATLAB codes used in this talk can be found at <http://brainimaging.waisman.wisc.edu/-chung/lb>.

**Anqi Qiu, Department of Bioengineering, Clinical Imaging Research Centre,  
National University of Singapore**

***Brain Morphological Shape Markers for Alzheimer's Disease and Vascular Dementia***

Structural magnetic resonance imaging (MRI) techniques have been widely used to investigate imaging markers associated with psychiatric disorder and neurodegenerative diseases. In this talk, I will move away from traditional volumetric analysis to sophisticated morphological shape analysis for subcortical structures assessed using conventional T1-weighted MRI. I will demonstrate it in early detection of mild cognitive impairment (MCI), Alzheimer's disease (AD), and vascular dementia (VaD) using the datasets of ADNI, South Korean ADNI, and Singapore Memory Aging Cognition Study.

Short Bio: Qiu Anqi received her BS in Biomedical Engineering from Tsinghua University in 1999, MS degrees in Biomedical Engineering and Applied Mathematics and Statistics from University of Connecticut in 2002 and from the Johns Hopkins University in 2005, respectively. She obtained her PhD degree at the Johns Hopkins University in 2006. After one-year postgraduate training, she joined the National University of Singapore as assistant professor and launched her own Computational Functional Anatomy Laboratory at both the Faculty of Engineering and the School of Medicine.

Since her PhD study, she has worked on the field of medical image analysis. Her research focuses on the translation of mathematical modeling to quantitative medicine. Especially, she has been interested in extracting anatomical and functional information from magnetic resonance images in order to identify neuroimaging biomarkers associated with neurodegenerative diseases and neuropsychiatric disorders. Her group is currently leading the neuroimaging core of two major national projects: infant brain development and dementia. For more information, please visit website <http://www.bioeng.nus.edu.sg/cfa/>.

**Michael H. Coen, Ph.D., Department of Biostatistics and Medical Informatics**

***Analyzing Neuroimaging Data via In-Situ Statistics***

I discuss a new statistical approach to measuring minute, short-term changes in neural microstructure that are clinically meaningful yet unobservable to human experts. These methods have proved highly accurate in predicting longitudinal white matter changes in preclinical Alzheimer's disease. I will outline our approach, present ongoing work and results, and discuss its general applicability for other problems.

Rasmus M. Birn, Ph.D., Department of Psychiatry and Medical Physics

### *Processing Choices in Resting-state Functional Magnetic Resonance Imaging*

Resting-state functional magnetic resonance imaging (rs-fMRI) is a technique to measure functional connections in the brain using MRI. The use of this technique has virtually exploded in the past few years. However, this technique is highly sensitive to various sources of noise, such as scanner instabilities, head motion, cardiac pulsation, and respiration. While a number of correction techniques have been developed, there is currently no consensus for the processing steps that should be used. In our study, we examine the test-retest reliability of functional connectivity estimated from rs-fMRI, and the impact of various acquisition choices and processing steps.

Iain P. Bruce, Marquette University

### *Using the G-factor and SENSE Induced Correlations for Optimizing fcMRI Study Specific RF Coil Design*

In typical parallel MRI RF coil design, the g-factor is the de-facto metric for assessing the amplification of noise that arises in SENSE reconstructed images as a result of overlapping coil magnetic fields. Recently, however, it has been shown that an additional artifact of the SENSE reconstruction process is an artificially induced correlation between previously aliased voxels. As these correlations can have null-hypothesis implications in fcMRI studies, where no correlation is assumed between voxels, optimal coil designs that simultaneously minimize a metric of the traditional g-factor and the correlation induced between voxels in a ROI would be beneficial. With such a framework, RF coils can be designed for specific fcMRI studies, in which the noise and correlations induced by the SENSE process are minimized within particular regions of the brain. This is a joint work with Daniel B. Rowe.

M. Muge Karaman, Marquette University

### *A Statistical fMRI Model for Differential $T_2^*$ Contrast Incorporating $T_1$ and $T_2^*$ of Gray Matter*

Relaxation parameter estimation and brain activation detection are two main areas of study in magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI). Relaxation parameters can be used to distinguish voxels containing different types of tissue whereas activation determines voxels that are associated with neuronal activity. In fMRI, the standard practice has been to discard the first scans to avoid magnetic saturation effects. However, these first images have important information on the MR relaxivities for the type of tissue contained in voxels, which could provide pathological tissue discrimination. It is also well-known that the voxels located in gray matter (GM) contain neurons that are to be active while the subject is performing a task. As such, GM MR relaxivities can be incorporated into a statistical model in order to better detect brain activation. Moreover, although the MR magnetization physically depends on tissue and imaging parameters in a nonlinear fashion, a linear model is what is conventionally used in fMRI activation studies. In this study, we develop a statistical fMRI model for Differential  $T_2^*$  Contrast Incorporating  $T_1$  and  $T_2^*$  of GM, so-called DeTeCT-ING Model, that considers the physical magnetization equation to model MR magnetization; uses complex-valued time courses to estimate  $T_1$  and  $T_2^*$  for each voxel; then incorporates gray matter MR relaxivities into statistical model in order to better detect brain activation, all from a single pulse sequence by utilizing the first scans. This is a joint work with Daniel B. Rowe.

Mary Kociuba, Marquette University

*A Temporal Frequency Description of the Spatial Correlation Between Voxels in fMRI Due to Spatial Processing*

To correct the noise inherent within an acquired signal in fMRI and identify true biological spatio-temporal correlations, spatial and temporal filters are applied during the time series data processing. It is well known that spatial preprocessing induces correlation between voxels; applying a low pass spatial filter produces a smoother image, yet artificially increases the correlations between neighboring neural regions. The exact theoretical statistical relationships for the spatial covariance and spatial correlation matrices can be represented as a linear combination of second order voxel temporal frequencies. Developing this framework provides a means for quantifying the consequences of reconstruction and processing operations on the voxel temporal frequency spectrums, through identifying the temporal frequency bands that contribute significantly to induced correlations of no biological origin. This is a joint work with Daniel B. Rowe.