Methods for Neuroimaging Research (MP / NTP 651)

Must be registered for 3 credits

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Time: Twice per week for 75 minutes

Office Hours: By request

Class Overview:

The main objectives for this course are to provide a foundation in methods for magnetic resonance imaging (MRI) studies of the brain with statistical image analysis. The course will cover many of the most widely used methods for human neuroimaging studies including functional BOLD MRI, structural MRI morphometry, diffusion tensor imaging. Other neuroimaging MRI methods will also be covered. The course will cover methods for statistical image analysis, the physics and methods of image acquisition, discuss steps and tools for image analyses and the interpretation of the results.

Learning Outcomes:

• Develop a basic understanding of magnetic resonance imaging, anatomical imaging methods, functional BOLD MRI (fMRI), and diffusion tensor imaging

(DTI).

• Learn and apply basic methods for statistical image analyses.

• Gain hands-on experience with tools for processing and analyses of fMRI, DTI and anatomic brain images.

• Develop skills to independently process, analyze, troubleshoot and interpret MRI neuroimaging data.

Textbook and Materials:

Lectures will be supplemented with relevant articles provided by instructors as needed. For the fMRI lectures, we also strongly recommend Functional Magnetic Resonance Imaging by Huettel, Song and

McCarthy. Introduction to Functional Magnetic Resonance Imaging: Principles and Techniques by Buxton is also excellent. There are also excellent books on Diffusion Tensor Imaging: Introduction to Diffusion Tensor Imaging by Mori (basic) and Diffusion MRI: Theory, Methods and Applications by DK Jones.

Grades:

Note graded materials will be weighted differently for undergraduate and graduate students

Undergraduate Students:

Homework: 40%

Computer Exercises: 40%

Neuroimaging Literature Review: 20%

Graduate Students:

Homework: 30%

Computer Exercises: 30%

Semester Project: 40%

Homework Assignments are Assigned Weekly

Late Homework and Computer Exercise Reports will be penalized 10% and 10% for each additional week (e.g., up to 2 weeks late – 20%).

Computer Exercise Reports should be 1 page typed summary of the work with additional pages for figures. Each report must have title, objective, introduction, methods, results, discussion.

Assignments will be graded on a point scale between 0 and 100. Final course grades will be a weighted score of all assignments and will be set according to

Course Grade Scale: A:90-100; AB:80-89; B:70-79; BC:60-69; C:50-59; D:40-49; F:<40

Semester Project (Graduate Students):

In the early part of the semester, class projects will be defined and/or assigned for an independent neuroimaging project. This project should require a minimum of 20 additional hours of lab work outside of class. The project does not need to be novel, but should emphasize some aspect of neuroimaging methodology. It may be scanner-related experiments, or computer simulations. MR data sets can be provided by the instructor per request for simulation or image analysis projects. A project report will be required at the end of the semester.

Please do not simply pursue a project related to previous neuroimaging projects unless approved by instructor.

Neuroimaging Literature Review (Undergraduate Students):

In the early part of the semester, topics will be defined and/or assigned for an independent literature review project. This project will require a review of at least 5 published neuroimaging papers on a specific topic that is approved by the instructor. Students are responsible for researching (finding, reading and summarizing) the papers. A project report will be required at the end of the semester. The report should summarize the key findings of the papers and critically evaluate the neuroimaging methods used in each of the studies.

Please do not simply pursue a project related to previous neuroimaging projects unless approved by instructor.

Neuroimaging Methods – Class Schedule

Week 1: Overview of Class & Intro to Class Computers and Linux

Objectives: Present course overview, introduce students to the basics utilization of class computers and system software. This includes account login, basic linux commands, file management.

Materials: Computer Exercise Instructions; Links to On-Line Linux Tutorials

(http://www.ee.surrey.ac.uk/Teaching/Unix/)

Assignments: Survey of previous experience and interests. Computer exercises to learn computer basics for class.

Week 2: Introduction to MRI - Precession, Resonance, Relaxation

Objectives: Introduce the basics of how magnetic resonance imaging (MRI) works. Topics include the use of a magnetic field to align nuclear spins, the precession of nuclear spins around a magnetic field, the use of radio waves to perturb the nuclear spins (resonance), the property of relaxation that provides the basis for MRI image contrast, and the way in which spatial information is encoded.

Materials: Lecture notes. Computer exercise Instructions.

Assignments: Homework assignment on MRI contrast and how images are created. Computer exercises to learn how to convert between common MRI file formats.

Week 3: MRI pulse sequences for Neuroimaging research

Objectives: Introduce the many different ways that magnetic resonance images are acquired in neuroimaging research. This includes more rapid imaging techniques (e.g. echo-planar imaging); ways to make the signal sensitive to specific tissue properties, such as diffusion; recent advances that improve spatial and temporal resolution (e.g. parallel imaging); and the tradeoffs between resolution and signal-to-noise. Students will also observe an MRI scanning session.

Materials: Lecture notes. MRI screening form to screen for contraindications to observing the MRI scanning session.

Assignments: Homework assignment to test knowledge about 1) the ways MRI data is acquired in neuroimaging research and 2) the differences in image contrast observed in the MRI scanner demonstration.

Week 4: Basic Statistical Analysis Methods

Objectives: Introduce basic methods for statistical analysis of neuroimaging data. Topics include definition of terminology (probability distributions, bias, variance, covariance), hypothesis testing, models (regression, general linear model), and least squares estimation methods.

Materials: Lecture notes.

Assignments: Homework assignment on the general linear model, hypothesis testing, and design matrix.

Week 5: Advanced Statistical Analysis Methods

Objectives: Continue presentation of statistical image analysis techniques. Topics include statistical contrast, the problem of multiple comparisons in statistical image analyses and controlling for multiple comparisons (Bonferroni, Cluster based, Family-Wise Error, False Discovery Rate), nonparametric methods (Permutation methods). Both lectures and in-class computer exercises are used to cover material.

Materials: Lecture notes. Computer exercise instructions.

Assignments: Homework assignment on statistical model contrast, multiple comparisons. Computer exercise on comparing multiple comparisons corrections with cluster-based and permutation based methods.

Week 6: Structural MRI and Morphometry

Objectives: Introduce MRI acquisition and image analysis methods for assessing brain volume and morphometry. Topics include methods for image segmentation (Gray Matter, White Matter and CSF), spatial normalization (affine and diffeomorphic), brain template matching, and voxel-based morphometry. In-Class computer exercise focuses on tools for voxel based morphometry with FSL (similar to http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLVBM/UserGuide ) Materials: Lecture notes. Computer exercise instructions. Manual for ANTS spatial normalization software. Paper: Mechelli A. et al., Voxel Based Morphometry of the Human Brain: Methods and Applications (Curr Med Imag Rev. 2005).

Assignments: Homework assignment on image segmentation, registration and morphometry. Report summary of computer exercise to demonstrate voxel based morphometry using FSL.

Week 7: fMRI - Mechanisms

Objectives: Introduce the way that brain function is measured with MRI (functional MRI, fMRI). Topics include the origin of the fMRI signal, spatial and temporal characteristics of the fMRI signal, practical considerations in acquiring fMRI data, and a broad overview of current research in fMRI. In-class computer exercises introduce the students to one of the more commonly used fMRI data analysis software packages, Analysis of Functional NeuroImages (AFNI).

Materials: Lecture notes. Computer exercise instructions. Link to the AFNI user manual (https://afni.nimh.nih.gov/afni/doc ).

Assignments: Homework assignment on fMRI contrast mechanisms. Report summary of computer exercises to demonstrate familiarity with the AFNI software package.

Week 8: fMRI – Analysis (single subject and group)

Objectives: Introduce the steps necessary to analyze fMRI data. Topics include the steps necessary to correct for signal distortions (e.g. motion), different ways to estimate brain function, and common problems in fMRI data analysis. In-class computer exercises provide students with hands-on experience in analyzing fMRI data, estimating the brain activation in both an individual subject and on a group of subjects.

Materials: Lecture notes. Computer exercise instructions. Link to YouTube videos giving step-by-step instructions for the in-class exercises, by Andrew Jahn.

(https://www.youtube.com/watch?v=3QzEdYggEfs&list=PLIQIswOrUH6-v5EWwFdMsTZttt4407KW9 ).

Assignments: Homework assignment on the steps necessary to analyze fMRI data. Report summary of computer exercise to estimate brain activation in one individual and a group of subjects.

Week 9: fMRI - Resting state and Connectivity

Objectives: Introduce the way that functional connections between brain regions can be estimated from fMRI data, including data acquired while the subject is in a “resting-state.” Topics include the history of resting-state functional connectivity, the evidence that resting-state functional MRI signals are neuronal in origin, and the processing steps necessary to estimate functional connectivity. In-class computer exercises provide students with hands-on experience in computing functional connectivity estimates from fMRI data.

Materials: Lecture notes. Computer exercise instructions. Paper: Biswal B., et al., Functional Connectivity in the Motor Cortex of Resting Human Brain using Echo-planar MRI. Magn. Res. Med. 1995.

Assignments: Homework assignment on the processing steps necessary to estimate functional connectivity and the evidence that resting-state functional connectivity is neuronal in origin.

Report summary of computer exercise to estimate resting-state functional connectivity in one test subject.

Week 10: fMRI – paradigm design, advanced fMRI

Objectives: Introduce ways to design fMRI studies. Topics include methods to determine optimal stimulus timing, limitations in paradigm design due to the temporal dynamics of the fMRI signal, and alternative strategies to measure brain function with MRI (e.g. natural viewing paradigms). In-class computer exercises provide students with hands-on experience in designing an fMRI study and determining the optimal stimulus timing.

Materials: Lecture notes. Computer exercise instructions. Paper: Birn RM et al., Detection Versus Estimation in Event-Related fMRI: Choosing the Optimal Stimulus Timing (NeuroImage, 15, 252-264 (2002)).

Assignments: Homework assignment on the concepts in fMRI paradigm design. Report summary of computer exercise to optimize the stimulus timing in an fMRI study.

Week 11: Diffusion Tensor Imaging

Objectives: Introduction to Diffusion Tensor Imaging (DTI) including basic physics, acquisition methods, encoding, protocols, common artifacts and corrections (eddy currents, B0 distortion), quantitative DTI estimation, scalar measures (fractional anisotropy, mean diffusivity, axial and radial diffusivities). In-class computer exercises provide students with hands-on experience with diffusion-weighted images, diffusion tensor encoding, tools for correcting head motion and eddy current distortion, tensor estimation, and quantitative DTI maps (FA, MD, AD, RD).

Materials: Lecture notes. Computer exercise instructions. Papers: Alexander AL. et al., Diffusion Tensor Imaging of the Brain (Neurotherapeutics 4:316-329; (2007)). Jones DK. et al, White matter integrity, fiber count and other fallacies: The do's and don'ts of diffusion MRI.

(Neuroimage 73:239-54 (2013)). Tournier JD et al., Diffusion Tensor Imaging and Beyond

(Magn Reson Med 65:1532-56 (2011)).

Assignments: Homework assignment on DTI encoding, quantitative measures. Report summary of computer exercise to correct and compute quantitative DTI maps.

Week 12: Diffusion Tensor Imaging Analyses

Objectives: Review various methods for DTI analyses that are commonly used in neuroimaging research. Topics include a survey of DTI applications, challenges with analyses (heterogeneity of DTI measures across the brain) and analysis techniques (whole brain histograms, anatomical templates/regions-of-interest, tract based spatial statistics, voxel based analyses). In class computer exercise provides exposure to DTI spatial normalization (with DTI-TK), creating a DTI brain template, and voxel-based statistical testing with FSL.

Materials: Lecture notes. Computer exercise instructions. Papers:

Zhang H et al., Deformable Registration of Diffusion Tensor MR Images with Explicit Orientation Optimization (Med Imag Anal. 10:764-85 (2006)).

Lee JE et al., A study of diffusion tensor imaging by tissue-specific, smoothing compensated voxel-based analysis (Neuroimage 44: 870-83 (2007)).

Smith SM et al. Tract-based spatial statistics (Neuroimage 31:1487-505 (2006)).

Assignments: Homework assignment on DTI spatial normalization, analysis methods. Report summary of computer exercise on DTI spatial normalization and voxel-based analysis.

Week 13: Advanced Diffusion Imaging

Objectives: Lecture on advanced diffusion-weighted imaging methods beyond the diffusion tensor. Topics include limitations of the diffusion tensor, diffusion-weighted signal behavior at high diffusion-weighting, high angular diffusion imaging models (HARDI, Q-ball), parametric models (Kurtosis, NODDI), q-space and diffusion spectrum imaging.

Materials: Lecture notes. Papers: Wedeen VJ et al., Mapping Complex Tissue Architecture with Diffusion Spectrum Magnetic Resonance Imaging (Magn Reson Med. 54:1377-86 (2005)).

Zhang H et al., NODDI: Practical in vivo neurite orientation dispersion and density imaging fo the human brain (Neuroimage 61: 1000-16 (2012)).

Assignments: Homework assignment on advanced diffusion imaging methods.

Week 14: Tractography

Objectives: Review methods and applications for white matter tractography. Topics include estimation of white matter orientation using DTI and other diffusion-weighted imaging methods, tractography algorithms for estimating white matter tract trajectories, deterministic tractography, and probabilistic tractography. In class computer exercise provides experience with DTI tractography reconstruction of human white matter tracts.

Materials: Lecture notes. Computer exercise instructions. Papers:

Lazar M. Mapping brain anatomical connectivity using white matter tractography (NMR Biomed. 23:821-35 (2010)).

Catani M & de Schotten MT. A diffusion tensor imaging tractography atlas for virtual in vivo dissections (Cortex 44: 1105-1132 (2008)).

Assignments: Homework assignment on DTI tractography. Report summary of computer exercise on DTI tractography.

Week 15: Connectomics

Objectives: Provide a basic overview of the rapidly evolving field of brain connectomics using fMRI and DTI. Topics include state-of-the-art neuroimaging hardware and methods

(connectome gradients, simultaneous multi-slice, high resolution DWI and fMRI), generating individual connectomes, graph theory, and statistical analyses of connectomes.

Materials: Lecture notes. Papers:

Sporns O et al., The human connectome: a structural description of the human brain (PLoS Comput Biol 1:e42 (2005)).

Bullmore E et al., Complex brain networks: graph theoretical analysis of structural and functional systems (Nat Rev Neurosci. 10:186-98 (2009)).

Assignments: Homework assignment on graph theory and connectomics.