# Connectomics: The Functional and Structural Wiring of the Human Brain

Syllabus MBB 980V Spring 2021

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**Time:** Tuesdays 3 PM – 5 PM
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## General Information

Magnetic Resonance Imaging (MRI) has revolutionized our ability to study the living human brain. Studies of the wiring or connections between different regions of the human brain using a technique called functional MRI have transformed our understanding of the brain's organization, revealing that at the macroscale, the brain is a complex network with properties that complex networks in nature typically exhibit. From functional MRI, we see that the brain is organized into a set of modules, which we just refer to as brain networks, that are active when we engage in our every day activities. More recently, advances in diffusion MRI have made it possible to study the white matter structural connectome via *in vivo* fiber tracking to reveal how this information highway system in the brain physically connects different gray matter regions. MRI-based connectomics is the study of the connectivity of the brain and is a rapidly growing field, with new methods and applications evolving at an incredibly fast pace. The goal of this class is to understand how MRI methods are used to study the living human brain connectome. This course is designed for students in the MBB programs who are interested in learning about neuroimaging techniques for studying brain connectivity, including those who are interested in neuroscience applications and brain disorders and those interested in bioinformatics/computer science/statistics/physics applications in neuroimaging.

In this course, we will learn the basics of the workhorse MRI methods used for connectomics research, functional and diffusion MRI. The basics of each method will be primarily conceptual, with some exposure to the physics and math underlying each technique. We will learn how each of these techniques is used to study the structural and functional connectome of the human brain. Key methodological and interpretational issues for each technique will be discussed, including comparative neuroanatomy research that aims to integrate MRI connectomic measures with findings from translational studies using tracer injections to gain an understanding of the mechanisms underpinning MRI measures of connectivity. We will discuss brain networks that have been reported in the literature using these methods, and the links between structural and functional connectomes. We will do a survey of widely used open access tools for connectivity and connectome analyses. Last, throughout the course we will discuss open access connectome datasets, including the Human Connectome Lifespan and Disease Connectome studies, the ABCD study, and the UK Biobank, which will be the hypothetical data sources for your final research projects. The research project will be modeled after an HMS postdoctoral fellowship application to provide experience in designing your own hypothetical research study and in writing research proposals. Students may also use this opportunity to develop their proposal for a senior thesis or other real-life project (for example, NIH pre-doctoral fellowships) focused on connectomics/machine learning if appropriate.

## Grading is based on the following:

| | |
|---|---|
| Class Participation: | 25% |
| Pre-Proposal: | 10% |
| Presentations on Aims & Significance | 15% |
| Presentation on Final Project | 15% |
| Final Project (Written): | 35% |

Class Participation: The success of this course depends upon your participation. You will be expected to read all assigned articles ***prior*** to each class and be prepared to discuss your thoughts, ideas, and questions on each topic. There will be a combination of activities and assignments in and out of class that will be required to facilitate student participation. Class attendance is required.

Extra readings are provided in case you are interested in exploring a topic in more depth, but are not required reading.

Assigned readings may be changed a bit if I find something that seems like a better compliment to the topic.

Pre-Proposal: Each student will submit a couple of candidate ideas for the Final Project. There should be about a paragraph for each candidate idea, with a few key references, so I can provide feedback to guide your choice of topic for the Final Project.

Final Project: Each student will prepare a four-page research paper modeled after the Research Plan for an HMS fellowship application. I will provide additional details of the structure of the application.

Presentations on Final Project Elements: Each student will do two short presentations on the elements of the Final Project. The first will be on the Specific Aims & Significance to get feedback from the class on your project topic, the second will be on the final project (all sections). You will be expected to prepare a powerpoint (or similar) presentations. The length of the presentations will depend on final class enrollment. Guidelines on the elements of the Final Project, including all presentations, will be given to you.

**Academic Honesty**

I expect that all students will uphold the standards of academic integrity according to the Harvard honor code. You are strongly encouraged to interact with your classmates on your Final Project to refine, focus, and develop your research study, and you will have ample opportunities in class to obtain feedback from me and your classmates on your proposed study. However, your written project must be the result of your own research and writing. You will be expected to produce your own academic work of integrity – that is, work that adheres to the scholarly and intellectual standards of *accurate attribution of sources and transparent acknowledgement of the contribution of others to their ideas, discoveries, interpretations, and conclusions*. Please see the Harvard Guide to Using Sources for further information (https://usingsources.fas.harvard.edu/). Cheating on quizzes also will not be tolerated and will result in a failure for that quiz.

**Syllabus (Tentative)**

**Week 1 (1/26): Introduction and History of the Human Connectome.**

Assigned Readings:
Sporns O. 2011. The human connectome: A complex network. Annals NY Acad Sci 1224: 109-125.
Catani M et al. 2013. Connectomic approaches before the connectome. Neuroimage 80:2-13.

**Week 2 (2/2): Properties of Brain Networks, Parcellation and the Connectome. (Leo out)**

Assigned Readings:
Laio, et al., 2017. Small-world human brain networks: Perspectives and challenges. Neurosci and Biobeh Reviews 77:286-300. **Read sections 2.1 and 2.2 only (pp. 287-289).**

Ardesch D., et al. 2019. The human connectome from an evolutionary perspective. Progress in Brain Research 250:129-151. **Read all.**

Sporns O. 2013. The human connectome: Origins and challenges. Neuroimage 80:53-61. **Only the section on "Challenges" (pp. 56-58).**

**Week 3 (2/9): The HCP Lifespan and Disease Connectome Projects and Other Open Access Datasets (Leo out)**

Assigned Readings:
Barch D. 2017. Resting state functional connectivity in the Human Connectome Project: Current status and relevance to understanding psychopathology. Harvard Rev Psychiatry 25:209-217.

**Week 4 (2/16): Fundamentals of MRI Part 1**

Assigned Readings:
Huettel S., et al. 2009. Functional Magnetic Resonance Imaging, 2nd Edition. Sinauer Associates, Inc., Sunderland, MA. pp. 31-43, 57-67.

**Week 5 (2/23): Fundamentals of MRI Part 2**

Assigned Readings:
Huettel S., et al. 2009. Functional Magnetic Resonance Imaging, 2nd Edition. Sinauer Associates, Inc., Sunderland, MA. pp. 90-97, 121-131.

**Week 6 (3/2): Introduction to Functional MRI and Functional Connectivity Part 1**

Assigned Readings:
Bandettini P. 2012. Functional MRI: A confluence of fortunate circumstances. NeuroImage 61:A3-A11.

**Week 7 (3/9): Introduction to Functional MRI and Functional Connectivity Part 2**

**Project Pre-Proposal Due**

Fox M. and Raichle M. 2007. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nature Neuroscience Reviews 8:700-711.

**Week 8 (3/16): No Class, Wellness Day**

**Week 9 (3/23): Intrinsic Connectivity Networks and Challenges of FMRI Connectivity**

Assigned Readings:
Uddin et al. 2019. Towards a universal taxonomy of macro-scale functional human brain networks. Brain Topography 32:926-942.
Buckner R. et al. 2013. Opportunities and limitations of intrinsic functional connectivity MRI. Nature Neuroscience 16:832-837.

**Due 3/26 Recorded presentations: Aims and Significance**

**Week 10 (3/30): Introduction to Diffusion MRI and Structural Connectivity with Tractography**

Guest speaker: Anastasia Yendiki, PhD. Associate Professor HMS
https://scholar.harvard.edu/a-y/research

Assigned Readings:
Mueller et al. 2015. Diffusion MRI and its role in neuropsychology. Neuropsychol Rev 25:250-271.

Extra:
Assaf Y., et al. 2019. The role of diffusion MRI in neuroscience. NMR in Biomed 32e3762, pp. 1-16.

**Week 11 (4/6): Interpretation and Validation of dMRI Measures of White Matter Structure**

Beaulieu C. 2014. The Biological Basis of Diffusion MRI in *Diffusion MRI 2nd Edition*. Edited by Heidi Johansen-Berg and Timothy Behrens. Elsevier. Pp. 155-183.

**Due Student Reviews of Significance and Aims Presentations**
**In class discussion of presentations**

**Week 12 (4/13): Data Analysis Tools and Methods for MRI Connectomics**

Assigned Readings:
TBD

**Week 13 (4/20): In class presentations on Final Projects**

**Week 14 (4/27): Cross-Modal and Cross-Species Comparisons of Structural and Functional Connectivity**

Assigned Readings:
Reid et al. 2016. A cross-modal, cross-species comparison of connectivity measures in the primate brain. Neuroimage 125:311-331.

**Final Exam Period:** **Final Project papers due, exact date TBD.**

Some learning activities:

1) white board to answer questions
2) twitter tasks
3) how do you do a literature search – have them figure out how many citations, scan some of them pick out interesting one and present it to the class
4) create a slide on a section of the reading to present to the class
5) post survey answers to the chat
6) these tasks in breakout rooms
7) live google doc/breakout room
8) view addiction/network real-time feedback video
9) OHBM On Demand
10) how do you engage with your academic/career community?
11) See https://poorvucenter.yale.edu/Classroom-Assessment-Techniques for more ideas, including the minute paper (!), empty outlines, background knowledge probe
12) students create test questions for a lecture
13) for first lecture, pick a picture or milestone that is of interest to you and do some further research on it, google, Wikipedia or other

If Leo is TA, have her monitor the chat