COLUMBIA | ENGINEERING
The Fu Foundation School of Engineering and Applied Science

COLUMBIA UNIVERSITY MEDICAL CENTER

Syllabus

In Vivo Magnetic Resonance Spectroscopy - from Data to Clinical Benefit

BME Topic Class, Fall 2018

Date/Time:	Thursdays, 4:10-6:40 PM
Location:	TBD
Instructors:	1. Christoph Juchem, PhD, christoph.juchem@columbia.edu Office hours: TBD 2. Lawrence Kegeles, MD, PhD, lsk5@cumc.columbia.edu Office hours: TBD
Teaching Assistants:	1. SEAS: TBD Office hours: TBD 2. CUMC: TBD Office hours: TBD
Prerequisites:	none
Credits:	3 points

Course Description

Magnetic resonance spectroscopy (MRS) allows the detection and quantification of chemical compounds from localized regions in living tissue, e.g., the brain, in a noninvasive fashion. It thereby provides a powerful tool to assess key aspects of brain metabolism and function. The repertoire of measurable compounds along with the quantitative character of the derived information makes MRS a versatile tool for the identification of clinical conditions, for longitudinal patient monitoring and for treatment control and monitoring of virtually all disorders with a metabolic signature.

This educational course comprises all aspects of *in vivo* MRS from theory to experiment, from data acquisition to the derivation of metabolic signatures, and from study design to clinical interpretation. Anyone interested in gaining an understanding of MRS techniques, their potential and the limitations of their application *in vivo* will find this course useful. The course bridges the gap between theoretical concepts, hands-on training in MRS data literacy and direct experimental experience on a human 3T MR scanner. This 16-session combined academic course and “boot-camp” will provide novices in MRS the requisite know-how for future engagement in MRS research and diagnostics.

Course Objectives

At the end of the course, attendees should

- be familiar with the concepts of magnetic resonance and MRS
- understand the basic magnetic resonance scanner and hardware architecture
- have a basic overview of research and clinical/neuroscience MRS applications
- have a basic understanding of the biochemistry targeted with *in vivo* MRS
- recognize metabolic signatures in clinical diagnostics and pathology
- have a basic understanding of MRS study design and execution
- be able to handle, correct and process MRS data
- be able to quantify MRS data and to derive metabolic profiles
- be able to provide a basic clinical/neuroscience interpretation of biochemical results
- be able to describe the potential, limitations and pitfalls of MRS
- be able to provide some critique of MRS projects and manuscripts before an audience of peers

Suggested Textbooks

1. *Magnetic Resonance Spectroscopy: Tools for Neuroscientific Research and Emerging Clinical Applications.* Edited by Charlotte C. Stagg, Douglas L. Rothman, ISBN 9780124016880, https://clio.columbia.edu/catalog/10748129
2. *Magnetic Resonance Spectroscopy Diagnosis of Neurological Diseases.* Edited by Else R. Danielsen, Brian Ross, ISBN 0824702387, https://clio.columbia.edu/catalog/4059334
3. *Magnetic Resonance Spectroscopy of Degenerative Brain Diseases.* Edited by Gulin Oz, ISBN 9783319335551, https://clio.columbia.edu/catalog/12260315
4. *MRI: Basic Principles and Applications*, Brian M. Dale, Mark A. Brown, and Richard C. Semelka, ISBN 9781119013037, https://clio.columbia.edu/catalog/11720594
5. *The Mathematics of Medical Imaging: A Beginner's Guide*, Timothy G. Feeman, ISBN 9783319226651, https://clio.columbia.edu/catalog/11685941
6. *In Vivo NMR Spectroscopy: Principles and Techniques*, Robin A. de Graaf, ISBN 9780470512968, https://clio.columbia.edu/catalog/4059444

Note that electronic versions of all books are available through Columbia's online library free of charge

Grading Criteria

12 problem sets at 3% each:	36%
Midterm exam:	30%
Final exam:	34%

Policies

The course follows Columbia University policies, including those describing the Rights and Responsibilities of its members. Also, please note the Faculty Statement on Academic Integrity.

Homework Assignments
All homework is due at the beginning of the next class and to be submitted via CourseWorks (courseworks2.columbia.edu).

Make Up Exams
Only students with legitimate reasons will be allowed to postpone examinations or make up for missed ones. Note that
1) students are expected to present appropriate documentation, e.g. a doctor's note
2) all make-up exams will be oral - no exceptions.

Additional
All aspects of this syllabus are subject to change.
Suggestions and feedback are welcome.

Course Outline

1. *Classroom: Basics of Nuclear Magnetic Resonance*

   Magnetic resonance, gyromagnetic ratio, Larmor condition, energy levels, spin polarization, magnetization, Bloch equations, dipole-dipole interaction, relaxation, radio-frequency pulses, pulse-acquire, saturation, inversion, spin-echo

2. *Classroom: Basics of Magnetic Resonance Spectroscopy*

   Concept of Fourier MRS, chemical shift, J-coupling, localization, water-suppression, outer volume suppression, STEAM, PRESS, LASER, J-difference editing, ^{1}H, X nuclei, adjustments, data acquisition, frequency demodulation, analog-to-digital conversion

3. *Classroom: Basics of Biochemistry*

   Biochemistry review, metabolites-of-interest (^{1}H, ^{13}C, ^{31}P, ^{17}O, ^{19}F), non-invasive quantification with MRS, cellular integrity (NAA, choline, myo-inositol), neurotransmission (Glutamate, Glutamine, GABA), energy metabolism (^{13}C, ^{31}P, Cr/PCr, glucose, lactate), oxidative stress and antioxidant potential (GSH, ascorbic acid), psychotropic medication (^{19}F, ^{7}Li)

4. *Classroom: MRS in Mood/Anxiety Disorders*

   MRS in unipolar major depression, bipolar disorder, anxiety disorders, obsessive compulsive disorder, post-traumatic stress disorder: roles of GABA and glutamate, evaluation of ECT, rTMS, and tDCS therapeutics, evaluation of ketamine treatment

5. *Classroom: MRS in Psychotic and Substance Use Disorders*

   MRS in clinical high-risk for psychosis, first-degree relatives, first-episode schizophrenia, chronic schizophrenia, unmedicated state, effects of medication and other treatment modalities, addiction (ethanol, nicotine, cocaine), acute pharmacological challenge paradigms, pharmacological models of illness

6. *Classroom: MRS of Neurodegenerative Disorders*

   MRS in multiple sclerosis, Alzheimer's disease, Parkinson's disease, fronto-temporal dementia, Lewy body disease, amyotrophic lateral sclerosis: disturbances in myo-inositol, GABA, glutamate, and high-energy phosphates as indicators of glial integrity, excitation-inhibition disturbances, and tissue bioenergetic status

7. *Computer Lab: Data Processing Strategies*

   Data handling, apodization, filtering, zero-filling, quality assessment, J-difference processing, phase/frequency/line shape/eddy current correction, combination of multi-dimensional data (Rx, NR), SVD water removal, concepts and strategies of Fourier processing

8. *Computer Lab: Data Analysis Strategies*

   Model-based analysis, spectral fitting algorithms, Lorentzian/Gaussian/Voigt shapes, prior knowledge, identification of resonances, quantitative referencing, absolute quantification, Cramer-Rao lower bonds, Hessian error, Monte-Carlo error estimation, statistical testing, comparison of time- and frequency-domain approaches

9. *Computer Lab: Data Interpretation*

   Metabolic modeling, clinical diagnosis and pathophysiological interpretation, treatment monitoring, biomarkers as treatment targets, prediction of disease onset, prediction of illness exacerbation

10. *Classroom: Potential, Limitations and Future Directions*

    Promises and pitfalls, new neurochemicals, labeling, hyperpolarization, task-based MRS, multi-dimensional MRS, regression analysis (ridge/Tikhonov, Lasso), sparse MRS acquisition, information theoretical approaches (compressed sensing, Dantzig selector), machine learning

11. *MR Scanner: Introduction to MR Scanner Environment and Hardware*

    MR scanner, gradient system, gradient amplifiers, RF coils, RF filters, RF amplifier, controller / acquisition system, patient bed, patient monitoring, informed consent, metal detector, subject safety, pregnancy test, presentation software for functional tasks, stimulus paradigms, acquisition computer, acquisition software

12. *MR Scanner: Basic Experiment Setup (Phantom)*

    Phantoms, phantom placement, MR system setup, RF coil setup, functionality testing, scout image, B_0 shimming, FASTMAP, B_1 shimming

13. *MR Scanner: MRS Experiment Setup (Phantom)*

    MRS voxel placement, RF power optimization, outer-volume suppression, water suppression, protocol design and execution, MRS problems and remedies: eddy currents, sequence timing, phase, baseline, residual water

14. *MR Scanner: MRS Experiment Execution (Phantom)*

    STEAM, PRESS, semi-LASER, J-difference editing (JDE), spectroscopic imaging (MRSI), multi-planar chemical shift imaging (MPCSI)

15. *MR Scanner: In Vivo MRS Investigation (Healthy Volunteer)*

    Representative *in vivo* MRS study procedure (comprising all aspect of classes 11-15) including informed consent, safety, subject preparation, anatomy and calibration, MRS setup, selective illustrative MRS protocols: STEAM, JDE

16. *Classroom: Processing, Quantification and Interpretation of In Vivo MRS*

    Analysis of data acquired during class #15 with method and techniques discussed in classes #7-9.