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

COLUMBIA UNIVERSITY MEDICAL CENTER

Syllabus

Principles and Practices of In Vivo Magnetic Resonance Spectroscopy

BMEN E6410, Fall 2020

Date/Time:	Thursdays, 4:10-6:40 PM
Locations:	1) Lectures online 2) Live practical sessions at 3T MRI scanner (TBD)
	This course is open to both undergraduates and graduate students. The option to virtually participate in all course activities online will be fully available to any students who do not attend in person. Students with questions or concerns about course logistics should feel free to email the instruction team for clarification.
Instructors:	1. Christoph Juchem, Ph.D. cwj2112@columbia.edu Office hours (Online): Thursday, 2-3 PM 2. Lawrence Kegeles, M.D., Ph.D. lsk5@cumc.columbia.edu Office hours (Online): Tuesday, 2:30-3:30 PM
Teaching Assistants:	1. SEAS: Kelley Swanberg, M.Sc. kswanberg@columbia.edu Office hours (Online): Tuesday, 2:30-3:30 PM (with Dr. Kegeles) 2. CUMC: Jodi Weinstein, M.D. jodi.weinstein@stonybrookmedicine.edu Office hours (Online): Thursday, 2-3 PM (with Dr. Juchem)
Prerequisites:	Quantitative Physiology I or II (or instructor permission) Undergraduates as well as MS or PhD students welcome
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 13-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 Gülin Öz, 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 9781119382546, https://clio.columbia.edu/catalog/13906052

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

Grading Criteria

11 problem sets at 3% each:	33%
Participation:	20%
Midterm exam:	20%
Final exam:	27%

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).

Course Participation Grade

To receive full points for participation, in addition to remaining generally engaged and vocal during class lectures and discussions, students will be expected to participate in the following activities:

> **PollEverywhere quizzes during lecture:** Every course lecture will involve a variable number of live quiz questions to which students will be expected to submit answers in real time for a participation score. Everyone enrolled in the class via Courseworks is automatically enrolled in PollEverywhere; this can be confirmed on https://www.polleverywhere.com/login by submitting either one's Columbia (UNI) email address or, for non-UNI students, the non-Columbia email address through which one enrolled in Courseworks and clicking "Log In Via Columbia." Students should confirm at the beginning of each lecture that they are logged in to PollEverywhere, and at quiz time students will be directed to a URL that will enable them to participate in live questions.
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> **Piazza discussion:** Every week students will be expected to post at least one question and at least one answer to another student's question on our Piazza forum, moderated regularly by the course instruction team:
> https://piazza.com/columbia/fall2020/bmene6410principlesandpracticesofinvivomrs

Please let the instruction team know if you have any trouble accessing either PollEverywhere or Piazza. Students who anticipate needing to miss a lecture should contact the instruction team in advance so that alternate assignments can be arranged.

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.

Camera During Online Participation

Course participants attending online are expected to keep their camera on at all times.

Additional

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

Course Outline

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Week	Date	Lecture	Topics	Assignments
1	09/10/20	#1	**Basics of Nuclear Magnetic Resonance** (Online) 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	HW1 out, due 9/17/2020
2	09/17/20	#2	**Basics of Magnetic Resonance Spectroscopy** (Online) Concept of Fourier MRS, chemical shift, J-coupling, localization, water suppression, outer volume suppression, STEAM, PRESS, LASER, J-difference editing, 1H, X nuclei, adjustments, data acquisition, frequency demodulation, analog-to-digital conversion	HW2 out, due 9/24/2020
3	09/24/20	#3	**Basics of Biochemistry** (Online) Biochemistry review, metabolites of interest (1H, 13C, 31P, 17O, 19F), non-invasive quantification with MRS, cellular integrity (NAA, choline, myo-inositol), neurotransmission (glutamate, glutamine, GABA), energy metabolism (13C, 31P, Cr/PCr, glucose, lactate), oxidative stress and antioxidant potential (GSH, ascorbic acid), psychotropic medication (19F, 7Li)	HW3 out, due 10/1/2020
4	10/01/20	#4	**Data Processing Strategies** (Online) 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	HW4 out, due 10/8/2020
5	10/08/20	#5	**MRS in Mood / Anxiety Disorders** (Online) 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	HW5 out, due 10/15/2020
6	10/15/20	#6	**MRS in Psychotic and Substance Use Disorders** (Online) 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	no HW
7	10/22/20	-	**Final Fall A / Midterm Exam** (Online)	
8	10/29/20	#7	**MRS in Neurodegenerative Disorders** (Online) 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	HW6 out, due 11/5/2020
9	11/05/20	#8	**Data Analysis and Interpretation** (Online) Model-based analysis, spectral fitting algorithms, Lorentzian/Gaussian/Voigt shapes, prior knowledge, identification of resonances, absolute quantification, Cramer-Rao lower bonds, Hessian error, Monte-Carlo error estimation, statistical testing, metabolic modeling, clinical diagnosis and pathophysiological interpretation, treatment monitoring, biomarkers as treatment targets, prediction of disease onset, prediction of illness exacerbation	HW7 out, due 11/12/2020
10	11/12/20	#9	**Introduction to Environment and Hardware, Overall Experiment Setup** (MR Scanner) MR scanner, gradient system, gradient amplifiers, RF coils, RF filters, RF amplifier, controller / acquisition system, patient bed, patient monitoring, metal detector, subject safety, presentation software for functional tasks, stimulus paradigms, acquisition computer, acquisition software, Phantoms, phantom placement, RF coil setup, functionality testing, scout image, B0 shimming	HW8 out, due 11/19/2020
11	11/19/20	#10	**MRS Experiment Setup and Execution: Phantom** (MR Scanner) MRS voxel placement, MRS problems and remedies: eddy currents, sequence timing, phase, baseline, residual water, STEAM, PRESS, semi-LASER, J-difference editing (JDE), spectroscopic imaging (MRSI), multi-planar chemical shift imaging (MPCSI)	HW9 out, due 11/24/2020
12	*Thanksgiving* **Tuesday 11/24/2020**	#11	**In Vivo MRS Investigation: Volunteer** (MR Scanner) Representative in vivo MRS study procedure (comprising all aspect of classes #9 and #10) including informed consent, safety, subject preparation, anatomy and calibration, MRS setup, selective illustrative MRS protocols: STEAM, JDE	HW10 out, due 12/3/2020
13	12/03/20	#12	**Processing, Quantification and Interpretation of In Vivo MRS** (Online) Analysis of data acquired during class #11 with method and techniques discussed previously.	HW11 out, due 12/10/2020
14	12/10/20	#13	**Potential, Limitations and Future Directions** (TBD) TBD	Guest speaker: TBD (no HW)
15	12/17/20		**Final Exam** (Online)	