

Syllabus
Magnetic Resonance Spectroscopy: A Window to the Living Brain
BMEN 4490, Fall 2022

Date/Time:	Thursdays, 4:10-6:40 PM Optional weekly discussions/office hours
Locations:	1) Lectures: Mudd 327 or Hammer Health Sciences Center 303 2) Discussion and office hours: Wednesdays, 4:00-5:00 PM (Zoom, accessible from Courseworks) Thursdays, 2:30-3:30 PM (Mudd 343) 3) Live practical sessions at 3T MRI scanner (Jerome L. Greene Science Center) <i>Students with questions or concerns about course logistics should feel free to email the instruction team for clarification.</i>
Instructors:	1. Christoph Juchem, Ph.D. cwj2112@columbia.edu Discussion and office hours (Mudd 343): Thursdays, 2:30-3:30 P.M. 2. Lawrence Kegeles, M.D., Ph.D. lsk5@cumc.columbia.edu Discussion and office hours (online): Wednesdays, 4:00-5:00 P.M.
Teaching Assistants:	1. SEAS: Ronald Instrella, M.Sc. ronald.instrella@columbia.edu Discussion and office hours (online): Wednesdays, 4:00-5:00 P.M. (with Prof. Kegeles) 2. CUMC: Jonathan Wai, M.D. Jonathan.Wai@nyspi.columbia.edu Discussion and office hours (Mudd 343): Thursdays, 2:30-3:30 P.M. (with Prof. Juchem)
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 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

10 problem sets at 3% each:	30%
Participation:	20%
Midterm exam:	20%
Final exam:	30%

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](#). Academic integrity violations will be referred to the Student Conduct and Community Standards Office and may constitute grounds for automatic failure of the course.

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, students will be expected to remain generally engaged and vocal during class lectures and discussions.

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.

Office of Equal Opportunity and Affirmative Action (EOAA): Course Environment

Names/Pronouns. You deserve to be addressed in a manner that reflects your identity. You are welcome to tell us your [pronoun\(s\)](#) and/or name (if different from University records) at any time, either in person or via email.

Discrimination. We embrace the diversity of gender, gender identity & expression, sex, sexual orientation, race, ethnicity, national origin, age, religion, disability status, family status, socioeconomic background, and other visible and non-visible identities. Columbia University does not tolerate unlawful discrimination, discriminatory harassment, sexual assault, domestic violence, dating violence, stalking, or sexual exploitation and all such conduct is forbidden by [Columbia University Policy](#).

Accessibility. We want you to succeed in this course. Contact disability@columbia.edu for learning accommodations.

Duty to Report. You deserve a University community free from discrimination, harassment, and gender-based misconduct including sexual harassment, sexual assault, domestic and dating violence, stalking, and sexual exploitation. It is therefore University policy to require Columbia faculty and staff to report to EOAA any instance or allegation of prohibited conduct involving any undergraduate or any graduate student that is disclosed to, observed by, or otherwise known to that employee. This requirement to report is in place to help ensure that students are provided appropriate resources and to allow the University to mitigate harm to our community.

There are confidential resources on campus who do not have a Duty to Report, including: Sexual Violence Response & Rape Crisis/Anti-Violence Support Center (SVR), Ombuds Office, Medical Services, University Counseling and Psychological Services, University Pastoral Counseling, Columbia Office of Disability Services. University employees working in a confidential capacity will not report information shared with them.

Additional

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

Course Outline (next page)

Week	Date	Lecture	Topics	Assignments
			Basics of Nuclear Magnetic Resonance (Mudd 327)	
1	09/08/22	#1	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 09/15/2022
			Basics of Biochemistry (Hammer 303)	
2	09/15/22	#2	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)	HW2 out, due 09/22/2022
			Basics of Magnetic Resonance Spectroscopy (Hammer 303)	
3	09/22/22	#3	Concept of Fourier MRS, chemical shift, J-coupling, localization, water suppression, outer volume suppression, STEAM, PRESS, LASER, J-difference editing (JDE), 1H, X nuclei, adjustments, data acquisition, frequency demodulation, analog-to-digital conversion	HW3 out, due 09/29/2022
			MRS in Mood and Anxiety Disorders (Hammer 303)	
4	09/29/22	#4	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	HW4 out, due 10/06/2022
			Data Processing Strategies (Mudd 327)	
5	10/06/22	#5	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	no HW
6	10/13/22	-	Final Fall A / Midterm Exam	
			MRS in Psychotic and Substance Use Disorders (Mudd 327)	
7	10/20/22	#6	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	HW5 out, due 10/27/2022
			Data Analysis and Interpretation (Mudd 327)	
8	10/27/22	#7	Model-based analysis, spectral fitting algorithms, Lorentzian/Gaussian/Voigt shapes, prior knowledge, identification of resonances, absolute quantification, Cramer-Rao lower bounds, 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	HW6 out, due 11/03/2022
			MRS in Developmental and Neurodegenerative Disorders (Hammer 303)	
9	11/03/22	#8	MRS in autism, 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	HW7 out, due 11/10/2022
			Introduction to Environment and Hardware, Overall Experiment Setup (Mudd 327)	
10	11/10/22	#9	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 11/17/2022
			MRS Experiment Setup and Execution: Phantom (MR Scanner)	
11	11/17/22	#10	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 11/24/2022
	Thanksgiving		In Vivo MRS Investigation: Volunteer (MR Scanner)	
12	Tuesday 11/22/2022	#11	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	no HW
			Processing, Quantification and Interpretation of In Vivo MRS (Hammer 303)	
13	12/01/22	#12	Analysis of data acquired during class #11 with method and techniques discussed previously.	HW10 out, due 12/08/2022
			Potential, Limitations and Future Directions (Mudd 327)	
14	12/08/22	#13	TBD	Guest speaker: TBD (no HW)
15	12/15/22	-	Study Days (no class)	
16	12/22/22	-	Final Exam (4:10-7:00 PM)	