BCHM669E   Biomolecular NMR: Theory and Applications   FALL 2020

Course meets Mon/Wed 11:00am-12:15pm
Due to the COVID-19 pandemic the lectures will be performed either synchronously on-line via zoom or in some cases asynchronously using video recordings posted on ELMS. Some classes might be held in-person.

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This graduate level course is designed as an introduction to modern biomolecular NMR and its applications to biological problems, including determination of the structure and dynamics of biomacromolecules and characterization of macromolecular interactions. The course covers fundamentals of nuclear magnetic resonance (NMR), including quantum-mechanical treatment, vector models, spin density operator approach and product operator formalism. The students will learn NMR pulse sequence design (including product operator formalism), principles of multidimensional NMR, methods for protein signal assignment and structure calculation, studies of protein-ligand interactions, and NMR approaches to protein dynamics. In addition to theory of NMR, we will also cover NMR data analysis using downloadable and online computer tools and simulation of the outcome of NMR experiments on a computer using Virtual NMR Spectrometer.

Course prerequisites: calculus, undergraduate level biochemistry and physical chemistry.

Topics Wish List (subtopics not necessarily in this order)**:**
1. *Nuclear Magnetic Resonance, basics*:
    general principles of NMR spectroscopy, classical/vector description, Bloch equations, chemical shift, quantum mechanical description of NMR spectroscopy, spin-Hamiltonian, eigenstates, transitions, spin density operator, product operator formalism and how to use it, understanding NMR pulse sequences.
2. *Multidimensional NMR Spectroscopy*:
    From 1-D to 2-D to n-D, homonuclear coherence transfer and mixing: COSY, NOESY, TOCSY; heteronuclear coherence transfer: INEPT, HSQC, HMQC, TROSY.
3. *Some Practical Aspects of Experimental NMR*:
    quadrature detection, sign discrimination, coherence selection, phase cycling, gradients; data processing: window function, zero-filling, linear prediction, isotope filtering/editing; solvent-signal suppression; computer simulations of the outcome of NMR experiments.
4. *NMR for biomolecular structure determination*:
    NOEs, J-couplings, H-bonding; spin system assignment, NOESY signal assignment, triple-resonance methods for spin system typing, sequential assignment; 2° structure prediction (J-couplings, Karplus equation, H-D exchange, CSI); from NOEs to structure, example of structure assignment and calculation.
5. *NMR for protein dynamics studies:*
    nuclear spin relaxation as a unique tool to study biomolecular dynamics; overall and internal motions.

6. *Novel methods for structure determination*:
   long-range orientational constraints from molecular alignment, anisotropic rotational diffusion, paramagnetic effects, CSA tensors.
7. *NMR methods to study protein-ligand interactions*:
   mapping interaction interfaces, from fast to slow exchange, determining binding affinities and stoichiometries.
8. *Computer tools for data analysis.*

Textbooks:
1. M. Levitt, Spin Dynamics: basics of nuclear magnetic resonance, Wiley, 2001
2. G. Rule, T. K. Hitchens, Fundamentals of Protein NMR Spectroscopy, Springer, 2005
3. Cavanagh et al., Protein NMR Spectroscopy. Academic Press, 1996
4. F. Van de Ven, Multidimensional NMR in Liquids, Wiley-VCH.
5. J. Keeler, Understanding NMR Spectroscopy.

Grading:
Homework reading and problems (not graded) will be assigned during the semester. Students will be given two major midterm projects that will be due in class on the assigned dates. The final exam/project will be a take-home exam. The scores on all three exams/projects will be added, and the final grades will be based on the total score.
Contributions to the total grade:

Project #1	33%
Project #2	33%
Final Exam	34%

You will be guaranteed an A if your total score is above 85% and a B if it is above 60% of the maximum possible total score.

Academic integrity. Students are expected to observe the University's *Code of Academic Integrity* (**http://shc.umd.edu/SHC/Default.aspx, http://www.president.umd.edu/policies/iii100a.html**). Students are responsible for knowing, understanding and behave accordingly to the content of the Code. Cheating on the exams or problem sets is not acceptable and will be met with zero tolerance. All work submitted for grading in this course (i.e. examinations and homework projects) must be the original work of the student whose name is on the work.

This syllabus was updated on 08/31/2020.