BCHM669E Biomolecular NMR: Theory and Applications FALL 2012

Course meets in CBSO 2118, Mo 11:00am-1:30pm (altern: Tue 3:30-6pm)

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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, including quantum-mechanical treatment, vector models, 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 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 (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, product operator formalism and how to use it.
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. *Experimental aspects of NMR*:
   quadrature detection, sign discrimination, coherence selection, phase cycling, gradients; data processing: window function, zero-filling, linear prediction, isotope filtering/editing; computer simulations of the outcome of NMR experiments: the "Virtual NMR spectrometer".
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^o 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*:
   orientational constraints from molecular alignment, anisotropic rotational diffusion, CSA tensors, paramagnetic effects.

7. *NMR methods to study protein-ligand interactions.*
mapping interaction interface, from fast to slow exchange, determining binding affinities.

Textbooks:

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

Grading:

Homework problems (not graded) will be assigned during the semester. Students will be given two major projects that will be due in class on the assigned dates. In addition, every student will be assigned a topic for oral presentation in class, on the last day(s) of classes.
Contributions to the total grade:

Projects #1 & #2	40%
Topic presentation	30%
Final Exam	30%