Course location: Lectures: MWF, 4th period, 10:40 – 11:30 ARB R3-265. Labs: Wed, Group A (macromolecules) 7th-9th periods; Thur, Group B (small molecule mixtures) 7th-9th periods AMRIS facility. First lab will meet in MBI LG-110 initially for safety video.

Credit: 1 hr for lecture, 1 hr for lab

Prerequisites: BCH 6740 or equivalent or consent of instructor.

Recommended Texts:

High-Resolution NMR Techniques in Organic Chemistry, T. Claridge ~$50

*Text for those interested in metabolite mixtures

Spin Dynamics: Basics of Nuclear Magnetic Resonance, M. Levitt ~$60

*Text for those wanting a more physics-rich description

Protein NMR spectroscopy: Principles and Practice, J. Cavanagh et al. ~$80

*Text for those interested in protein structure and dynamics

200 and More NMR Experiments: A Practical Approach, S. Berger & S. Braun ~$90

*Text used in the labs (150 and More… is also sufficient)

Bruker Avance 1D/2D Techniques Manual pdf available online

*Manual for AMRIS NMR spectrometers; relevant sections for labs will be provided

***If you are unsure which text you should get, get Claridge. I have all these texts in my office and you are welcome to come peruse them to help in making your choice.

Tests and Grading: Lecture grade will be 50% homework and 50% based on a final project.

Students will be required to process and analyze NMR data using freeware. Laboratory grade will be 20% participation, 40% processed data and 40% completed laboratory project report

Instructor Contacts: Dr. Joanna Long

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Schedule of lectures and labs:

1) Wed, Sep 30: **Nuclear Magnetic Resonance: A Classical Picture**

1. Spin angular momentum and magnetic dipoles
2. Precession and the Larmor frequency
3. RF fields and the rotating frame
4. The Basic NMR/MRI machine

2) Fri, Oct 2: **Nuclear Magnetic Resonance: Thermodynamics**

1. Bloch equations
2. Phenomenological introduction to T_1 and T_2

3. RF Pulses
4. The Hahn echo and T_1 relaxation experiments
5. NMR and MRI: two sides of the same coin

3) Mon, Oct 5: **Nuclear Magnetic Resonance: The molecular picture**

1. Larmor frequencies, abundance of various nuclei
2. Chemical shift and molecular/spatial information
3. Chemical shift databases: proteins and small molecules
4. Dipolar Couplings
5. Quadrapolar coupling
6. Solution NMR : T_1, T_2, and NOE

4) Wed, Oct 7: **Data Collection**

1. Time vs. Frequency
2. Hz vs. PPM
3. Fourier Transform
4. Digitization and Spectral Width
5. Quadrature detection
6. Multiple pulse experiments

1 Lab) Wed Oct 7 / Thur, Oct 8: Basics of NMR

1. Safety class
2. Sample preparation
3. Introduction to Bruker topspin software
4. Sample insertion, tuning, shimming, and 1D spectrum
5. Data processing and phasing
6. Relaxation measurements

NO CLASS ON FRIDAY OCTOBER 9

5) Mon Oct 12: **Nuclear Magnetic Resonance: A Quantum Mechanical Picture**

1. Energy levels and polarization
2. RF pulses
3. Chemical shift
4. 1D NMR spectrum explained (part of it)
5. Product operators as a tool to simplify the quantum mechanics

6) Wed, Oct 14: **Product operators**

1. RF and Chemical shift product operators
2. Scalar (J) coupling
3. 1D NMR spectrum explained more completely
4. Product operators for J coupling
5. zero and double quantum states

2 Lab) Wed, 14 / Thur, Oct 15:

Group a) 1D NMR—^{15}N, ^{13}C-labeled ubiquitin

Group b) 1D NMR—small molecule mixtures

1. gradient shimming.
2. Pulse width calibration
3. Radiation damping
4. solvent suppression
5. Test of experimental parameters: SW, O1, pw, D1, acq, etc
6. ^{1}H vs ^{13}C detection

7) Fri, Oct 16: **Introduction to 2D NMR**

1. 2D Exchange
2. NOE –measuring distances
3. COSY—measuring bonding
4. TOCSY

8) Mon, Oct 19: **Heteronuclear 2D NMR**

1. HMQC
2. HSQC
3. HMBC

9) Wed, Oct 21: **Protein structure determination**

1. Basic strategy
2. Principles of triple resonance experiments, what can we get from chemical shifts?
3. Real-life experiments
4. Assignment of side-chains
5. Practical sample requirements and isotopic enrichment
6. What if the protein is not recombinant – natural abundance methods

3 Lab) Wed, Oct 21 / Thur, Oct 22:

Group a) 2D NMR—^{15}N, ^{13}C-labeled ubiquitin

Group b) 2D NMR— small molecule mixtures

1. NOESY
2. TOCSY
3. X-pw calibration
4. ^{1}H-^{13}C HMBC (group A) or ^{1}H-^{15}N HSQC (group B)

10) Fri, Oct 23: **Introduction to solid state NMR**

1. Time scales of molecular motion
2. Revisiting spin interactions from solids perspective
3. Spin vs. space
4. Static experiments
5. Magic angle spinning

11) Mon, Oct 26: **solid state NMR and polarization enhancement**

1. solid state NMR : T_1, T_2, and MAS
2. Chemical shift anisotropy
3. Dipolar recoupling
4. Quadrupolar nuclei
5. Protein assignments in the solid state
6. DNP

NO CLASS WEDNESDAY, OCTOBER 28

NO LABS WEDSNESDAY-THURSDAY, OCT. 29-29

12) Fri, Oct 30: **Dynamics**

1. Correlation functions
2. Time scales of molecular motion
3. Experiments to probe dynamics in solution
4. Dynamics and mixture analysis
5. Protein dynamics measurements
6. Real-life examples

13) Mon, Nov 2: **Dynamics and diffusion**

1. Dynamics in the solid state and lineshapes
2. Diffusion and coherence lifetimes
3. Experiments to probe dynamics
4. Experiments to probe diffusion
5. Real-life examples

14) Wed, Nov 4: **In vivo spectroscopy**

1. In vivo considerations
2. ^{1}H and solvent suppression
3. ^{31}P measurements
4. ^{13}C and metabolic flux measurements

4a Lab) Wed, Nov 4: Solid State NMR

1. Setting the magic angle
2. 1D static and MAS spectrum
3. Cross polarization
4. Dynamics experiment

4b Lab) Thur, Nov 5: HRMAS

1. Setting the magic angle
2. Shimming
3. 1D static and MAS spectrum
4. Solvent suppression

15) Fri, Nov 6: **Protein structure calculations**

1. Chemical shifts and structure

2. Building a secondary structure model
3. Course tuning – adding in distance geometry
4. Fine tuning – molecular dynamics
5. NMR restraints

5b Lab) Wed, Nov 18: Diffusion and Dynamics

1. ^{2}H of Lipid dynamics and temperature
2. ^{1}H measurements of protein diffusion
3. ^{1}H-^{15}N relaxation measurement

5a Lab) Thur, Nov 19: Diffusion and Dynamics

1. ^{2}H of Lipid dynamics and temperature
2. ^{1}H measurements of small molecule diffusion
3. PFG calibrations

Fri, 11/13 Final Project due

Mon, 11/30 Lab Report due