

CHEM590N1, NMR of Macromolecules: Survey and Practice.

CHEM590N1, Spring 2008, Session 1
MWF, 1-1:50 pm, Noyes 163
F, 2-5 pm, Vizlab (Noyes 151)

Prof. Chad M. Rienstra, A120 CLSL, 244-4655
rienstra@scs.uiuc.edu
http://scs.uiuc.edu/~rienstra/chem590n_s08

A. Course Synopsis. This course covers modern applications of multidimensional solution and solid-state protein NMR, emphasizing review of the recent literature, qualitative discussion and applications to biochemical structure and function. Students will learn practical aspects of data acquisition, processing, interpretation and structure determination, including hands-on experience with data processing and structure determination software (NMRPipe, Sparky, NMRView, XPLOR-NIH, CNS). This course is suitable for advanced undergraduates or graduate students in all areas of Chemistry, Biophysics, Biochemistry and related disciplines in the life sciences. Prerequisites: familiarity with basic principles of protein structure, such as from an undergraduate biochemistry course; ability to work very hard and learn quickly.

B. Course Goals (In Logical Order)

1. To provide students with a *qualitative* introduction into protein NMR spectroscopy (*quantitative*, rigorous quantum mechanical theory will be reserved for CHEM590N2). This knowledge should allow students to determine whether NMR is suitable for their biochemical research problem.
2. To introduce the language of NMR and its modern implementation on commercial spectrometers. This should allow students to choose experiments and reasonable parameter values with a specific goal in mind. At this level of understanding, students will still require advice about which experiment is best for their application.
3. To describe pulse sequences at a diagrammatic (qualitative) level, using certain resulting equations to illustrate important points. This knowledge should allow students to select optimal parameters for pulse sequences, even if they are quite different from the default situation, based on the particular properties of their samples and instrument on a given day. This requires a somewhat more detailed understanding than simply selecting an experiment and running it from automated software packages such as BioPack.
4. To provide skill sets to process 2D, 3D and 4D NMR data sets in an optimal fashion. This requires description of data sets at a simple level of theory, including trigonometric and exponential functions, in order to appreciate the effect of various processing functions applied to data. This knowledge should allow students to get the most out of their hard-earned experimental data.
5. To provide an overall framework for understanding modern NMR research and its applications to chemistry and biochemistry, with a particular emphasis on studies of protein structure and dynamics. The framework also aids in understanding NMR of nucleic acids and small organic molecules. This knowledge should allow students to progress towards a real NMR research project, such as a structure determination.

The following are explicitly not goals of this course:

1. To provide hands-on data collection experience or training at the spectrometers. The VOICE NMR Facility provides this service, aided by representatives from each research group. All students are strongly encouraged to get adequate training and acquire data sets of interest to them on their research compounds. This data may then be used during computational laboratory exercises and/or as part of the final course project.
2. To derive equations or demonstrate the instructor's theoretical abilities. That will be reserved for CHEM590N2, a separate course that will offer students the opportunity to understand pulse sequences deeply, at the level required to design new pulse sequences.

C. Practical Details

1. This course is a half-semester long (1/14 to 3/7). (CHEM590N2 runs from 3/10 to 5/10.) Plan on a fast pace, although we will skip many equations and derivations.

2. There will be short (15-20 minute) as necessary to test comprehension of material covered and to help the instructors pace the material appropriately for the audience.

3. There will be an oral exam in which you will present your final project to the class and Prof. Rienstra. Plan on the project requiring at least 20 hours of your time during the last 2-3 weeks of the course. The presentation will be informal but you will be expected to answer questions about your project.

D. Course Textbook

1. Required: *Protein NMR Spectroscopy: Principles and Practice*, Cavanagh, Fairbrother, Palmer, Rance and Skelton, Academic Press, 2007, ISBN 978-0-12-164491-8 ([Elsevier link](#)) ([Amazon link](#)). This is a new version of the text. It should be available at the campus bookstore.

2. Recommended: *Multidimensional Solid-State NMR and Polymers*, Schmidt-Rohr and Spiess, Academic Press, 1994, ISBN 978-0-12-626630-6 ([Amazon link](#)) This book is rather pricey (\$195). Several copies are available in the Rienstra group. You may borrow one if you wish from the student office (please sign out).

3. Potentially useful as supplements:

a. *Spin Dynamics: Basics of Nuclear Magnetic Resonance*, Malcolm H. Levitt, John Wiley & Sons, 2001, ISBN 978-0-47-148922-1 ([Amazon link](#)). The Rienstra group also has a few copies of this book.

b. *Fundamentals of Protein NMR Spectroscopy*, Gordon S. Rule & T. Kevin Hitchens, Springer, 2005, ISBN 978-1-40-203499-2 ([Amazon link](#))

E. Teaching Assistants

Due to the small enrollment this semester, there is not a full-time TA assigned to this class, although you are welcome to ask questions of advanced members of the Rienstra group. Also feel free to schedule meetings to get your questions answered. Prof. Rienstra will be doing all the grading himself!

Dr. Donghua Zhou (A124 CLSL, dhzhou@scs.uiuc.edu) will be giving several lectures during January. You are welcome to send him email to schedule meetings as well.

F. Expectations

CHEM590N is a graduate course. N1 is aimed primarily towards Chemical Biology students, but Physical, Analytical, Organic, Biochemistry and Biophysics students are also welcome. As a survey course, N1 will necessarily cover a large quantity of material, requiring a fast pace of coverage. You will need to do readings in advance, keep up with the lectures, review material, ask plenty of questions, do all the computational lab exercises and understand them in detail. Theoretical (time-consuming) analysis of pulse sequences will be reserved for the N2 course.

Daily Calendar for CHEM590N1, Spring 2008

| Date | Lecturer (Helper) | Topic | Assigned Reading from Palmer (2007) | Pulse Sequences or Key Concepts |
|----------|-------------------|---|---|---|
| | WEEK 1 | BASIC CONCEPTS | | |
| 1/14 | CMR | Overview and Basic Concepts: Bloch Equations, T_1 , T_2 , T_2^* | Chapter 1 (all); skip Chapter 2 | Bloch decay, Hahn echo |
| 1/16 | CMR | Experimental NMR | Chapter 3.1-3.2, 3.8 (also 3.3 for Lab) | Magnets, probes, resonance, 1D NMR |
| 1/18 | CMR | Time-Frequency Domain Relationships | Chapter 3.3 | Signal-to-noise ratio, digital resolution |
| 1/18 Lab | CMR | Fourier Transforms, Apodization Functions | See website for links to exercise | |
| | WEEK 2 | THE BIG PICTURE | | |
| 1/21 | DHZ | Overview of Other Practical Issues and Techniques | Chapter 3.4-3.7 | Pulses (composite, shaped, decoupling, gradients, solvent suppression) |
| 1/23 | DHZ | 2D NMR in Simple Terms | Chapter 4.1-4.3 | COSY, HETCOR in very general terms |
| 1/25 | DHZ | 2D, 3D, 4D: Sensitivity & Resolution | Chapter 4.4-4.5 | Maximizing sensolution and resitivity |
| 1/25 Lab | HLF & KDK | <i>Processing 2Ds: Tradeoffs in S&R by Parameter Selection</i> | Chapter 4.4-4.5 | How to work processing for S&R (apodization in nD) |
| | WEEK 3 | SMALL MOLECULE | | |
| 1/28 | DHZ | Experimental ^1H Methods: More about COSY | Chapter 6.1-6.3 | COSY: R, 2QF, 3QF, E |
| 1/30 | DHZ | Multiple Quantum, TOCSY | Chapter 6.4-6.5 | 2Q, 3Q, TOCSY, NOESY, ROESY |
| 2/1 | DHZ and/or CMR | HETCOR Basics and 3Ds | Chapter 7.1-7.2 | HSQC, HMQC, TROSY; combinations with NOESY |
| 2/1 Lab | LJS & AJN | <i>Advanced 3D+ Processing of Solution NMR Data Sets</i> | Chapter 3.3 (review); Hoch & Stern handouts | Linear prediction, maximum entropy, sine bells and whistles |
| | WEEK 4 | PROTEIN ASSIGNMENTS | | |
| 2/4 | CMR | 3D HNC Experiments For Protein Assignment | Chapter 7.3-7.4, 10.1 | HNCO, HNCA, HN(CO)CA, H(CA)NH, HN(CA)CO, CBCA(CO)NH, CBCANH, HNCACB |
| 2/6 | CMR | Scalar and residual dipolar couplings | Chapter 7.5-7.6 | HNCA-J, HNHA, RDC |
| 2/8 | CMR | Assignment and structure | Chapter 10 | Backbone walk, structural constraints, simulated annealing calculations |
| 2/8 Lab | CMR | <i>Backbone Assignments of Protein Solution NMR Data</i> | Chapter 10 | |
| | WEEK 5 | SOLID-STATE NMR | | |
| 2/11 | CMR | Solid-State NMR Basics | Classic papers: Pines, Gibby & | CP, MAS, proton decoupling; chemical shift |

| | | | | |
|----------|---------------|---|---|--|
| | | | Waugh; Herzfeld & Berger; Maricq & Waugh; Stejskal & Schaefer | tensors (qualitative treatment) |
| 2/13 | CMR | SSNMR Pulse Sequences | More classic literature | TPPM, RFDR, R2, REDOR, TEDOR, DCP, DARR |
| 2/15 | tbd | Advanced Concepts in Polarization Transfer | Meier; Baldus; Takegoshi | Adiabatic CP; SPECIFIC CP; R2TR; DREAM |
| 2/15 Lab | tbd | <i>Calculation of Protein NMR Structures with XPLOR-NIH</i> | Herzfeld-Berger | Simulated annealing; distance constraints; dihedral angles |
| | WEEK 6 | ADVANCED SSNMR | | |
| 2/18 | CMR | Advanced Concepts in Polarization Transfer (cont.) | | |
| 2/20 | CMR | Assignment Strategies for Solid-State NMR | Recent literature (see website) | NCACX, NCOCX, CCC CONCACX, CANCOCX |
| 2/22 | CMR | Distance Measurements Strategies for SSNMR | Recent literature (see website) | PDSD, DARR, ZF-TEDOR, BASE-TEDOR, SPECIFIC, CHHC, NHHC |
| 2/22 Lab | CMR | <i>Assignments of Protein Solid-State NMR Data</i> | Recent literature (see website) | |
| | WEEK 7 | ADVANCED TOPICS | | |
| 2/25 | CMR | Dynamics | Chapter 8 | |
| 2/27 | CMR | Large Molecules | Chapter 9.1 | |
| 2/29 | CMR | Intermolecular Interactions | Chapter 9.2 | |
| 2/29 Lab | CMR | <i>Final Projects*</i> | | |
| | WEEK 8 | LAST WEEK | | |
| 3/3 | CMR | Rapid Acquisition Methods | Chapter 9.3 | |
| 3/5 | CMR | Leftovers | | |
| 3/7 | Off to ENC | <i>Final Projects*</i> | | |

**Presentation schedules will be discussed on the first day of class.*