Chemistry C613: Introduction to Mass Spectrometry (3 credits)

Department of Chemistry, Indiana University, Bloomington, IN
Spring 2008, two of the following three days M/W/F (room A400)
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Office hours: Tues: 10-12 (or by appt.)

Course objectives: This course presents material designed to familiarize graduate level students with modern techniques in mass spectrometry (MS). Throughout the semester the instructor will present historical perspectives with scientific discussions on why and how many of the modern technologies were developed. Students will gain an appreciation for the strengths and weaknesses of MS methods as applied to traditional problems of quantifying analytes in samples and determination of molecular structures of unknowns in addition to an understanding of evolving areas in the field (especially those relating to problems of biological and environmental importance). This course is firmly rooted in a physical understanding of small molecules including electronic structure, dynamics and energetics. Students will be given some review of thermodynamics and kinetics as they apply to MS technologies. The development of instrumentation central to MS methods including (but not limited to) fundamentals in vacuum systems, pressure measurement devices, methods for ion detection, fragmentation and mass-to-charge measurement will be discussed.

Lectures: The class meets twice a week for course lectures from 1:00 to 3:00 (it will probably let out between ~2:15 to 2:30) on M, W, or F (lab lectures will be given during a third lecture period). Class lectures will consist of time spent presenting new material and time spent for student questions and discussion. Students are strongly encouraged to ask questions. *All material presented in lectures is fair game for testing. In addition, students are encouraged to supplement information in the course by attending all seminars within the department that involve mass spectrometry. Thus, it is useful to keep 3:00 to 4:00 (Tues) and 2:30 to 3:30 (Thurs) open if possible. In some cases, seminars will be discussed in class as well.*

Labs: Over the course of the semester students will complete four laboratory assignments. Three of the assignments are carried out in the mass spectrometry facility (MSF, located in room A411 of the Chemistry Building); one will be completed using SIMION software (available in C-006). For the laboratory experiments the class is divided into small groups that are scheduled to use the MSF on specific dates (See attached sheet). The laboratory assignments are factored into the final grade (see below); thus, attendance is important. In extreme circumstances it may be possible to reschedule lab experiments [e.g., conference attendance (reschedule in advance), or documented illness].

Texts: *Mass Spectrometry: A textbook* by Jürgen H. Gross (required). The text can be purchased at the IU bookstore or online.

Other suggested reading material: *Mass Spectrometry Basics* by Herbert and Johnstone; *Interpretation of mass spectra* by F. W. McLafferty; *Time-of-Flight Mass Spectrometry* by R. J. Cotter; Standard biochemistry texts (e.g., Voet/Voet, Stryer, and Creighton; *Spectrochemical Analysis* by Ingle and Crouch. Additional assignments from the literature will be given throughout the course.

Grading: Grades will be assigned based on scores obtained on four exams (120 pts. each, three exams during the term: two in class and one take home; and a comprehensive final exam, given on Wednesday April 30th, in A-400 from 1:00 to 3:00 p.m.). Additionally, students will carry out a series of laboratory assignments covering multiple topics in the area of mass spectrometry including the design of mass spectrometry instrumentation. The laboratory assignments will be worth a combined total of 120 pts. Six problem sets will be assigned throughout the course worth a total of 120 pts. combined. Students must take all exams. If an exam is missed the student must meet with the professor. In some cases the instructor may arrange for a makeup. The only reason to need a makeup is a true medical or family emergency. If it is not possible to give a written makeup exam the instructor will conduct the exam in person by asking the student to work out problems on the board. The course is based on a 720 pt total.

Exams: The exam dates will be arranged to fit the schedules of students in the class. The final exam will be given during finals week.

What students should show that they know -for exams: In addition to the material presented in class, students should bring a working knowledge of chemistry (bonding, energetics, kinetics and thermodynamics).

Course Schedule: The following dates apply to C-613 for the Spring of 2008.

Jan. 7 (M), Lecture 1: *Course description and administrative details; beginning lecture associated with the history of mass spectrometry. Handout given.*

Jan. 9 (W), Lecture 2: *Finishing the history of Mass Spectrometry, Beginning Ion formation (fundamentals of ion formation: associated reading)*
Problem set 1 (history of MS) handed out

Jan. 14 (M), Lecture 3: *Ion formation (part I) –fundamentals of ion formation: constants, potential energy surfaces associated with neutrals and ions.*

Jan. 16 (W), Lecture 4: *Ion formation (part II) –kinetics, thermodynamics and ion structure.*
Problem set 1 (hand in at the beginning of class)
Problem set 2 (potential energy surface diagrams assigned)

Jan. 18 (F), Lecture 5 (laboratory lecture 1, given by Jon Karty): *Electron Ionization: fundamentals and quantitation. Handout given.*

Jan. 21 (M): *No class (MLK day)*

Jan. 23 (W) Lecture 6: *Considering a Mass Spectrum: basic definitions (resolution, resolving power, capacity, sensitivity, mass scale, etc…).*
Problem set 2 is due (no problem set this week is assigned as student will be in the lab)

Jan 25 (F): Complete laboratory 1 (there is no lecture on this day). Note the lab report will be due on JAN 30 at the beginning of class.

Jan. 28 (M) Lecture 7: *Fragmentation (physical and chemical considerations associated with bond cleavage); begin spectrum interpretation -homolytic, heterolytic and sigma bond cleavage.*
Problem set 3 (interpreting EI mass spectra) handed out

Jan. 30 (W) Lecture 8: *Continue interpretation of mass spectra and fragmentation patterns (isotopic structure, rearrangements and eliminations to produce stable ions and neutrals).*
Laboratory 1 due (hand in at the beginning of class)

Feb. 1 (F) Lecture 9 (laboratory lecture 2 given by Jon Karty): *High-resolution mass spectrometry and collision induced dissociation. Handout given.*

Feb. 4 (M). Lecture 10 (catch up/review for exam 1).
Problem set 3 is due (at the beginning of class)

Feb. 6 (W) Complete laboratory 2 (there is no lecture on this day). Study for exam and complete the lab report. Note the lab report will be due on FEB 11 at the beginning of class.

Feb. 11 (M): IN CLASS EXAM 1 Exam 1 will cover all aspects of Mass Spectrometry History, Ion formation, fragmentation and interpretation of mass spectra. Be ready to interpret some spectra as a part of this exam.
[turn in lab 2 report at the beginning of class]

Feb. 13 (W) Lecture 11: *Instrumentation overview and practical considerations for designing vacuum systems.*

Feb 18. (M) Lecture 12: *SIMION basics and demonstrations (Chem - C006).*
Problem set 4 (SIMION) handed out in class

Feb. 20. (W) Lecture 13: *RF and DC fields (Quadrupoles I).*

Feb. 25 (M) Lecture 14: *Quadrupoles II; stability diagrams (a-q).*
Problem set 4 due at the beginning of class.

Feb 27 (W) Lecture 15: *Quadrupoles III: Triple Quadrupoles and tandem MS introduction.*

Mar. 3 (M) Lecture 16: *Trapping devices I (paul traps, linear ion traps).*

Mar. 5 (W) Lecture 17: *Trapping devices II (tandem-MS, orbitraps, etc.).*

Mar. 7 (F) Lecture 18 (laboratory lecture 3 given by Manny Plasencia): Advanced SIMION Techniques Lab, handout given.

Mar. 10 - 15 : *Spring Break – No classes.*

Mar. 17 (M) Lecture 19: *Magnetic Sectors/ICR (designs and instrumentation).*

Mar. 19 (W) Lecture 20: *Time-of-flight systems: linear, reflectron, operational, resolution and design considerations.*
Problem set 5 (analyzers and practical considerations) handed out.

Mar. 21 (F): **Laboratory 3 (SIMION) reports due**.

Mar. 24 (M) Lecture 21: *Drift tubes and ion mobility techniques.*

Mar. 26 (W) Lecture 22: *Ion sources (part I) –formation of ions from droplets (ESI, APCI, DART and DESI).*
Problem set 5 due at the beginning of class.

Mar. 31 (M) Lecture 23: *Ion sources (part II) – CI, FAB, ICP, MALDI, APPI (ohh, and others).*

Apr. 2 (W) Lecture 24: *Detectors and review for in class exam 2.*

Apr. 7 (M) EXAM 2: The in class portion will cover all material since exam 1 (given on Feb. 11). Note: be sure to pick up the take home exam, which is due on M April 14.

Apr. 9 (W) Lecture 25: *Applications (part I), Proteomics I. Peptide mass fingerprinting and bottom up approaches*
Problem set 6 (Proteomics) handed out.

Apr. 11 (F) Lecture 27 (laboratory lecture 4 given by Jon Karty): Protein identification by mass spectrometry (handout given).

Apr. 14 (M) Lecture 28: *Applications (part II)*, Proteomics II. *Top down approaches and protein modifications.* ***(Students submit topics for lecture 31)***

Apr. 16 (W) Lecture 29: *Applications (part III), Biomolecules: metabolomics and glycomics.*
Problem set 6 due at the beginning of class.

Apr. 18 (F): Complete laboratory 4 (there is no lecture on this day). Note the lab report will be due on APR 23rd at the beginning of class.

Apr. 21 (M) Lecture 30: *Applications (part IV) Environmental mass spectrometry and stable isotopes.*

Apr. 23. (W) Lecture 31: Student selected topic.
Laboratory 4 report due at beginning of class.

Apr. 28. (M): *Review for Final exam and course evaluations.*

Apr. 30 (W) 1:00 to 3:00 p.m. FINAL EXAM (room A400 Chemistry). Final grades will be available by Monday morning.