

CHEMISTRY 529 SYLLABUS ULTRA HIGH MASS SPECTROMETRY

LECTURE: Fulmer Hall 1:10-2:00 PM Monday and Wednesday
INSTRUCTOR: Professor Peter Reilly
OFFICE: Fulmer 128 PHONE: 335-0042 Email: pete.reilly@wsu.edu
OFFICE HOURS: by appointment

GRADING: Base on oral presentations and class participation. Attendance is mandatory. Students will be assigned papers from the current literature to present, review and discuss in class. There are no formal examinations.

SUGGESTED PREREQUISITES:

1. Undergraduate physical chemistry and/or
2. Undergraduate physics
3. Chem 514
4. Graduate standing

NOTE:
This is an advanced course. It is not a prerequisite for the analytical qualifying exams. Mass spectrometry topics covered on the qualifying exams can be found in Harris.

SYNOPSIS:

This is an advanced graduate level class. The material presented represents the next frontier in mass spectrometry—the ultra high mass range. Ultra high mass spectrometry is the mass analysis of analytes with molecular masses generally much greater than 20 kDa. This is an area of science that is currently rapidly advancing. Because of recent advances in instrumentation, the rate of growth in this area is expected to increase exponentially. The procedures and methods for analyzing large molecules will be changing rapidly. This course will have to evolve with the changes in the field. It is the goal of this course to prepare you for these changes.

The recent advances in this area are based on new methods for handling ions. This course thoroughly covers the fundamentals of ion handling in the ultra high mass range. You will learn how to sample ions with molecular masses ranging into the 10^9 Da range and well beyond from the atmosphere into vacuum and trap them. You will then learn to isolate ions with specific value of m/z and then move them into a mass analyzer and analyze them. You will learn how to use time-of-flight and digital ion trap analyzers for ultra high mass analysis and what to expect from each analyzer. Strategies for differentiating and quantifying biomolecules and complexes by determining cross sections, retention time and mass will be explored.

The literature relating to the analysis of intact proteins, protein complexes, RNA, DNA and viruses will be covered. Students will present, discuss and review assigned papers. We will discuss how the state of the art will change with the advent of the new technology.

All required reading will be sent as pdf files through email at least a week before being covered in class.

Schedule

Topics: Ion formation, controlling charge, moving into vacuum, slowing them down, moving them in vacuum and trapping massive ions.

Required reading:

Ion slowing and trapping and mass analysis

1-11a H. Koizumi, W.B. Whitten, P.T.A. Reilly, *Controlling the Expansion into Vacuum—the Enabling Technology for Trapping Atmosphere-Sampled Particulate Ions* J Am Soc Mass Spectr, 21 (2010) 242-248.

1-11b X. Wang, H. Chen, J. Lee, P.T.A. Reilly, *Increasing the Trapping Mass Range to $m/z = 10^9$ —A Major Step Toward High Resolution Mass Analysis of Intact RNA, DNA and Viruses*, Int. J. Mass Spectrom., 328-329 (2012) 28-35.

1-13a J. Lee, M.A. Marino, H. Koizumi, P.T.A. Reilly, *Simulation of duty cycle-based trapping and ejection of massive ions using linear digital quadrupoles: The enabling technology for high resolution time-of-flight mass spectrometry in the ultrahigh mass range*, Int. J. Mass Spectrom., 304 (2011) 36-40.

1-13b H.J. Chen, J. Lee, P.T.A. Reilly, *High-resolution ultra-high mass spectrometry: Increasing the m/z range of protein analysis*, Proteomics, 12 (2012) 3020-3029.

1-13c J. Lee, H. Chen, T. Liu, C.E. Berkman, P.T.A. Reilly, *High Resolution Time-of-Flight Mass Analysis of the Entire Range of Intact Singly-Charged Proteins*, Analytical Chemistry, 83 (2011) 9406-9412.

1-18 MLK Holiday

Controlling the Charge:

1-20a S. Cristoni, L.R. Bernardi, I. Biunno, F. Guidugli, *Analysis of protein ions in the range 3000–12000 Th under partial (no discharge) atmospheric pressure chemical ionization conditions using ion trap mass spectrometry*, Rapid Communications in Mass Spectrometry, 16 (2002) 1153-1159.

1-20b Yang, S.H., et al., *Manipulation of Protein Charge States through Continuous Flow-Extractive Desorption Electrospray Ionization: A New Ambient Ionization Technique*. Analytical Chemistry, 2011. **83**(3): p. 643-647.

1-25a M. Scalf, M.S. Westphall, J. Krause, S.L. Kaufman, L.M. Smith, *Controlling charge states of large ions*, Science, 283 (1999) 194-197.

1-25b M. Scalf, M.S. Westphall, L.M. Smith, *Charge Reduction Electrospray Mass Spectrometry*, Analytical Chemistry, 72 (1999) 52-60.

1-25c D.D. Ebeling, M.S. Westphall, M. Scalf, L.M. Smith, *Corona Discharge in Charge Reduction Electrospray Mass Spectrometry*, *Analytical Chemistry*, 72 (2000) 5158-5161.

Topics: Duty Cycle Waveform Manipulation of Ions and Isolation.

Required reading:

1-27a Brabeck, G.F. and P.T.A. Reilly, *Mapping ion stability in digitally driven ion traps and guides*. *International Journal of Mass Spectrometry*, 2014. **364**(0): p. 1-8.

1-27b F.L. Brancia, B. McCullough, A. Entwistle, J.G. Grossmann, L. Ding, *Digital Asymmetric Waveform Isolation (DAWI) in a Digital Linear Ion Trap*, *J Am Soc Mass Spectr*, 21 (2010) 1530-1533.

2-1a Singh, R., V. Jayaram, and P.T.A. Reilly, *Duty Cycle-Based Isolation in Linear Quadrupole Ion Traps*. *International Journal of Mass Spectrometry*, 2013. **343-344**: p. 45-49.

2-1b Brabeck, G.F., et al., *Development of MSⁿ in Digitally Operated Linear Ion Guides*. *Analytical Chemistry*, 2014. **86**(15): p. 7757-7763.

2-3 and 2-8 Fun with stability diagrams programs. You will download Excel Spreadsheet programs to directly observe the effects of changing the duty cycle. You will learn to perform ion isolation and MS/MS. Bring a laptop to class.

Ultra High Mass Detectors

2-10a Liu, R., Q. Li, and L. Smith, *Detection of Large Ions in Time-of-Flight Mass Spectrometry: Effects of Ion Mass and Acceleration Voltage on Microchannel Plate Detector Response*. *Journal of the American Society for Mass Spectrometry*, 2014. **25**(8): p. 1374-1383.

2-10b A. Aksenov, M. Bier, *The analysis of polystyrene and polystyrene aggregates into the mega dalton mass range by cryodetection MALDI TOF MS*, *J Am Soc Mass Spectr*, 19 (2008) 219-230.

2-15 Presidents Day Holiday

2-17a Bahr, U., et al., *A charge detector for time-of-flight mass analysis of high mass ions produced by matrix-assisted laser desorption/ionization (MALDI)*. *International Journal of Mass Spectrometry and Ion Processes*, 1996. **153**(1): p. 9-21.

2-17b J.H. Barnes IV, G.M. Hieftje, *Recent advances in detector-array technology for mass spectrometry*, *Int. J. Mass Spectrom.*, 238 (2004) 33-46. AND A.K. Knight, R.P. Sperline, G.M. Hieftje, E. Young, C.J. Barinaga, D.W. Koppelaar, M.B. Denton, *The development of a micro-Faraday array for ion detection*, *Int. J. Mass Spectrom.*, 215 (2002) 131-139.

Ultra-High Mass Analyzers:

- 2-22 TOF—limits: Resolution, Mass Accuracy, Mass Limit, Detectors
- 2-24 Traps: ICR, Orbitrap and DITs—limits: Resolution, Mass Accuracy, Mass Limit, Detectors

Cross section measurement, IMS, MS/MS

Required reading:

- 2-29a T. Covey, D.J. Douglas, *Collision cross sections for protein ions*, J Am Soc Mass Spectr, 4 (1993) 616-623.
- 2-29b Y.L. Chen, B.A. Collings, D.J. Douglas, *Collision cross sections of myoglobin and cytochrome c ions with Ne, Ar, and Kr*, J Am Soc Mass Spectr, 8 (1997) 681-687.
- 3-2 S.L. Kaufman, *Analysis of biomolecules using electrospray and nanoparticle methods: The gas-phase electrophoretic mobility molecular analyzer (GEMMA)*, Journal of Aerosol Science, 29 (1998) 537-552.
- 3-7a A.B. Kanu, P. Dwivedi, M. Tam, L. Matz, H.H. Hill Jr., *Ion Mobility-Mass Spectrometry*, Journal of Mass Spectrometry, 43 (2008) 1-22.
- 3-7b Brabeck, G.F., et al. *Duty Cycle-Based Cross Section Measurement of Large Singly-Charged Proteins*. in *American Society for Mass Spectrometry Conference*. 2013. Minneapolis, MN
- 3-9a L. Ding, F.L. Brancia, *Electron capture dissociation in a digital ion trap mass spectrometer*, Analytical Chemistry, 78 (2006) 1995-2000.
- 3-9b C. Rose, J. Russell, A. Ledvina, G. McAlister, M. Westphall, J. Griep-Raming, J. Schwartz, J. Coon, J.P. Syka, *Multipurpose Dissociation Cell for Enhanced ETD of Intact Protein Species*, J Am Soc Mass Spectr, 24 (2013) 816-827.

3-14 to 3-18 Spring Break

Chromatography and MS of intact proteins.

Required reading:

- 3-21 F.Y. Meng, B.J. Cargile, S.M. Patrie, J.R. Johnson, S.M. McLoughlin, N.L. Kelleher, *Processing complex mixtures of intact proteins for direct analysis by mass spectrometry*, Analytical Chemistry, 74 (2002) 2923-2929
- 3-23 J.D. Tipton, J.C. Tran, A.D. Catherman, D.R. Ahlf, K.R. Durbin, J.E. Lee, J.F. Kellie, N.L. Kelleher, C.L. Hendrickson, A.G. Marshall, *Nano-LC FTICR Tandem Mass Spectrometry for Top-Down Proteomics: Routine Baseline Unit Mass Resolution of Whole Cell Lysate Proteins up to 72 kDa*, Analytical Chemistry, 84 (2012) 2111-2117.

- 3-28 P.D. Compton, L. Zamdborg, P.M. Thomas, N.L. Kelleher, *On the Scalability and Requirements of Whole Protein Mass Spectrometry*, *Analytical Chemistry*, 83 (2011) 6868-6874.
- 3-30 J.C. Tran, L. Zamdborg, D.R. Ahlf, J.E. Lee, A.D. Catherman, K.R. Durbin, J.D. Tipton, A. Vellaichamy, J.F. Kellie, M. Li, C. Wu, S.M.M. Sweet, B.P. Early, N. Siuti, R.D. LeDuc, P.D. Compton, P.M. Thomas, N.L. Kelleher, *Mapping intact protein isoforms in discovery mode using top-down proteomics*, *Nature*, 480 (2011) 254-258

Analysis of Protein Complexes

- 4-4 Z. Hall, A. Politis, M.F. Bush, L.J. Smith, C.V. Robinson, *Charge-State Dependent Compaction and Dissociation of Protein Complexes: Insights from Ion Mobility and Molecular Dynamics*, *J. Am. Chem. Soc.*, 134 (2012) 3429-3438.
- 4-6 B.T. Ruotolo, J.L.P. Benesch, A.M. Sandercock, S.-J. Hyung, C.V. Robinson, *Ion mobility-mass spectrometry analysis of large protein complexes*, *Nat. Protocols*, 3 (2008) 1139-1152.

Week 13-14: Analysis of RNA and DNA

- 4-11 M.B. Beverly, *Applications of mass spectrometry to the study of siRNA*, *Mass Spectrometry Reviews*, 30 (2011) 979-998.
- 4-13 K.K. Murray, *DNA Sequencing by Mass Spectrometry*, *Journal of Mass Spectrometry*, 31 (1996) 1203-1215.
- 4-18 M. Zhaojing, P.A. Limbach, *Mass spectrometry of RNA: linking the genome to the proteome*, *Briefings in Functional Genomics & Proteomics*, 5 (2006) 87-95.

Analysis of Viruses

- 4-20a J.J. Thomas, B. Bothner, J. Traina, W.H. Benner, G. Siuzdak, *Electrospray ion mobility spectrometry of intact viruses*, *Spectroscopy*, 18 (2004) 31-36.
- 4-20b Downard, K.M., B. Morrissey, and A.B. Schwahn, *Mass spectrometry analysis of the influenza virus*. *Mass Spectrometry Reviews*, 2009. **28**(1): p. 35-49.
- 4-25a C. Uetrecht, I.M. Barbu, G.K. Shoemaker, E. van Duijn, A.J.R. Heck, *Interrogating viral capsid assembly with ion mobility-mass spectrometry*, *Nature Chemistry*, 3 (2011) 126-132.
- 4-25b J.Z. Bereszczak, I.M. Barbu, M. Tan, M. Xia, X. Jiang, E. van Duijn, A.J.R. Heck, *Structure, stability and dynamics of norovirus P domain derived protein complexes studied by native mass spectrometry*, *Journal of Structural Biology*, 177 (2012) 273-282.

4-27 H.-C. Chang, *Ultrahigh-Mass Mass Spectrometry of Single Biomolecules and Bioparticles*, Annual Review of Analytical Chemistry, 2 (2009).

5-2 to 5-6 Final Exam week

The precise schedule and reading material are subject to change at the discretion of the instructor.

University required disclaimers:

ACCOMMODATIONS: Students with Disabilities: Reasonable accommodations are available for students with a documented disability. If you have a disability and need accommodations to fully participate in this class, please either visit or call the Access Center (Washington Building 217; 509-335-3417) to schedule an appointment with an Access Advisor. All accommodations **MUST** be approved through the Access Center.

ACADEMIC INTEGRITY: Cheating or plagiarism in any form will not be tolerated by University policy. Given the current grading system for this course is based on presentation and in class discussion, it is not really possible in any case.

SAFETY: The campus safety plan is at <http://safetyplan.wsu.edu/>.
Go to <http://oem.wsu.edu/Planning.html> to prepare for emergencies.
The campus-wide alert system is at <http://alert.wsu.edu/>.