

**TWO-DAY COURSE, Saturday and Sunday**  
**07 LC-MS: Advanced Techniques and Applications**

**Instructor**



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This two-day course presents a comprehensive overview of technology and techniques of analytical mass spectrometry and from that foundation extends into exciting, disruptive recent developments.

1. Sample preparation
  - Topics: Types of extraction, Objectives of extraction, Prefractionation techniques, Sample types, Issues to consider, Isolation of proteins from biological samples, Liquid-solid extraction, Liquid-liquid extraction, Solid-phase (micro) extraction, multi-well format SPE, Mixed mode SPE, On-line SPE, Automation, Micro SPE (pipette tip-based), Ultrafiltration, Affinity techniques, Molecularly Imprinted Polymers (MIP's), Thermo's MSIA pipette tips, Electro Extraction, Quechers, SISCAPA, Dried blood spots (DBS), Dried Plasma Spots (DPS).
  - Topics: Recent alternatives to established sample preparation of drugs in biological samples, biologics (peptides, proteins, etc.) in biological samples, drugs and biomarkers from clinical samples and chemicals in food matrices associated with food safety issues.
2. Advanced separation techniques
  - Topics: UHPLC, Superficially porous particle LC, HILIC, Porous Graphite Carbon, Hydrophobic Interaction Chromatography (HIC), Nano-UHPLC, Capillary Electrophoresis (CE), Differential Mobility Spectrometry (DMS), Size Exclusion Chromatography (SEC).
3. Ionization techniques for MS
  - Topics: Electrospray ionization (ESI), Nano ESI, Atmospheric pressure chemical ionization (APCI), Atmospheric pressure photoionization (APPI), Matrix assisted laser desorption ionization (MALDI), LAESI, Direct analysis in real time (DART), Desorption electrospray ionization (DESI), Atmospheric sampling analysis probe (ASAP), Electron Ionization (EI) and its potential for LC/MS.
  - Topics: New ionization techniques which may be used with or without on-line separation science technology such as HPLC, UPLC or capillary electrophoresis (CE). This area has evolved into a variety of ambient ionization techniques such as DESI, DART, ASAP, etc. - examples and comparisons of the potential and pitfalls associated with these techniques will be explored. The analytical potential of coupling ambient ionization with DMS will be covered.
4. Mass Analyzers
  - Quadrupoles, Ion traps, linear and quadrupole, Time-of-Flight (TOF), Orbitraps, Hybrid mass analyzer systems, Ion mobility spectrometers, Differential mobility Spectrometry (DMS), and FTMS.
  - Topics: Developments and improvements in mass analyzers including linear ion traps, FTMS, time-of-flight (TOF), orbitraps, and accelerator mass spectrometry (AMS), the latter currently being applied to micro-dosing experiments by the pharmaceutical industry. Issues such as full-scan acquisition rates, high-resolution mass spectrometry (HRMS), the importance and usefulness of exact mass measurements for qualitative and quantitative analysis, and the analytical merits compared with modern SRM LC/MS experiments will be discussed with many practical examples and applications. The latter will include clinical chemistry issues as well as pharmaceutical, food safety, environmental and industrial examples.
5. Imaging and profiling by MS

- Applications of recently reported ionization techniques for imaging the location of chemicals in various matrices employing MALDI, DESI, LAESI, LESA and other techniques.
  - Topics: The technique of MALDI and its applications to tissue imaging as well as DESI, LAESI and also liquid extraction surface analysis (LESA) employing nano-electrospray. A comparison of the various classes of compounds where MALDI and nano ESI provide complimentary coverage of certain compounds found in biological and other matrices.
6. High resolution MS
    - Topics: Fundamentals, Mass Defects, Isotopic patterns, Mass axis calibration, Types of HRMS systems, Qual/Quan Analysis, Data mining processes, Future directions
    - Topics: The analytical merits of HRAMS from QTOF as well as orbitraps and FTMS systems will be presented. Instances where either SRM LC/MS or LC HRAMS may be preferred for optimal selectivity due to chemical background or other interference issues.
  7. Miniaturization in MS
    - Topics: Purdue University "Mini 11", Torion, Microsaic, Agilent Chip Cube, Waters QDa, Advion expression
    - Topics: The benefits and limitations of smaller analytical instrumentation systems will be compared. This includes miniaturization of HPLC systems as well as the mass spectrometers themselves. The commercial introduction of chip-based HPLC systems closely integrated with mass spectrometers offers a glimpse of future directions in analytical chemistry.
  8. Synergistic Integration
    - A systematic overview via specific examples with applications highlighting noted examples of innovative novel and non-standard technologies which demonstrate the analytical potential of new analytical technologies.
    - Topics: Developing instrumentation and technologies are will be important aspects of future mass spectrometry techniques and its expansion to important new applications. An extremely important example is the need for LC/MS bioanalysis (quantitation) of biologics (ADC's, large molecules, RNA, etc.) in biological samples employing both bottom up and top down methods. HRAMS coupled with 'protein friendly' chromatography will significantly expand our present analytical capabilities. Ion mobility spectrometry (IMS) and transportable mass spectrometers could lead to point-of-care applications and other far reaching applications of mass spectrometry beyond what we are doing today. The future is very exciting!

**Prerequisites:** Students who sign up for this advanced course should either have five years or more of personal LC/MS/MS experience and familiarity with the scientific literature or have taken one or more introductory courses which cover atmospheric pressure ionization (API) techniques as well as the basics involved in routine LC/MS and LC/MS/MS analyses.