50th Annual Conference • 2002 • Orlando, FL

2019 History Committee
American Society for Mass Spectrometry

Biology Meets Mass Spectrometry

During the '90s and beyond, mass spectrometrists began to capitalize on the instrumentation developments of previous years. Almost every area of the mass spectrometer had undergone significant improvement: sampling, ionization, mass analyzers and detectors. In addition new methods had evolved for coupling MS with separation techniques like liquid chromatography. These instrument developments enabled larger biomolecular compounds to be analyzed and this led to an explosion of new applications in the biological and medical sciences.

A Pioneer's Vision Realized

At the 1962 New Orleans ASTM E-14 meeting (the predecessor to today's ASMS conference) organizers were sufficiently intrigued to include an outlier paper among the 20 papers accepted for the *Hydrocarbon Studies* session: "Spectra of Compounds of Biological Interest" submitted by Klaus Biemann and James McCloskey. This submission was in stark contrast to the vast number of papers discussing applications in the petroleum industry. At the time, biological applications were limited to the analysis of relatively small and volatile compounds. Nonetheless, Biemann and McCloskey showed that MS was capable of analyzing biomolecules on the order of several hundreds of Daltons in size. Their paper described a sample introduction technique for low volatility compounds that would later be refined to yield a method of sample introduction that became ubiquitous: the solids probe.

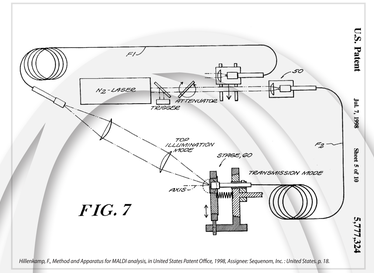
By 1967 the ASTM E-14 meeting had begun to include a session devoted to biological applications, and within ten years various researchers were using mass spectrometry in conjunction with other techniques to sequence small peptides. In 1977, a 94-residue protein, monellin, was sequenced in Biemann's laboratory by acid/enzymatic digestion followed by a variety of derivatization techniques to enhance amino acid volatility. During and following this period, as new ionization techniques became available, the general theme of such sessions was how to overcome the analytical difficulties posed by the study of peptides and proteins by mass spectrometry.

As larger and more complex proteins were being investigated, it became clear that the fickle nature of many of the current ion sources would not facilitate their widespread adoption outside the die-hard researchers in this niche area of analytical mass spectrometry. The first widely adopted breakthrough in the analysis of large biomolecules was the development of Fast Atom Bombardment (FAB) by Barber and co-workers in 1980. The first practical result was the elucidation of the amino acid sequence of efrapeptin D, which contained several unusual amino acids, as reported by Morris, Barber, et al in 1981. FAB was rapidly coupled with tandem mass spectrometry, which led to the development of a nomenclature system for protonated peptide/protein fragments. At the time, the practical upper mass limit of analytes was several thousand Da, however, which prevented FAB from holding the community's interest for too long. FAB was supplanted in the 1990s by the commercialization of electrospray ionization (ESI) and matrix-assisted laser desorption (MALDI).

As a direct consequence of ESI and MALDI in 1980s, the analysis of proteins by mass spectrometry began to expand into the larger community of biologists. Complementary to these two huge breakthroughs in sample introduction/ionization were advances in mass analyzers that extended the range of m/z values that could be measured. Deconvolution protocols developed by Mann and others helped to unravel the identities of multiply-charged ions that dominated ESI spectra. Adding reflectors to the designs of Time-of-Flight (TOF) mass analyzers provided longer path lengths and thus increased resolving power in MALDI instruments, allowing useful access to a larger portion of the theoretically limitless mass range of TOFs. Orthogonal acceleration in TOFs, another instrumentation development of the late 1980s, increased the ion sampling efficiency of TOFs by 2-3 orders of magnitude.

A search of "mass spectrometric studies of peptides and proteins" in SciFinder for the year 2002 produced almost 500 publications. The persistence of many researchers since Biemann brought mass spectrometry to the field of biology 40 years ago has paid off dramatically, as seen in today's Conference.

Lasers and Mass Spectrometry



Hillenkamp, F., Method and Apparatus for MALDI analysis, in United States Patent Office, 1998, Assignee: Sequenom, Inc. - United States. p. 18.

Beginning in the 1990s, the technique known as Matrix-Assisted Laser Desorption Ionization or MALDI became a staple of many laboratories engaged in the analysis of oligonucleotides, peptides and proteins. The use of lasers as a source of ionization for mass spectrometry had been explored since the mid 1960s, but the real potential of the technique to produce ions from solid surfaces didn't emerge until the 1970s with the advent of the Laser Microprobe Mass Analyzer (LAMMA). Molecular ions were observed in spectra of underivatized oligosaccharides, cardiac glycosides, and nucleosides produced by laser desorption as early as the late 1970s; however, much of the laser desorption research during this early period focused on the effect of laser irradiation wavelength on the ionization process rather than on its potential for desorbing large molecules intact.

With discovery in the mid-1980s that mixing an organic acid (matrix) with the surface-mounted sample could greatly enhance the ion signal from large and more interesting biomolecules, MALDI drew more and more interest. The pulsed cloud of ionized sample molecules created by laser desorption was ideally suited for analysis with the TOF mass analyzer, which at the time was undergoing significant improvements in resolving power and accessible mass range. Today, most major laboratories still employ MALDI in various areas of their research activities.

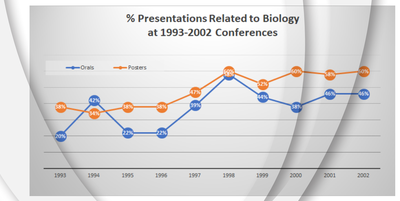
The John B. Fenn Distinguished Contribution Award presented to recognize a focused or singular achievement in fundamental or applied mass spectrometry

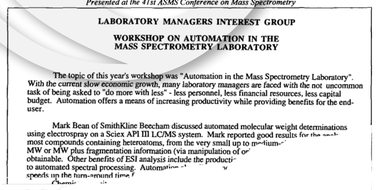
1993 **Chris Enke & Richard Yost**	*Triple Quadrupole mass spectrometry*
1994 **Donald F. Hunt**	*Negative Ion Chemical Ionization*
1995 **Keith R. Jennings**	*Collisional Dissociation*
1996 **Burnaby Munson & Frank Field**	*Chemical Ionization*
1997 **Franz Hillenkamp & Michael Karas**	*MALDI*
1998 **David Dahl & Don McGilvery**	*SIMION*
1999 **Melvin Comisarow & Alan Marshall**	*FTICR*
2000 **Boris Mamyrin**	*Reflectron TOF*
2001 **George Stafford**	*Mass-Selective Axial Instability Scans for QITs*
2002 **William Henzel, John Stults, & Colin Watanabe**	*Peptide Mass Fingerprinting*

Mass Spectrometry and Pharmaceuticals

The 1990s saw a meteoric rise in the use of mass spectrometry in pharmaceutical research. Long a standard tool for molecular weight determination and structural elucidation in pharma, mass spectrometers almost overnight became the instrument of choice for combinatorial chemistry in drug discovery, pharmacokinetic analysis, and biotransformation studies. The advent of ESI and MALDI as ionization techniques, and the availability of extended mass ranges in both time-of-flight (TOF) and quadrupole analyzers, were coupled with the emerging field of robotics to deliver the selectivity, sensitivity, and speed required to meet ever-increasing demands of the biological communities.

This wide-scale adoption in the industry is reflected in both the growth of Society membership and in the programs of annual conferences. The number of oral and poster presentations focusing on pharma-related topics increased steadily over the decade. By 2002, fully half the presentations were devoted to small molecule, peptide, and protein studies of interest to the drug industry.





Presented at the 41st ASMS Conference on Mass Spectrometry

LABORATORY MANAGERS INTEREST GROUP

WORKSHOP ON AUTOMATION IN THE MASS SPECTROMETRY LABORATORY

The topic of this year's workshop was "Automation in the Mass Spectrometry Laboratory". With the current slow economic growth, many laboratory managers are faced with the not uncommon task of being asked to "do more with less" - less personnel, less financial resources, less capital budget. Automation offers a means of increasing productivity while providing benefits for the end-user.

Mark Bean of SmithKline Beecham discussed automated molecular weight determinations using electrospray on a Sciex API III LC/MS system. Mark reported good results for the most most compounds containing heteroatoms, from the very small up to m-fium- MW or MW plus fragmentation information (via manipulation of or obtainable. Other benefits of ESI analysis include the producti- to automated spectral processing. Automation sponds up the turn-around time f-

Forensic Applications of Mass Spectrometry

In the 1950s-60s, the earliest examples of forensic mass spectrometry focused on the structural characterization of psychoactive and medical compounds from botanic matter. In the 1970s, applications shifted to the characterization of drugs and poisons in human stomach contents. With the availability of commercial gas chromatography-mass spectrometry (GC-MS) instruments in the 1970s, forensic applications expanded to include the analysis of explosives and ignitable liquids in arson investigations. However, the forensic community was not engaged with ASMS during this period, so the number of presentations involving forensic applications at ASMS conferences remained low relative to other topics.

In the early '90s, acts of terrorism were so uncommon on US soil that most US citizens were only peripherally aware of threats to their personal safety. The public's mindset changed when a truck bomb exploded on a lower level of the World Trade Center in New York City in 1993. The seeming randomness of the event and the potential for thousands to suffer injury brought terrorism to national attention. Acts of terrorism remained in the public's eye thanks to a string of high profile bombings, including the bombing of the Alfred P. Murrah Federal Building in Oklahoma City in 1995 and the unexploded pipe bomb found in Centennial Olympic Park in Atlanta just as the Olympics began in 1996. Anxiety peaked in 2001 with the attacks on the World Trade Center, the Pentagon, and United Airlines flight 93 over Shanksville, PA. The mailing of anthrax-laced letters to politicians and media personnel during the autumn of 2001 that year kept the public on high alert. Concurrent with the increase in terrorist activities in the US was the significant expansion of forensic applications of mass spectrometry in the analysis of home-made bombs, chemical warfare agents, and toxins. Despite the rich literature in these areas of security, much of this work was conducted with Department of Defense funds and remains unpublished. During the same period, the development and availability of field portable instruments became an important contributor to the use of mass spectrometry in forensic settings.

The bombing of the Alfred P. Murrah Federal Building in Oklahoma City in 1995 brought terrorism to the public's attention and raised awareness in the MS community for the need to detect trace levels of explosives in post-blast debris.

During the 1990s, and into the 2000s, forensic applications became a steady and important feature of the Annual Conference. A special workshop on Forensic Mass Spectrometry was held in 1996 that covered analytical topics as diverse as illicit drugs, gunshot residues, explosives, the decomposition of human remains, and the chemical characterization of finger prints. In 2000, an oral session on Forensic Mass Spectrometry was included in the program; in 2001, both an oral and a poster session appeared, and in 2002 there were three sessions: an oral session entitled, "MS and Homeland Security," and two poster sessions titled, "Anti-terrorism and MS" and "Forensic Applications." Since then, a 2005 Sanibel Meeting on "MS in Forensic Science and Counterterrorism" drew participants from across the US, and the world, and another Sanibel Conference in 2015 focused on "Forensic and Security Applications of MS". Clearly, mass spectrometry has become an important tool in the arsenal of researchers who seek to keep the public safe. By the end of this decade, the publications of forensic mass spectrometry research and applications had almost tripled, reaching nearly 120 manuscripts in 2003 (citations counted using SciFinder database for the term "forensic mass spectrometry").

Biemann Medal established in 1996 and endowed by former students, postdoctoral associates and friends to recognize significant achievements in the early stages of scientists' careers

Presented "in honor of Professor Klaus Biemann as an educator and scientist and in honor of his lasting legacy resulting from the training of students and postdoctoral associates over a 40 year period at the Massachusetts Institute of Technology."

1997 **Scott McLuckey**	*Fundamental studies of multiply-charged ions in ion traps*
1998 **Robert Squires**	*Structural and thermochemical characterization of reactive organic and organometallic intermediates*
1999 **Mattias Mann**	*Applications of mass spectrometry to protein chemistry and molecular biology*
2000 **Julie Leary**	*Metal ions coordinated with carbohydrates*
2001 **Peter Armentrout**	*Reactivity and thermochemistry of metallated molecules*
2002 **Ruedi Aebersold**	*Identification and characterization of proteins with mass spectrometry*

MASS SPECTROMETRY	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002
	Lab Managers Interest Group: "Automation in the Mass Spectrometry Laboratory" first formal discussion of robotics and MS analyses	Process MS Interest Group Workshop with topic "On-Line Mass Spectrometry for Process Control and Diagnostics"	GLP Workshop lasts 4 hours (7-11 PM) with controversial talk by Charles Snipes (FDA CDER) on computer validation in GLP environment	ASMS adopts 4-day format; oral & posters sessions Mon-Thurs Nobel prize to Curl, Kroto and Smalley for the discovery of Fullerenes using TOF-MS	Immuno-Affinity MS - A New Dimension for the Study of Alzheimer's Disease Amyloid beta-Protein.	Molecular Shape Determination Using FTICR/MS Linewidth Measurements	Makarov first describes orbitrap mass analyzer at ASMS	Analysis of human metabolites of chemical warfare agents in urine using GC/MS/MS	Annual Conference Program published in JASMS special issue	Nobel Prize awarded to John Fenn and Koichi Tanaka for methods for the MS analysis of biological macromolecules

HISTORY	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002
	First attempt to destroy World Trade Center unsuccessful CERN puts software into public domain, launching the World Wide Web	Nelson Mandela is inaugurated president of South Africa. Jeff Bezos founds Amazon	Yahoo founded in Santa Clara, CA Sarin gas attack in Tokyo subway kills 12 and injures thousands	Unexploded pipe bomb found in Centennial Olympic Stadium, Atlanta The first successfully cloned mammal, Dolly the sheep, is born	President Clinton bars federal funding for research on human cloning IBM Deep Blue defeats Garry Kasparov in chess match giving boost to Artificial Intelligence research	Iraq suspends all cooperation with UN weapons inspectors Google is founded in Menlo Park, CA	Dow Jones Industrial Average closes above 11,000 Origin of HIV virus traced to Chimps Y2K panic because of concern for two-digit date codes	Y2K a non-event The "Dot-Com bubble" bursts and thousands of dot.coms go under	Wikipedia is launched Human genome sequenced World Trade Center destroyed	Larson B Ice Shelf, 3,250 square km, breaks apart The Euro is launched in Euro Zone countries US President George Bush establishes Department of Homeland Security