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# International Journal of Mass Spectrometry

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## Foreword

The current issue of IJMS honors Robert J. Cotter for his seminal contributions to mass spectrometry that include fundamental studies and instrumentation developments as well as many important biological applications. An overview of the areas his work has covered would be rather long! Indeed, his bibliography contains more than 320 papers in immensely diverse areas - from ion-hydrogen molecule cross section measurements, to miniaturized mass analyzers in search for extraterrestrial life, to the structure of major histocompatibility complex (MHC) class I peptides. Overall, his work has a very high scientific impact. Bob's *h-index* is 55, i.e., he has (co)authored 55 papers, each of which has been cited at least 55 times (according to the Citation Index)! More importantly, Bob and his numerous students and collaborators have successfully demonstrated the power of mass spectrometry by applying it to a variety of biochemical, biomedical problems and chemical problems - from protein and DNA structure elucidation and functional transformations to analysis of intact microorganisms - lending credence to the maxim that "a method is only as good as the problems it solves".

Robert James Cotter was born on July 15, 1943 in Walter Reed Hospital in Washington D.C. and grew up in the New England area. He obtained his undergraduate degree in chemistry from the College of Holy Cross (1965). Bob's graduate studies in physical chemistry at Johns Hopkins University (Baltimore, Maryland) were under the direction of Walter Koski, who had worked on the Manhattan project. Bob's thesis work (MS, 1971 and PhD, 1972) involved mass spectrometer construction and the study of reaction cross-sections of ions with hydrogen and deuterium. As Bob himself semi-jokingly points out, even then he had started using mass spectrometry for studies of biomolecules by working with the most important biomolecule for life - the water molecule! Notably, the instrument used in these early experiments was a home-built tandem mass spectrometer of BB geometry (two magnetic sectors with a collision chamber in between).

Since 1978 Bob Cotter has been linked with the Johns Hopkins University School of Medicine in Baltimore. Together with Catherine Fenselau, Bob co-founded (1979) the Middle Atlantic Mass Spectrometry (MAMS) Laboratory - a shared instrumentation facility funded at the time by the National Science Foundation. Catherine and Bob not only have shared their professional interest in MS instrumentation and its biological applications, but since 1984 they shared their personal lives as well, successfully raising three sons from previous marriages. Bob is currently Professor of Pharmacology and Molecular Sciences, and Professor of Biophysics and Biophysical

Chemistry at the School of Medicine. In parallel, he has been the Director of the MAMS Laboratory for over 20 years. He also served as President of the American Society for Mass Spectrometry (1998–1999) and is currently on the Board of the US Human Proteome Organization. He has been a member of the editorial board of several journals and has served on numerous federal review panels. Many of his former students and collaborators (more than 70) successfully continue to develop and apply MS in academia, industry or government (with a larger proportion in the latter two entities).



Bob has been a pioneer in developing both advanced mass spectrometry methods and novel and unique instrumentation, reflected in his 13 issued US patents. His contributions in various mass spectrometry areas - from ionization methods and ion analyzer miniaturization to applications in microbiology, immunology, and proteomics - are well known. Some of the earliest applications of lasers in mass spectrometry for ionization and desorption of biomolecules in the "pre-MALDI era" come from his laboratory. He has elucidated mechanisms of laser desorption, and contributed to understanding chemical ionization/thermal desorption, field desorption, plasma desorption and FAB. His was one of the first three labs world-wide to demonstrate the utility of TOF instruments in biological mass spectrometry long before they became popular and commercially ubiquitous. In 1978 he interfaced a 10.6  $\mu\text{m}$   $\text{CO}_2$  laser to a Wiley-McLaren TOF instrument. With that setup he studied not only the fundamental mechanisms of laser desorption, but the capability to

sequence small peptides by time-delayed extraction (“time-lag”) measurements. Using this early LD TOF setup, Bob and his collaborators elucidated the structures of lipid A - toxic complex lipopolysaccharides found in bacterial cell walls. Further instrumental developments in the MAMS lab include the curved-field reflectron (CFR). The CFR has been the basis for several TOF and tandem TOF (TOF/TOF) configurations, some of which have been commercialized. In parallel, TOF instrument miniaturization in Bob’s lab has been driven by potential mass spectrometry applications for defenses against chemical and biological weapons. Bob and his students co-developed the hybridized mass extension assay for DNA SNP analysis (currently commercialized by a biotech company) as well as the use of MALDI MS for genetic tissue typing for organ transplantation based



upon the hypervariable region encoding class II molecules. We are certain that many in the community share Bob’s vision for a desk-top mass spectrometer in each doctor’s office for rapid clinical diagnostics.

The MAMS facility’s location within the Johns Hopkins School of Medicine - one of the premier biomedical research establishments in the world - has provided the framework for several important groundbreaking collaborations. In addition to working on MHC class I peptide structure, Bob and his students were the first to show that other classes of compounds (e.g., glycosylphosphatidylinositol) can also be MHC ligands. Also in the field of immunology, Bob’s lab collaborated in the demonstration of the antigenic mimic properties of Salmonella. Mass spectrometry work at MAMS has had a critical input in elucidating the structural alterations of various beta-amyloid proteins with implications for the development of Alzheimer’s disease.

The most recent work coming from Bob Cotter’s lab is as exciting as ever. In one effort, protein microarrays have been coupled to a MALDI tandem TOF mass spectrometer to provide identification of peptides in plasma without fluorescent labeling. Continuing a successful series of ion trap modifications, a miniature ion trap mass spectrometer is being developed to fly on a future ESA/NASA mission as a detector for life on Mars.



Throughout his career, Bob has been a dedicated teacher, reflected not only in the successes of his many students but in his hugely popular book on “Time-of-flight Mass Spectrometry: Instrumentation and Applications in Biological Research”. Bob has taught his students not only excellent science but many important life lessons as well – one of us (PAD) will always remember Bob’s advice “to see straight” and not lose one’s goal and dedication.

Among his many pastimes, Bob enjoys photography – many of his former and present students feature prominently in slides taken during the years, in and out of the laboratory, for example, during the traditional 4th of July bicycle rides along the Chesapeake & Ohio Canal or while watching the firework displays in the Baltimore Inner Harbor. Bob’s enthusiasm for the visual arts is also evident in the annual MAMS T-shirt edition, a new one appearing almost every summer before each ASMS Conference. Indeed, from these T-shirts one can trace both the history of mass spectrometry and also date a particular MAMS achievement, correlating it with the respective blockbuster movie release (as illustrated in the selection accompanying this text). We are also certain that many attendees to the ASMS conferences in the last two decades or so have enjoyed Bob’s late night impromptu jazz piano sessions, well past hospitality suite closings!

Together with his many friends and colleagues we congratulate Bob on his 65th anniversary with our wishes for many more years of exciting research ahead!

Plamen A. Demirev and Amina Woods,  
Guest Editors