

# THE CONTRIBUTION OF MASS SPECTROMETRY TO THE BIOSCIENCES

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It is at least arguable that the analysis of biologically important molecules has provided the major driving force for the development of mass spectrometry (MS) since the 1960s. It is incontrovertible that the introduction of ionization methods suitable for the analysis of biopolymers in the 1980s propelled the technique to the forefront of biochemical methods. Yet MS has intrinsic limitations for the study of biomolecules: the characterisation of analyte stereochemistry is difficult to achieve directly, for example, and analysis is performed in the gas-phase, a medium of limited immediate biological relevance. The strengths of MS, on the other hand, are clear. The method achieves very high sensitivity (though there remains significant scope for improvement), can provide great detail of primary structure (particularly when tandem MS is employed), effectively handles complex mixtures (again aided by tandem MS), and, perhaps most importantly, is able to provide rigorous quantitative information. These attributes are critical to the contribution of MS to the emerging field of systems biology, which seeks to define cellular processes by modeling the enormously complex interactions that take place between components at the levels of genome, transcriptome, proteome and metabolome. Rigorous and effective modeling requires extensive qualitative and quantitative analytical data and MS has a clear role to play.

This lecture develops and illustrates these ideas with particular reference to the study of the proteome – the full complement of proteins in a cell or organism. The analytical problem is defined by the “multi-dimensionality” of the proteome. Thus, the definition of primary protein sequence must be accompanied by complementary data on post-translational modification, protein/protein interactions, sub-cellular location, etc. Qualitative data must be accompanied by relative and absolute quantification, and by an understanding of the dynamic nature of the proteome: individual proteins are continuously synthesized and degraded, and the rate of turnover represents an important biochemical parameter. To an extent, familiar analytical approaches may be applied in addressing these challenges; stable isotope dilution, for example, represents a suitable conceptual framework for absolute quantification. Proteomics, however, provides challenges that place unique demands on both instrumentation and analytical strategy. These will be explored in this lecture and novel analytical approaches will be described.