Current Topics

Challenge of Mass Spectrometry toward the Elucidation of Life Phenomena

Foreword

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Mass spectrometry (MS) is an analytical technique by which chemical substances are identified by measuring the mass-to-charge ratio \((m/z)\) of ions. MS analysis provides the molecular weight (MW) or structural information of a compound. A mass spectrometer consists of three basic compartments: an ionization source for ion generation; a mass analyzer for ion separation; and an ion detector. Characteristic performance is available with different combinations of an ionization source with a mass analyzer.

The basis for MS was established by J. J. Thomson at the beginning of the twentieth century. Early MS was exclusively employed to the study of atomic weights and isotopes. From the 1950s and into the 1960s, some important advances in MS were made especially to the mass analyzer: time of flight (TOF) and quadrupole analyzers were developed. A hyphenated analytical method, gas chromatography-MS (GC-MS), was also developed in the 1950s, which allowed the separation of molecules online to the mass spectrometer. However, MS was still restricted to small and thermally stable compounds, and thus was insufficient for application to the analysis of biological molecules, which often have high polarity and high molecular weight.

Innovative techniques for “soft” ionization, such as electron spray ionization (ESI) and matrix-assisted laser desorption/ionization (MALDI), were developed over the last 30 years and drastically extended the applicability of MS to biological and clinical chemistry. ESI can be applied to qualitative and quantitative analysis of a wide variety of nonvolatile and thermally labile compounds. Because ESI permits the ionization of molecules directly from solution, it can efficiently be interfaced with liquid separation techniques such as high-performance liquid chromatography (HPLC) and capillary electrophoresis (CE). These separation techniques are generally more suitable for the separation of polar or macro molecules in complex biological matrices when compared versus GC. On the other hand, MALDI source has high ionization efficiency for large biological molecules including proteins and peptides, and is most often used in combination with TOF analyzer since both MALDI and TOF are based on pulsed techniques. The development of both “soft” ionization techniques, as acknowledged by the award of the 2002 Nobel Prize in Chemistry to Koichi Tanaka and John B. Fenn, extended the applicability of MS to the measurement of polar and thermally labile biological molecules without prior derivatization.

Another important aspect of MS analysis is the development of tandem MS instruments composed of two or more mass analyzers coupled together. In this technique, a precursor ion of interest is selected in the first mass analyzer then fragmented to generate characteristic secondary fragment ions that are selected in the following mass analyzer. The main advantage of MS/MS technique is to obtain MS/MS spectrum that is helpful in identification of compounds. Currently, LC-MS/MS has emerged as one of the most valuable tools in the field of “-omics” such as proteomics and metabolomics due to its sensitivity, selectivity, and rapidity. Different configurations of mass analyzers to perform MS/MS (e.g., triple quadrupole, three-dimensional (3D) ion trap, and quadruple-TOF) are commonly used for these purposes.

Modern MS techniques with high sensitivity, selectivity, resolution, accuracy, and throughput have become the dominant tools for characterization of a broad range of biological molecules. In addition to qualitative and quantitative analyses by MS techniques, the application of MS is now extended to chemical imaging techniques (imaging mass spectrometry; IMS) allowing the visualization of spatial distribution of biological molecules. Among the MS techniques, IMS currently provides one of the most attractive approaches for the elucidation of biological events.

The progress of MS technology is supported by a very broad-based research including fundamental and applied studies. This mini review series is intended to provide recent advances of MS for understanding life phenomena. This review includes a wide variety of progress in MS methodology and application. As LC-MS/MS-based studies, 1) a novel approach for quantitative proteomics in which fluorogenic derivatization-HPLC is combined with LC-MS/MS (FD-LC-MS/MS), 2) recent advances in the determination of salivary hormones that include derivatization method to increase the sensitivity, and 3) immunoproteomics and immune complexome analysis as a new variation of proteomic analysis are described. 4) Recent advances in quantitative approach for laser desorption/ionization MS (LDI-MS) and its related techniques for labeling are also reviewed. IMS is one of the most innovative techniques in the MS community and therefore 5) a mass microscope in which a microscope is combined with high-resolution MALDI-IMS and its clinical applications are included in this review. Finally, 6) single cell mass spectrometry involving Live Single-cell MS for the molecular and functional analysis of cellular phenomena is presented.

As M. S. Tswett (1872–1919), the inventor of chromatography, said, “Every scientific advance is an advance in method,” scientific advances are often led by improvements in measurement techniques. Although MS technologies have contributed to significant progresses in life science to date, they will continue to play important roles in biological and pharmaceutical sciences including biomarker searching, clinical diagnostics, and drug discovery in the future.

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