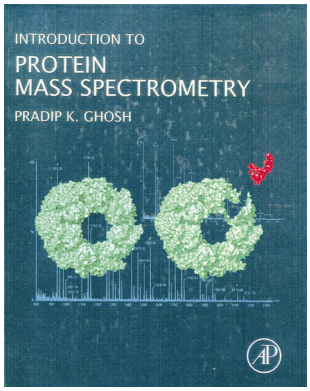

Introduction to Protein Mass Spectrometry. Pradip K. Ghosh. Academic Press, An Imprint of Elsevier, 125, London Wall, EC2Y 5AS, UK. 2015. xxii + 880 pages. Price: US$ 150.00.

Mass spectrometry is one of the oldest analytical techniques used by chemists for unambiguous characterization of a chemical compound. This technique is being routinely used since a long time by organic chemists. Earlier it was considered that only volatile compounds that can be charged by electron ionization or other techniques could be investigated using mass spectrometry. The path-breaking discovery of soft ionization techniques such as electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) in the late nineties opened the window for mass spectrometric studies of large macromolecules such as proteins, lipids and nucleic acids.

This book is a nice account of the basic methods used in different mass spectrometric techniques for the study of proteins. It begins with a chapter on sample preparation for mass spectrometry, which indeed is a critical step as the soft ionization methods in protein mass spectrometry often suffer from formation of ion-pairs at the surface of the biomolecules by non-volatile buffers and counter ions, decreasing the sensitivity of the technique. The author describes various ionization techniques used in protein mass spectrometry and outlines the newer techniques such as laser-induced liquid beam/bead ionization desorption (LILBID) and laser ablation with electrospray ionization (LAESI). Desorption electrospray ionization (DESI) is also rapidly becoming a powerful method for rapid imaging of a wide range of biological samples, which could have also be outlined. Multidimensional protein identification by combining multiple chromatographic methods to separate peptides from the mixture followed by tandem mass analyses in shotgun proteomics has immensely improved the sensitivity of the technique. The author highlights important applications of selective labelling methods and electrophoretic separation methods which have added further improvements in the separation of peptides/proteins. He discusses various developments in the ionization methods such as electrospray, MALDI, LILBID, LAESI with examples, which provides a nice overview of the applications of these techniques in macromolecular mass spectrometry. Latest developments in the mass spectrometric instrumentation have been well described, giving a brief outline of the principles of mass analyses by various techniques. This would indeed be helpful for understanding the fundamentals of the mass spectrometric techniques for a beginner as well as a practising user. The author has outlined the basic electrodynamics in the quadrupole mass filter, ion trap, orbitrap as well as ion mobility techniques. He has described basic instrumentation and technical features of some state-of-the-art commercial instruments and highlighted the multidimensional tandem analyses methods, which are also a useful compilation of information in one reference book.

Mass spectrometry of peptides and proteins has grown far beyond just determination of the molecular mass of the intact molecule (or the protonated species). Sequencing of peptides by mass spectrometry has become an extremely important tool in modern proteomics. The identification of peptides by tandem mass spectrometry from the fragmentation pattern of the secondary ions produced by collisional dissociation of the peptide ions is now a part of the routine application of mass spectrometry. This method is based on different models of fragmentation of the peptide ions, which have been nicely discussed giving simple examples. The major challenge of mass spectrometric sequencing methods is the distinction between various isobaric amino acids. The author has highlighted some of the known methods of selective identification of such isobaric residues. However, there are new methods evolving rapidly, and it is indeed not easy to have all such methods covered in one book. The author has also outlined the use of multiple reaction monitoring methods for making selective fragmentation of peptides. The label-free, as well as various labelling approaches for quantitation of proteins or peptides form important component of proteomic application of mass spectrometry. The book has dedicated a section in the fourth chapter to provide details on various types of labelling methods used for rapid quantification of peptides by mass spectrometry.

The most significant benefit of mass spectrometric techniques in proteomics is the high-throughput detection and quantification of proteins in biofluids. The development of newer methods in mass spectrometry primarily aims at improving the sensitivity and resolution to reach a level of quantitative determination of various components and to identify the relative level of expression in a cell or tissue sample. The issue of quantification of proteins is possibly the most challenging problem, and there have been several concerns about accuracy of the methods of peptide/protein quantification by mass spectrometry. Various iTRAQ methods have been developed, which have been found to give satisfactory results for many isobaric residues in peptide fragments. Several other approaches have also been discovered, some of which are specific for certain types of instrumentation. The book gives a nice background of these methods and highlights the interactions of different reagents in achieving efficient tagging of the peptide fragments.

The fragmentation of peptides during tandem mass analyses has been a subject of immense interest. The author has lucidly explained various pathways for fragmentation, highlighting the chemical reactions in gas phase of the peptide ions that may take place in different cases. He has described several residue-specific reactions which may give rise to 'anomalous' fragmentation peaks, that are indeed important for residue-specific sequential identification of the peptides. However, there are often several secondary ions formed by gas-phase reactions of the peptide ions, which are not identified unambiguously. These ions are the key to identification of many isobaric amino acids and can also help in the precise identification of post-translational modifications. The book has outlined many such reactions; however, there are several developments in this area, and I hope the author will include them in the

subsequent editions of the book. The author has dedicated a full chapter describing various applications of mass spectrometry to protein science. Mapping of intact protein isoforms using top-down approach by multidimensional separation techniques followed by mass spectrometric analyses of peptides and fragments analysed with the help of proteome database has become a versatile technique today. Combination of this technique with differential mass spectrometric analyses has been used to achieve label-free detection and quantification of even low-abundance proteins and peptides. High-throughout mass fingerprinting is one of the major breakthroughs in mass spectrometric applications in proteomics. Rapid analyses of human plasma proteome by exploiting multidimensional ion mobility mass spectrometry have revolutionized the capabilities of this versatile technique. Combining electrospray ionization travelling wave ion mobility spectrometry with tandem mass analyses has been shown to yield information on topology along with the mass of the large macromolecular systems. These are some of the frontier developments in the area where the mass spectrometric studies are used to determine structural properties of the biomolecular complexes. The author has provided a lucid discussion on such developments citing suitable examples and also highlighted laser-based high-speed mass spectrometric techniques (e.g. MALDI, LAESI) which have been developed to image biological materials such as tissue samples. Some of these techniques can provide high-throughput imaging methods for potential clinical and pathological applications. The author has also briefly described developments of bioinformatics tools for analyses and interpretation of mass spectrometric results. Several software have been developed to identify the tandem mass spectral signatures of peptides using protein or genomic databases using different models of fragmentation pathways of peptide ions. These bioinformatic tools have enabled fast analyses of a large number of samples with significant accuracy. Some of the software also interface with the instrument for suitable data-dependent acquisition of MS/MS spectra, leading to substantial reduction in the time of experiment.

Overall, this is a well-written textbook highlighting recent developments and challenges in protein mass spectrometry. The organization of the chapters in the book has been thoughtful and is meant for a non-expert and beginner in the area. The author has also described some of the most difficult methods and latest developments in the area, making the book an important source of information even for experts and practitioners of protein mass spectrometry. It would indeed be a priced collection for any science library and would serve as a useful reference to the latest developments in the subject.

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Annual Review of Genetics, 2016. Nancy M. Bonini, Michael Lichten and Gerturd Schüpbach (eds). Annual Reviews, 4139 El Camino Way, Palo Alto, CA 94303-0139, USA. Vol. 50. vii + 618 pp. Price: US$ 102.

Since the last *Annual Review of Genetics* was published, the world saw the launch of the *Human Cell Atlas* – a multi-institute, multi-country endeavour to create a profile of all the different kinds of cells in a human body in terms of their gene expression and other molecules[1]. This has been possible due to the unprecedented advances made in the field of sequencing single DNA/RNA molecules. On the other hand, discovery of ancient remains of both *Homo sapiens* and other hominins continues to revolutionize our understanding of human evolution[2–4]. Recent findings have pushed the history of *H. sapiens* at least 100,000 years further back than that considered earlier[5,6] and have thrown light on the food habits of the Neanderthals[7]. Genetics, as it has since its inception, retains its position at the helm of biological research.

This volume opens with an article by James Haber, in which he summarizes his life's work on double-stand break (DSB) repair. For the last 40 years Haber has been studying the role of homologous recombination (HR) and other processes in the repair of such potentially lethal DNA damages using the model, budding yeast *Saccharomyces cerevisiae*. A couple of other articles in this volume also deal with HR. Gray and Cohen discuss the role of HR in meiotic crossover. During prophase I, the number of DSBs introduced in the chromosomes, is at least an order of magnitude larger than the final number of crossovers. The process of selection of these DSBs is known as designation. Gray and Cohen discuss the mechanism of DSB formation and designation, and also the proteins involved in the process. On the other hand, McVey *et al.* take a detailed look at the role of eukaryotic DNA polymerases in HR across diverse taxa. As has been mentioned above, HR is involved in DNA repair in a variety of contexts such as in meiosis and DSB repair. This review gives a detailed description of the different DNA polymerases and how they mediate such processes.

It is a delight to notice that in this volume the idea of evolution forms a common thread in majority of the reviews, including those mentioned above. Both McVey *et al.* as well as Gray and Cohen take a comparative approach in their respective reviews. A detailed comparison of meiosis across different eukaryotes is the focus of a review by Loidl. It also provides some interesting insights about the origin and diversification of the meiotic process. Loid argues that although meiosis has had a single origin in the common ancestor of all eukaryotes, there are substantial differences in its detail across taxa. Moreover, he notes that the synaptonemal complex is absent in several scattered taxa across distant lineages, suggesting its later origin. Loidl emphasizes the lack of detailed study on meiosis in non-model organisms. The life cycle of several multicellular eukaryotes such as many plants and fungi alternates between haploid and diploid states, a phenomenon termed alternation of generations (AOGs). The proportion of an organism's life cycle spent as haploid and diploid is also extremely variable across lineages. The genetic basis of the origin and maintenance of AOGs in land plants is discussed in the review by Bowman *et al*. The authors provide a detailed description of the genes involved in this process across different major plant groups such as bryophytes, angiosperms, etc. The role of two homeobox