Preface

Nucleic acids and their components play an important role in a variety of fundamental biological processes. The elucidation of the molecular structure of deoxyribonucleic acid (DNA) in 1953 by Watson and Crick led to the so-called *central dogma of molecular biology*. This dogma proclaims that DNA is transcribed to form messenger ribonucleic acid (mRNA) of a complementary sequence that directs its own replication and the sequence of nucleobases in the RNA is then translated to the corresponding sequence of amino acids to form a protein. In addition to mRNA, two other RNA species, transfer RNA (tRNA) and ribosomal RNA (rRNA), are required for this translation process.

The field of genomics has evolved over the last few years, culminating in the sequencing and characterization of the entire human genome. Furthermore, genetic theory contributed to the concept of coding by genes. A gene is defined, biochemically, as a segment of DNA (or, in a few cases, RNA) that encodes the information required to produce a functional biological product—a protein. Current challenges include the unraveling of the relationship between the genome and the proteome. The genome can be used to predict the total potential proteome, including all of the modifications that can be carried out after the initial translation of mRNA to protein by tRNAs and rRNAs.

Consequently, nucleic acid research has had a most profound impact on molecular biology. The study of noncovalent interactions between nucleic acids and peptides or proteins is a highly active research field. Such interactions are involved in many cellular processes, including replication, regulation of gene expression, and DNA packaging. Nearly all the functions of nucleic acids are accomplished by interacting with proteins. Recognition and selectivity are achieved through noncovalent contacts between virtually all biopolymers (proteins, DNA, RNA, polysaccharides, and membrane lipids) that are present in living organisms. The formation and dissociation of these weak interactions are crucial in a vast number of biochemical events. In addition, weak interactions between nucleases and DNA or RNA are central to the recombination, repair, and replication of these molecules in cells.

It is not possible to overestimate the role of metal ions in determining the three-dimensional architecture of nucleic acids, their helices, and higher-order molecular assemblies. Protein–protein, protein–nucleic acid, protein–ligand, and antibody–antigen interactions are other examples that involve noncovalent interactions, which are also of fundamental importance for the pharmaceutical industry in the evaluation of potential drug candidates.

The ability of DNA adducts to induce mutagenesis and carcinogenesis is dependent on their chemical structure, stability, and ability to be recognized by specialized DNA repair proteins. The local DNA sequence context plays a major role in mediating the rate of nucleobase adducts repair and their mispairing potency. Furthermore, the exact location of a DNA adduct within the gene determines whether the resulting mutation affects the structure and function of the gene product.

Among the biophysical techniques employed to study the large biomolecular assemblies involved in these tasks, mass spectrometry presents the greatest potential based on its intrinsic characteristics and accessible information. Therefore, mass spectrometry has had a major role in elucidating the regulatory components and mechanisms involved in the progression from gene to functional protein. Furthermore, analyses of nucleic acids is required to establish their size, purity, and sequence as a prerequisite to their use as molecular probes or therapeutics in biomedical science.

The development of soft-ionization techniques for mass spectrometry has, without question, transformed the field of nucleic acid chemistry. Significant progress in the area of accurate mass

determination, sequencing, and the study of noncovalent interactions has been made possible by the use of ionization techniques such as matrix-assisted laser desorption ionization coupled to time-of-flight (MALDI-TOF) mass analyzers and electrospray ionization (ESI) coupled to conventional analyzers and to tandem mass spectrometric (MS/MS) instruments. Mass spectrometry is now one of the definitive methods for the characterization of isolated and synthetic DNA, RNA, and related products. In addition to accurately determining an intact mass, one can obtain information on the molecular structure and biopolymer sequence using a number of different mass spectrometry approaches. These approaches have provided valuable information on structurally specific biomolecular DNA and RNA interactions. They can also enable the direct determination of stoichiometry for post-translational modifications of specific DNA–drug, DNA–protein, RNA–protein, and DNA–RNA noncovalent and covalent associations. Furthermore, these mass spectrometry approaches can be applied to DNA and RNA sequencing analyses, single-nucleotide polymorphisms, genotyping, mutation detection, genetic diagnosis, and probing of viral structures.

The editors acknowledge the special efforts of the contributors to this CRC/Taylor & Francis publication: Diethard K. Bohme (Canada), William Buchmann (France), Ed Dudley (UK), Daniele Fabris (USA), Valérie Gabelica (Belgium), Kristina Håkansson (USA), Filip Lemière (Belgium), Russell P. Newton (UK), Natalia Y. Tretyakova (USA), Antonio Triolo (Italy), Jean-Jacques Vasseur (France), and Yinsheng Wang (USA). Each contributor, an expert in their particular discipline, has shared their knowledge and understanding of the field of nucleic acid mass spectrometry.

Our aim is to expose you, the reader, to the latest developments in the field of nucleic acid mass spectrometry. The past 15 years have seen dramatic progress in this field. Thus, in addition to contributions that review and summarize these developments and advances, this book also contains chapters describing the next generation of mass spectrometry analyses of nucleic acids and their complexes that have been enabled by such past accomplishments.

This book should be equally accessible to the nucleic acids expert who is a mass spectrometry novice as well as to those with expertise in mass spectrometry but a minimal appreciation of nucleic acids. The exciting developments in mass spectrometry technology have fueled incredible advances in our understanding of nucleic acids and their complexes. We believe these contributions have captured these advances in outstanding fashion, serving to inspire new findings and developments of interest to all in this field.

Finally, no work of this scope is possible without the guidance and support of the publisher. The editors wish to especially acknowledge Ms. Jill J. Jurgensen for her expert help in preparing and producing this book.

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