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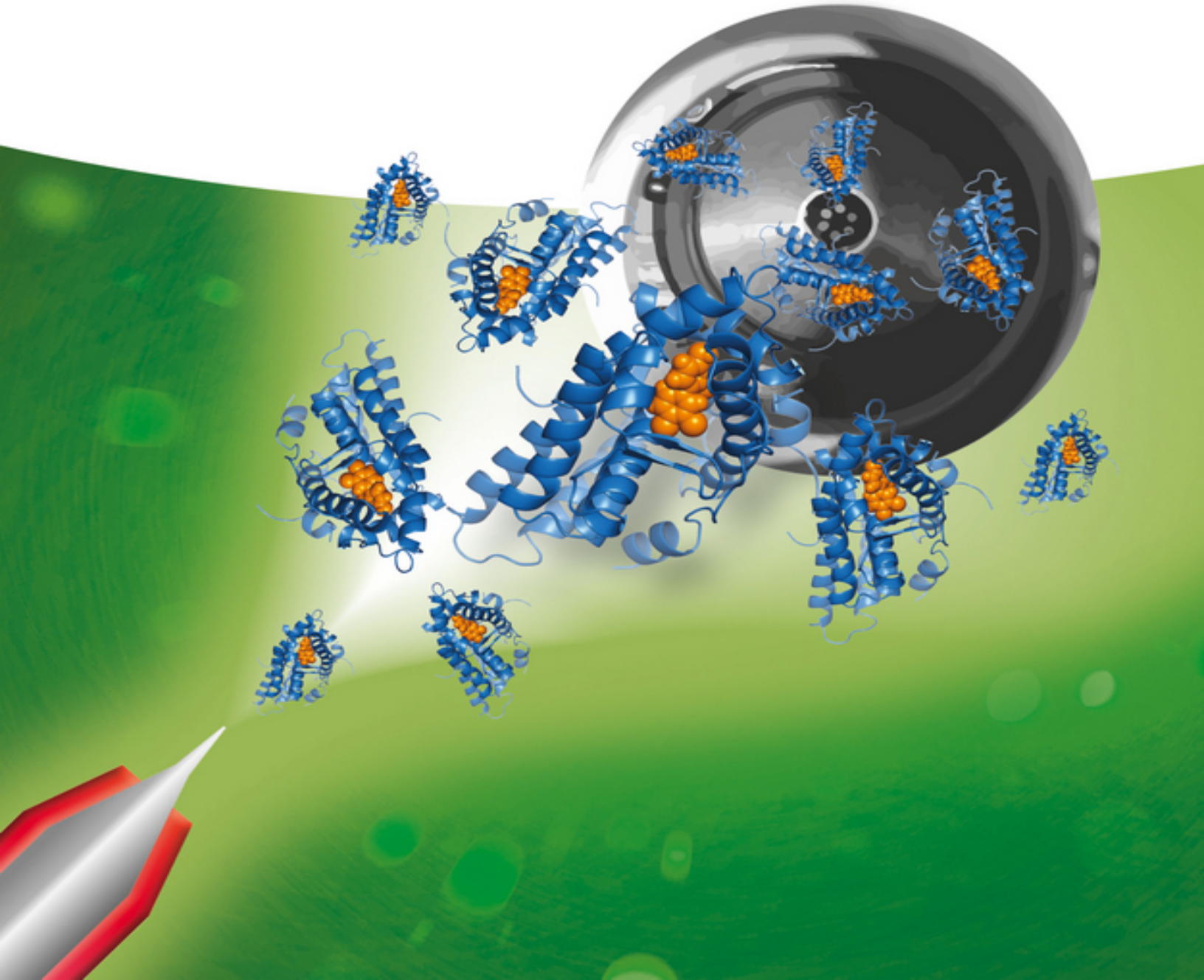

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Preface

The introduction, in 1988, of two new ionization methods for mass spectrometry (MS) has greatly changed the application areas of MS, especially in the biochemical and biological fields. Electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) enabled the efficient analysis of highly polar biomolecules as well as complex biomacromolecules in an easy and user-friendly way and with excellent sensitivity. Multiple charging of proteins in ESI-MS enables the use of simple and relatively cheap mass analyzers in the analysis of peptides and proteins and even opened the way to study intact noncovalent complexes of proteins and drugs or other molecules, including protein–protein complexes. In addition, ESI provided an excellent means to perform online coupling of liquid chromatography (LC) to MS. MALDI-MS with its high level of user-friendliness and excellent sensitivity also boosted the applications of MS in studying biomacromolecules, being more recently even extended to the characterization of complete microorganisms. These developments encouraged further instrumental developments toward highly advanced (and more expensive) mass spectrometers, which provide additional possibilities in the study of biomolecules and their interactions. These new technologies opened a wide range of new application areas, of which perhaps proteomics and all derived strategies and applications belong to the most marked accomplishments. ESI-MS and MALDI-MS changed the way biochemists and biologists perform their research into molecular structures and (patho)physiological processes. Along similar lines, it also changed the ways drug discovery and development is being performed within the pharmaceutical industries. And in the

slipstream of this, it changed analytical chemical research efforts in many other application areas.

The ability to study intact biomacromolecules and especially noncovalent complexes between biomolecules as well as other developments in the field, initiated by the introduction of ESI-MS and MALDI-MS, opened extensive research into the way MS can be used in the study of biomolecular interactions. Different distinct areas for analysis of bioaffinity interactions, and for analysis of biologically active molecules in general, can be recognized in this regard. These areas include precolumn-based ligand trapping followed by MS analysis, affinity chromatography following MS, and postcolumn online affinity profiling. Other methodologies are more indirect and relate to separately performed bioassays and (LC)-MS analysis, such as effect-directed analysis, metabolic profiling, and antivenomics approaches. Besides these, direct approaches without the use of chromatography are nowadays also used in several research areas. These include direct MS-based bioassays and native MS studies in which the latter looks at intact protein complexes in the gas phase. Affinity techniques for trapping proteins and protein complexes toward bottom-up proteomics analysis could also be mentioned in this regard although these techniques are actually specific sample preparation strategies for proteomics research.

With so many new approaches and technologies being introduced in this area in the past 10–15 years, it seems appropriate to compile a thorough review of the current state of the art in the analysis of biomolecular interactions by MS. That is what this book provides in 12 chapters. Apart from a tutorial chapter on MS in the beginning and a conclusive overview at the end of the book, the various chapters are grouped into four themes:

- Native MS, that is, the study of liquid-phase and gas-phase protein–protein interactions by MS and ion-mobility MS
- The use of LC–MS to study biomolecular interactions via indirect assays, as, for instance, applied in effect-directed analysis and related approaches, MS-based binding and activity assays, and other ways to study and identify bioactive molecules, for example, via metabolic profiling or antivenomics.
- Precolumn and on-column technologies to assess bioaffinity, involving frontal and zone affinity chromatography, ultrafiltration and size exclusion chromatography, affinity capillary electrophoresis, and biosensor affinity analysis coupled to MS.
- Online postcolumn continuous-flow bioassays to study bioactivity or bioaffinity of compounds after chromatographic separation.

The contributors to this book did a great job in writing very good reviews and providing beautiful artwork to illustrate the principles and applications of their specific areas within the analysis of biomolecular interactions by MS. For us, it was a pleasure to work with them in this project. We would like to thank them all for their work and for their patience with us in finalizing the final versions of the various chapters.

We hope the readers will benefit from this book, value the overview provided in the various chapters, and perhaps even get stimuli for new research areas or new approaches to perform their research, for instance, by combining ideas and approaches from various chapters of the book into new advanced technologies.

Enjoy reading and get a high affinity with MS!

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Abbreviations

μ	Electrophoretic mobility
2DE	Two-dimensional electrophoresis
5-HT	5-Hydroxytryptamine, serotonin
5-HT_{2A}	5-Hydroxytryptamine (serotonin) receptor subtype 2A
Ab	Antibody
ACE	Affinity capillary electrophoresis
ACE	Angiotensin converting enzyme
AChBP	Acetyl choline binding protein
Ag	Antigen
Ag–Ab	Antigen–antibody complex
AhR	Aryl hydrocarbon receptor
AMAC	Accelerated membrane assisted clean-up
APCI	Atmospheric pressure chemical ionization
API	Atmospheric pressure ionization
AR-CALUX	Androgen chemically activated luciferase expression
BGE	Background electrolyte
BGF	Bioassay guided fractionation
BGT1	Betaine-GABA transporter
BLAST	Basic local alignment search tool
BS^2G	Bis(sulfosuccinimidyl)suberate
CCT	Chaperonin containing Tcp1
CDER	Center for drug evaluation and research
CE	Capillary electrophoresis
CECs	Chemicals of emerging concern
CHCA	α-Cyano-4-hydroxy cinnamic acid
CI	Chemical ionization
CID	Collision-induced dissociation