Metal Complex–DNA Interactions

Interactions of metal complexes with DNA have been fascinating chemists for a long time. The discovery of the antitumor activity of *cis*-$[PtCl_2(NH_3)_2]$ (cisplatin) in the late 1960s and the subsequent investigation of its DNA-binding properties have certainly resulted in one of the best-known examples of metal-complex–DNA interactions, but that is by no means the only example. Nick Hadjiliadis and Einar Sletten have now taken on the challenging task of compiling a book that brings together the highly diverse aspects of this ever-growing area of research. They have managed to recruit an impressive number of authors from more than a dozen countries to aid them in their endeavor. The resulting book, *Metal Complex–DNA Interactions*, is divided into 18 stand-alone chapters. For the sake of clarity and to better organize the wealth of available information, the editors have divided the book into four sections, namely "Basic Structural and Kinetic Aspects", "Medicinal Applications", "DNA Recognition: Nucleases and Sensors", and "Toxicological Aspects".

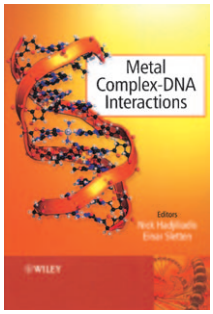
The introductory section dealing with "Basic Structural and Kinetic Aspects" comprises four chapters. The first of these presents an introduction to NMR spectroscopic studies of sequence-selective binding of transition metal ions and platinum complexes to DNA. The section also contains a chapter on the thermodynamics of metal-ion–DNA interactions, and provides an insight into how metal-ion binding can be investigated by optical spectroscopy. The third chapter gives a detailed description of the various possible folding topologies of guanine quadruplexes, and specifies how (or whether) these are correlated with the type of metal ions present. The final chapter provides an overview of supramolecular aspects of transition-metal–nucleobase chemistry; here the focus is not on metal binding to DNA as such but rather on the structural chemistry of metal complexes of its nucleobase building blocks.

The second section, devoted to "Medicinal Applications", contains six chapters, four of which deal with the applications of platinum complexes. The first chapter, after a brief introduction to the mode of action of the well-known antitumor drug cisplatin, provides a detailed insight into possible conformers of model complexes of the main cisplatin adduct. The next chapter covers the biological reactions to DNA damage induced by platinum drugs. Next there is a discussion of the telomers and of the RNA component of telomerase as potential targets for platinum complexes, and that is followed by an introduction to the basic principles and concepts of photodynamic cancer therapy using ruthenium, osmium, and rhodium complexes. The remaining two chapters report on the application of platinated oligonucleotides as potential antisense or antigene agents for the regulation of gene expression, and on the interactions of rhodium complexes and organotin complexes with DNA. From this list it becomes clear that readers expecting detailed reports on traditional platinum–DNA chemistry, with an emphasis on how complex formation distorts duplex DNA, might be somewhat disappointed. However, several of the less thoroughly studied aspects of platinum-complex–DNA interactions reported here surely deserve a large audience, and the editors' decision to include them in their book will certainly help to propagate these new approaches.

The third section, "DNA Recognition: Nucleases and Sensors", starts with a chapter on groove-binding ruthenium(II) complexes as probes for the recognition of non-duplex DNA, which also includes a brief discussion of intercalating complexes. The second chapter describes conjugates of small peptides with DNA-binding metal complexes, which are designed with the intention to introduce sequence-specificity during DNA binding. The remaining three chapters highlight various aspects of nucleic acid hydrolysis. They report on artificial restriction agents with metal-dependent reactivity, on catalytic DNA species (DNAzymes) as sensors for metal ions, and on enzymes for the processing of nucleic acids in which the catalytic action depends critically on the two metal ions.

The final section, "Toxicological Aspects", consists of three chapters dealing with mercury(II), chromium, and arsenic, respectively. The first of these gives a detailed insight into mercury(II) binding sites in DNA, and in particular into the mercury(II)-mediated thymine–thymine mispairing. The next chapter summarizes different types of DNA damage induced by chromium(VI) compounds, including direct chromium–DNA adducts as well as oxidative action. Finally, possible mechanisms for arsenic-induced carcinogenicity are discussed. Contrary to the information given on the book cover, the final section does not deal with the effect of nickel on DNA integrity.

When thumbing through the book, one immediately notices that the term "metal complex" is used in a broad sense throughout. While it is certainly true that metal ions in biological systems are hydrated, and therefore are in fact metal complexes, it is still surprising in a book entitled *Metal Complex–DNA Interactions* that about half of the chapters report on the interaction of DNA with metal *ions* or metal *species*. The editors' attempt to condense as many aspects of the interaction of metal species with DNA as possible into one compendium has unfortunately resulted in



Metal Complex–DNA Interactions
Edited by Nick Hadjiliadis and Einar Sletten. Wiley-VCH, Weinheim 2009. 544 pp., hardcover € 125.00.—ISBN 978-1405176293

parts of the book appearing fragmented. For example, there are many toxic metal species, and the choice to include mercury(II), chromium, and arsenic in the section on toxicological aspects seems arbitrary. Moreover, the damaging effects of the latter two elements appear to arise mainly from the generation of oxidative stress rather than from a direct interaction with DNA. For these reasons the final section—although it certainly reports on highly interesting and topical research—seems like a foreign body within the book. Instead, interesting developments in the field of medicinal applications that are not mentioned in the book could have been included, for example research on trinuclear platinum complexes or on the nature of platinum–DNA interactions at the level of the nucleosome.

On a more technical note, most chapters cover recent literature up to 2007, with rare appearances of references to publications of early 2008. All the lists of references include the titles of the publications, which allows one to quickly choose items for further reading. The positioning of the color plates section in the middle of the book appears somewhat out-dated. A comparison with other similarly priced books shows that it is nowadays preferred to incorporate high quality color figures within the main text.

Taken together, the book provides an impressive overview of the great diversity of current research on metal-complex–DNA interactions. It shows that the targets of interest are no longer limited to regular DNA duplexes, but that they extend to more complex conformations such as single strands, bulged duplexes, and quadruple helices. As this broad range of topics is covered in a form that also includes some highly specialized stand-alone chapters, the book is suitable for academic researchers from a variety of disciplines, including inorganic chemists, biochemists, and medicinal chemists. It is a good reference book for scientists already familiar with the subject, can be used for background reading in graduate courses on metal–DNA interactions, and certainly deserves a place in every scientific library.

Jens Müller
Westfälische Wilhelms-Universität Münster
(Germany)

DOI: 10.1002/anie.200906042