Platinum and Biological Systems

Metal Ions in Biological Systems, Volume 33: Probing of Nucleic Acids by Metal Ion Complexes of Small Molecules

EDITED BY ASTRID SIGEL AND HELMUT SIGEL, Marcel Dekker, New York, 1996, 678 pages, ISBN 0-8247-9688-8, U.S.$195.00

Metal ions perform an important role in the structure and stability of the DNA double helix, and many DNA-protein interactions, including both gene expression and DNA replication, are dependent upon metals. It is therefore not surprising that metals and metal compounds have become important both as tools for probing nucleic acid structure and, as in the case of platinum compounds, chemotherapeutic agents. This volume (and Volume 32 reviewed in *Platinum Metals Rev.*, 1996, **40**, (3), 117) draws upon the experience of recognised international experts to review the present status of research in this area. The various chapters describe experimental and theoretical techniques for examining metal-nucleic acid interactions, such as optical and NMR spectroscopy, electrochemistry, thermodynamic and kinetic analysis, the use of metals as probes, and molecular modelling. Specific metal-DNA interactions are discussed, as are metal complexes as artificial nucleases.

The platinum group metals feature in a number of chapters; in Chapter 1, J. Kozelka describes the molecular modelling of transition metal complexes with nucleic acids, where the cisplatin-DNA adduct is used to compare theoretical predictions versus empirical data. In Chapter 4, the role of the double helix as an active promoter of Pt-DNA adduct formation with *cis* and *trans* diamminedichloro platinum(II) is discussed by M. Boudvillain and co-workers, and in Chapter 5, B. Lippert asks why the *cis* and *trans* isomers are so different, and what makes the *cis* isomer (cisplatin) a good antitumour drug?

Ruthenium and rhodium complexes are frequently used as probes for DNA, particularly ruthenium phenanthroline (phen) complexes, and rhodium bipyridyl (bpy) and phenanthrenequinone diimine (phi) complexes. These compounds, unlike cisplatin which forms covalent bonds with DNA, bind to DNA via outer sphere interactions, such as intercalation, groove binding or electrostatic binding. As described by B. Nordén and co-workers, in Chapter 7, these probes are substitution-inert, however, they can be activated by light or electrochemically. M. A. Billadeau and H. Morrison, Chapter 9, discuss the potential use of Rh(phen) and Rh(bpy) as photoactive, "photocisplatin", chemotherapeutic agents, the activated compounds being able to react chemically with DNA. The use of these compounds is limited by the requirement of UV light for photoactivation.

Electrochemical activation of ruthenium and rhodium complexes is proposed by D. H. Johnston and co-workers, Chapter 10, as a route to design diagnostic electrode probes, while the electroactive properties of DNA are discussed by E. D. A. Stemp and J. K. Barton in Chapter 11. Here, [Ru(II)(phen)] and [Rh(III)$(phi)_2$(phen)] complexes are used to investigate long range charge transfer through the DNA double helix. The latter compound, when bound to a DNA-binding oligopeptide, is used as a probe for DNA-protein interactions; this is described by E. C. Long and colleagues, in Chapter 14.

The use of numerous transition metal complexes is described, and of particular interest to the inorganic biochemist are chapters featuring the so-called artificial nucleases: metal compounds capable of breaking the DNA strands of the double helix. Chapters 20 and 21 describe the clinically important interactions of metals with the anticancer drug bleomycin which result in the DNA strand being broken and leading to tumour cell death.

Metal ions thus play a significant role in many biological processes. This book is a very useful volume, complementing Volume 32. It is recommended to all those with an interest in this area of bioinorganic chemistry. S.P.F.