Historical Development and Perspectives
of the Series

Metal Ions in Life Sciences

It is an old wisdom that metals are indispensable for life. Indeed, several of them, like sodium, potassium, and calcium, are easily discovered in living matter. However, the role of metals and their impact on life remained largely hidden until inorganic chemistry and coordination chemistry experienced a pronounced revival in the 1950s. The experimental and theoretical tools created in this period and their application to biochemical problems led to the development of the field or discipline now known as Bioinorganic Chemistry, Inorganic Biochemistry, or more recently also often addressed as Biological Inorganic Chemistry.

By 1970 Bioinorganic Chemistry was established and further promoted by the book series Metal Ions in Biological Systems founded in 1973 (edited by H.S., who was soon joined by A.S.) and published by Marcel Dekker, Inc., New York, for more than 30 years. After this company ceased to be a family endeavor and its acquisition by another company, we decided, after having edited 44 volumes of the MIBS series (the last two together with R.K.O.S.) to launch a new and broader-minded series to cover today’s needs in the Life Sciences. Therefore, the Sigels’ new series is entitled

Metal Ions in Life Sciences

and we are happy to join forces in this new endeavor with a most experienced publisher in the Sciences, John Wiley & Sons, Ltd, Chichester, UK.

The development of Biological Inorganic Chemistry during the past 40 years was and still is driven by several factors; among these are: (i) the attempts to reveal the interplay between metal ions and peptides, nucleotides, hormones or vitamins, etc.; (ii) the efforts regarding the understanding of accumulation, transport, metabolism and toxicity of metal ions; (iii) the development and application of metal-based drugs; (iv) biomimetic syntheses with the aim to understand biological processes as well as to create efficient catalysts; (v) the determination of high-resolution structures of proteins, nucleic acids, and other biomolecules; (vi) the utilization of powerful spectroscopic tools allowing studies of structures and dynamics; and (vii), more recently, the widespread use of
macromolecular engineering to create new biologically relevant structures at will. All this and more is and will be reflected in the volumes of the series *Metal Ions in Life Sciences*.

The importance of metal ions to the vital functions of living organisms, hence, to their health and well-being, is nowadays well accepted. However, in spite of all the progress made, we are still only on the brink of understanding these processes. Therefore, the series *Metal Ions in Life Sciences* will endeavor to link coordination chemistry and biochemistry in their widest sense. Despite the evident expectation that a great deal of future outstanding discoveries will be made in the interdisciplinary areas of science, there are still ‘language’ barriers between the historically separate spheres of chemistry, biology, medicine, and physics. Thus, it is one of the aims of this series to catalyze mutual ‘understanding’.

It is our hope that *Metal Ions in Life Sciences* proves a stimulus for new activities in the fascinating ‘field’ of *Biological Inorganic Chemistry*. If so, it will well serve its purpose and be a rewarding result for the efforts spent by the authors.

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Preface to Volume 1

Neurodegenerative Diseases and Metal Ions

Over the years substantial evidence has accumulated implicating that metal ions play a role in the pathophysiology and pathogenesis of neurodegenerative disorders. This is emphasized in Chapter 1, which sets the scene for this volume and provides an organizational frame for metal-related disorders, namely: (i) those caused by a defect in metal ion transport or homeostasis; (ii) those caused by toxicological exposure to metals; and (iii) those caused or associated with metalloprotein aggregation and/or misfolding.

Indeed, misfolded proteins are implicated in a rapidly growing list of debilitating illnesses like Alzheimer’s, Parkinson’s, and Creutzfeldt–Jakob diseases. Therefore Chapter 2 deals with protein folding and misfolding; structures, energetics, and dynamics of transient species are considered in detail because their characterization is an essential step in understanding the benign and malignant pathways of protein folding.

The three chapters following these general considerations are devoted to metal ion interactions, mainly of copper, with mammalian prion proteins and their fragments, to transmissible spongiform encephalopathies (Creutzfeldt–Jakob and related diseases) as well as to the amyloid precursor protein (Alzheimer’s disease). Chapters 6 and 7 consider in particular the role of iron in Parkinson’s and Huntington’s diseases, respectively, whereas Chapter 8 details the interrelation between copper–zinc superoxide dismutase and familial amyotrophic lateral sclerosis. The malfunctioning of copper transport in Wilson and Menkes diseases, where copper accumulates or is not absorbed, respectively, is dealt with in Chapter 9. The special role of iron in neurodegenerative diseases and the chemical interplay between catecholamines and metal ions are in the focus of Chapters 10 and 11, respectively; in this context Parkinson’s, Alzheimer’s and Huntington’s diseases are considered again, but from a different viewpoint, in addition to neurodegeneration with brain iron accumulation (NBIA, formerly Hallervorden–Spatz syndrome), neuroferritinopathy, aceruloplasminemia, Friedreich’s ataxia, and taupathies.

The disruption of the homeostasis of metal ions can have devastating effects as is evident throughout the book. This also holds for the essential zinc; its
metalloneurochemistry, i.e. its physiology and pathology as well as probes and sensors to detect it, are covered extensively in Chapter 12.

Next to metal ions like manganese, iron, copper, and zinc, which are essential but may also be toxic due to the creation of reactive oxygen species resulting in oxidative stress, there are other metal ions which are a priori neurotoxic. Among these is aluminum, and its role in neurodegenerative processes is reviewed in Chapter 13. Cadmium, lead, and mercury are important from the viewpoint of public health because they are released into the environment by human activities; their neurotoxicity is covered in Chapter 14.

The terminating Chapter 15 summarizes in a general way the medicinal chemistry of metal-centered brain diseases and indicates other neurological disorders that may involve metal ions like polyneuropathy, multiple sclerosis, macular degeneration, progressive supranuclear palsy or the restless leg syndrome which are not otherwise covered in the book because knowledge is scarce.

It is clear that there is an urgent need for developing novel drugs and classes of drugs that manipulate metal-centered neuropathology more precisely and elegantly than the presently (only partly) available chelation therapies. It is hoped that this volume stimulates research into this direction.

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