Preface

Metals are essential for life, as well as for around one-third of the proteins that require the interaction with metal ions or metal containing cofactors to carry out a particular biological function. This interplay has been extensively explored in the past, as metalloproteins are involved in key biological processes, from energy production to the synthesis of DNA building blocks. Here we took the challenge to organize a book focusing on an essential aspect of the metal-protein interaction, relating to the role of metal ions in protein folding and structure, which we felt needed to be addressed, aiming at merging topical contributions in fundamental aspects of the folding, stability, and design of metal-binding proteins or peptides, with more biological aspects related the action of metallochaperones or with the intervention of metals in determining protein conformations associated with disease. With this purpose we have commissioned 13 chapters that provide a comprehensive, state-of-the-art perspective of the topic under discussion, which we have organized in four sections.

Section I, Folding and Stability of Metalloproteins, comprises contributions that provide case study examples of protein folding and stability studies in particular systems or proteins that comprise different metal ions (zinc, copper) or cofactors (iron-sulfur centers, heme). It aims to provide a view on more fundamental aspects such as for example those related to the influence of metal sites and respective redox state in the energetics of the folding reaction, interactions with nonnative protein states, or influence in folding pathways. Section II, Mechanisms of Metal Transporters and Assembly reviews the proteins that shuttle metal ions in the cell (iron and copper chaperones in the selected examples) to a particular target metalloprotein. A structural understanding of these proteins and of metal-mediated conformational changes is fundamental to characterize the *in vivo* insertion of metals into apoproteins, and protein-protein interactions. Section III, Metal Ions, Protein Conformation, and Disease, illustrates how metal binding can be connected to pathological protein conformations in unrelated diseases, from cancer to protein deposition disorders such as Parkinson's disease. This is an emerging field in which the role of metal ions is becoming increasingly more relevant, in a large number of different proteins and pathologies. Section IV, Metalloprotein Design, Simulation, and Models, gathers contributions addressing protein redesign of metal-containing proteins by computational methods, folding simulation studies, and work on model peptides, dissecting the relative energetic contribution of metals sites to protein folding and stability. It provides a key view on how computational studies are relevant to understanding these biological processes.

Such a combination of contributions is expected to be of interest to a larger audience of protein chemists, biochemists, and biophysicists, from postgraduate level onward, with broad interests in aspects relating to structural biology, bioinorganic

chemistry, protein folding and disease, and molecular and cellular aspects of metals in biological systems. We hope that this overview on this key biological problem will make this volume a resourceful source of information as well as an attraction to new scientists to join the field.

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