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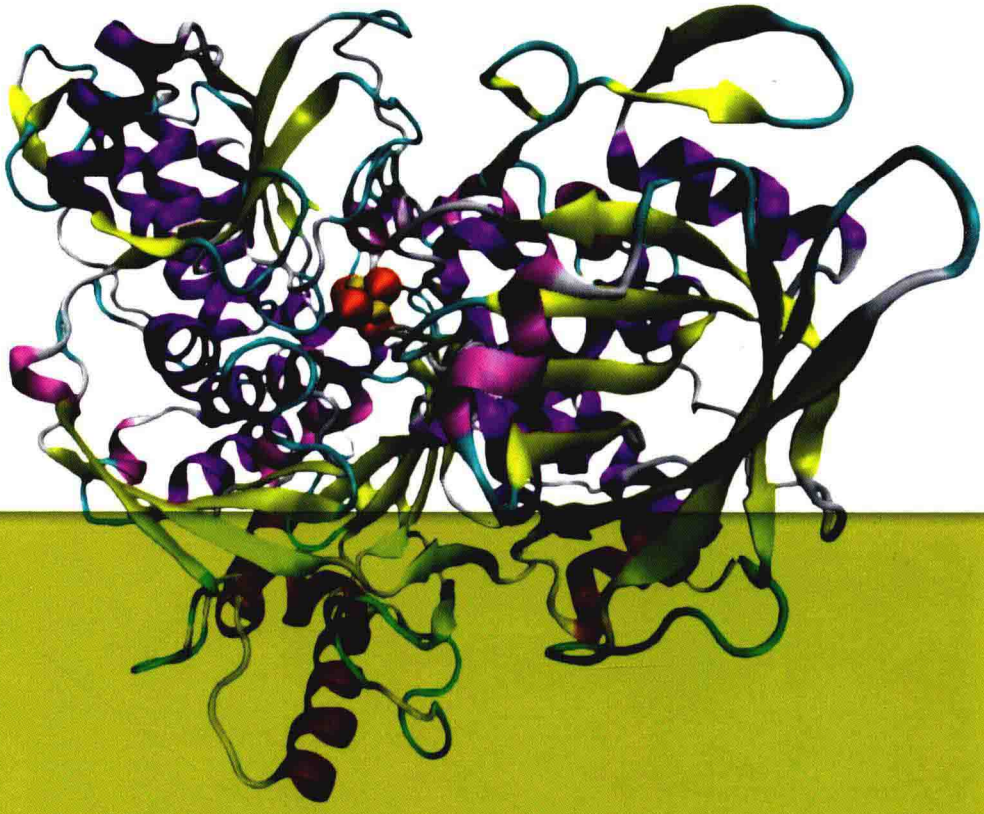

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Iron-Sulfur Clusters in Chemistry and Biology

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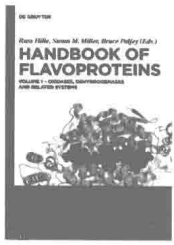

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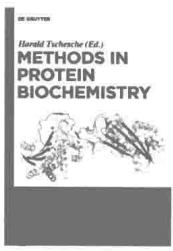

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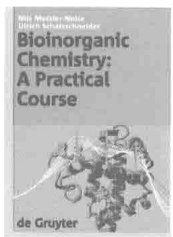

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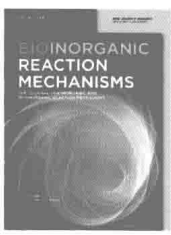

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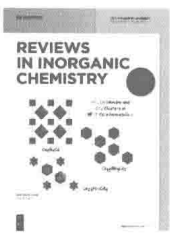

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Preface

Iron-sulfur (Fe-S) clusters are versatile prosthetic groups that enable their associated proteins to perform numerous functions, ranging from electron transport to substrate ligation, to structural support, and to DNA repair. Fe-S proteins did not become a focus of research until the late 1950s, when spectroscopy techniques evolved sufficiently to identify features that were specific for Fe-S clusters. Initially identified in mammalian succinate dehydrogenase, Fe-S clusters were subsequently found in numerous bacterial proteins that performed complex functions, including nitrogenase, which transforms atmospheric nitrogen into ammonia, generating an accessible source of nitrogen for synthesis of proteins and nucleic acids. Understanding how Fe-S clusters and proteins work has occupied many scientists for decades, and important breakthroughs regarding the mechanisms of nitrogenase and hydrogenase have occurred in just the last few years.

Not only is it a challenge to understand how Fe-S proteins work, but it is also a challenge to understand how Fe-S clusters are synthesized and inserted into Fe-S proteins in living organisms. Studies originally performed in bacterial model systems have revealed basic mechanisms of biogenesis that are conserved in all the kingdoms of life. Moreover, it has become apparent that flaws in the Fe-S assembly process cause several human diseases. As a result, biomedical researchers working on the pathophysiology of rare diseases such as Friedreich ataxia have begun attending conferences at which chemists and physicists discuss Fe-S research based on complex spectroscopic studies and computational analyses. Researchers from different ends of the spectrum have struggled to bridge the large gap between the physics and chemistry of Fe-S clusters and the important biological questions associated with their functions.

Despite a growing need for cross-disciplinary communication, there has been no single book devoted to Fe-S proteins that provided a basic and broad overview of the subject as it has evolved over the last several decades. This book was borne out of a desire to make the subject of Fe-S proteins more accessible by including a short history of Fe-S research, chapters that highlight the unique chemistry of Fe-S clusters and techniques important in analysis, and reviews from leading researchers on well-known Fe-S proteins such as nitrogenase and hydrogenase. In addition, numerous chapters focus on Fe-S synthesis and regulation in model organisms and in mammalian biogenesis, DNA metabolism, and human disease. Concluding with a discussion on the potential role of Fe-S clusters in capturing reducing power and contributing to the origin of life on earth, the final chapter touches on questions about how metabolic pathways initially developed.

I am indebted to my many outstanding and generous colleagues, who spent considerable time and effort in writing the chapters in this book. I hope that this book will be useful to those interested in the subject of Fe-S from many different perspectives

and that researchers from related disciplines will gain a greater sense for the context of their own work.

I want to thank Stephanie Dawson, who perceived that there was an unmet intellectual need and initiated this project while she was an editor at De Gruyter. I also thank Julia Lauterbach of De Gruyter for her tireless support and guidance in turning this book into a reality. My family and friends graciously supported me when I needed time to work on the project known to them as "the book", and I am thankful for their help.

Tracey A. Rouault

Tracey A. Rouault biography

Tracey A. Rouault is a leading researcher in the area of mammalian iron-sulfur proteins, an area she began to pursue after discovering an important role for an iron-sulfur protein in the regulation of mammalian iron metabolism. She received a degree in Biology from Yale College and an MD degree from Duke University Medical School, where she completed her training in internal medicine. She completed a medical fellowship at the National Institutes of Health in Bethesda, Maryland, and has since focused on the regulation of mammalian iron metabolism and its relationship to human diseases. Her main interests include elucidating mechanisms of mammalian iron-sulfur cluster biogenesis and exploring the pathophysiology of diseases related to ineffective iron-sulfur cluster biogenesis, several hematologic disorders, genetic cancer syndromes, and neurodegenerative diseases. Her early research in the role of iron-sulfur proteins in regulation led to a productive collaboration with Helmut Beinert, a researcher responsible for numerous ground-breaking advances related to iron-sulfur proteins. She has also collaborated with Richard Holm, whose pioneering work led to the inorganic synthesis of numerous iron-sulfur clusters and revealed that many properties of iron-sulfur proteins derive from intrinsic features of their iron-sulfur clusters. She is an active member of the rapidly growing iron-sulfur protein research community.

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