METALLOENZYMES AND CHEMICAL BIOMIMETICS

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Bioinorganic enzymology, the chemistry of metalloenzymes and closely related areas dealing with metalloprotein functions, is a broad interdisciplinary research field, representing an intellectually attractive and experimentally demanding frontier in modern chemical and biological sciences. Inorganic chemists should play a major role in this area because metal ions and their properties/reactivity are a primary feature characterizing these biological systems. Metalloproteins are basically highly elaborated metal complexes where the ligand is a structured polypeptide chain. They contain one or more metal ions in the active site and are optimally designed to accomplish evolutionary directed functions. The ultimate goal of biological inorganic chemistry research is to gain an understanding of these functions in terms of structure and reactivity. Inorganic chemists, in particular, recognize that the structural and electronic properties of biological metal centres are often modulated from those of small molecules containing the same metal ion. Understanding these differences is essential for understanding function, and for this reason the contribution of synthetic and biomimetic chemistry is extremely important for the progress of this field.

Major role for Inorganic Chemisty

The significance of the metal-centred chemistry performed by metalloenzymes is not limited to the biological environment. It has a strong impact on the medical sciences (e.g. generation of oxygen radicals, production and reactions of nitric oxide), pharmacological sciences (e.g. enzyme inhibition, protein receptors, metal toxicity), and environmental sciences (e.g. nitrogen and sulphur cycles, soil and water detoxification). But the capacity of metalloenzymes to carry out energetically difficult processes efficiently under mild conditions should also be attractive to chemical industry, with the aim of developing environmentally friendly processes.

As with other interdisciplinary research fields, it is clear that bringing together scientists with different expertise is essential for the progress in the area. The key importance of metallobiochemistry has been recognized at the European level with the launch of several COST Actions, and ultimately D21 (2000−2006) had the objective of coordinating the research efforts by a large number of European groups on topics of timely and relevant interest, and promoting more intensive exchange between individual groups. More than 100 laboratories were involved in this programme, which developed along the following priority areas: (a) structural, mechanistic and spectroscopic studies of metalloenzymes; (b) synthetic studies of mononuclear and polynuclear metal complexes with biomimetic ligands as active site models and biomimetic catalysts; (c) structural and spectro-

Interdisciplinary exchange promoted

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scopic studies on electron transfer proteins; (d) characterisation and biological role of metal-protein interactions; (e) small molecules activation at biological and biomimetic metal centres. A large body of high quality scientific progress has been made during the years through this COST Action. Much of this would have probably been made also in the absence of this programme, but it is true that facilitating the collaborations increased the scientific impact that would have been obtained if individual groups carried out their research independently. Given the dimension of COST D21, a huge number of papers have been published in the literature within this programme. A "flavour" of the broad scope of D21 "Metalloenzymes and chemical biomimetics" is given by the fully peer-reviewed microreviews and research papers appearing in the present and following issues of the European Journal of Inorganic Chemistry. These papers span several research topics which characterized D21, and in particular focus on insulin mimetic vanadium complexes (Gätjens et al., Kiss et al.), DNA cleavage by artificial nucleases (Borras et al.), metal-protein interactions (Kiss et al.), enzyme inactivation by radical species (Golding et al.), protein-protein interactions (Moura et al.), enzymatic production of toxic small inorganic molecules (Obinger et al.), inhibition of zinc enzymes (Santos et al.), distribution of vanadate in human blood (Gorzsas et al.), biomimetic chemistry of dinuclear zinc complexes (Meyer et al.), vanadium complexes (Pessoa et al., Geraldes et al.) and manganese clusters (McKenzie et al.), and engineering of electron transfer proteins (Canters et al.). We hope that this collection will stimulate more inorganic chemists to be involved into the field of metallobiochemistry, perhaps initiating interdisciplinary collaborations.

Collaboration raised scientific impact

