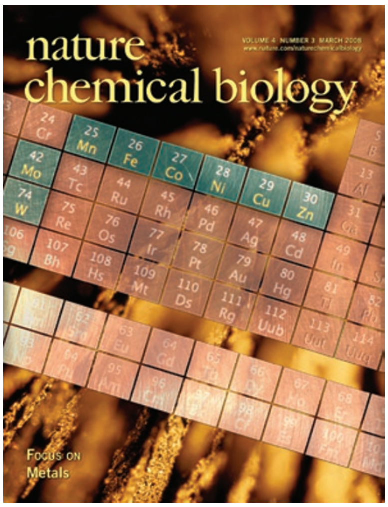
nature
chemical biology

Metals in chemical biology

As scientists move towards a more comprehensive understanding of the role of metals in biology, bioinorganic chemistry will be an increasingly important component of chemical biology.

Bioinorganic chemistry—the interface of biology and inorganic chemistry—first emerged as a distinct discipline around 1962 with the first "Metals in Biology" Gordon Research Conference (originally called "Metals and Metal Binding in Biology"). The field exploded in the early 1980s, with 1983 marking the first International Conference on Biological Inorganic Chemistry (ICBIC) (p. 157). Since this period, tremendous advances have been made in understanding the mechanisms and functions of metals in biological systems (*Proc. Natl. Acad. Sci. USA* **100**, 3563–3568, 2003), with many more on the horizon (*Nat. Chem. Biol.* **2**, 504–507, 2006). In this issue, we feature a collection of articles that describe important recent progress in the field from both the chemical and the biological perspective. These articles highlight the sophisticated understanding of the role of metals in biological pathways, but they also hint at the many biological functions of metals left to be discovered. As scientists move towards investigating the roles of metal ions within ever more complex biological systems, bioinorganic chemists are going to play an increasingly important role in the field of chemical biology.



Transition metal ions are components of biological processes from oxygen formation to hypoxia sensing and have been implicated in many diseases including microbial infections, cancer and neurodegenerative disorders. Iron and copper are two redox-active transition metals that have particularly intrigued bioinorganic chemists. In this issue we highlight some of the exciting new insights into the chemical mechanisms and biological functions of these metals. Kovaleva and Lipscomb describe the diverse chemical mechanisms (p. 186) and Loenarz and Schofield highlight the emerging biological roles (p. 152) of non-heme Fe(II) oxidases and oxygenase. Thiele and colleagues review the cellular and systemic pathways involved in regulating copper accumulation and distribution (p. 176), and Davis and O'Halloran discuss the unusual coordination chemistries being discovered in these copper trafficking pathways (p. 148).

With the unusual spectroscopic characteristics of metals, progress in the field of bioinorganic chemistry has been catalyzed by advancements in methods such as extended X-ray absorption fine structure (EXAFS) and electron paramagnetic resonance (EPR) spectroscopies. As bioinorganic chemists focus more on the roles of metal ions in cells and whole organisms, future developments in the field are likely to again result from methodological advances, including new approaches for imaging metals inside living systems. In this issue, Chang and colleagues highlight important progress in creating fluorescent small-molecule probes for studying metals in living cells and describe design considerations that will maximize the usefulness of these probes for cellular studies (p. 168).

Recent results, such as those linking the non-heme Fe(II) enzymes with epigenetic and obesity pathways, highlight the roles of metalloenzymes in complex biological systems, including ones with significant implications for disease. Bioinorganic chemists have already made important progress in understanding the roles of the metalloproteins in these and other biological pathways. In this issue, Thiele and Gitlin argue that it is now time to take the advances of the last decades in understanding the parts of these systems and "integrate these pieces into a systematic view of the dynamic metabolism of transition metals." They then highlight some new approaches that could be used to achieve an understanding of the "systems biology of transition metals" (p. 145).

Moving towards a broader understanding of how metals function within biological systems will require increasingly interdisciplinary research. The field of bioinorganic chemistry has always welcomed inorganic chemists and the biologists that share a common interest in metals. However, further integration of the bioinorganic community with other disciplines at the interface of chemistry, biology and medicine would open up additional avenues of research. For this to occur, bioinorganic chemists will need to interact broadly with scientists interested in the chemical mechanisms of biology and disease. At the same time, scientists in other disciplines will need to reach out to their bioinorganic colleagues and consider the perhaps undetected and unexpected roles that metals could be playing in their biological systems.

Journals that reach an interdisciplinary readership can also facilitate these types of cross-disciplinary interactions. Although chemical biology has a strong historic connection to bioorganic chemistry, at *Nature Chemical Biology* we have always considered the field to include all scientists interested in the interface of biology and chemistry (*Nat. Chem. Biol.* **1**, 3, 2005). As such, we consider bioinorganic chemists to be essential contributors to the chemical biology community. We are pleased to highlight some of the exciting advances in bioinorganic chemistry in this issue, and we look forward to continuing to publish papers that push the frontiers of 'metals in chemical biology'. ■