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## Metallomics. A Primer of Integrated Biometal Sciences.

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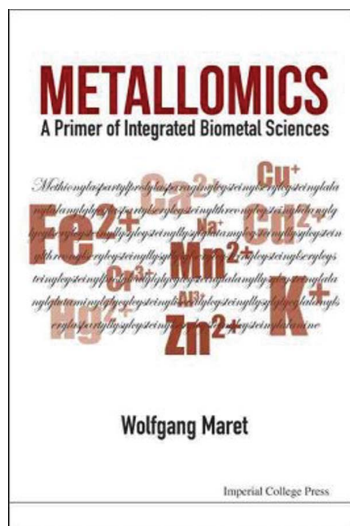
*Metallomics* is the science studying the metallome, *i.e.* the distribution of free metal ions in cellular compartments. This slim book serves as an introduction to the field and puts much emphasis on the fact that metallomics does not simply reduce to metal biochemistry: metals are not treated simply as cofactors, but as ‘critical, integral parts of cellular processes’ (quoted from the prologue). The terms metallome and metallomics were introduced at the beginning of the third millennium, so non-specialist readers may not be accustomed to the specificities of the field. *Metallomics*, which as the subtitle clearly states aims at being a *primer*, represents therefore a most welcome entry point.

*Metallomics* is composed of six chapters plus an *Epilogue and Summary*, preceded by a prologue and a list of abbreviations, and followed by a glossary (almost indispensable in a primer and certainly most welcome by the non-specialist reader) and the index. Each chapter ends with a summary, that helps the reader focus on the essential points.

The first chapter (five pages) is an *Introduction* where metallomics is cast as a field spanning beyond bioinorganic chemistry but with a different, more general approach studying the role of metal ions in biological systems rather than just the interaction of metals with biomolecules. The question of what elements are essential for life appears already in this introduction and will accompany the reader until the end of the journey, in which we learn not only that the question is still unanswered, but also that the answer is not unique but depends on the organism under investigation. Being a primer, *Metallomics* does not address all forms of life but concentrates on what may appear to be two extremes: bacteria and humans. The choice makes perfect sense once we think about the importance of human microbiota in health and disease.

Chapter 2 (24 pages) is true to the title of the book and provides the basic definitions. A clear distinction is made between *structural* and *functional* metallomics, to address coordination environments and functions of the metals, respectively. Some overlap does exist, in that among the various functions of metals we obviously also find a structural role. A large part of the chapter is devoted to the metallomes, with a distinction made between low and high molecular weight complexes, followed by a short survey of metalloproteins. The chapter ends naturally with a section on metalloproteomics, as the division of metallomics specifically devoted to proteins containing a metal ion.

Chapter 3 (23 pages) deals with *The chemical elements of life*. After a bit of taxonomy, the reader is briefly guided through cycles (carbon, oxygen, nitrogen, sulfur), before introducing a central topic of the book: the relationship between humans and bacteria, and the competition for metal ions that plays a fundamental role in the aggression of pathogens and the defence strategies against them. This is naturally followed by a presentation of the periodic system in biology. The abundance of the various elements in an organism is clearly not the key for rationalizing their occurrence; metals with no known functions do occur (Rb, Ti, Sr), sometimes in higher quantities than some essential metals (Co, Mo), which are even less abundant than some toxic metals (Pb). Elements that have no established functions in humans (Ni, V) or are even undoubtedly toxic (Cd) are essential in some other organisms.



Chapter 4 (20 pages) deals with *Essential elements* and starts with a discussion about the various estimated requirements and safe intakes. Deficiencies and excesses are considered not only in their direct effects but also for the influence they indirectly exert on the functions that primarily depend on other metals, like the role of zinc and copper in iron metabolism. A distinction is then introduced between *essential* and *beneficial*, depending on whether its function is related or not to survival of the organism. The complexity of the picture becomes clear when considering indirect essentiality, *i.e.* when an element is essential for an organism which is beneficial for its host [the analogy with the case of dietary fibre, essential for gut bacteria so beneficial for human health (Puddu *et al.*, 2014), comes naturally to one's mind]. Essential elements are then presented according to the group of the periodic table to which they belong.

Chapter 5 (17 pages) discusses *Non-essential elements*, in particular the many metals that are always present in our organism but whose function is (so far) unknown, and can be differentiated from the essential ones by their dose-response curve, showing regions of hormesis and pharmacological effects. Several of these, including toxic metals like Pb and Cd, are present at higher concentrations than essential elements like Mo, Co, I and Se; their bioaccumulation probably comes from a lack of selectivity. The issue of the toxicity of non-essential elements is addressed from a comprehensive perspective, which considers also cumulative risk factors, like deficiency of essential elements which causes oxidative stress (Zn) or increases the uptake of the non-essential ones (Fe versus Cd). A short but informative section about *metals in medicine* follows, which presents the use of non-essential

metals or their compounds as anti-cancer (*e.g.* As<sub>2</sub>O<sub>3</sub>, Pt) or anti-inflammatory (*e.g.* Au compounds) agents. The chapter ends with a survey of the main non-essential metals present in our body.

Chapter 6 (34 pages) discusses *Regulation of metal ions*, *i.e.* systemic and cellular homeostasis. We learn that each metal ion has two specific concentration ranges: one in which it can exist as a 'free' ion, the other in which it can function without interference from other ions ('working range'). How these ranges are controlled at the cellular level, through buffering, selectivity filters, sensors and so on, is the subject of a large part of the chapter. Special attention is paid to Zn and Fe, because of their many fundamental roles. The chapter ends with a section on detoxification.

The *Epilogue and Summary* spans five pages, resumes the main concepts presented in the previous chapters and presents the perspective for future research in the field.

Overall, *Metallomics* is a fascinating small book, easy to read for everybody with a basic knowledge of chemistry and biology, which will undoubtedly stimulate at least some of the readers to explore the field more in depth. Perhaps a short chapter about methodology and experimental techniques could have been included, although it is not absolutely necessary for a primer. The literature provided at the end of each chapter, although not extensive, is a good starting point to pursue the journey.

## References

- Puddu, A., Sanguineti, R., Montecucco, F. & Viviani, L. (2014). *Mediators Inflamm.* 162021.