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Bacterial Transition Metal Homeostasis

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Abstract Since details on metal cation transport proteins and on the allocation mechanisms for transition metals are provided elsewhere in this book, I will present aspects of transition metal homeostasis in a hopefully novel overview. We will start with a microbial look at the transition metal Periodic Table, cation speciation, and availability in the environment. This information provides rules that might govern microbial metal cation homeostasis from the outside of the cell. The fate of metal cations inside the cell is influenced by redox potentials and affinities to ligands in complex compounds. Understanding this topic requires study of interactions between metal cations and the consequences thereof. External availability and internal binding equilibria are connected by transport reactions. These lead to metal cation concentrations in cellular compartments, which are in flow equilibrium of import and export reactions. Thus, cellular cation homeostasis may be described as an interplay of transport flow backbone and competitive binding reactions. Both together provide an energy landscape for each metal cation and cellular compartment. As a recent part of the transport flow backbone in Gram-negative bacteria, efflux across the outer membrane from the periplasm to the outside has been identified. Active outer membrane efflux might indeed be taking place in Gram-negative bacteria. Thus, the periplasm is important in bacterial metal cation homeostasis.

1 Introduction

All living cells need transition metal cations. These elements share the same electronic configuration of their valence electron *s* orbitals but they differ in the occupation of their *d* orbitals. These incompletely filled *d* orbitals allow transition metals to form complex compounds, composed of a central metal cation and (mostly) four or six ligands, which are nonmetals with free electron pairs (Housecroft and Constable 2006). In living cells, these ligands in the first shell around a transition metal cation are mostly nitrogen, oxygen, or sulfur atoms. It is the formation of complex compounds (and reactions catalyzed by them) that makes transition metals so important for life. Without them, biochemistry would be impossible.

Before these cation-requiring biochemical reactions can be performed, the right metal cation has to be inserted into the catalytic site of the correct enzyme, and not the wrong one. How is this accomplished? In this chapter, we provide an overview of the series of partitioning events that result in the desired metal–enzyme complexes.

Three simple have rules seem to decide which element is used by a living cell and which is not (Nies 2004a). An ion must be biologically available to be of any use. Except for hydrogen (and partly for helium), which was there from the Big Bang 13.7 billion years ago, other elements were forged in the furnace of ancient stars and blown into space at the stars' death struggle. The synthesis routes of nuclear fusions in this hellfire and the relative stabilities of the atomic nuclei determine the elemental composition of the stellar dust at a given age of the universe (Schaifers 1984). This dust was used to form our sun 4.6 billion years ago, with some left over quickly creating the planets, including Earth. Red-hot and boiling in its infancy, heavy elements including nickel and iron sank to the middle of Earth while lighter elements formed its crust (Wood et al. 2006). This was the second element-partitioning event. The third one is determined by the solubility of the most stable ionic form of a metal ion in water. The elemental composition of seawater (Weast 1984) might serve as a standardized ecosystem to examine how much of a chemical element is available to a living cell today (Nies 2004a).

Living cells cannot influence the three first sorting events, which result in the elemental composition of seawater and other, more complicated, ecosystems. However, they control the next sorting step, the import into the cytoplasm. Since metal cations do not diffuse across the hydrophobic bilayer of a biological membrane, membrane-bound proteins or membrane-permeable carriers are needed for uptake of a metal ion. Table 1 takes a theoretical bacterial cell, assumes metal supply to this virtual bacterium by simple uptake systems ($\Delta\Psi$-driven uniport of metal cations or charge-neutral proton symport of oxyanions), and compares the amount of accu-