Metal Binding Proteins

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Metal ions play several major roles in proteins: structural, regulatory, and enzymatic. The binding of some metal ions increase stability of proteins or protein domains. Some metal ions can regulate various cell processes being first, second, or third messengers. Some metal ions, especially transition metal ions, take part in catalysis in many enzymes. From ten to twelve metals are vitally important for activity of living organisms: sodium, potassium, magnesium, calcium, manganese, iron, cobalt, zinc, nickel, vanadium, molybdenum, and tungsten. This short review is devoted to structural, physical, chemical, and physiological properties of proteins, which specifically bind these metal cations.

Keywords: metal binding protein ; metal binding site ; structure ; function

Metal ions play an extremely important role in functioning of all, without any exceptions, biological systems. Intracellular and extracellular fluids contain high concentrations of metal ions. Many biological events critically depend on metal ions. Metal ions interact with all charged and polar groups of biopolymers contacting with biological liquids, but their specific strong interactions with proteins play the most important role. More than a quarter of all the proteins contained in Protein Data Bank, possess bound metal ions. Most of all, these proteins contain bound zinc ions, followed by iron, calcium, and magnesium. In the modern literature, one can find quite a few reviews devoted to metal binding proteins (see, for example, [1][2][3]). This review aims to provide a general understanding of the structural, physicochemical, and functional properties of metal binding proteins.

Metal ions play three fundamental roles in proteins: structural, regulatory, and enzymatic. The binding of some metal ions stabilize proteins or protein domains. Some metal ions can take part in regulation of various cell processes being first, second, or third messengers. Some metal ions, especially transition metal ions, take part in catalysis in many enzymes. Between ten and twelve metals are vital for living organisms: sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), manganese (Mn), iron (Fe), cobalt (Co), zinc (Zn), nickel (Ni), vanadium (V), molybdenum (Mb), and tungsten (W). Sometimes these metals are called “life metals”. Below (**Table 1**) is a fragment of Mendelleev periodic table of elements, which shows positions of “life metals”.

Table 1. A fragment of Mendelleev periodic table of elements.

Periods	1	2	3	4	5	6	7	8	9	10	11	12
III	Na	Mg										
IV	K	Ca					Mn	Fe	Co	Ni	Cu	Zn
V						Mo						
VI						W						

Most of the biologically significant metals are located in the fourth period of the periodic table, except sodium and magnesium, which are in the third period, and molybdenum and tungsten, which are in the fifth and sixth periods, respectively. The biologically significant metals are divided into two groups: nontransition elements (Na, K, Mg, Ca, Zn) and transition elements (Mn, Fe, Co, Cu, Mo, W). Nontransition elements have constant oxidation state (valency) and their ions have completely filled electron shells. In contrast, transition elements have variable oxidation state (valency) and their ions have incompletely filled electron shells. Incompletely filled electron shells are reflected in special physical and chemical properties (absorption bands in ultraviolet and visible spectral regions, paramagnetism, and so on). Sometimes such properties facilitate their studies. Zinc is not a transition element since it has completely filled d-orbitals, at the same time Zn properties are very different from the properties of the rest of the nontransition metal ions. Below (**Table 2**) is a table of ionic radii of biologically significant metals in various oxidation states.

Table 2. Ionic radii of biologically significant metals.

Metal	Ion	Ionic Radius, Å
Na	Na^{+}	0.95
K	K^{+}	1.33
Mg	Mg^{2+}	0.66
Ca	Ca^{2+}	0.99
Mn	Mn^{2+}	0.80
	Mn^{3+}	0.66
	Mn^{4+}	0.52
Fe	Fe^{2+}	0.76
	Fe^{3+}	0.63
Co	Co^{2+}	0.76
	Co^{3+}	0.63
Ni	Ni^{2+}	0.83
	Ni^{3+}	0.74
Cu	Cu^{+}	0.91
	Cu^{2+}	0.69
Zn	Zn^{2+}	0.74
Mo	Mo^{+3}	0.83
	Mo^{+4}	0.79
	Mo^{+6}	0.73
W	W^{+4}	0.80
	W^{+5}	0.76
	W^{+6}	0.74

Na and K possess one s-electron on the outer shell besides the electron structure of rare gas atoms ([Ne] $3s^1$ and [Ar] $4s^1$, respectively). For this reason, they possess low ionization potentials and rather large size of their ions (0.95 and 1.33 Å, respectively). Mg and Ca are characterized by completely filled electron shells ($2s^2$ $2p^6$ and $3s^2$ $3p^6$); therefore, they have no preferences in respect to the direction of bonds formation. Their ionic radii are 0.65 and 0.99 Å, respectively.

Dipole water molecules, which surround metal ions in water solution, are oriented by the electric field of the ions (charge-dipole interaction). At least three layers of water molecules are influenced by the central ion. Geometry of the first hydration shell of calcium and monovalent metal cations can have various geometry. Some ions possess rather rigid and stable first hydration shell, which can have tetrahedral or octahedral (Mg^{2+}, Co^{2+}, Ni^{2+}) geometry. Zn^{2+} ion can have both tetrahedral and octahedral geometry of the first hydration shell.

References

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