

Chapter 14: Learning Objectives

- * One of the uses of metal cofactors in proteins is to maintain structural features that contribute to function. These are often Zn^{2+} ions, because Zn^{2+} binds tightly in a range of geometries, and is not redox-active.
- * The most common motif is the “zinc finger,” two antiparallel β -strands with Cys residues followed by an α -helix with two His residues. The resultant tetrahedral Cys_2His_2 coordination holds this section of protein in a “finger” shape that fits in the major groove of DNA for recognition.
- * Related zinc-binding domains also contain one or two Zn^{2+} ions.
- * In some cases, metal ion binding induces the metal-bound protein to assume a significantly different structure than the apo-protein. Proteins of this type are useful for signaling the presence of that metal ion.
- * Signaling proteins are also hugely important in neurochemistry, the study of how chemical signals are transmitted in the nervous system and brain.
- * An important class of signaling proteins use Ca^{2+} . The most common Ca-regulatory motif is the “EF-hand,” which undergoes a huge conformational change upon binding Ca^{2+} . This conformational change exposes a hydrophobic patch through which the protein (*e.g.* calmodulin) binds to another protein.
- * Metalloregulatory proteins are involved in positive and negative feedback systems that (1) prevent organisms from expressing (“down-regulate”) genes that encode proteins that cannot be used for lack of metal, (2) encourage synthesis of (“up-regulate”) genes that encode proteins that utilize that metal, or which regulate its concentration within acceptable levels (“homeostasis”).
- * Scientists have discovered transcription factors that are linked to many metals’ concentrations. These bind to the DNA or RNA in a way that inhibits transcription or translation of the given gene.
- * There is great current interest in the function and dysfunction of prion proteins, which form insoluble aggregates (“plaques”) in the brains of affected individuals. Prion diseases include Alzheimer’s, Creutzfeldt-Jacob disease, and BSE (“mad-cow disease”). Some recent research links Cu^{2+} and Zn^{2+} to the formation of plaques.
- * Nitric oxide (NO) is another important inorganic signaling molecule. It is synthesized from oxidation of arginine, and is used especially to control smooth muscle relaxation.