Metalloproteins with one labile coordination site around the metal centre are known as metalloenzyme. As with all enzymes, the shape of the active site is crucial. The metal ion is usually located in a pocket whose shape fits the substrate. The metal ion catalyzes reactions which are hard to achieve in organic chemistry.

**Carbonic anhydrase**

In all living organisms, Carbon dioxide (CO$_2$) is a key metabolite. It exists in equilibrium with bicarbonate (HCO$_3^-$) poorly soluble in lipid membranes compared to carbon dioxide. Carbon dioxide can easily move in and out of the cell whereas bicarbonate could not. Thus in vivo a critical balance between conversion of bicarbonate to carbon dioxide and the reverse is required. The interconversion process of carbon dioxide and bicarbonate proceeds quite slowly at physiological pH which is catalyzed in presence of enzyme, Carbonic anhydrases. These are zinc-containing enzymes found in almost all living organisms; catalyse the reversible reaction between carbon dioxide hydration and bicarbonate dehydration. They play critical roles in assisting the transportation of carbon dioxide and protons in the intracellular space, across the biological membranes and also in the layers of the extracellular space. They take part in other processes, such as from respiration and photosynthesis in eukaryotes to cyanate degradation in the prokaryotes.
The active site of carbonic anhydrases consists of a zinc ion, which is coordinated via three imidazole nitrogen atoms from three histidine units and coordination sphere is approximately tetrahedral in nature. Fourth coordination site is engaged with a water molecule. The coordinated water molecule gets polarized by the positively charged zinc ion and thus nucleophilic attack by the negatively charged hydroxide portion on carbon dioxide (carbonic anhydride) takes place very fast. Bicarbonate ion and hydrogen ions are produced in the catalytic cycle which remains in equilibrium.

\[ \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+ \]

**Vitamin B\textsubscript{12}-dependent enzymes**

Vitamin B\textsubscript{12} is known to catalyze transfer of methyl (-CH\textsubscript{3}) groups between two molecules a process which is energetically expensive in organic reactions and it involves the breaking of C-C bonds. The activation energy required for the process is lowered due to presence of metal ion which forms a transient Co-CH\textsubscript{3} bond. The coenzyme consists of a cobalt(II) ion coordinated via four nitrogen atoms of a corrin rings and a fifth Nitrogen atom from an imidazole group. In the latent state, formation of a Co—C σ bond occurs with the 5′ carbon atom of adenosine. This helps in understanding of its function in trans-methylation reactions as a naturally occurring organometallic compound such as the reaction carried out by methionine synthase.

**Nitrogenase (nitrogen fixation)**

The fixation of atmospheric nitrogen involves breaking very stable triple bond between the nitrogen atoms and thus requires intensive energy. This process is catalyzed by an enzyme known as nitrogenase, found in certain bacteria. There are three factors which enable it perform the necessary action and these are as follows: presence of a molybdenum atom at the active site, Iron-sulfur clusters engaged in transporting the electrons which are required to reduce the
nitrogen along with a rich energy source. The nitrogen fixation can be written in the following manner

\[
\text{N}_2 + 16 \text{MgATP} + 8e^- \rightarrow 2\text{NH}_3 + 16 \text{MgADP} + 16 \text{Pi} + \text{H}_2
\]

where Pi represents the inorganic phosphate. The active site contains a MoFe\text{7S8} cluster which binds the dinitrogen molecule and allows the reduction process to start. The electron transportation occurs via associated "P" cluster which comprised of two cubical Fe\text{4S4} clusters joined by sulfur bridges.

*In vivo* generation of the superoxide ion O$_2^{-}$ occurs due to reduction of molecular oxygen. It behaves as a free radical due to presence of an unpaired electron and thus becomes a powerful oxidizing agent. These properties altogether enables the superoxide ion (very toxic) advantageous for the phagocytes to kill the harmful micro organisms. Else the superoxide ion must be damaged before it does unwanted cell damage. This function is delicately maintained by the superoxide dismutase enzymes.
At neutral pH, in solution the superoxide ion disproportionate to molecular oxygen and hydrogen peroxide which is basically a dismutation reaction.

$$2O_2^- + 2H^+ \rightarrow O_2 + H_2O_2$$

Both oxidation and reduction of superoxide ions are involved in a dismutation reaction. The superoxide dismutase group of enzymes is commonly known as SOD. A metal ion exhibiting varying oxidation state either act as an oxidizing agent or as a reducing agent is involved which is the central reason responsible for the action of these enzymes.

Oxidation: \(M^{(n+1)+} + O_2^- \rightarrow Mn^+ + O_2\)

Reduction: \(Mn^+ + O_2^- + 2H^+ \rightarrow M^{(n+1)+} + H_2O_2.\)

An example of this category is where the active metal is copper exists as \(Cu^{2+}\) or \(Cu^+\) which is tetrahedrally coordinated by four histidine residues. Zinc ions in Human SOD are responsible for stabilization. Different other ions such as iron, manganese or nickel are found to be present in other isozymes. Another example which involves an unusual oxidation state of nickel that is nickel(III) is Ni-SOD. Ni geometry at the active site involves square planar Ni(II), thiolate (Cys2 and Cys6) and backbone nitrogen (His1 and Cys2) ligands and also square pyramidal Ni(III) with an added axial His1 side chain ligand.

**Chlorophyll-containing proteins**

Chlorophyll exhibits a central role during photosynthesis. Chlorin ring absorbs photon due to its well defined electronic structure. It contains magnesium which is not directly involved in the photosynthetic function but can be replaced by other divalent ions with a slight reduction in activity.

In this process absorption of photon causes an electron to be excited into a singlet state which further undergoes an intersystem crossing from singlet state to triplet state. Thus it becomes a free radical (very reactive) and results an electron transfer to the acceptors which are adjacent to the chlorophyll in the chloroplast. In this phosynthetic cycle chlorophyll is oxidized and re-
reduced. Finally molecular oxygen evolves as a final oxidation product as this process involves electrons withdrawal from water.

Signal-transduction metalloproteins

Calmodulin

Calmodulin is an example of a signal-transduction protein. It contains four EF-hand (helix-loop-helix structural domain) motifs, which can binds Ca\(^{2+}\) ions. The ligating environment around calcium ion is adopts a pentagonal bipyramidal geometry. Calmodulin consist of two symmetrical globular domains (the N- and C-domain), separated by a by a flexible "hinge" region. The calcium ion acts as a diffusible second messenger to the initial stimuli and contributes in an intracellular signalling system.

Transcription factors

The transcription factors are known to binds with DNA and are thus plays an important role in gene regulation. Zinc finger protein is known to be integral part of many transcription factors. Zinc finger is model where zinc ion at the centre of the protein surrounded by specific residues. Zinc finger proteins are known to binds with DNA but zinc ion does not directly participate in the process rather it is essential for the folding pattern of the protein. The ligating environment around the Zn\(^{2+}\) ion in these proteins usually have cysteine and histidine side chains.