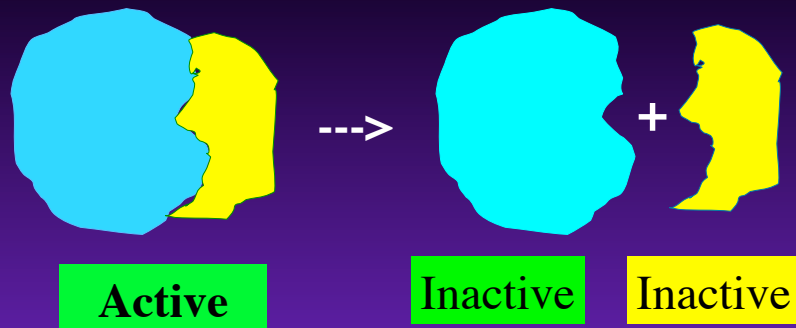


Cofactors

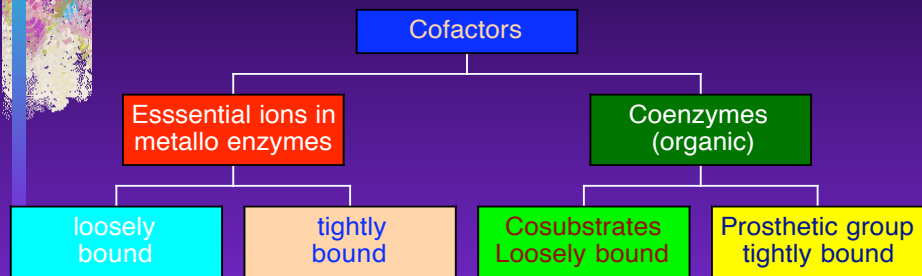
Manickam Sugumaran
Department of Biology
University of Massachusetts
Boston, MA 02125

Holoenzyme can be dissociated into inactive apoenzyme and cofactor.

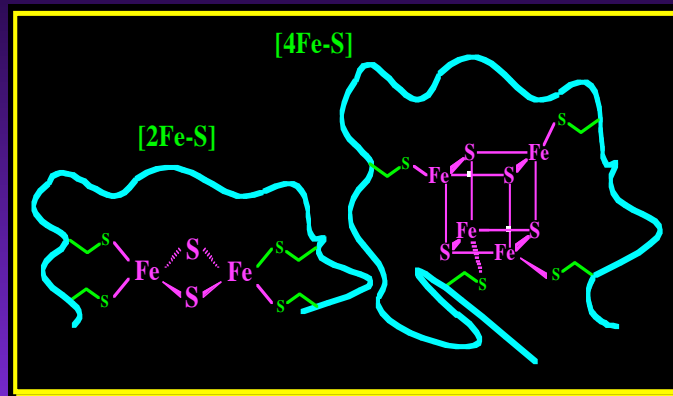
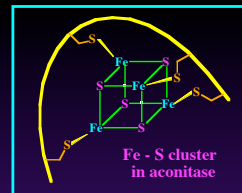


HOLOENZYME \dashrightarrow APOENZYME + COFACTOR

Cofactors are derived from vitamins and other small molecules. Some times they are simply inorganic ions.



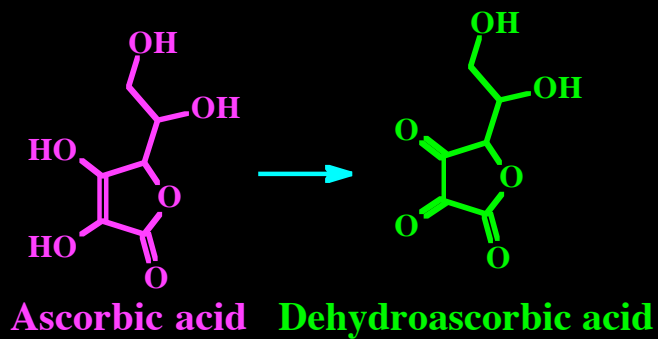
Iron - sulfur cluster found in some proteins



Vitamins and coenzymes

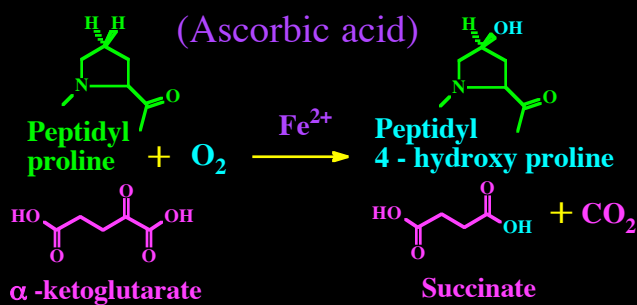
- **Vitamins are usually converted into coenzymes by simple biochemical reactions.**
- **One exception - Vitamin C is both the vitamin form and the coenzyme form.**

Vitamin C - Ascorbic acid

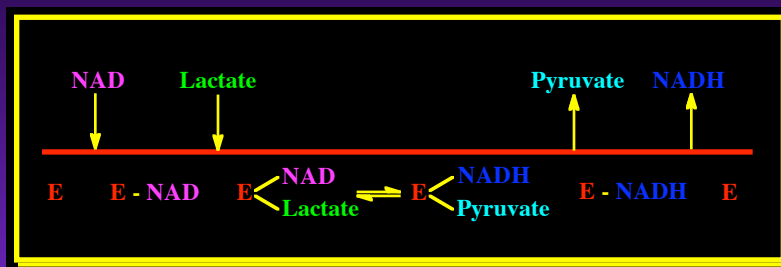


Ascorbic acid is required for collagen proline hydroxylase reaction

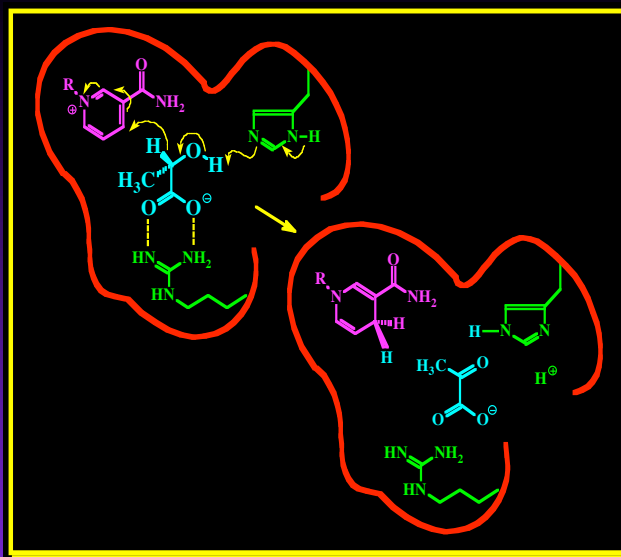
Collagen Proline Hydroxylase reaction



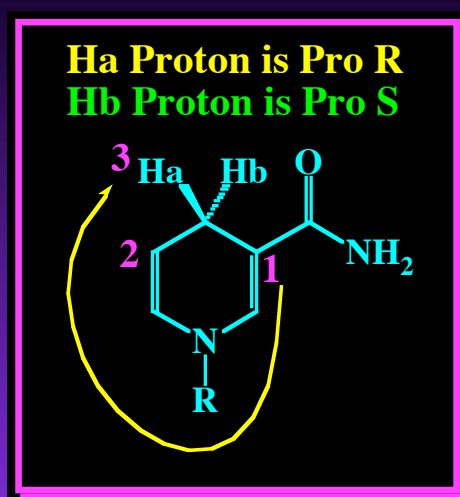
Lactate dehydrogenase follows sequential Bi Bi Mechanism



Lactate Dehydrogenase reaction



Pro R and Pro S hydrogen and A and B side of NAD.



Stereospecificity of NAD



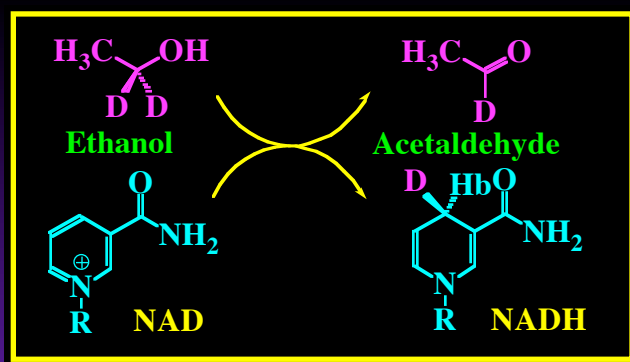
When labeled ethanol was used with NAD, one atom of deuterium was transferred to NAD and one atom was retained in acetaldehyde. None was lost to the solvent.



When labeled resultant NAD(D) was used to reduce acetaldehyde, all the deuterium was transferred from NAD(D) quantitatively to the ethanol that was formed. None was lost to solvent again.

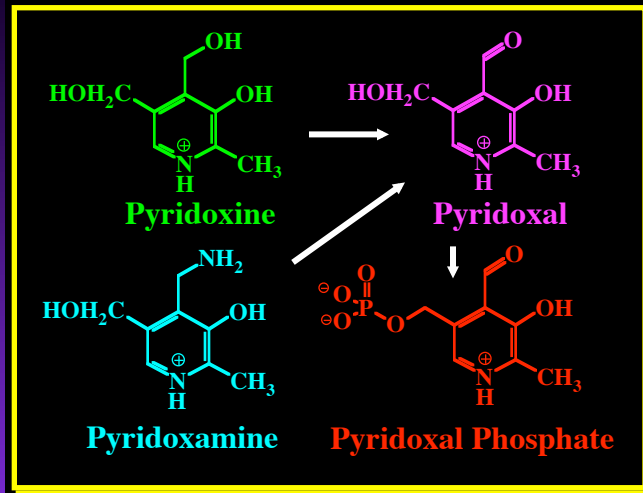
Thus NAD stereospecifically transfers hydrogen atom to its substrates

Stereospecificity of Alcohol dehydrogenase reaction - (A side specific dehydrogenase)

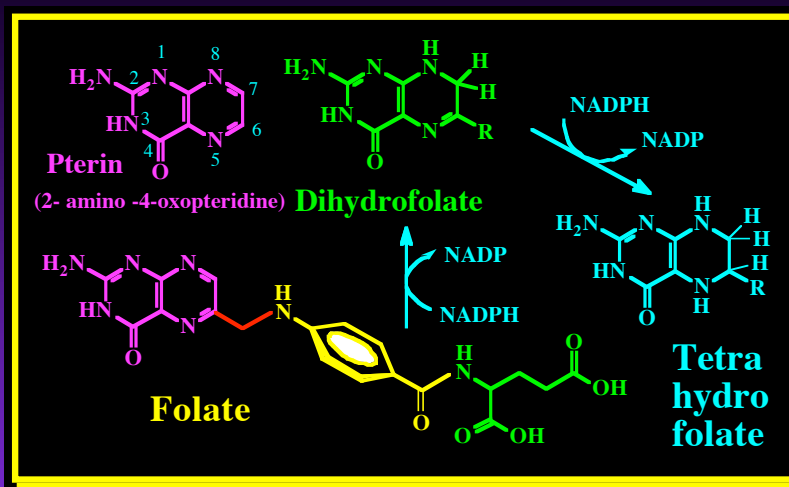


One atom of D is specifically transferred to Pro R position (A side) of NAD by the enzyme. In the reverse direction, the Pro R hydrogen from NADH is specifically transferred to acetaldehyde to generate stereospecifically labeled ethanol.

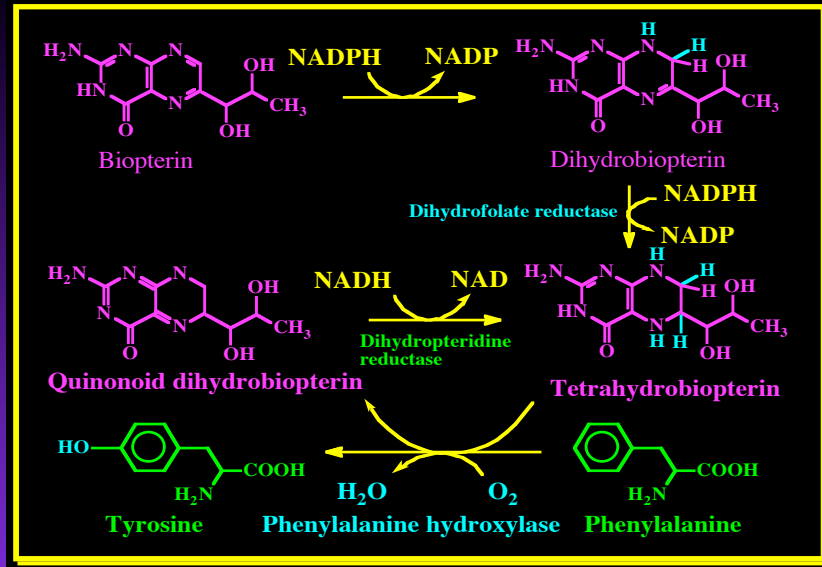
Pyridoxine is converted to pyridoxal phosphate, the coenzyme form of this vitamin.



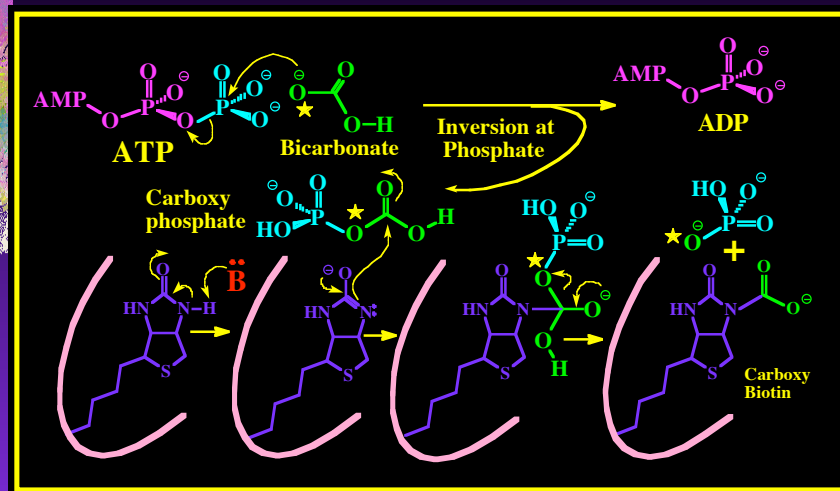
Folate coenzymes



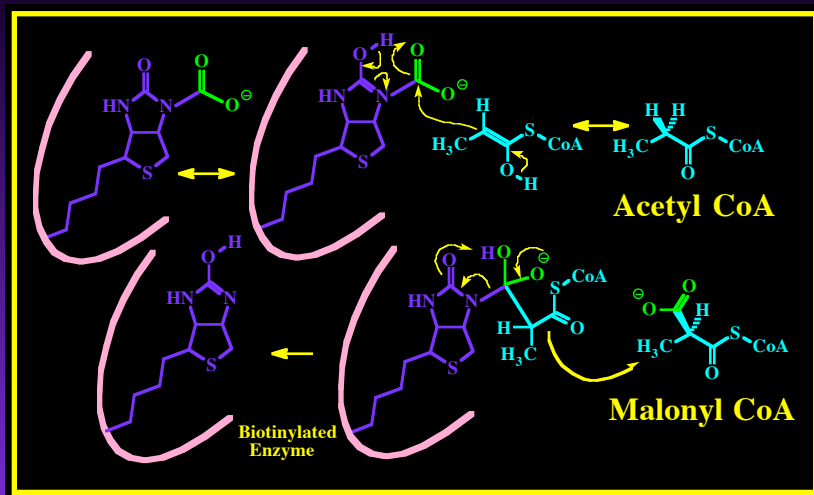
Biopterin and amino acid hydroxylases



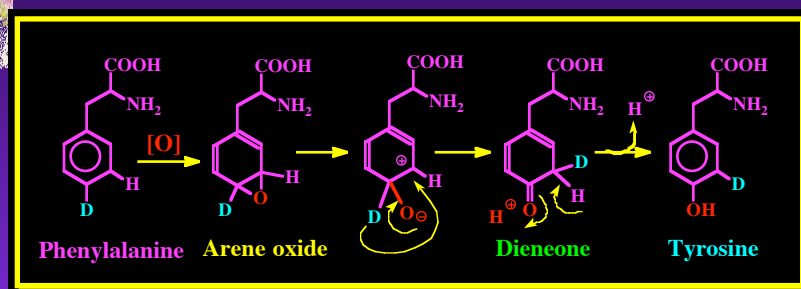
Biotin - carboxylation reaction



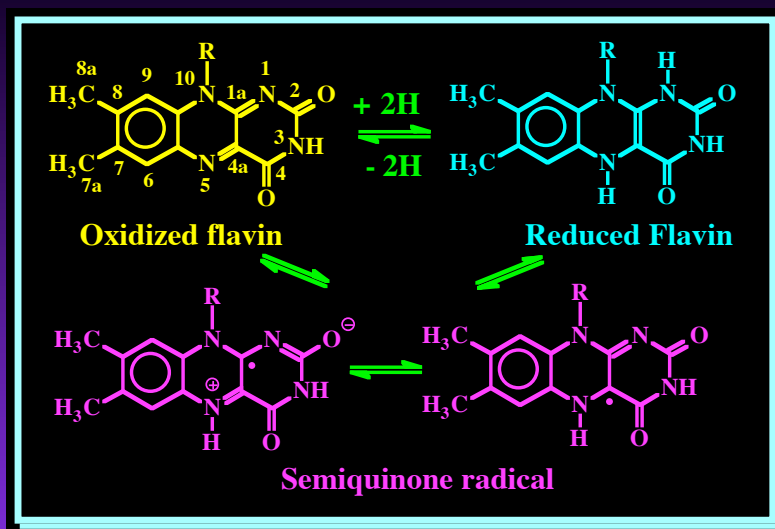
Biotin - carboxylation reaction



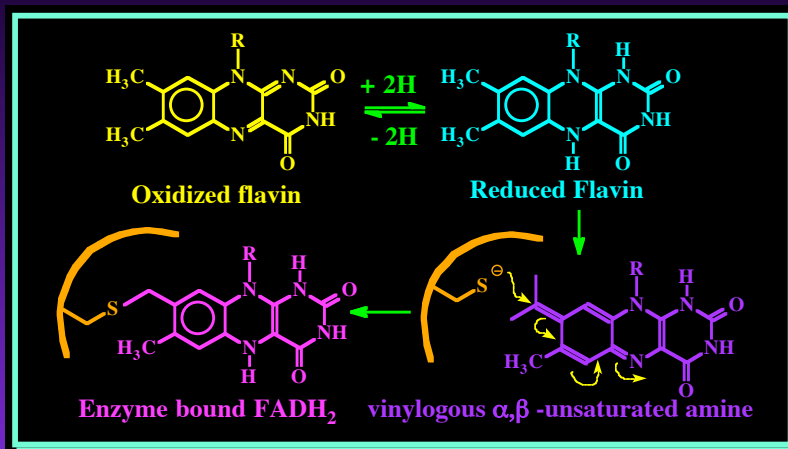
NIH shift



Different states of flavins

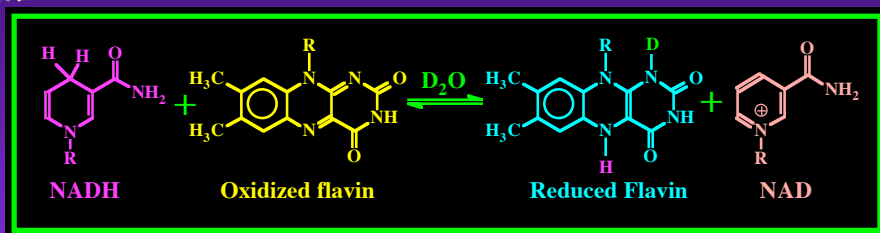


Covalent attachment of FAD to some enzymes

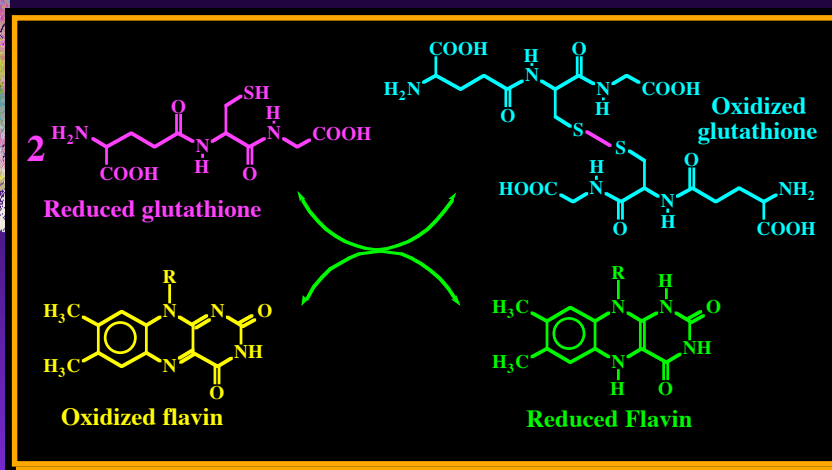


FAD - two electron reduction

From model compounds, the following generalized reduction scheme has been derived for FADH₂ formation. The hydride is transferred to the N-5 and a proton from water is incorporated into N-1 during the reduction of FAD by NADH in water.



Glutathione reduction/oxidation



Mechanism of thiol - disulfide exchange catalyzed by Flavin

