Chapter 8-II:

Amino Acid Metabolism

Amino acid biosynthesis

Essential amino acids

Nonessential amino acids

Table 20-3 Essential and Nonessential Amino Acids in Humans

Essential	Nonessential
Arginine[a]	Alanine
Histidine	Asparagine
Isoleucine	Aspartate
Leucine	Cysteine
Lysine	Glutamate
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Proline
Tryptophan	Serine
Valine	Tyrosine

[a]Although mammals synthesize arginine, they cleave most of it to form urea (Section 20-3A).

Table 20-3 Fundamentals of Biochemistry, 2/e

The synthesis of ANDEQ

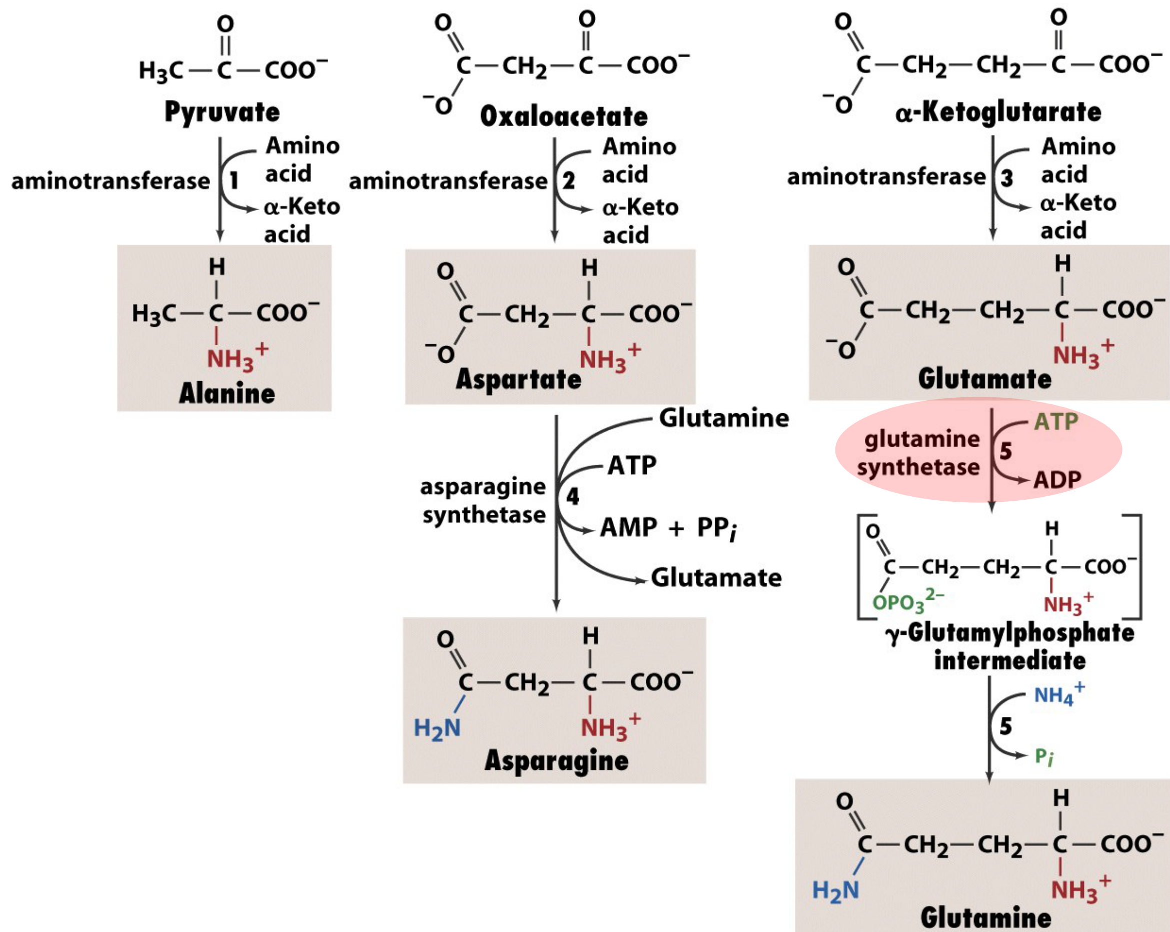


Figure 20-27 Fundamentals of Biochemistry, 2/e

Glutamine synthetase: vital for regulating nitrogen metabolism

Glutamine: amino group donor & storage form of ammonia

Activated by α-ketoglutarate in mammalian enzyme: prevent accumulation of ammonia

Bacterial glutamine synthetase: more elaborate control

- 9 allosteric feedback inhibitors, each with its own binding site
  - His, Trp, carbamoyl phosphate, glucosamine 6-P, AMP, CTP (end product from glutamine)
  - Ala, Ser, Gly
- Covalent modification by adenylylation

Glutamine synthetase from *Salmonella typhimurium*

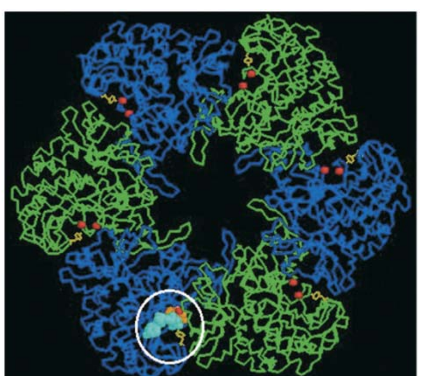


Figure 20-28a Fundamentals of Biochemistry, 2/e

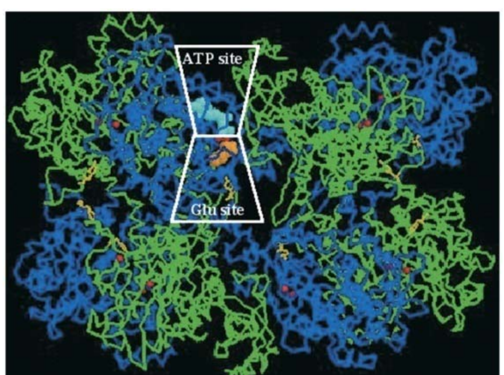


Figure 20-28b Fundamentals of Biochemistry, 2/e

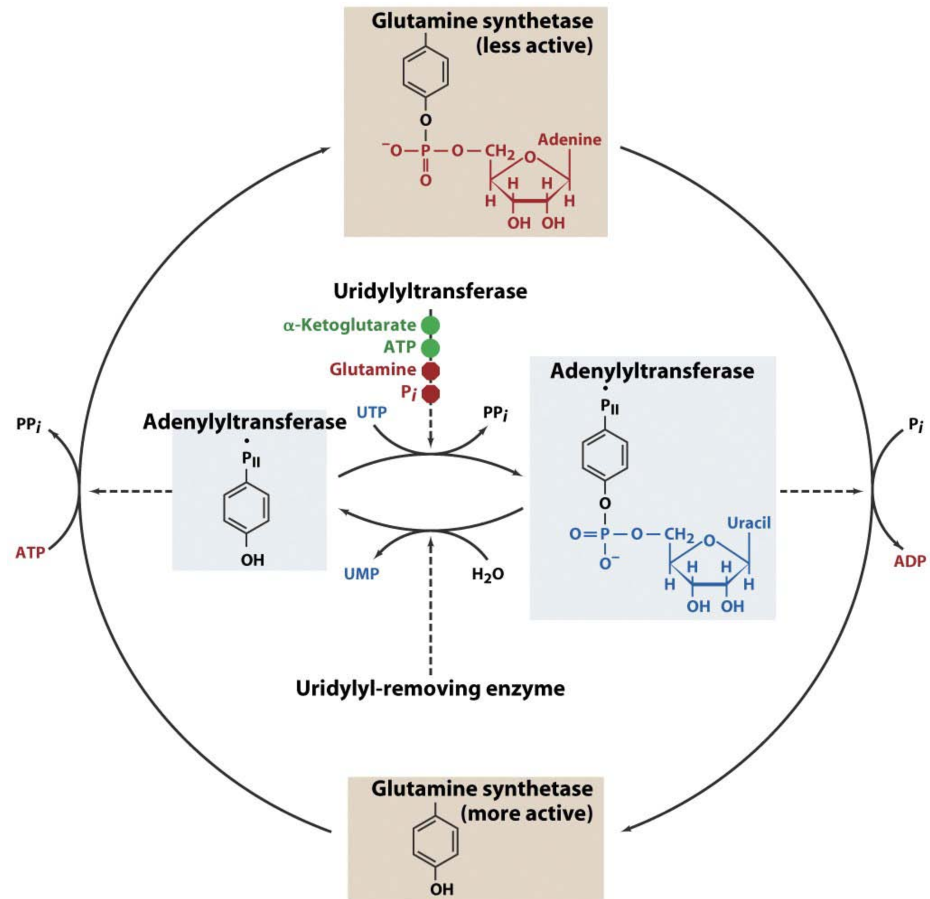
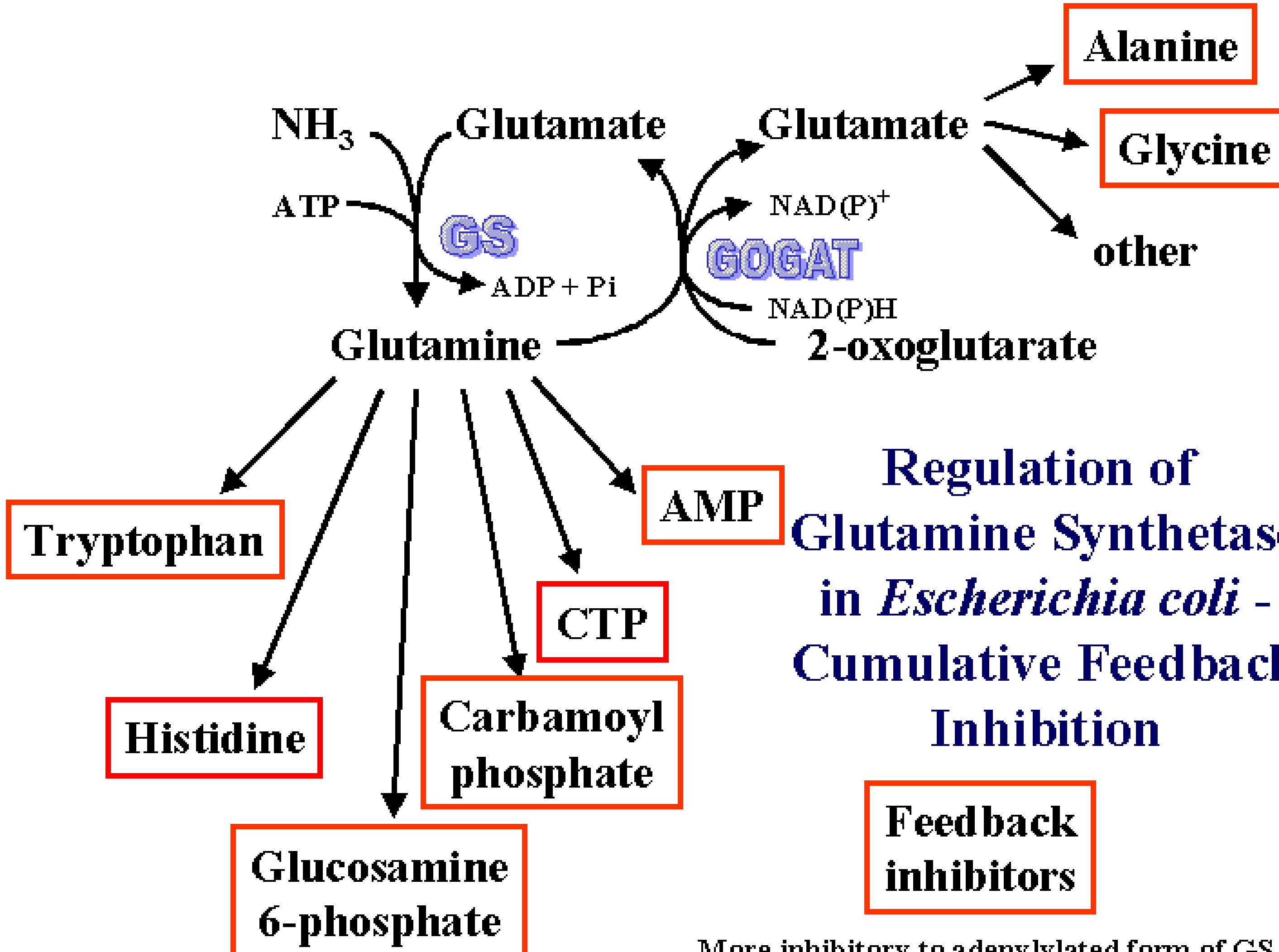


Figure 20-29 Fundamentals of Biochemistry, 2/e

Regulation of Glutamine Synthetase in *Escherichia coli* - Cumulative Feedback Inhibition



Feedback inhibitors

More inhibitory to adenylylated form of GS

The biosynthesis of the glutamate family of amino acids

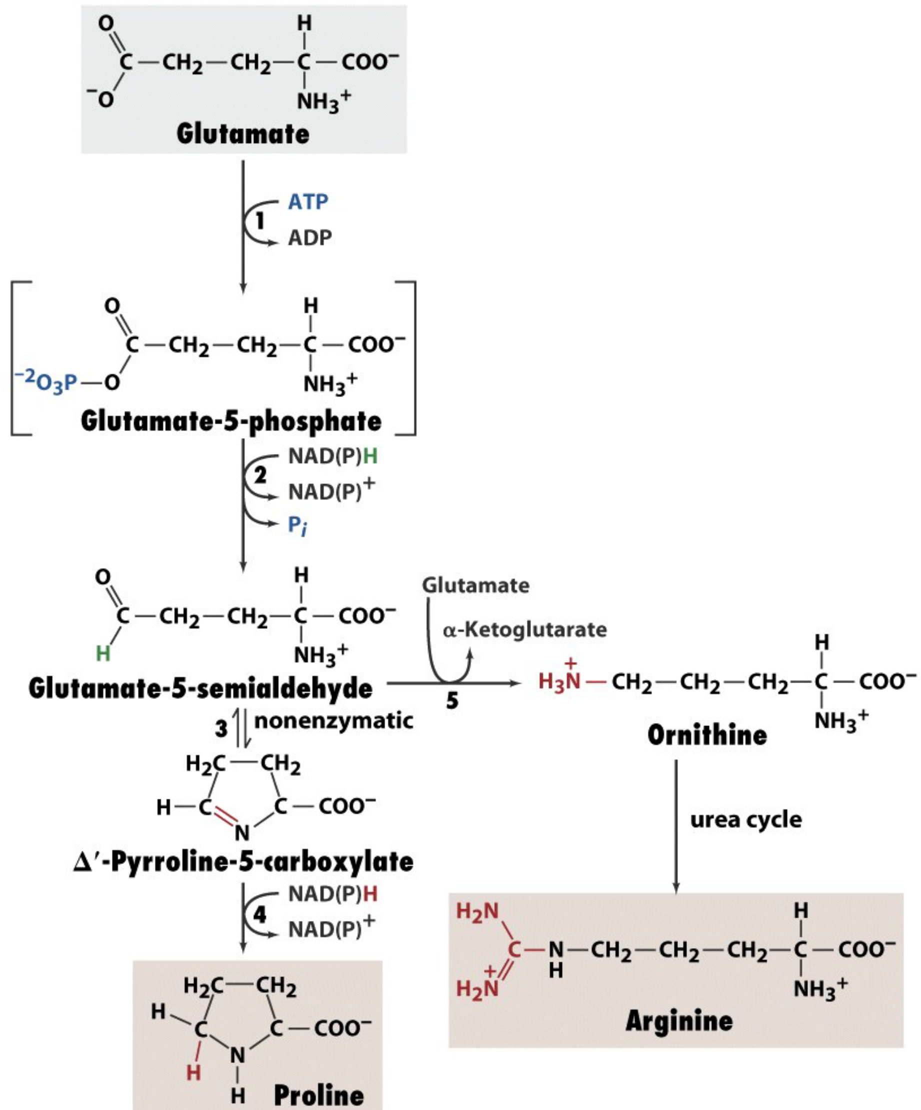


Figure 20-30 Fundamentals of Biochemistry, 2/e

The conversion of 3-phosphoglycerate to serine

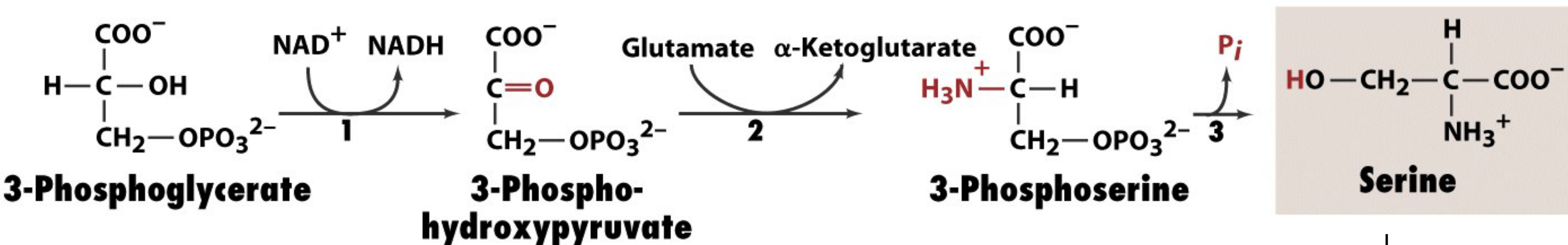


Figure 20-31 Fundamentals of Biochemistry, 2/e

homocysteine →

Cystathionine

↓

Cysteine
α-ketobutyrate

Aspartate family
KMT

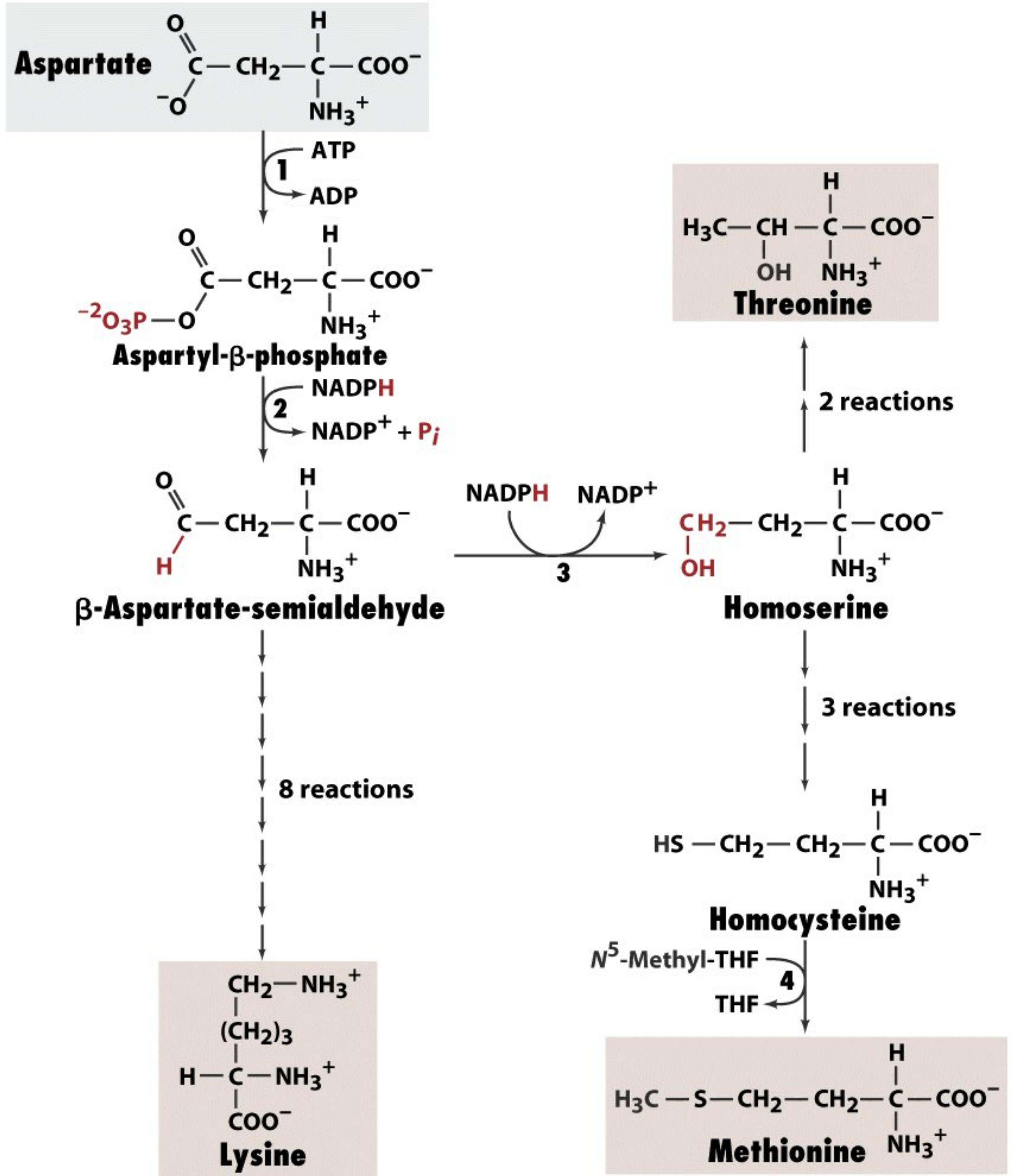


Figure 20-32 Fundamentals of Biochemistry, 2/e

Pyruvate family: ILV

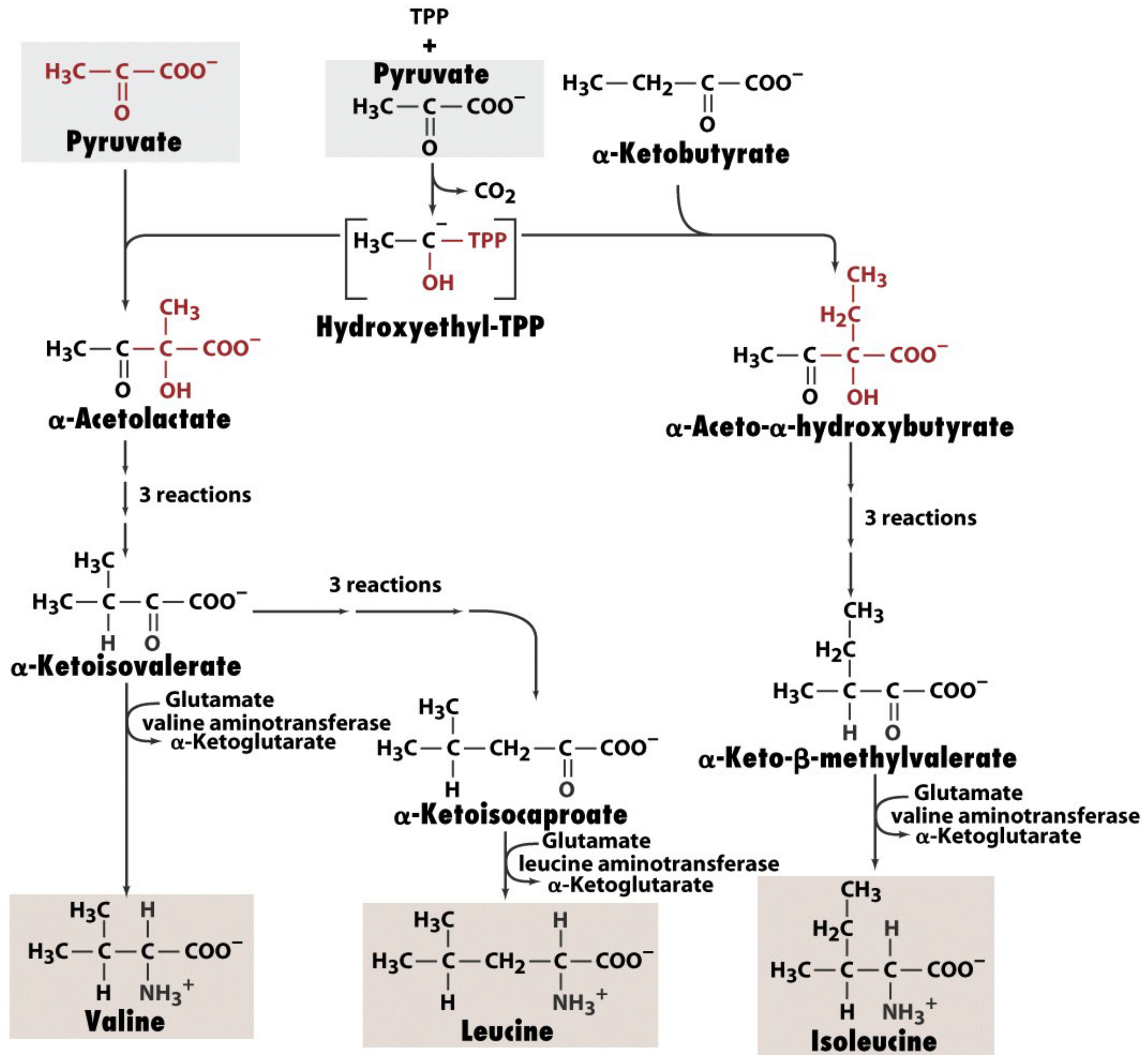


Figure 20-33 Fundamentals of Biochemistry, 2/e

The biosynthesis of FWY

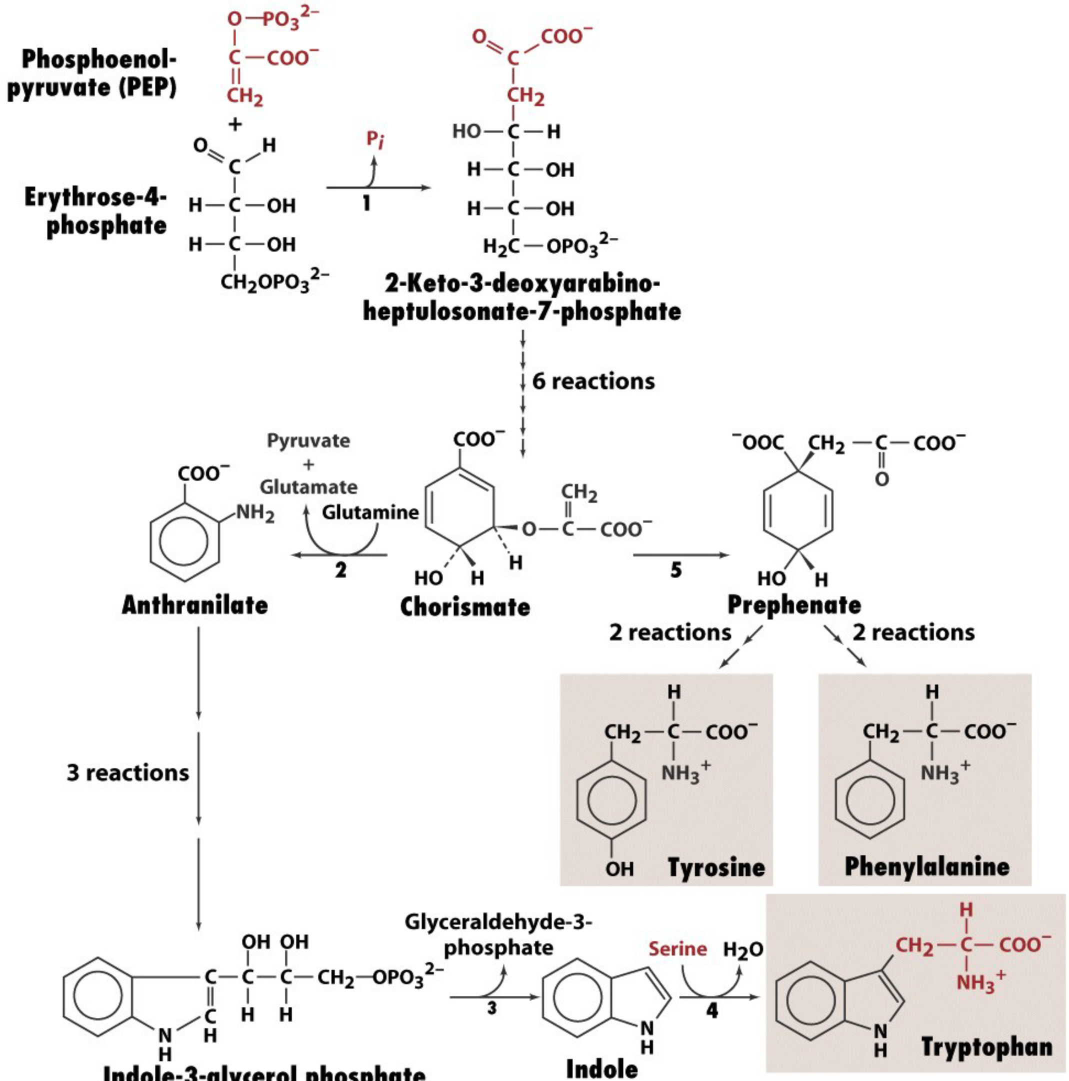


Figure 20-34 Fundamentals of Biochemistry, 2/e

Tryptophan synthase from S. typhimurium

$\alpha 2\beta 2$ bifunctional enzyme
Indole-3-glycerol phosphate to indole and glyceraldehyde-3-P
Indole plus serine to form Trp
Indole is channeled between the two subunits

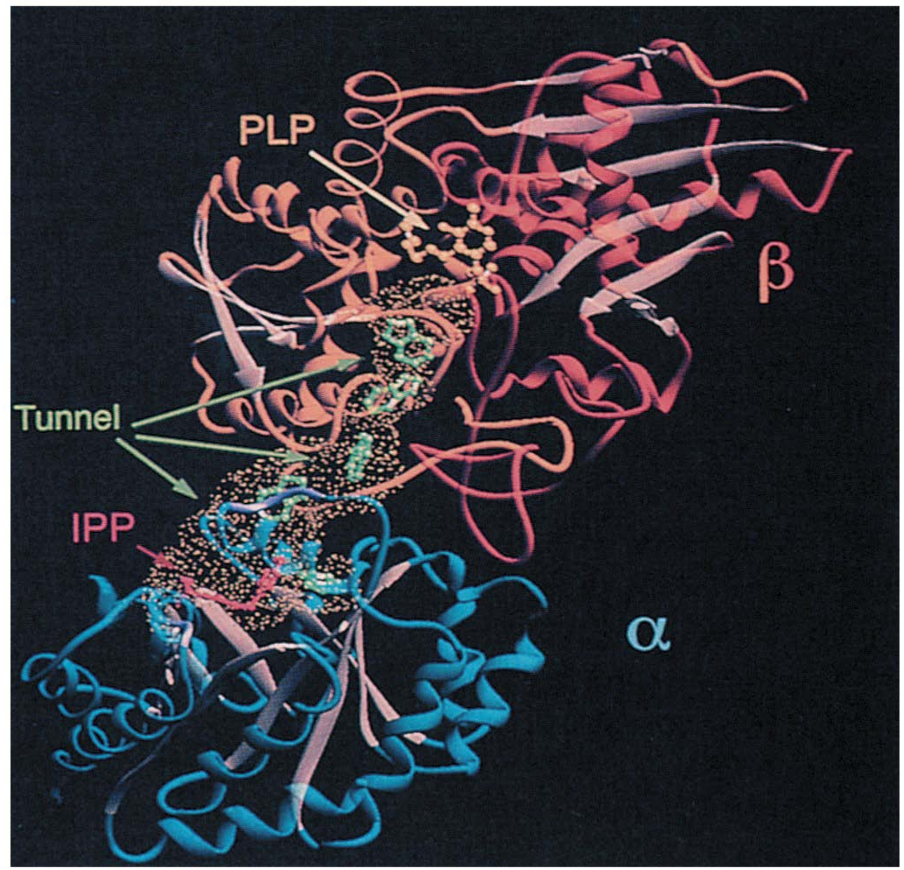


Figure 20-35 Fundamentals of Biochemistry, 2/e

Histidine biosynthesis

Start from PRPP (5-phosphoribosyl-α-pyrophosphate)
His involves in catalysis as nucleophile and/or general acid-base catalysis
His originate from a purine (5’-phosphoribosyl ATP): support RNA world hypothesis

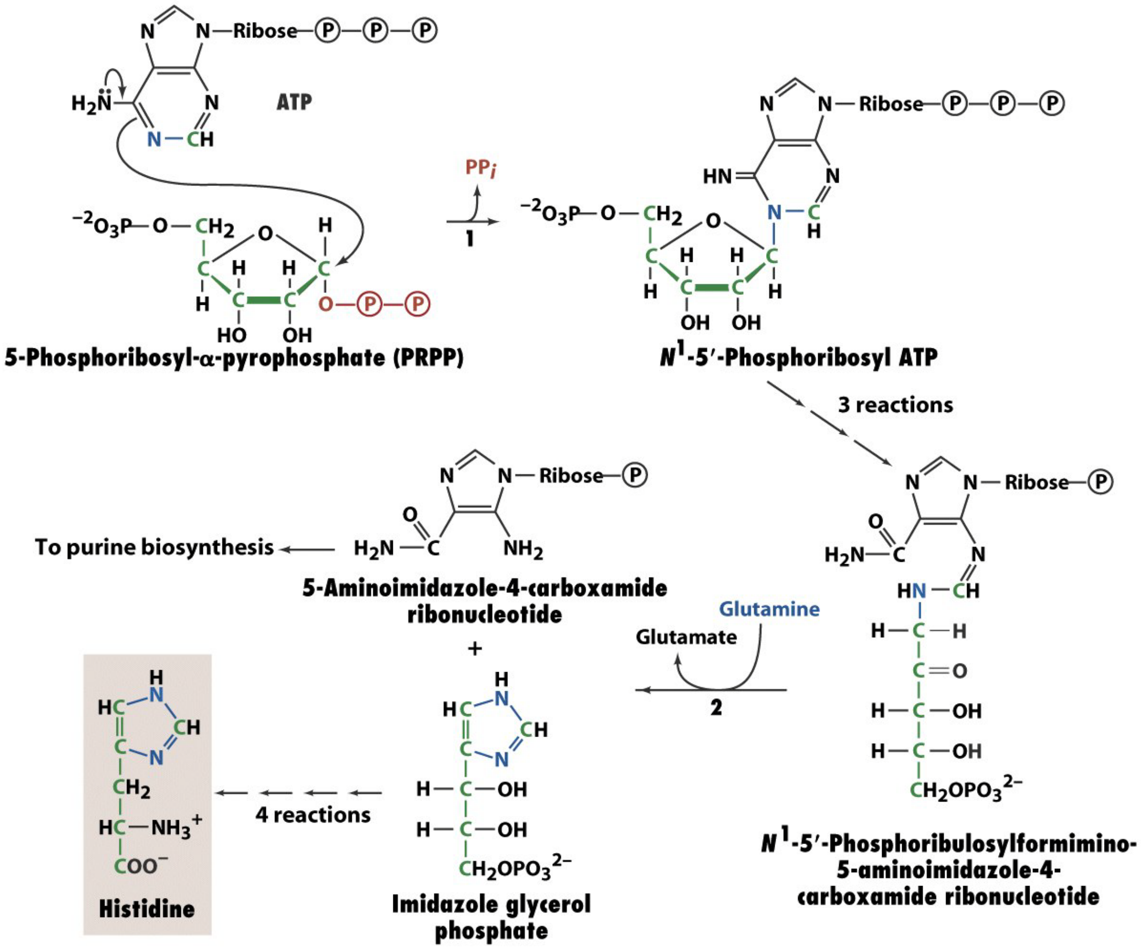


Figure 20-36 Fundamentals of Biochemistry, 2/e

Heme biosynthesis and degradation

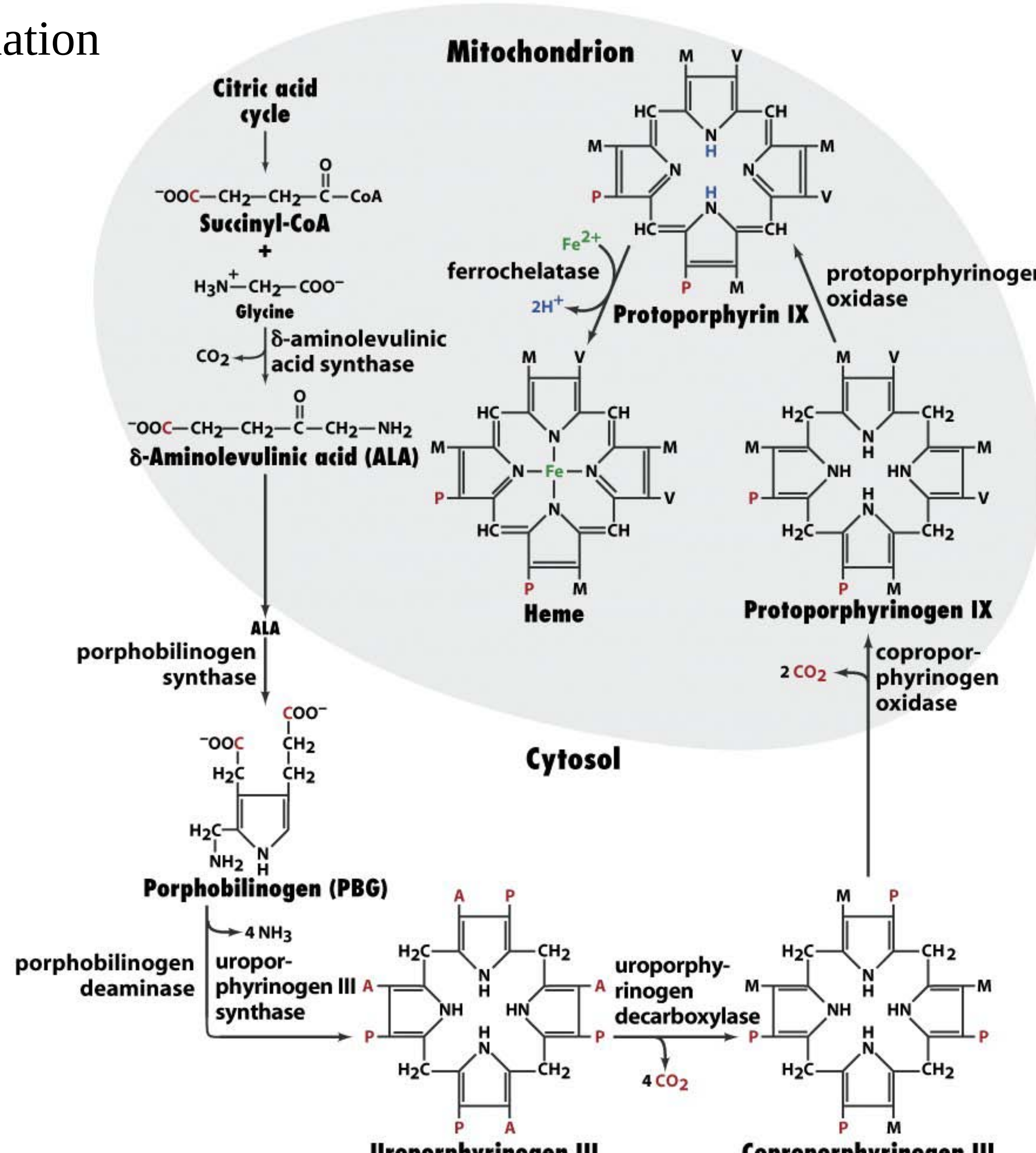
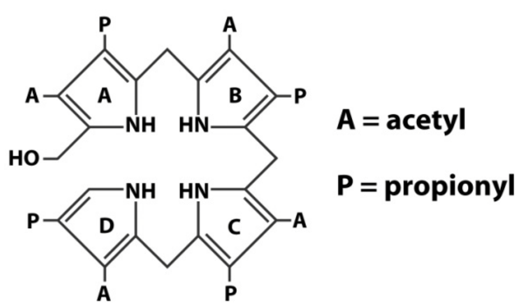


Figure 20-37 Fundamentals of Biochemistry, 2/e



Hydroxymethylbilane

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Heme degradation

Jaundice: excess amount of bilirubin (insoluble)
signals RBC destruction, liver dysfunction,
and bile duct obstruction

green

red orange

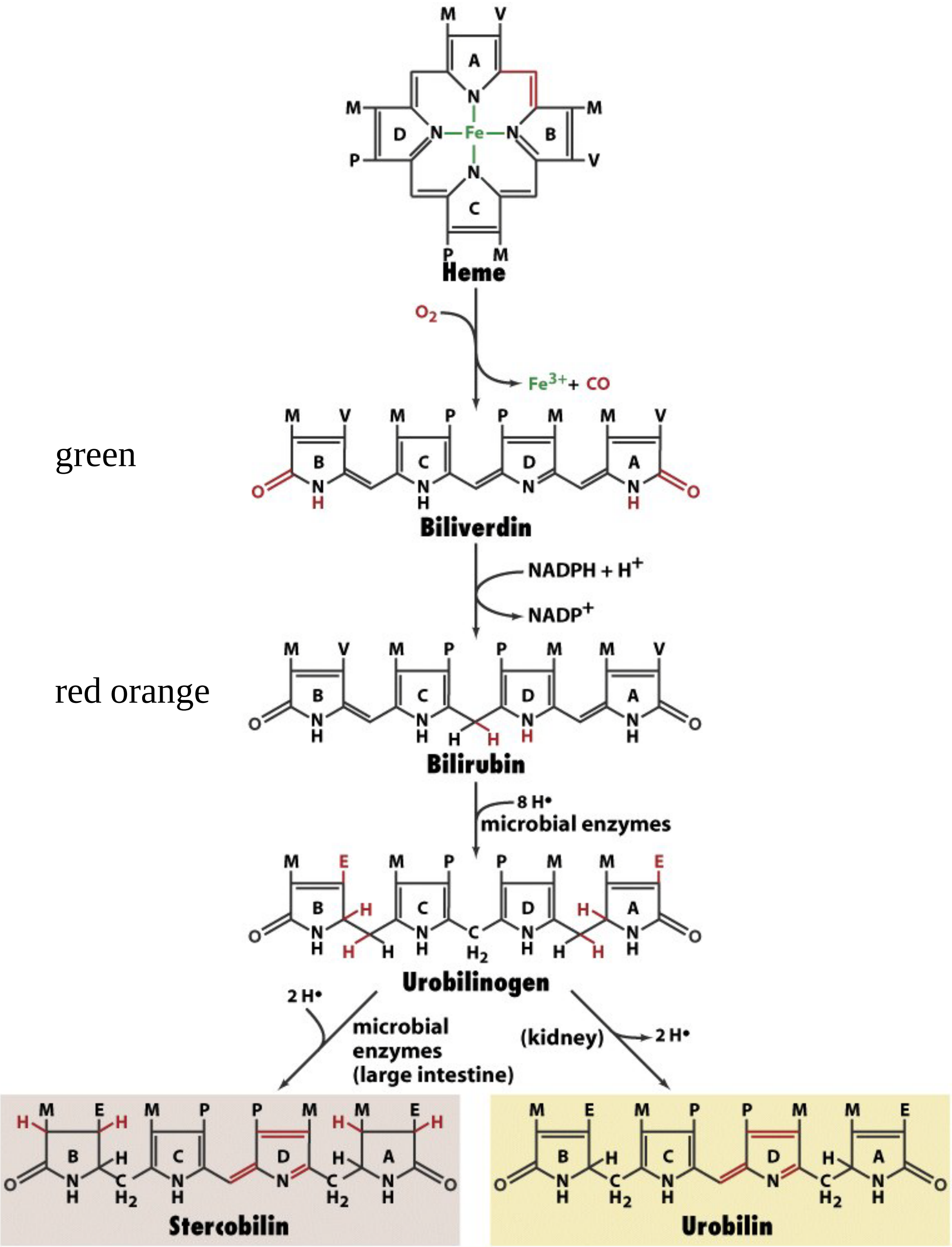


Figure 20-38 Fundamentals of Biochemistry, 2/e

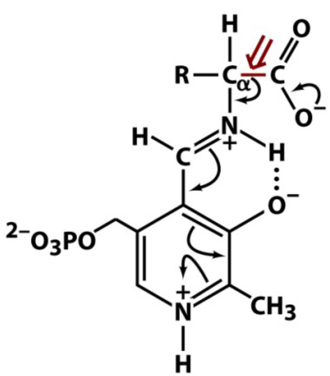
Biosynthesis of physiologically active amines

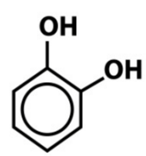
Epinephrine (adrenalin), norepinephrine, dopamine, serotonin (5-hydroxytryptamine),
γ-aminobutyric acid (GABA), and histamine

Hormones and/or neurotransmitters

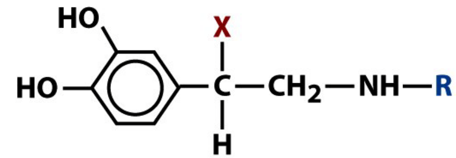
Catechol amines & Indole amines

Amino acid decarboxylase (PLP-dependent rxn)





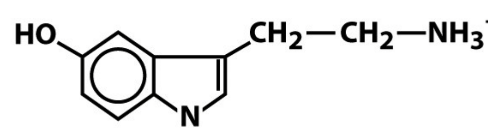
Catechol



X = OH, R = CH_3 **Epinephrine (Adrenalin)**

X = OH, R = H **Norepinephrine**

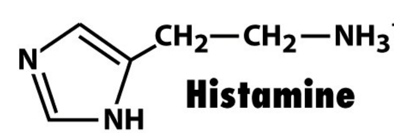
X = H, R = H **Dopamine**



Serotonin (5-hydroxytryptamine)

$^{-}OOC-CH_2-CH_2-CH_2-NH_3^+$

γ-Aminobutyric acid (GABA)



Histamine

The sequential synthesis of L-DOPA, dopamine, norepinephrine, and epinephrine

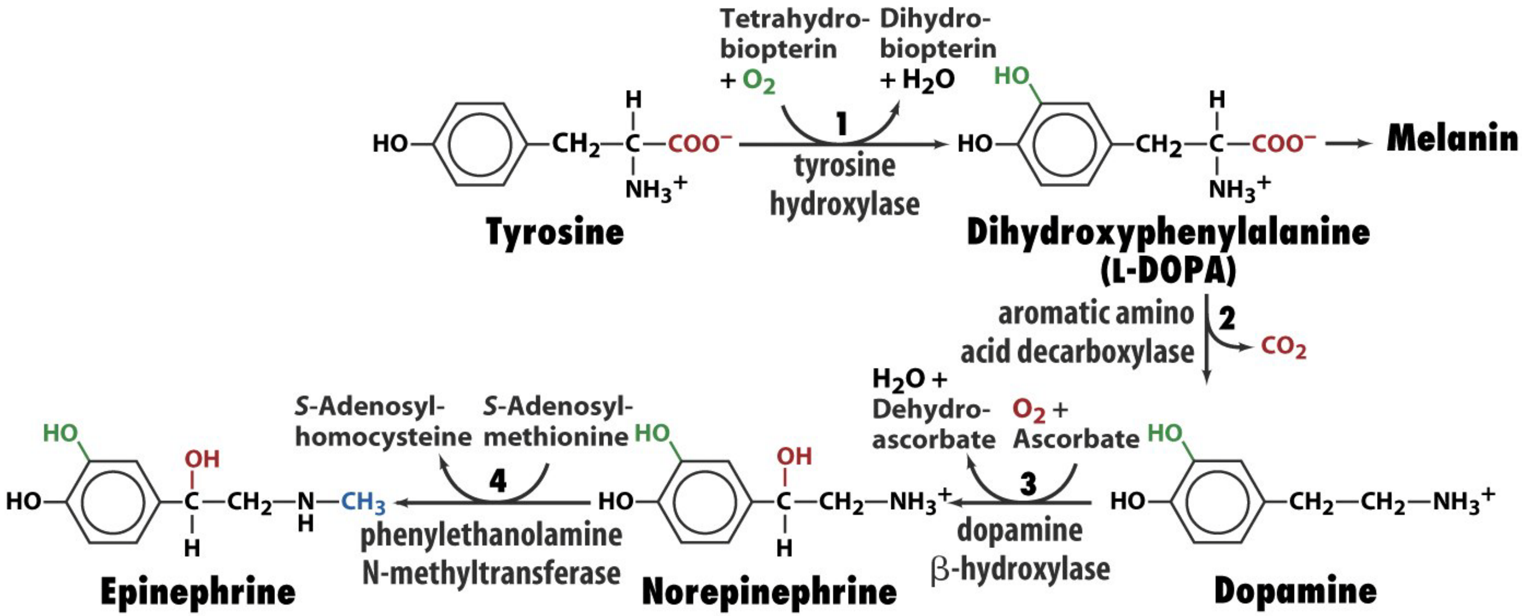
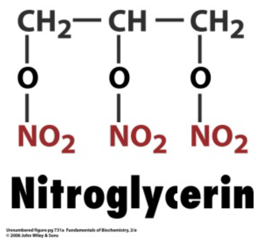


Figure 20-39 Fundamentals of Biochemistry, 2/e

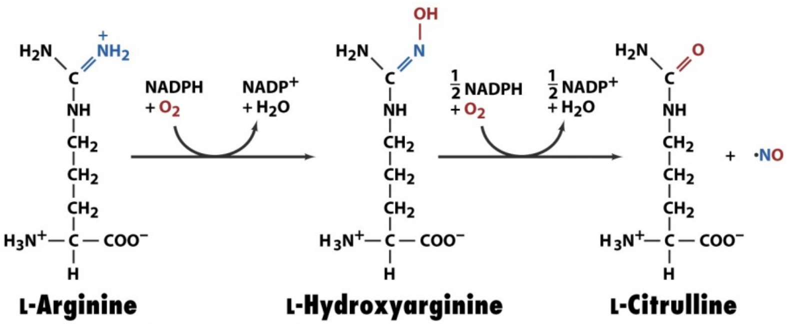
Nitric oxide

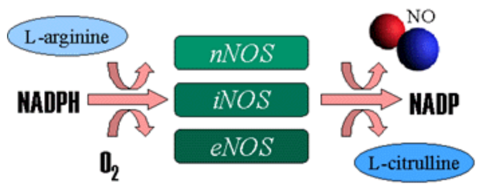
Arginine: endothelium-derived relaxing factor (EDRF)
making underlying smooth muscle relax



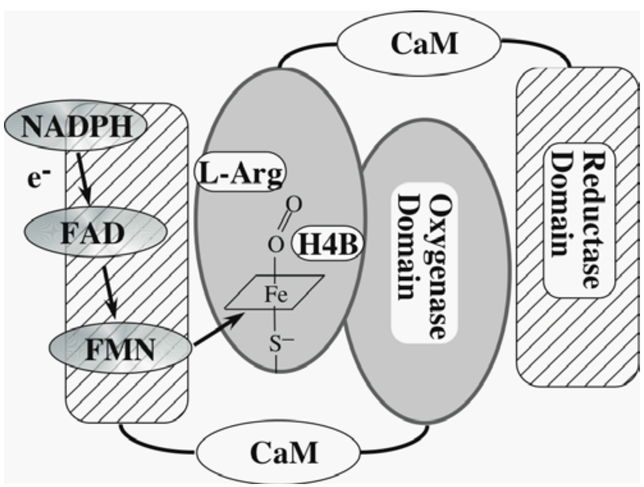
NOS: a homodimeric protein, 3 isoforms

Angina pectoris
(협심증)

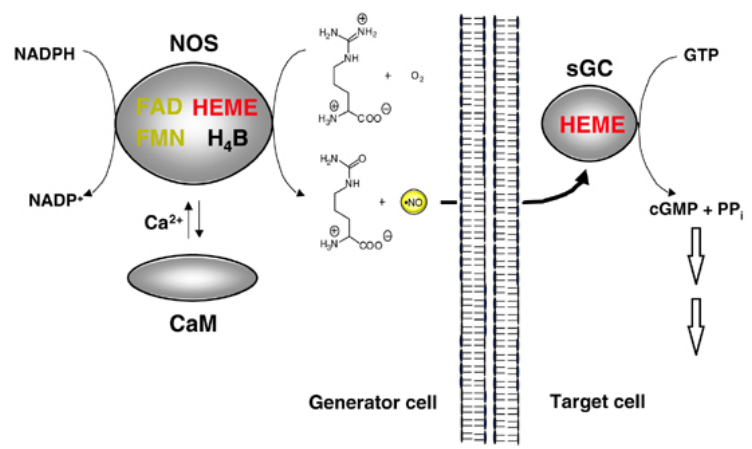




http://www.sgul.ac.uk/depts/immunology/~dash/no/nos.html

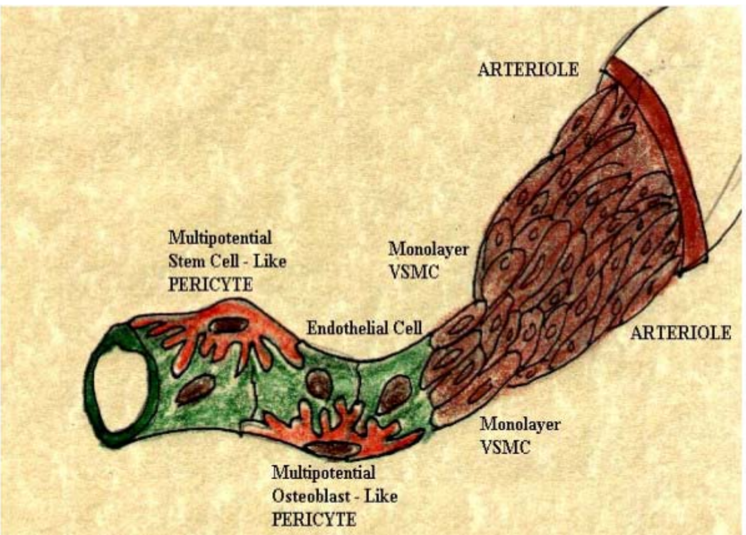


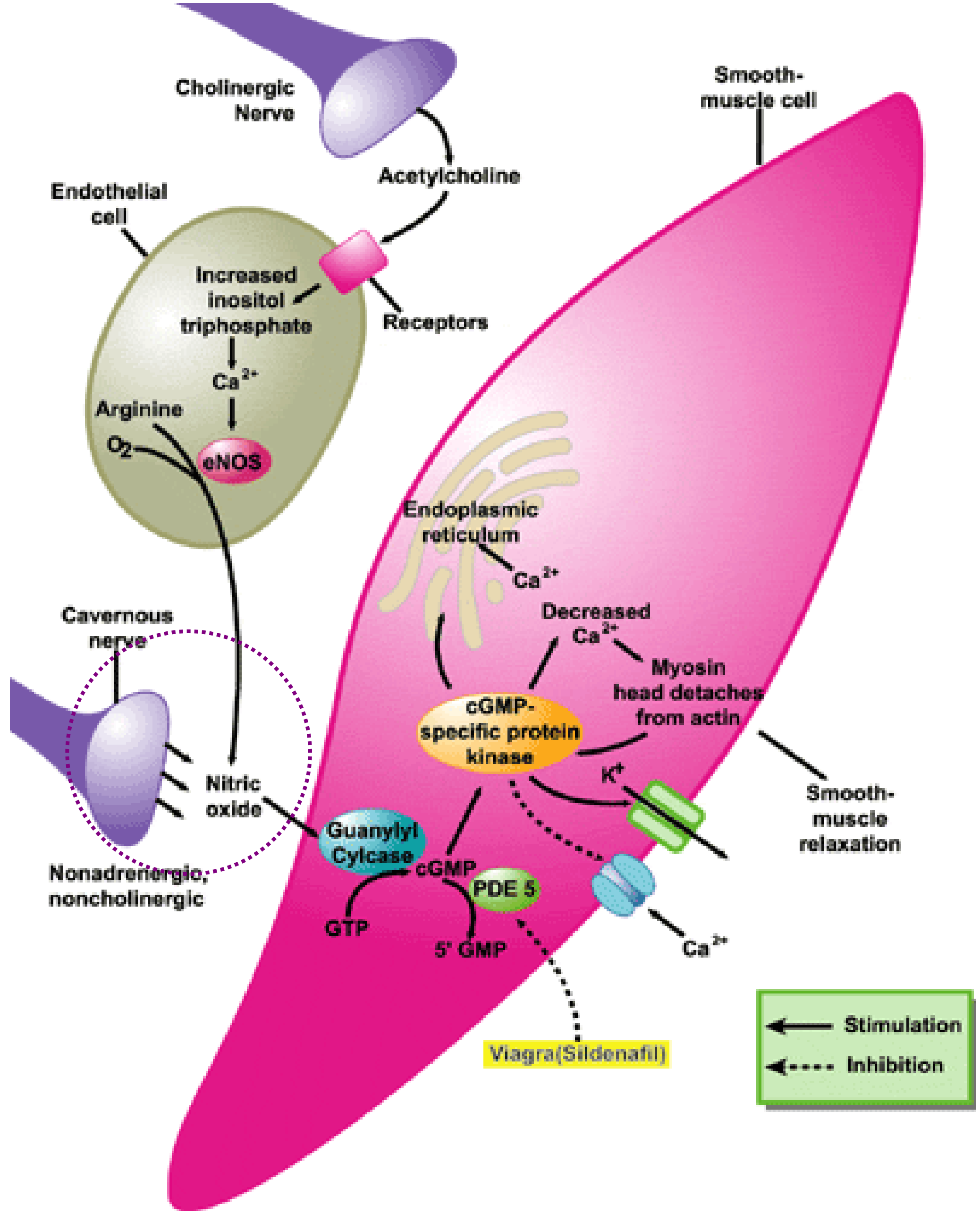
NO and cGMP



NO & cGMP

NO: half life of ~5 s, diffusion of ~1 mm





http://www.wiley.com/legacy/college/boyer/0470003790/cutting_edge/viagra/viagra.htm

Nitrogen fixation

N_2 is stable (N≡N bond *E* is 945 kJ/mol)
Converted to metabolically useful form by diazotrophs
Nitrogenase reduces N_2 to NH_3
Fe-protein: a homodimer containing one [4Fe-4S] cluster and two ATP binding sites
MoFe-protein: $\alpha 2\beta 2$ tetramer containing Fe and Mo

P cluster: consists of 2 [4Fe-3S] clusters linked through an additional sulfide ion
FeMo-cofactor: consists of a [4Fe-3S] cluster and a [1Mo-3Fe-3S] cluster bridged by 3 sulfide ions

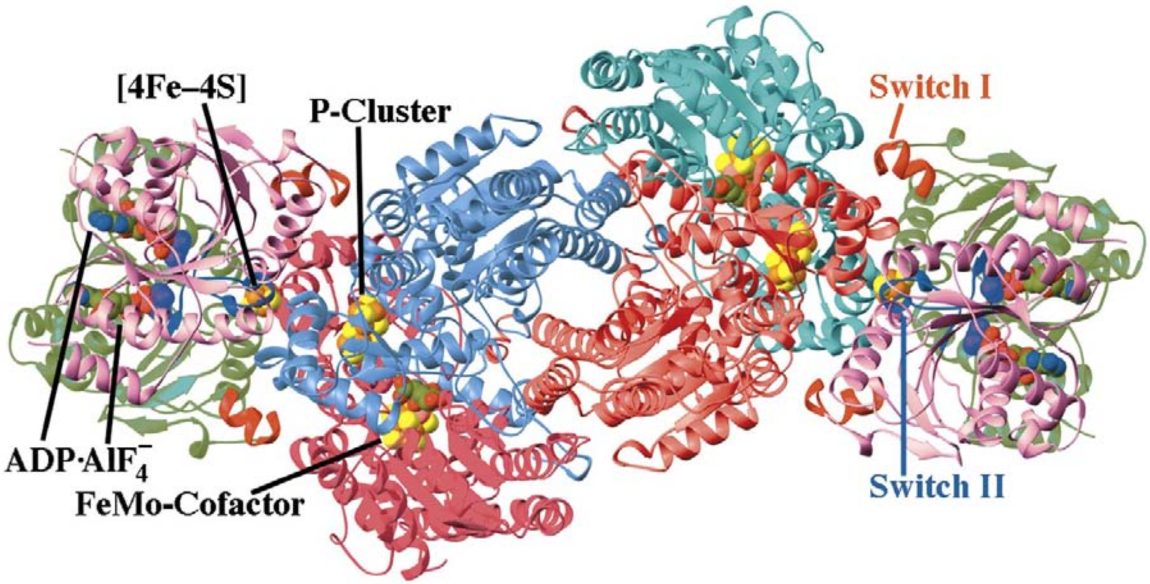
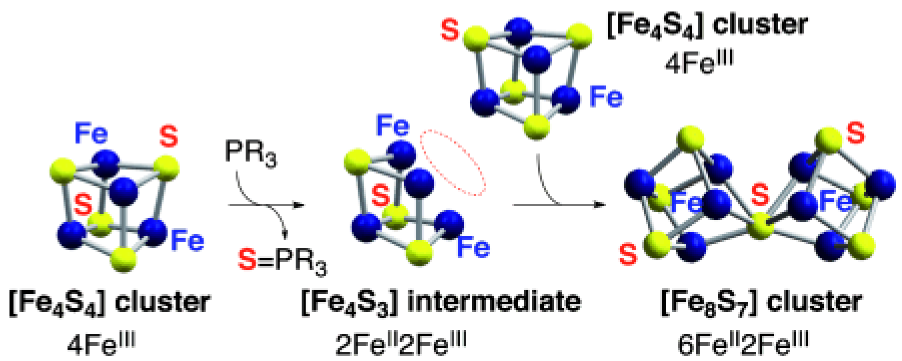


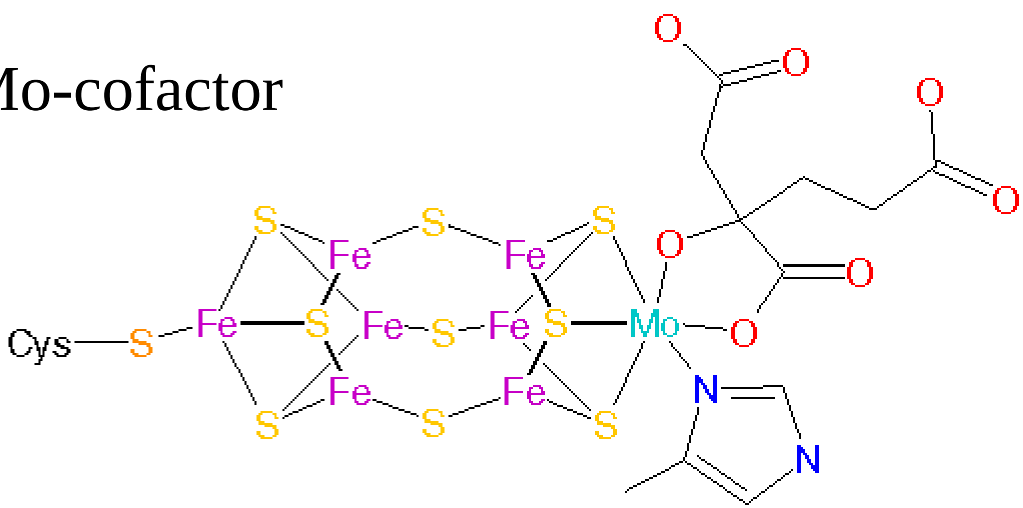
Figure 20-41 Fundamentals of Biochemistry, 2/e

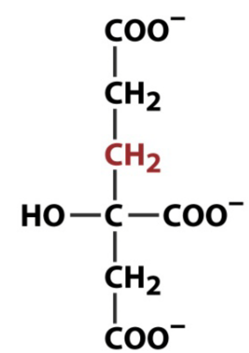
A. Vinelandii nitrogenase in complex

P-cluster



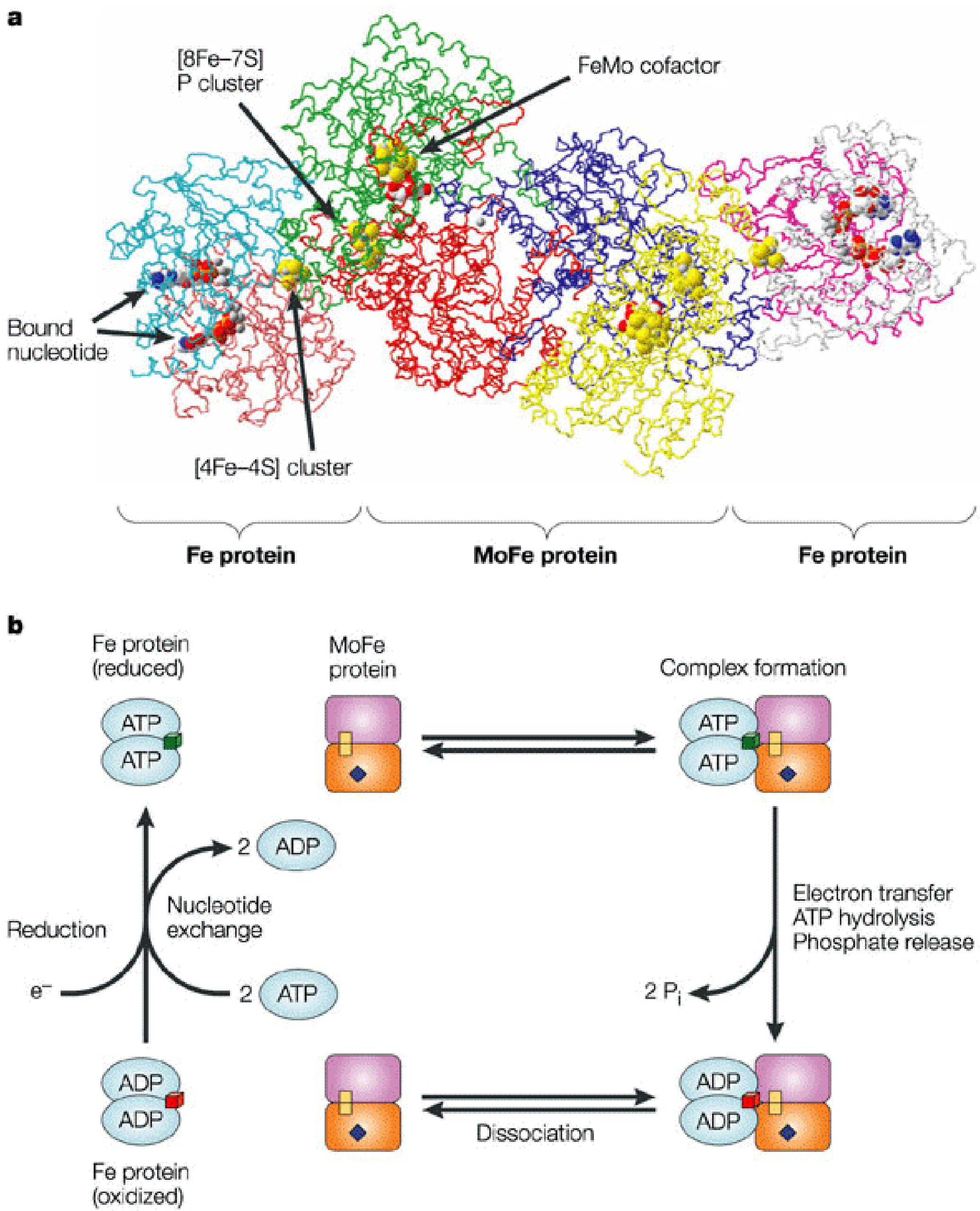
FeMo-cofactor





Homocitrate

Unnumbered figure pg 734 Fundamentals of Biochemistry, 2/e



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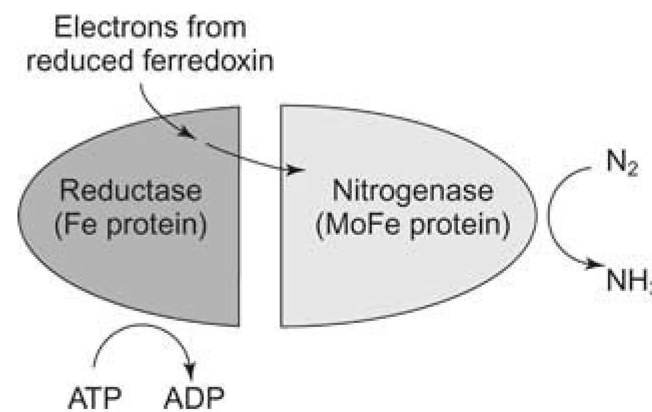


The flow of electrons in the nitrogenase-catalyzed reduction of N_2

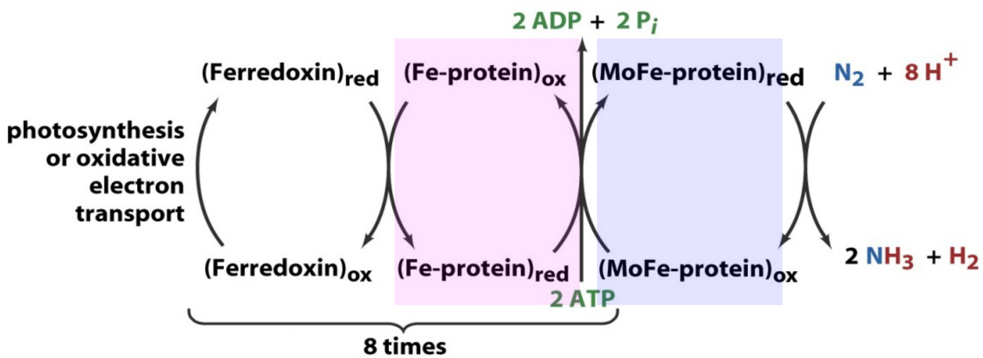
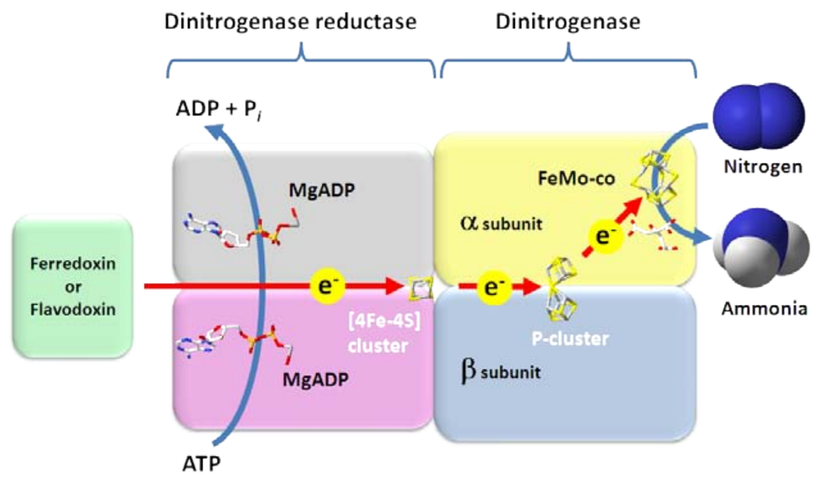
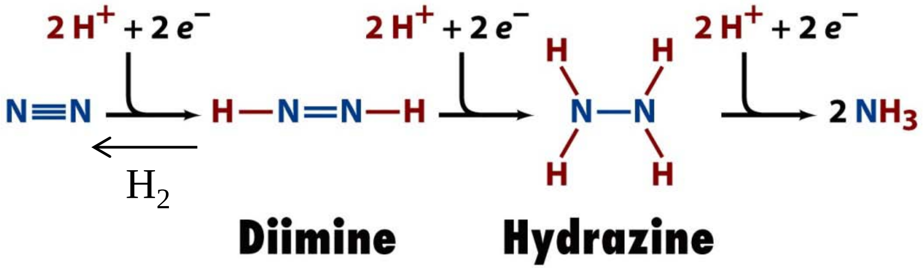


Figure 20-43 Fundamentals of Biochemistry, 2/e



ATP dependent conformational changes in nitrogenase
ATP binding to Fe-protein
ATP hydrolysis induced conformational change
Alternation of redox potential from -0.29 to -0.4 V
(reduction potential of N2 reduction is -0.34 V)

N_2 reduction is energetically costly

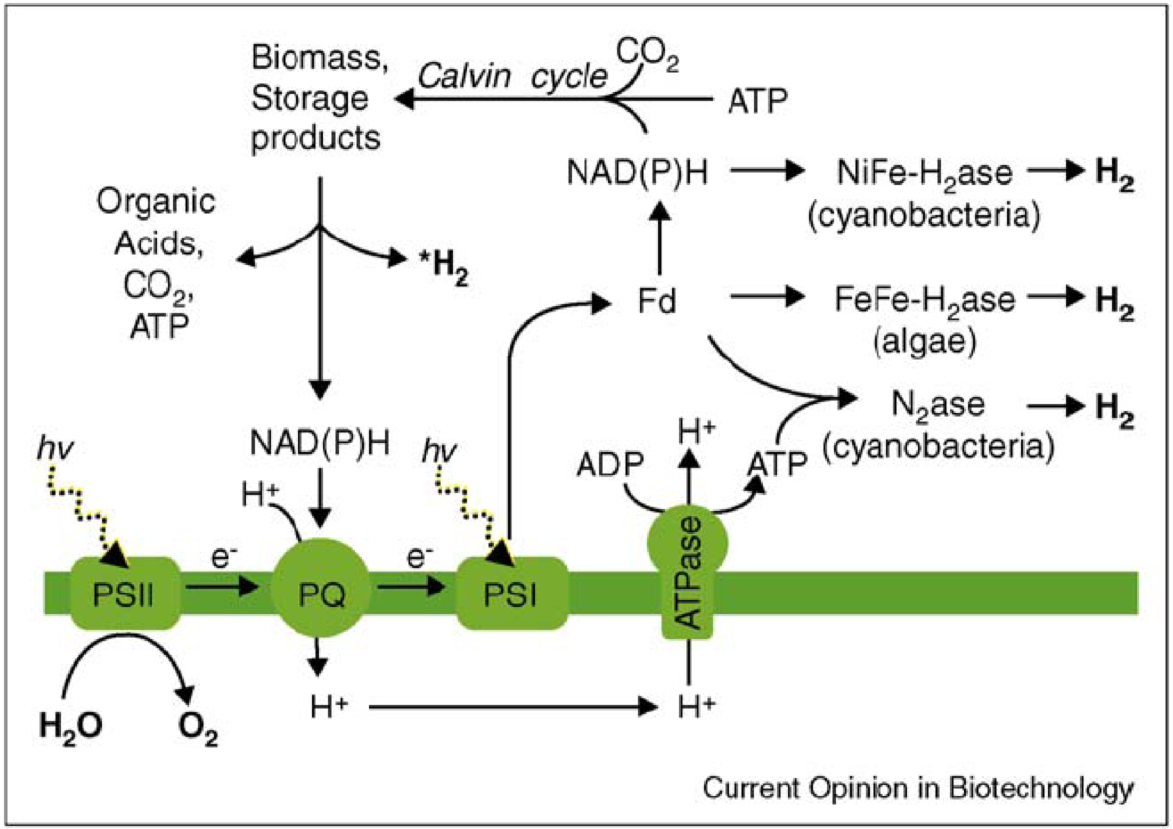


Unnumbered figure pg 736 Fundamentals of Biochemistry, 2/e

$$N_2 + 8\,H^+ + 8e^- + 16\,ATP \rightarrow 2\,NH_3 + H_2 + 16\,ADP + 16\,P_i$$

6 times of electron transfer per N2 fixed: 12 ATP
Futile cycle: diimine to nitrogen, 2 electrons transfer and 4 ATP
Total: 16 ATP

Photobiological production of hydrogen gas as a biofuel

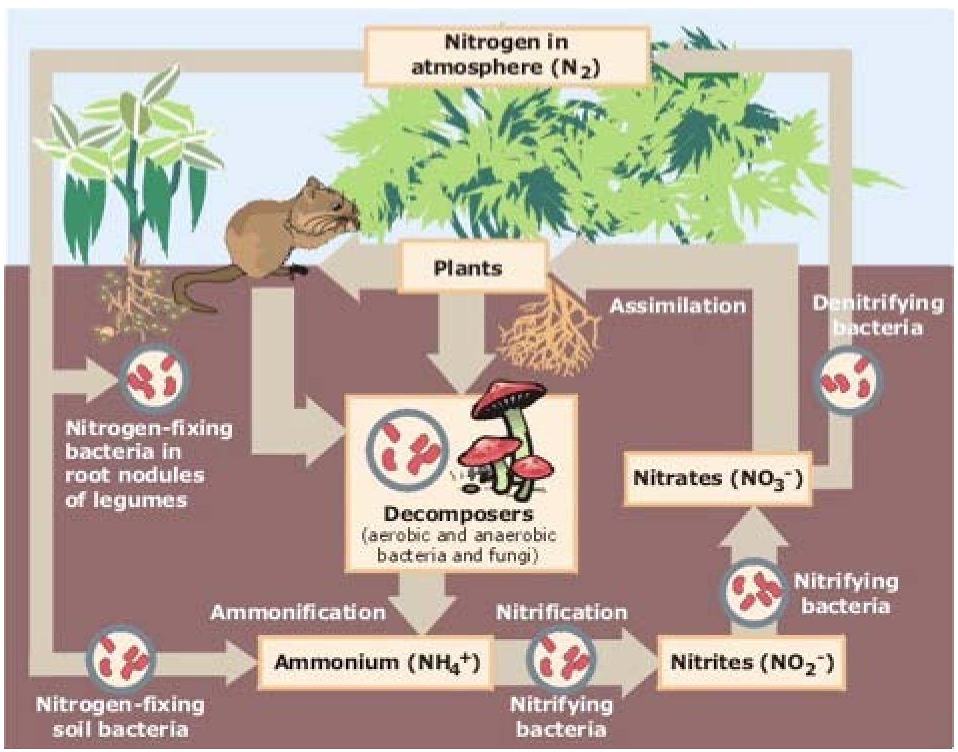


$$\text{Hydrogenase}: \quad 2H^+ + 2e^- \leftrightarrow H_2 \qquad (1)$$

$$\text{Mo-nitrogenase}: \quad N_2 + 8H^+ + 8e^- + 16ATP \rightarrow 2NH_3 + H_2 + 16ADP \qquad (2)$$

The nitrogen cycle

Interconversion of nitrogen in the biosphere



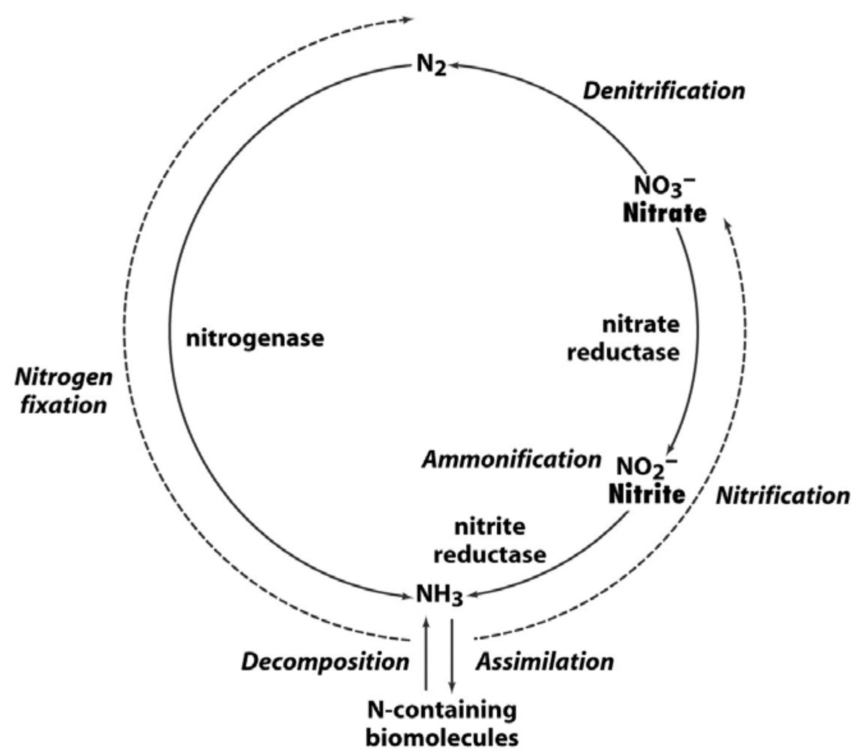


Figure 20-44 Fundamentals of Biochemistry, 2/e

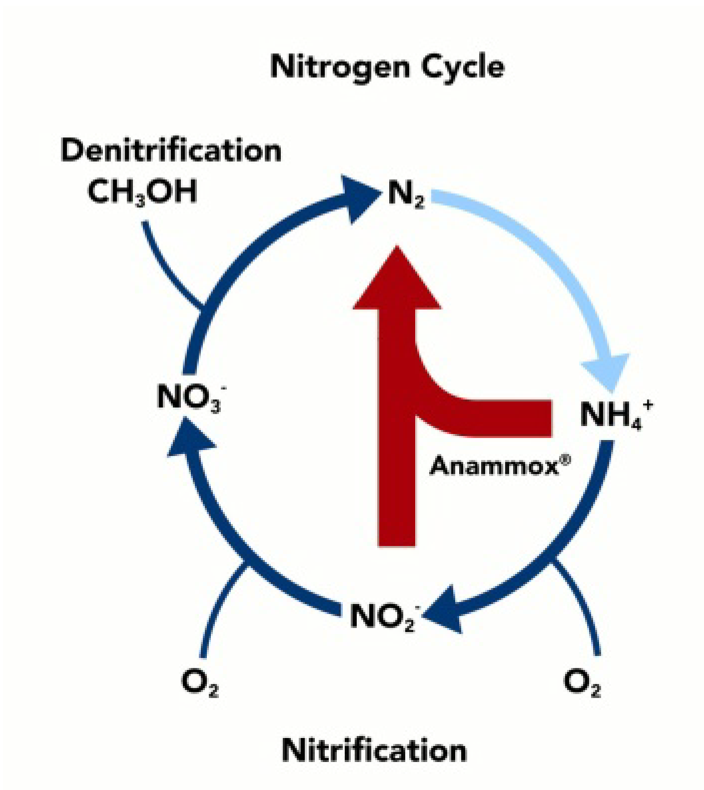
Anammox bacteria

Anaerobic oxidation of ammonia to N_2 in the anaerobic environment

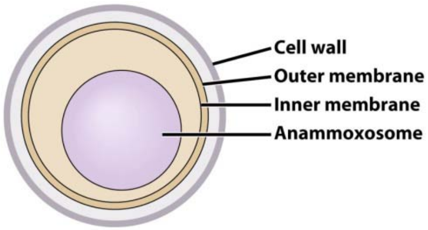
Anammox reaction in anammoxosome

$NH_4^+ + NO_2^- \rightarrow N_2 + 2\ H_2O$

Unusual lipid (ladderanes) provides rigidity, thereby decreasing permeability



http://www.paques.nl/?pid=46



Box 20-4 figure 1 Fundamentals of Biochemistry, 2/e
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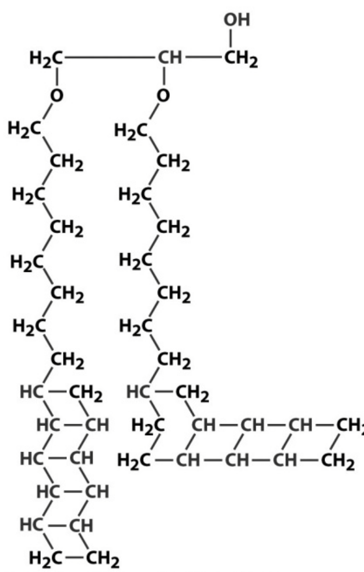

Box 20-4 figure 2 Fundamentals of Biochemistry, 2/e
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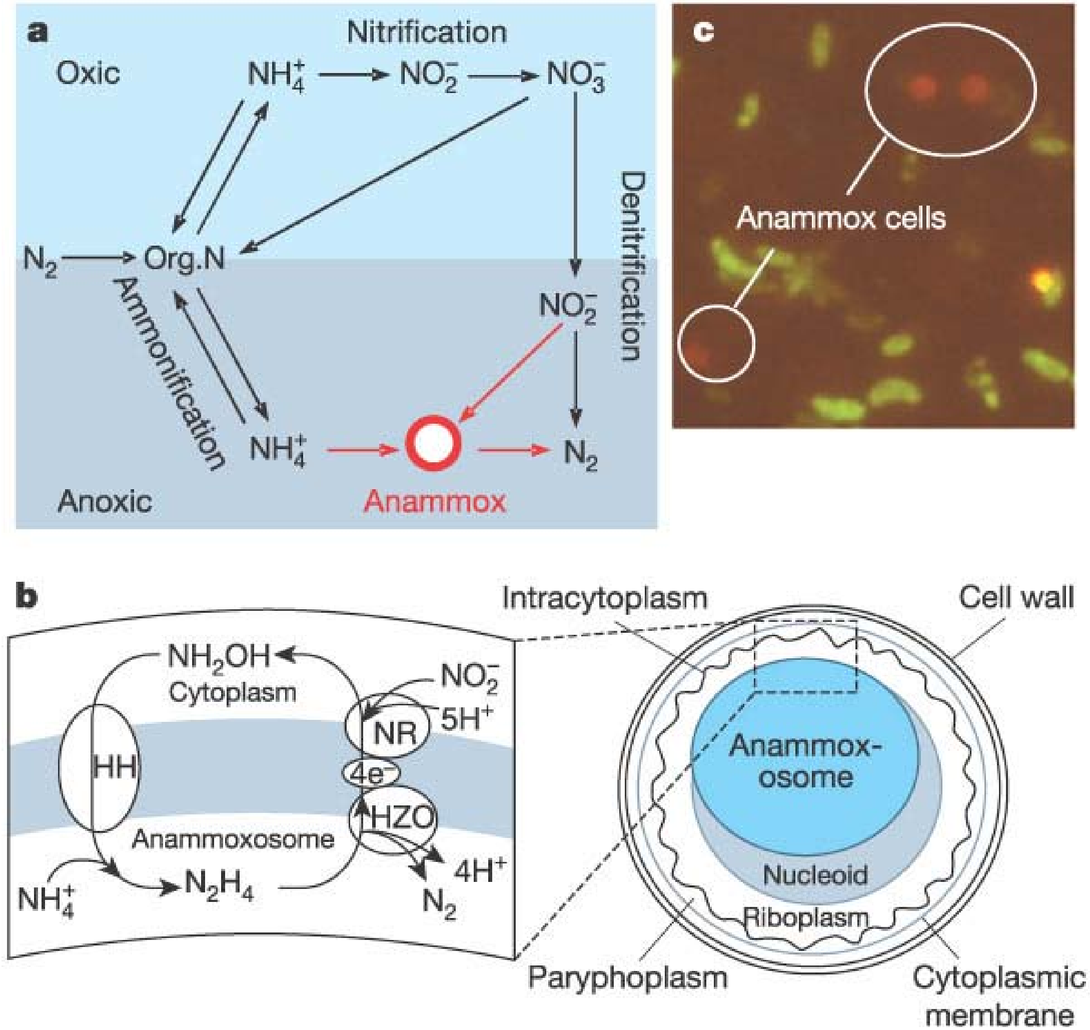


a, Simplified marine nitrogen cycle including the anammox 'sink'. Org.N, organic nitrogen. **b**, Morphology of the anammox cell and proposed model for the anammox process. HH, hydrazine (N2H4) hydrolase; HZO, hydrazine oxidizing enzyme; NR, nitrite reducing enzyme. **c**, Fluorescence *in situ* hybridization of filter material from station 7617 (142 m water depth). Green cells are total Eubacteria stained with EUB338 probe; red cells (encircled) are anammox bacteria stained with a new specific probe (AmxBS820). Nature 422, 608-611(10 April 2003)

Assimilation of fixed nitrogen

Glutamine synthetase + glutamate synthase

In bacteria & plants

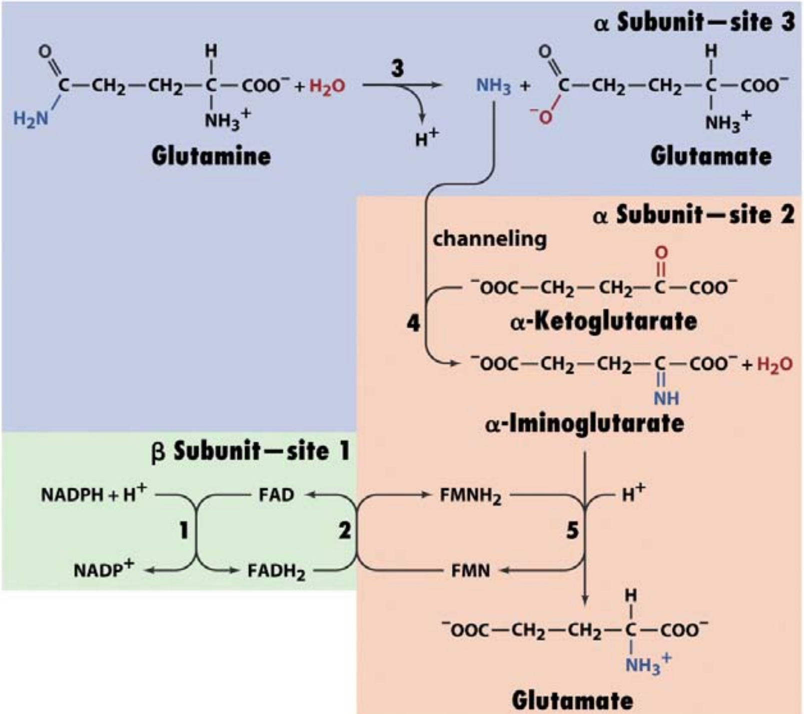
Glutamate synthase: α-ketoglutarate + glutamine + NADPH + H^+ → 2 glutamate + $NADP^+$

Glutamine synthetase : glutamate + ATP + $NH4^+$ ⟶ glutamine + ADP + Pi

The net result of glutamine synthetase & glutamate synthase

α-ketoglutarate + NH_4^+ + NADPH + ATP → glutamate + $NADP^+$ + ADP + Pi

The glutamate synthase reaction



Overall: NADPH + H^+ + glutamine + α-ketoglutarate ⟶ 2 glutamate + $NADP^+$

Figure 20-45 Fundamentals of Biochemistry, 2/e