Biochemistry

Metabolism

22.11.2018 – 11.12.2018

Glyoxylate cycle
Respiratory chain

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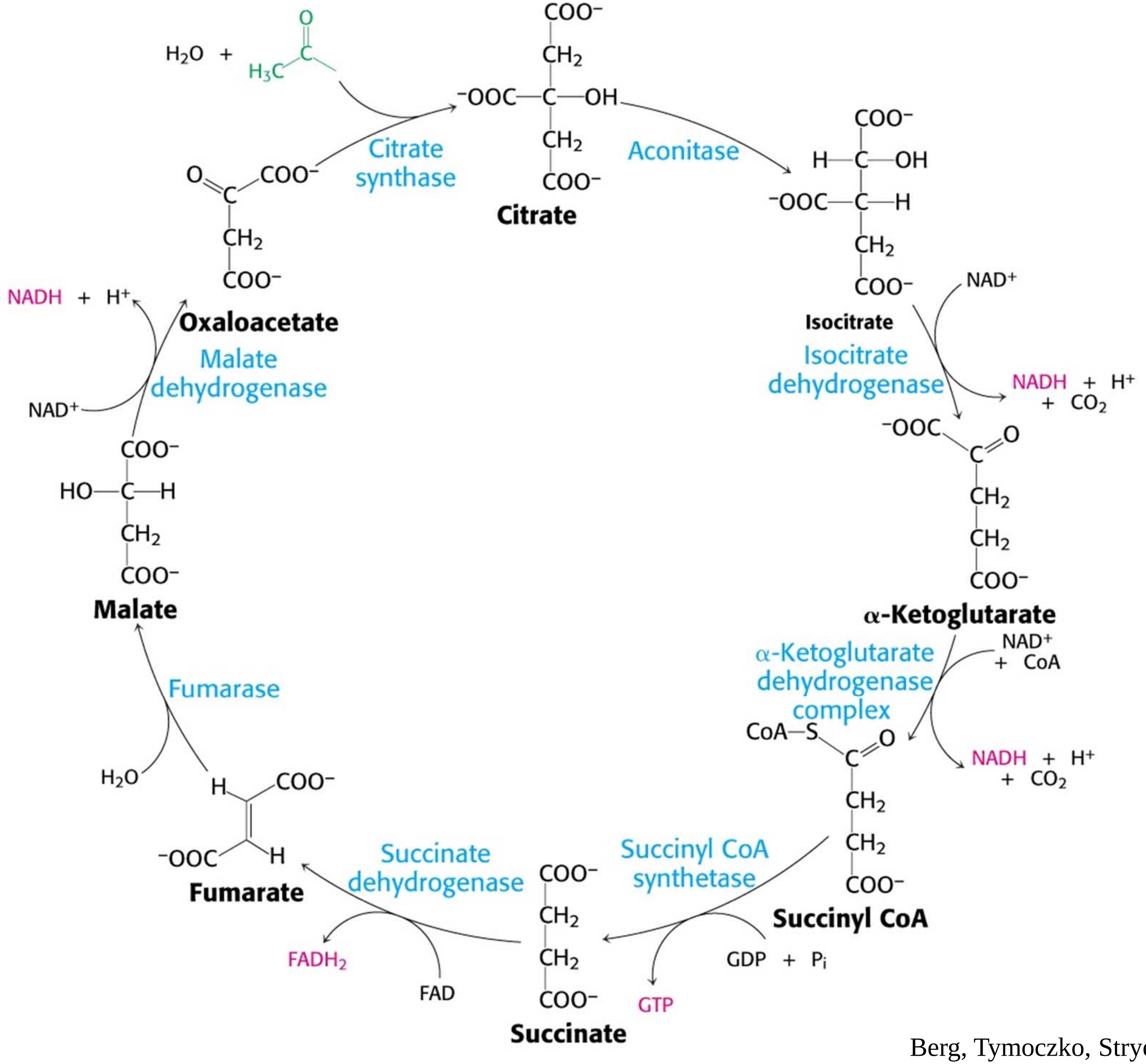
Reactions of the citric acid cycle



Berg, Tymoczko, Stryer: Biochemistry

The glyoxylate cycle

„a short circuit“

from isocitrate to malate

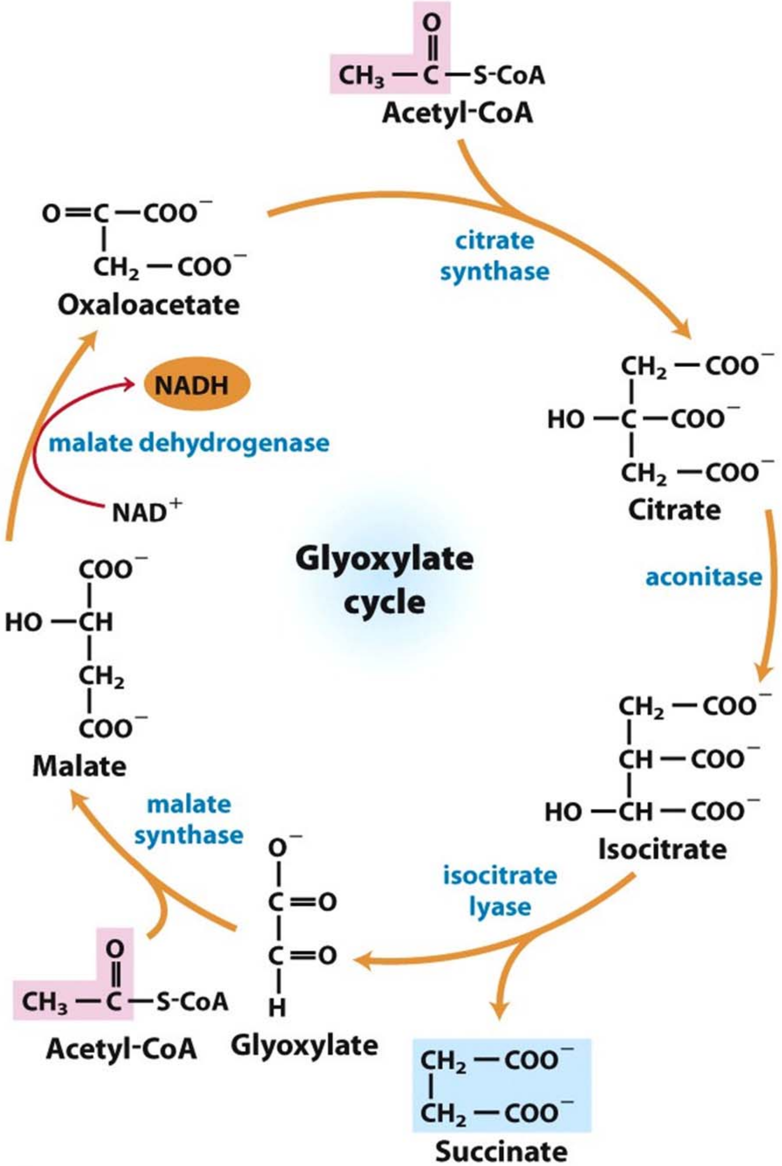


Figure 16-20
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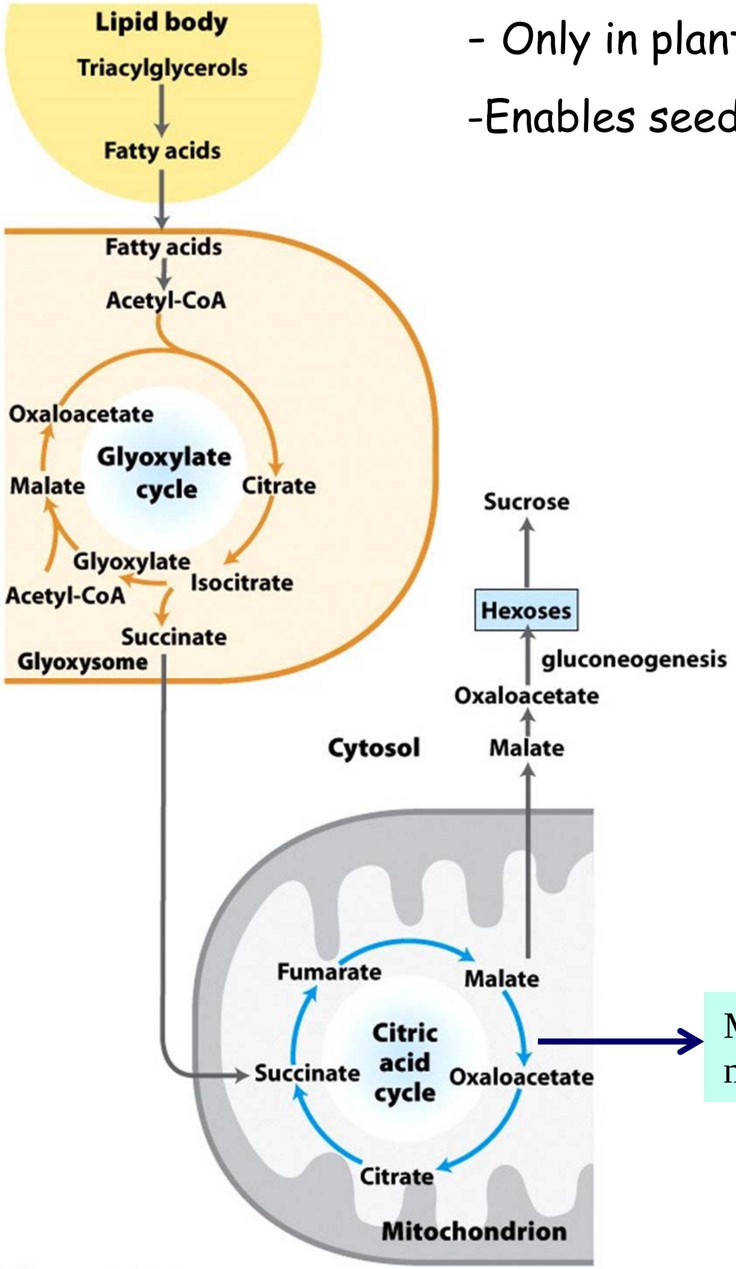
- net conversion of 2 AcCoA to succinate in the glyoxysome, which can be converted to malate in the mitochondrion for use in gluconeogenesis in the cytosol

2AcetylCoA+NAD$^+$ +2 H_2O → Succinate+2CoA+2NADH+H$^+$

- Only in plants (glyoxisomes)

-Enables seeds to convert fats into sugars



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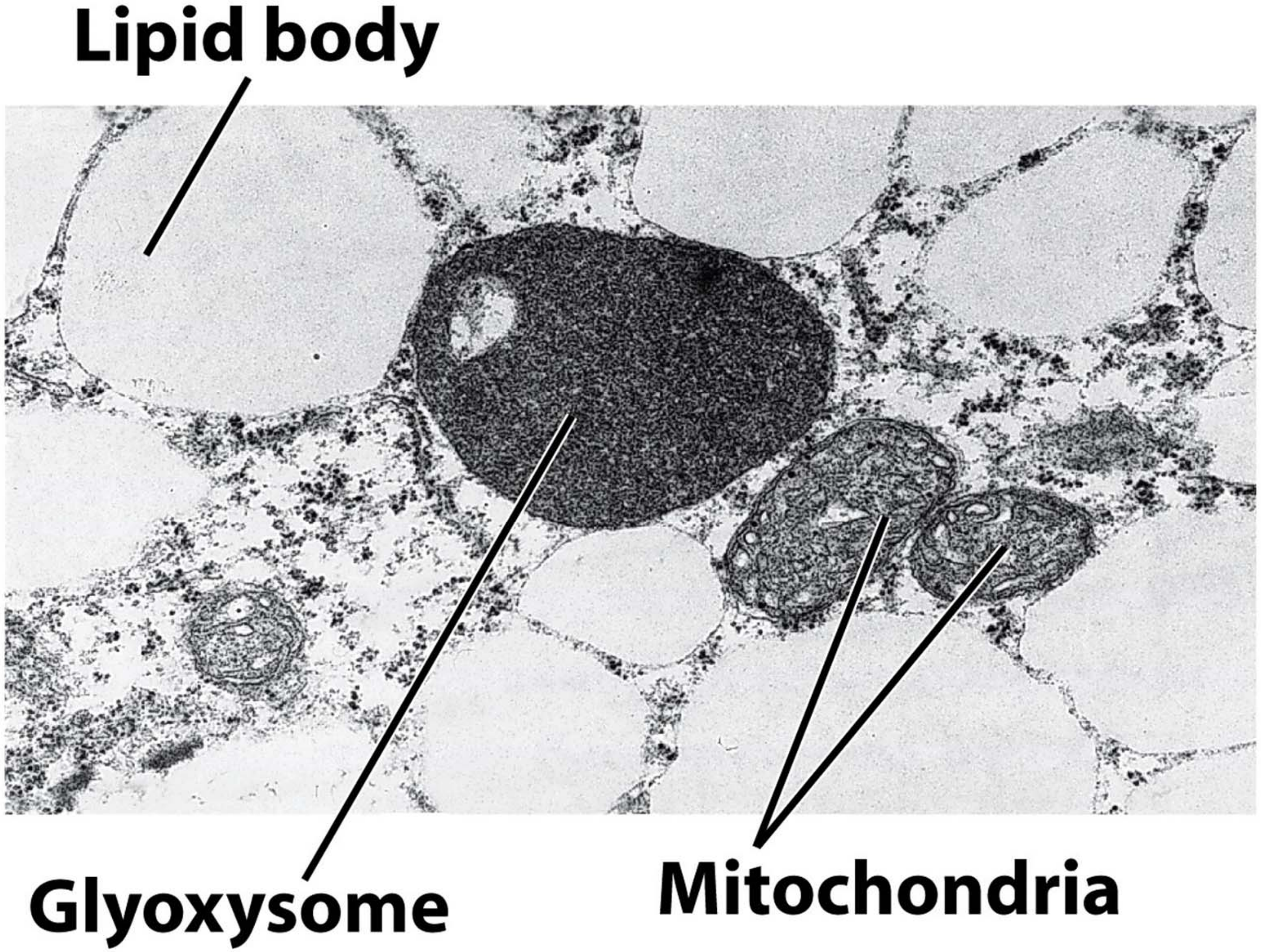
Malate can continue in the TCA making the glyoxylate cycle anaplerotic

Electron micrograph of a germinating cucumber seed



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Citric acid cycle is the common final oxidative path linking catabolism to respiratory chain

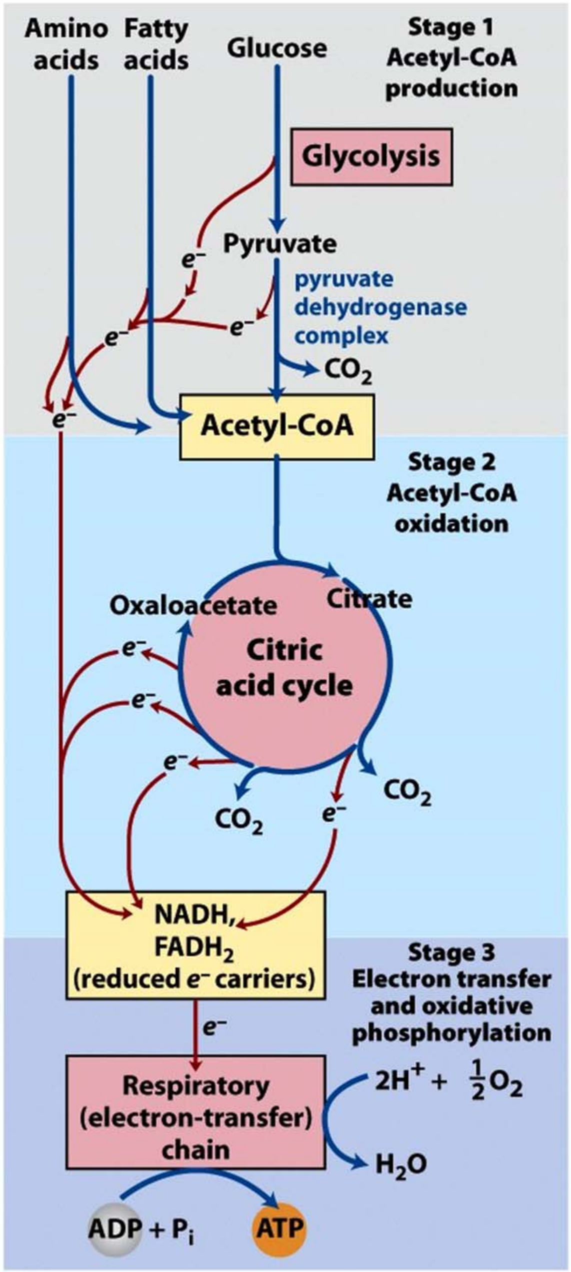

Figure 16-1
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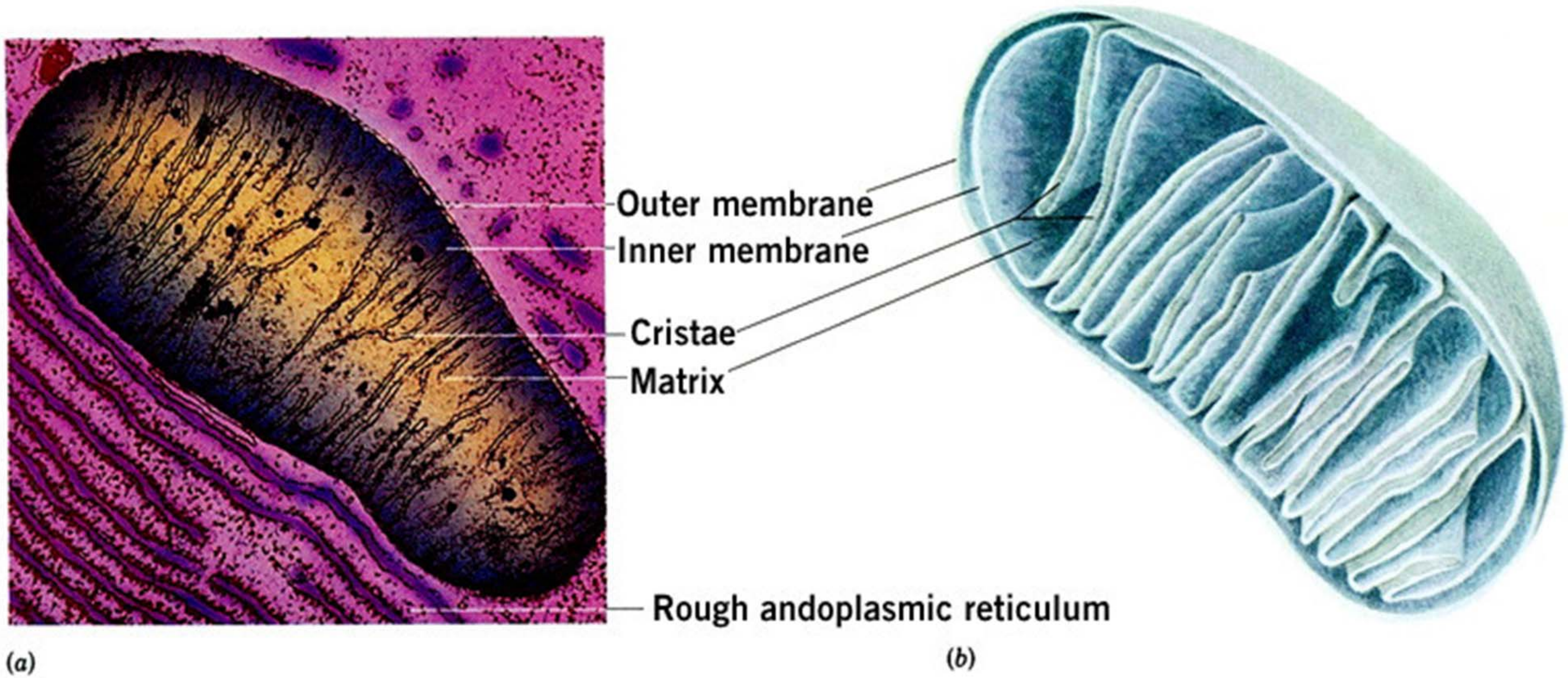
Stage 1:
Acetyl-CoA production

Stage 2:
Acetyl-CoA oxidation

Stage 3:
Electron transfer and oxidative phosphorylation

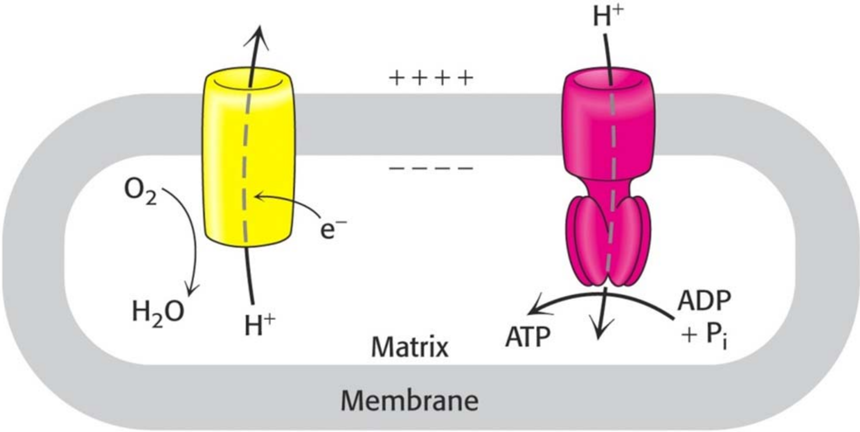


Inner membrane: enzymes of the respiratory chain, transporters

Matrix: catabolic enzymes : citric acid cycle, β-oxidation of fatty acids
mitochondrial DNA and RNA, ribosomes

Function: energy production (ATP)

Generation of reducing equivalents during glucose degradation and their utilization in the oxidative phosphorylation.



$$1/2O_2 + NADH + H^+ \rightleftharpoons H_2O + NAD^+$$

$$\Delta G^{o\prime} = -218 \text{ kJ/mol}$$

$$\Delta G^{o\prime} = - n \times F \times \Delta E^{o\prime}$$

$$= - 2 \times 96{,}5 \times 1.14$$

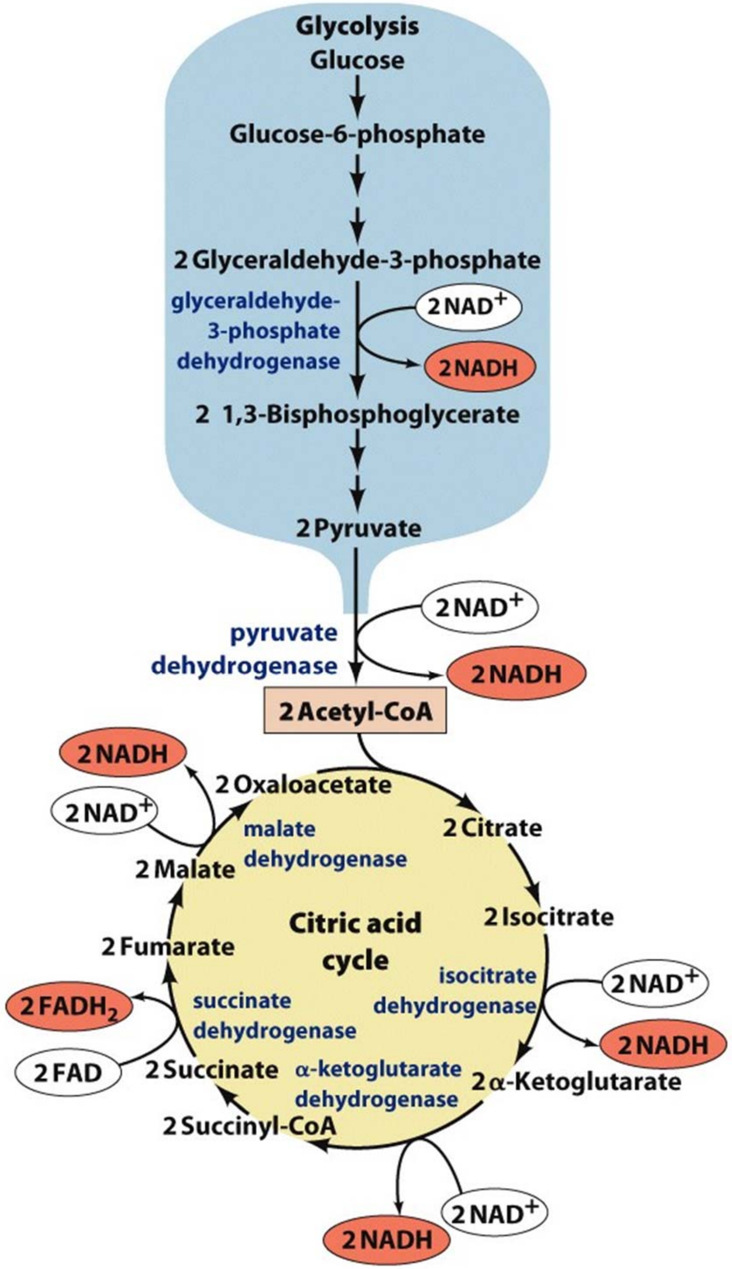


Figure 22-1

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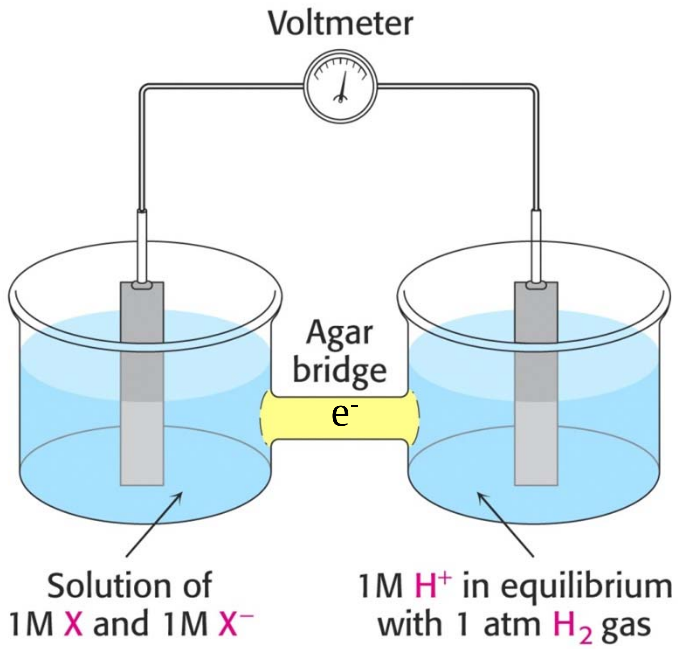
Measurement of the redox potential



Sample half-cell | Standard half-cell

$X^{-} + H^{+} = X + ½ H_2$

$X^{-} = X + e^{-}$

$H^{+} + e^{-} = ½ H_2$

TABLE 18.1 Standard reduction potentials of some reactions

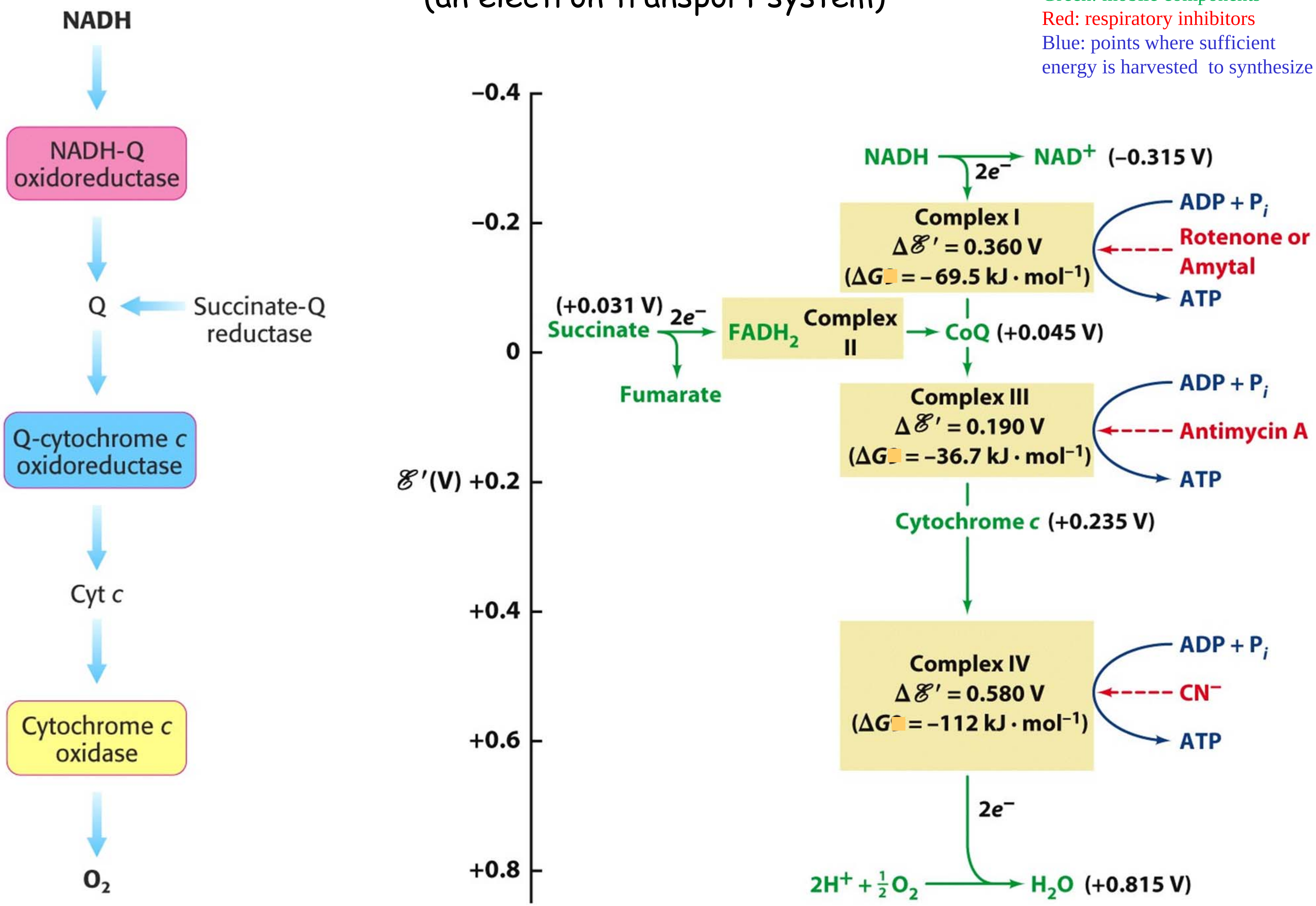
Oxidant	Reductant	n	E'_0 (V)
Succinate + CO_2	α-Ketoglutarate	2	− 0.67
Acetate	Acetaldehyde	2	− 0.60
Ferredoxin (oxidized)	Ferredoxin (reduced)	1	− 0.43
2 H^+	H_2	2	− 0.42
NAD^+	NADH + H^+	2	− 0.32
$NADP^+$	NADPH + H^+	2	− 0.32
Lipoate (oxidized)	Lipoate (reduced)	2	− 0.29
Glutathione (oxidized)	Glutathione (reduced)	2	− 0.23
FAD	$FADH_2$	2	− 0.22
Acetaldehyde	Ethanol	2	− 0.20
Pyruvate	Lactate	2	− 0.19
Fumarate	Succinate	2	0.03
Cytochrome *b* (+3)	Cytochrome *b* (+2)	1	0.07
Dehydroascorbate	Ascorbate	2	0.08
Ubiquinone (oxidized)	Ubiquinone (reduced)	2	0.10
Cytochrome *c* (+3)	Cytochrome *c* (+2)	1	0.22
Fe (+3)	Fe (+2)	1	0.77
$\frac{1}{2} O_2 + 2 H^+$	H_2O	2	0.82

Note: E'_0 is the standard oxidation–reduction potential (pH 7, 25°C) and n is the number of electrons transferred. E'_0 refers to the partial reaction written as

$$\text{Oxidant} + e^{-} \longrightarrow \text{reductant}$$

The mitochondrial respiratory chain
(an electron transport system)

Green: mobile components
Red: respiratory inhibitors
Blue: points where sufficient energy is harvested to synthesize ATP



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The path of e^- and p^+ along the mitochondrial respiratory chain

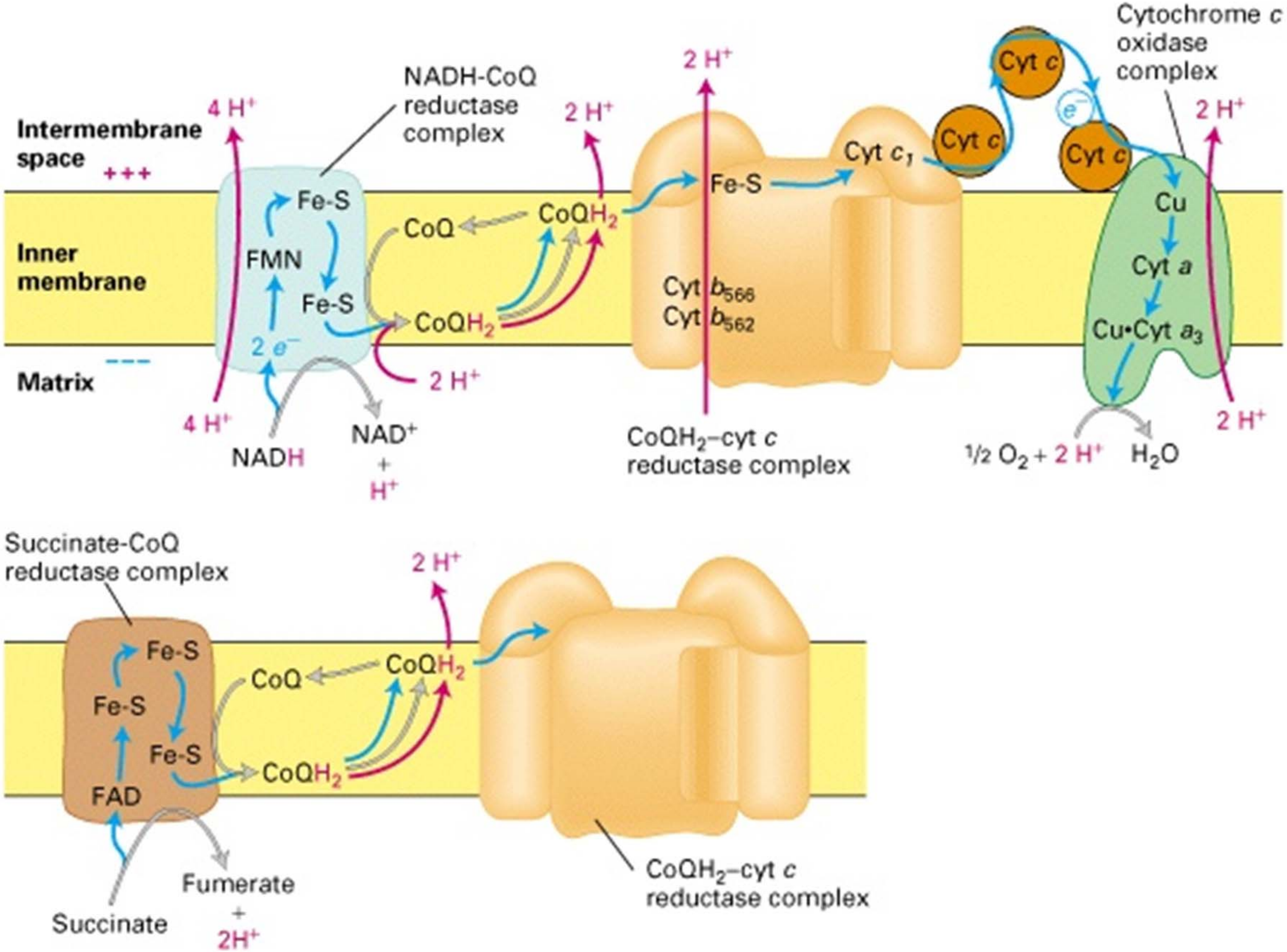

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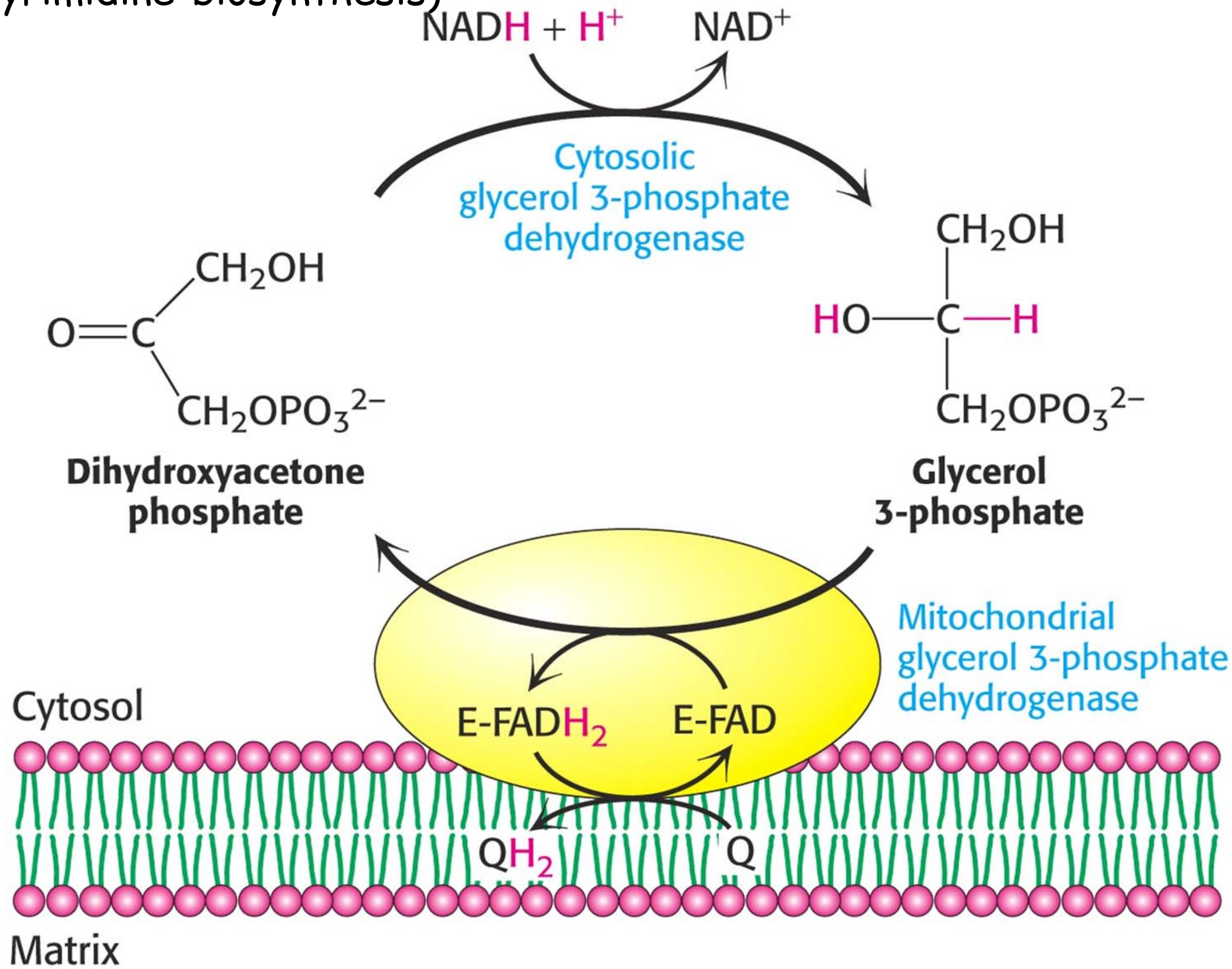
TABLE 18.2 Components of the mitochondrial electron-transport chain

Enzyme complex	Mass (kd)	Subunits	Prosthetic group	Oxidant or reductant: Matrix side	Oxidant or reductant: Membrane core	Oxidant or reductant: Cytosolic side
NADH-Q oxidoreductase	880	≥ 34	FMN Fe-S	NADH	Q	
Succinate-Q reductase	140	4	FAD Fe-S	Succinate	Q	
Q-cytochrome *c* oxidoreductase	250	10	Heme b_H Heme b_L Heme c_1 Fe-S		Q	Cytochrome *c*
Cytochrome *c* oxidase	160	10	Heme *a* Heme a_3 Cu_A and Cu_B			Cytochrome *c*

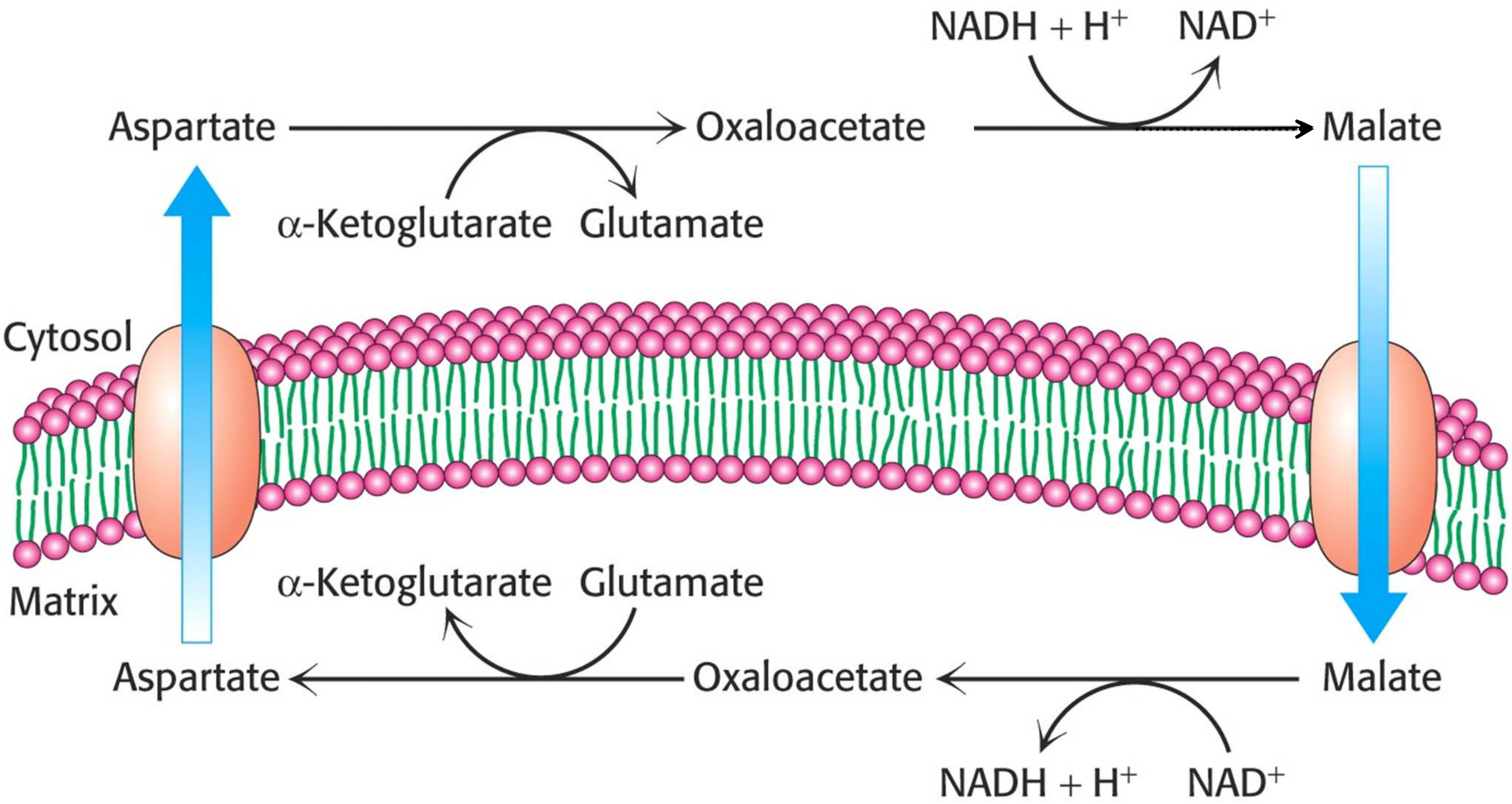
Sources: J. W. DePierre and L. Ernster, *Annu. Rev. Biochem.* 46(1977):215; Y. Hatefi, *Annu Rev. Biochem.* 54(1985);1015; and J. E. Walker, *Q. Rev. Biophys.* 25(1992):253.

Coenzym Q: a collecting pool for electrons derived from :

- Complex I
- Complex II (succinate-DH)
- Glycerol 3-phosphate-DH (see below)
- AcylCoA-DH (β-oxidation of fatty acids)
- Dihydroorotate-DH (pyrimidine-biosynthesis)



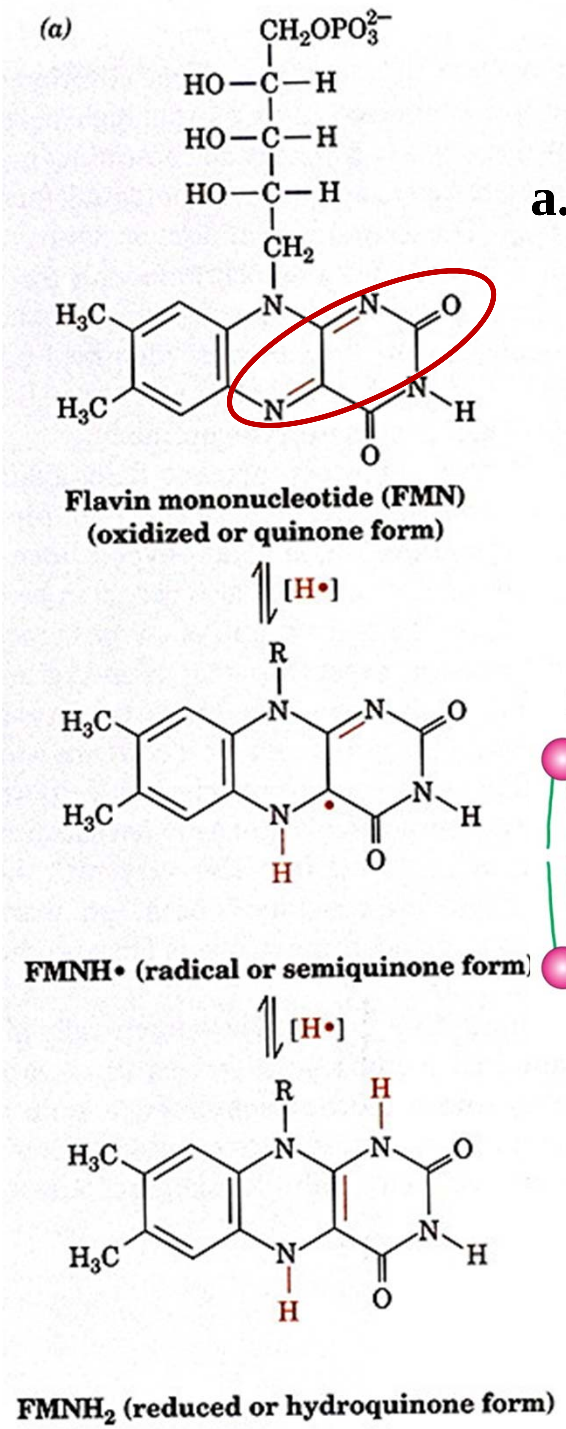
The malate-aspartate-shuttle enables the shift of cytosolic NADH into the mitochondria

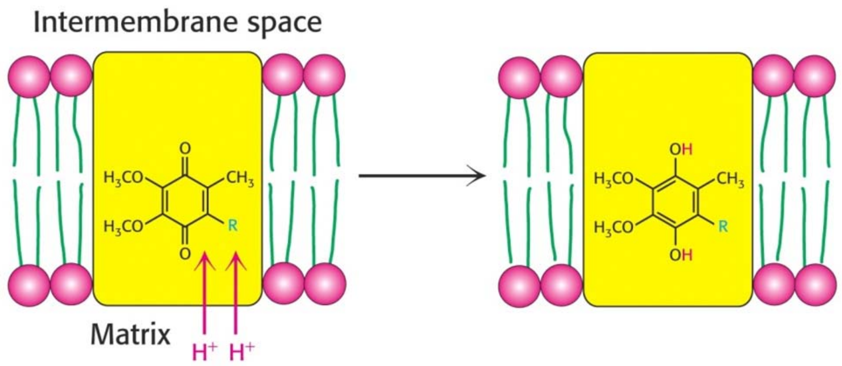


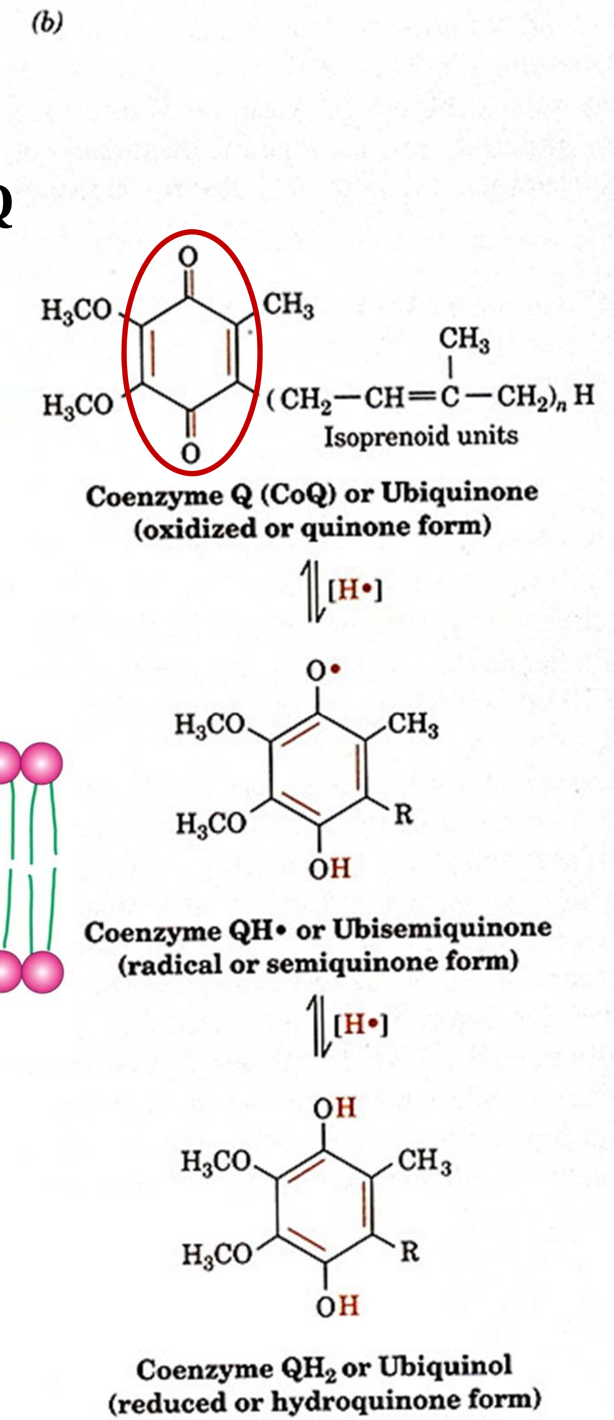
The oxidation states of:

a.) FMN b.)CoQ

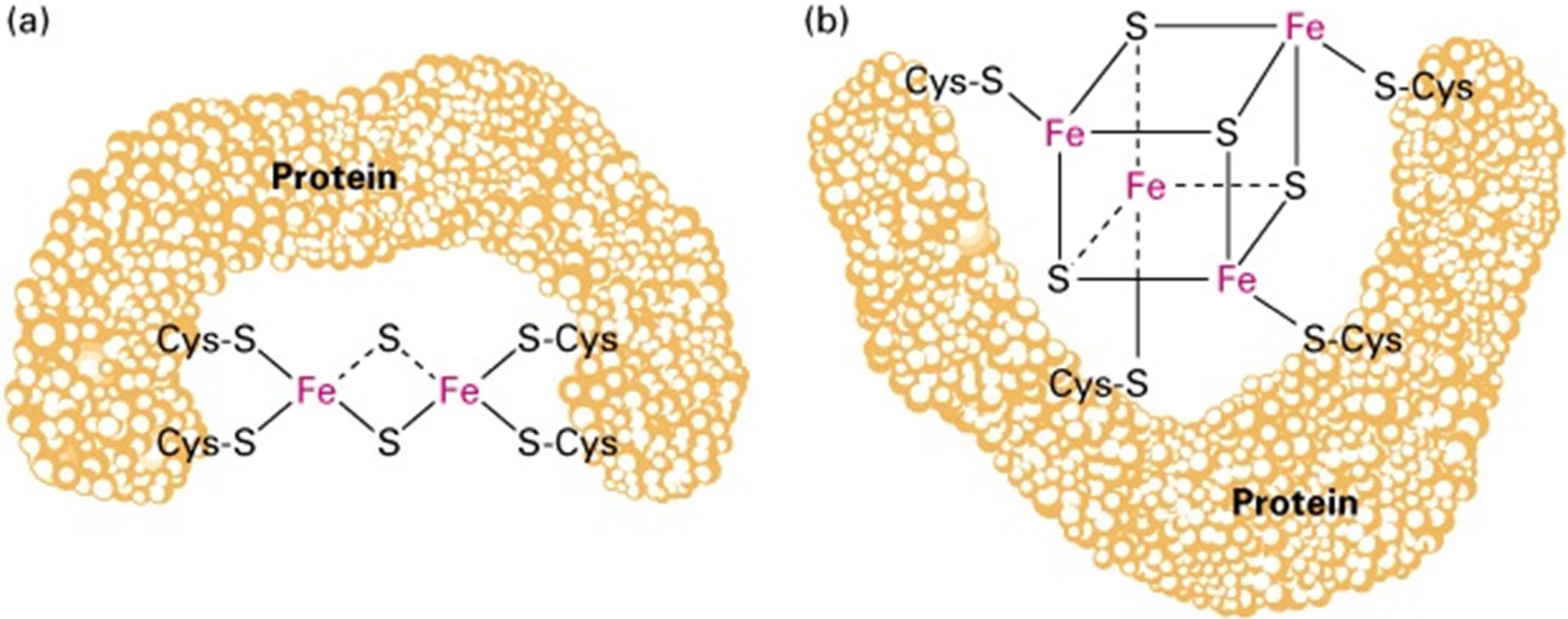
Both co-enzymes form stabile semiquinones (radicals)

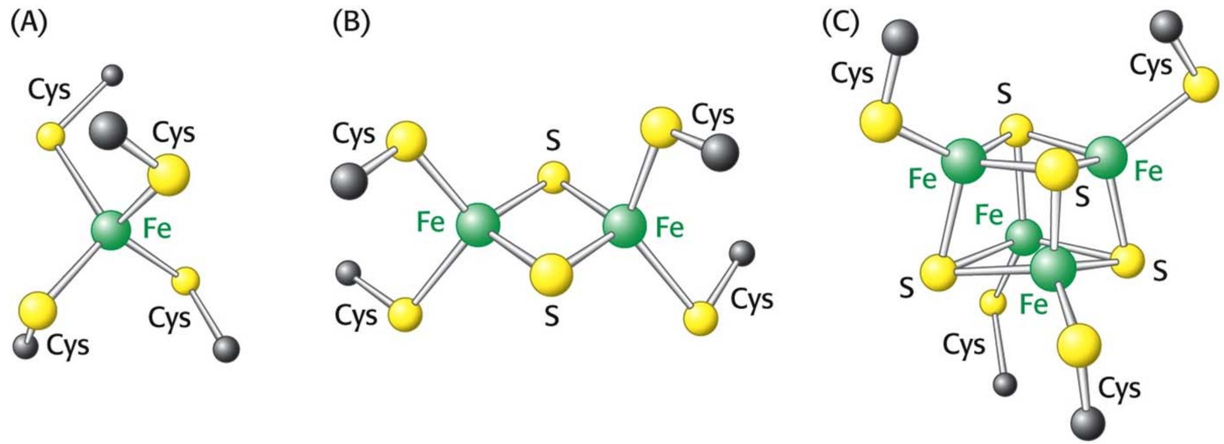




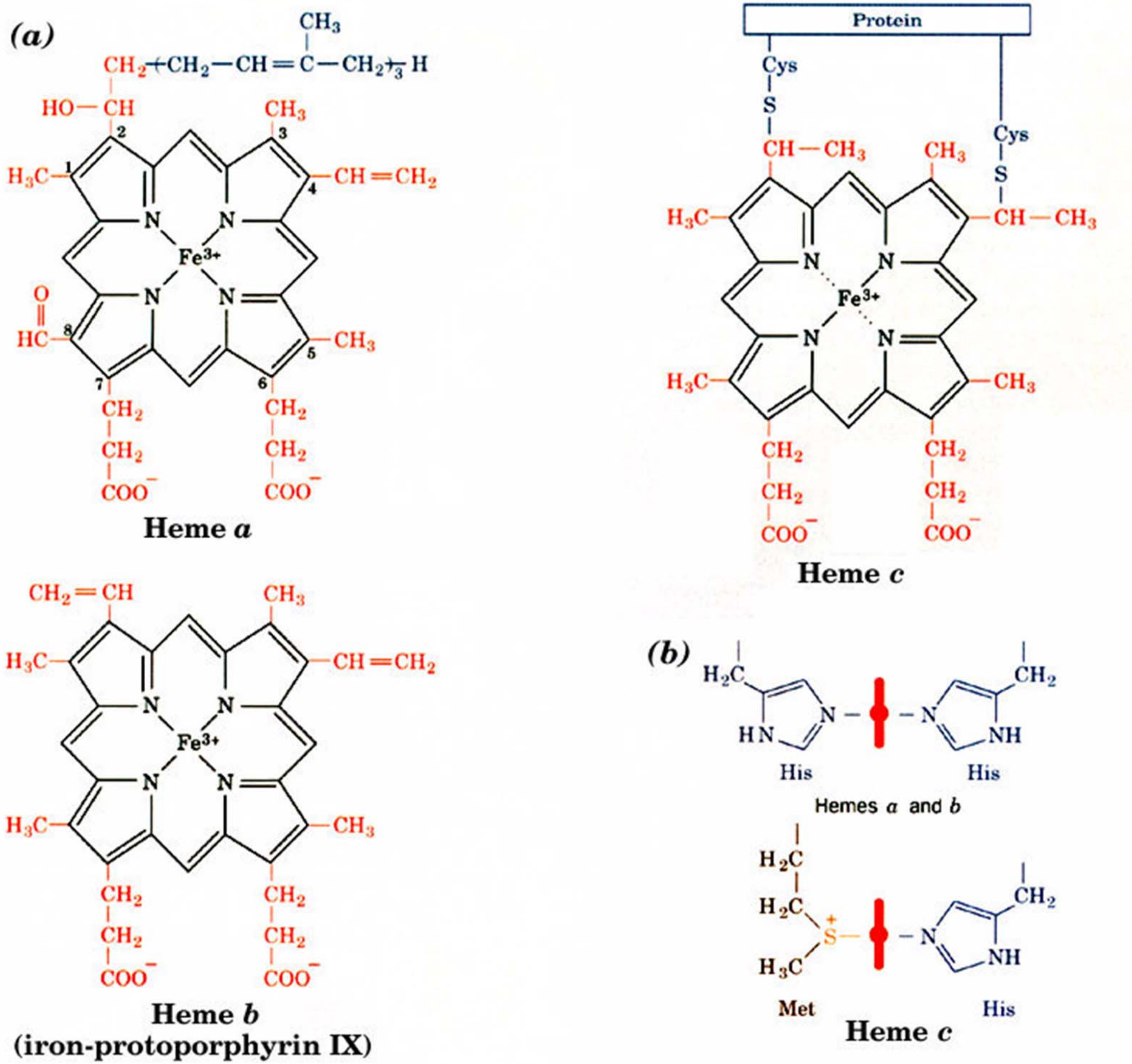


Spatial structure of protein-bound iron-sulfur centres

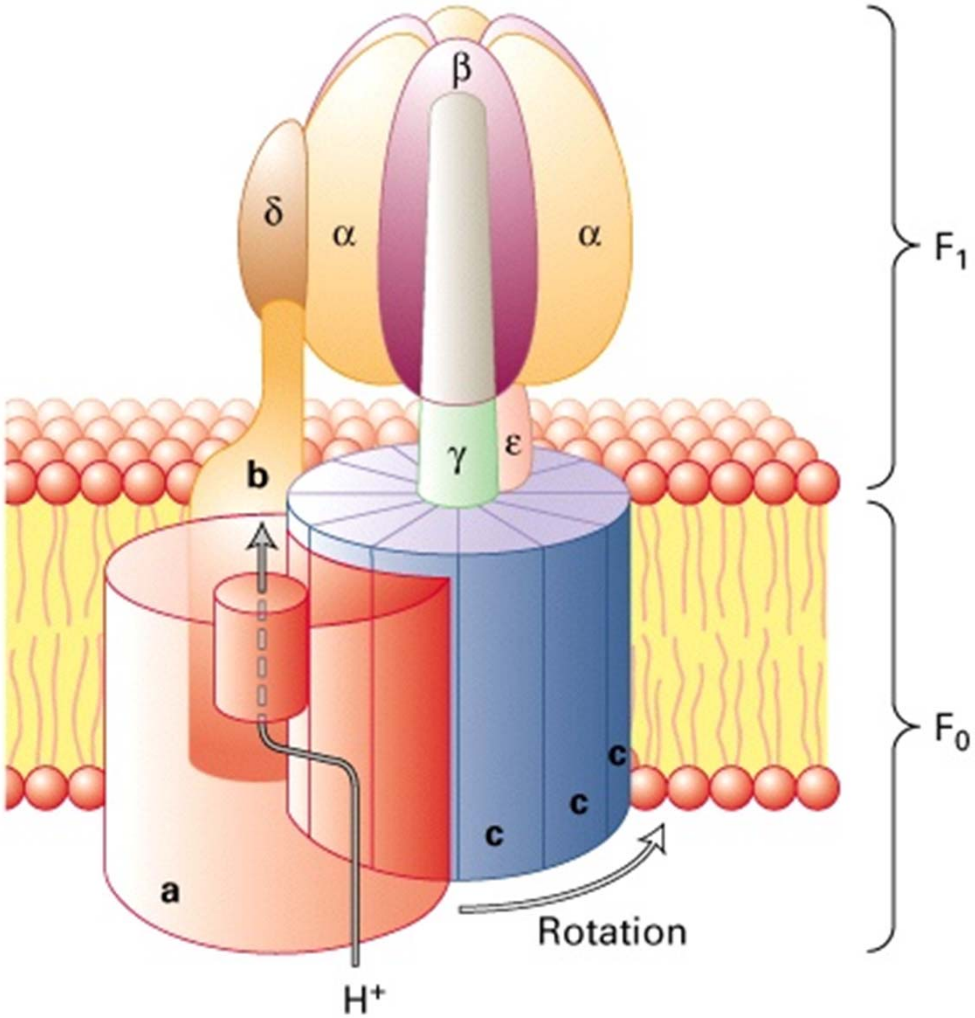




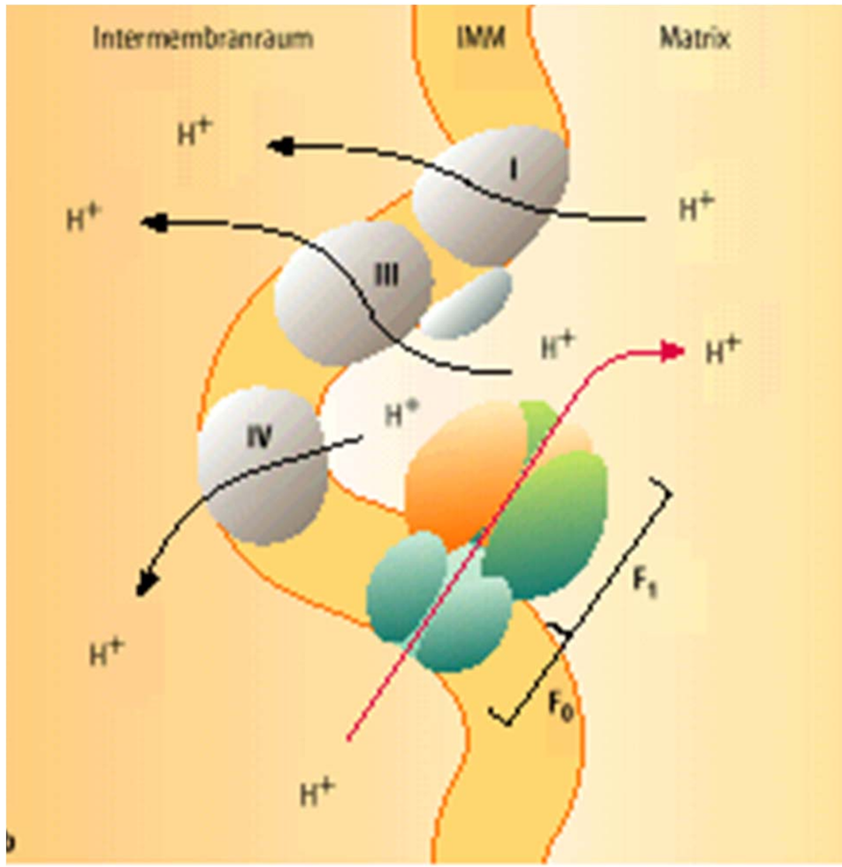
Prosthetic groups of cytochromes contain heme-bound iron



Structure and topology of F_1/F_0-ATPase



Eukaryotes



The proton-motive force drives p^+ back into the matrix providing energy for ATP formation catalyzed by F_1/F_0-ATP-ase.

Experimental evidence for the rotation of the c ring in E. coli F_1/F_0-ATPase

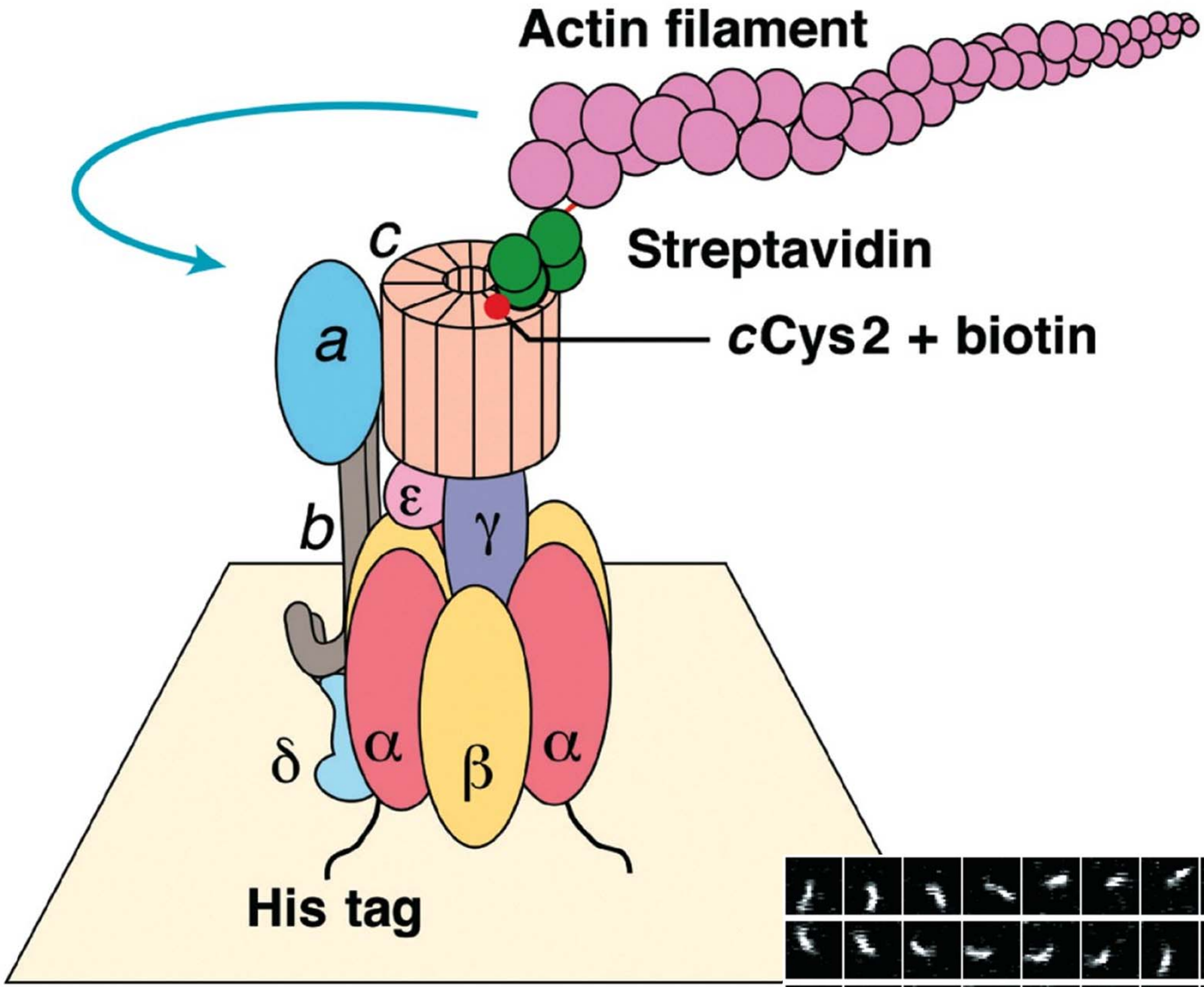


Figure 22-43a
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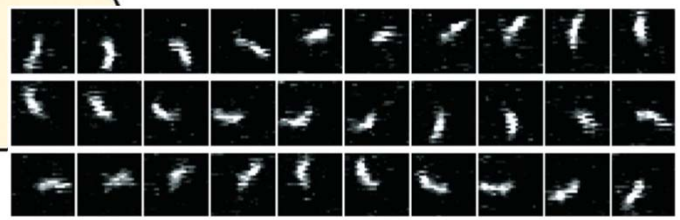


Figure 22-43b
Courtesy of Masamitsu Futai, Osaka University, Osaka, Japan

Schematic diagram of the action of the E. coli F_1/F_0-ATPase

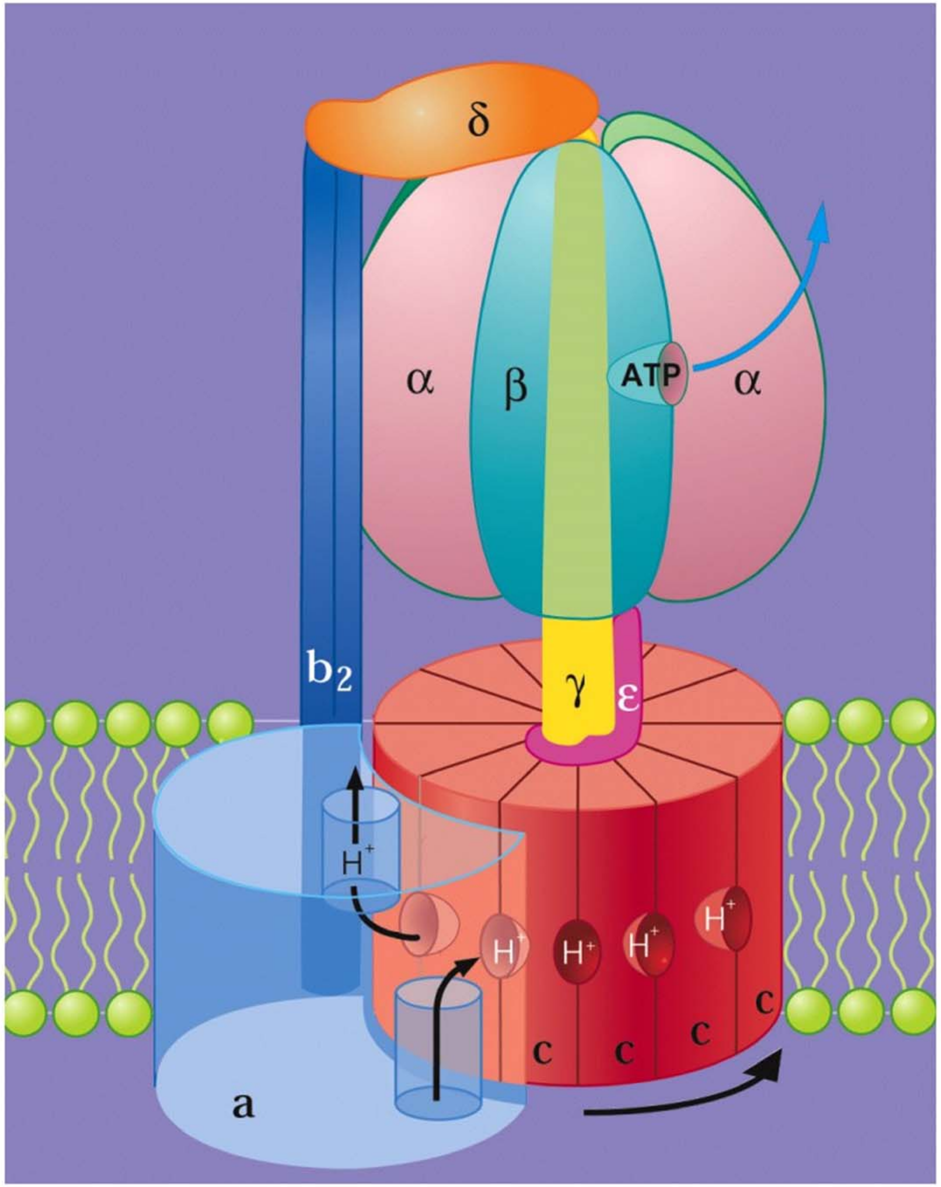
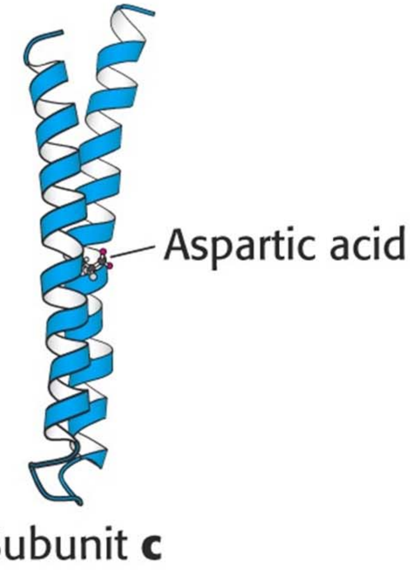
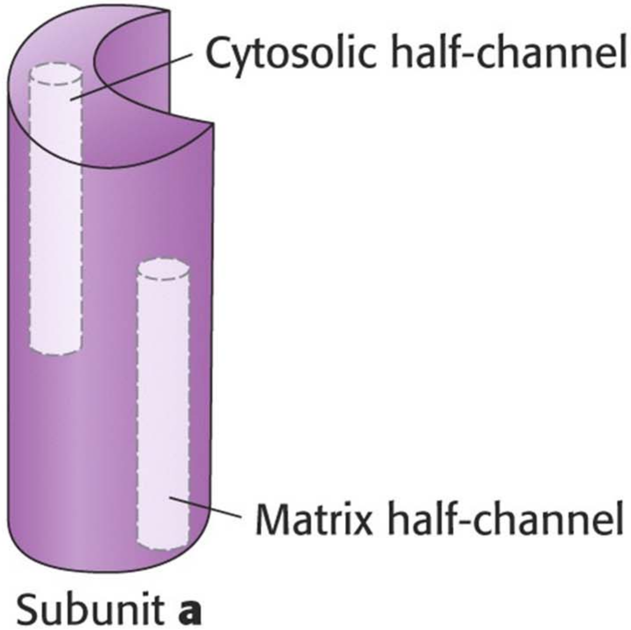
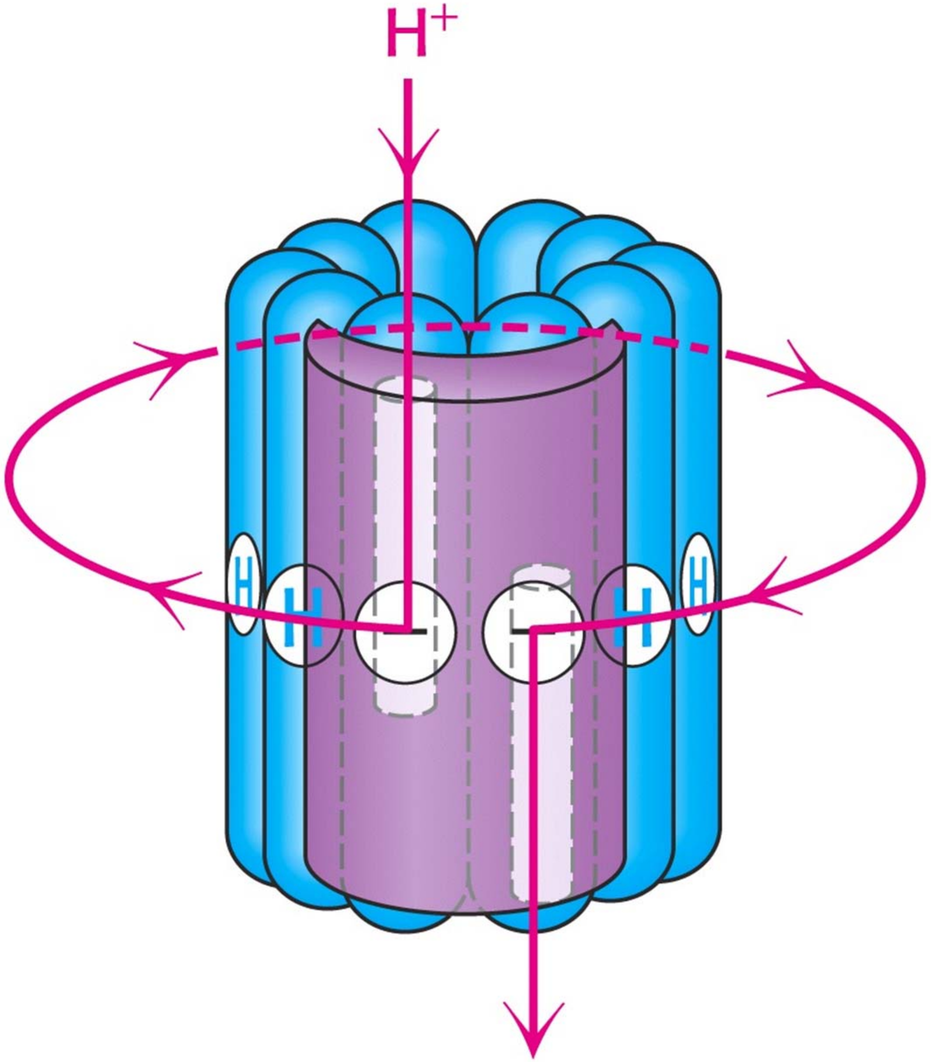


Figure 22-45
Courtesy of Richard Cross, State University of New York, Syracuse, New York

ATP synthase: conversion of electro-chemical energy into mechanical energy







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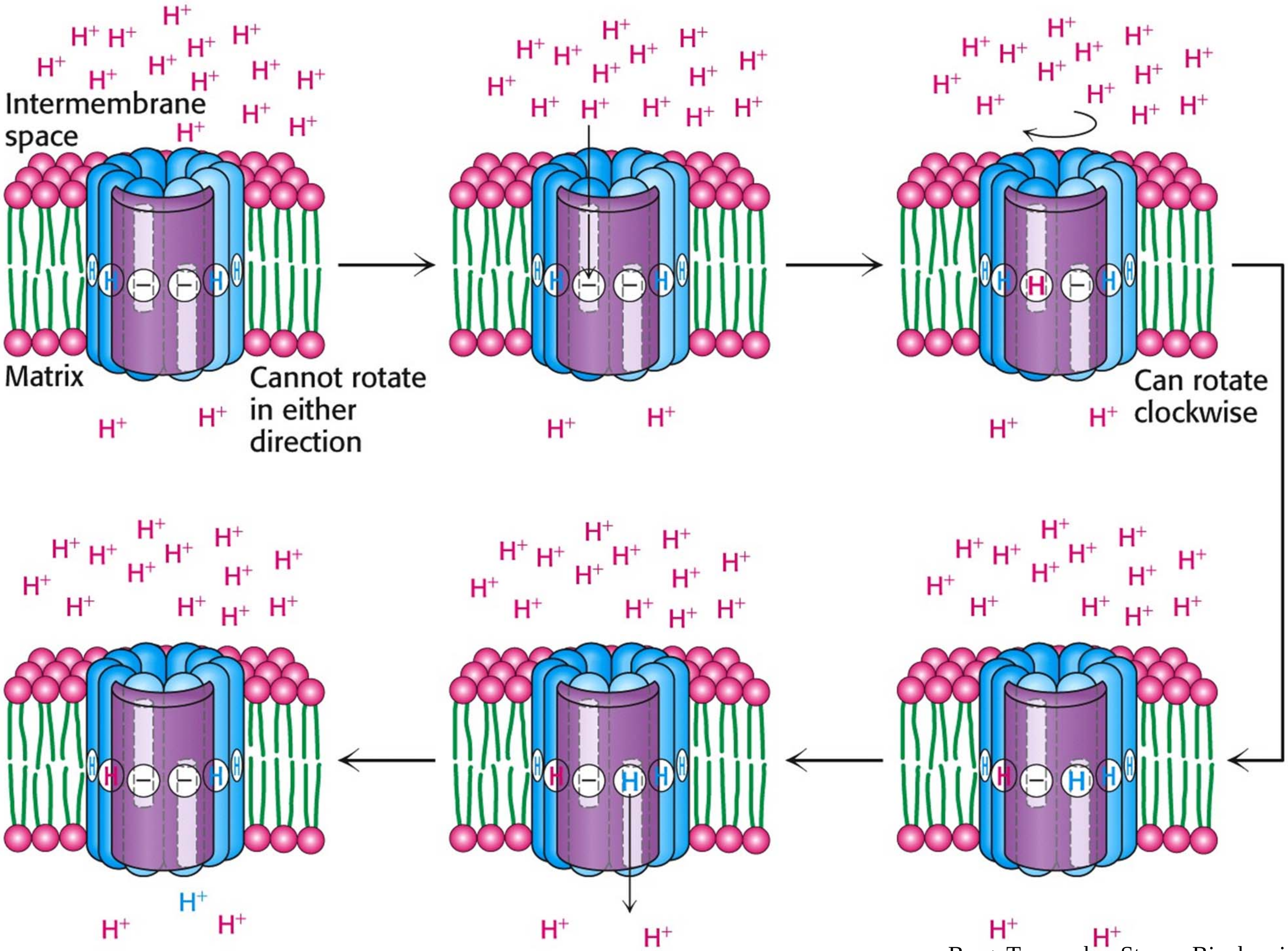
Proton path through the F_0-unit of ATP-synthase



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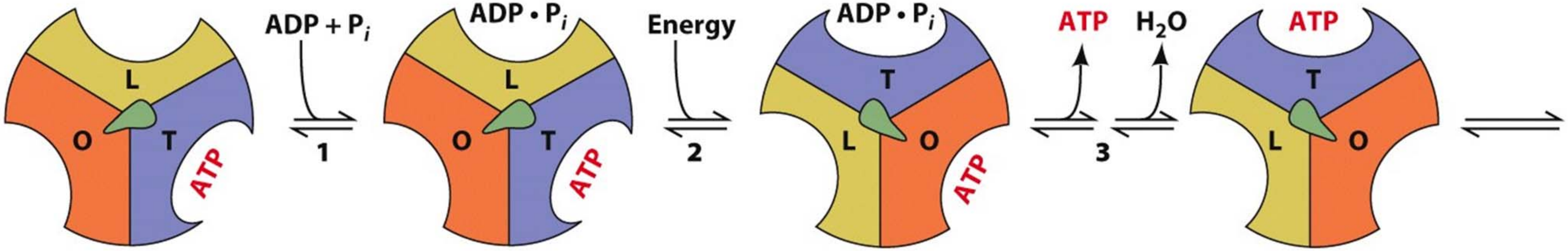
Mechanism of ATP synthase

Energy-dependent conformational changes: O = open, T = tight, L = loose



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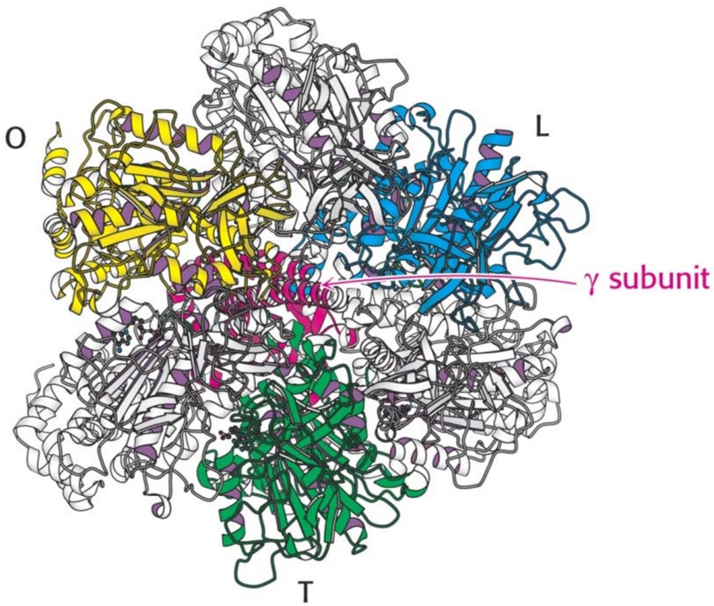

ATP yield from glucose degradation:

Anaerobic: 2 ATP

Aerobic: 30 ATP from 10 NADH
4 ATP from 2 FADH
2 ATP corresp. 2 GTP
2 ATP from glycolysis

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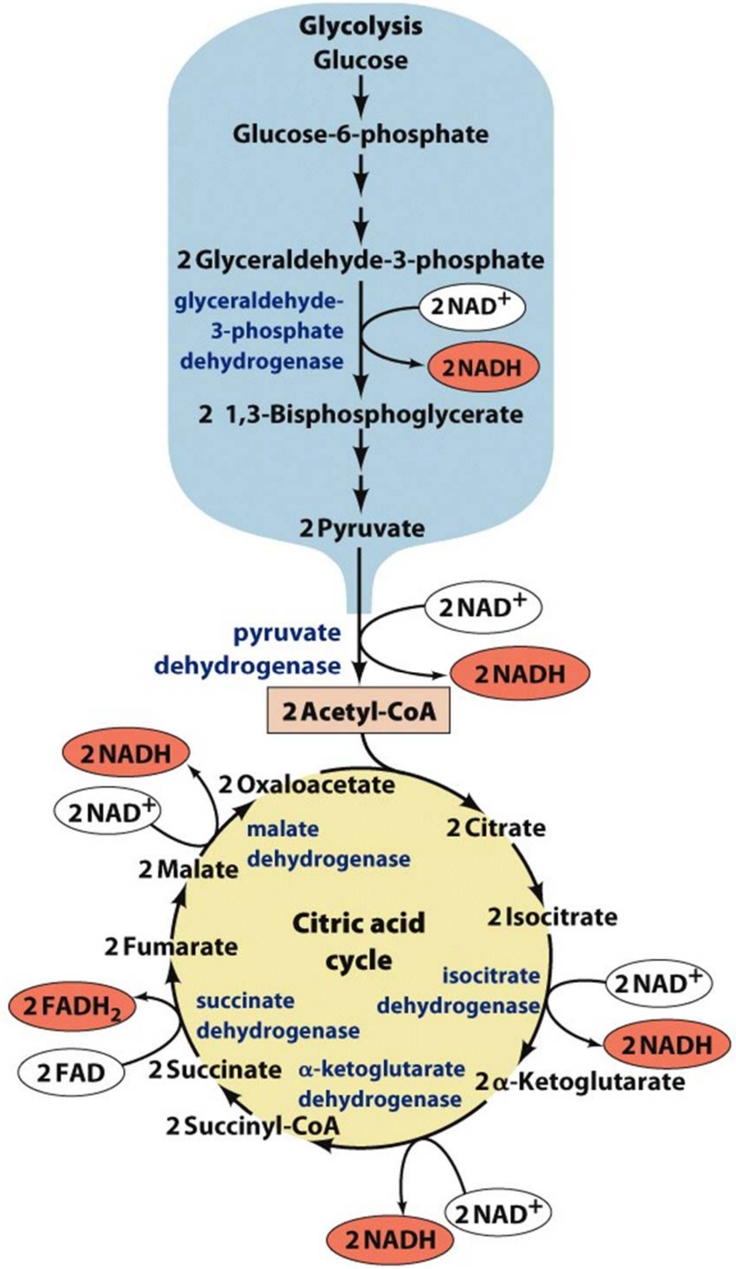
38 ATP

Pasteur effect!!!



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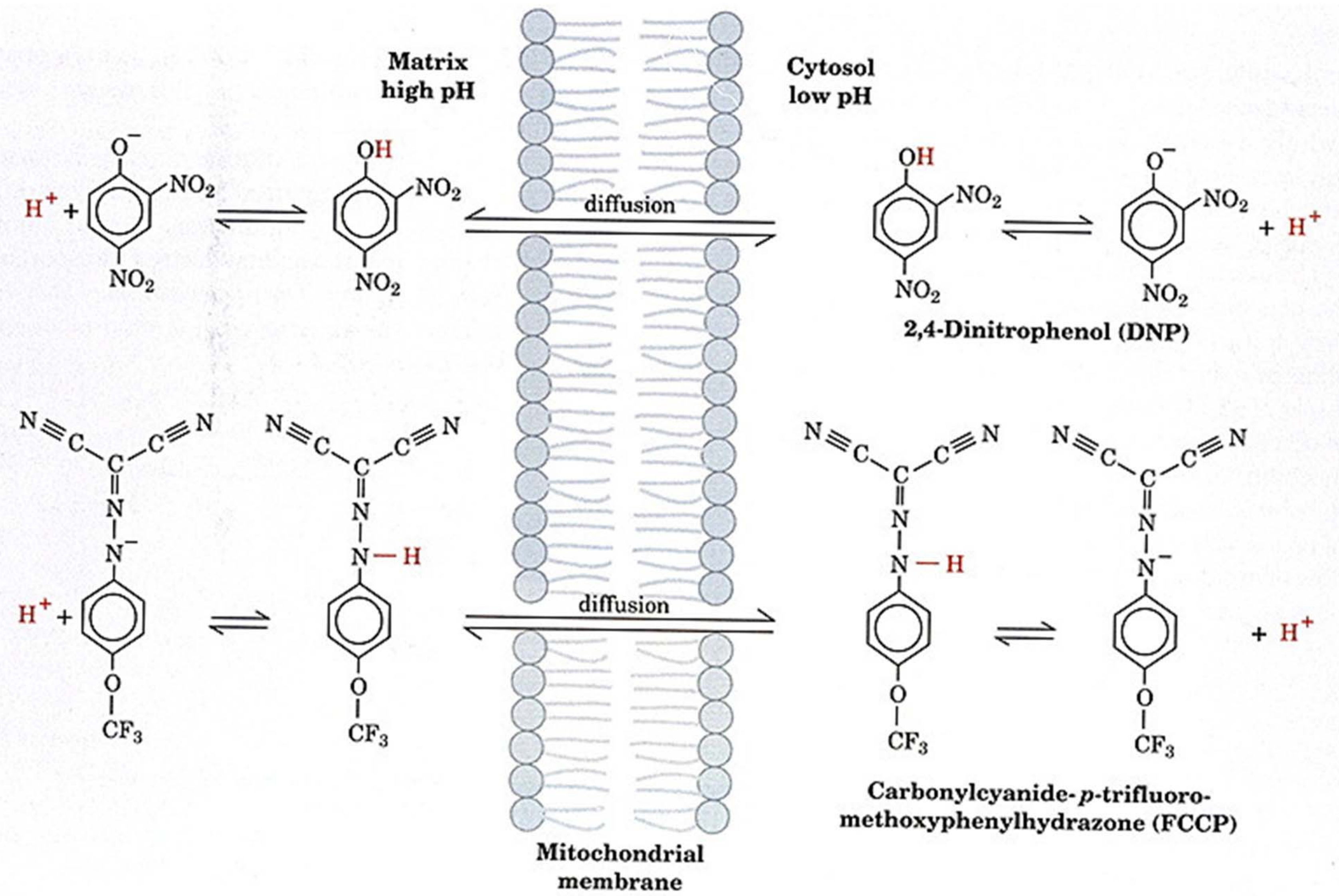
Proton-transporting ionophores uncouple oxidative phosphorylation



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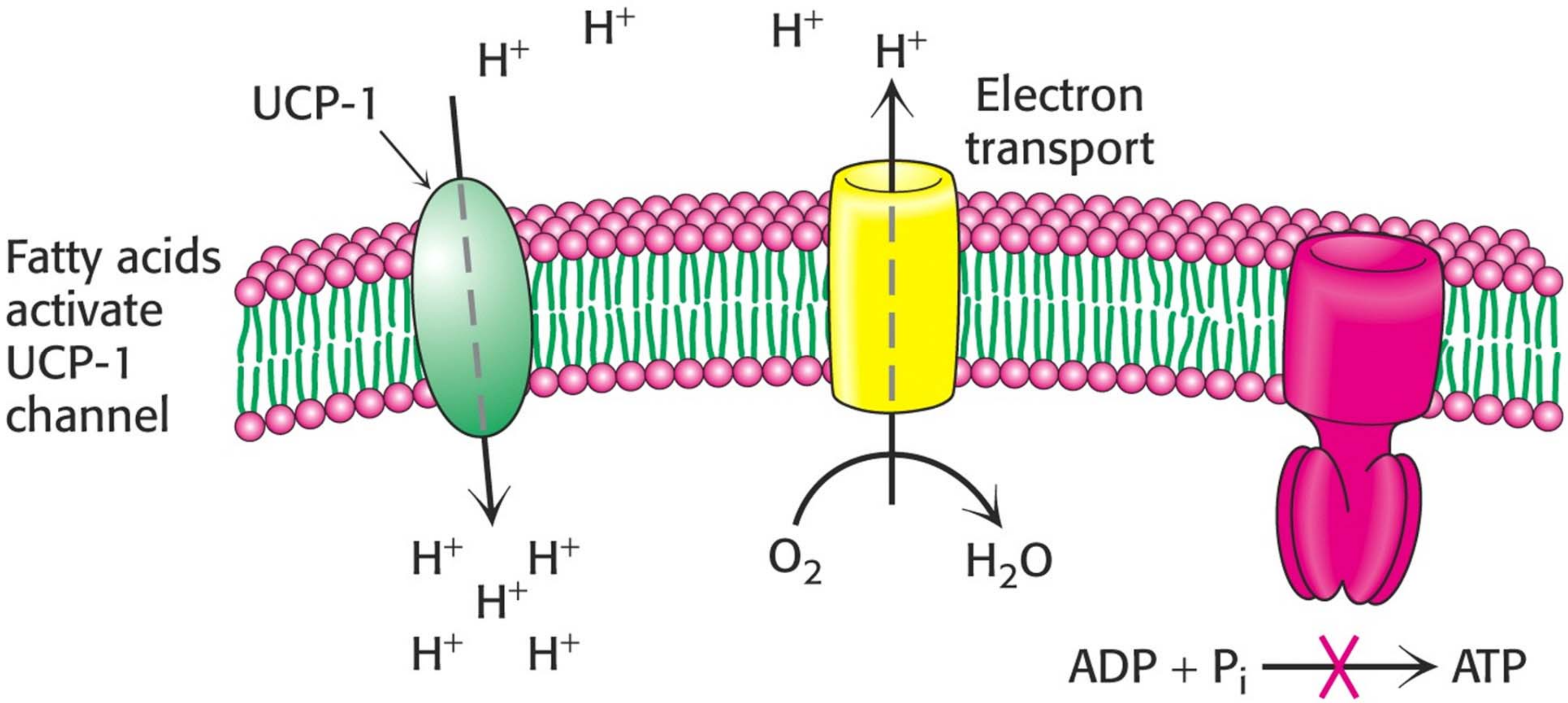
Heat generation by uncoupled brown fat mitochondria

Thermogenin (UCP, uncoupling protein):



GDP: inhibitor of UCP-1

The topology of the F_0/F_1-ATPase in membranes and the direction of proton flow in bacteria, mitochondria, chloroplasts