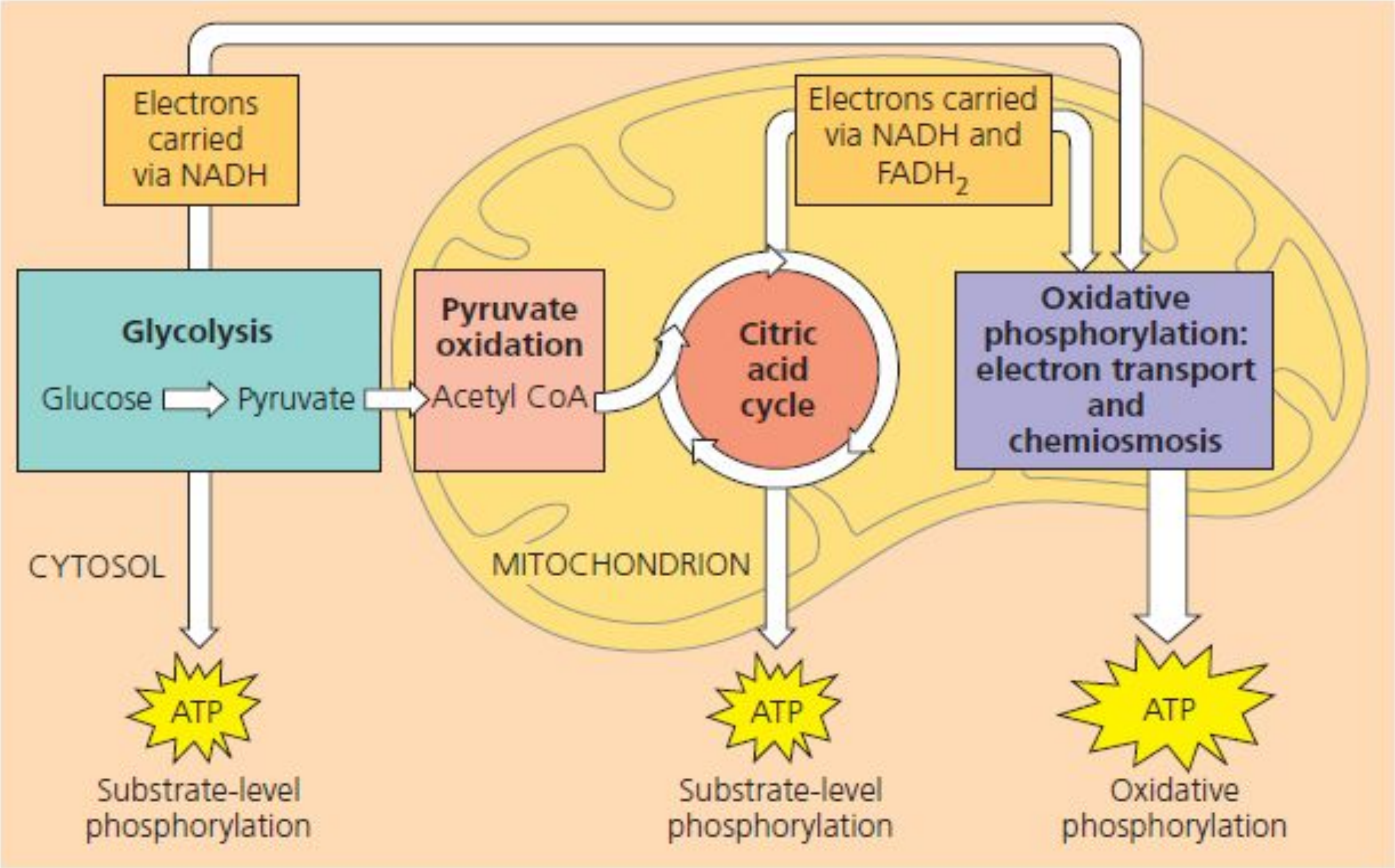
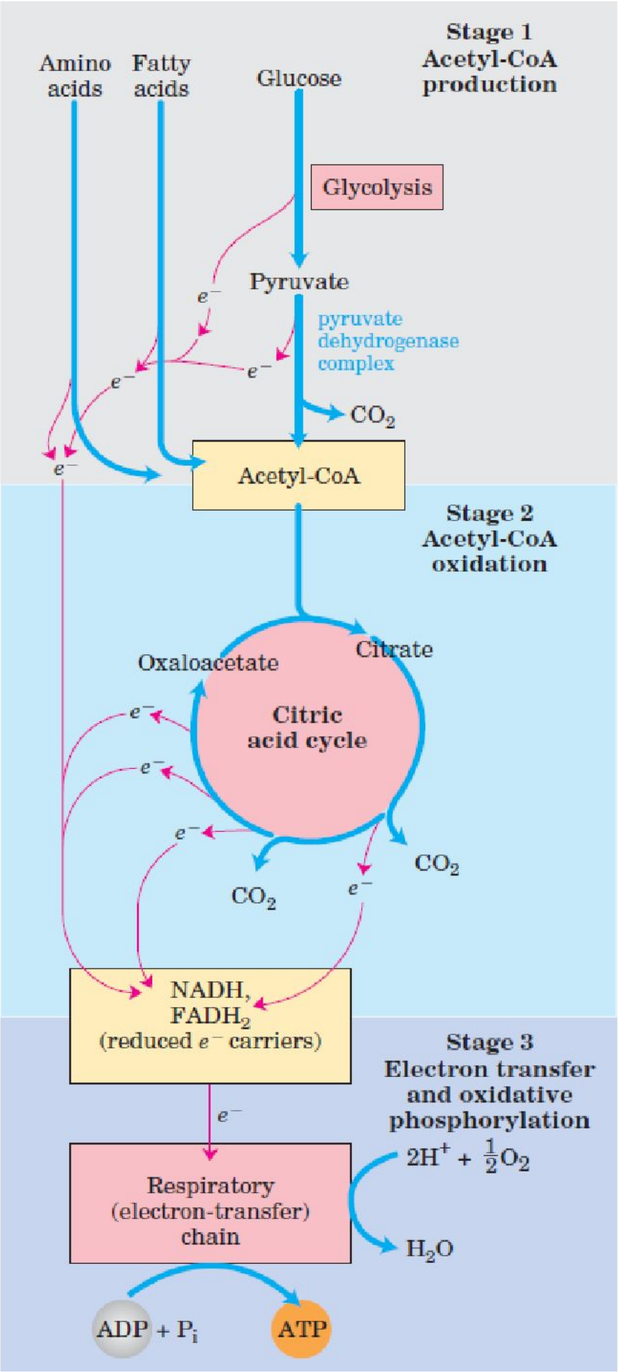
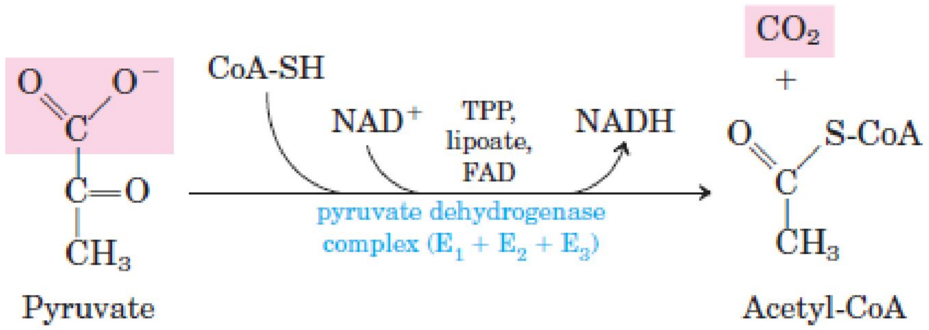
Цикл Кребса.

Дыхательная цепь.

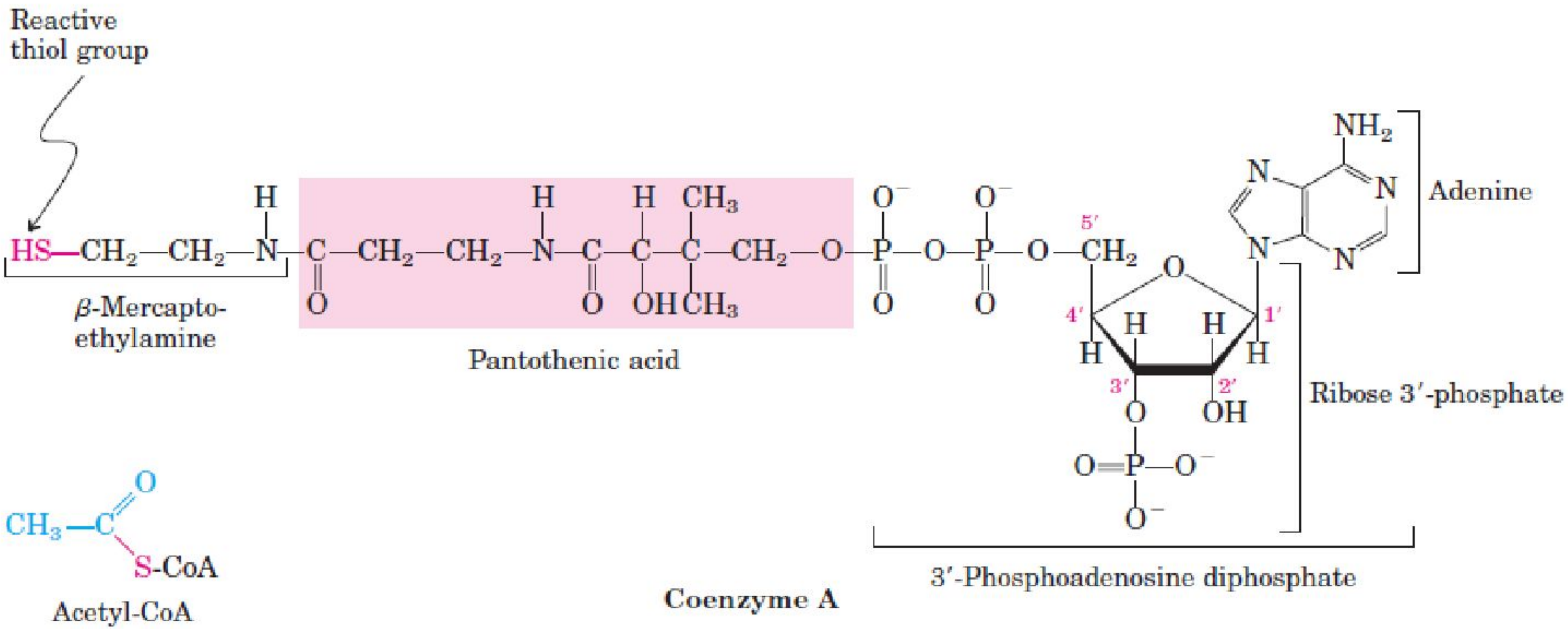

Electrons carried via NADH
Electrons carried via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Pyruvate oxidation
Acetyl CoA
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
CYTOSOL
MITOCHONDRION
ATP
ATP
ATP
Substrate-level phosphorylation
Substrate-level phosphorylation
Oxidative phosphorylation


Stage 1
Acetyl-CoA
production
Amino acids
Fatty acids
Glucose
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
e^-
CO_2
Acetyl-CoA
Stage 2
Acetyl-CoA
oxidation
Oxaloacetate
Citrate
Citric acid cycle
CO_2
CO_2
NADH,
$FADH_2$
(reduced e^- carriers)
Stage 3
Electron transfer
and oxidative
phosphorylation
$2H^+ + \frac{1}{2}O_2$
H_2O
Respiratory (electron-transfer) chain
ADP + P_i
ATP

Окислительное декарбоксилирование Pyr (PDH)



$\Delta G'^{\circ} = -33.4$ kJ/mol



Coenzyme A

Коферменты PDH

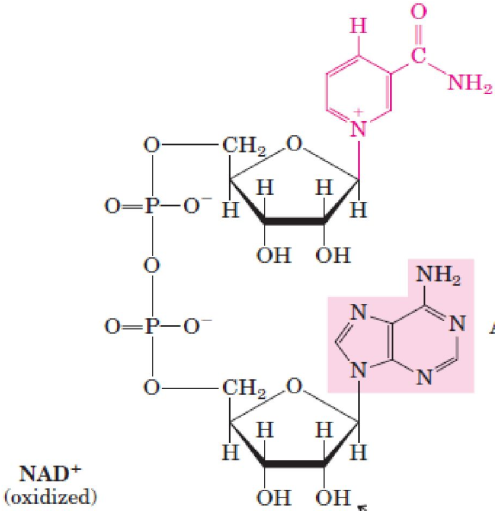
1) CoA

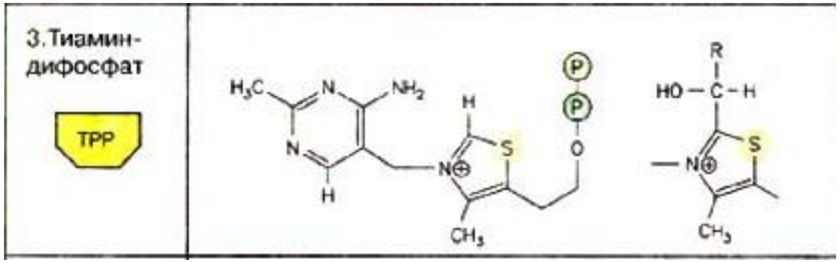
2) NAD

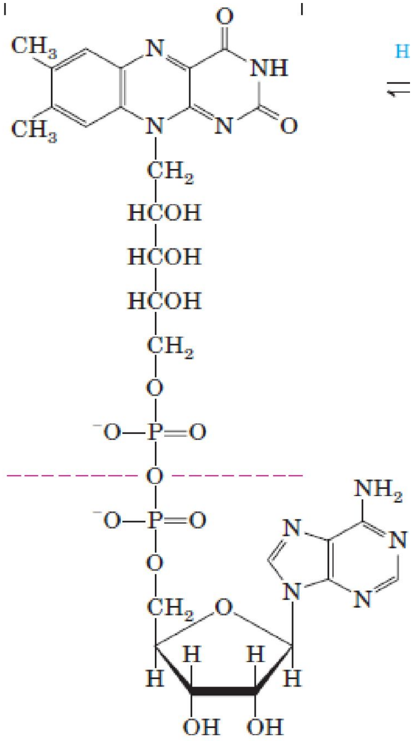
3) TPP

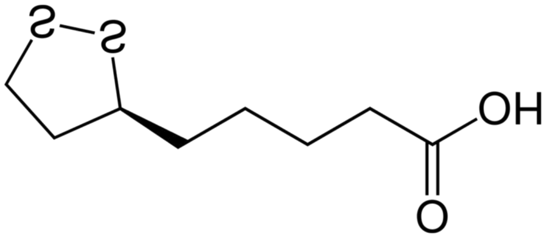
4) FAD

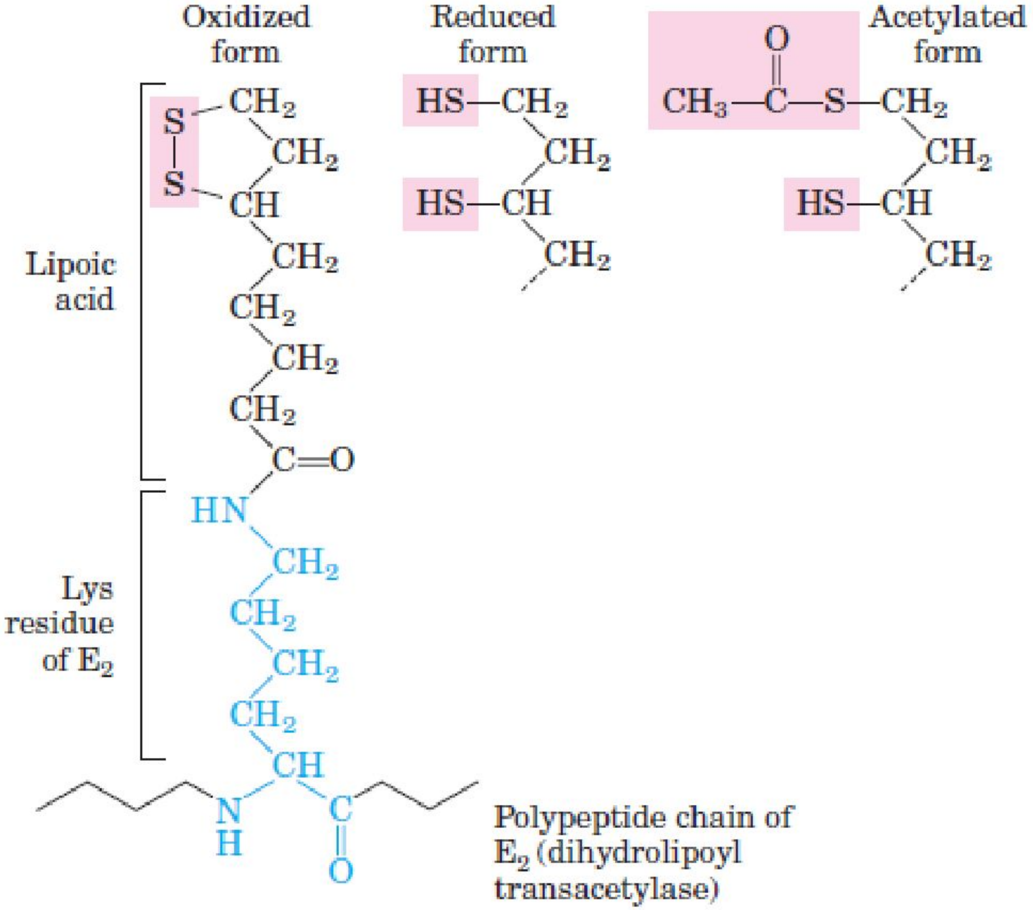
5) липоат










Oxidized form

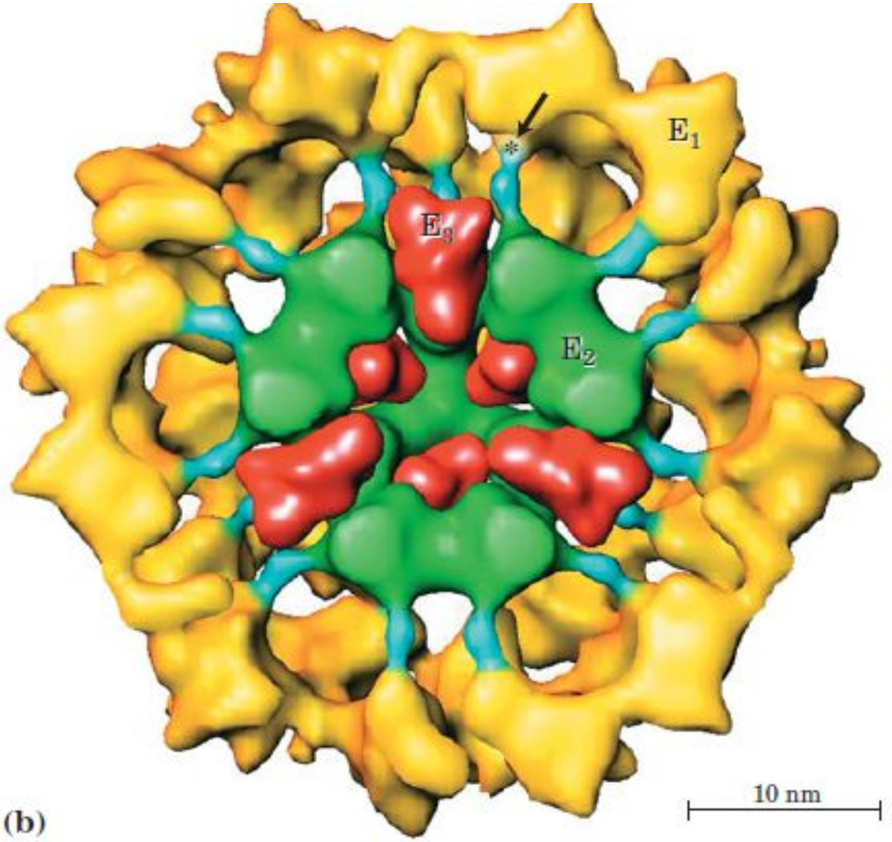
Reduced form

Acetylated form

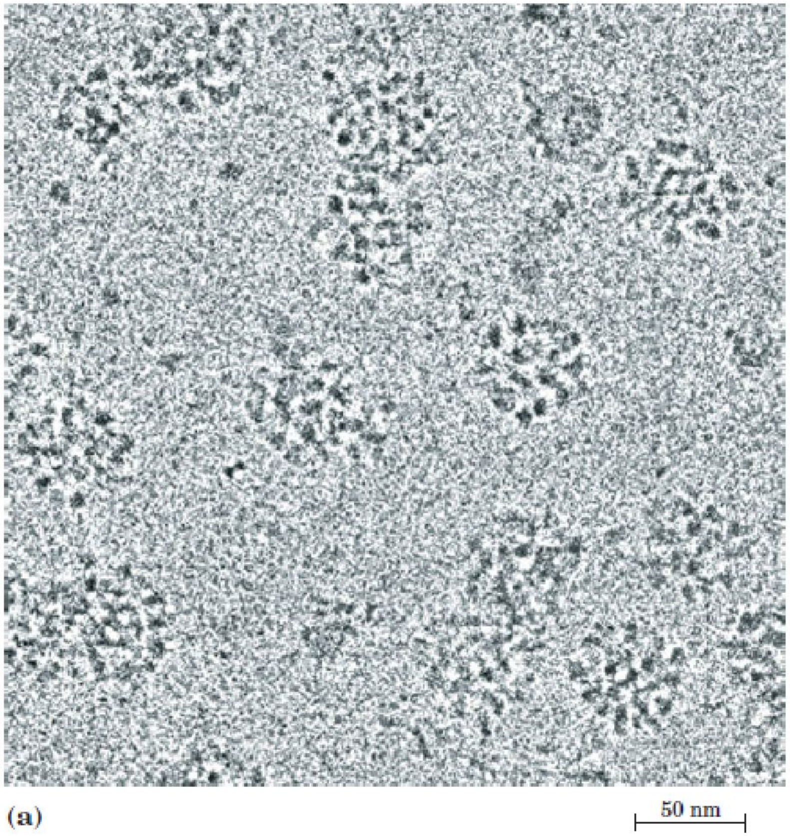
Lipoic acid

Lys residue of E_2

Polypeptide chain of E_2 (dihydrolipoyl transacetylase)



(b)

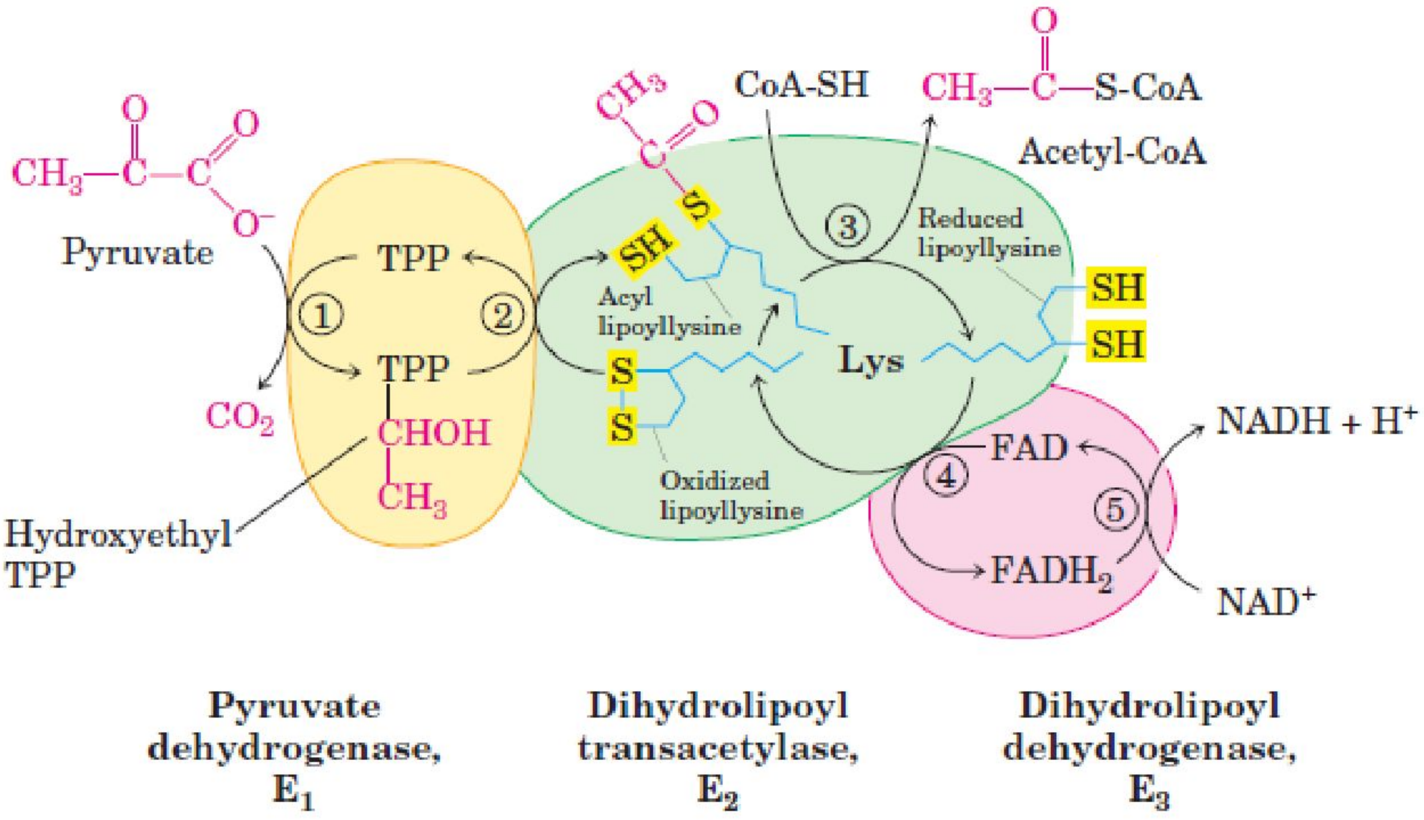


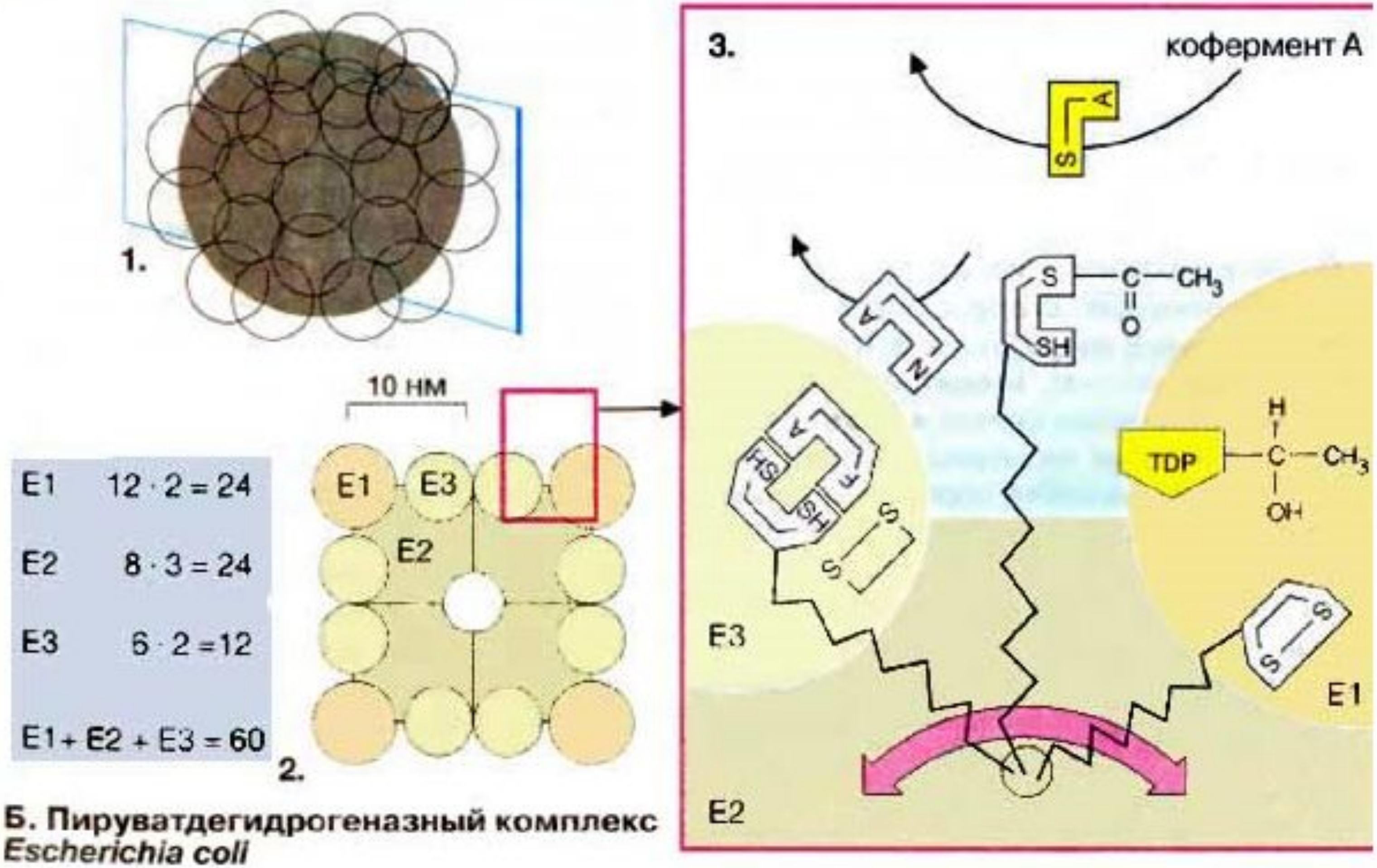
(a)

E1 – пируват дегидрогеназа

E2 – дигидролипоил трансацетилаза

E3 – дигидролипоил дегидрогеназа

CoA-SH
CH3—C—S-CoA
O
Acetyl-CoA
CH3
C=O
S
SH
O
CH3—C—C
O
O−
Pyruvate
TPP
①
②
TPP
CO2
CHOH
CH3
Hydroxyethyl TPP
Acyl lipoyllysine
S
S
Oxidized lipoyllysine
③
Reduced lipoyllysine
Lys
SH
SH
④
FAD
⑤
FADH2
NADH + H+
NAD+
Pyruvate dehydrogenase, E1
Dihydrolipoyl transacetylase, E2
Dihydrolipoyl dehydrogenase, E3

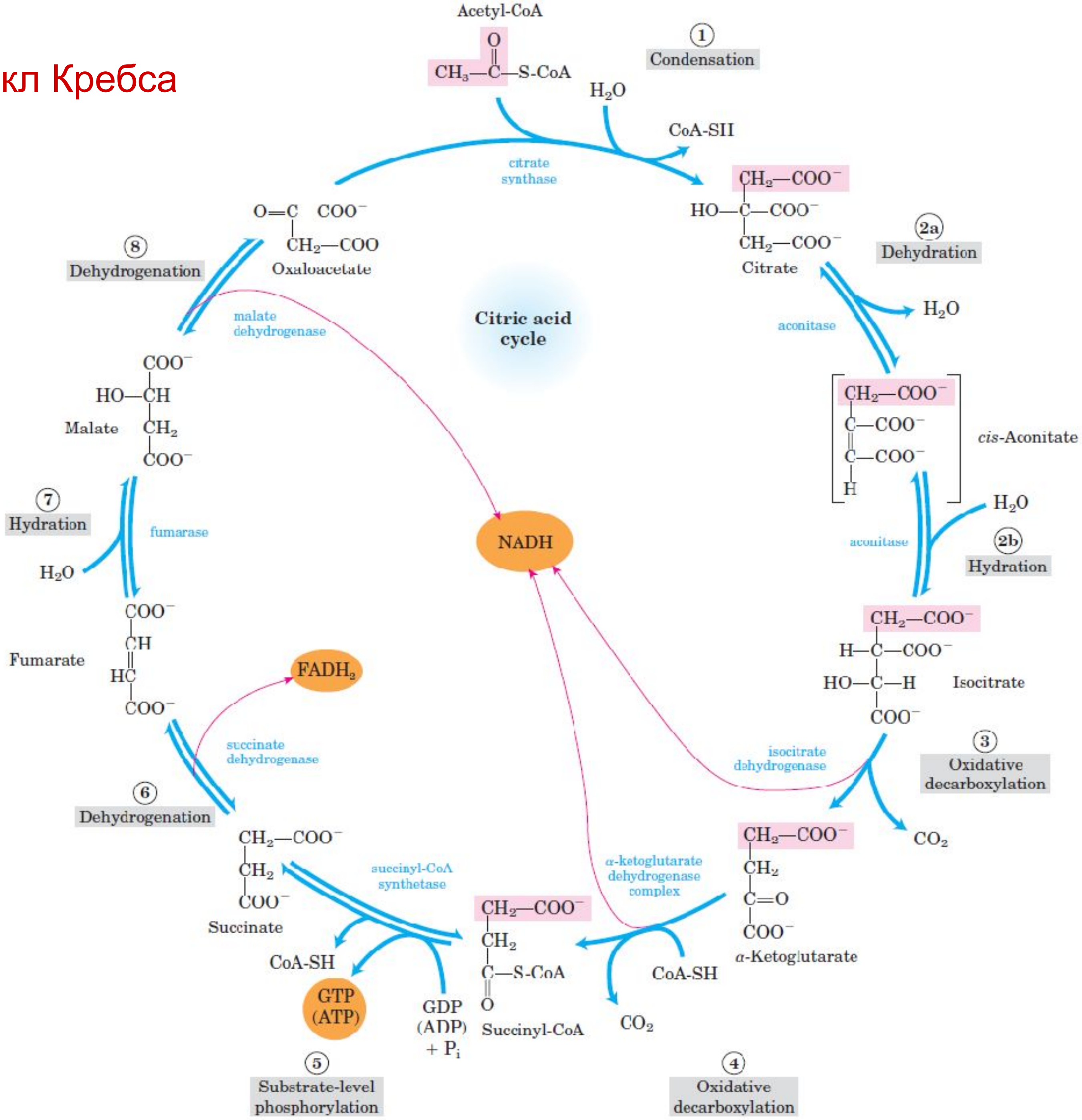


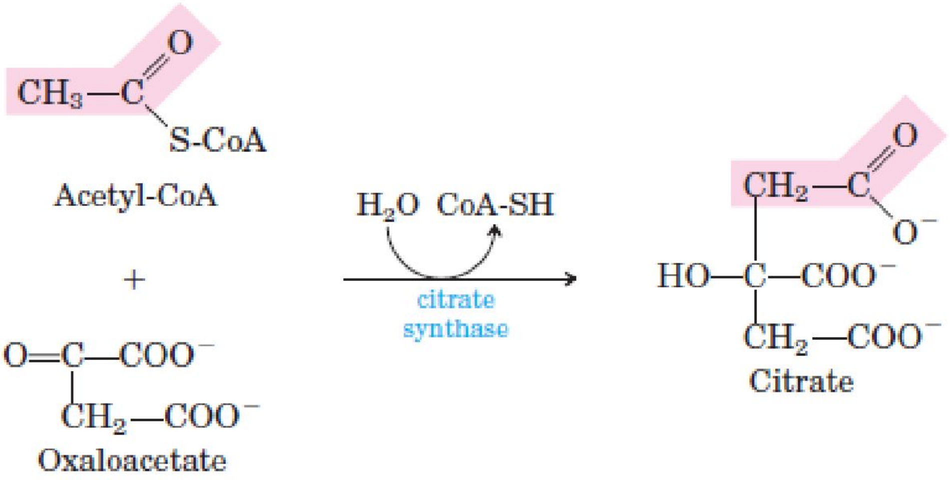
E1	12 · 2 = 24
E2	8 · 3 = 24
E3	6 · 2 = 12

E1 + E2 + E3 = 60

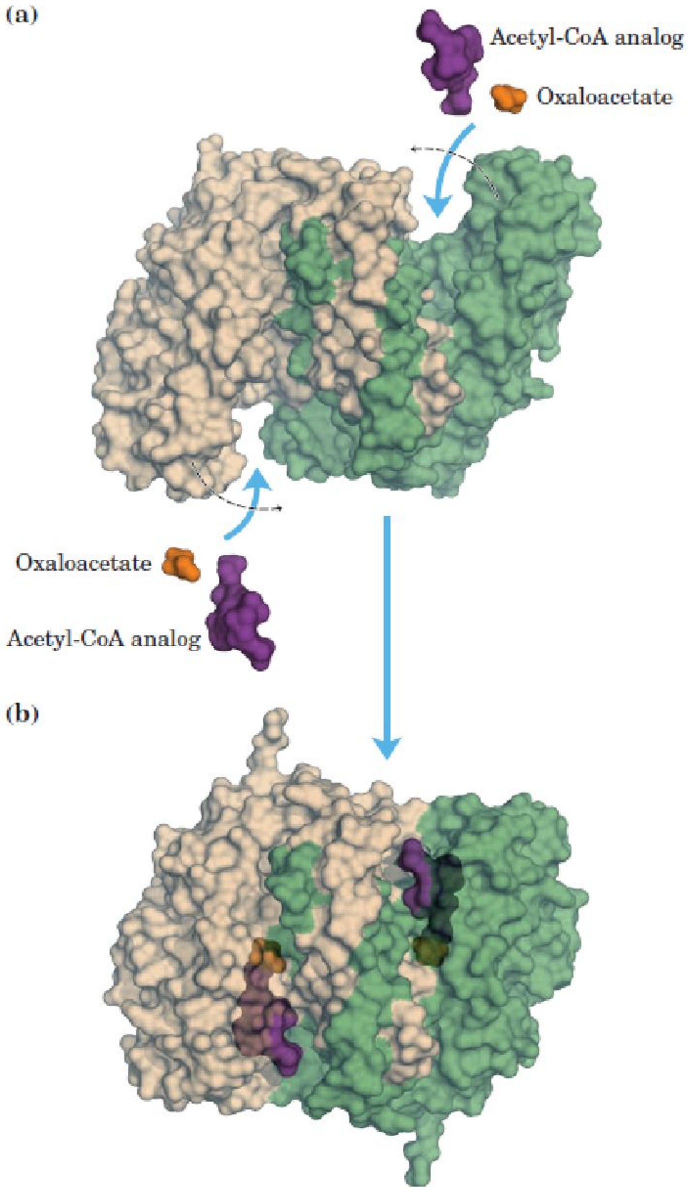
Б. Пируватдегидрогеназный комплекс ***Escherichia coli***

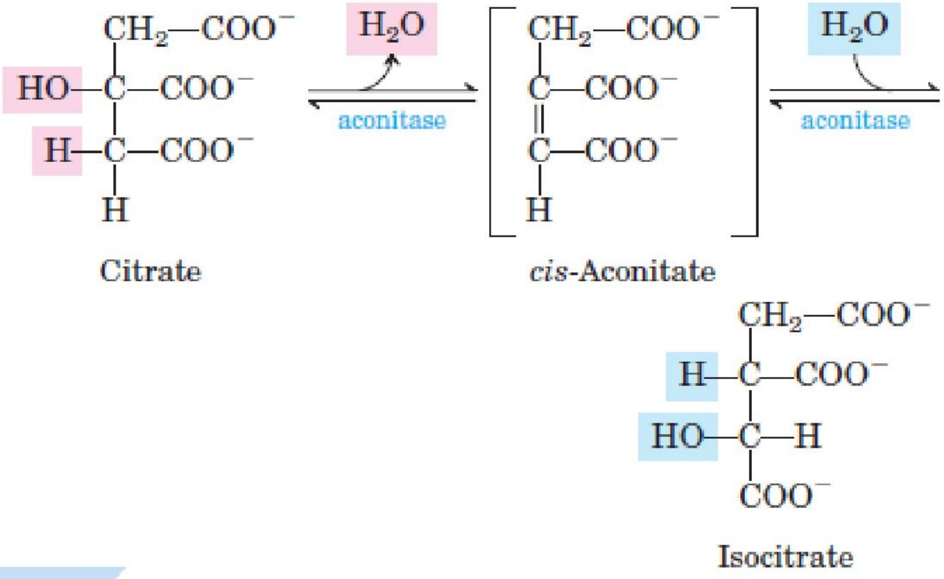
Цикл Кребса


Acetyl-CoA
O
CH₃—C—S-CoA
① Condensation
H₂O
CoA-SH
citrate synthase
CH₂—COO⁻
HO—C—COO⁻
CH₂—COO⁻
Citrate
2a Dehydration
aconitase
H₂O
CH₂—COO⁻
C—COO⁻
C—COO⁻
H
cis-Aconitate
H₂O
aconitase
2b Hydration
CH₂—COO⁻
H—C—COO⁻
HO—C—H
COO⁻
Isocitrate
③ Oxidative decarboxylation
isocitrate dehydrogenase
CO₂
CH₂—COO⁻
CH₂
C=O
COO⁻
α-Ketoglutarate
α-ketoglutarate dehydrogenase complex
CoA-SH
CO₂
④ Oxidative decarboxylation
CH₂—COO⁻
CH₂
C—S-CoA
O
Succinyl-CoA
succinyl-CoA synthetase
GDP (ADP) + Pᵢ
GTP (ATP)
CoA-SH
⑤ Substrate-level phosphorylation
CH₂—COO⁻
CH₂
COO⁻
Succinate
⑥ Dehydrogenation
succinate dehydrogenase
FADH₂
COO⁻
CH
HC
COO⁻
Fumarate
fumarase
H₂O
⑦ Hydration
COO⁻
HO—CH
CH₂
COO⁻
Malate
malate dehydrogenase
⑧ Dehydrogenation
O=C COO⁻
CH₂—COO
Oxaloacetate
Citric acid cycle
NADH

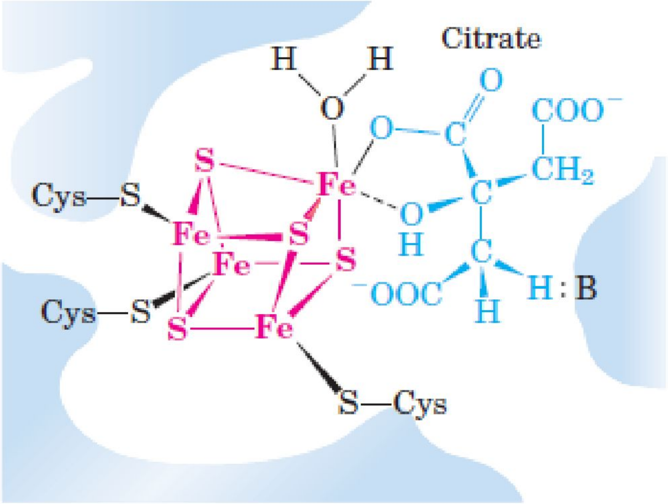


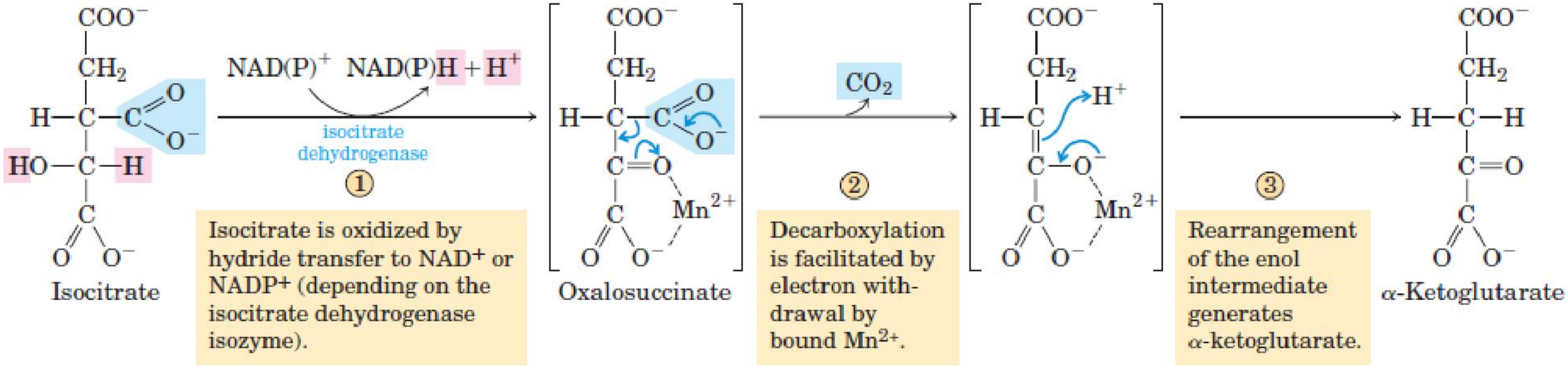
$\Delta G'^{\circ} = -32.2$ kJ/mol





$\Delta G'^{\circ} = 13.3$ kJ/mol

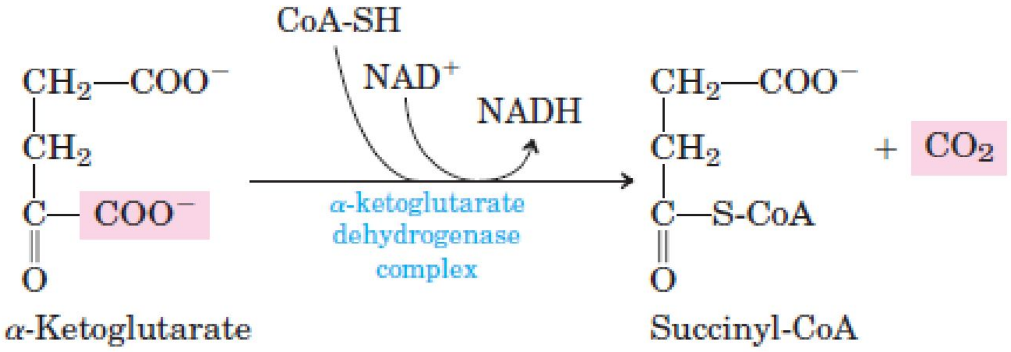




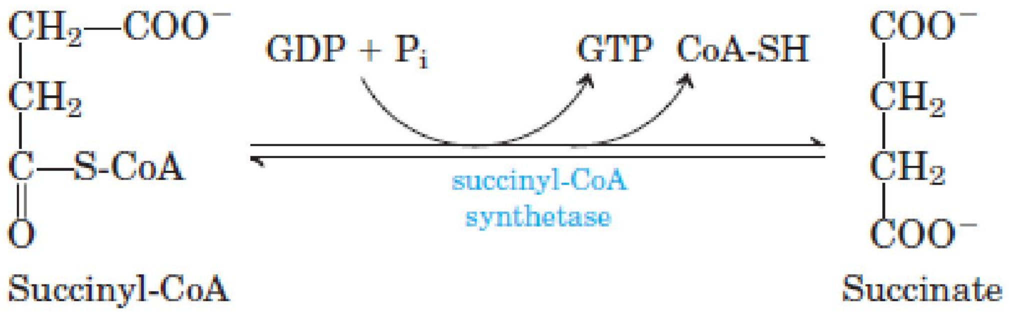
① Isocitrate is oxidized by hydride transfer to NAD$^+$ or NADP$^+$ (depending on the isocitrate dehydrogenase isozyme).

② Decarboxylation is facilitated by electron withdrawal by bound Mn^{2+}.

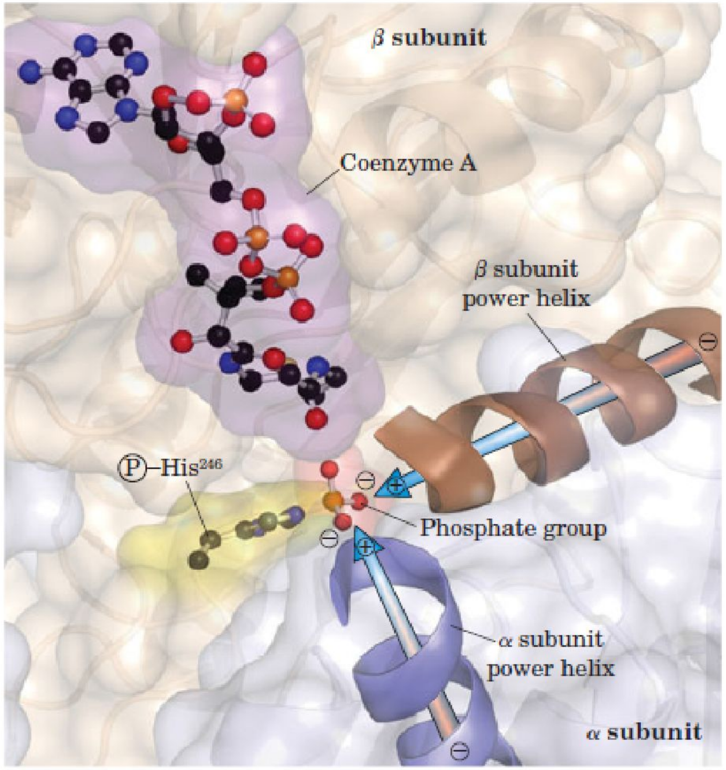
③ Rearrangement of the enol intermediate generates α-ketoglutarate.

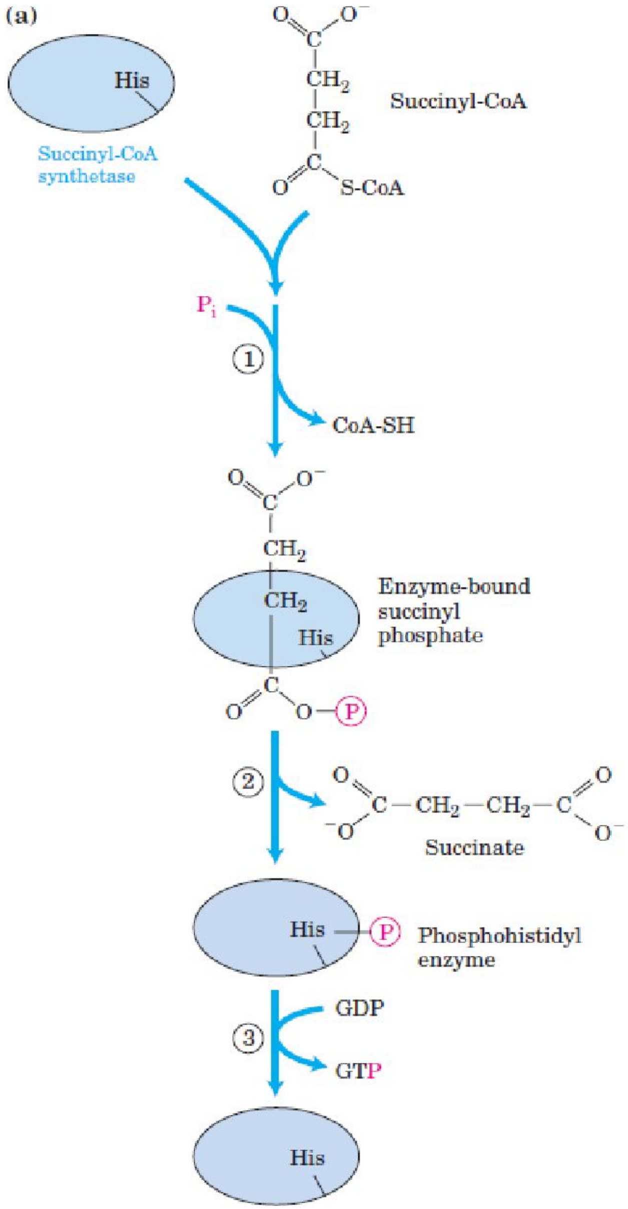


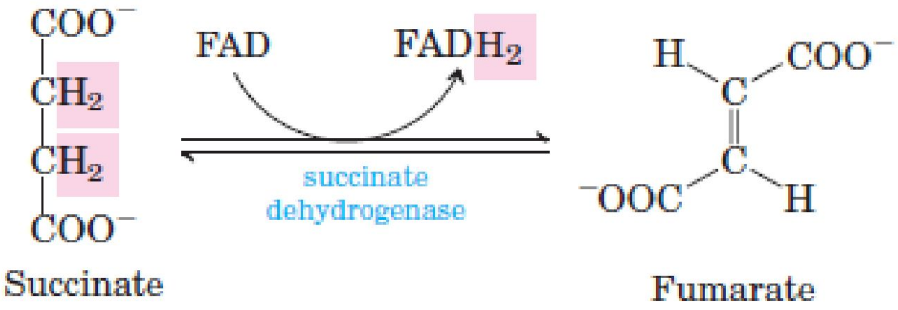
$\Delta G'^{\circ} = -33.5 \text{ kJ/mol}$



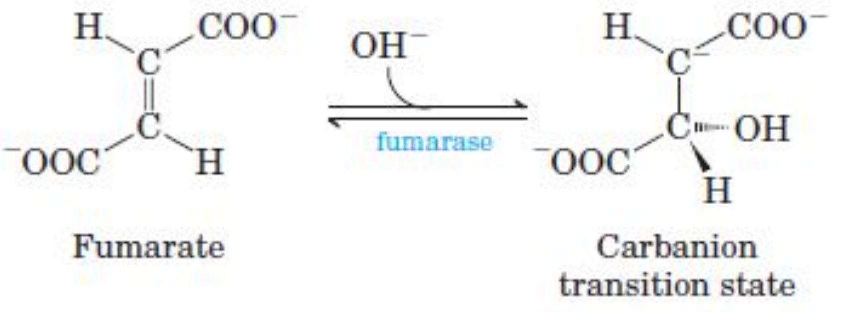
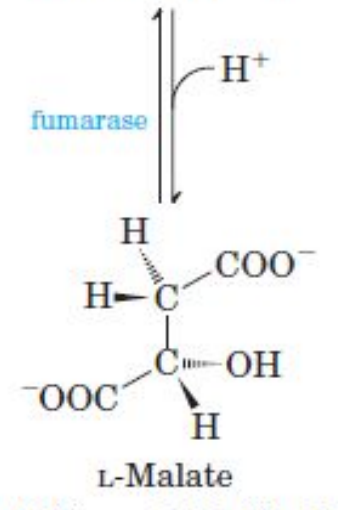
$\Delta G'^{\circ} = -2.9$ kJ/mol



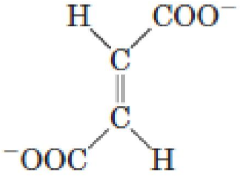


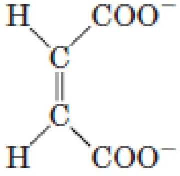


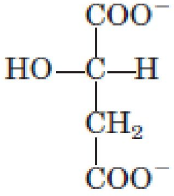
$\Delta G'^{\circ} = 0$ kJ/mol

$\Delta G'^{\circ} = -3.8$ kJ/mol

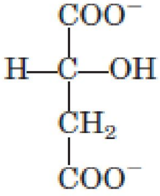

Fumarate


Maleate



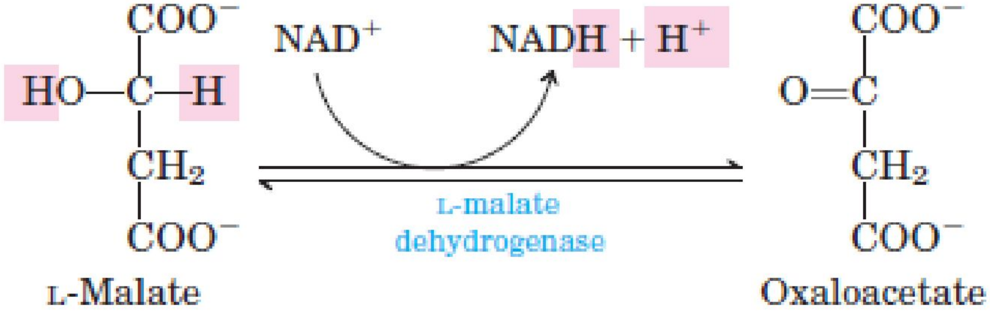
$$\begin{array}{c} COO^- \\ | \\ HO-C-H \\ | \\ CH_2 \\ | \\ COO^- \end{array}$$

L-Malate

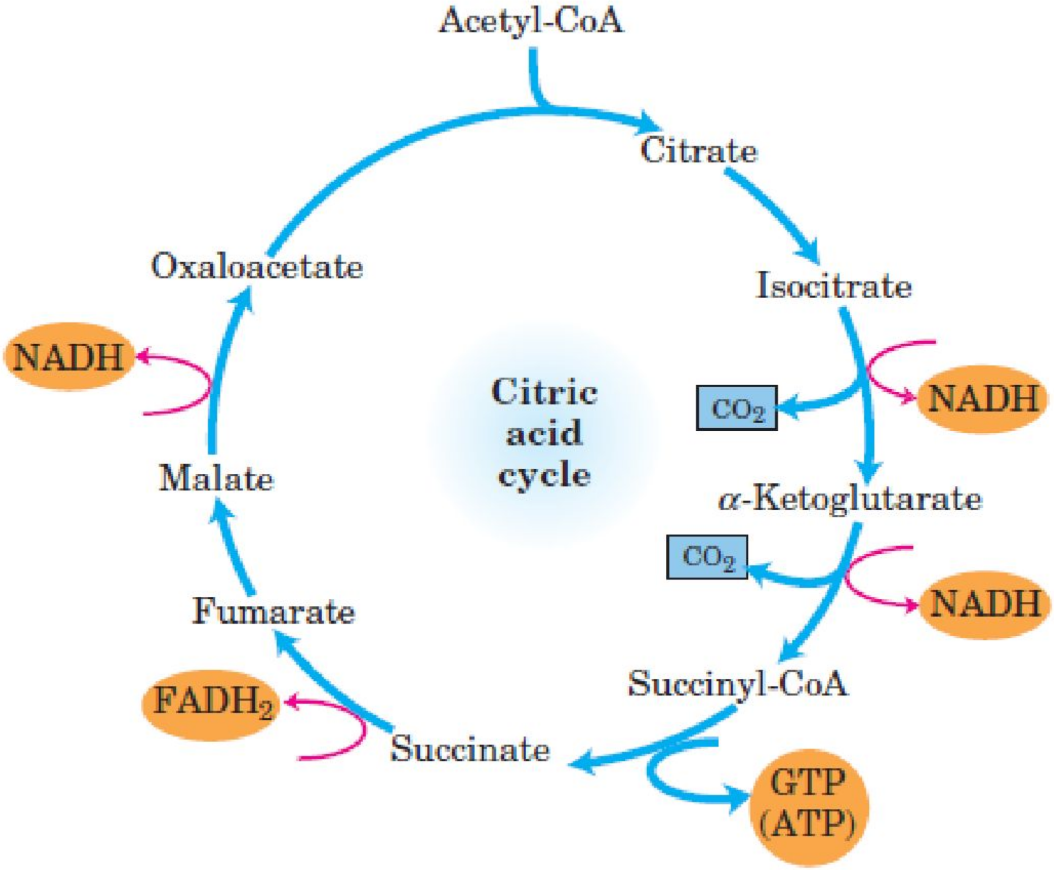


$$\begin{array}{c} COO^- \\ | \\ H-C-OH \\ | \\ CH_2 \\ | \\ COO^- \end{array}$$

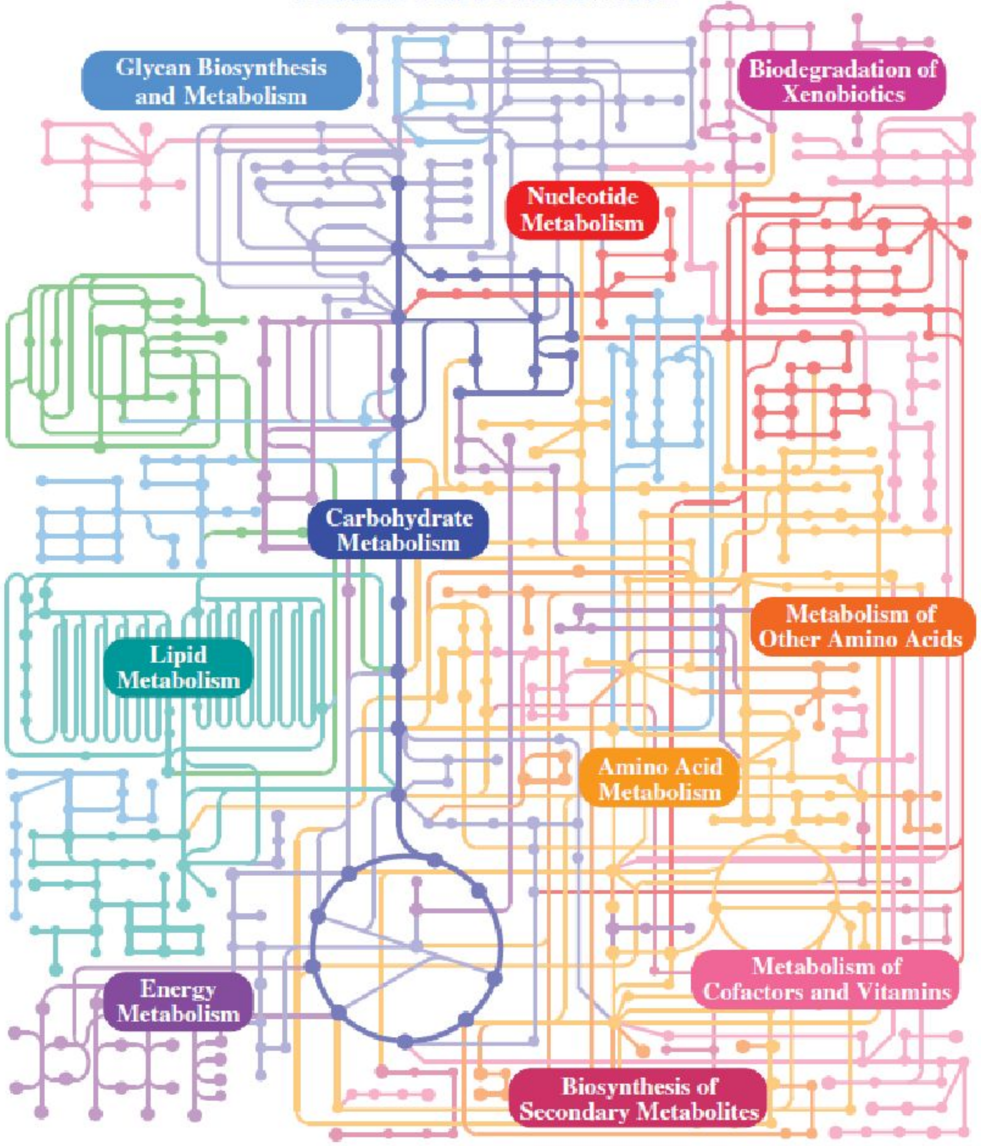
D-Malate

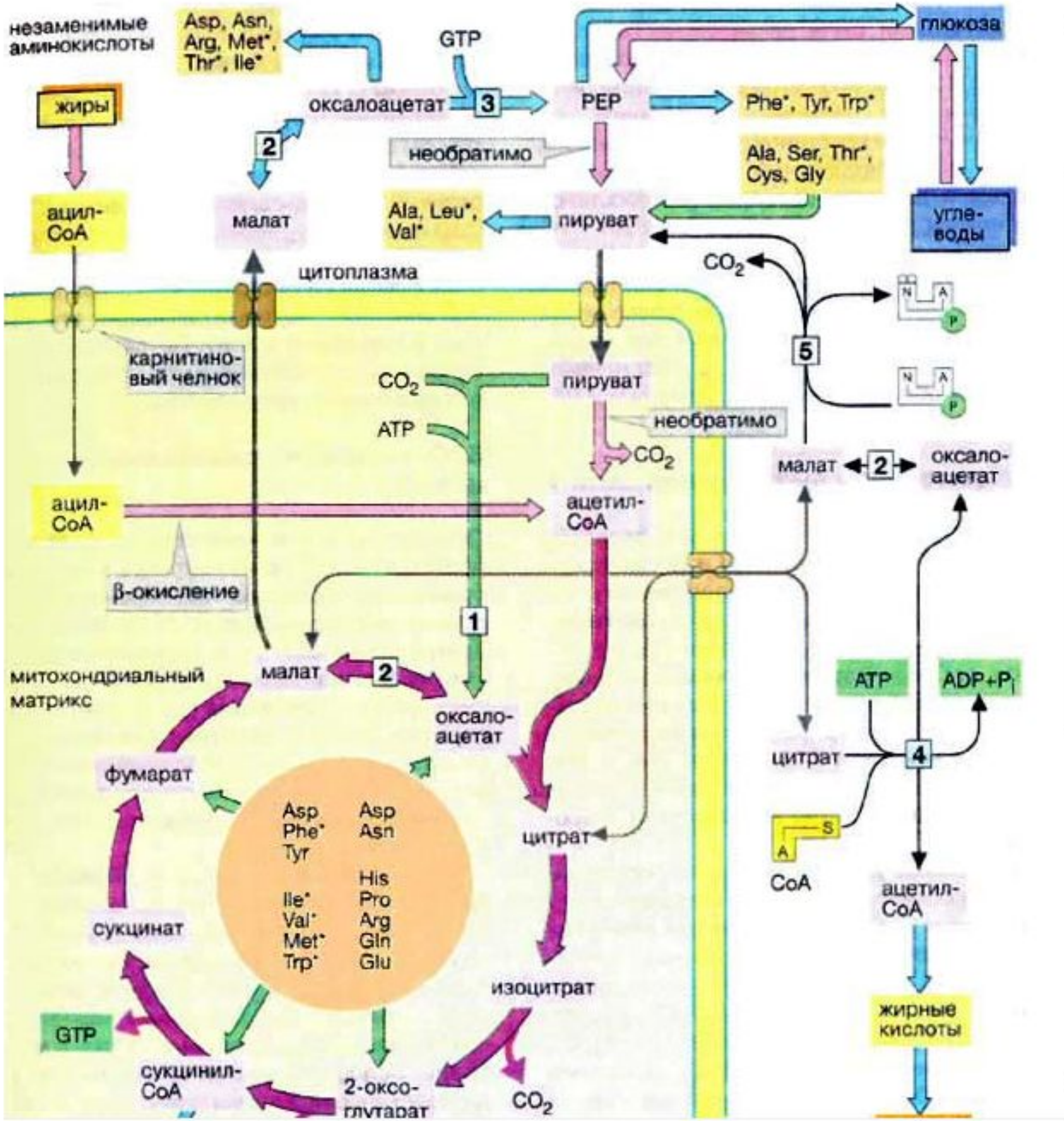


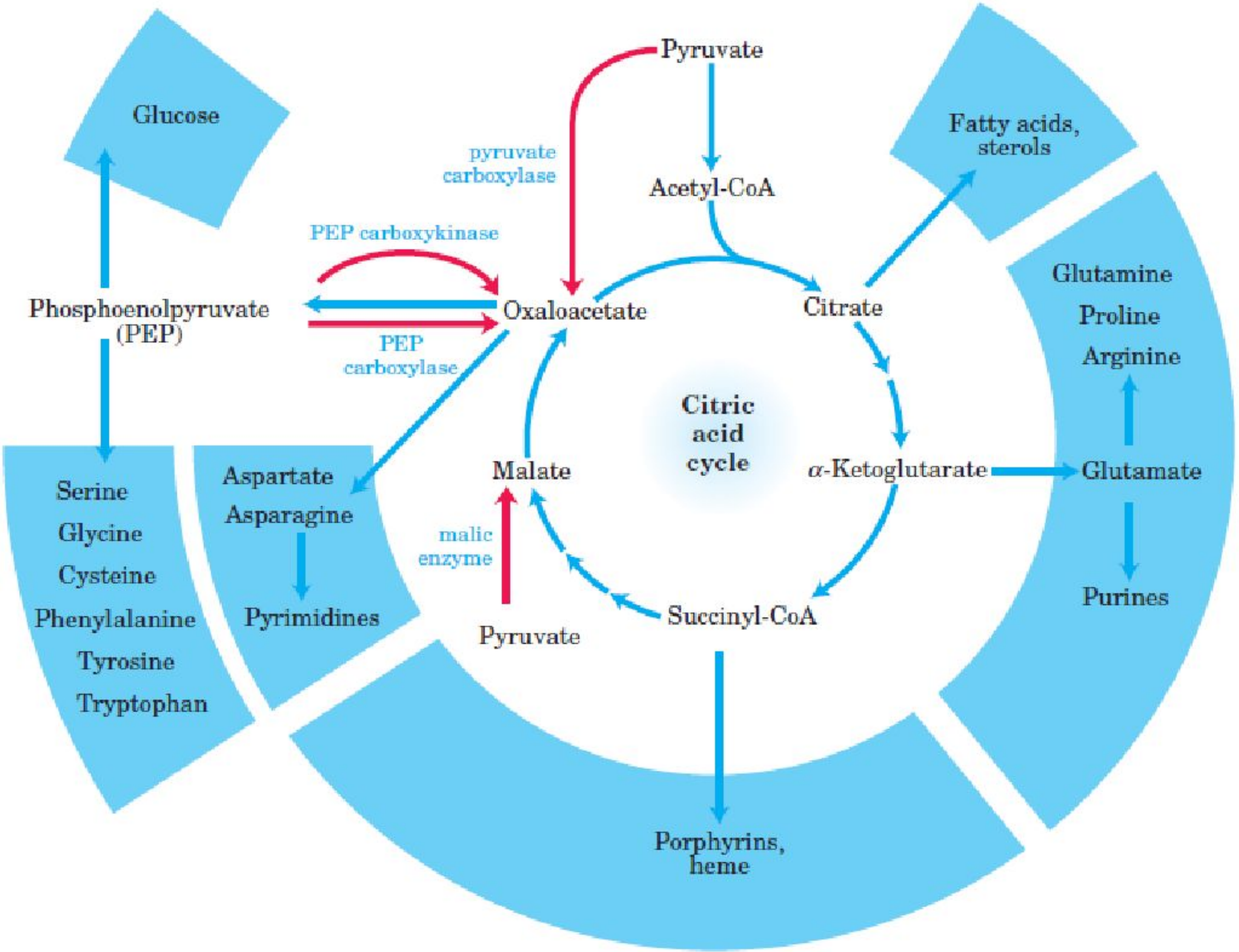
$$\Delta G'^{\circ} = 29.7\ \text{kJ/mol}$$

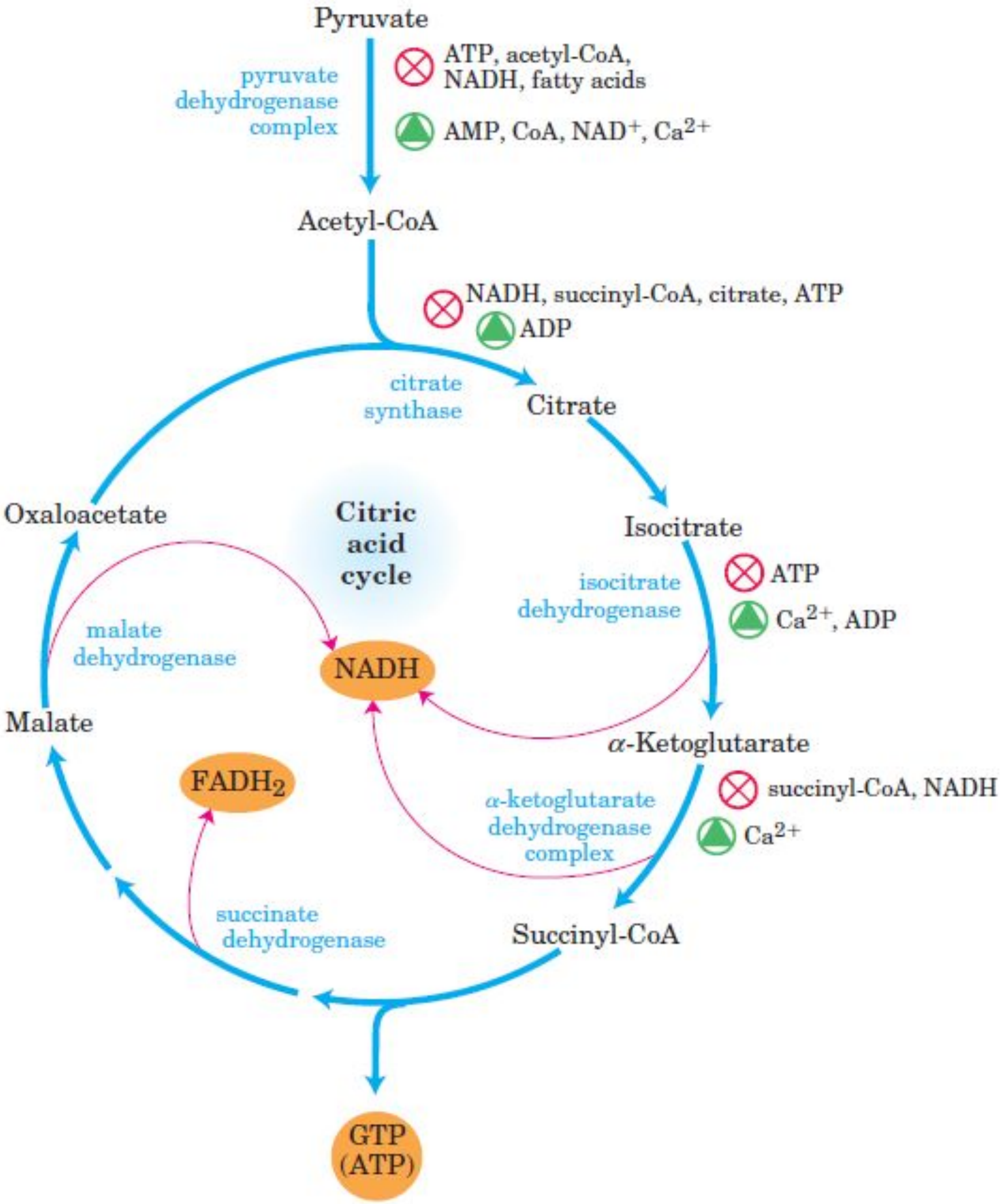

Acetyl-CoA
Citrate
Isocitrate
CO_2
NADH
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate
Citric
acid
cycle

METABOLIC PATHWAYS

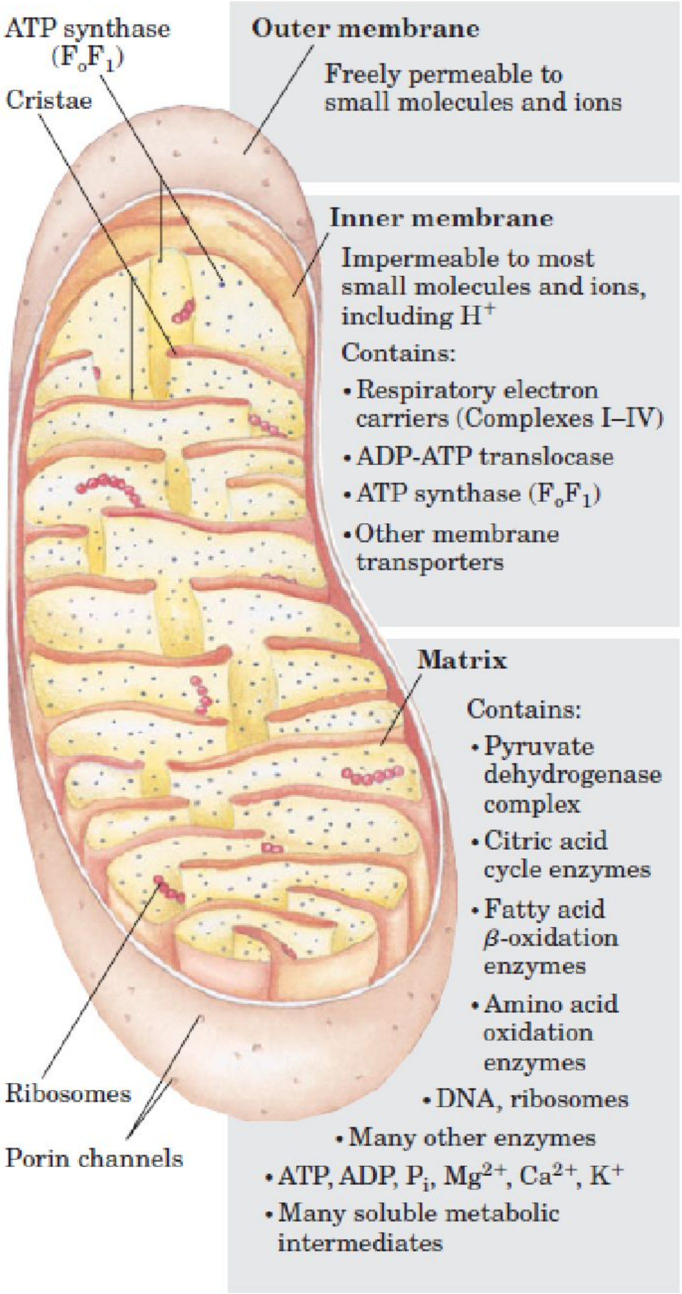



незаменимые аминокислоты
Asp, Asn, Arg, Met*, Thr*, Ile*
GTP
глюкоза
жиры
оксалоацетат
3
PEP
Phe*, Tyr, Trp*
2
необратимо
Ala, Ser, Thr*, Cys, Gly
ацил-CoA
малат
Ala, Leu*, Val*
пируват
угле-воды
цитоплазма
CO_2
карнитиновый челнок
5
CO_2
пируват
ATP
необратимо
CO_2
малат
2
оксало-ацетат
ацил-CoA
ацетил-CoA
β-окисление
1
митохондриальный матрикс
малат
2
оксало-ацетат
ATP
ADP+P_i
цитрат
4
фумарат
Asp
Phe*
Tyr
Ile*
Val*
Met*
Trp*
Asp
Asn
His
Pro
Arg
Gln
Glu
цитрат
CoA
ацетил-CoA
сукцинат
изоцитрат
жирные кислоты
GTP
сукцинил-CoA
2-оксо-глутарат
CO_2


Pyruvate
Glucose
Fatty acids, sterols
pyruvate carboxylase
Acetyl-CoA
PEP carboxykinase
Phosphoenolpyruvate (PEP)
Oxaloacetate
Citrate
PEP carboxylase
Glutamine
Proline
Arginine
Citric acid cycle
Malate
α-Ketoglutarate
Glutamate
Serine
Glycine
Cysteine
Phenylalanine
Tyrosine
Tryptophan
Aspartate
Asparagine
Pyrimidines
malic enzyme
Pyruvate
Succinyl-CoA
Purines
Porphyrins, heme


Pyruvate
pyruvate dehydrogenase complex
⊗ ATP, acetyl-CoA, NADH, fatty acids
▲ AMP, CoA, NAD^+, Ca^{2+}
Acetyl-CoA
⊗ NADH, succinyl-CoA, citrate, ATP
▲ ADP
citrate synthase
Citrate
Isocitrate
⊗ ATP
▲ Ca^{2+}, ADP
isocitrate dehydrogenase
Oxaloacetate
Citric acid cycle
malate dehydrogenase
NADH
Malate
α-Ketoglutarate
⊗ succinyl-CoA, NADH
▲ Ca^{2+}
α-ketoglutarate dehydrogenase complex
$FADH_2$
succinate dehydrogenase
Succinyl-CoA
GTP (ATP)

Дыхательная цепь



ATP synthase (F_oF_1)

Cristae

Ribosomes

Porin channels

Outer membrane

Freely permeable to small molecules and ions

Inner membrane

Impermeable to most small molecules and ions, including H^+

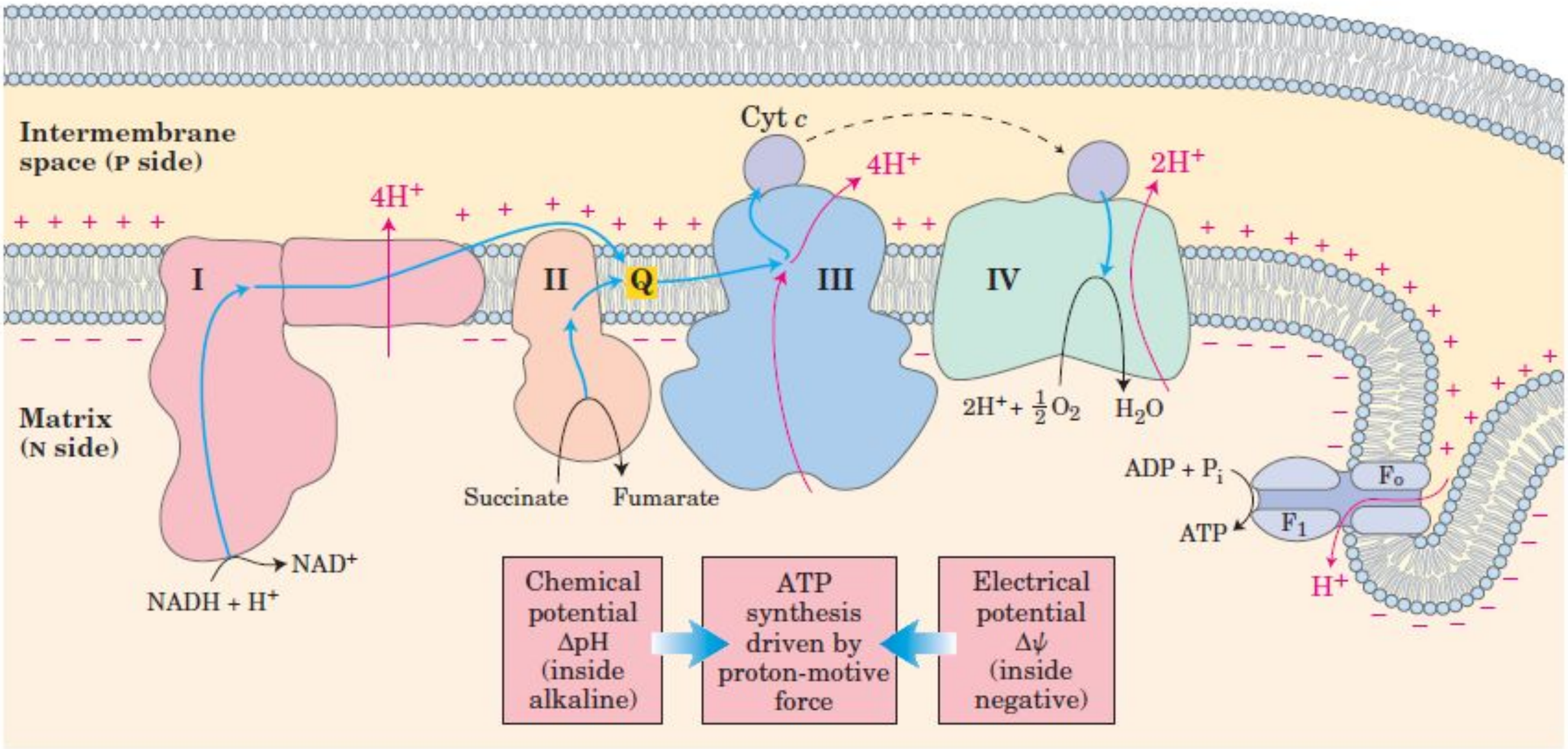
Contains:

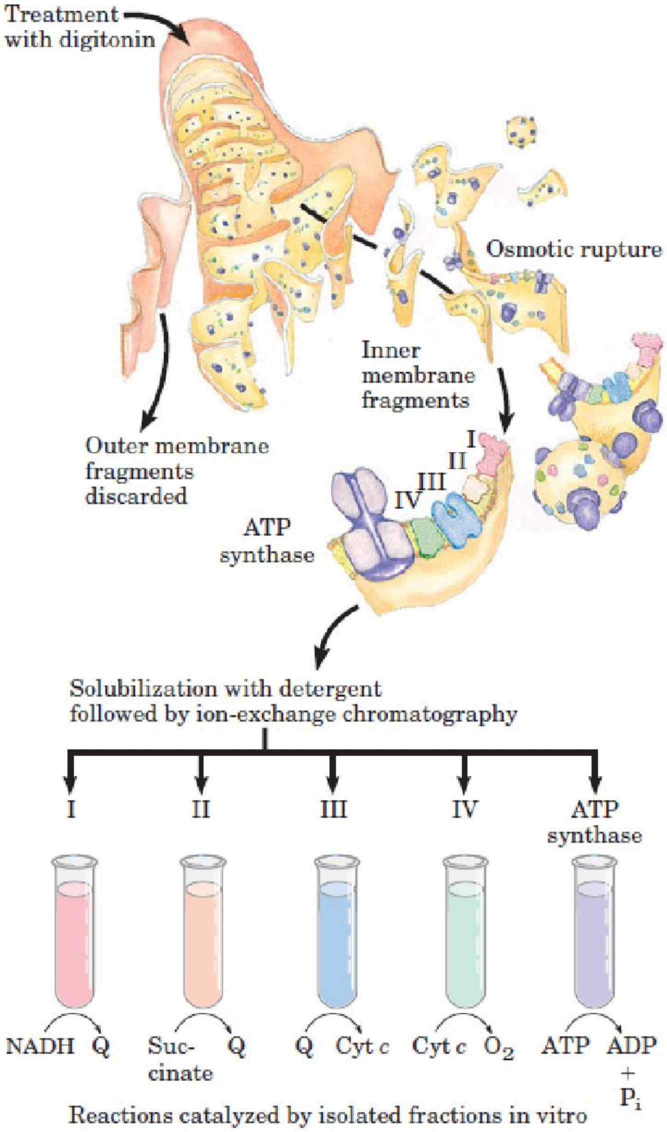
- Respiratory electron carriers (Complexes I–IV)
- ADP-ATP translocase
- ATP synthase (F_oF_1)
- Other membrane transporters

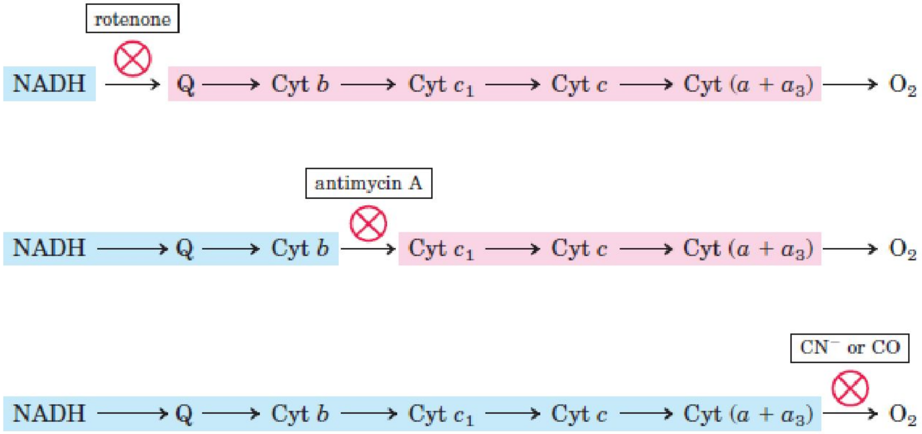
Matrix

Contains:

- Pyruvate dehydrogenase complex
- Citric acid cycle enzymes
- Fatty acid β-oxidation enzymes
- Amino acid oxidation enzymes
- DNA, ribosomes
- Many other enzymes
- ATP, ADP, P_i, Mg^{2+}, Ca^{2+}, K^+
- Many soluble metabolic intermediates


Intermembrane space (P side)
Matrix (N side)
Cyt c
$4H^+$
$4H^+$
$2H^+$
I
II
Q
III
IV
$NADH + H^+$
NAD^+
Succinate
Fumarate
$2H^+ + \frac{1}{2}O_2$
H_2O
$ADP + P_i$
ATP
F_o
F_1
H^+
Chemical potential ΔpH (inside alkaline)
ATP synthesis driven by proton-motive force
Electrical potential Δψ (inside negative)





rotenone

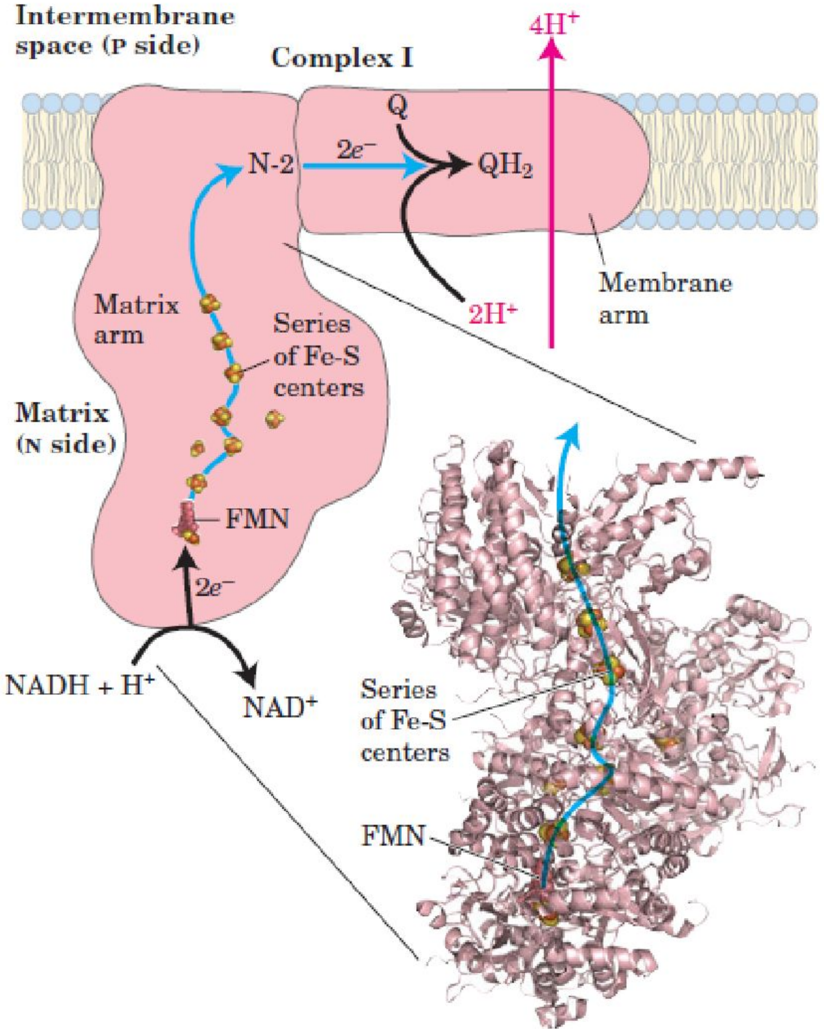
NADH $\longrightarrow$ Q $\longrightarrow$ Cyt *b* $\longrightarrow$ Cyt c_1 $\longrightarrow$ Cyt *c* $\longrightarrow$ Cyt ($a + a_3$) $\longrightarrow$ O_2

antimycin A

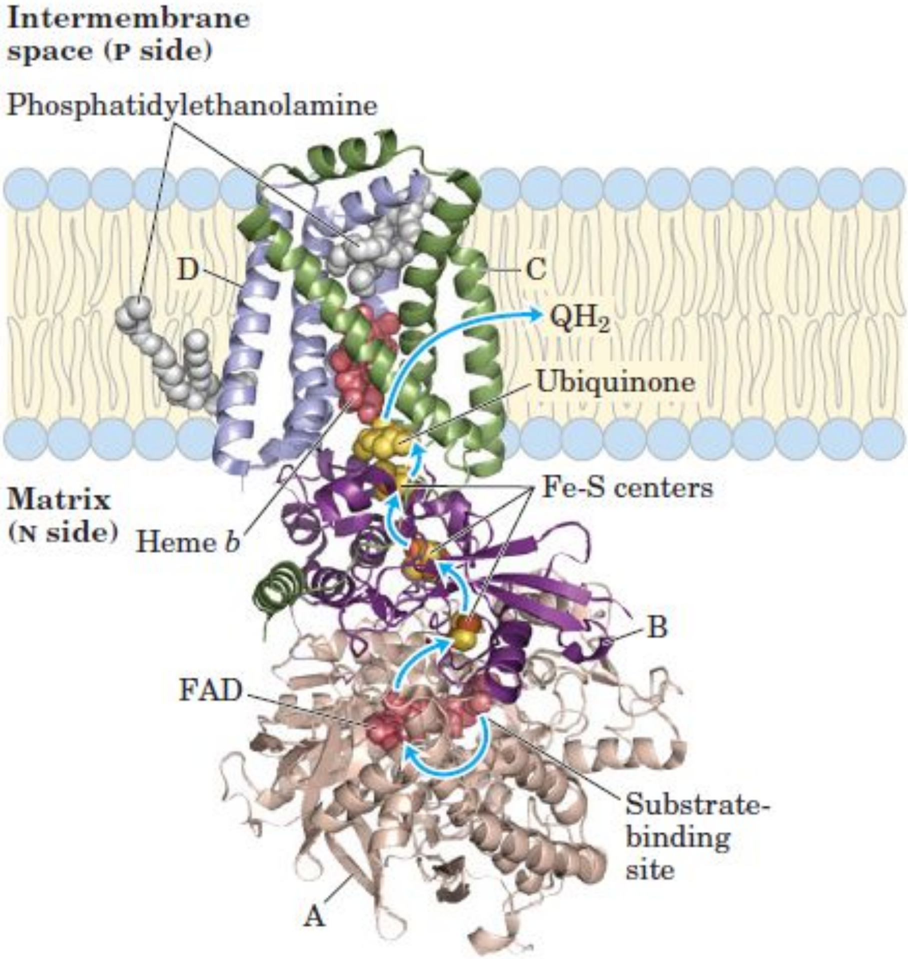
NADH $\longrightarrow$ Q $\longrightarrow$ Cyt *b* $\longrightarrow$ Cyt c_1 $\longrightarrow$ Cyt *c* $\longrightarrow$ Cyt ($a + a_3$) $\longrightarrow$ O_2

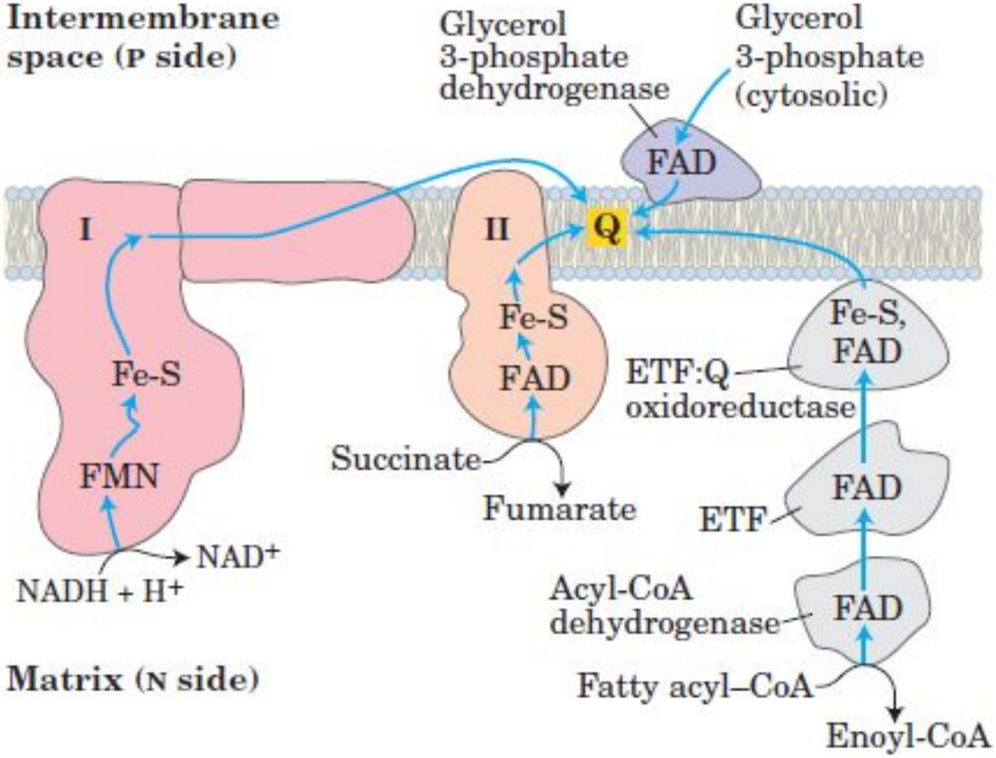
CN^- or CO

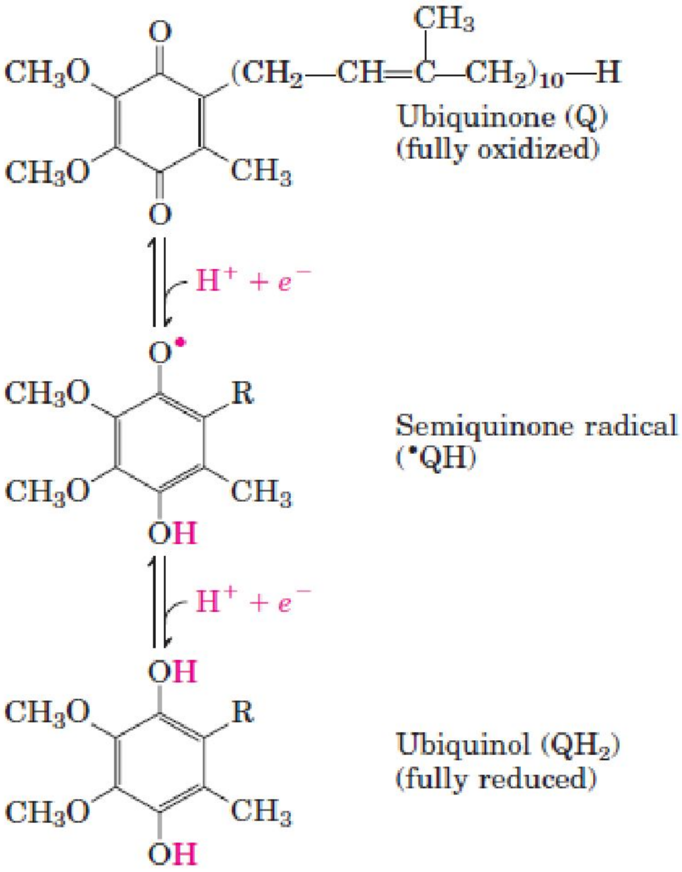
NADH $\longrightarrow$ Q $\longrightarrow$ Cyt *b* $\longrightarrow$ Cyt c_1 $\longrightarrow$ Cyt *c* $\longrightarrow$ Cyt ($a + a_3$) $\longrightarrow$ O_2



$$NADH + 5H_N^+ + Q \longrightarrow NAD^+ + QH_2 + 4H_P^+$$


Intermembrane space (P side)
Phosphatidylethanolamine
D
C
QH_2
Ubiquinone
Fe-S centers
Matrix (N side)
Heme *b*
B
FAD
Substrate-binding site
A

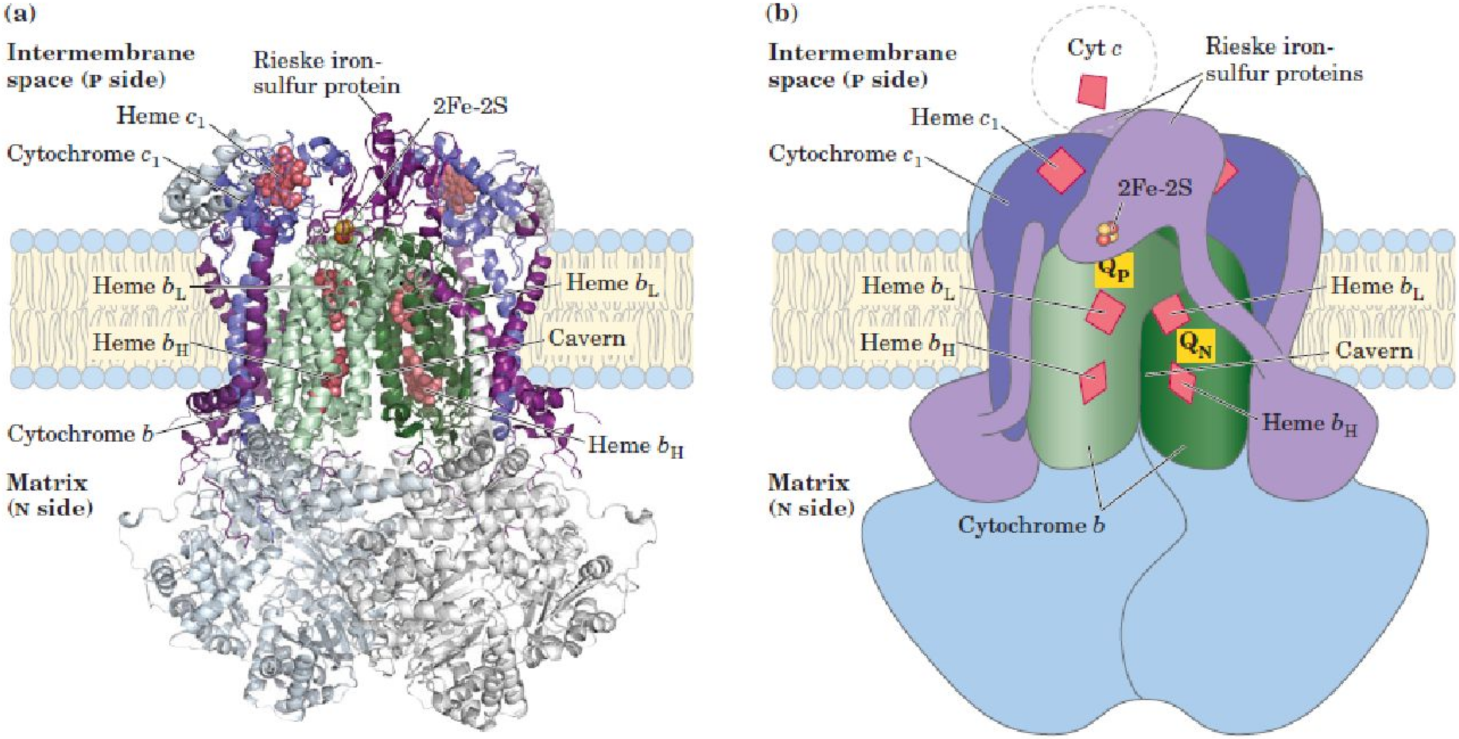

Intermembrane space (P side)
Glycerol 3-phosphate dehydrogenase
Glycerol 3-phosphate (cytosolic)
FAD
I
II
Q
Fe-S
FAD
Fe-S,
FAD
ETF:Q oxidoreductase
Fe-S
FMN
Succinate
Fumarate
FAD
ETF
NAD+
NADH + H+
Acyl-CoA dehydrogenase
FAD
Matrix (N side)
Fatty acyl–CoA
Enoyl-CoA



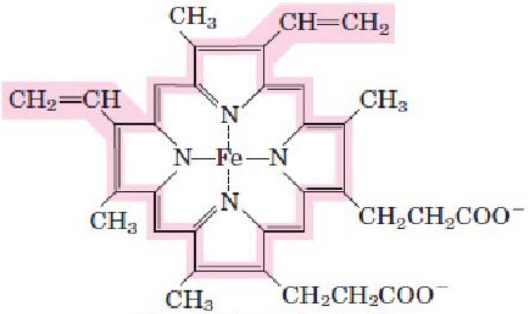
Ubiquinone (Q)
(fully oxidized)

Semiquinone radical
(•QH)

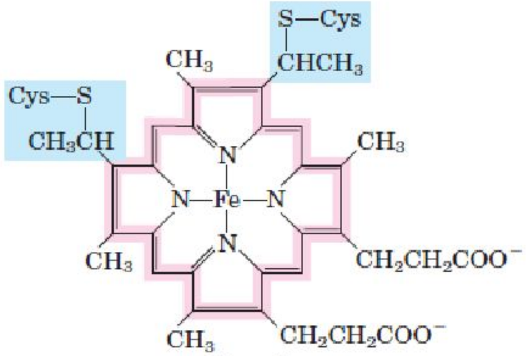
Ubiquinol (QH_2)
(fully reduced)



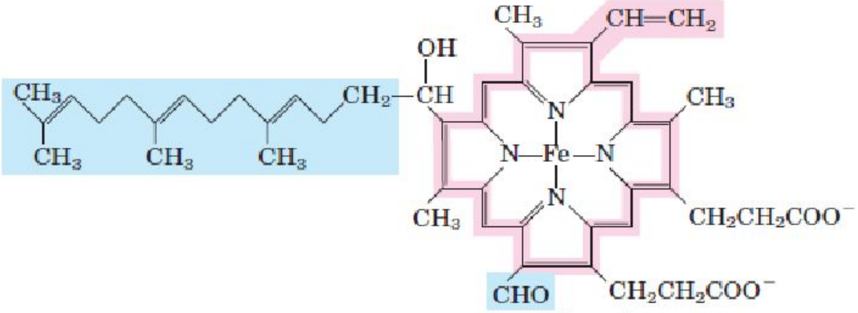
$$QH_2 + 2\ \text{cyt}\ c_1\ \text{(oxidized)} + 2H^+_N \longrightarrow Q + 2\ \text{cyt}\ c_1\ \text{(reduced)} + 4H^+_P$$



Iron protoporphyrin IX
(in *b*-type cytochromes)

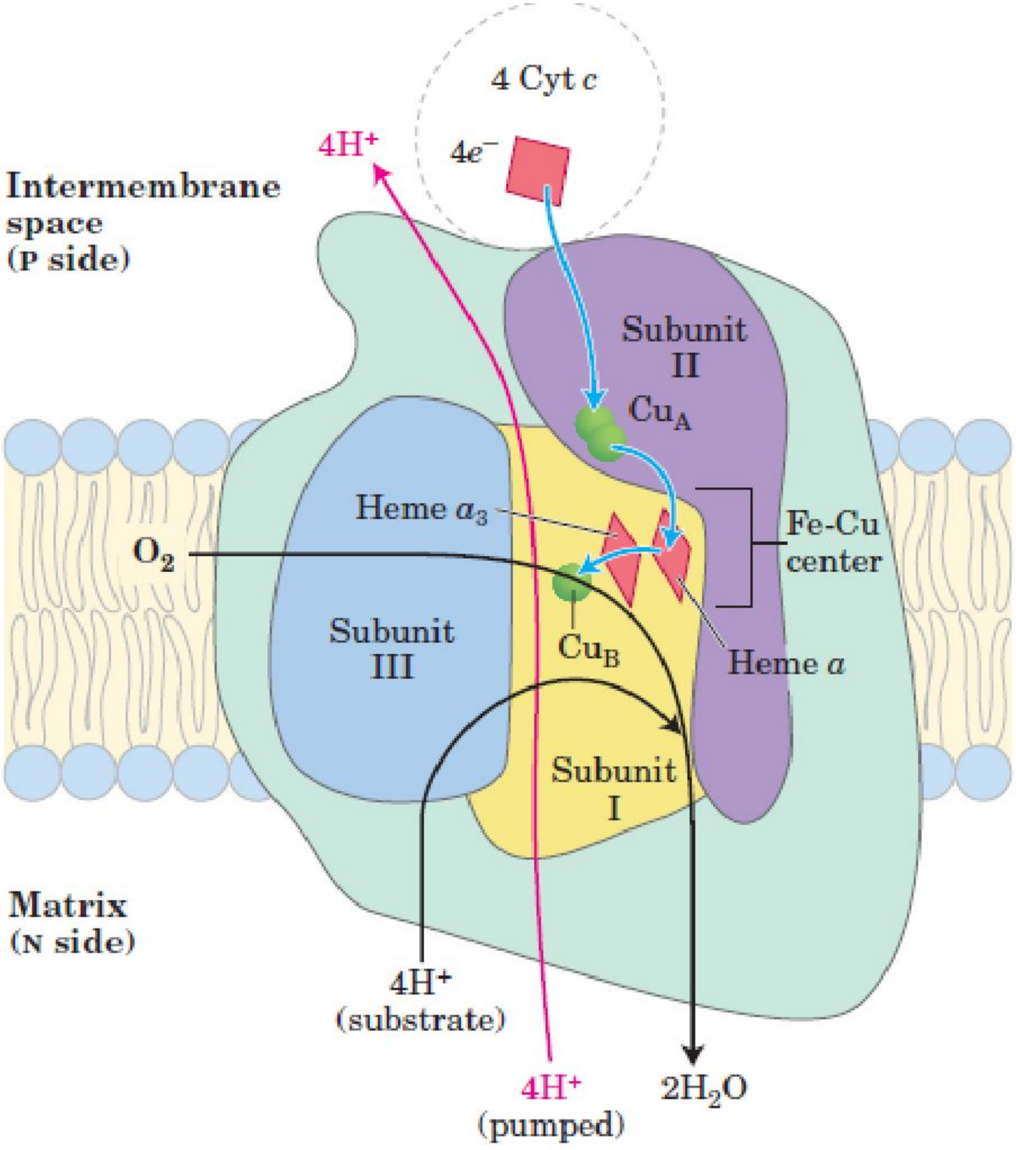


Heme C
(in *c*-type cytochromes)

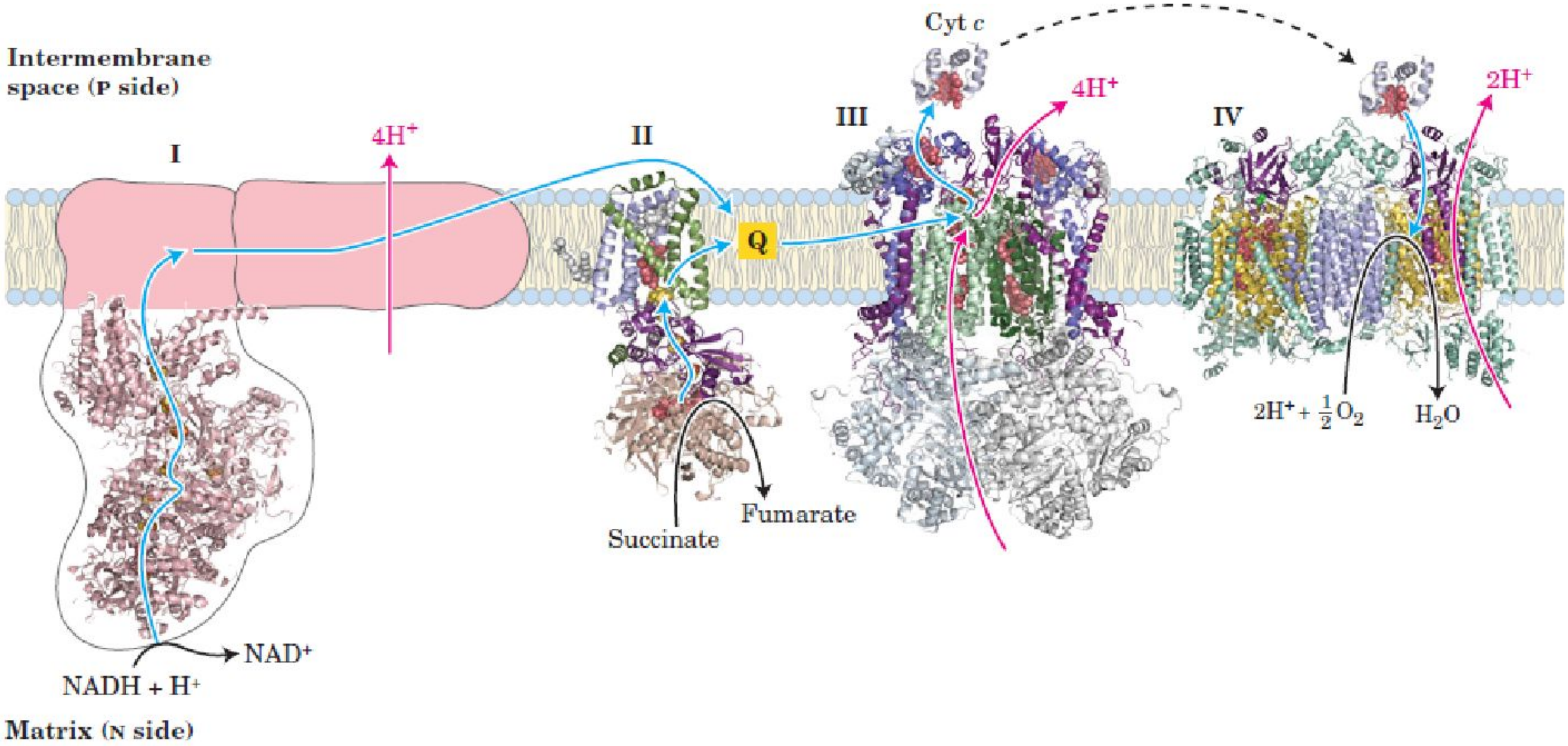


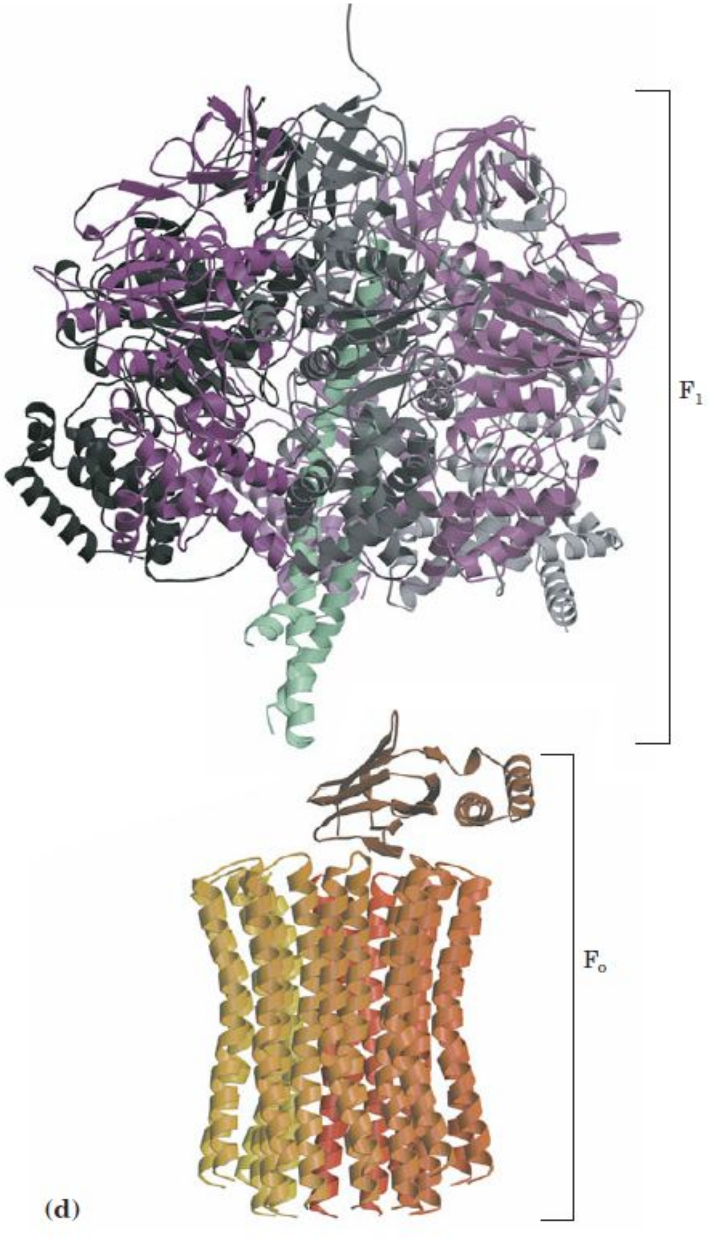
Heme A
(in *a*-type cytochromes)

FIGURE 19–3 **Prosthetic groups of cytochromes.** Each group consists of four five-membered, nitrogen-containing rings in a cyclic structure called a porphyrin. The four nitrogen atoms are coordinated with a central Fe ion, either Fe^{2+} or Fe^{3+}. Iron protoporphyrin IX is found in *b*-type cytochromes and in hemoglobin and myoglobin (see Fig. 4–16). Heme *c* is covalently bound to the protein of cytochrome *c* through thioether bonds to two Cys residues. Heme *a*, found in *a*-type cytochromes, has a long isoprenoid tail attached to one of the five-membered rings. The conjugated double-bond system (shaded pink) of the porphyrin ring accounts for the absorption of visible light by these hemes.

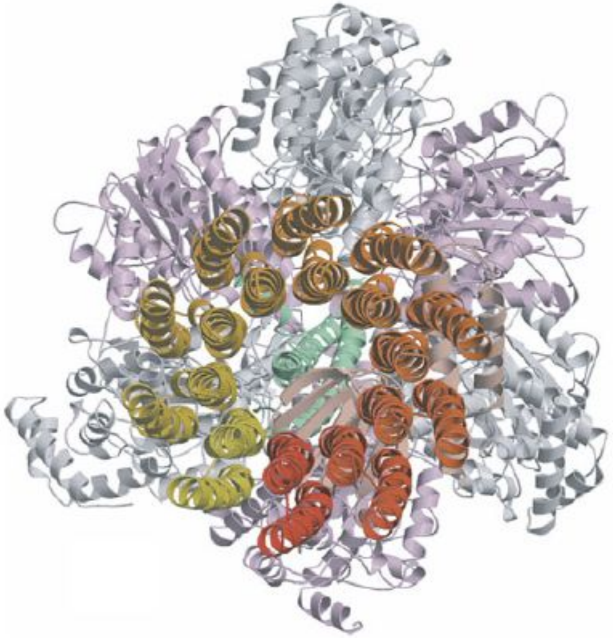


$$4\ \text{Cyt}\ c\ (\text{reduced}) + 8H_N^+ + O_2 \longrightarrow 4\ \text{cyt}\ c\ (\text{oxidized}) + 4H_P^+ + 2H_2O$$

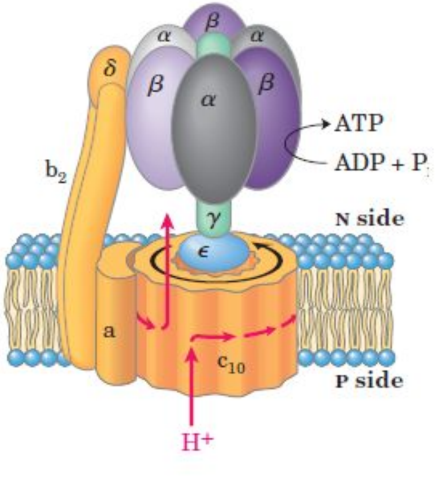

Intermembrane space (P side)
I
$4H^+$
II
Q
III
Cyt c
$4H^+$
IV
$2H^+$
Succinate
Fumarate
$2H^+ + \frac{1}{2}O_2$
H_2O
$NADH + H^+$
NAD^+
Matrix (N side)



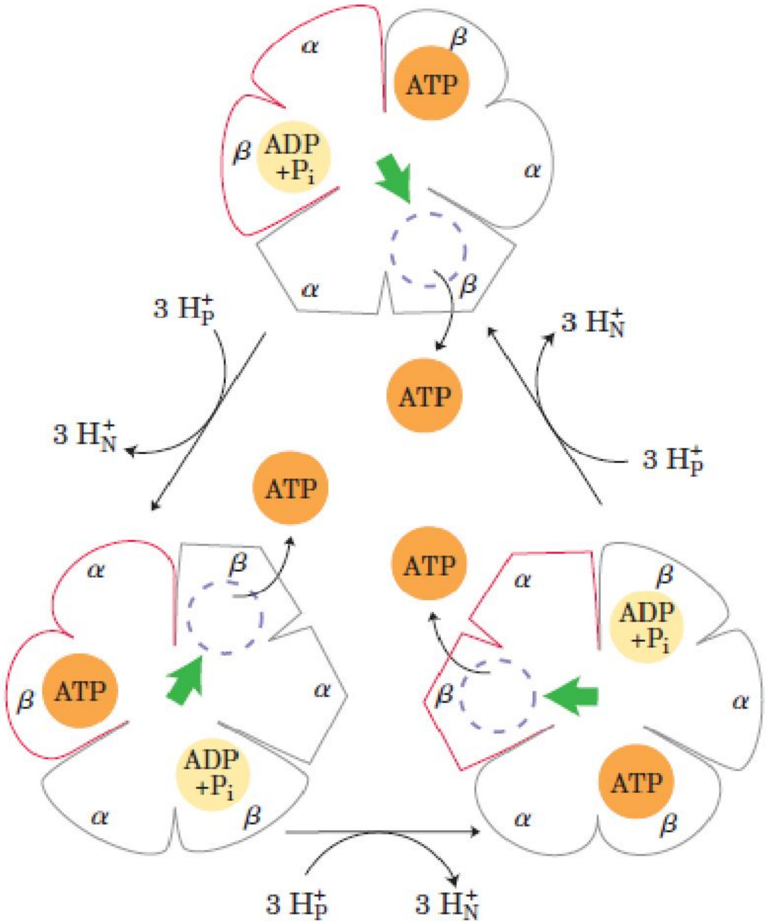
(d)

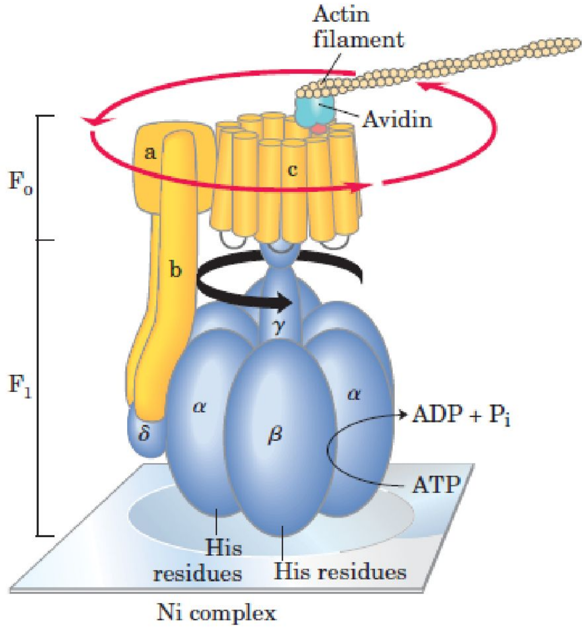


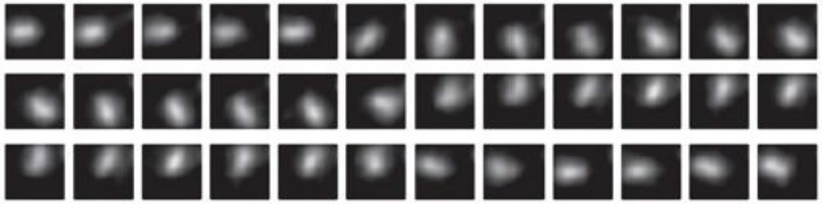
(e)



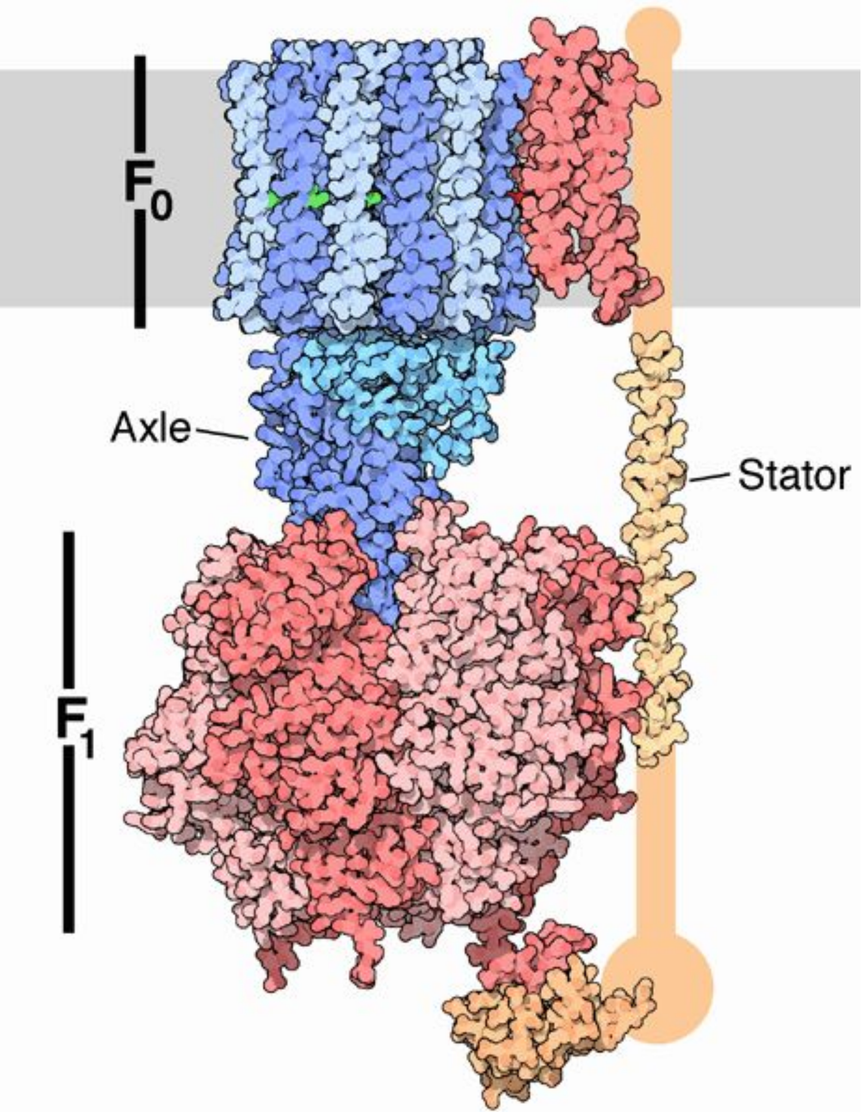
(f)

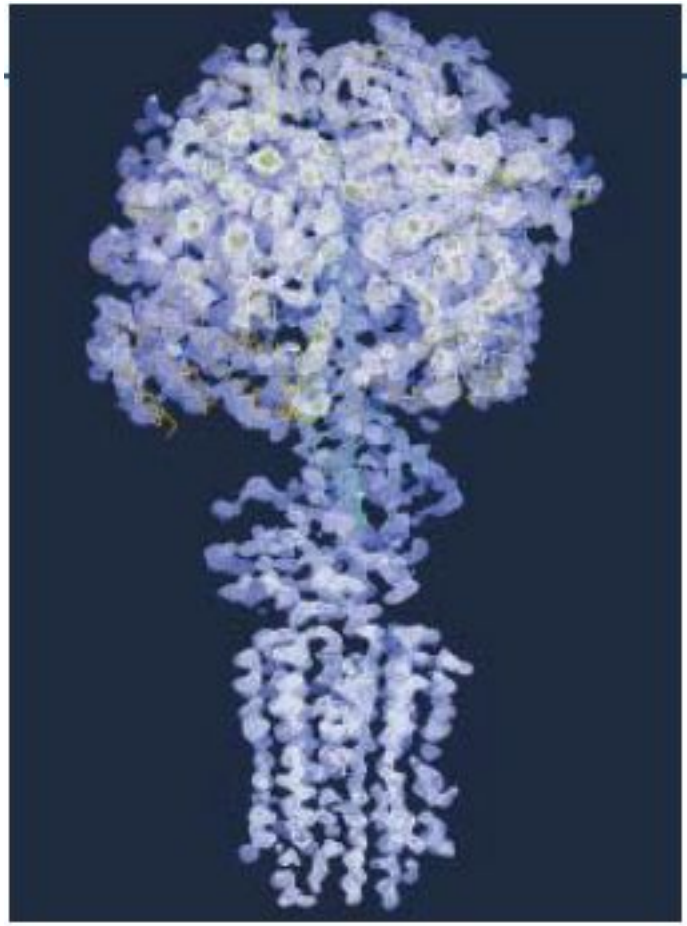

α
β
ATP
β
ADP
+P_i
α
α
β
3 H_P^+
3 H_N^+
3 H_N^+
3 H_P^+
ATP
ATP
ATP
α
β
β
ATP
α
ADP
+P_i
α
β
α
β
ADP
+P_i
β
α
ATP
α
β
3 H_P^+
3 H_N^+


Actin
filament
Avidin
F_o
a
c
b
γ
F_1
α
α
β
δ
ADP + P_i
ATP
His
residues
His residues
Ni complex

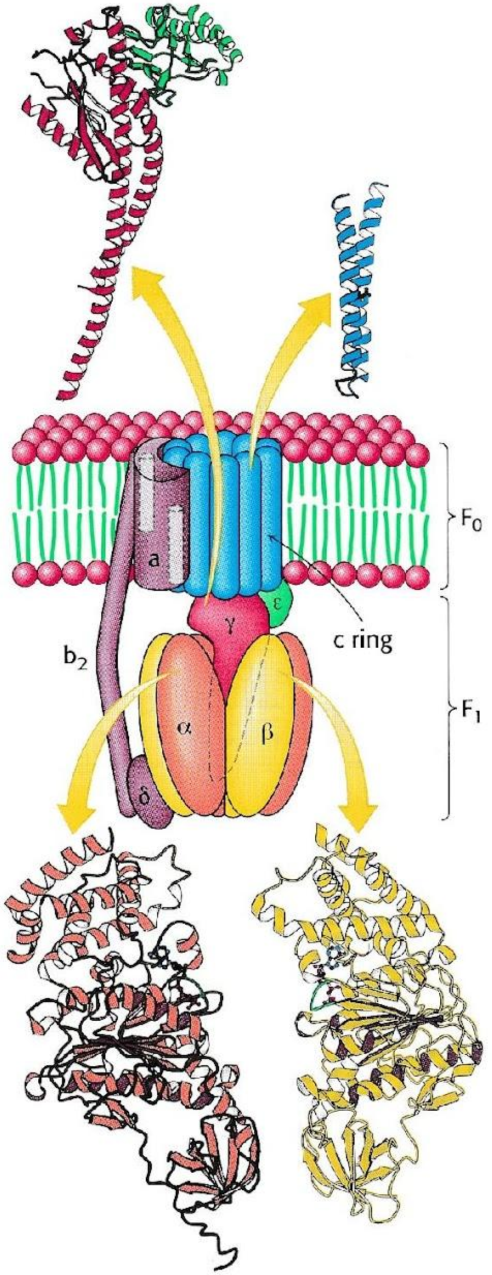


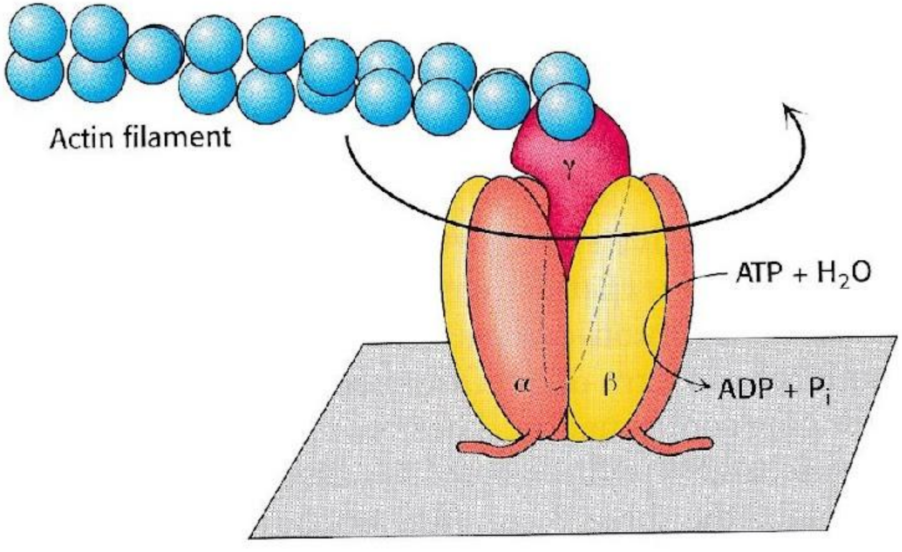
АТФ-синтаза



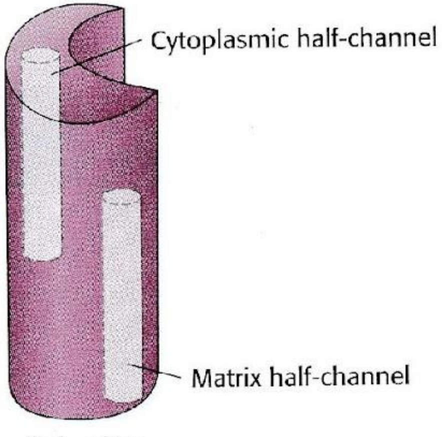


Electron density map of the F_1-ATPase associated with a ring of 10 c-subunits from the F_0 domain of ATP synthase, a molecular machine that carries out the synthesis of ATP in eubacteria, chloroplasts, and mitochondria. [Courtesy of Andrew Leslie, MRC Laboratory of Molecular Biology, Cambridge, UK.]

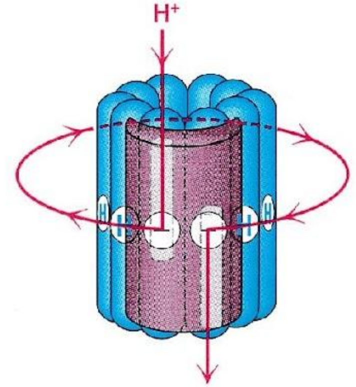


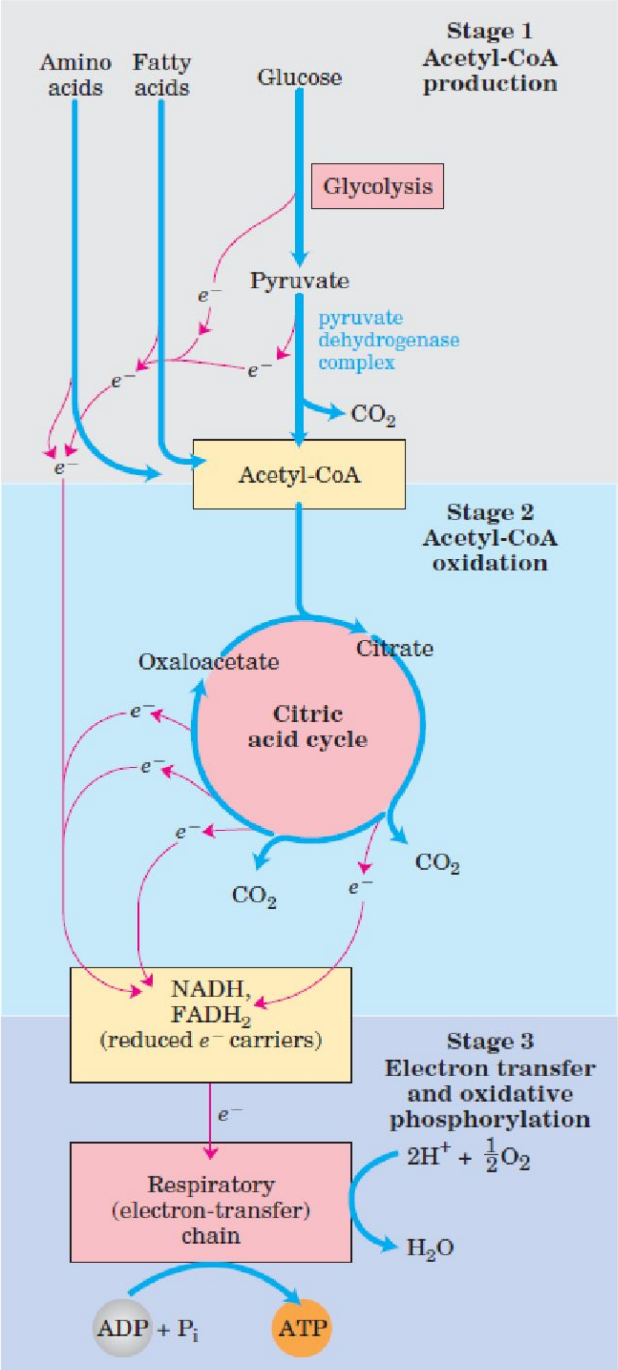


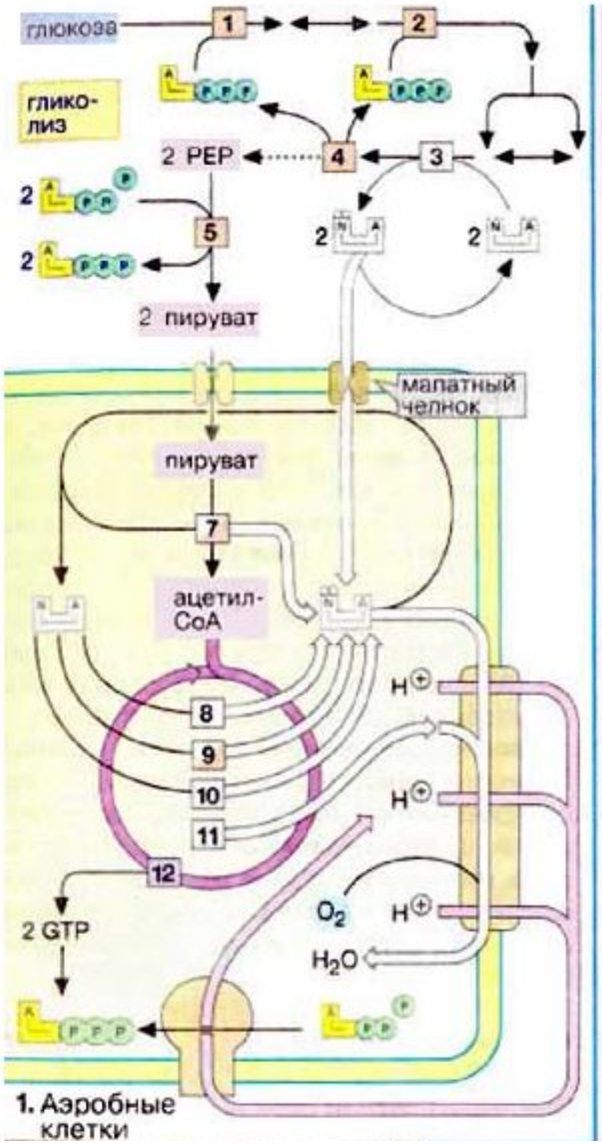
Subunit **c**



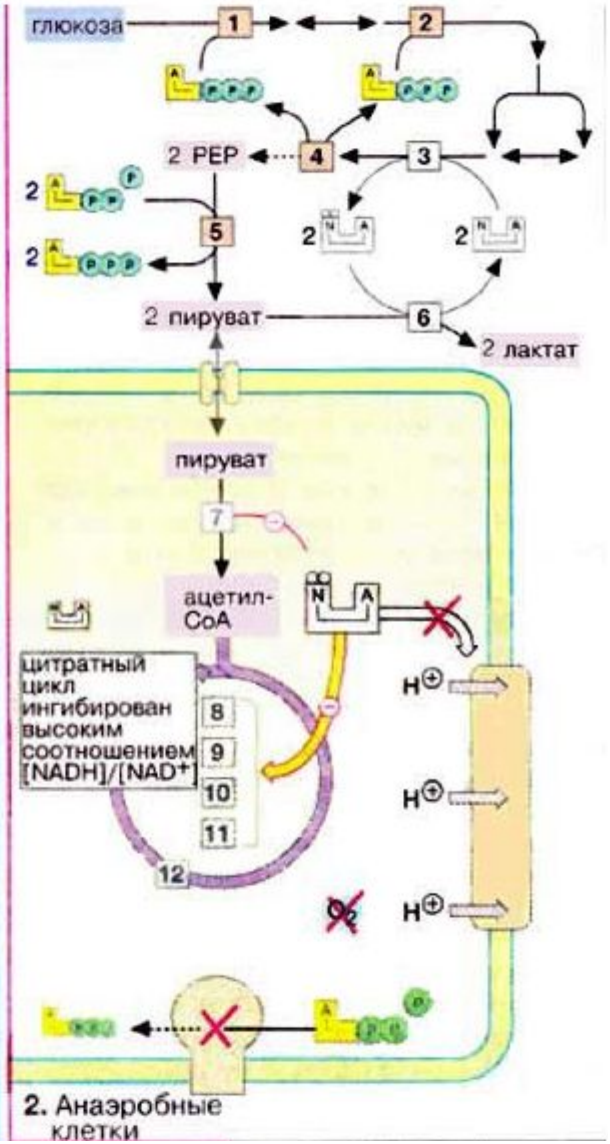
Subunit **a**




Stage 1
Acetyl-CoA
production
Amino acids
Fatty acids
Glucose
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
e^-
e^-
e^-
e^-
CO_2
Acetyl-CoA
Stage 2
Acetyl-CoA
oxidation
Citrate
Oxaloacetate
Citric acid cycle
e^-
e^-
e^-
e^-
CO_2
CO_2
NADH,
$FADH_2$
(reduced e^- carriers)
Stage 3
Electron transfer
and oxidative
phosphorylation
e^-
Respiratory (electron-transfer) chain
$2H^+ + \frac{1}{2}O_2$
H_2O
ADP + P_i
ATP

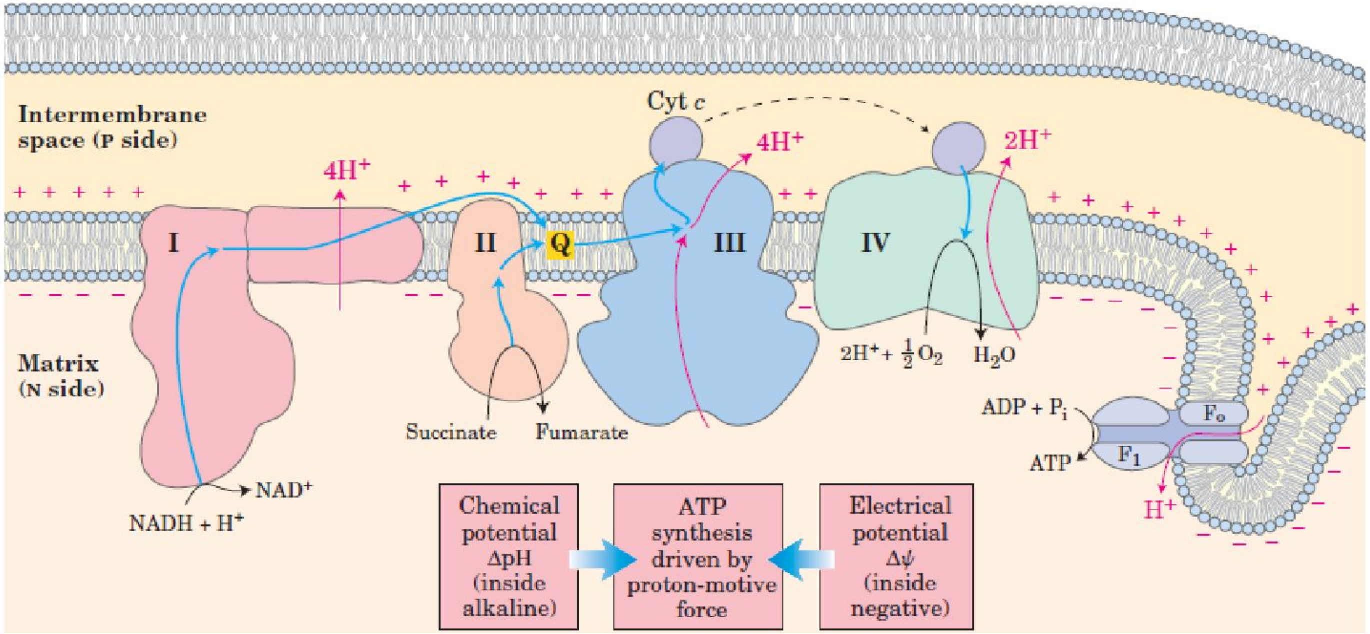


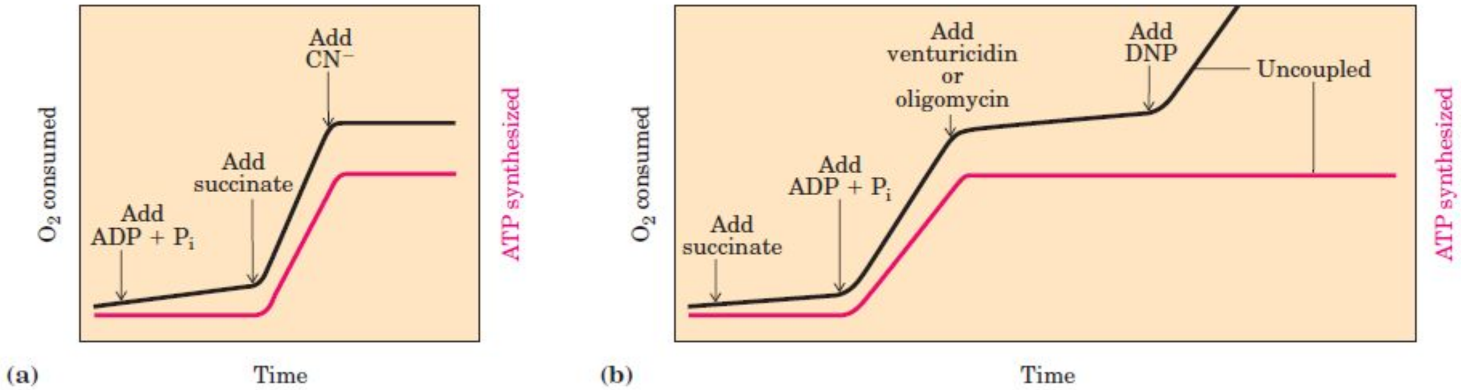
1. Аэробные клетки

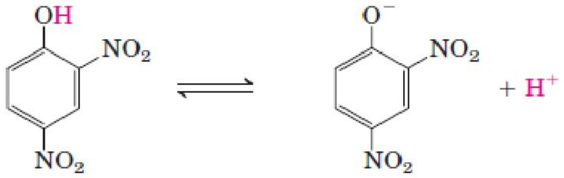


2. Анаэробные клетки

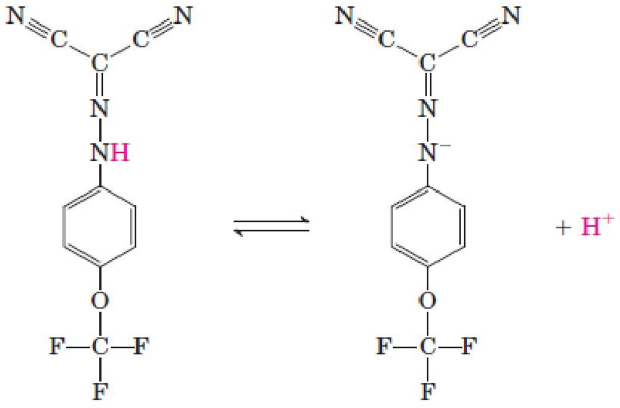
$$\mathrm{ADP} + \mathrm{P_i} + n\mathrm{H}^+_{\mathrm{P}} \longrightarrow \mathrm{ATP} + \mathrm{H_2O} + n\mathrm{H}^+_{\mathrm{N}}$$



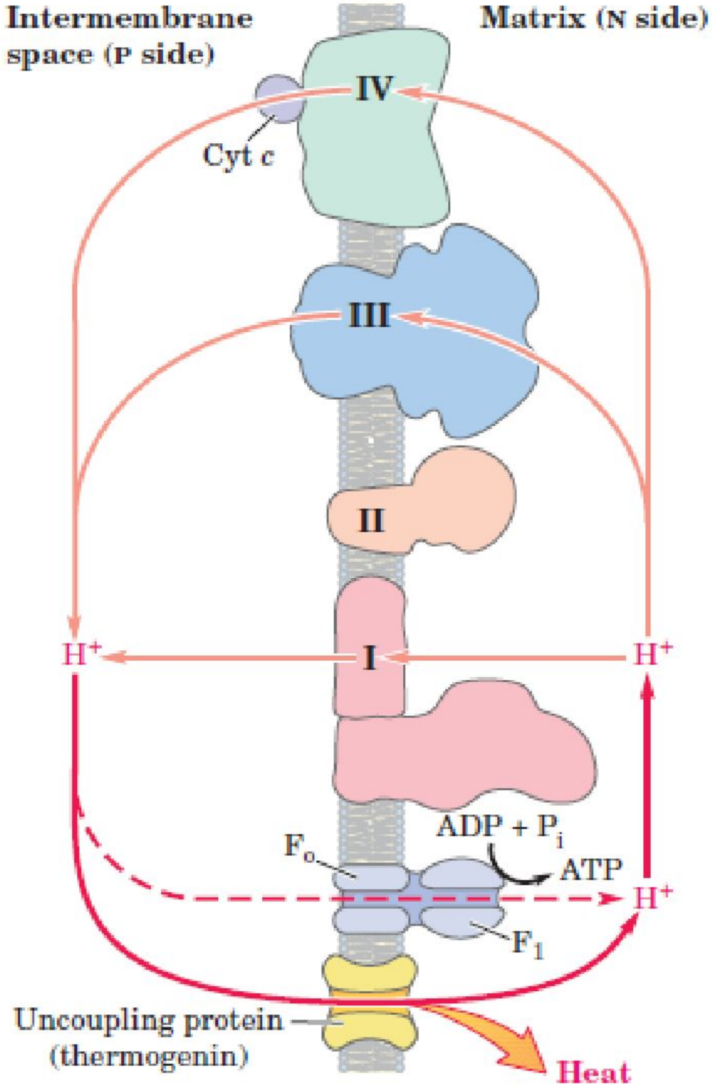




2,4-Dinitrophenol
(DNP)



Carbonylcyanide-*p*-
trifluoromethoxyphenylhydrazone
(FCCP)


Intermembrane space (P side)
Matrix (N side)
IV
Cyt c
III
II
I
H^+
H^+
F_o
ADP + P_i
ATP
H^+
F_1
Uncoupling protein (thermogenin)
Heat

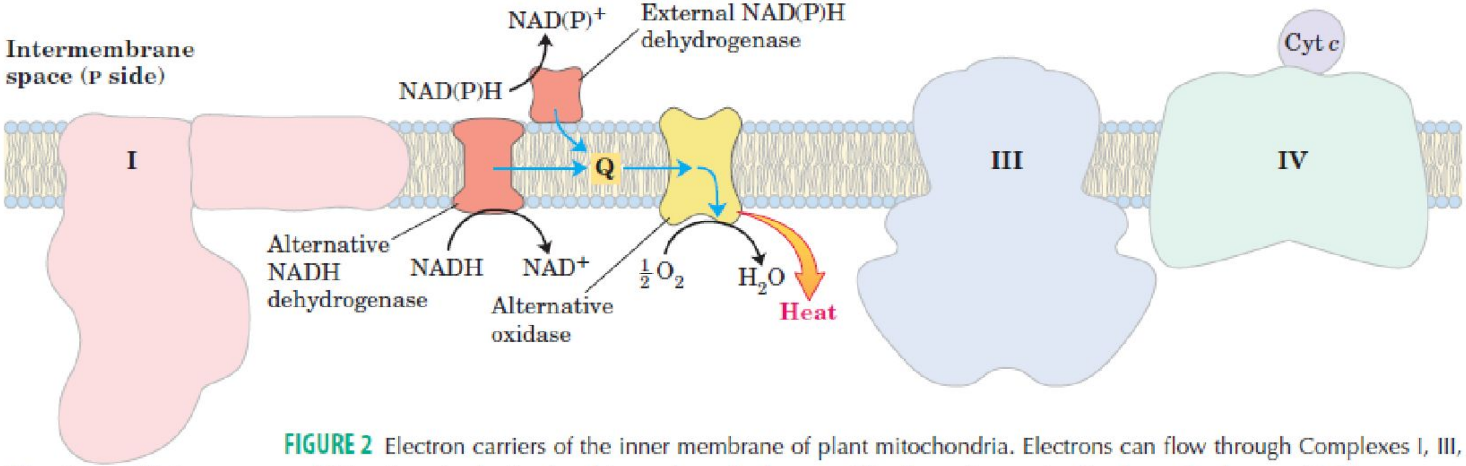
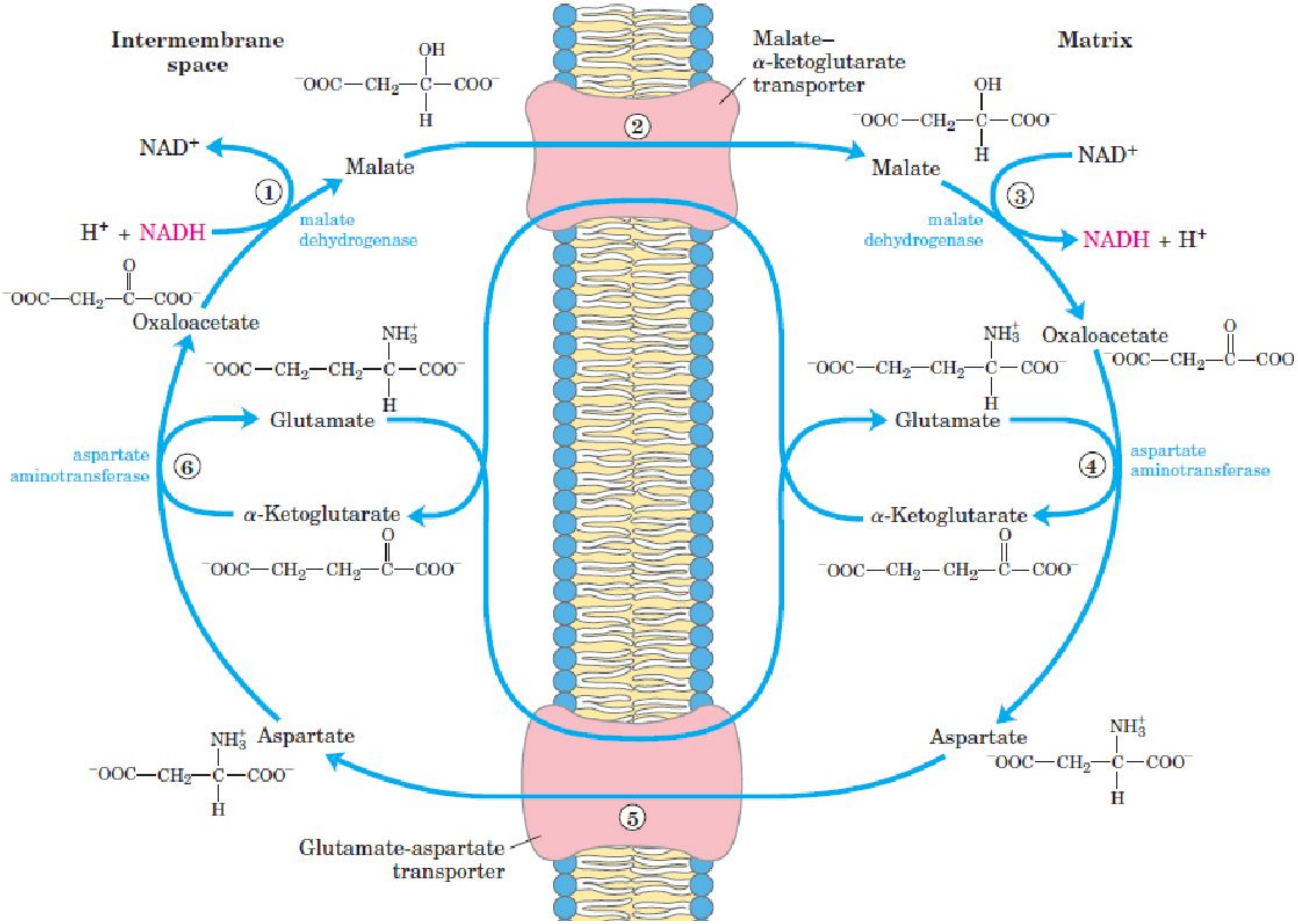
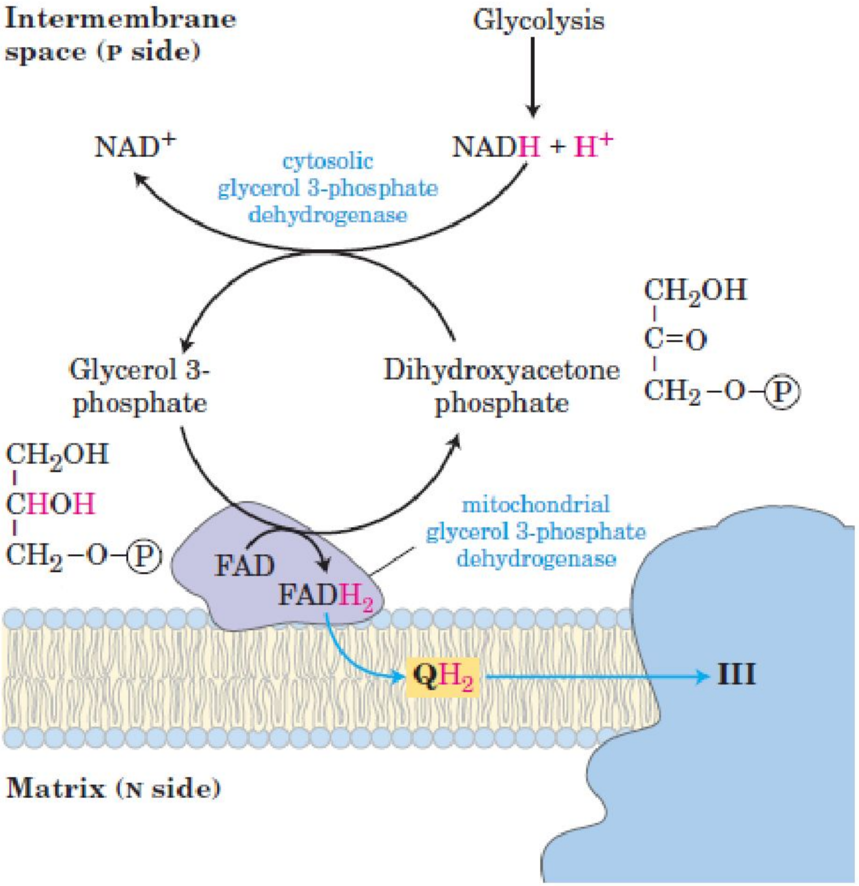
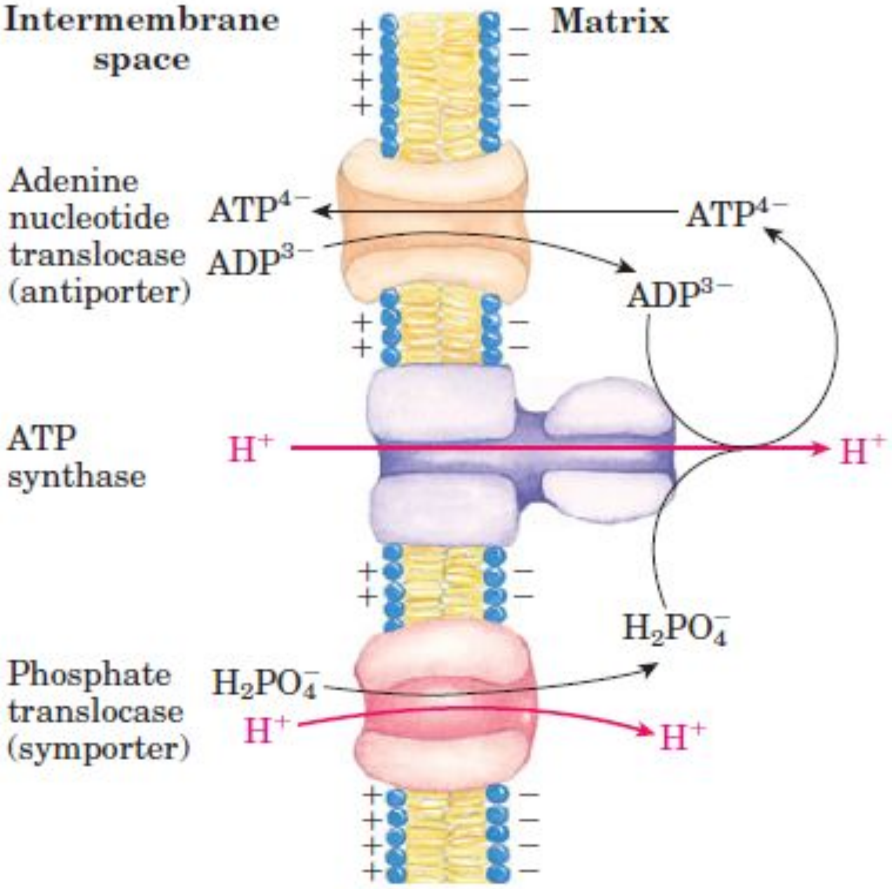


FIGURE 2 Electron carriers of the inner membrane of plant mitochondria. Electrons can flow through Complexes I, III, and IV, as in animal mitochondria, or through plant-specific alternative carriers by the paths shown with blue arrows.


Intermembrane space
Matrix
Malate–α-ketoglutarate transporter
Glutamate-aspartate transporter
①
②
③
④
⑤
⑥
NAD⁺
H⁺ + NADH
Malate
malate dehydrogenase
Oxaloacetate
Glutamate
α-Ketoglutarate
aspartate aminotransferase
Aspartate
NAD⁺
NADH + H⁺
⁻OOC—CH₂—C(OH)(H)—COO⁻
⁻OOC—CH₂—C(=O)—COO⁻
⁻OOC—CH₂—CH₂—C(NH₃⁺)(H)—COO⁻
⁻OOC—CH₂—CH₂—C(=O)—COO⁻
⁻OOC—CH₂—C(NH₃⁺)(H)—COO⁻


Intermembrane space (P side)
Glycolysis
NAD$^+$
NADH + H$^+$
cytosolic glycerol 3-phosphate dehydrogenase
Glycerol 3-phosphate
Dihydroxyacetone phosphate
CH_2OH
$C=O$
$CH_2-O-Ⓟ$
CH_2OH
$CHOH$
$CH_2-O-Ⓟ$
mitochondrial glycerol 3-phosphate dehydrogenase
FAD
FADH$_2$
QH$_2$
III
Matrix (N side)


Intermembrane space
Matrix
Adenine nucleotide translocase (antiporter)
ATP^{4-}
ADP^{3-}
ATP^{4-}
ADP^{3-}
ATP synthase
H^+
H^+
$H_2PO_4^-$
Phosphate translocase (symporter)
$H_2PO_4^-$
H^+
H^+
+
−

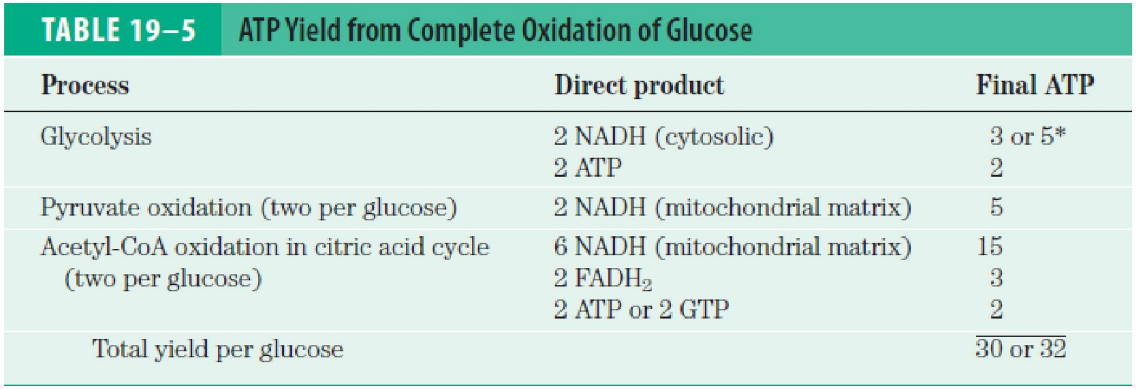


TABLE 19–5 ATP Yield from Complete Oxidation of Glucose

Process	Direct product	Final ATP
Glycolysis	2 NADH (cytosolic)	3 or 5*
	2 ATP	2
Pyruvate oxidation (two per glucose)	2 NADH (mitochondrial matrix)	5
Acetyl-CoA oxidation in citric acid cycle (two per glucose)	6 NADH (mitochondrial matrix)	15
	2 $FADH_2$	3
	2 ATP or 2 GTP	2
Total yield per glucose		30 or 32