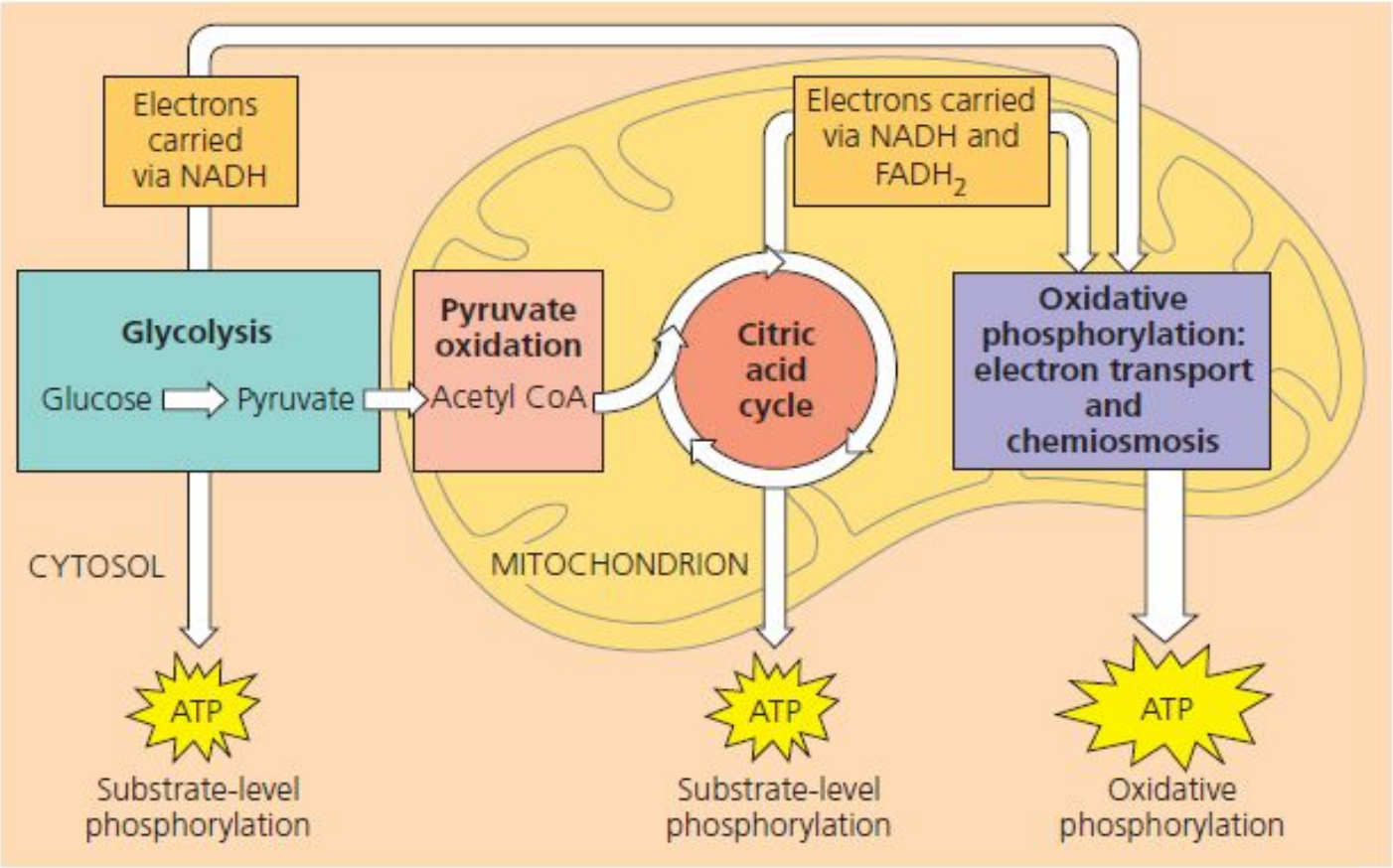
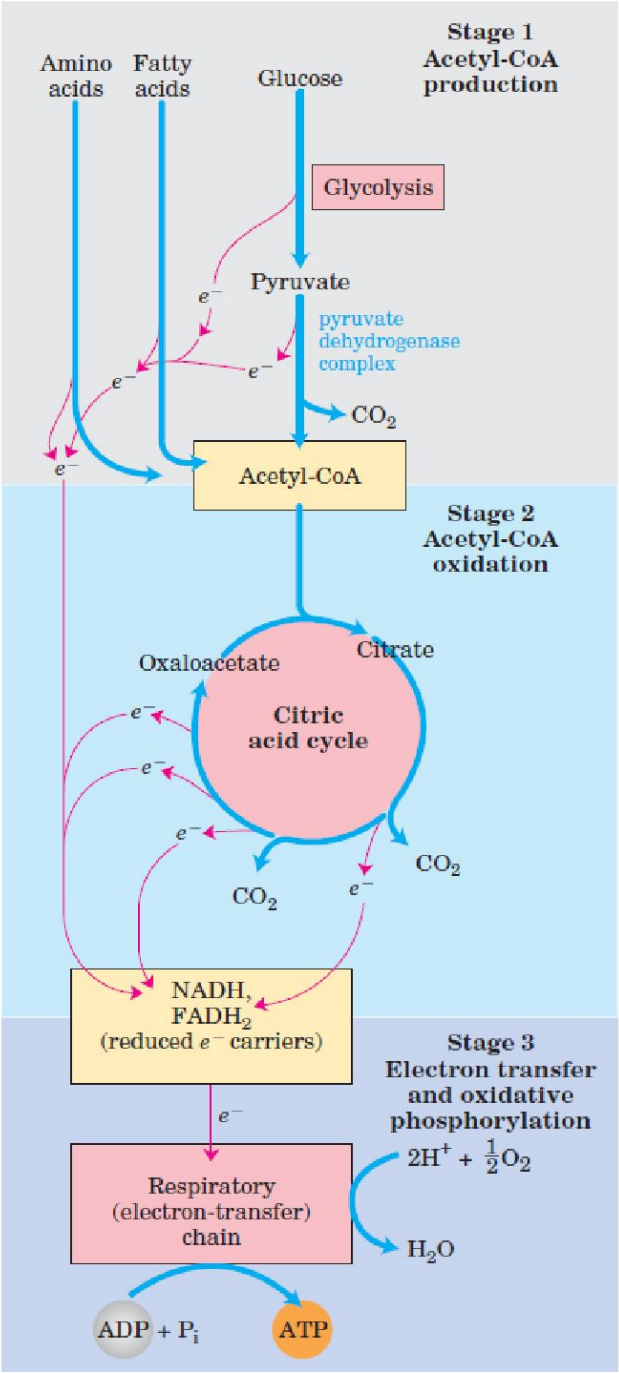
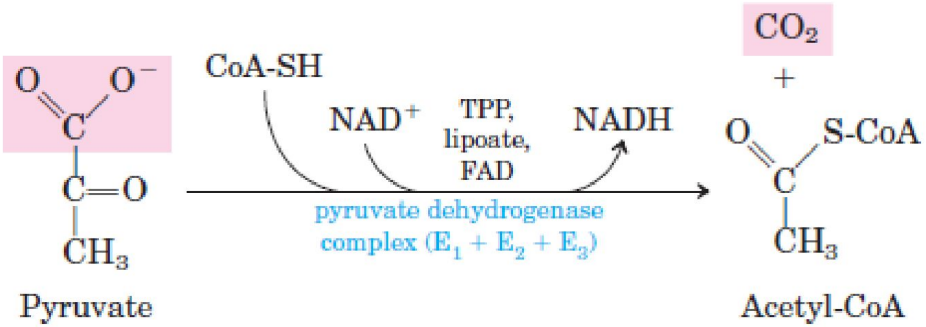
Цикл Кребса.

Дыхательная цепь.

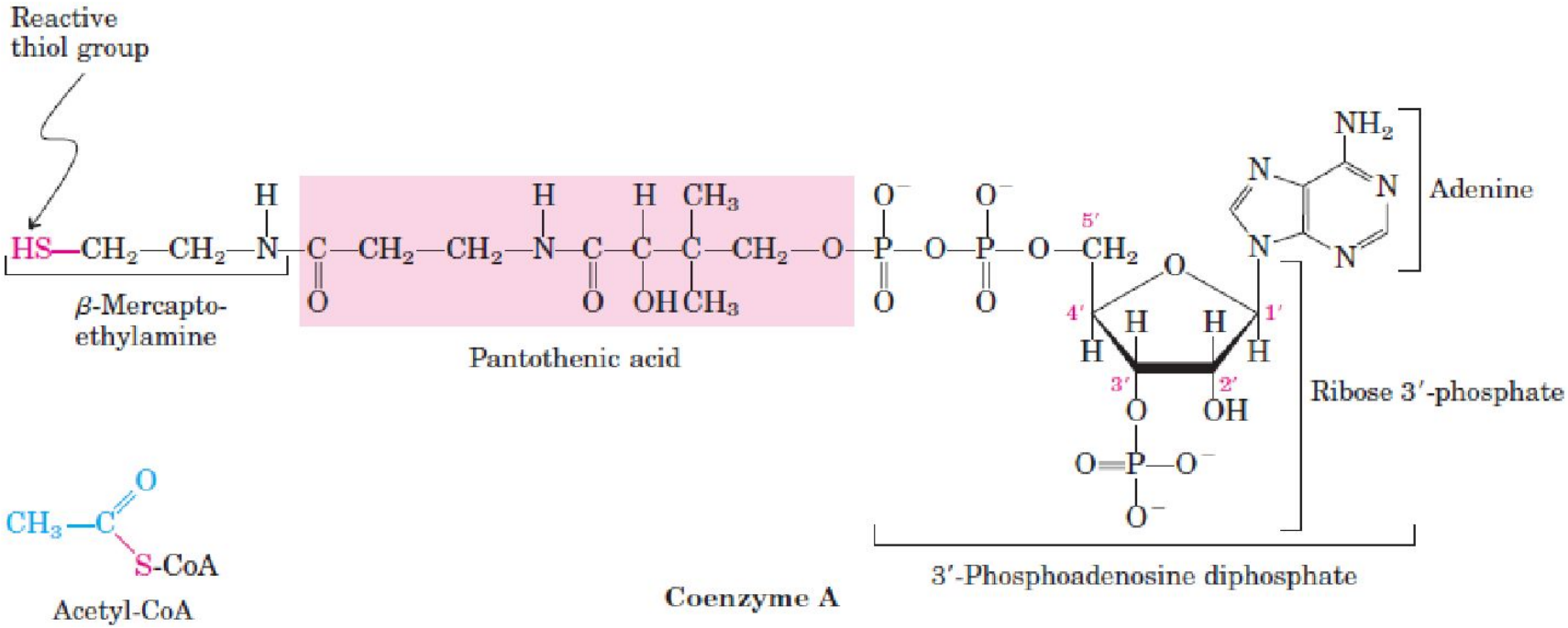

Electrons carried via NADH
Electrons carried via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Pyruvate oxidation
Acetyl CoA
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
CYTOSOL
MITOCHONDRION
ATP
Substrate-level phosphorylation
ATP
Substrate-level phosphorylation
ATP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


Stage 1
Acetyl-CoA
production
Amino acids
Fatty acids
Glucose
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
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
Respiratory (electron-transfer) chain
$2H^+ + \frac{1}{2}O_2$
H_2O
ADP + P_i
ATP

Окислительное декарбоксилирование Pyr (PDH)



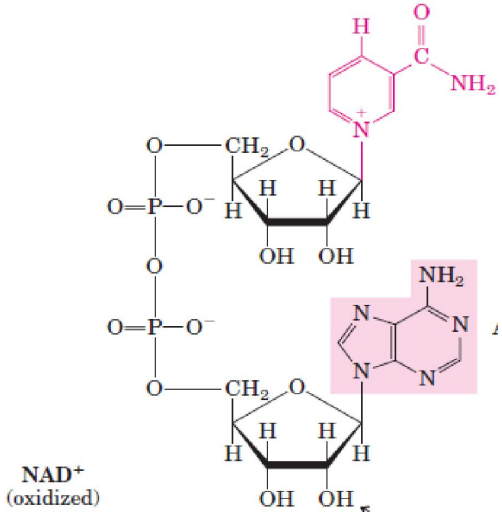
$\Delta G'^{\circ} = -33.4$ kJ/mol



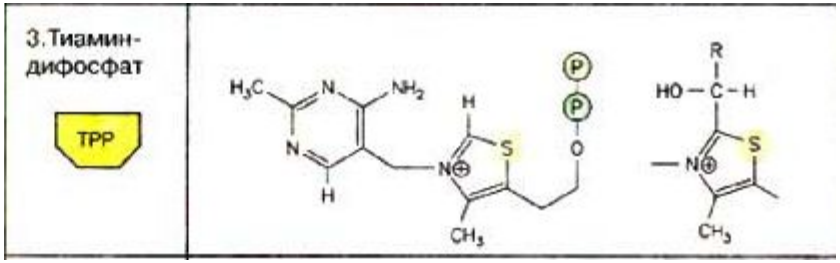
Коферменты PDH

1) CoA

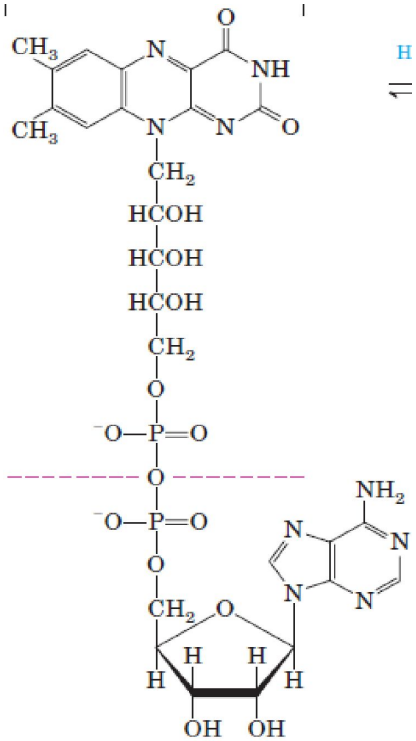
2) NAD



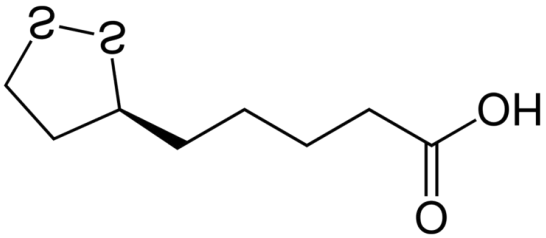
3) TPP

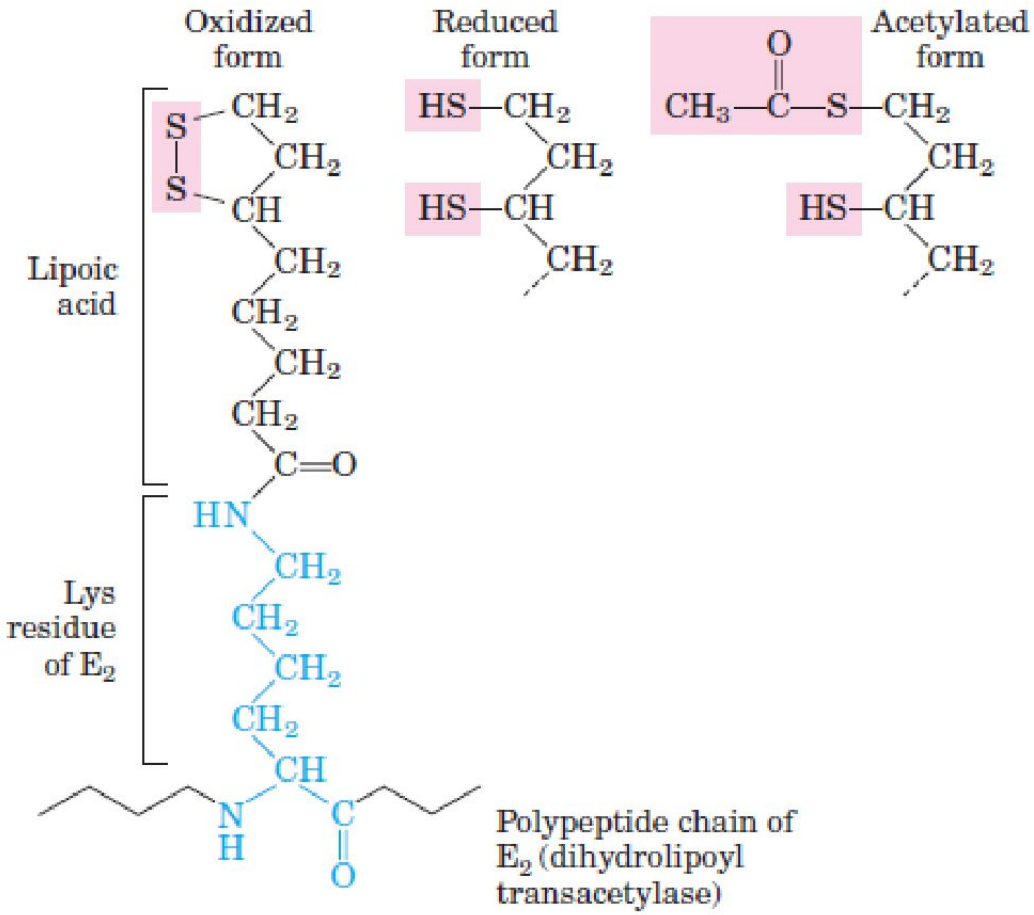


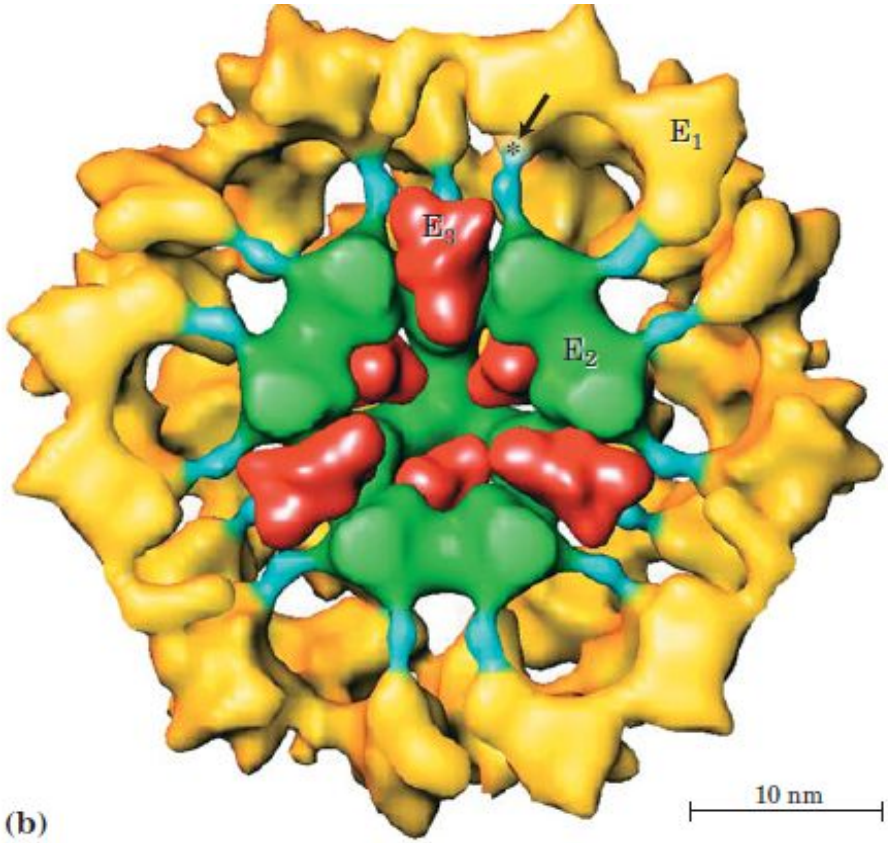
4) FAD

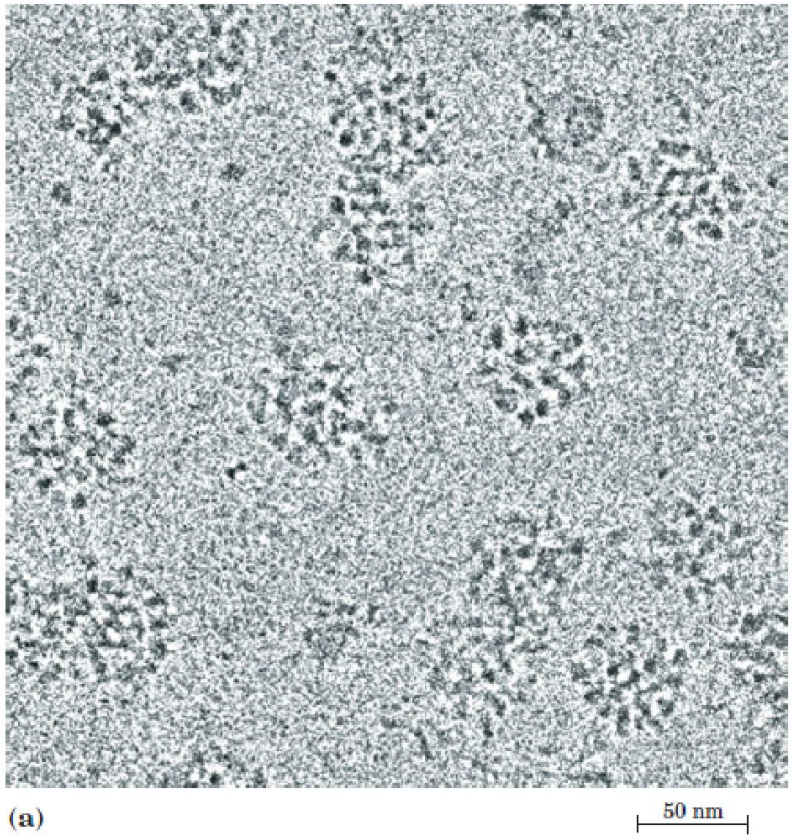


5) липоат




Oxidized form
Reduced form
Acetylated form
Lipoic acid
Lys residue of E_2
Polypeptide chain of E_2 (dihydrolipoyl transacetylase)

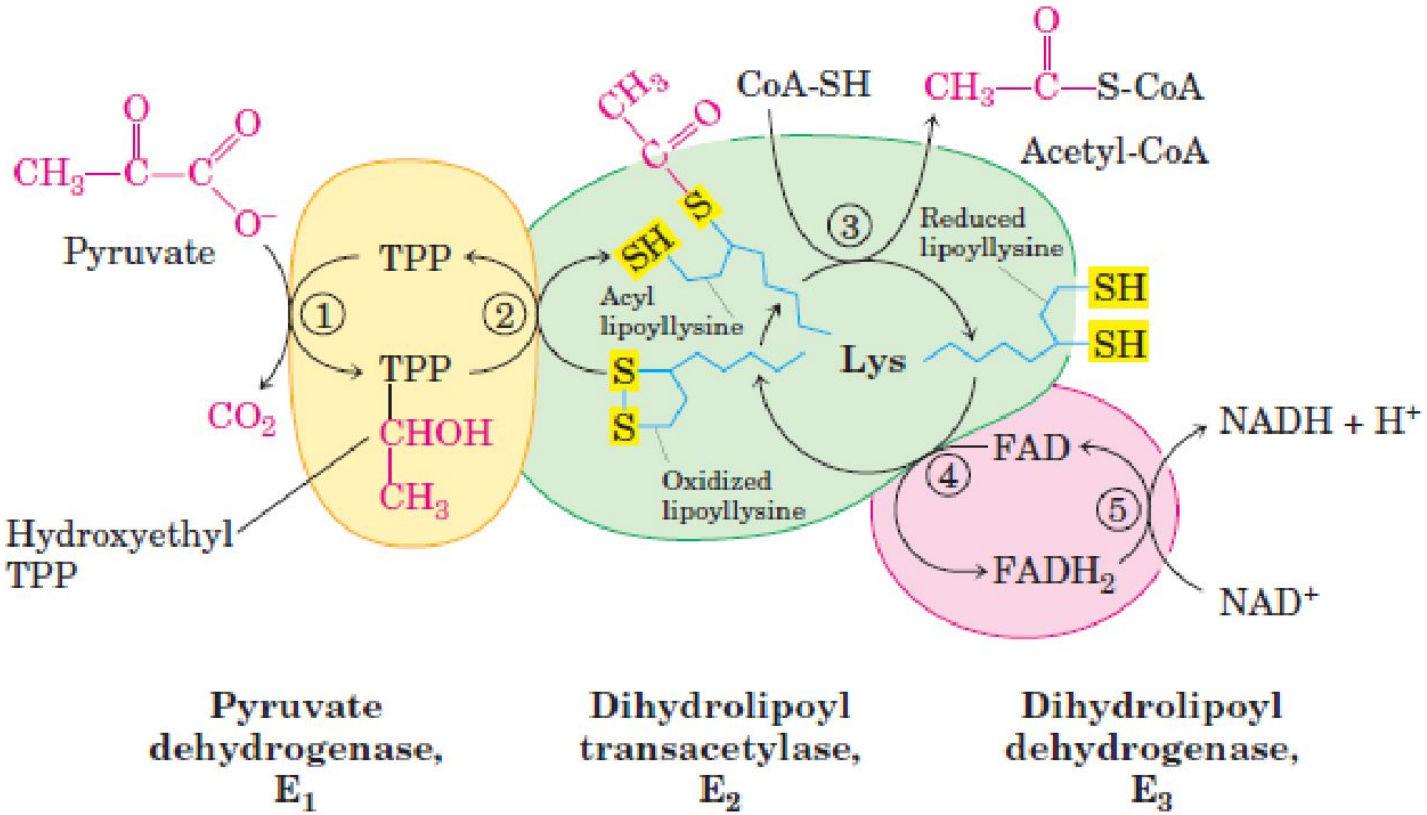


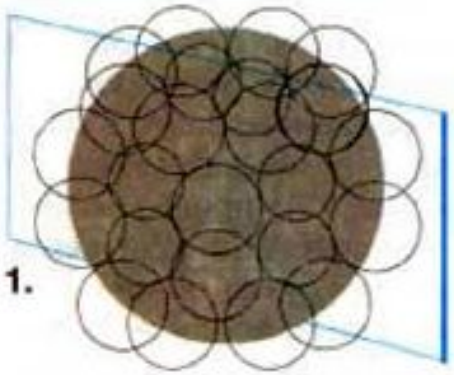


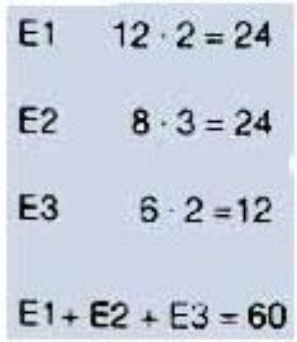
E1 – пируват дегидрогеназа

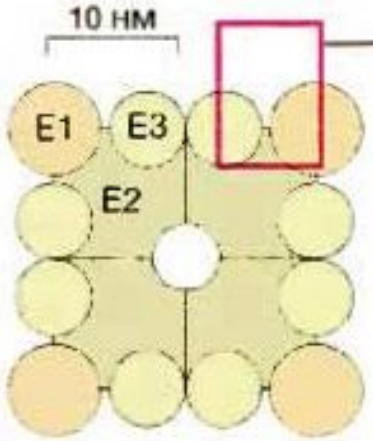
E2 – дигидролипоил трансацетилаза

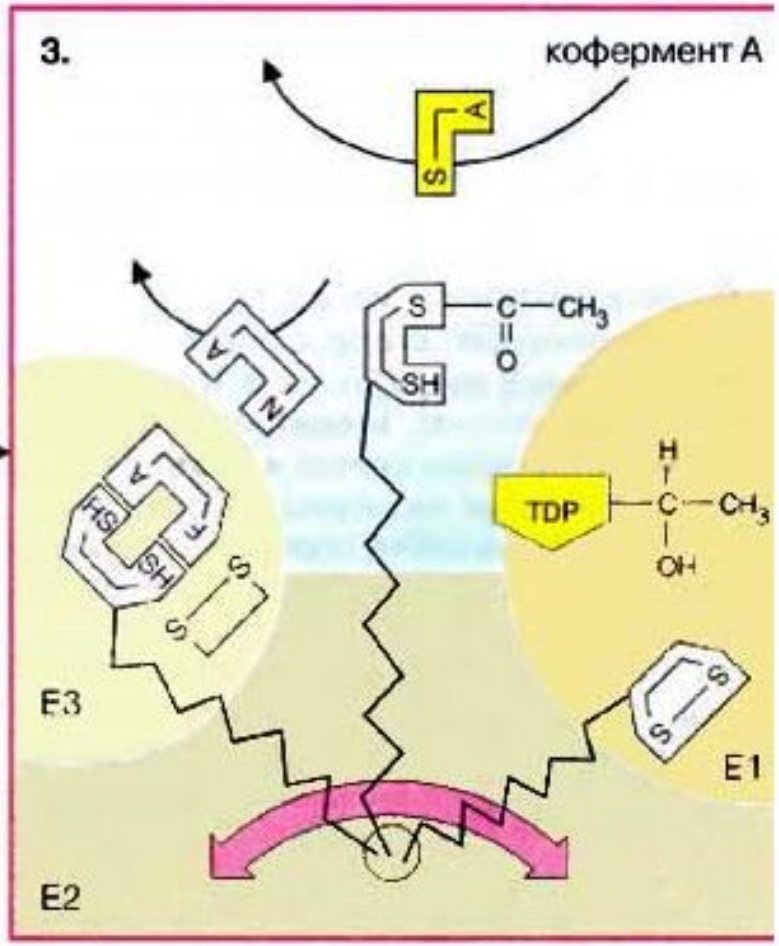
E3 – дигидролипоил дегидрогеназа


Pyruvate
TPP
TPP
CHOH
CH3
CO2
Hydroxyethyl TPP
CH3
CoA-SH
CH3—C—S-CoA
Acetyl-CoA
SH
S
Acyl lipoyllysine
S
S
Oxidized lipoyllysine
Lys
Reduced lipoyllysine
SH
SH
FAD
FADH2
NADH + H+
NAD+
Pyruvate dehydrogenase, E1
Dihydrolipoyl transacetylase, E2
Dihydrolipoyl dehydrogenase, E3



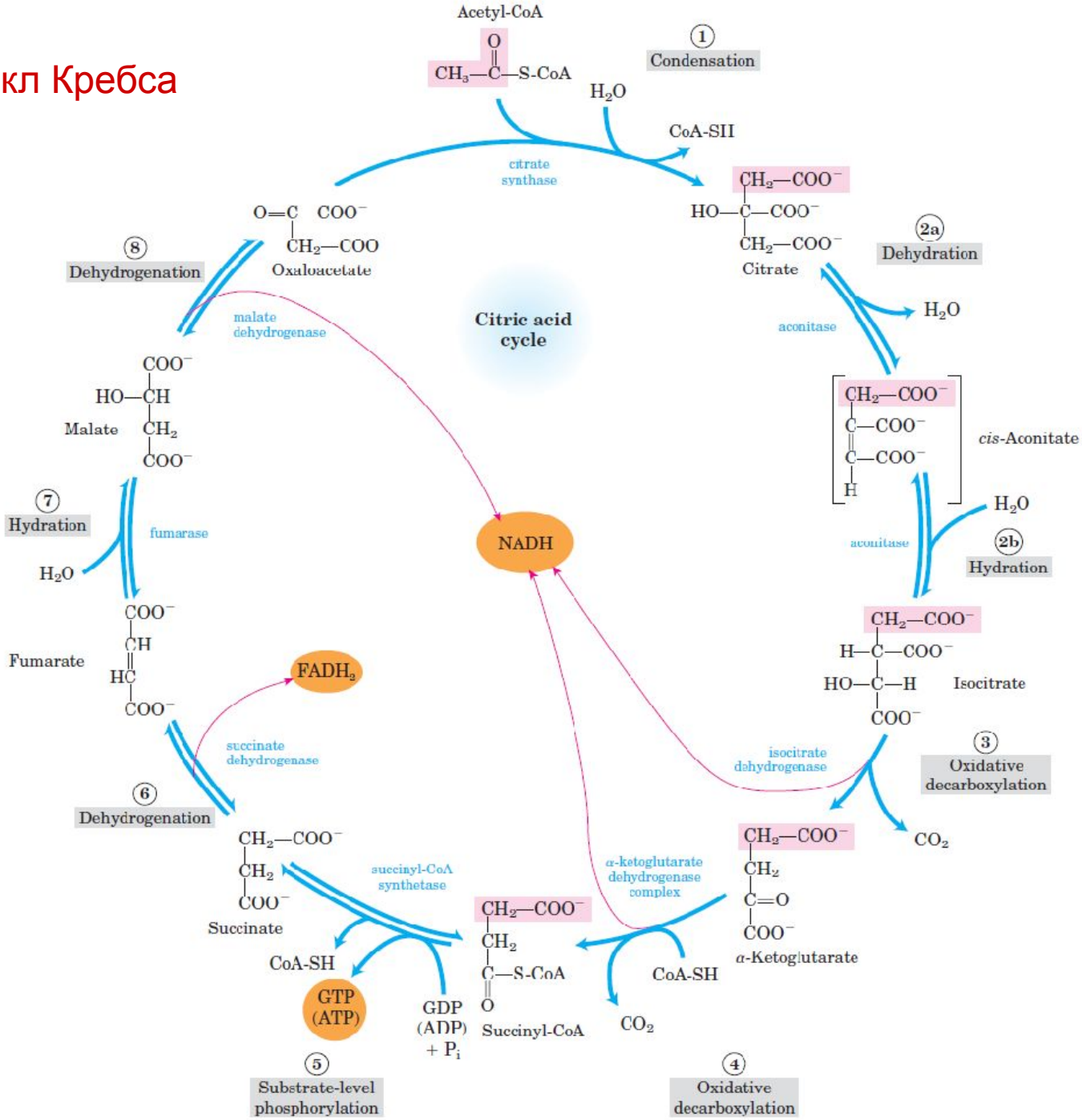


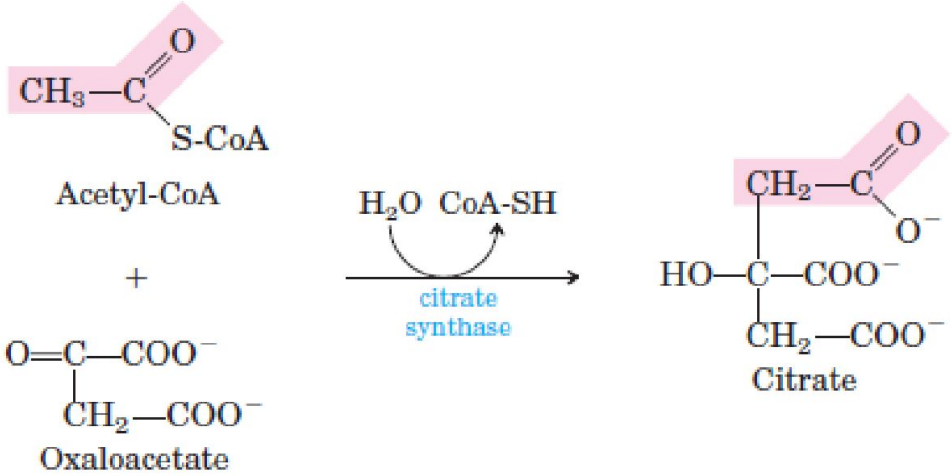




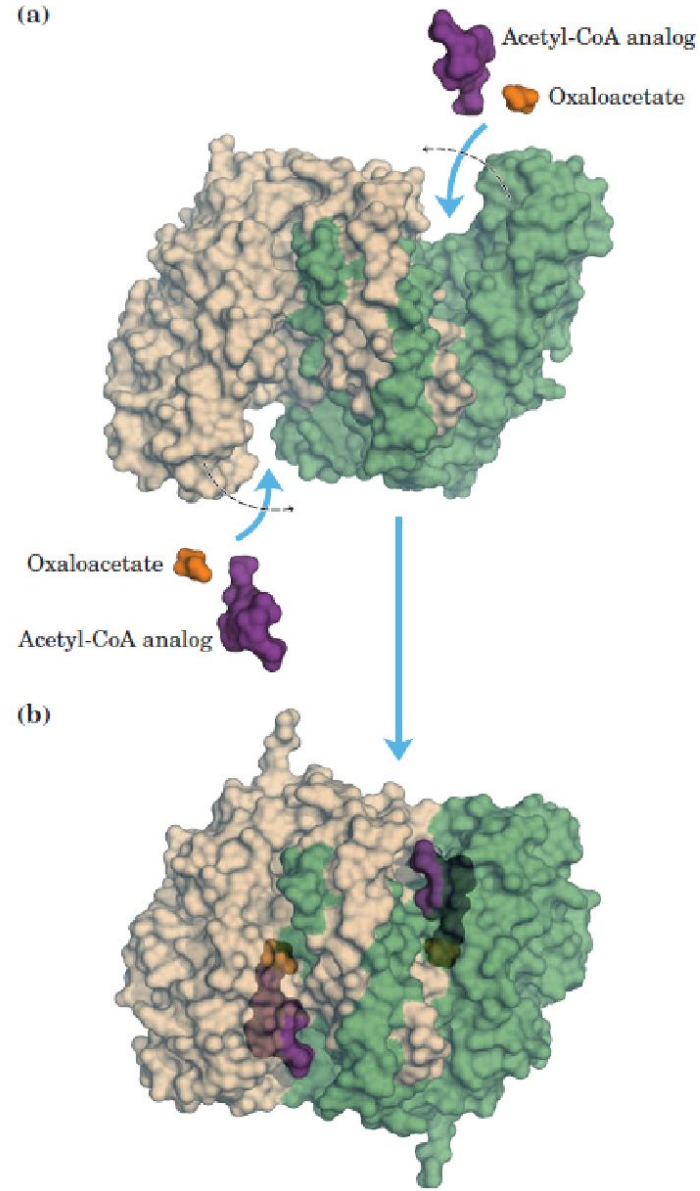
Б. Пируватдегидрогеназный комплекс *Escherichia coli*

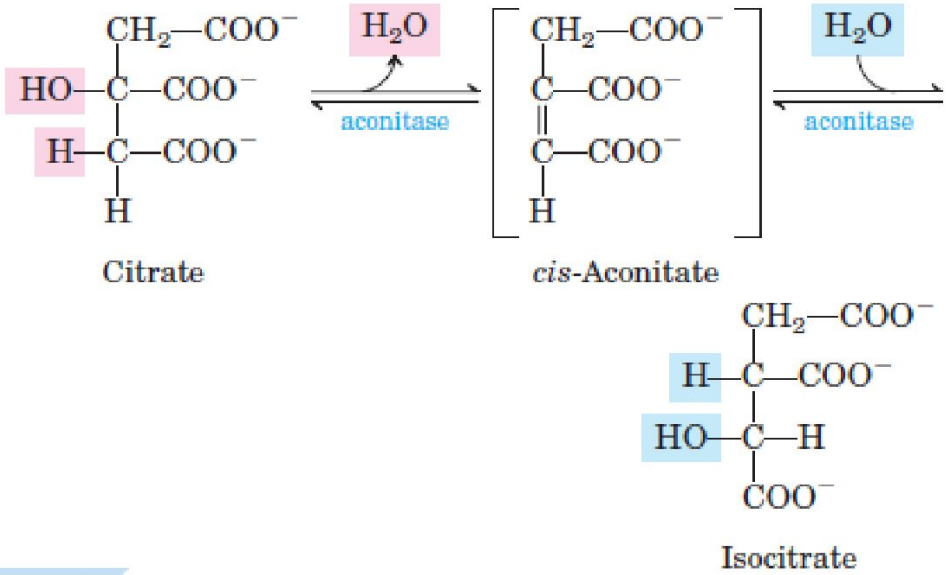
Цикл Кребса


Acetyl-CoA
CH3—C(=O)—S-CoA
H2O
1
Condensation
CoA-SH
citrate synthase
CH2—COO⁻
HO—C—COO⁻
CH2—COO⁻
Citrate
2a
Dehydration
H2O
aconitase
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
CH2—COO⁻
CH2
C—S-CoA
O
Succinyl-CoA
succinyl-CoA synthetase
GDP (ADP) + Pi
GTP (ATP)
CoA-SH
CH2—COO⁻
CH2
COO⁻
Succinate
5
Substrate-level phosphorylation
succinate dehydrogenase
FADH2
6
Dehydrogenation
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

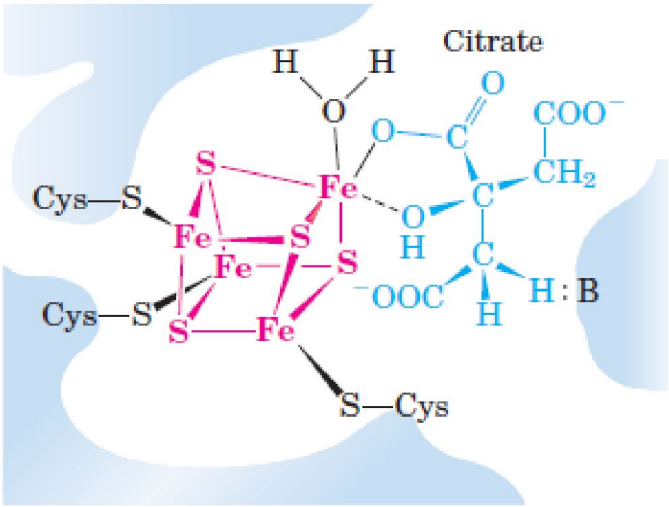


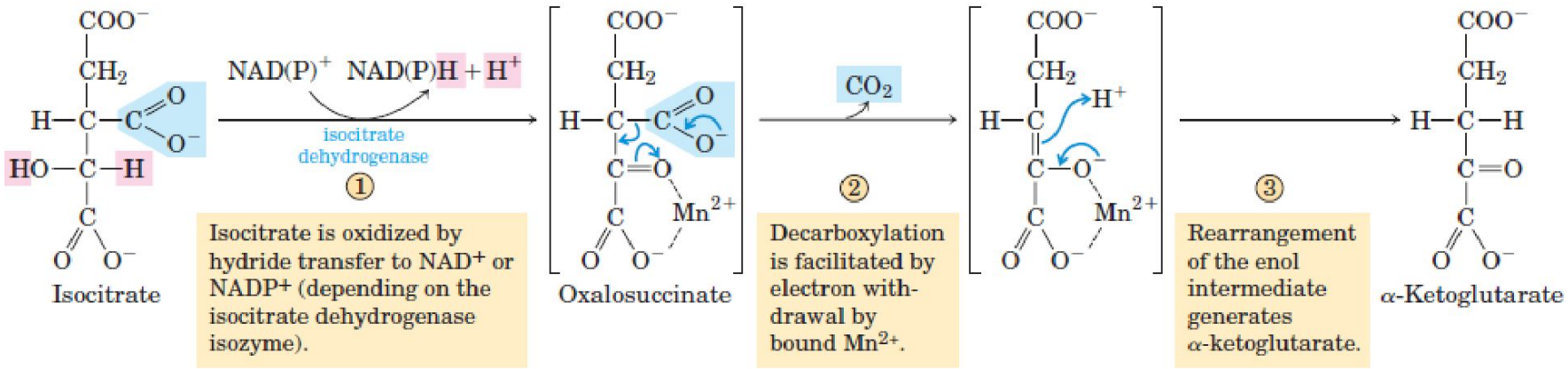
$\Delta G'^{\circ} = -32.2$ kJ/mol

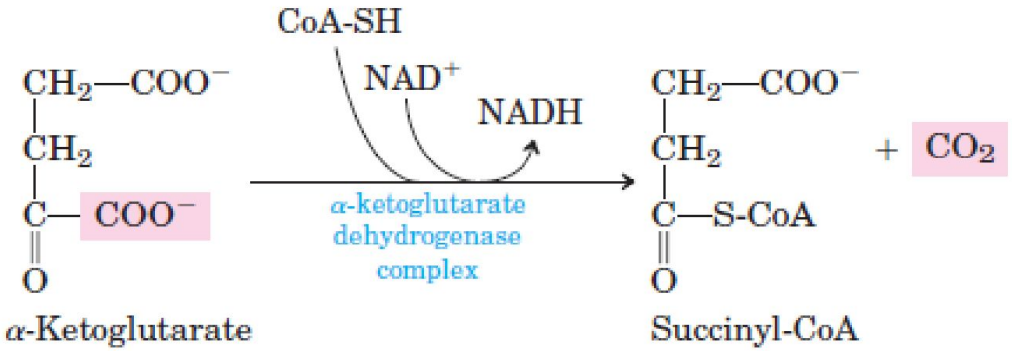




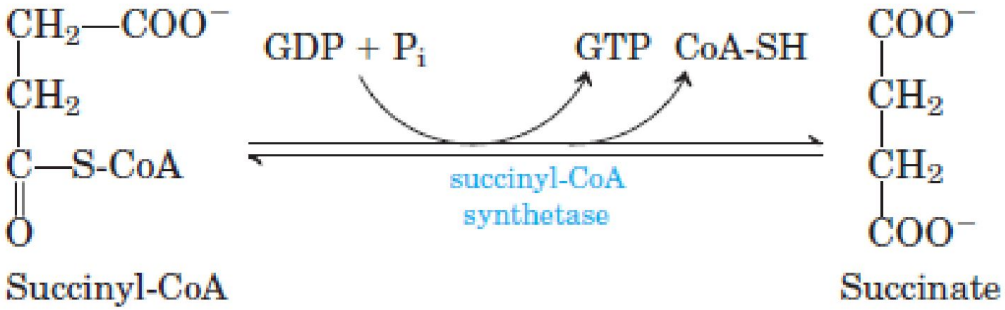
$\Delta G'^{\circ} = 13.3$ kJ/mol



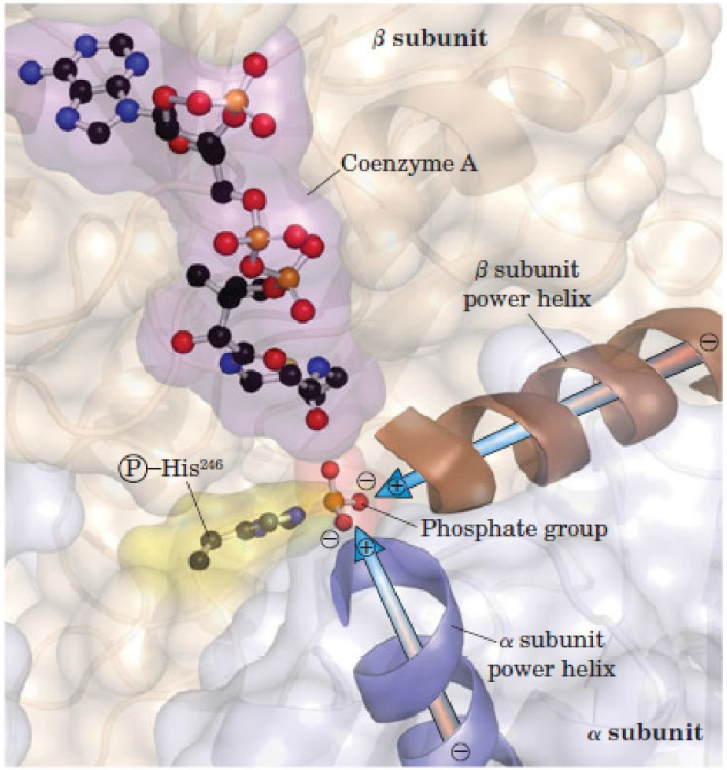

COO⁻
CH2
H—C—C
O
O⁻
HO—C—H
C
O O⁻
Isocitrate
NAD(P)+ NAD(P)H + H+
isocitrate dehydrogenase
1
Isocitrate is oxidized by hydride transfer to NAD+ or NADP+ (depending on the isocitrate dehydrogenase isozyme).
Mn2+
Oxalosuccinate
CO2
2
Decarboxylation is facilitated by electron withdrawal by bound Mn2+.
H+
3
Rearrangement of the enol intermediate generates α-ketoglutarate.
α-Ketoglutarate

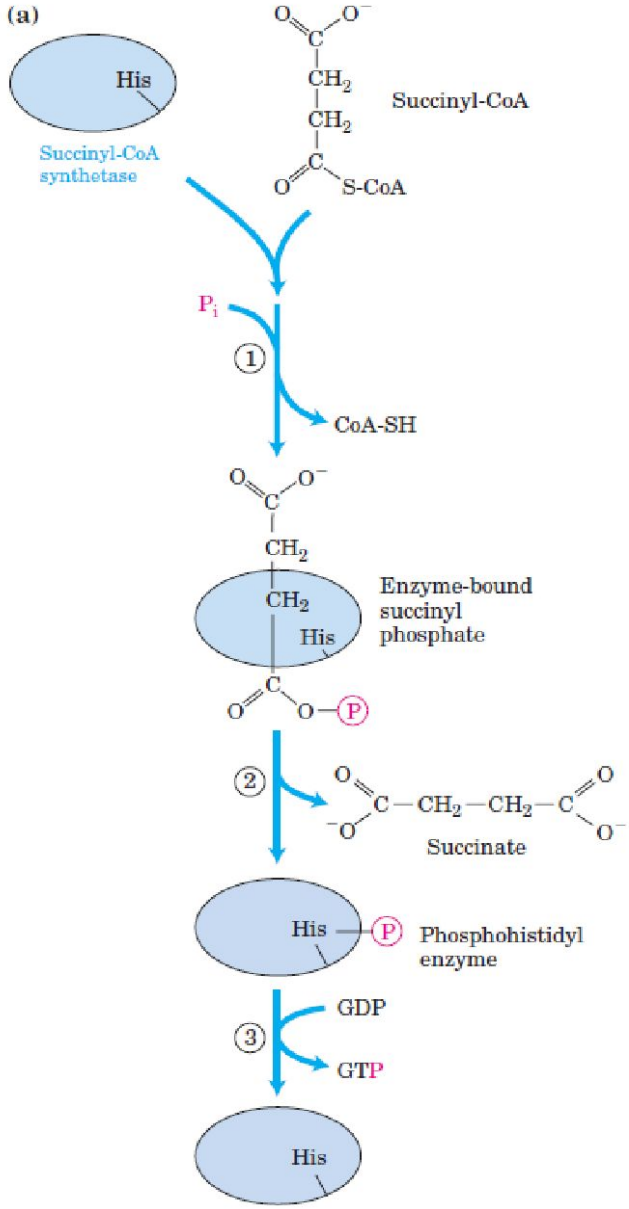


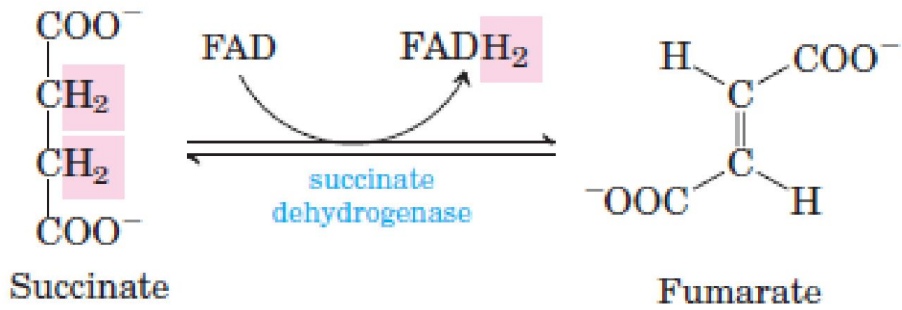
$\Delta G'^{\circ} = -33.5$ kJ/mol



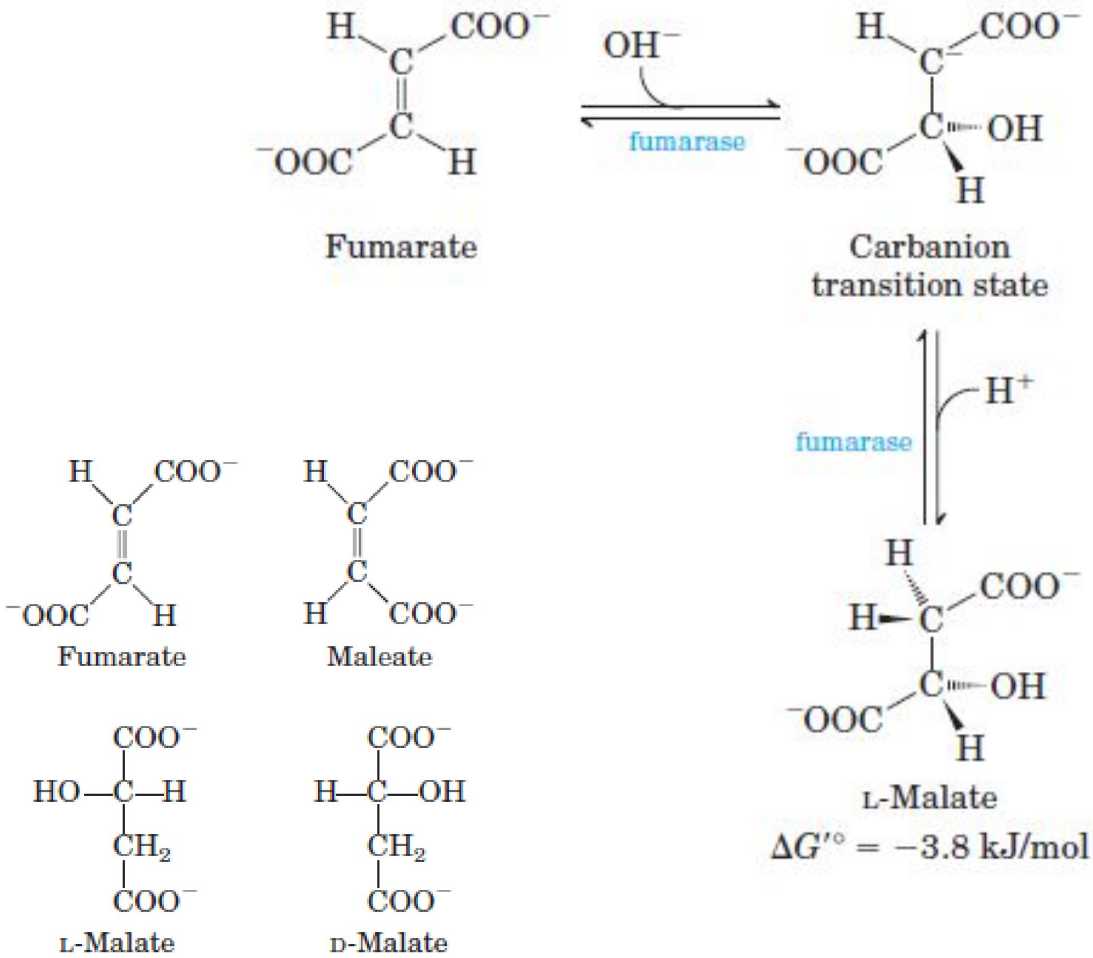
$$\Delta G'^{\circ} = -2.9 \text{ kJ/mol}$$

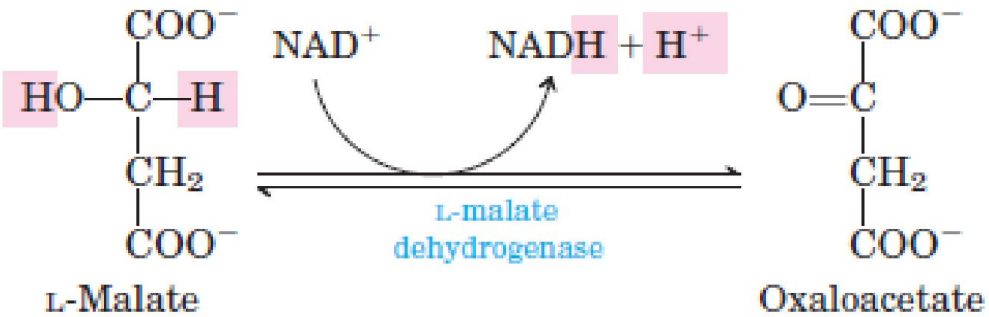




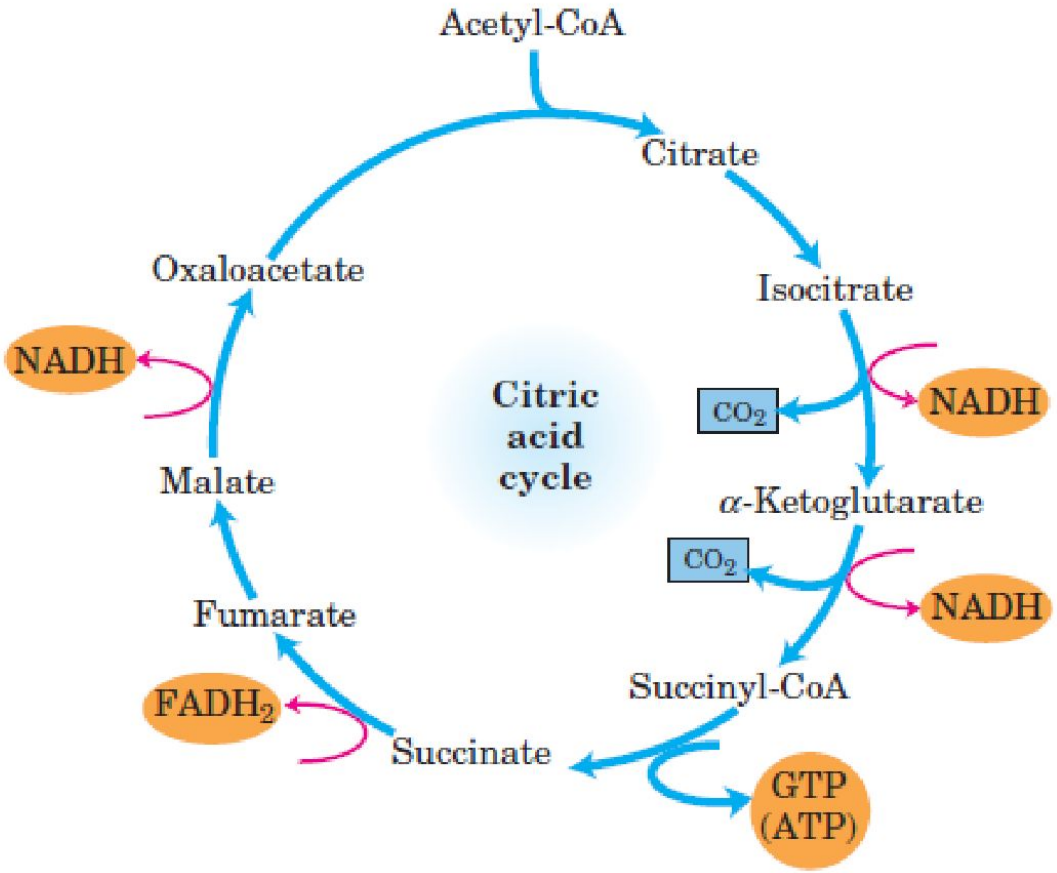


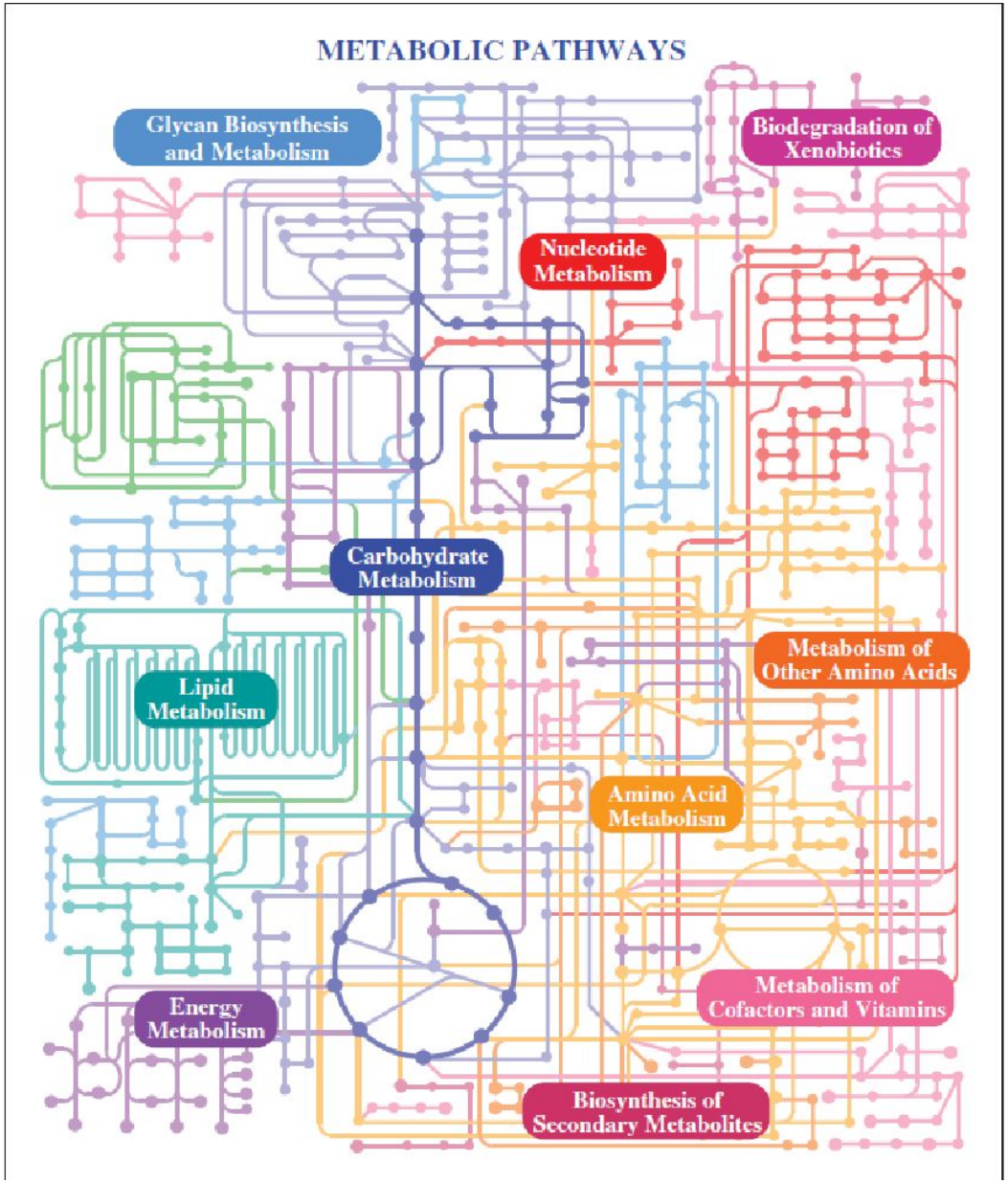
$\Delta G'^{\circ} = 0$ kJ/mol

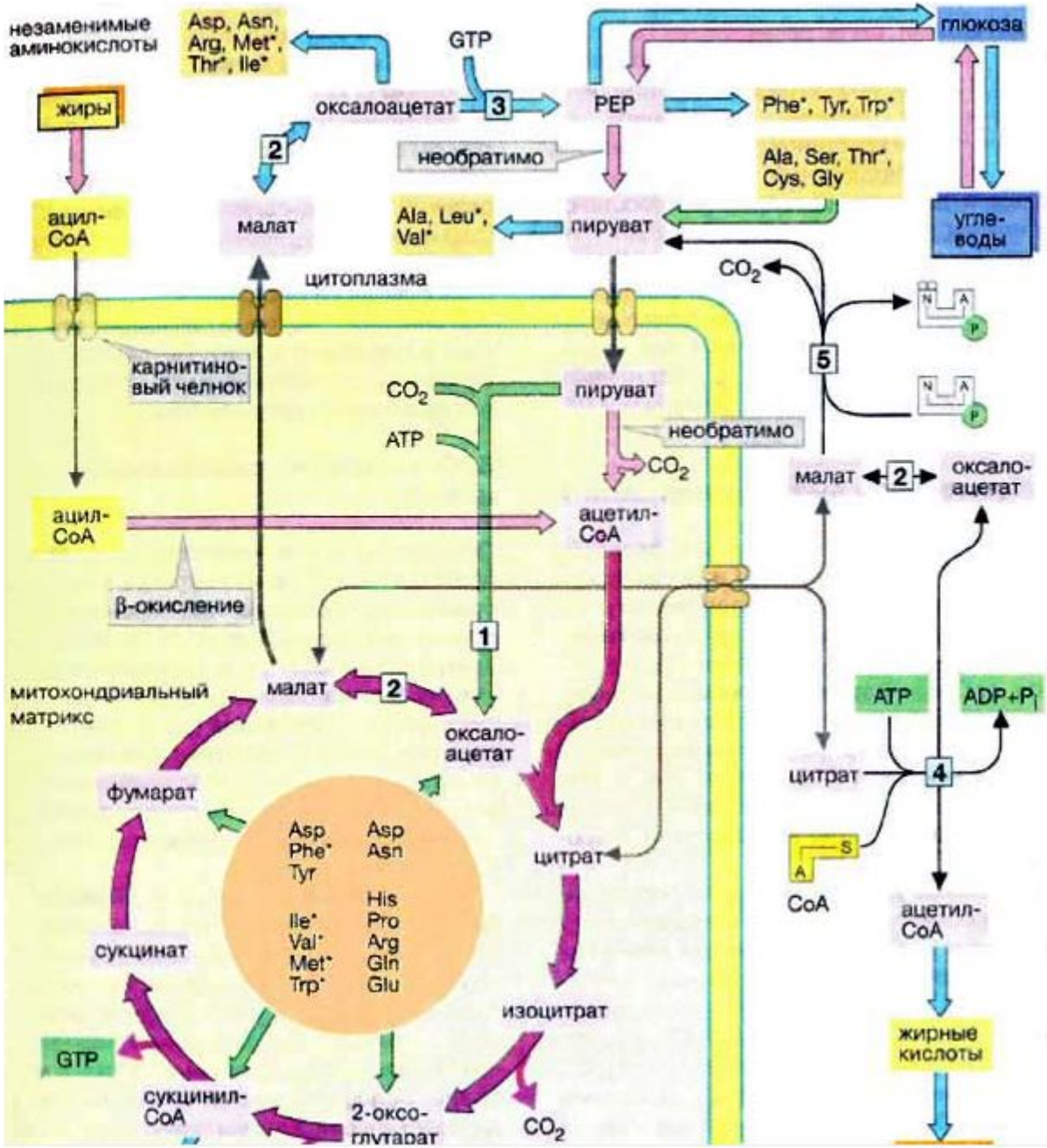

Fumarate
OH⁻
fumarase
Carbanion
transition state
H⁺
fumarase
L-Malate
ΔG′° = −3.8 kJ/mol
Fumarate
Maleate
L-Malate
D-Malate

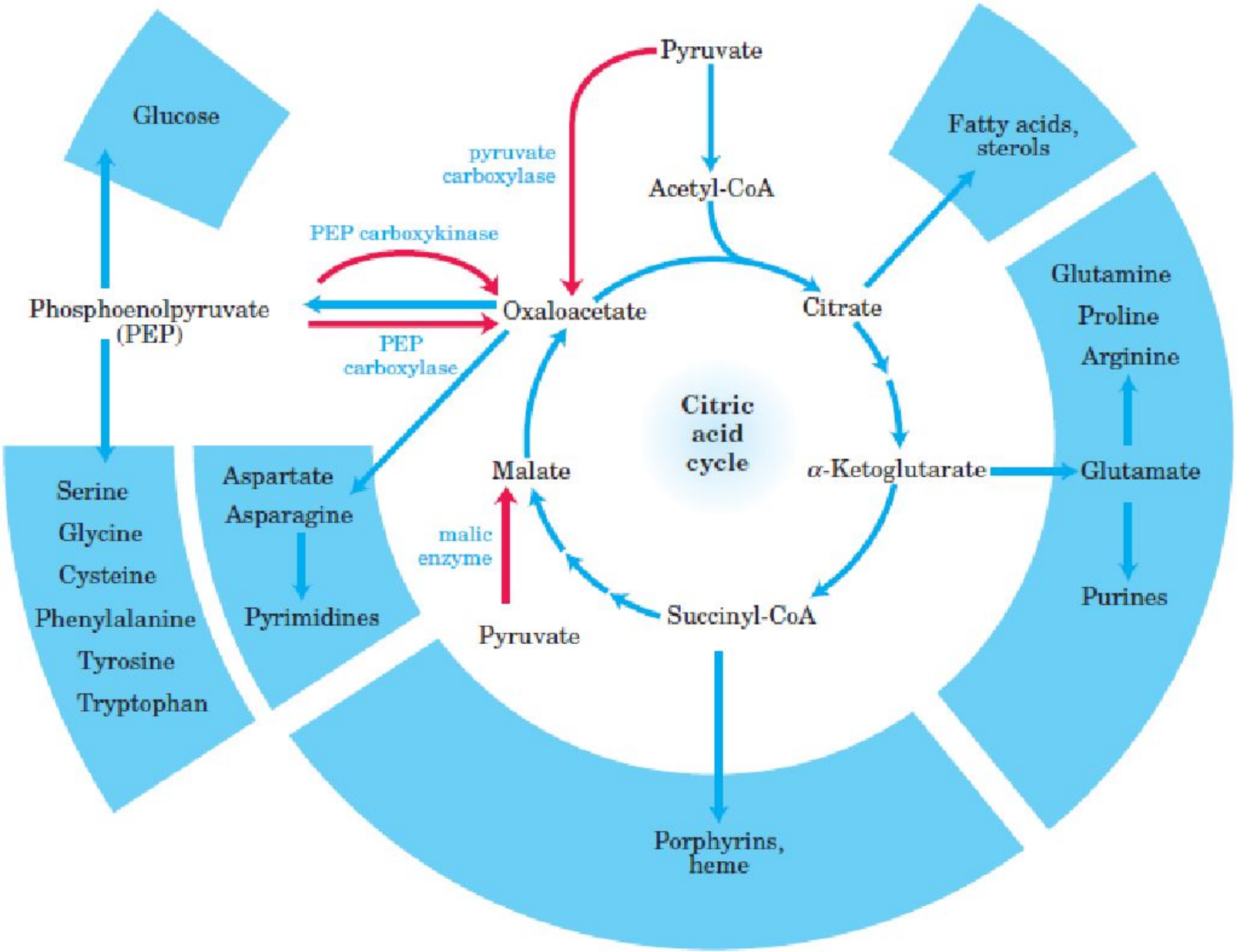


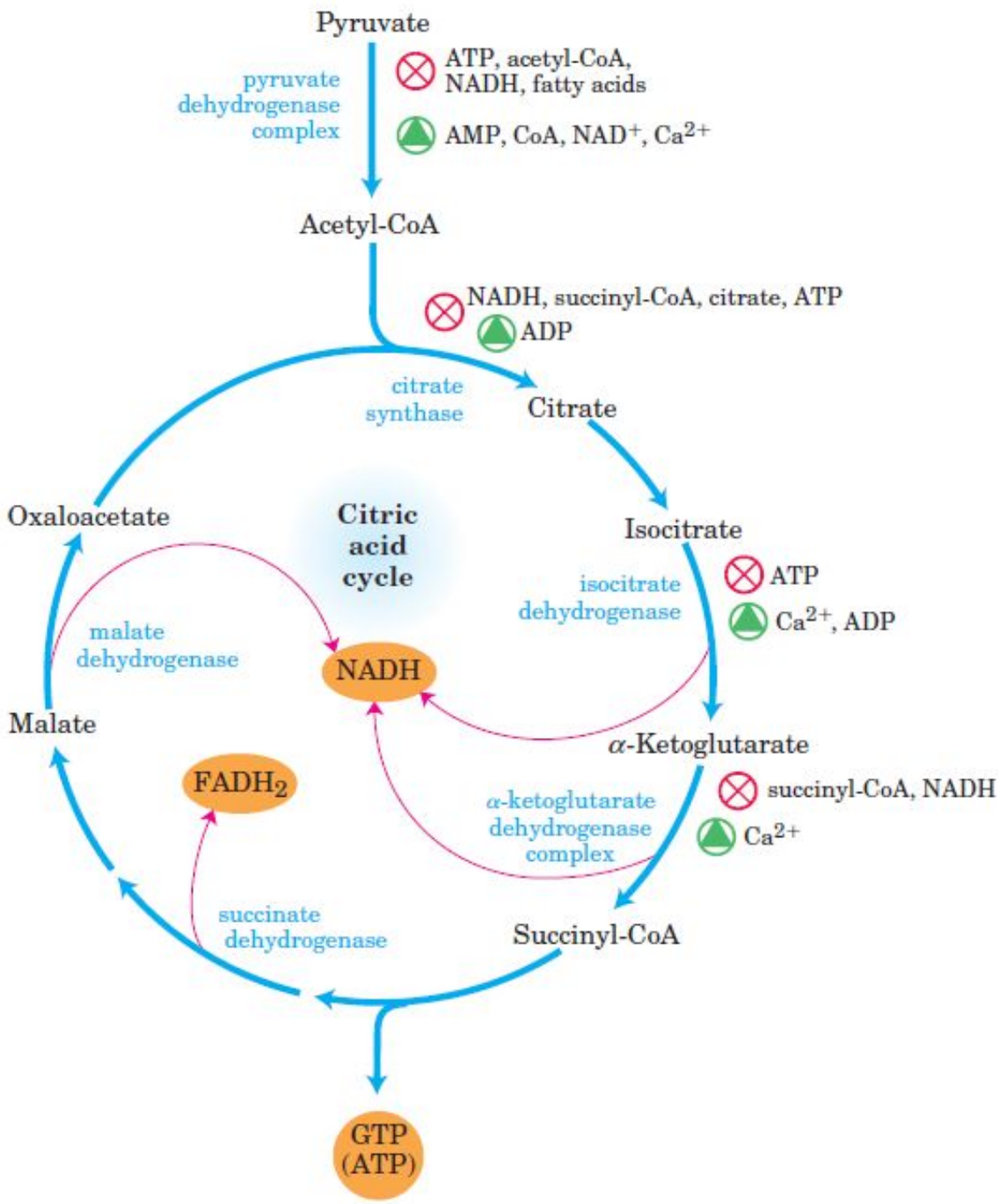
$\Delta G'^{\circ} = 29.7$ kJ/mol


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

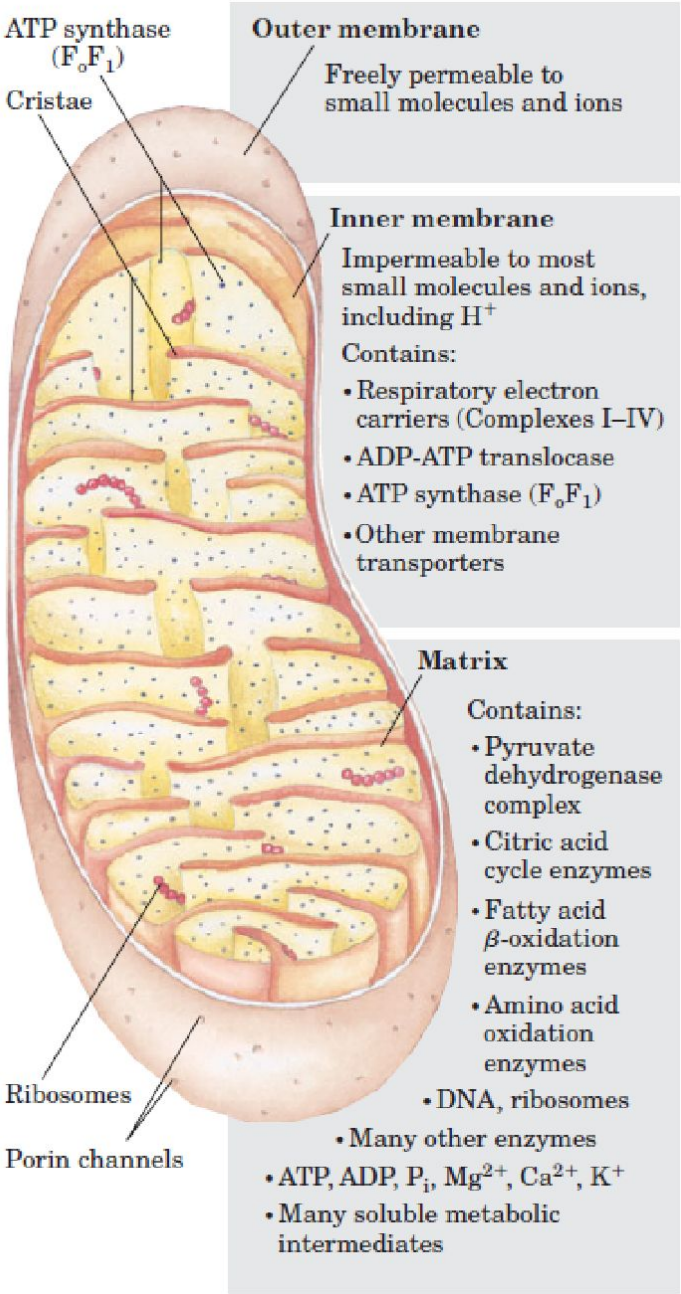

METABOLIC PATHWAYS
Glycan Biosynthesis and Metabolism
Biodegradation of Xenobiotics
Nucleotide Metabolism
Carbohydrate Metabolism
Metabolism of Other Amino Acids
Lipid Metabolism
Amino Acid Metabolism
Metabolism of Cofactors and Vitamins
Energy Metabolism
Biosynthesis of Secondary Metabolites

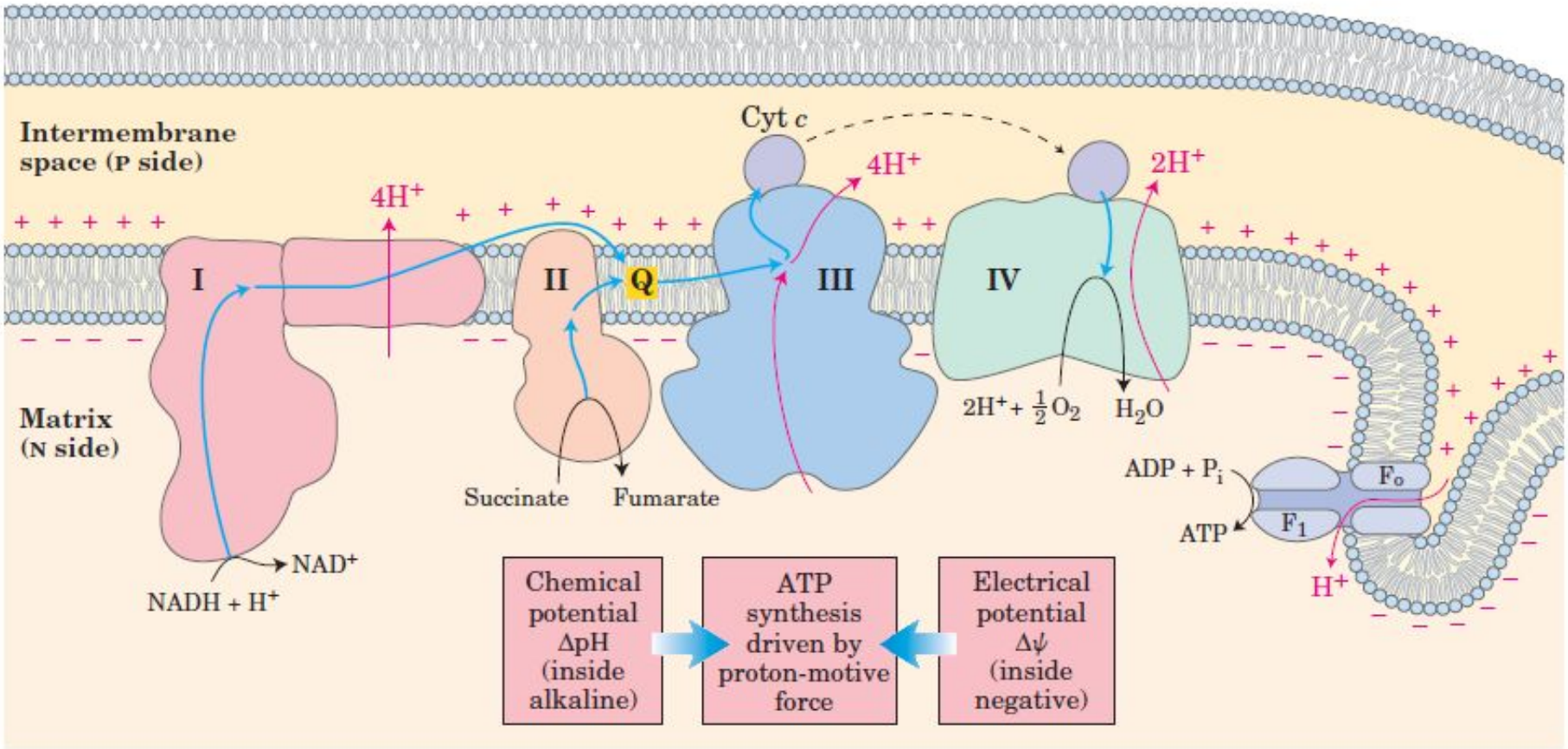

незаменимые аминокислоты
Asp, Asn, Arg, Met*, Thr*, Ile*
GTP
глюкоза
жиры
оксалоацетат
3
PEP
Phe*, Tyr, Trp*
2
необратимо
Ala, Ser, Thr*, Cys, Gly
ацил-CoA
малат
Ala, Leu*, Val*
пируват
углеводы
CO_2
цитоплазма
5
карнитиновый челнок
CO_2
пируват
ATP
необратимо
CO_2
малат
2
оксалоацетат
ацил-CoA
ацетил-CoA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

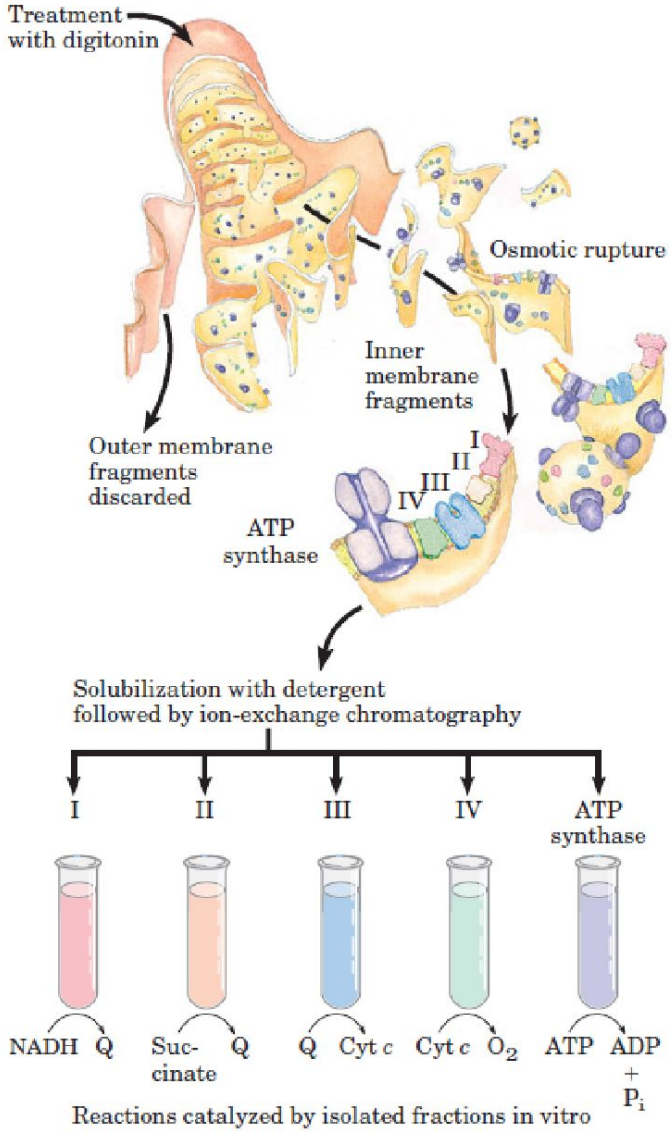

Glucose
Pyruvate
pyruvate carboxylase
Acetyl-CoA
Fatty acids, sterols
PEP carboxykinase
Phosphoenolpyruvate (PEP)
Oxaloacetate
Citrate
PEP carboxylase
Glutamine
Proline
Arginine
Citric acid cycle
Malate
α-Ketoglutarate
Glutamate
Serine
Glycine
Cysteine
Phenylalanine
Tyrosine
Tryptophan
Aspartate
Asparagine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

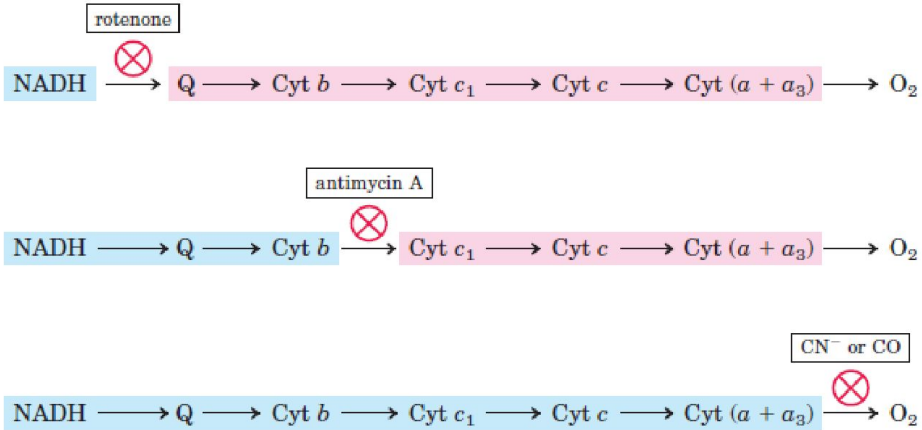

Pyruvate
pyruvate dehydrogenase complex
ATP, acetyl-CoA, NADH, fatty acids
AMP, CoA, NAD+, Ca2+
Acetyl-CoA
NADH, succinyl-CoA, citrate, ATP
ADP
citrate synthase
Citrate
Isocitrate
isocitrate dehydrogenase
ATP
Ca2+, ADP
α-Ketoglutarate
α-ketoglutarate dehydrogenase complex
succinyl-CoA, NADH
Ca2+
Succinyl-CoA
succinate dehydrogenase
Malate
malate dehydrogenase
Oxaloacetate
Citric acid cycle
NADH
FADH2
GTP (ATP)

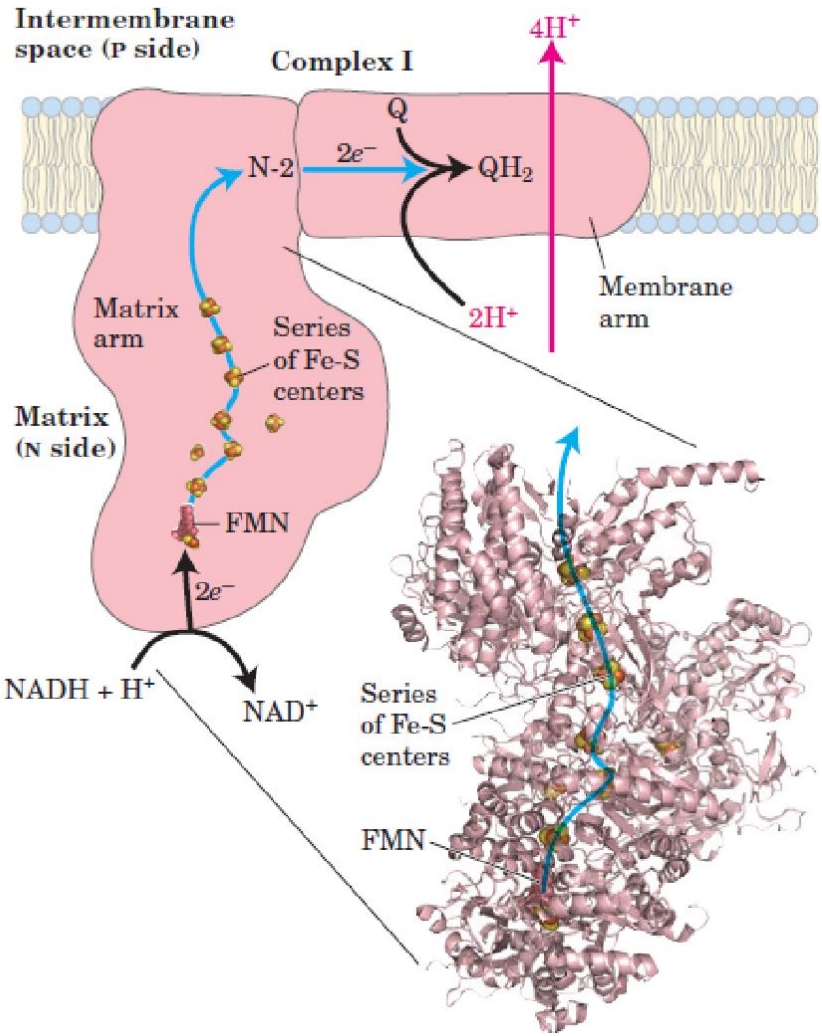
Дыхательная цепь



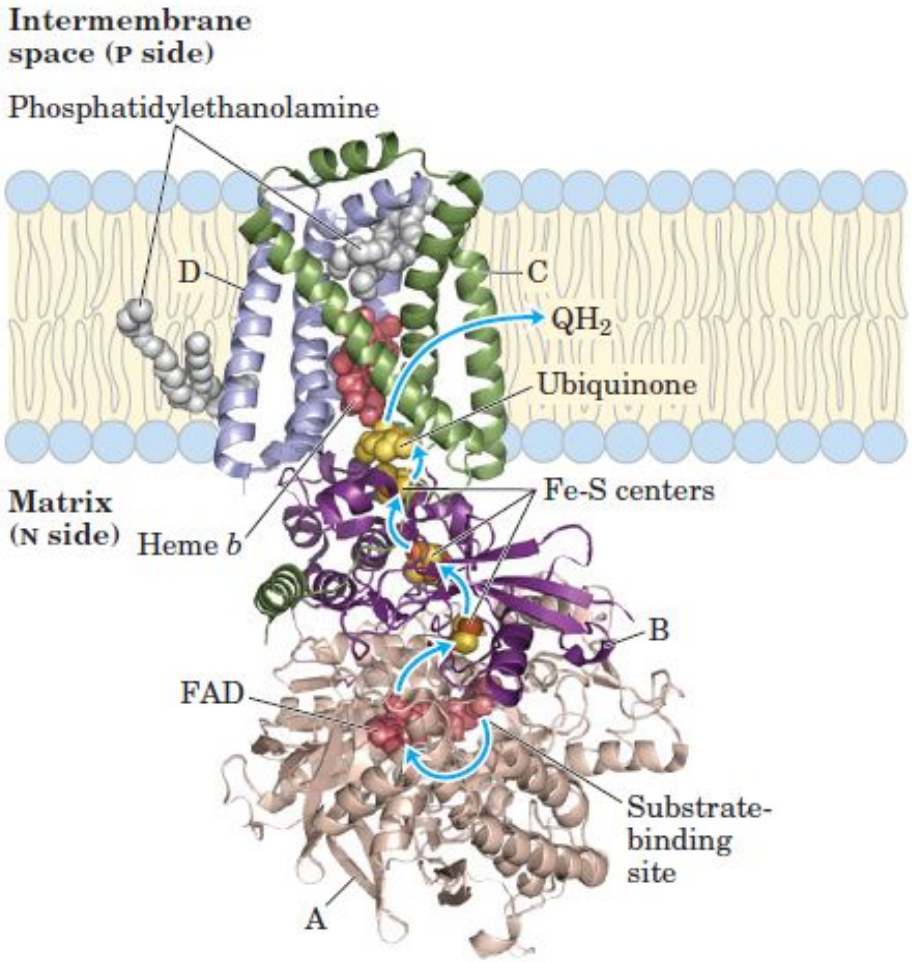

Intermembrane space (P side)
Matrix (N side)
Cyt c
4H+
4H+
2H+
I
II
Q
III
IV
NAD+
NADH + H+
Succinate
Fumarate
2H+ + ½ O2
H2O
ADP + Pi
ATP
Fo
F1
H+
Chemical potential ΔpH (inside alkaline)
ATP synthesis driven by proton-motive force
Electrical potential Δψ (inside negative)

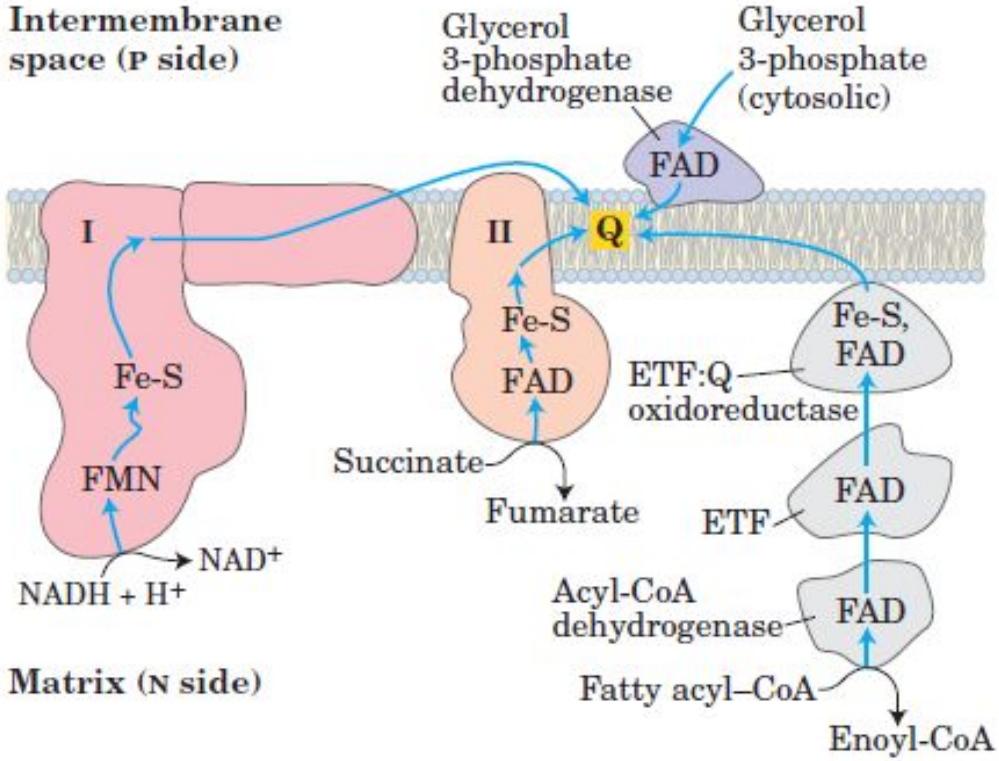

Treatment with digitonin
Osmotic rupture
Inner membrane fragments
Outer membrane fragments discarded
I
II
III
IV
ATP synthase
Solubilization with detergent followed by ion-exchange chromatography
I
II
III
IV
ATP synthase
NADH Q
Suc- cinate Q
Q Cyt c
Cyt c O2
ATP ADP + Pi
Reactions catalyzed by isolated fractions in vitro

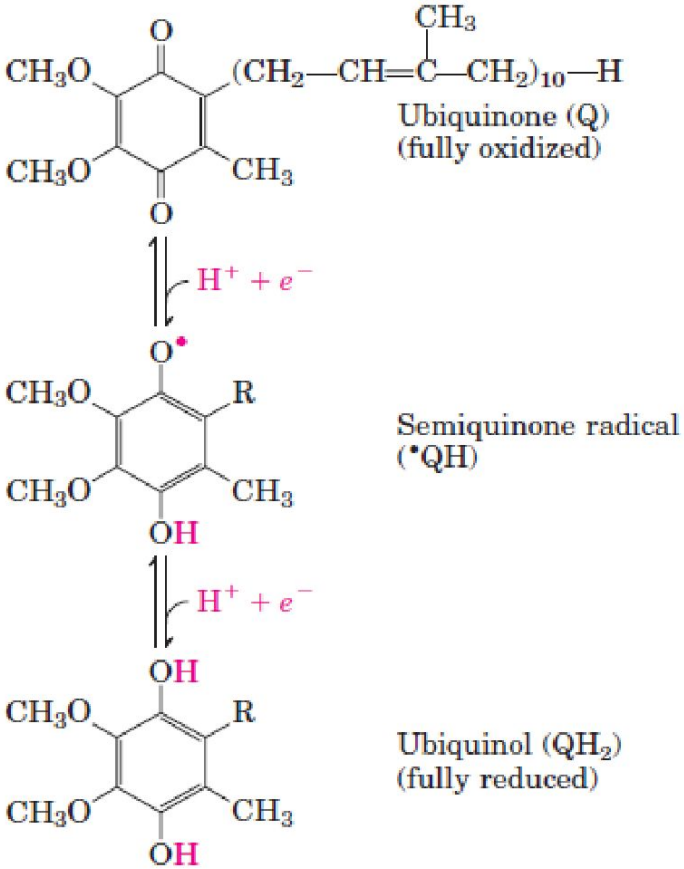

rotenone
NADH → Q → Cyt b → Cyt c1 → Cyt c → Cyt (a + a3) → O2
antimycin A
NADH → Q → Cyt b → Cyt c1 → Cyt c → Cyt (a + a3) → O2
CN⁻ or CO
NADH → Q → Cyt b → Cyt c1 → Cyt c → Cyt (a + a3) → O2

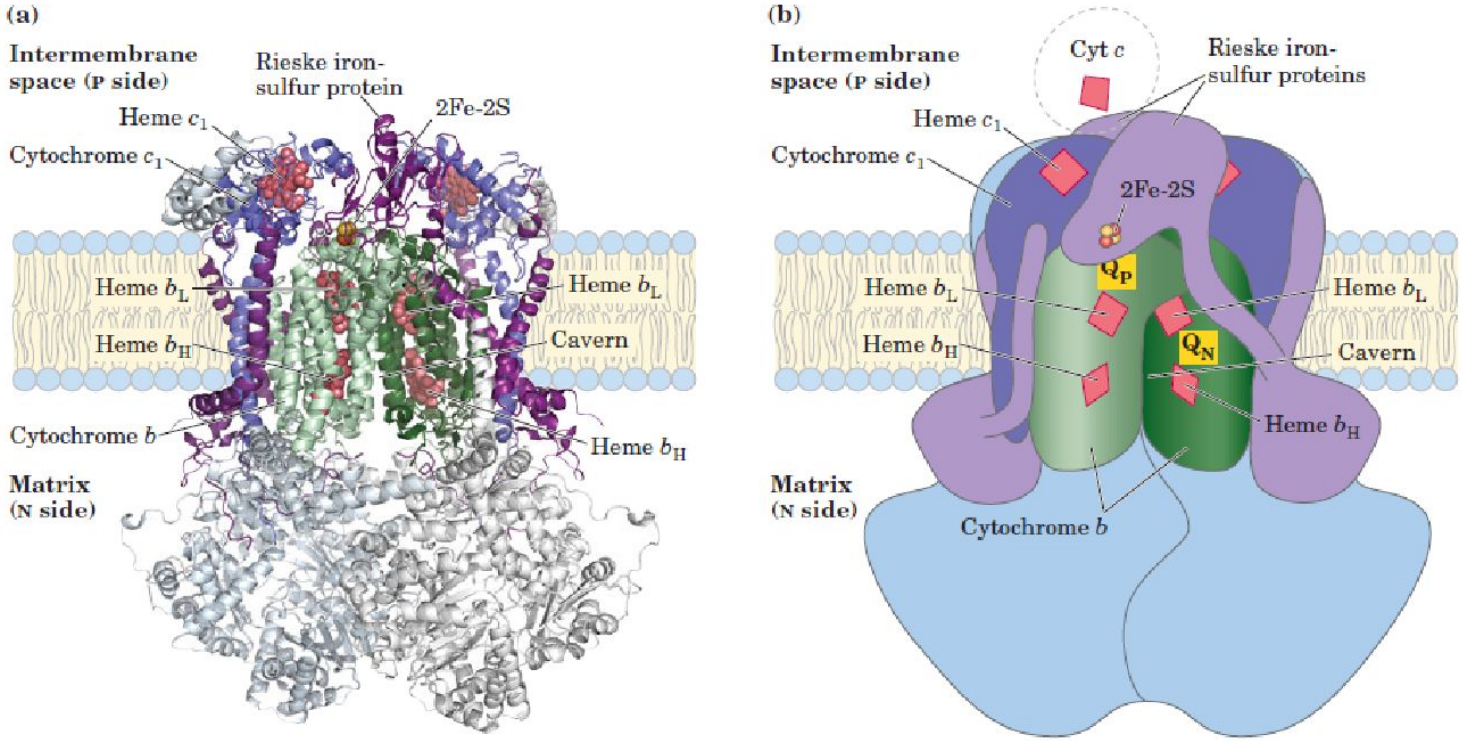


$$NADH + 5H_N^+ + Q \longrightarrow NAD^+ + QH_2 + 4H_P^+$$

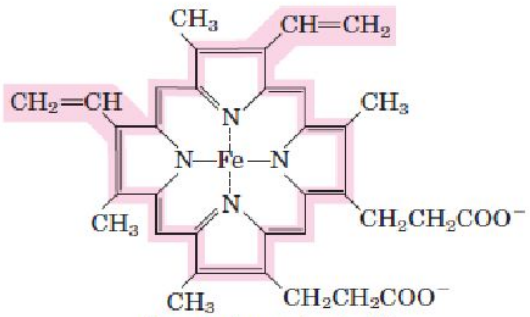

Intermembrane space (P side)
Phosphatidylethanolamine
D
C
QH_2
Ubiquinone
Fe-S centers
Matrix (N side)
Heme b
B
FAD
Substrate-binding site
A


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

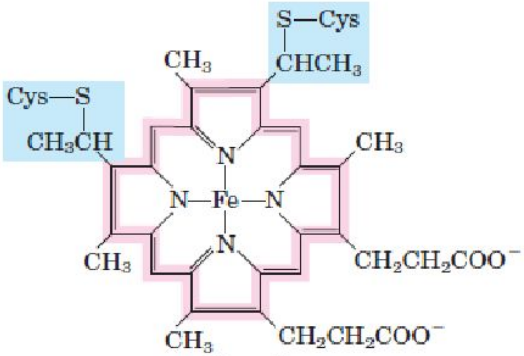

Ubiquinone (Q)
(fully oxidized)
$H^+ + e^-$
Semiquinone radical
(•QH)
$H^+ + e^-$
Ubiquinol (QH_2)
(fully reduced)



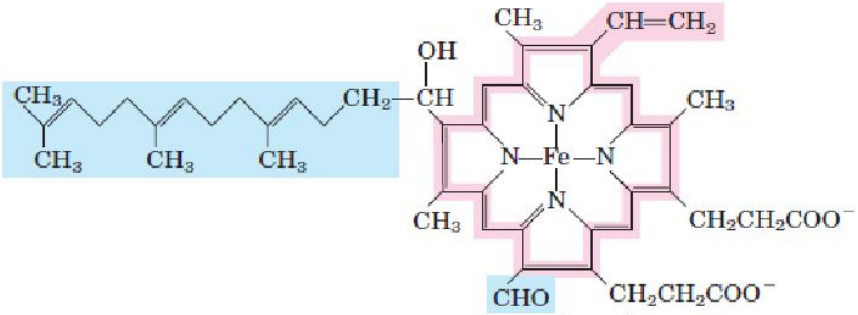
$$QH_2 + 2\ \text{cyt}\ c_1\ (\text{oxidized}) + 2H_N^+ \longrightarrow Q + 2\ \text{cyt}\ c_1\ (\text{reduced}) + 4H_P^+$$



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

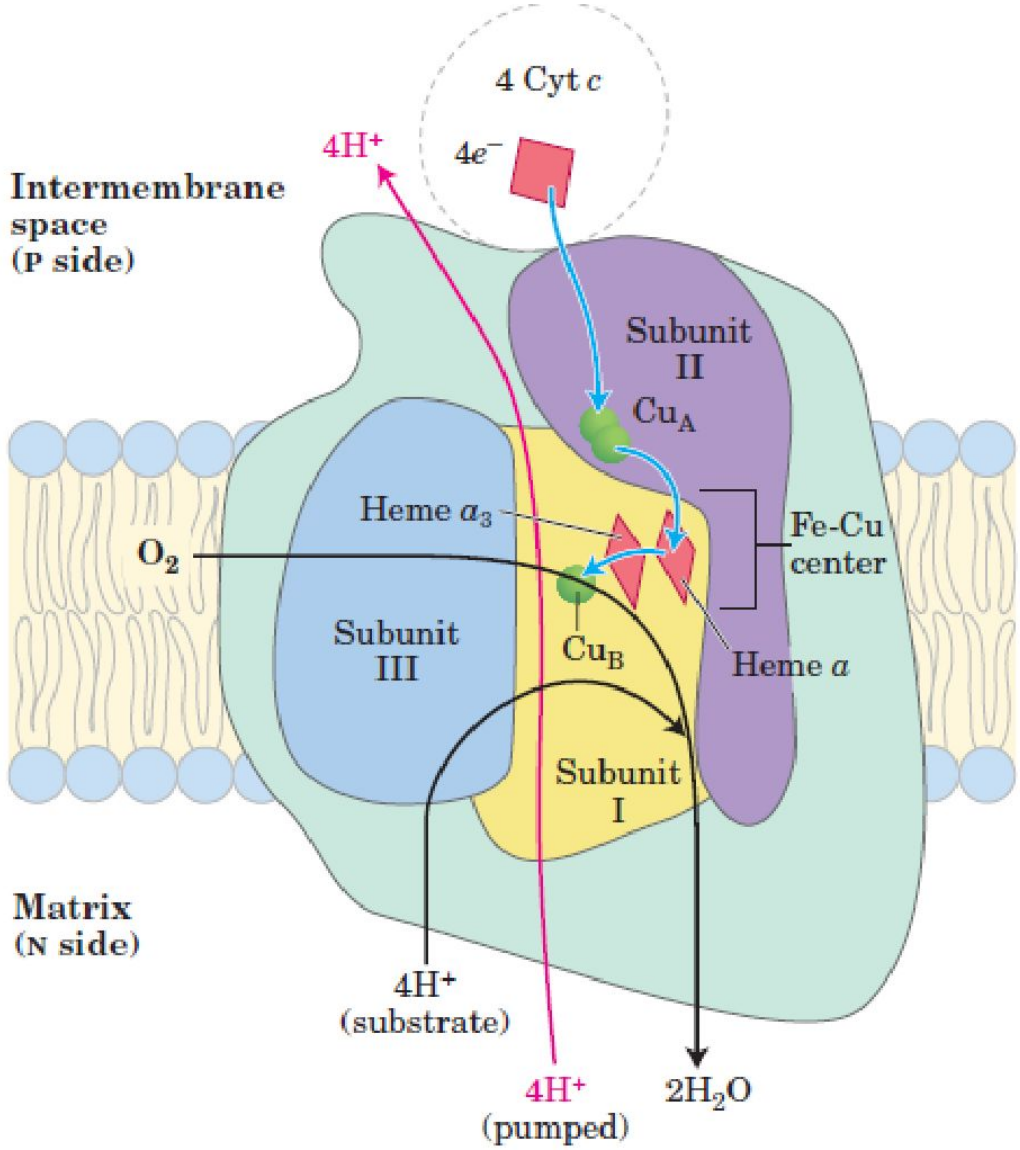


Heme C
(in *c*-type cytochromes)

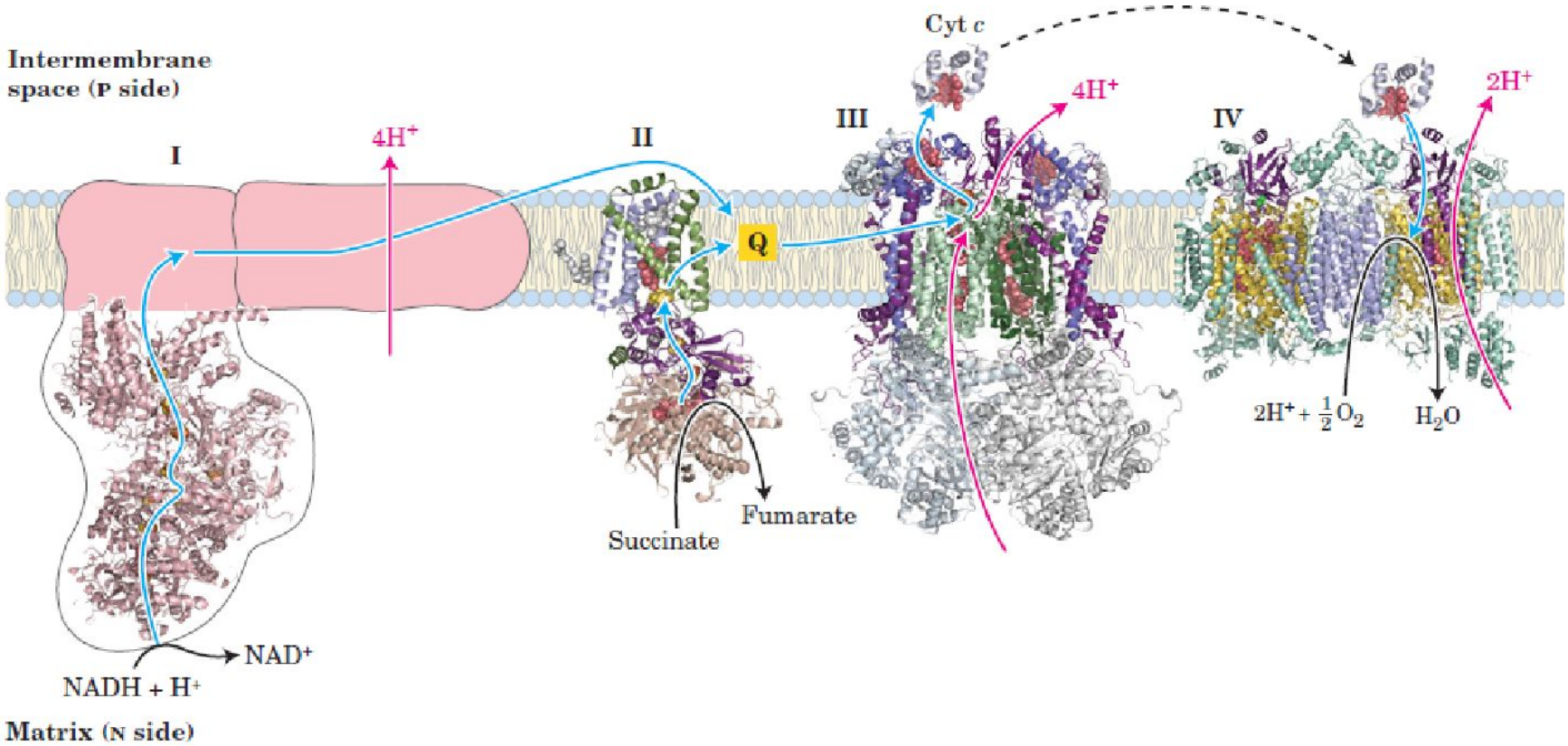


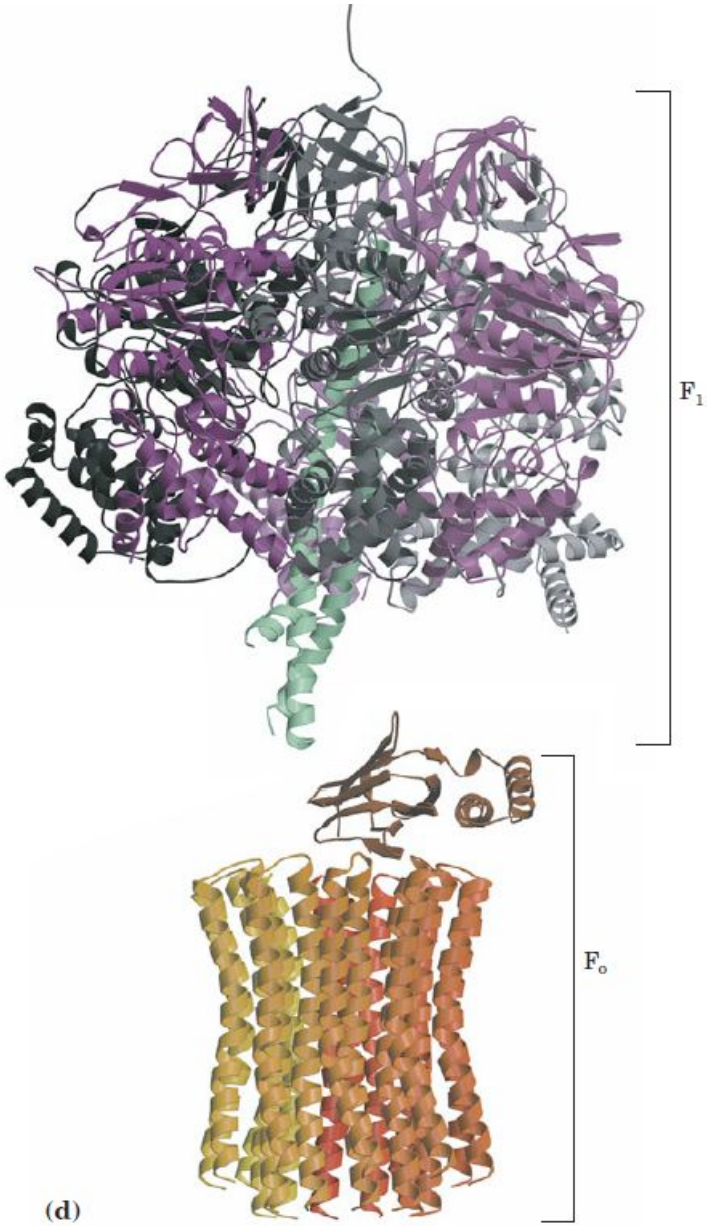
Heme A
(in *a*-type cytochromes)

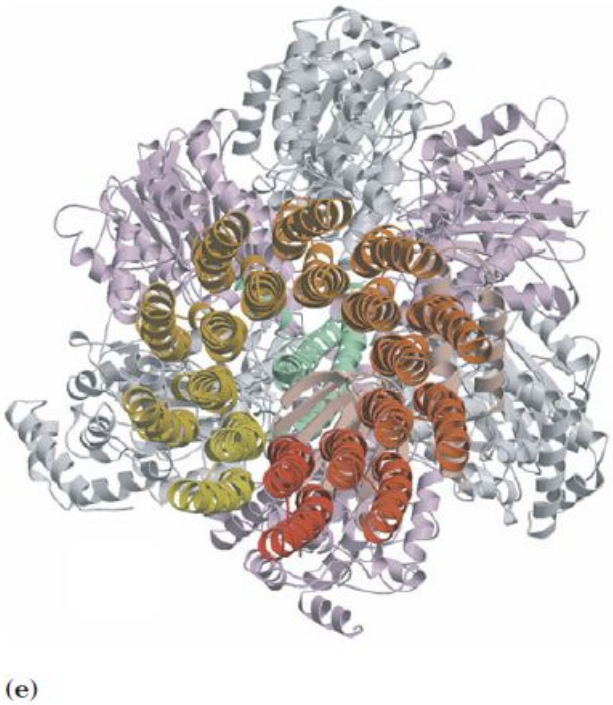
FIGURE 19–3 Prosthetic groups of cytochromes. Each group consists of four five-membered, nitrogen-containing rings in a cyclic structure called a porphyrin. The four nitrogen atoms are coordinated with a central Fe ion, either Fe^{2+} or Fe^{3+}. Iron protoporphyrin IX is found in *b*-type cytochromes 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.

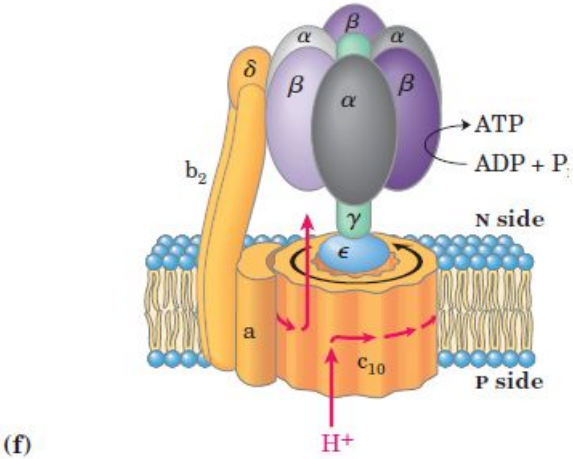


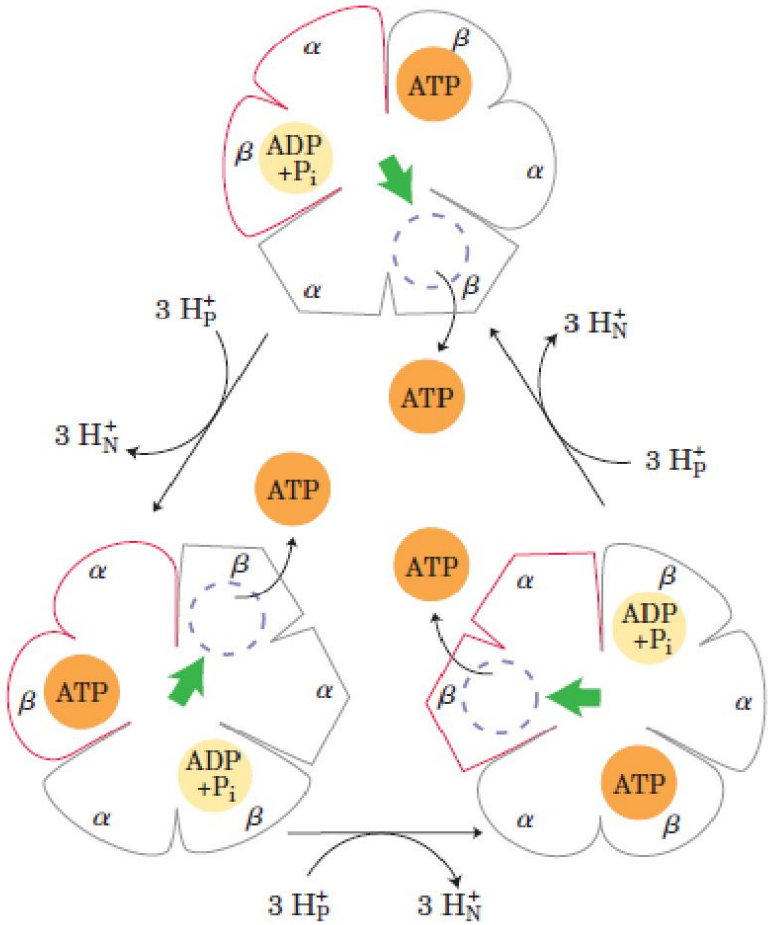
$$4\ \text{Cyt}\ c\ (\text{reduced}) + 8H_N^+ + O_2 \longrightarrow 4\ \text{cyt}\ c\ (\text{oxidized}) + 4H_P^+ + 2H_2O$$

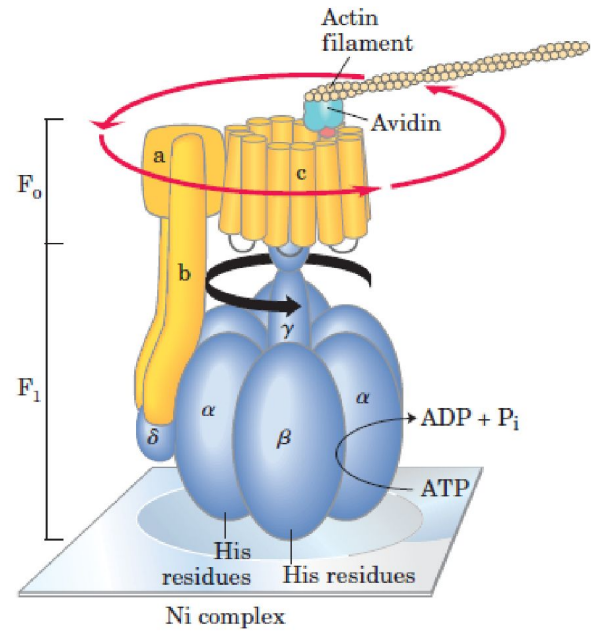

Intermembrane space (P side)
I
4H+
II
Q
III
Cyt c
4H+
IV
2H+
NADH + H+
NAD+
Succinate
Fumarate
2H+ + 1/2 O2
H2O
Matrix (N side)

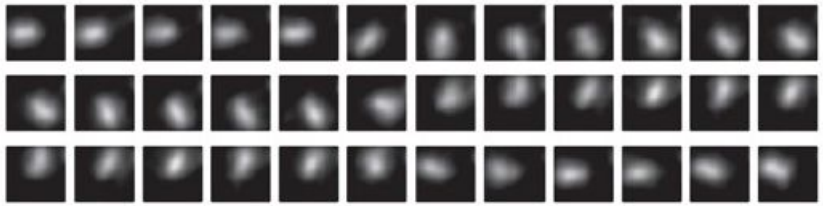

F1
Fo
(d)


(e)

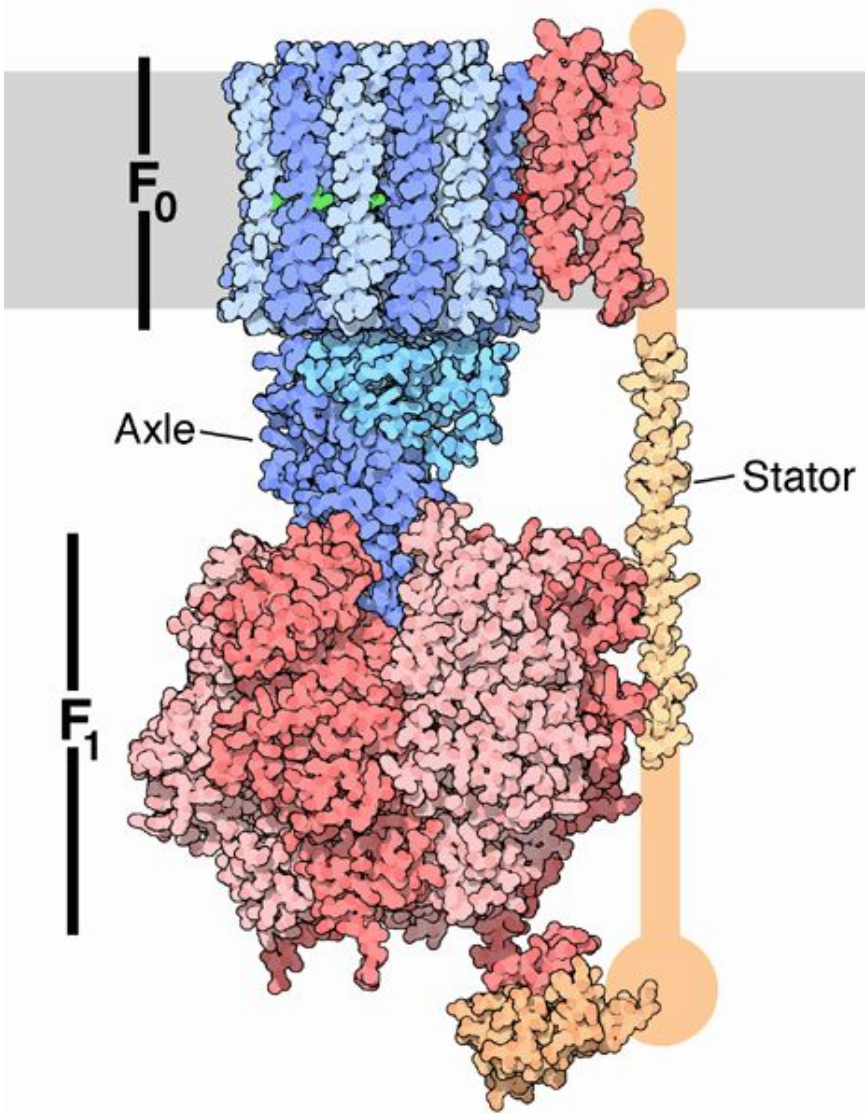

α
β
α
δ
β
α
β
ATP
ADP + Pi
b2
γ
N side
ε
a
c10
P side
H+
(f)

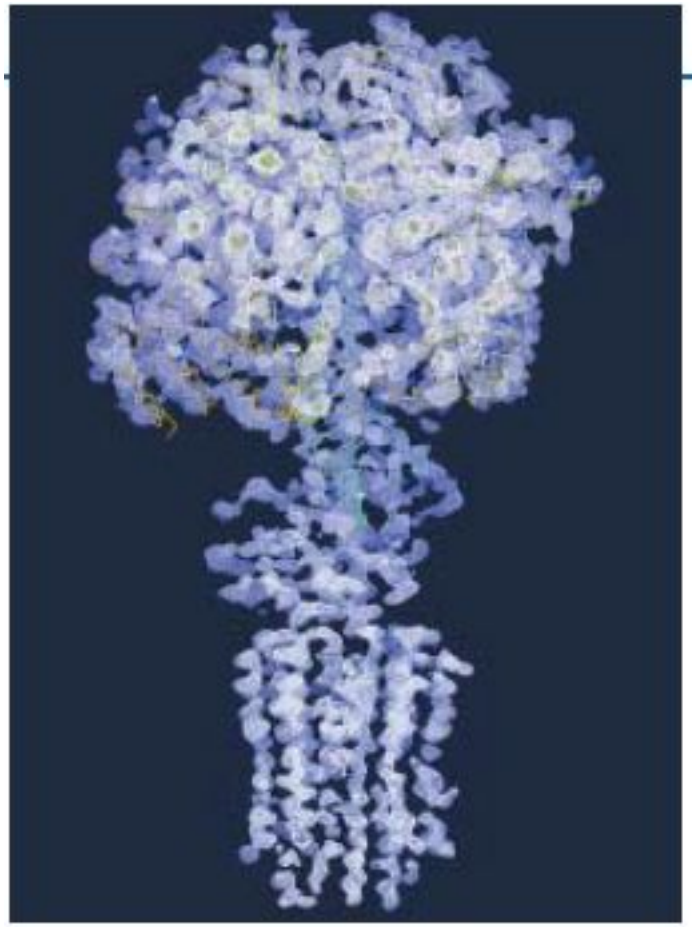

α
β
ATP
ADP
+Pi
3 H+P
3 H+N
3 H+N
3 H+P
3 H+P
3 H+N


Actin
filament
Avidin
a
c
b
γ
α
β
δ
Fo
F1
ADP + Pi
ATP
His
residues
His residues
Ni complex

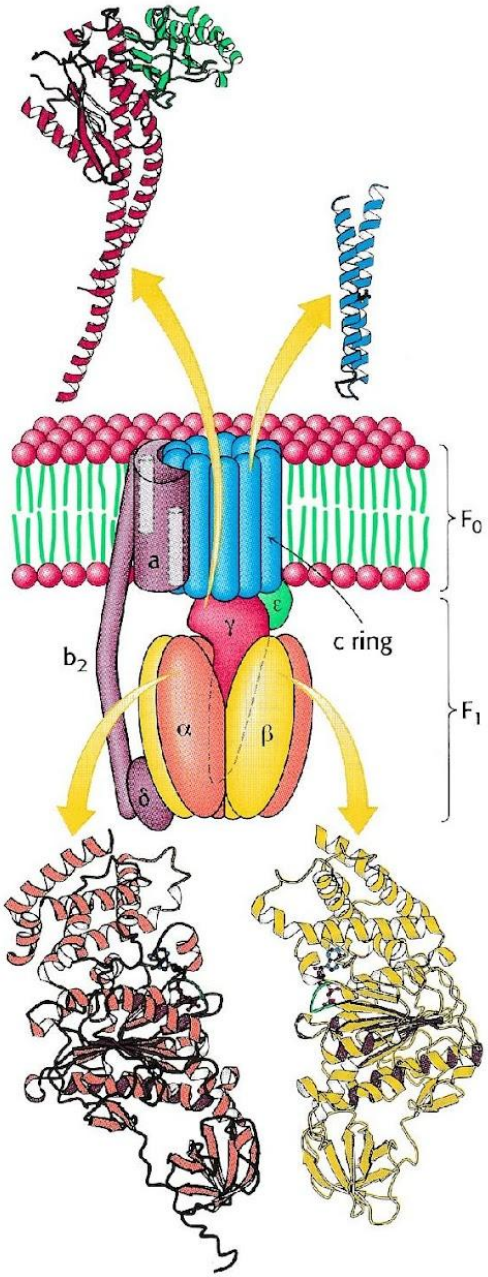


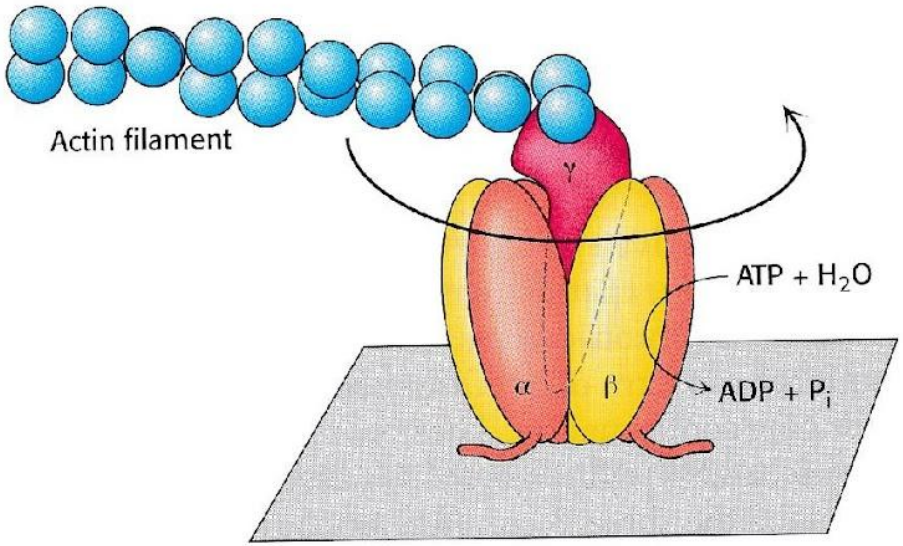
АТФ-синтаза



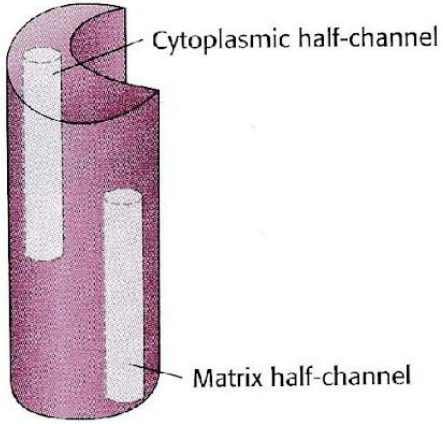


Electron density map of the F_1-ATPase associated with a ring of 10 c-subunits from the F_0 domain of ATP synthase, a molecular machine that carries out the synthesis of ATP in eubacteria, chloroplasts, and mitochondria. [Courtesy of Andrew Leslie, MRC Laboratory of Molecular Biology, Cambridge, UK.]

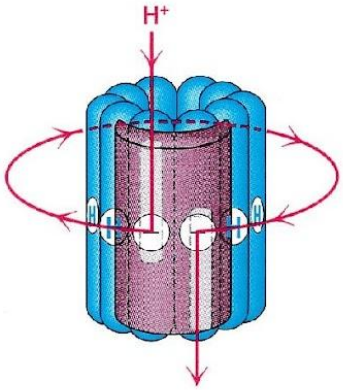


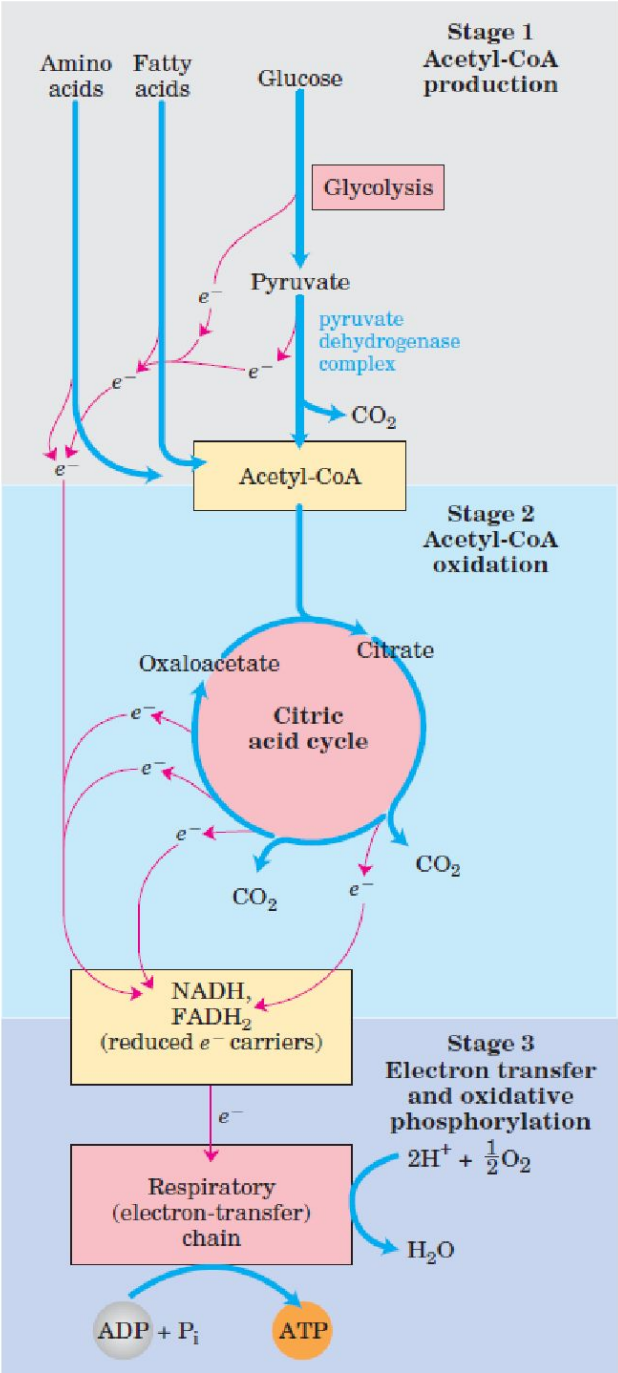


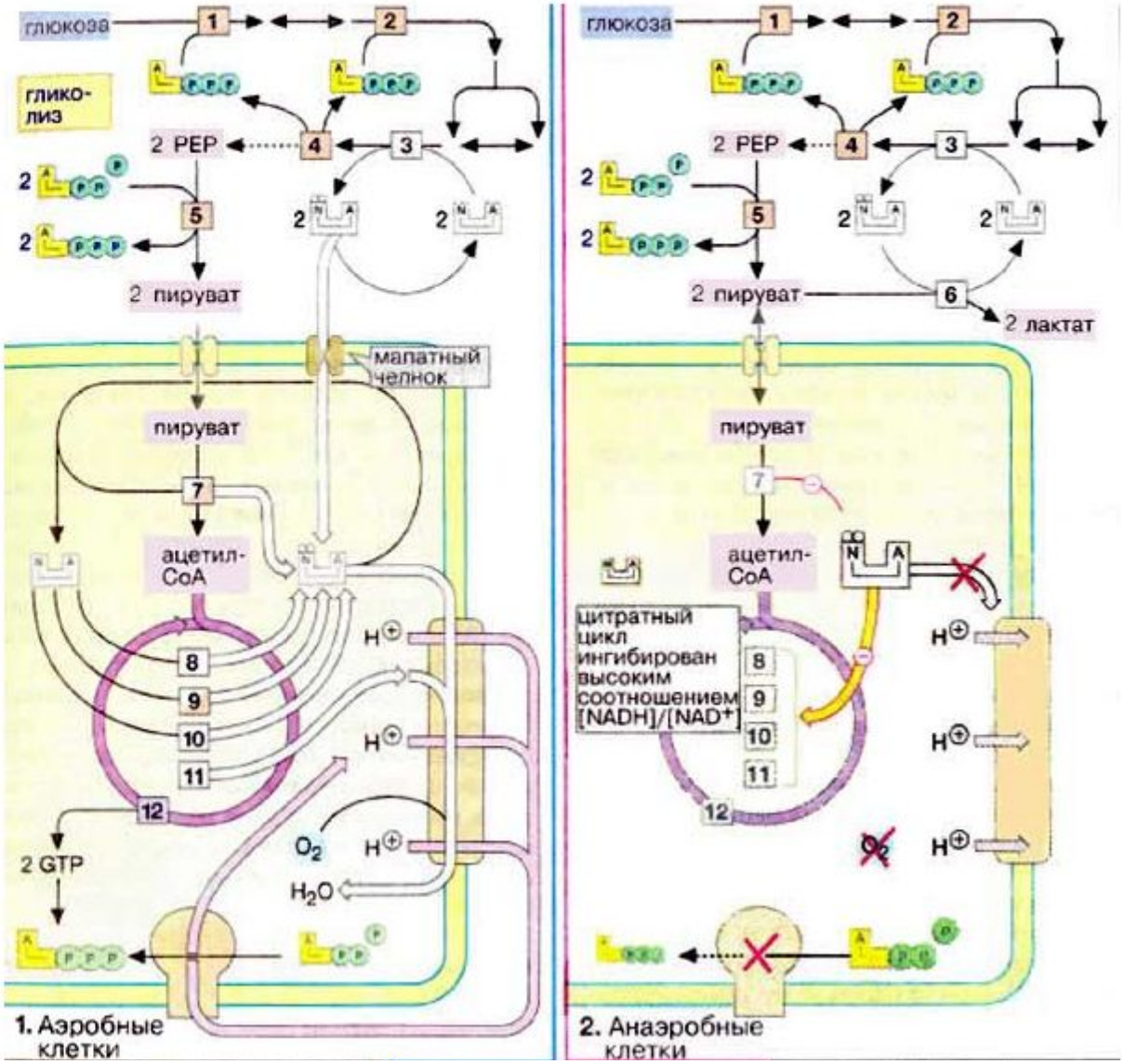
Subunit **c**



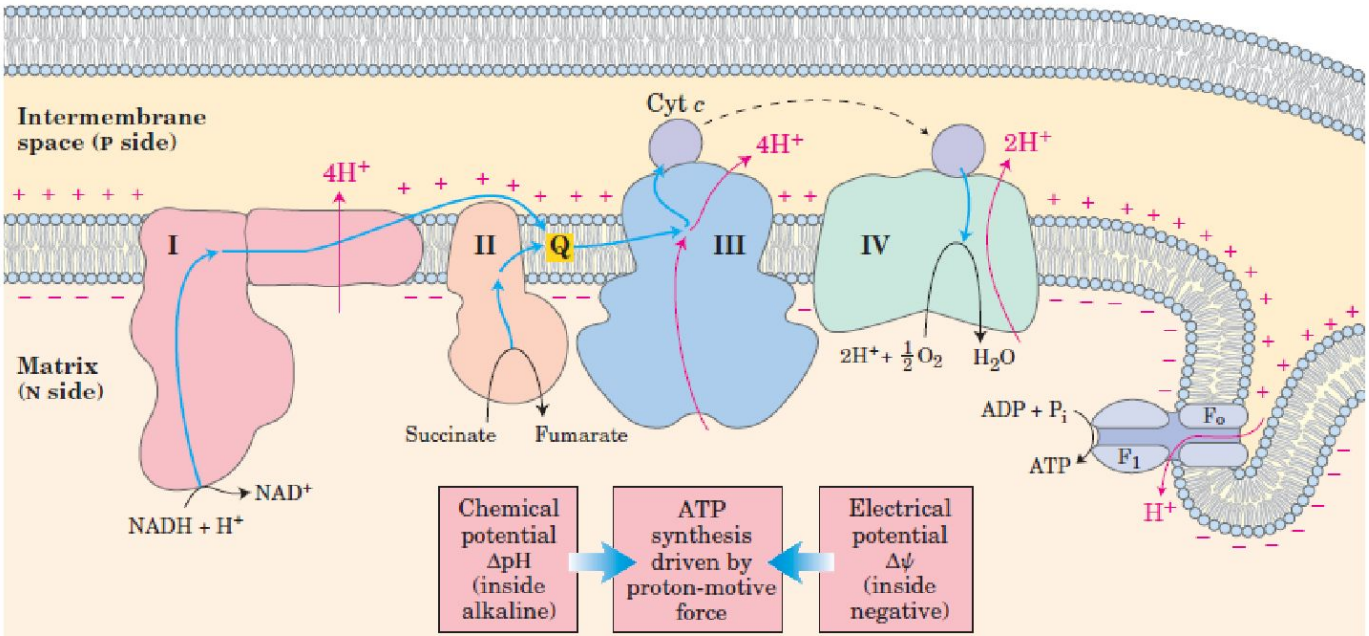
Subunit **a**

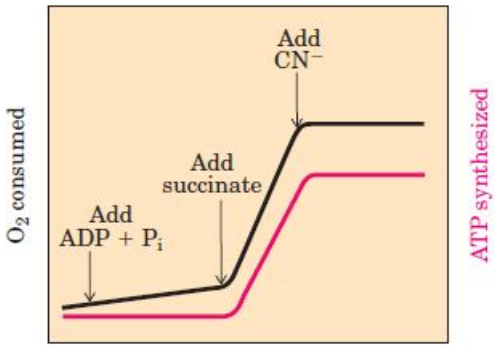


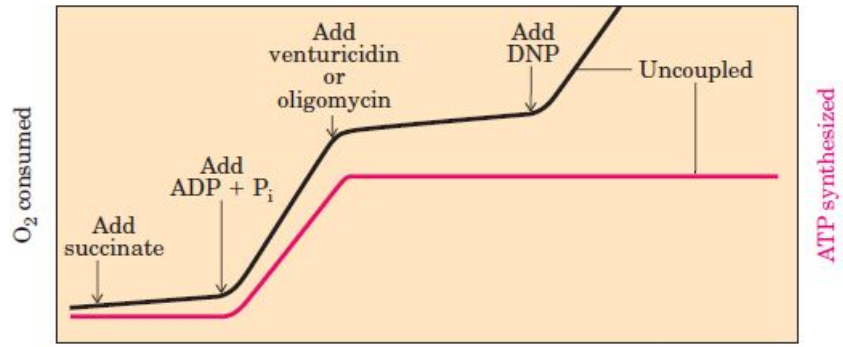

Stage 1
Acetyl-CoA
production
Amino acids
Fatty acids
Glucose
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
CO_2
Acetyl-CoA
Stage 2
Acetyl-CoA
oxidation
Oxaloacetate
Citrate
Citric acid cycle
CO_2
CO_2
NADH, $FADH_2$
(reduced e^- carriers)
Stage 3
Electron transfer and oxidative phosphorylation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

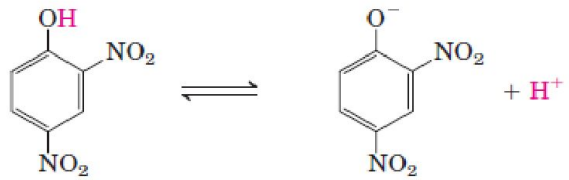

глюкоза
глико-
лиз
2 PEP
2 пируват
малатный
челнок
пируват
ацетил-
CoA
2 GTP
O_2
H_2O
1. Аэробные
клетки
глюкоза
2 PEP
2 пируват
2 лактат
пируват
ацетил-
CoA
цитратный
цикл
ингибирован
высоким
соотношением
[NADH]/[NAD+]
2. Анаэробные
клетки

$$ADP + P_i + nH^+_P \longrightarrow ATP + H_2O + nH^+_N$$

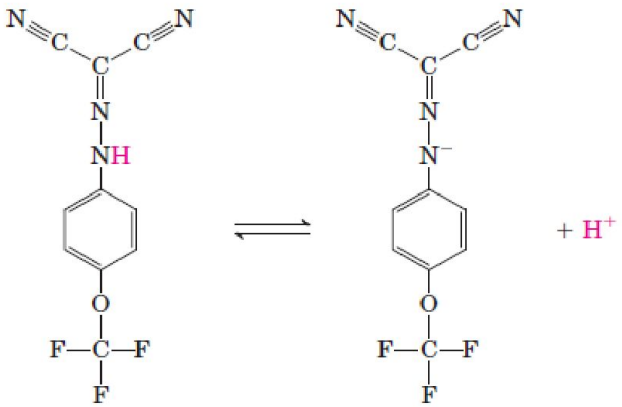




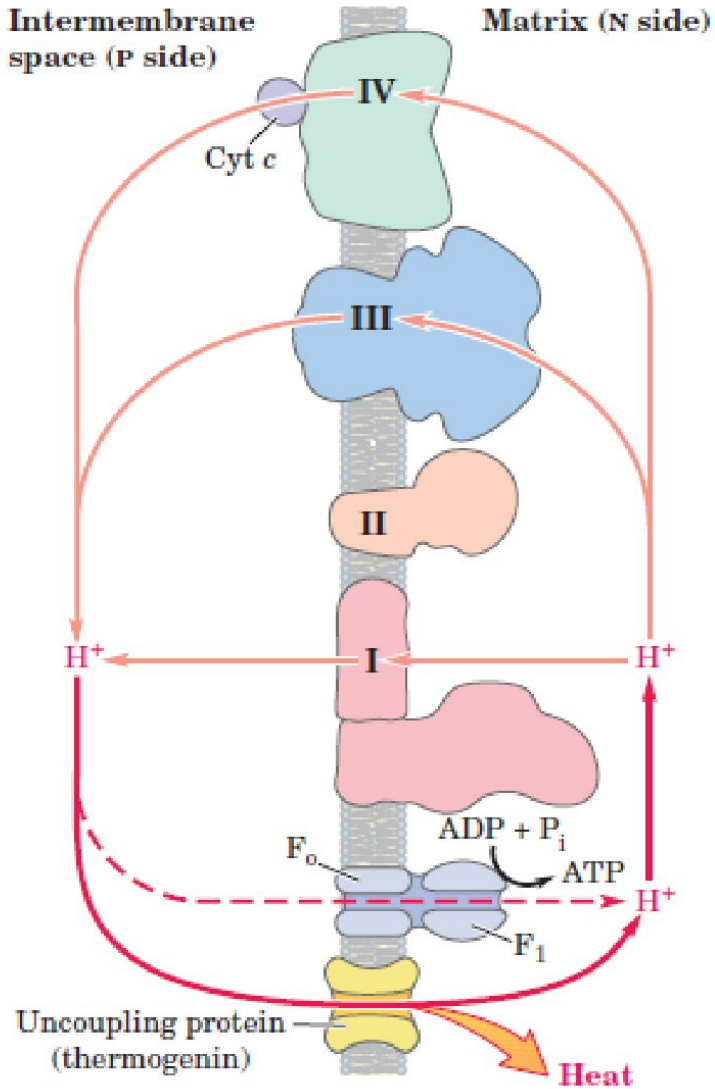




2,4-Dinitrophenol
(DNP)



Carbonylcyanide-*p*-
trifluoromethoxyphenylhydrazone
(FCCP)


Intermembrane space (P side)
Matrix (N side)
IV
Cyt c
III
II
I
H+
H+
ADP + Pi
ATP
Fo
F1
H+
Uncoupling protein (thermogenin)
Heat

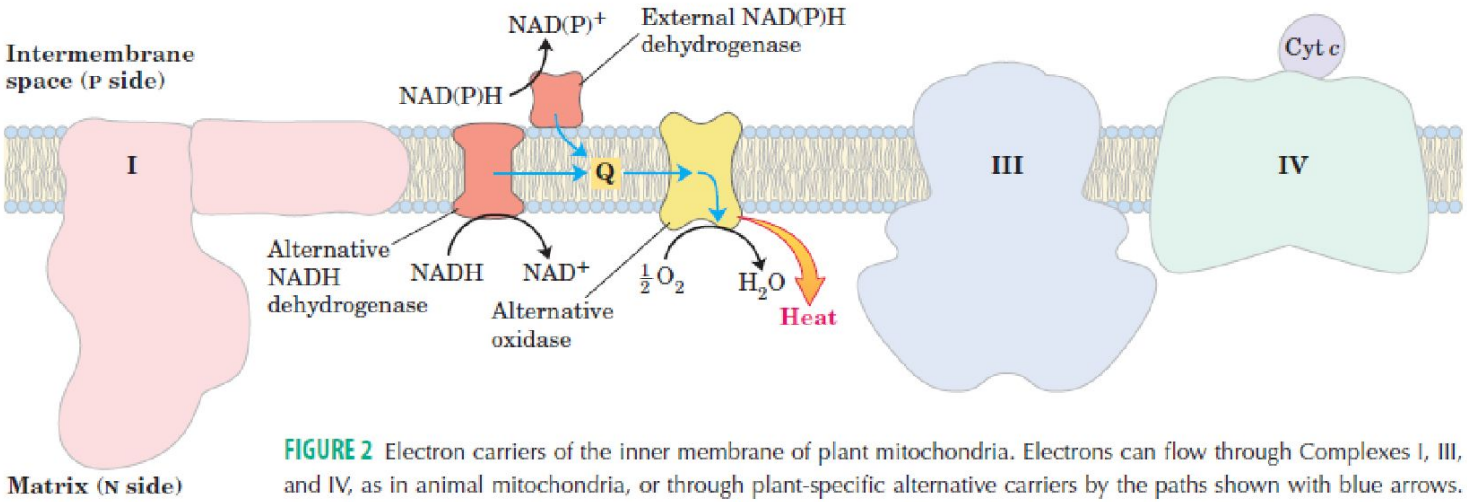
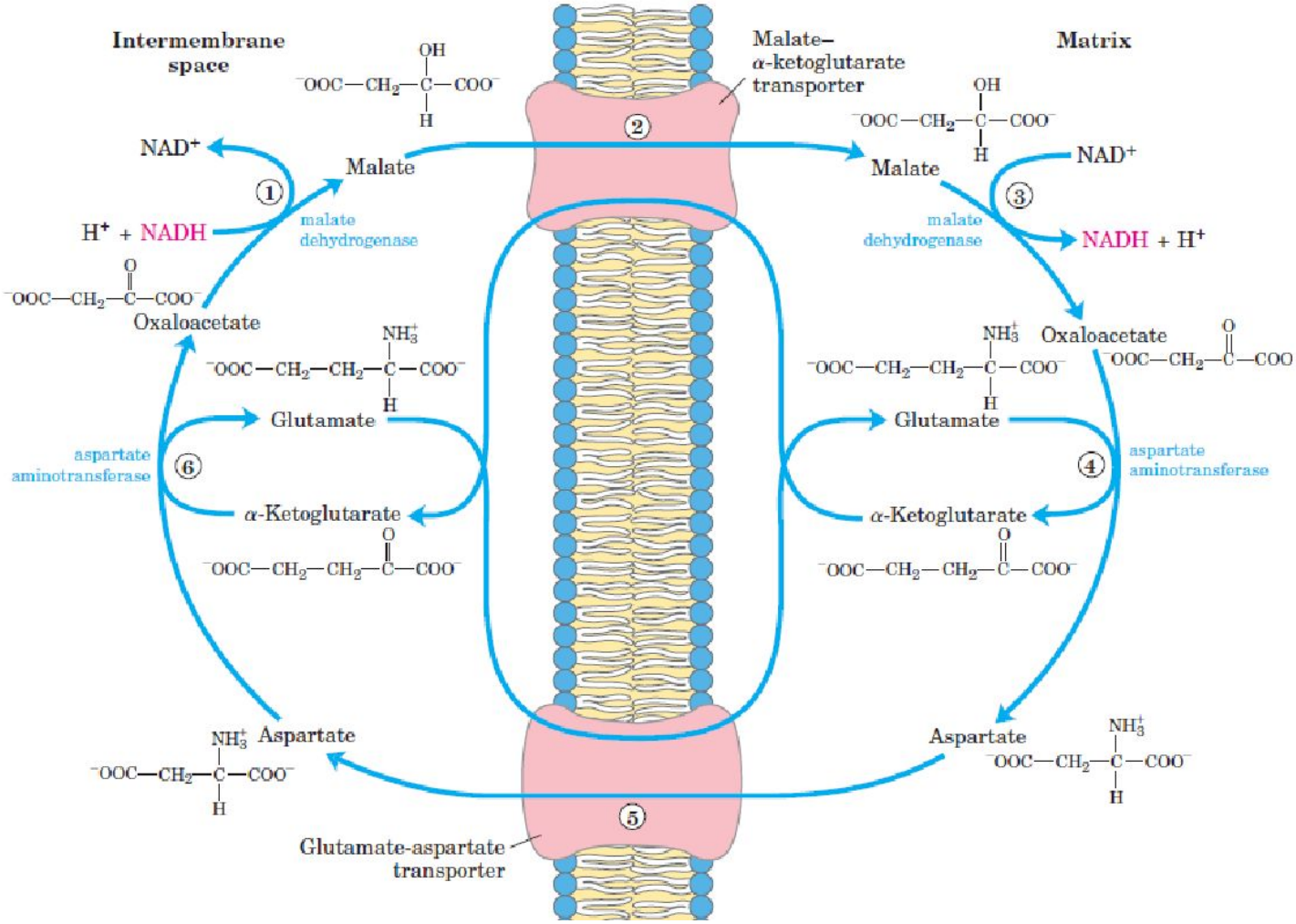
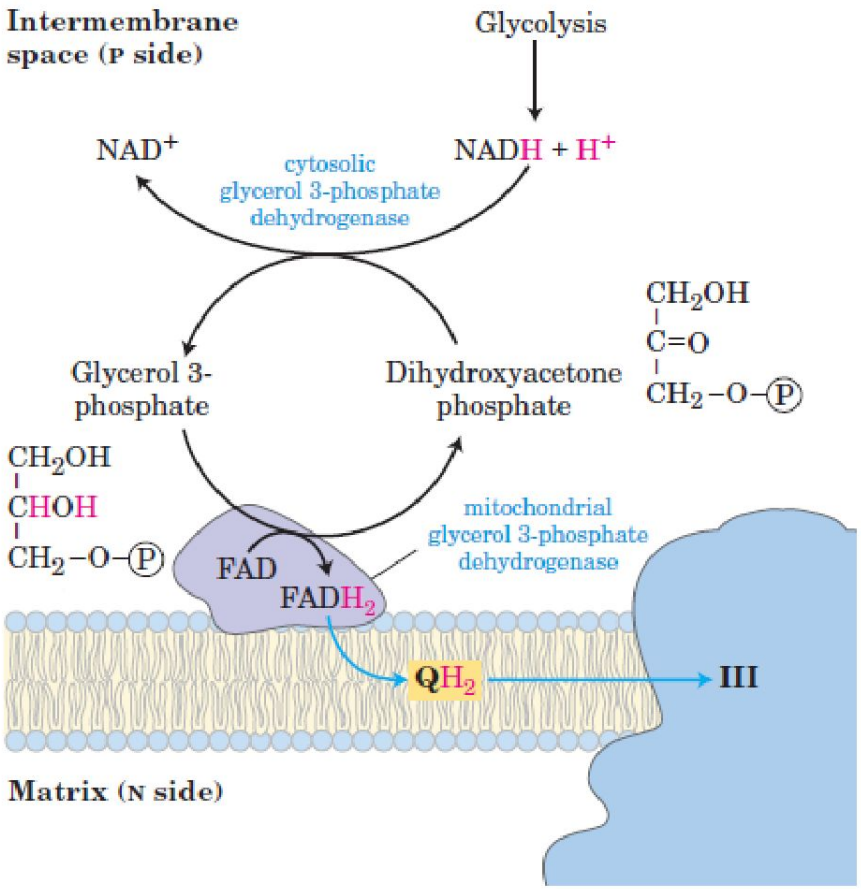


FIGURE 2 Electron carriers of the inner membrane of plant mitochondria. Electrons can flow through Complexes I, III, and IV, as in animal mitochondria, or through plant-specific alternative carriers by the paths shown with blue arrows.


Intermembrane space
Matrix
Malate–α-ketoglutarate transporter
Glutamate-aspartate transporter
Malate
Oxaloacetate
Glutamate
α-Ketoglutarate
Aspartate
NAD+
NADH + H+
H+ + NADH
malate dehydrogenase
aspartate aminotransferase
1
2
3
4
5
6


Intermembrane space (P side)
Glycolysis
NAD+
NADH + H+
cytosolic glycerol 3-phosphate dehydrogenase
Glycerol 3-phosphate
Dihydroxyacetone phosphate
CH2OH
C=O
CH2–O–P
CH2OH
CHOH
CH2–O–P
FAD
FADH2
mitochondrial glycerol 3-phosphate dehydrogenase
QH2
III
Matrix (N side)

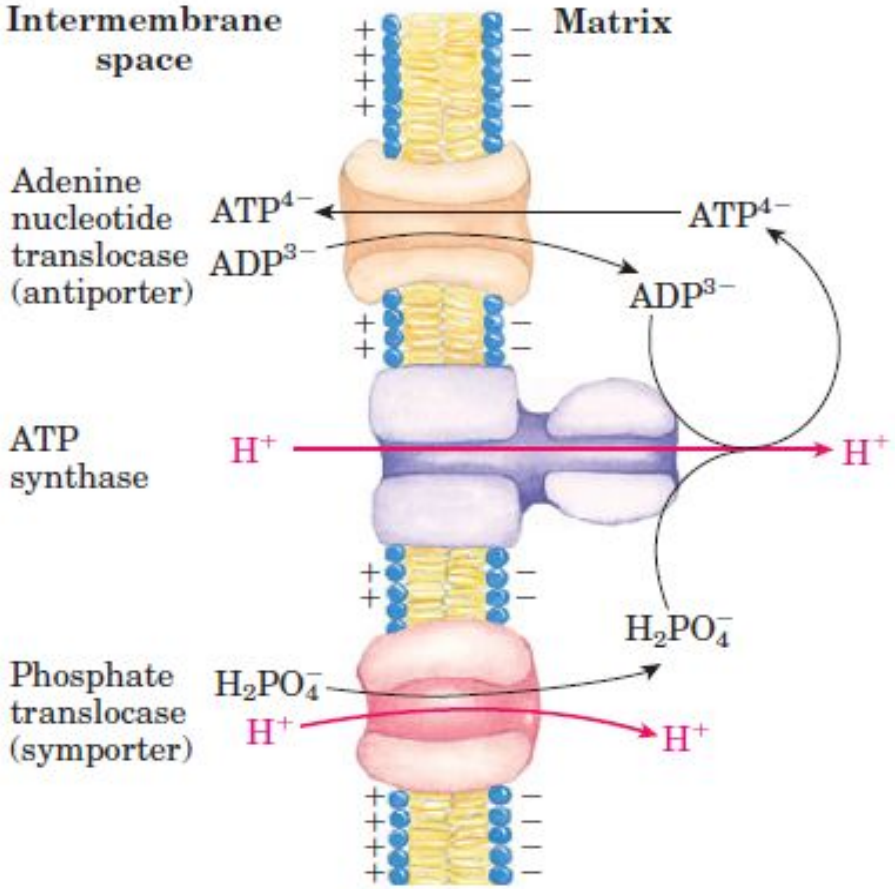

Intermembrane space
Matrix
Adenine nucleotide translocase (antiporter)
ATP^{4-}
ADP^{3-}
ATP^{4-}
ADP^{3-}
ATP synthase
H^+
H^+
$H_2PO_4^-$
Phosphate translocase (symporter)
$H_2PO_4^-$
H^+
H^+

TABLE 19–5 ATP Yield from Complete Oxidation of Glucose

Process	Direct product	Final ATP
Glycolysis	2 NADH (cytosolic) 2 ATP	3 or 5* 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) 2 $FADH_2$ 2 ATP or 2 GTP	15 3 2
Total yield per glucose		30 or 32