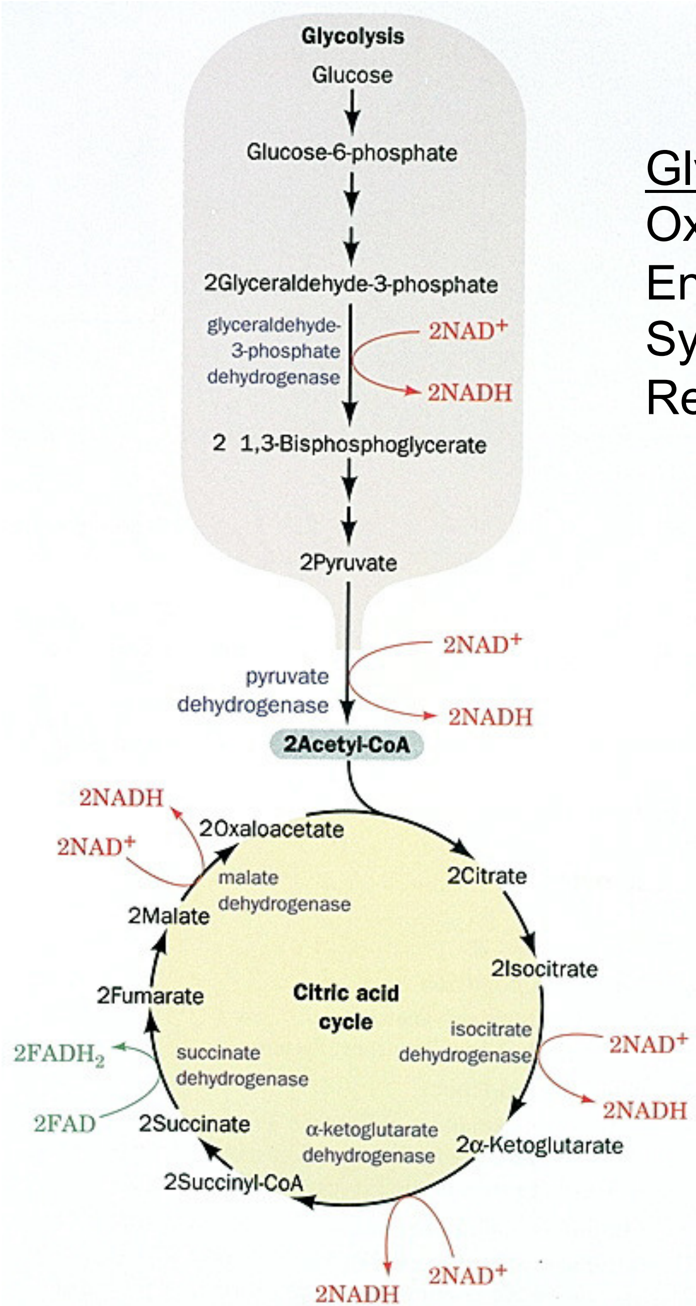
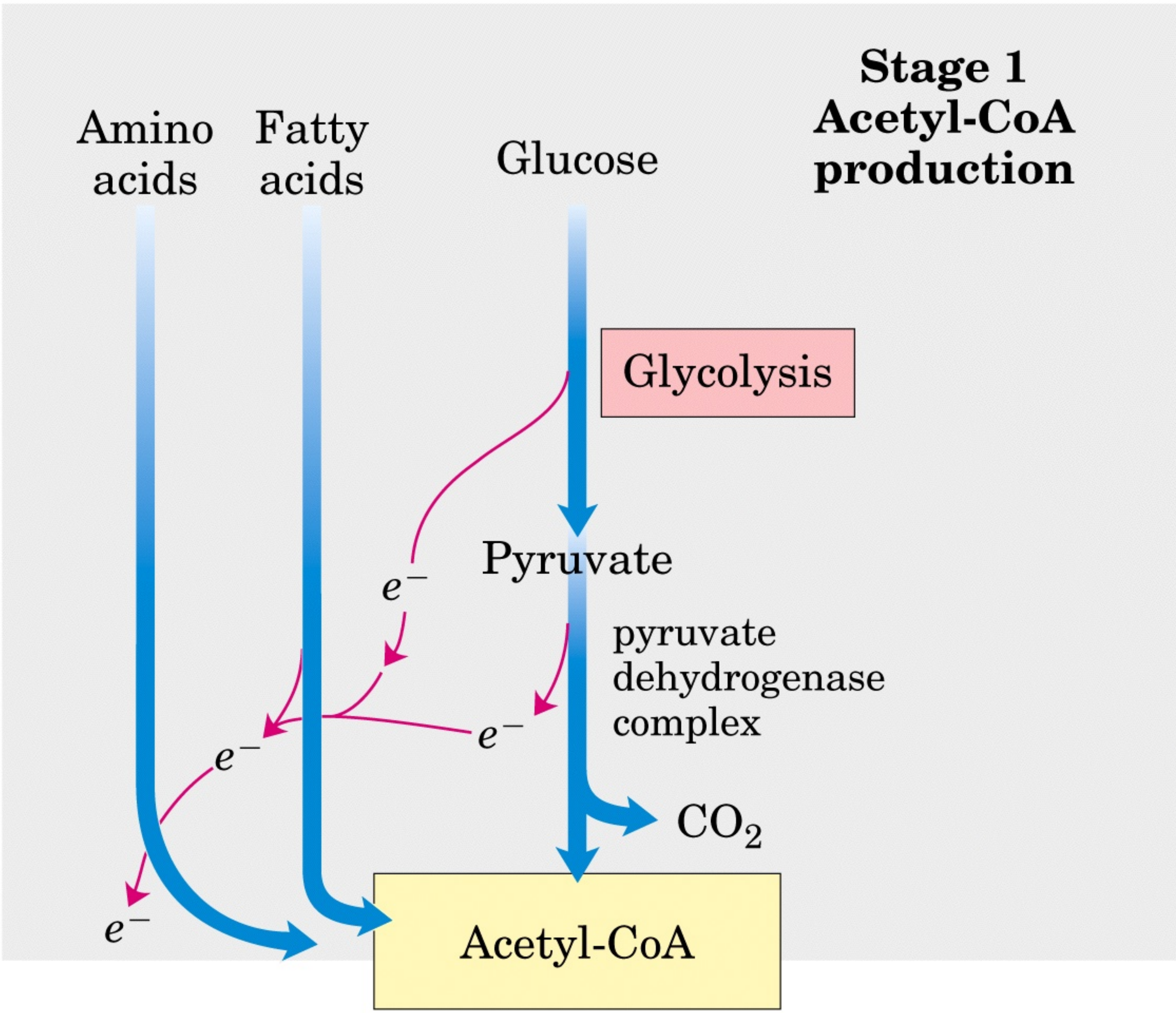
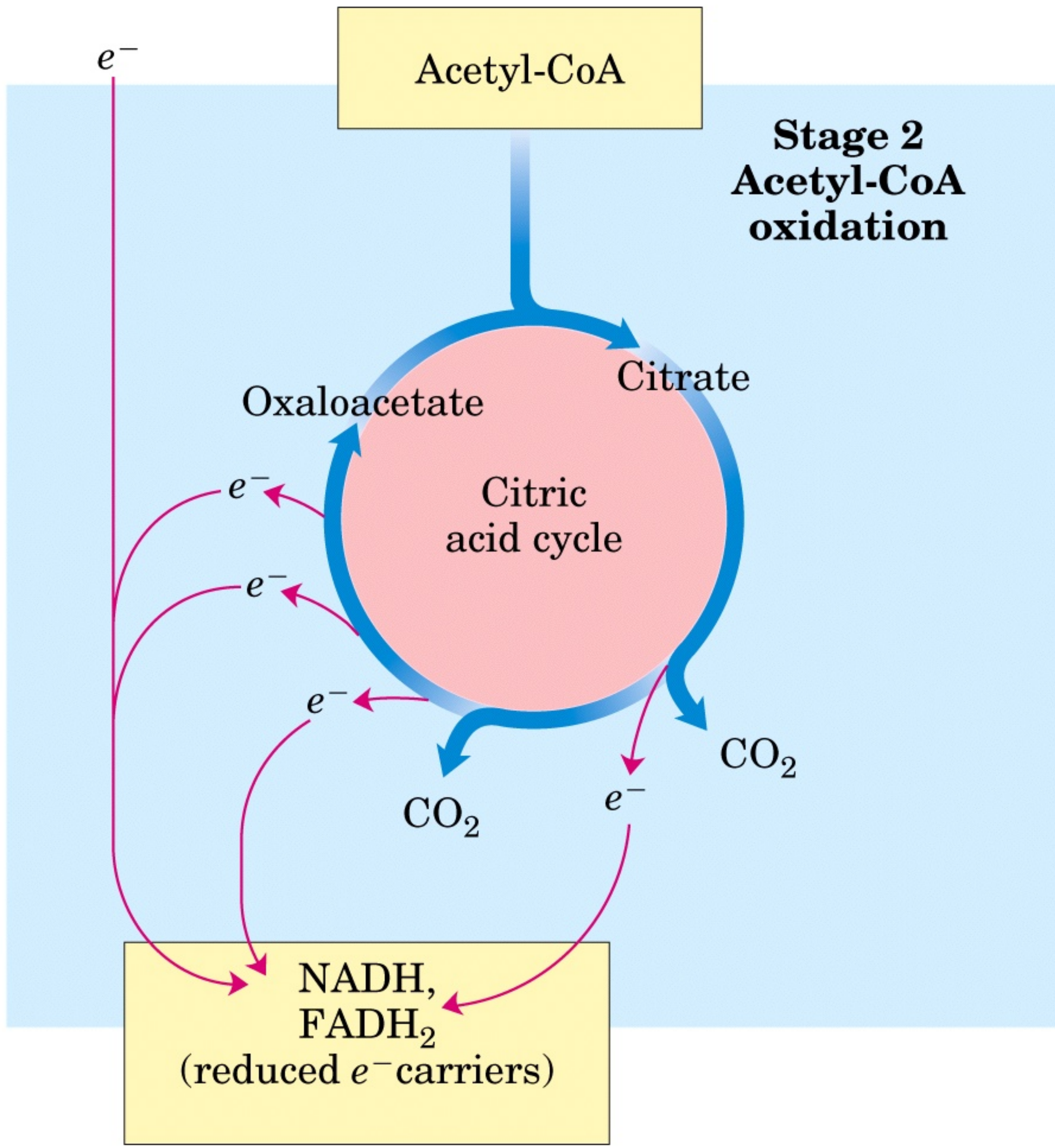


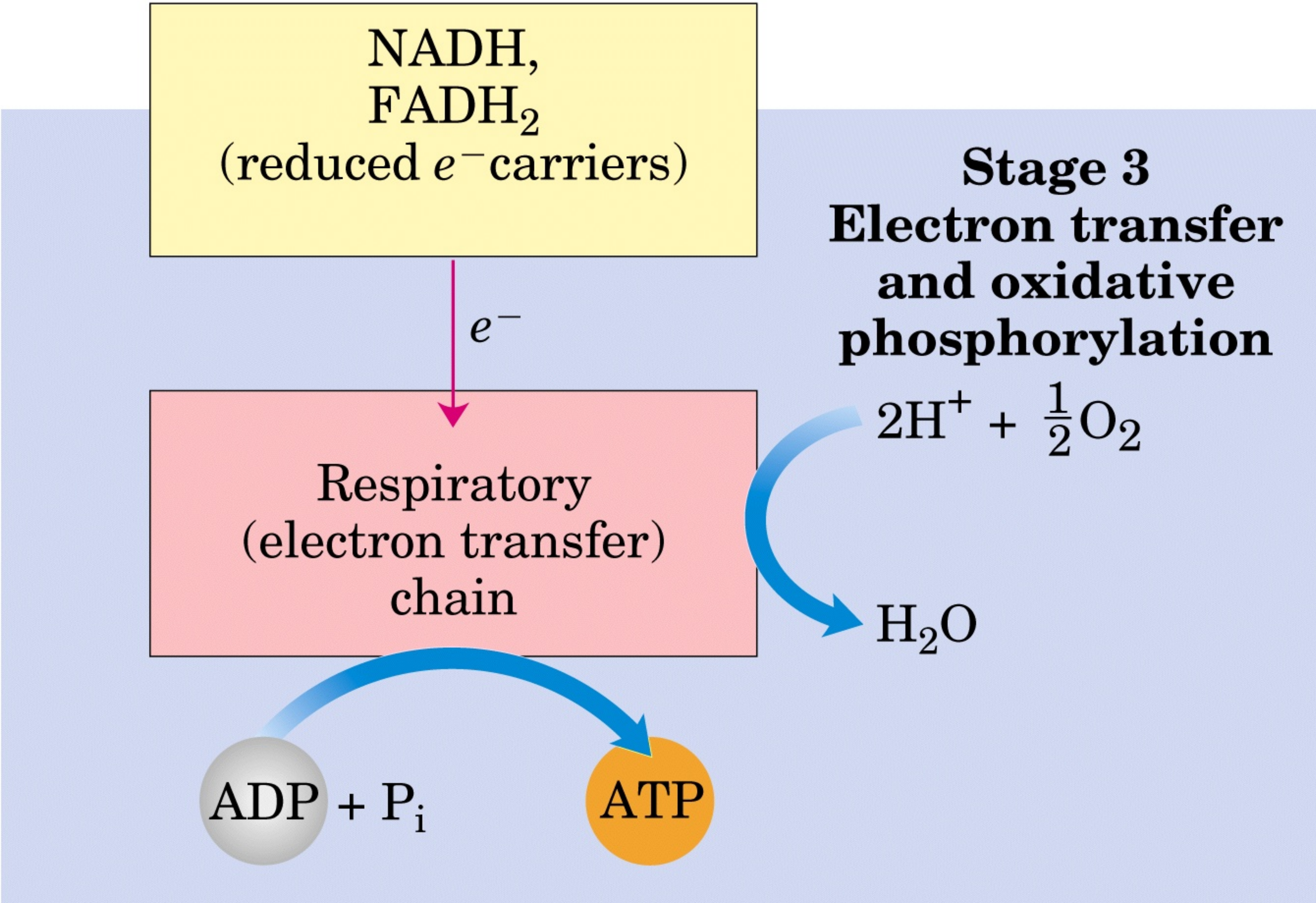
<u>Glycolyse:</u>
Oxidation von Glucose zu 2 Pyruvat
Energie wird konserviert durch:
Synthese von 2 ATP
Reduktion von 2 NAD^+ zu NADH

<u>Pyruvatdehydrogenase und Citratzyklus:</u>
Vollständige Oxidation von Pyruvat zu CO_2
Energie wird konserviert durch:
Synthese von ATP und Reduktionsäquivalenten

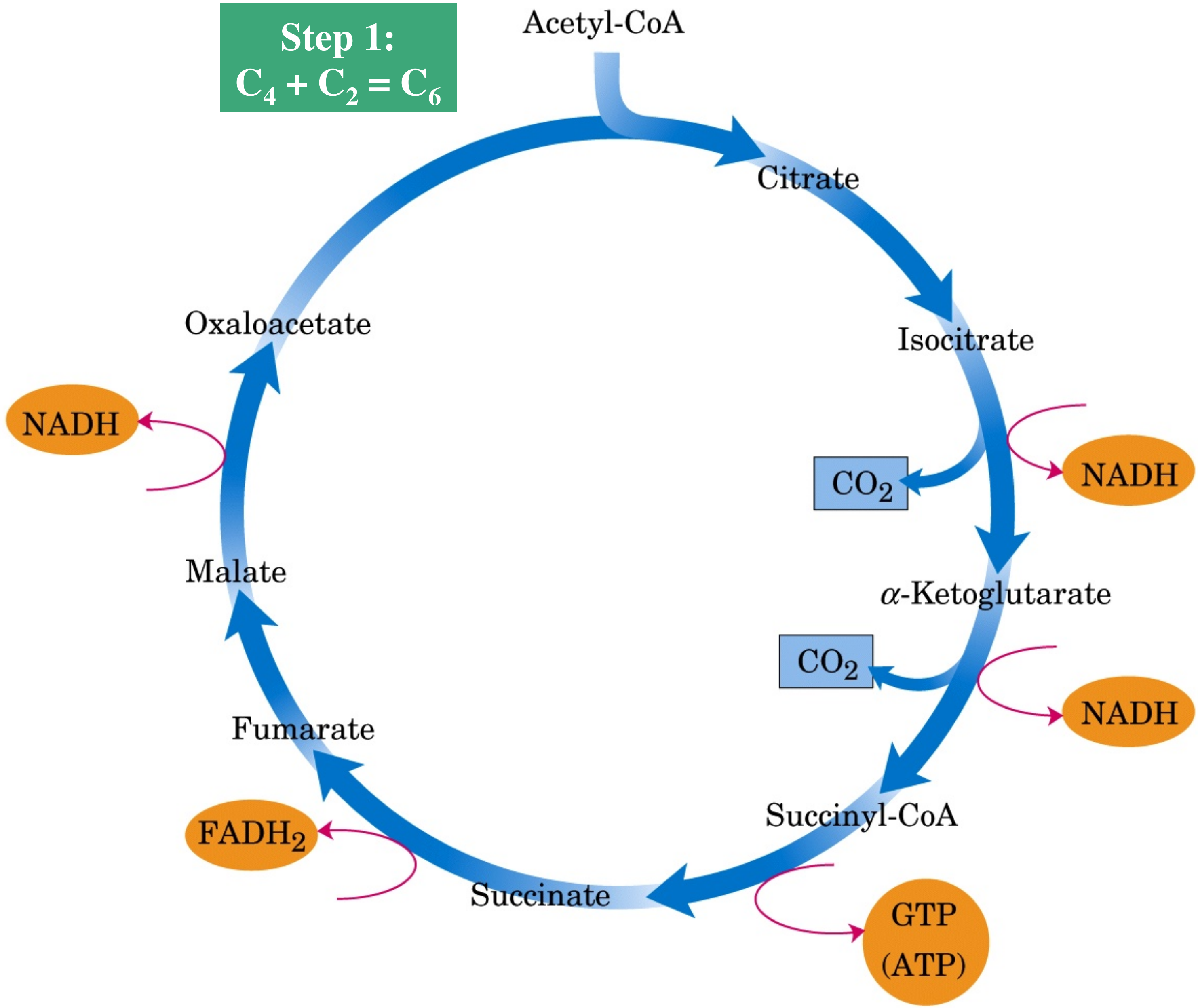

Stage 1
Acetyl-CoA
production
Amino
acids
Fatty
acids
Glucose
Glycolysis
Pyruvate
e^-
pyruvate
dehydrogenase
complex
e^-
e^-
CO_2
e^-
Acetyl-CoA



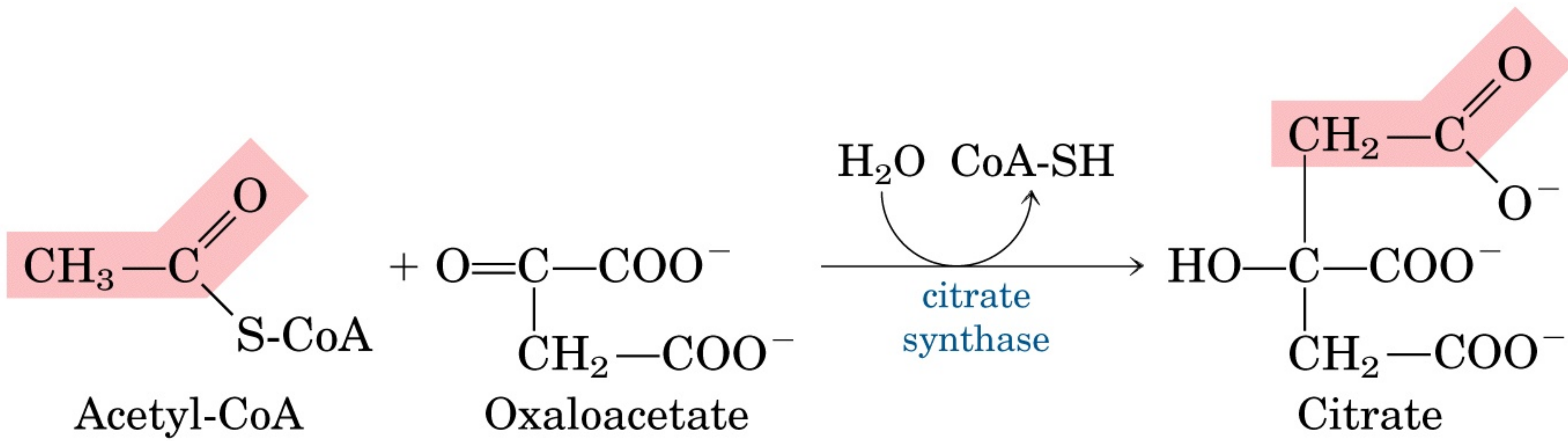
Acetyl-CoA
Stage 2
Acetyl-CoA
oxidation
Citrate
Oxaloacetate
Citric
acid cycle
e^-
e^-
e^-
e^-
e^-
CO_2
CO_2
NADH,
$FADH_2$
(reduced e^- carriers)


NADH,
$FADH_2$
(reduced e^- carriers)
e^-
Respiratory
(electron transfer)
chain
Stage 3
Electron transfer
and oxidative
phosphorylation
$2H^+ + \frac{1}{2}O_2$
H_2O
ADP + P_i
ATP

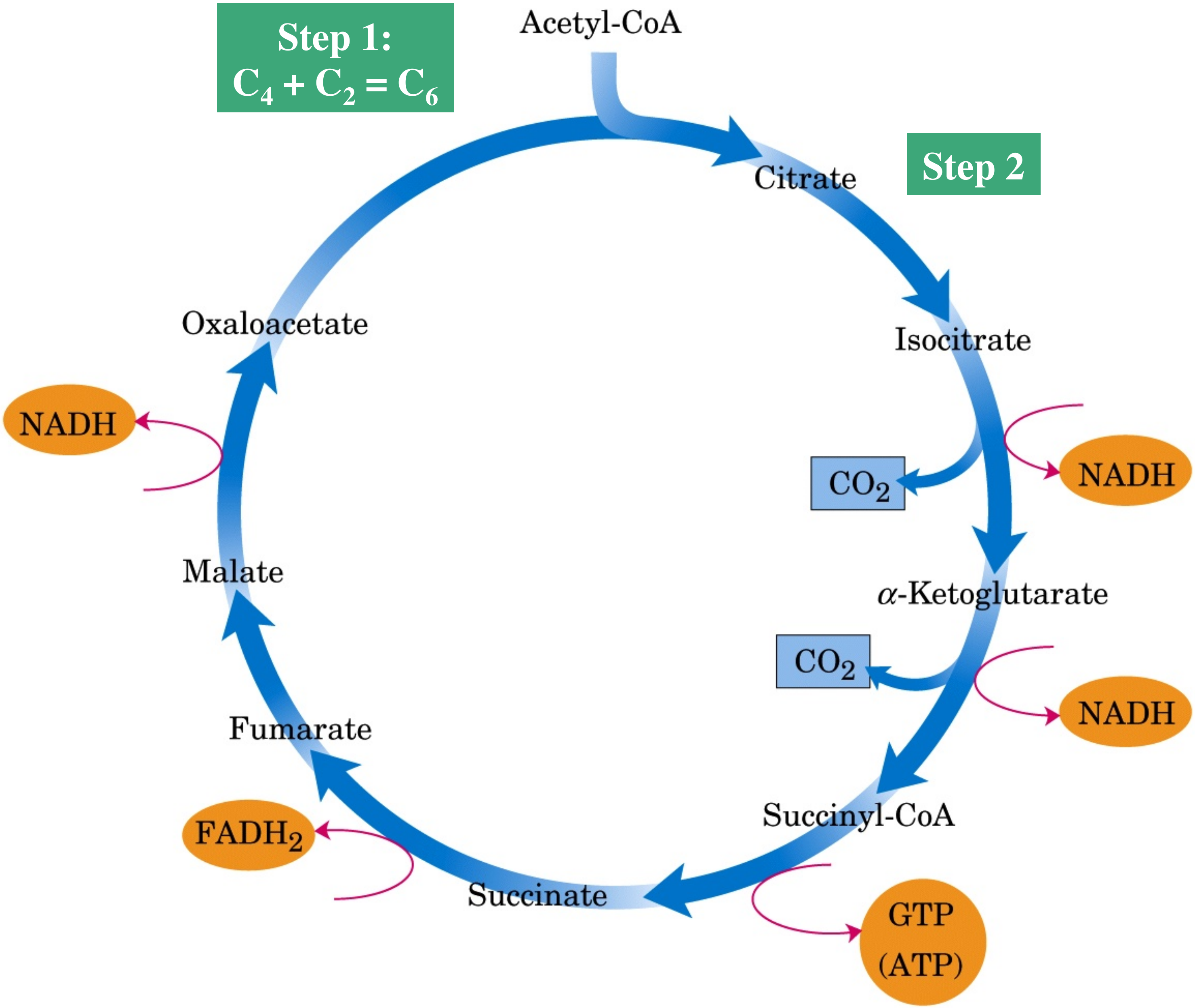
Step 1:
$C_4 + C_2 = C_6$



Step 1

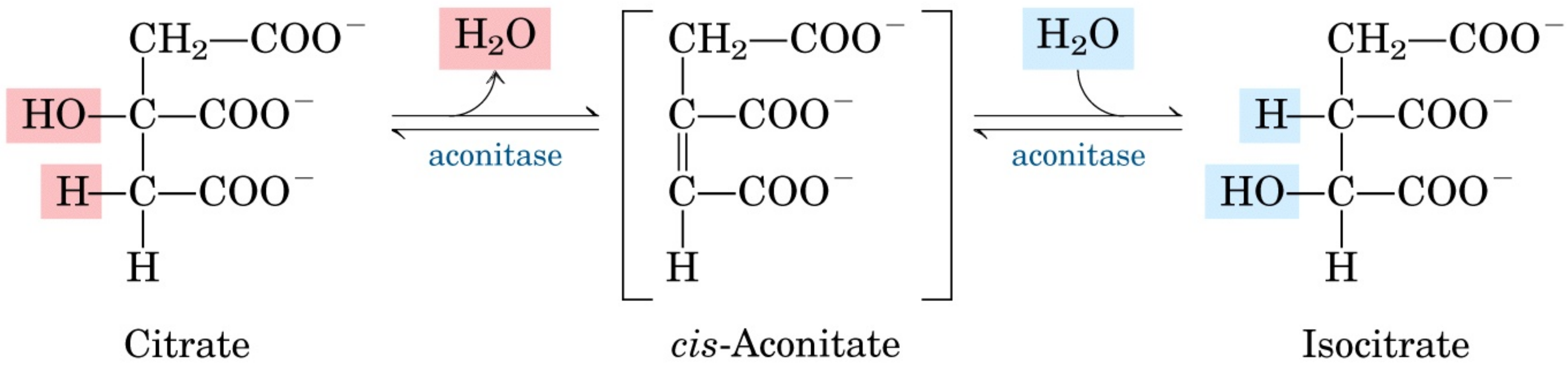


$$\Delta G'^{\circ} = -32.2\ \text{kJ/mol}$$

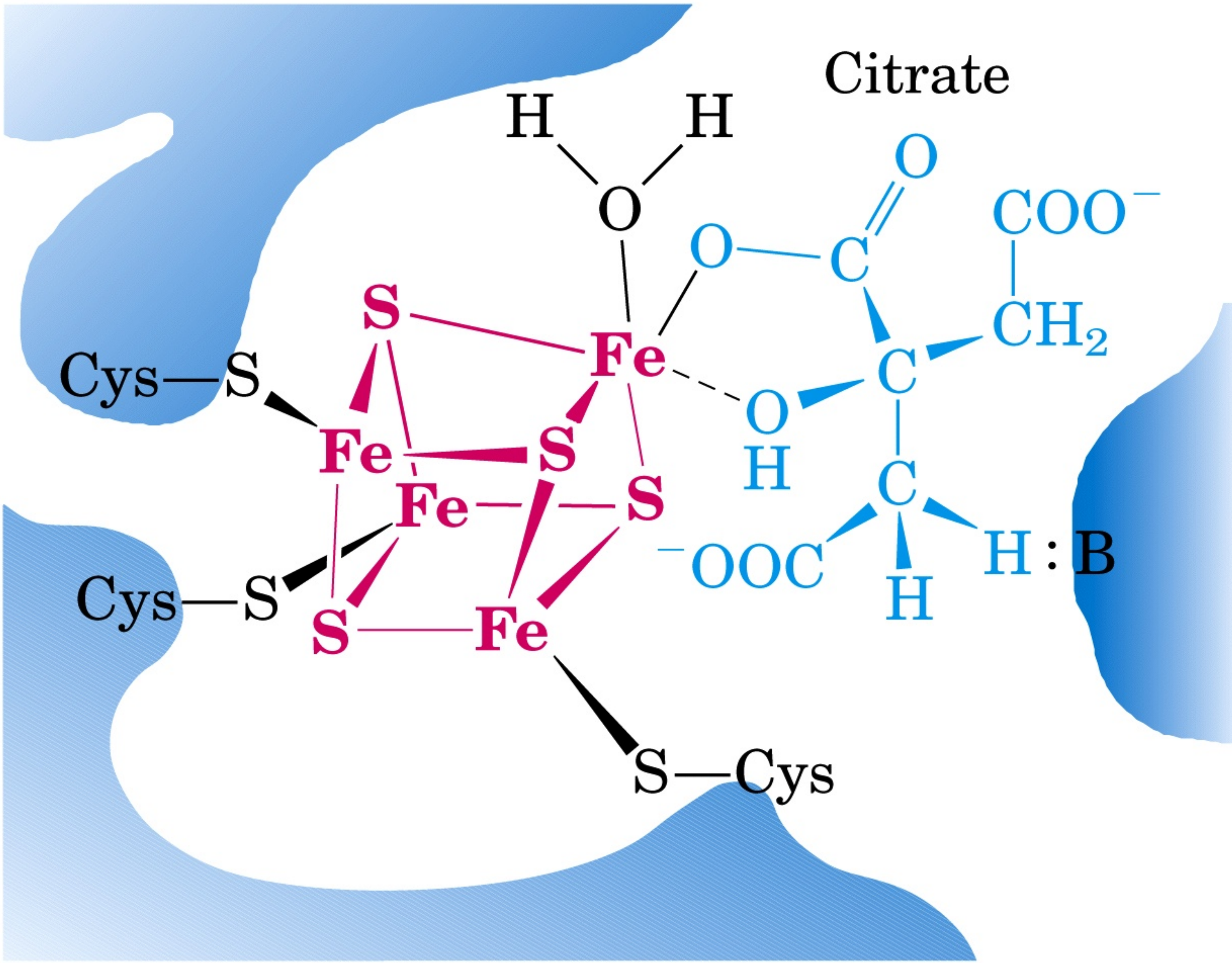


Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate

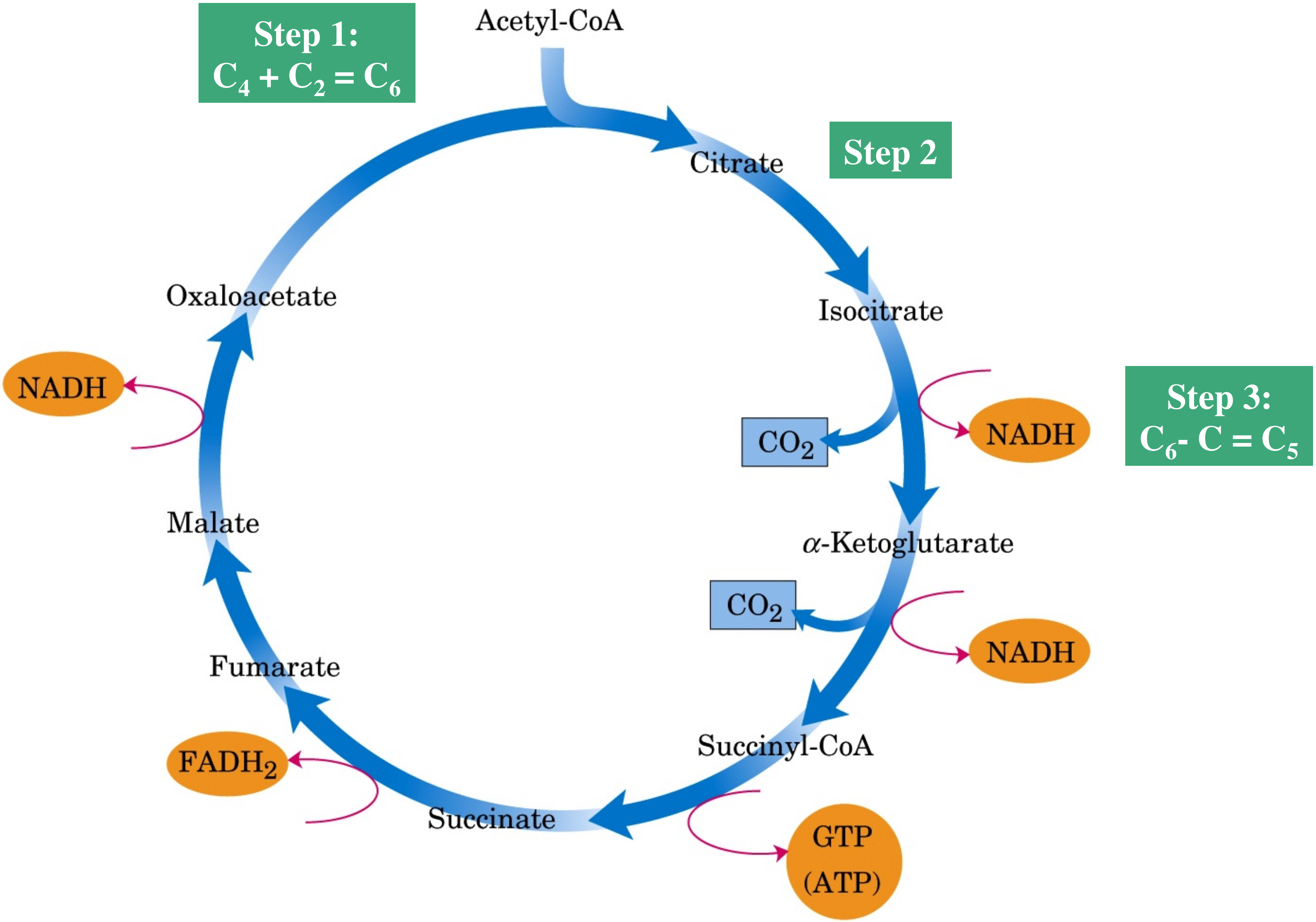
Step 2



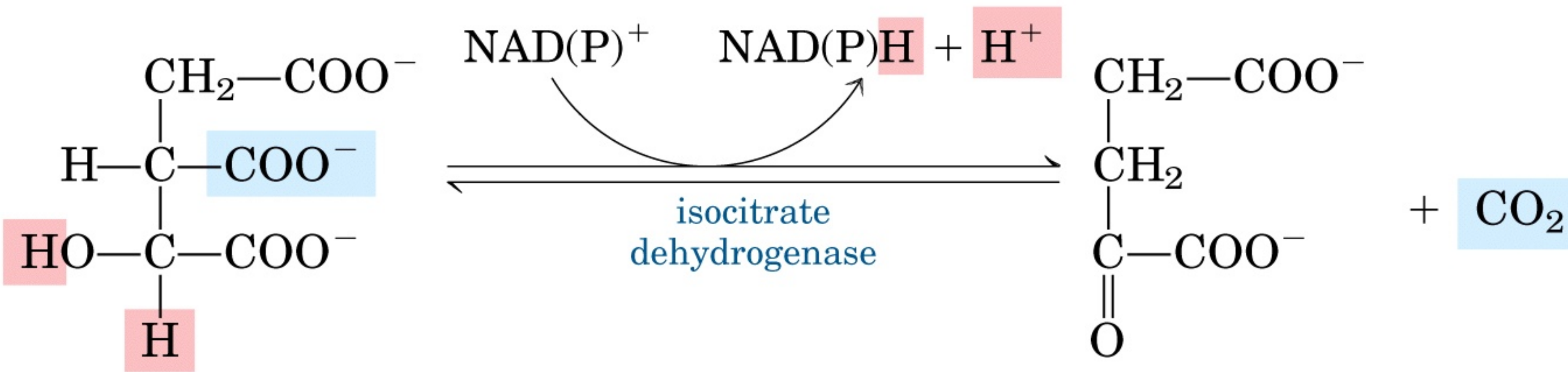
$\Delta G'^{\circ} = 13.3$ kJ/mol



Citrate
H
H
O
O
COO⁻
O
C
S
Fe
CH₂
Cys—S
C
O
Fe
S
H
S
C
Fe
⁻OOC
H : B
Cys—S
H
S
Fe
S—Cys


Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate

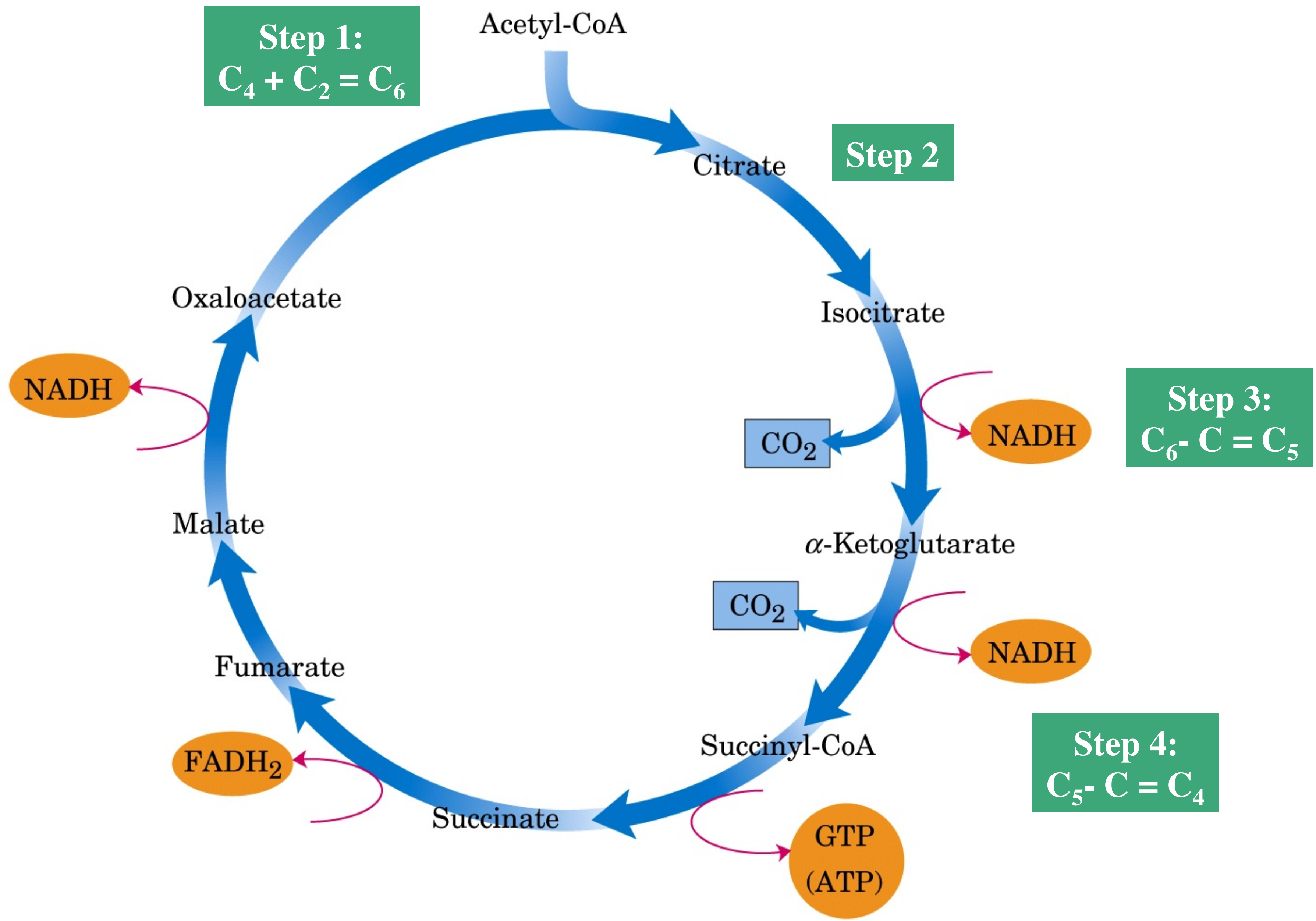
Step 3



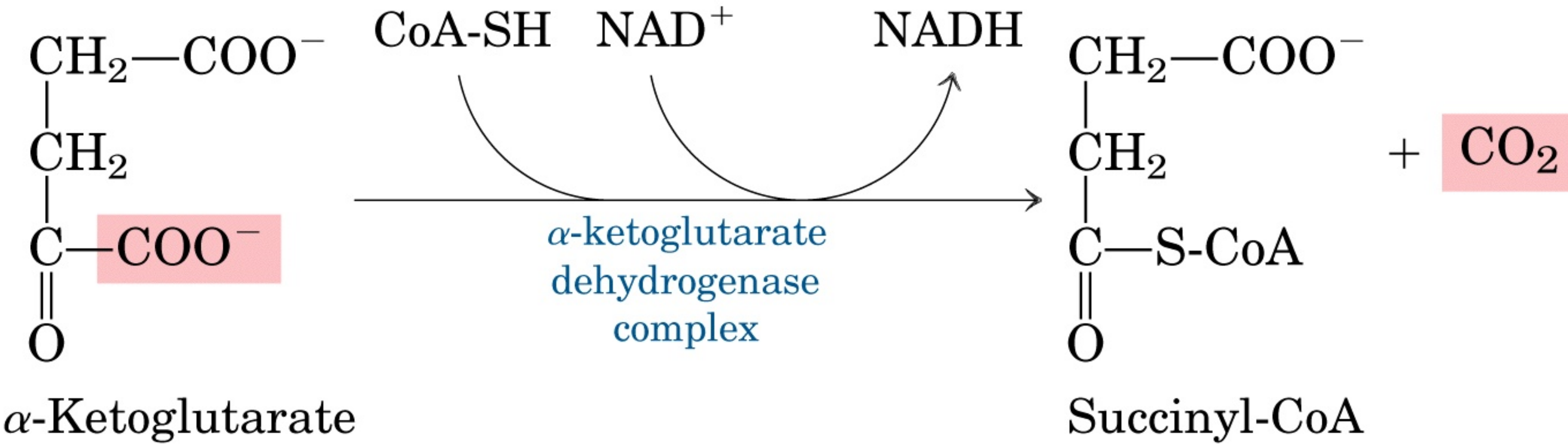
Isocitrate

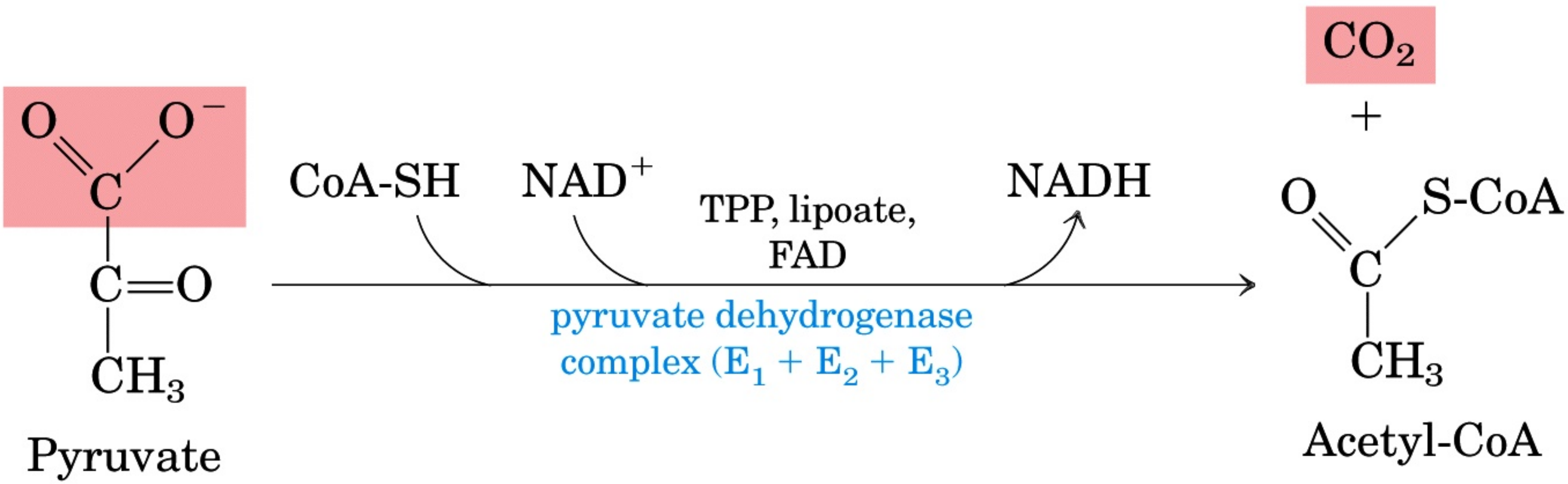
α-Ketoglutarate

$$\Delta G'^{\circ} = -20.9 \text{ kJ/mol}$$


Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Step 4:
$C_5 - C = C_4$
Succinyl-CoA
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate

Step 4



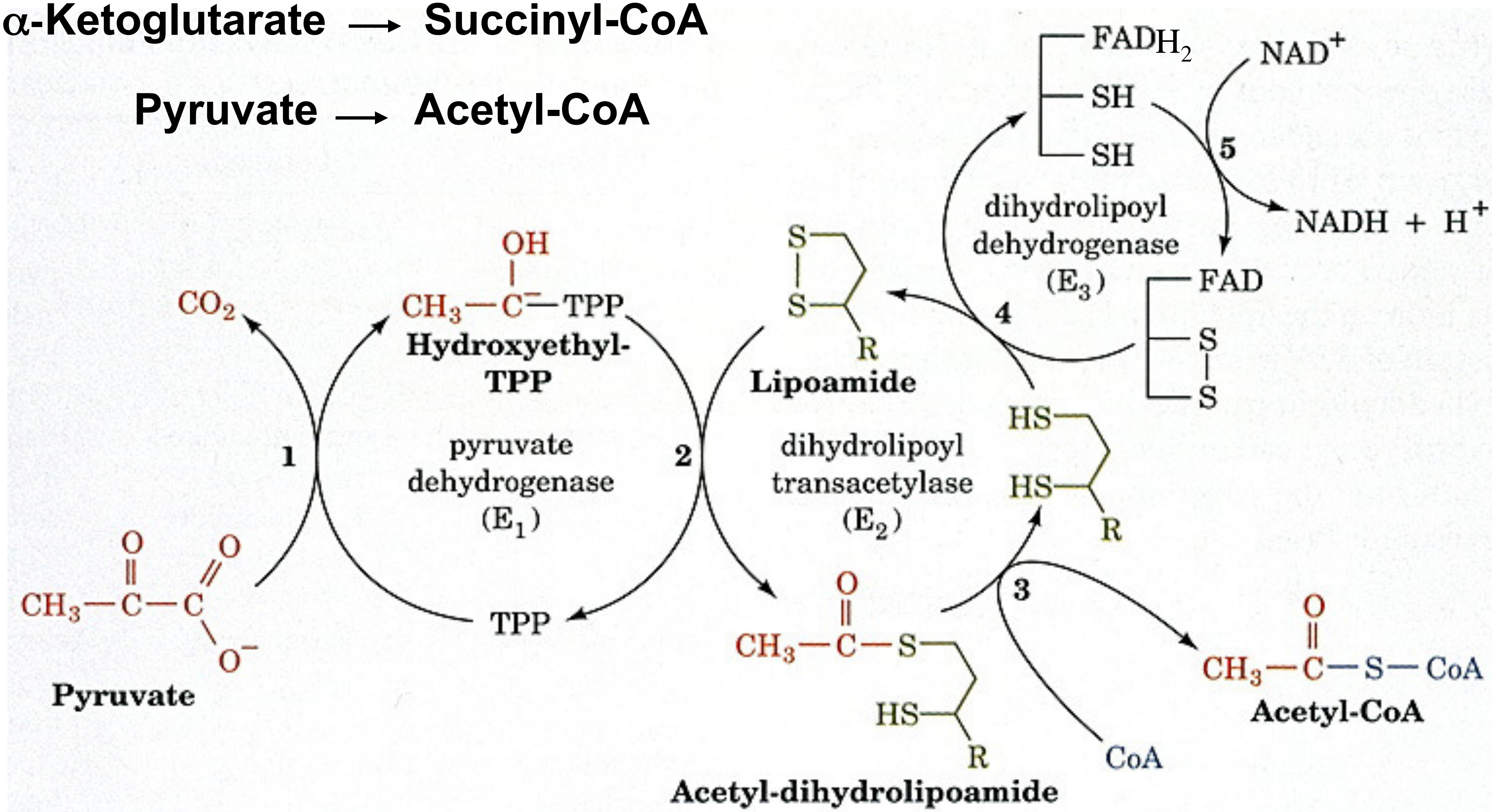


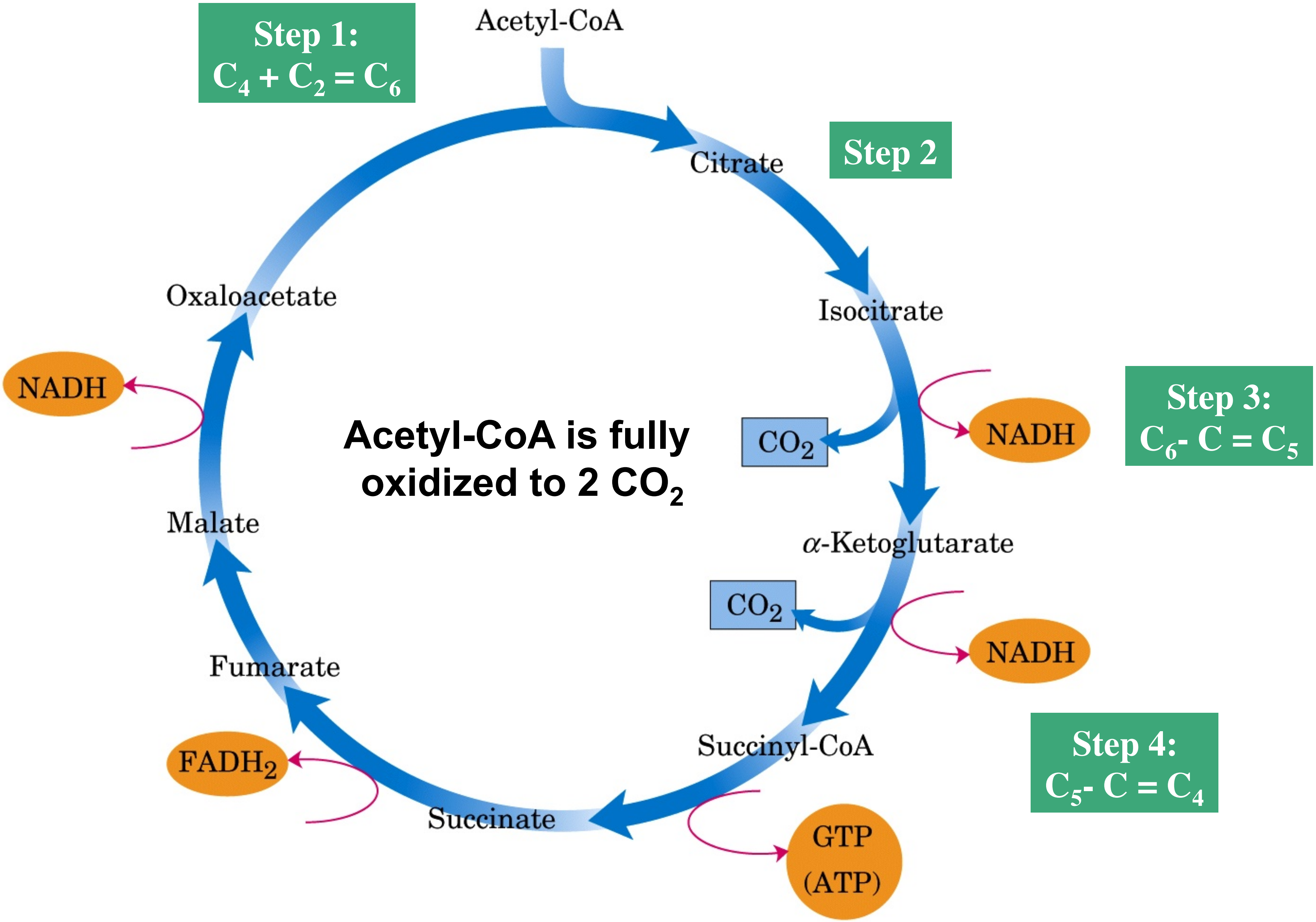
$\Delta G'^{\circ} = -33.4$ kJ/mol

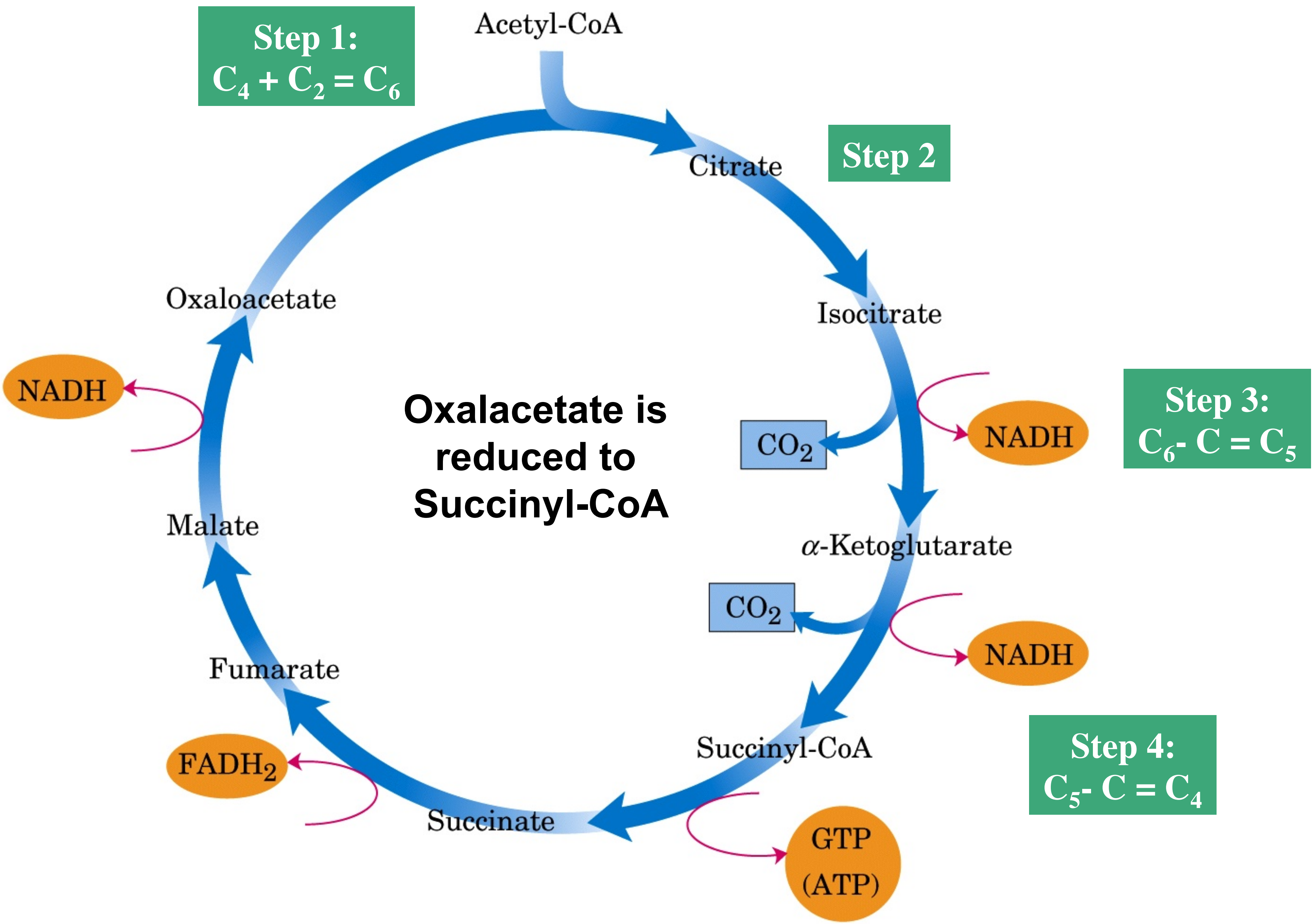
Step 4

α-Ketoglutarate ⟶ Succinyl-CoA

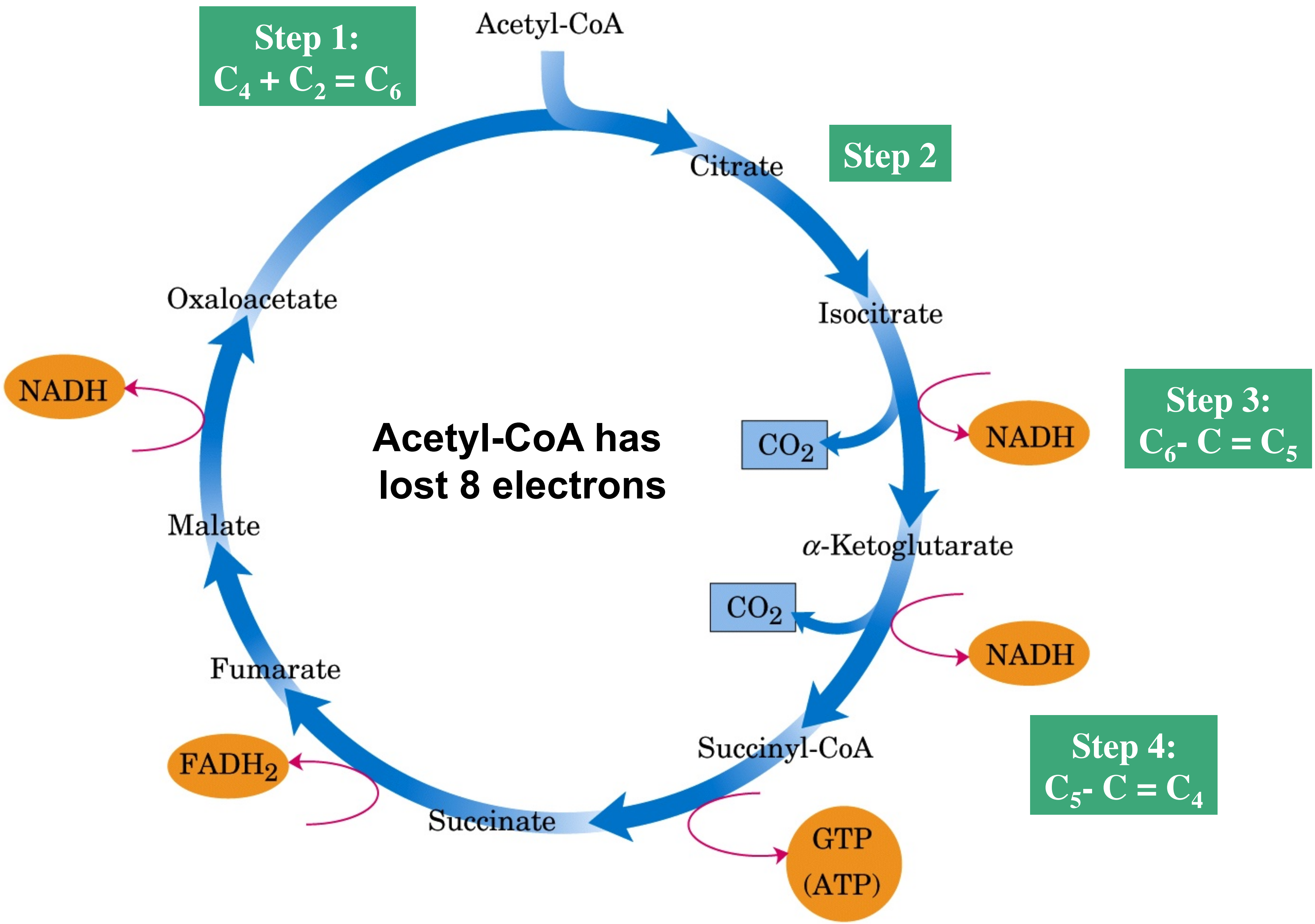
Pyruvate ⟶ Acetyl-CoA



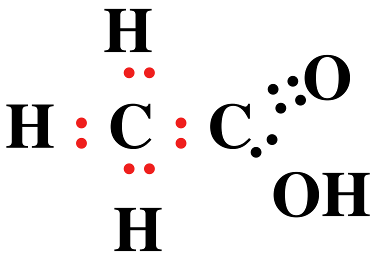

Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate
Acetyl-CoA is fully
oxidized to 2 CO_2



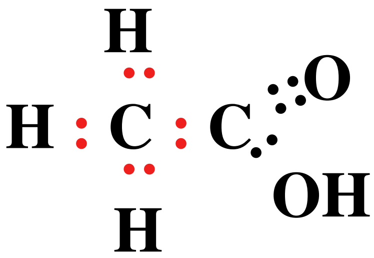
Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate
Oxalacetate is reduced to Succinyl-CoA


Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Step 4:
$C_5 - C = C_4$
Succinyl-CoA
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate
Acetyl-CoA has
lost 8 electrons

Acetic acid: 8 electrons

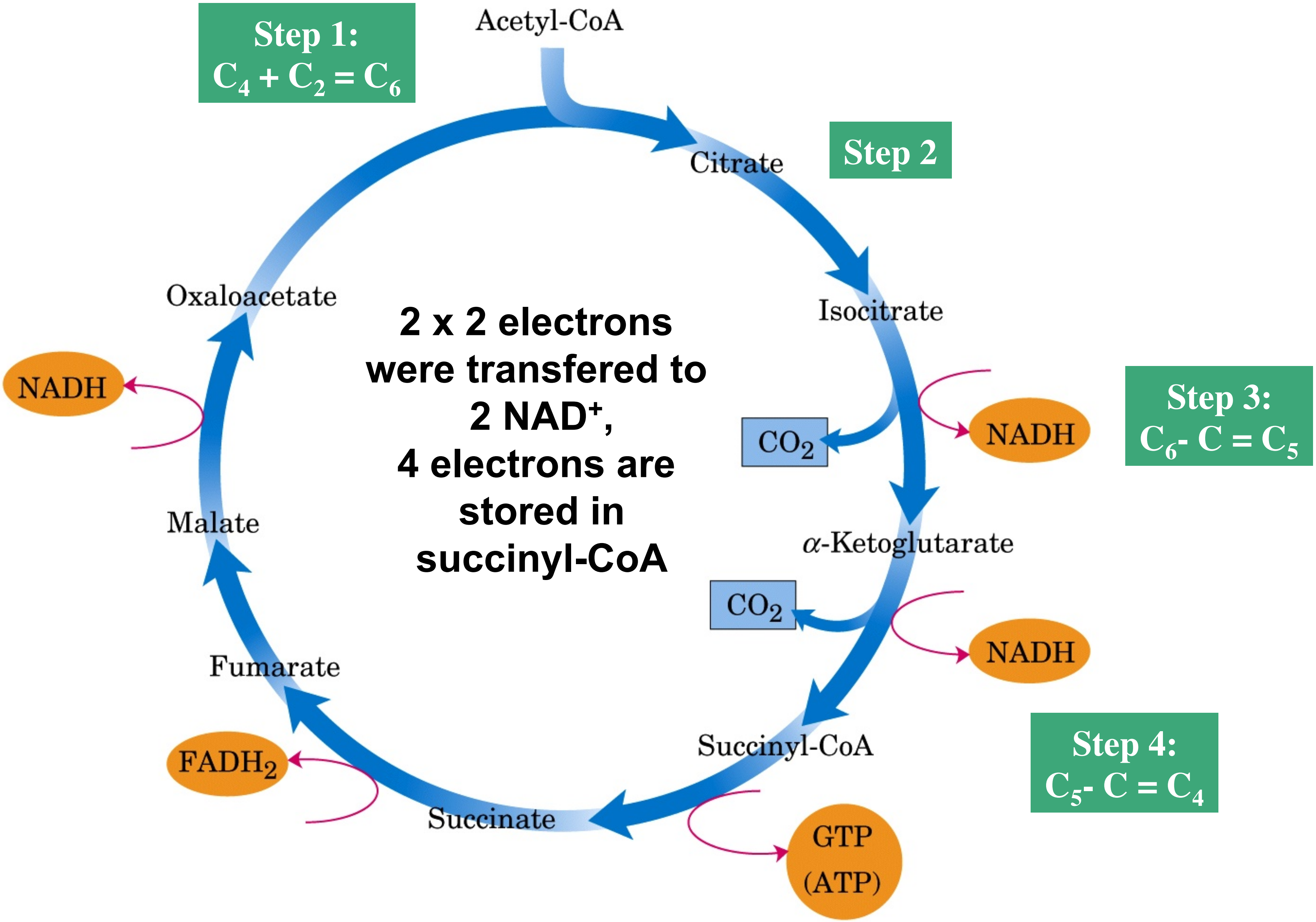


Acetic acid: 8 electrons

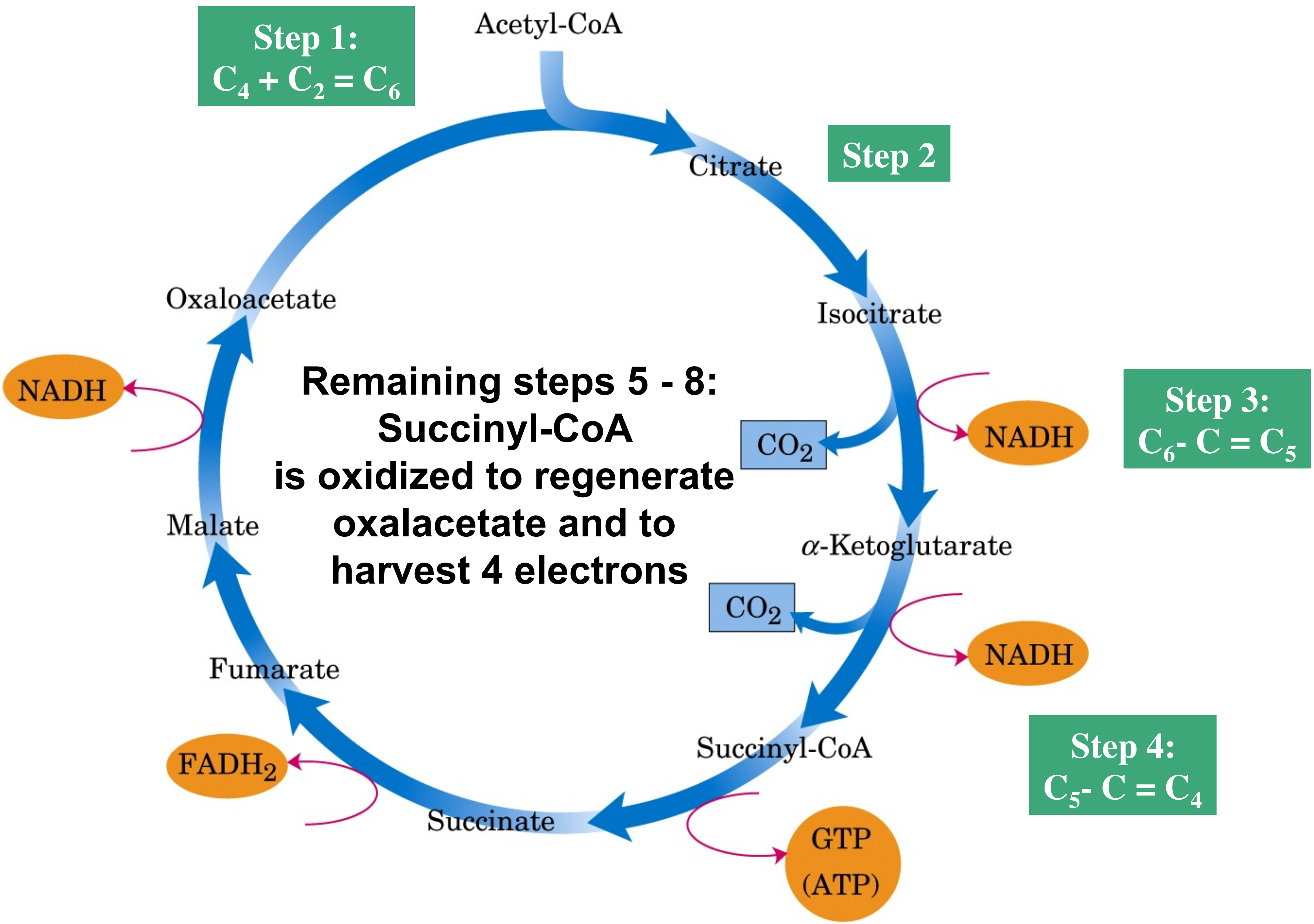


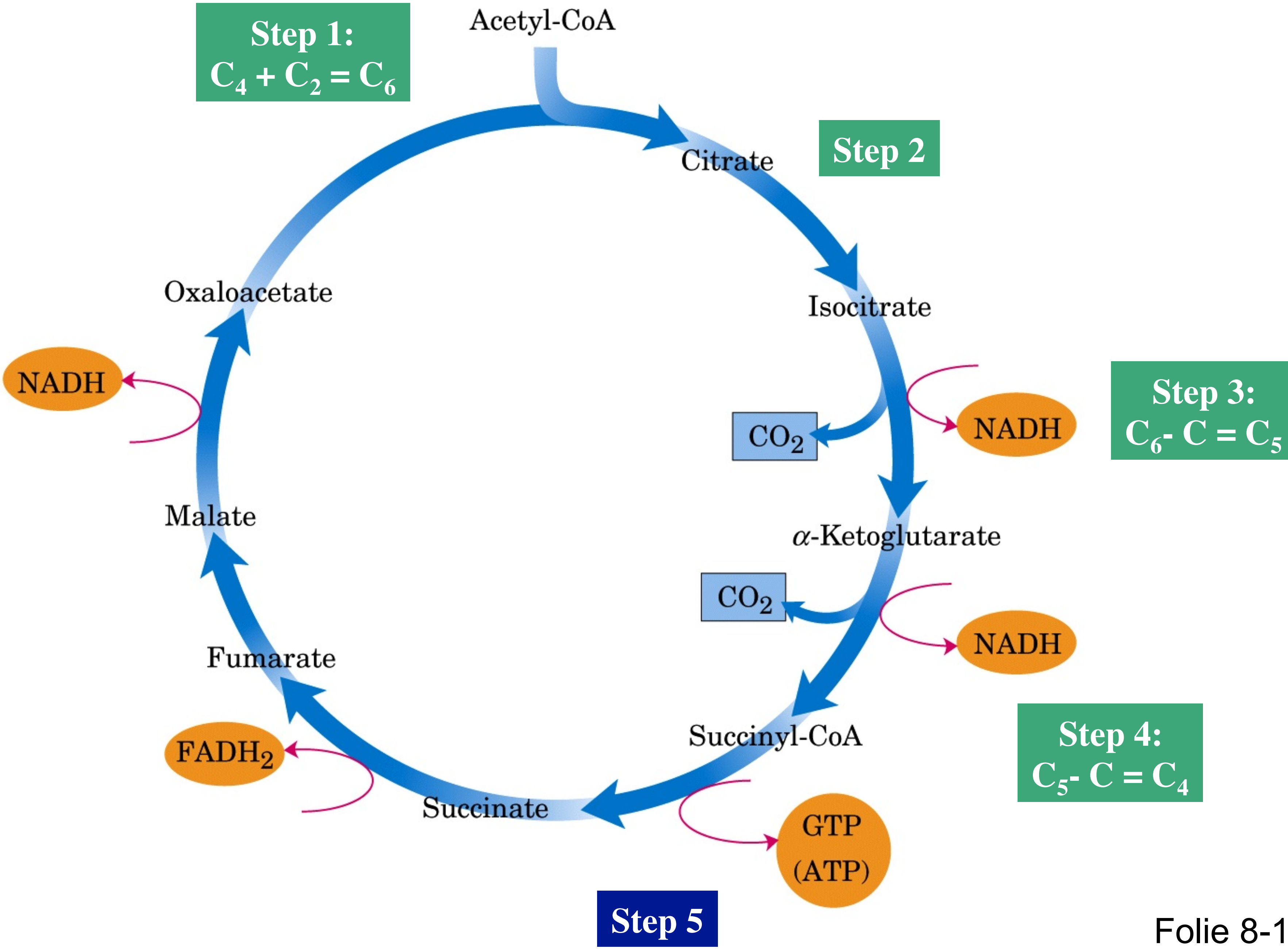
CO_2: 0 electrons

O :: C :: O



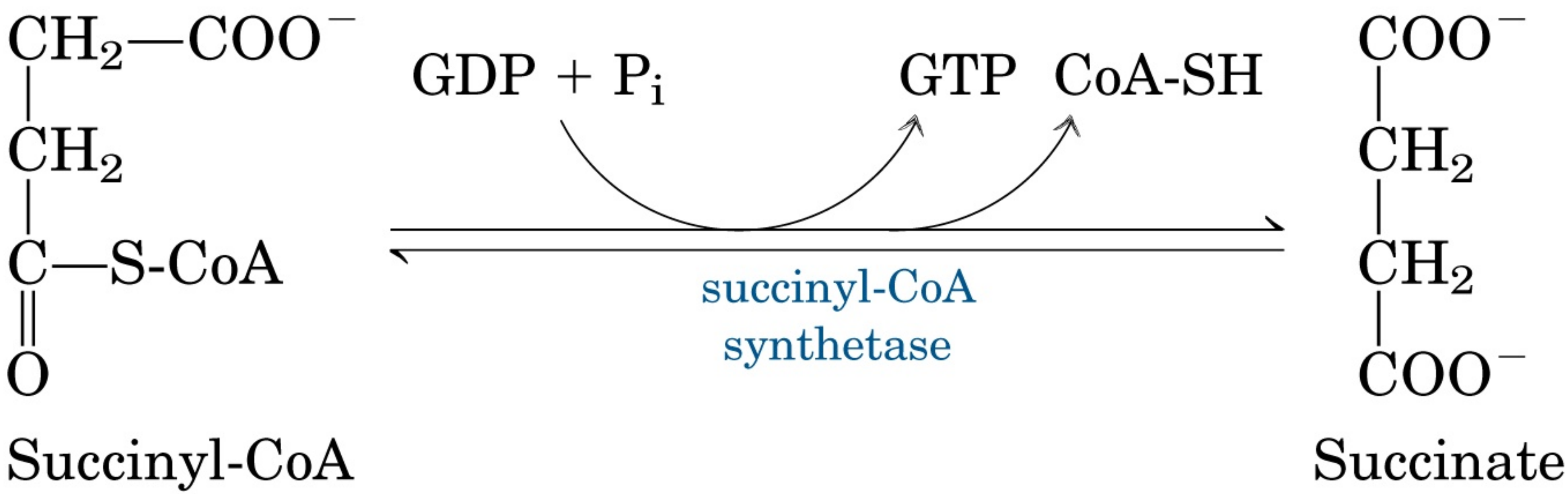
Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate
2 x 2 electrons
were transfered to
2 NAD^+,
4 electrons are
stored in
succinyl-CoA


Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
Oxaloacetate
NADH
Remaining steps 5 - 8:
Succinyl-CoA
is oxidized to regenerate
oxalacetate and to
harvest 4 electrons
CO_2
NADH
Step 3:
$C_6 - C = C_5$
Malate
α-Ketoglutarate
CO_2
NADH
Fumarate
$FADH_2$
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
Succinate
GTP
(ATP)



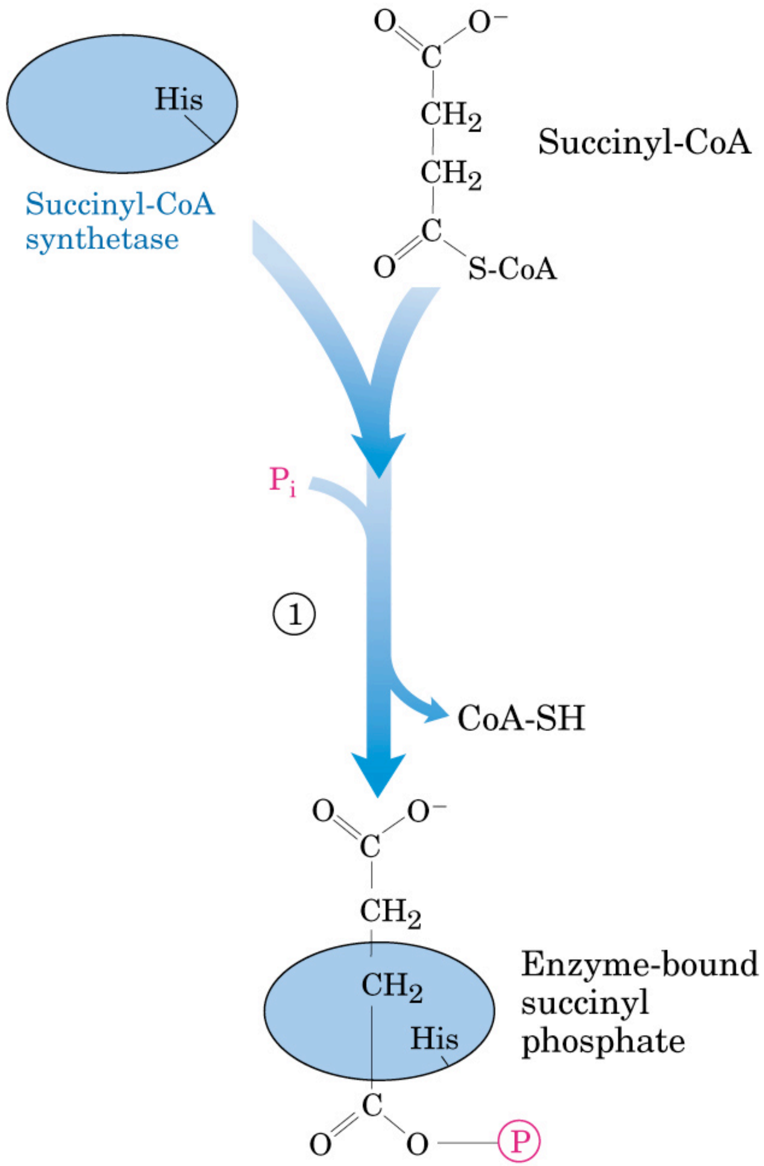
Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Step 5
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate

Step 5



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

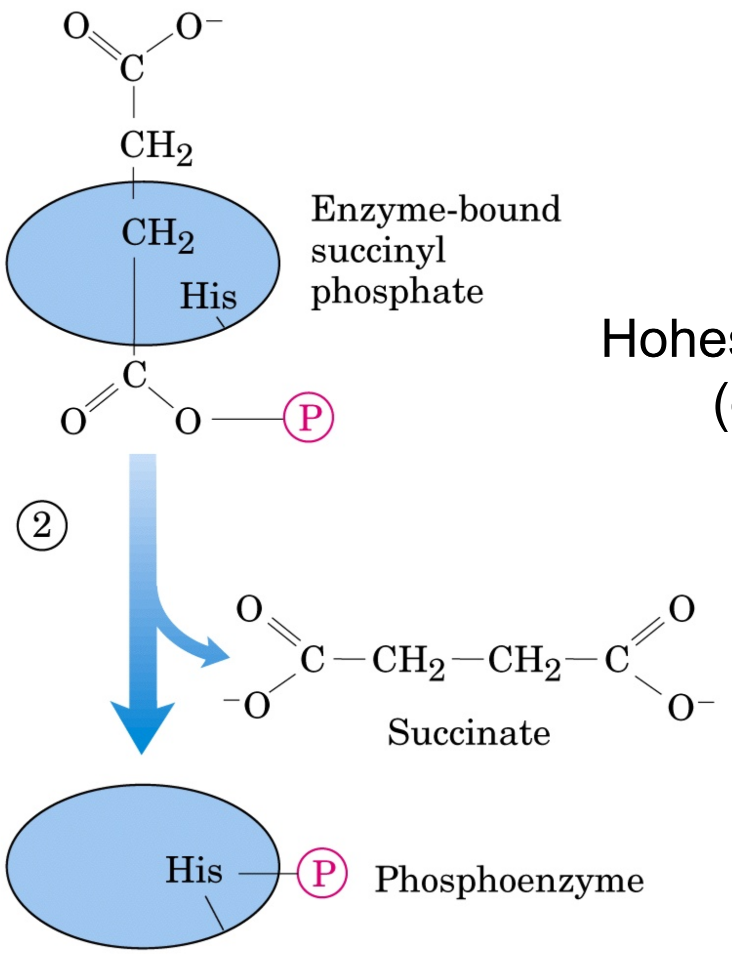
Step 5



Energiereicher Thioester

Spaltung mit P_i (nicht mit H_2O)
Energie wird konserviert.

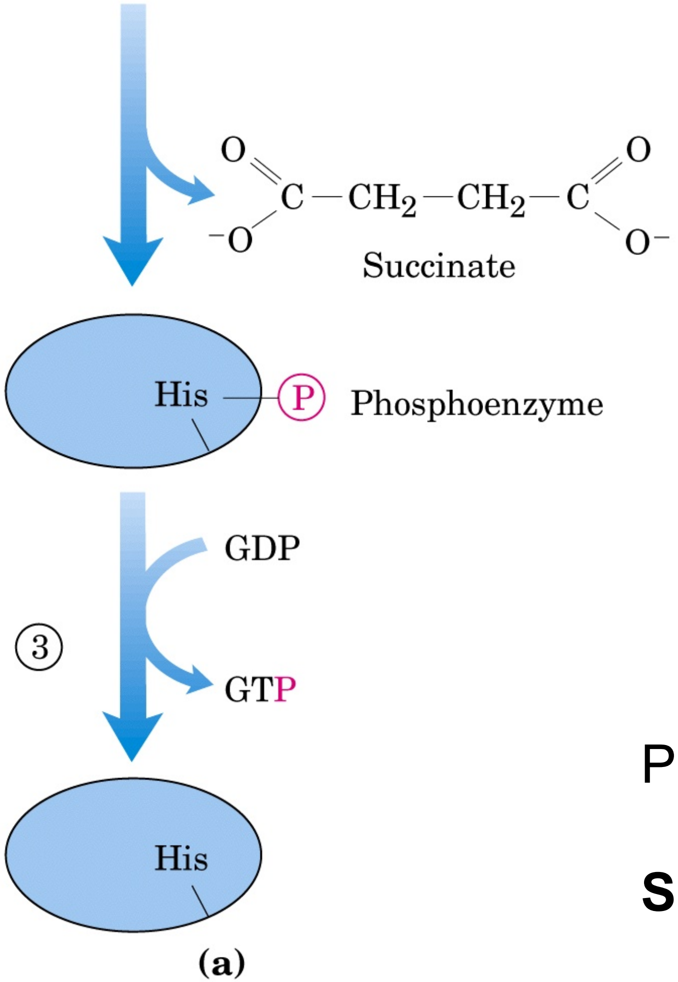
Step 5



Hohes Gruppenübertragungspotential (gemischtes Säureanhydrid)

P_i wird auf His übertragen.

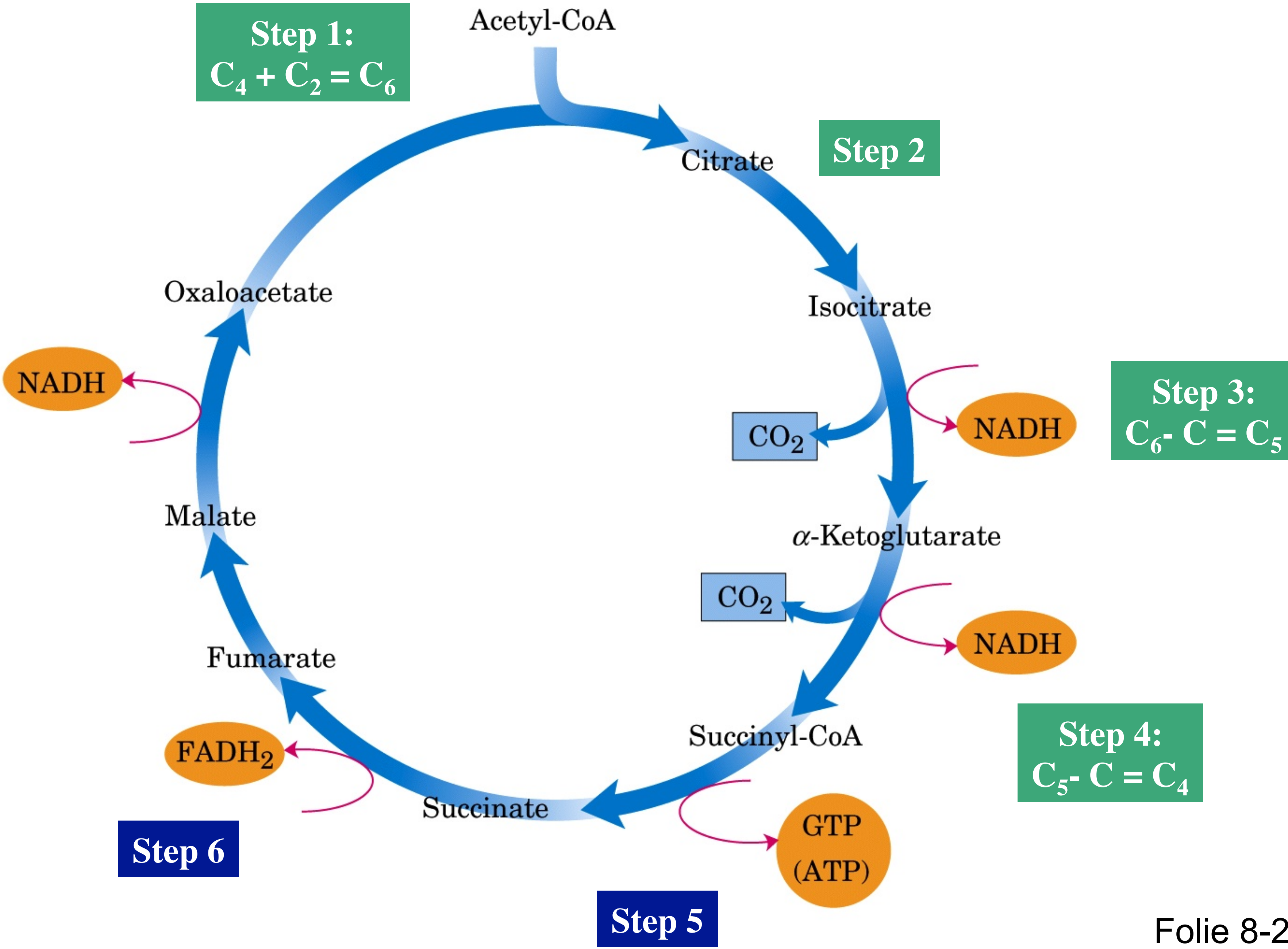
Step 5



Hohes Gruppenübertragungspotential ist in His-P konserviert.

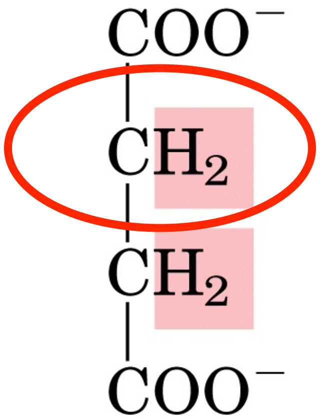
P_i wird auf GDP (ADP) übertragen.

Substratkettenphosphorylierung

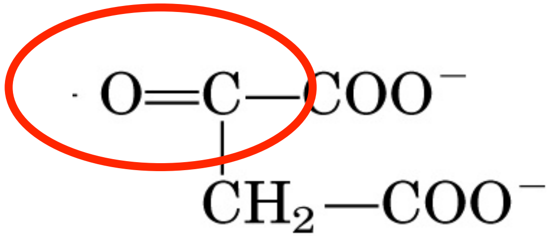

Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Step 5
Succinate
$FADH_2$
Step 6
Fumarate
Malate
NADH
Oxaloacetate

Step 6 - 8

Oxidation of Succinate to Oxalacetate



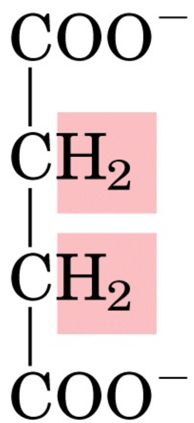
Succinate



Oxaloacetate

Step 6 - 8

Oxidation of Succinate to Oxalacetate

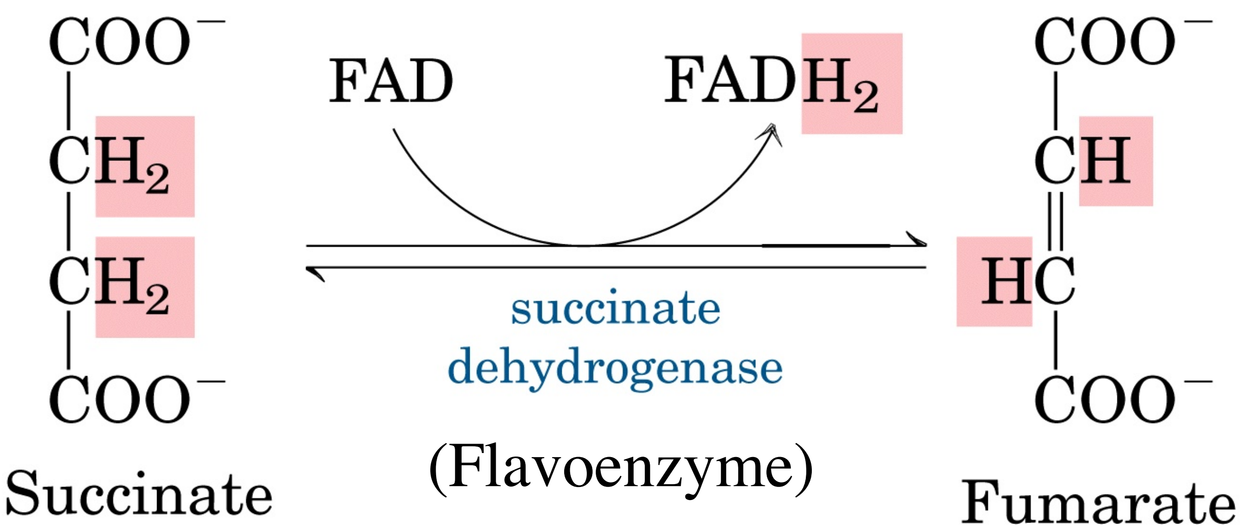


Succinate

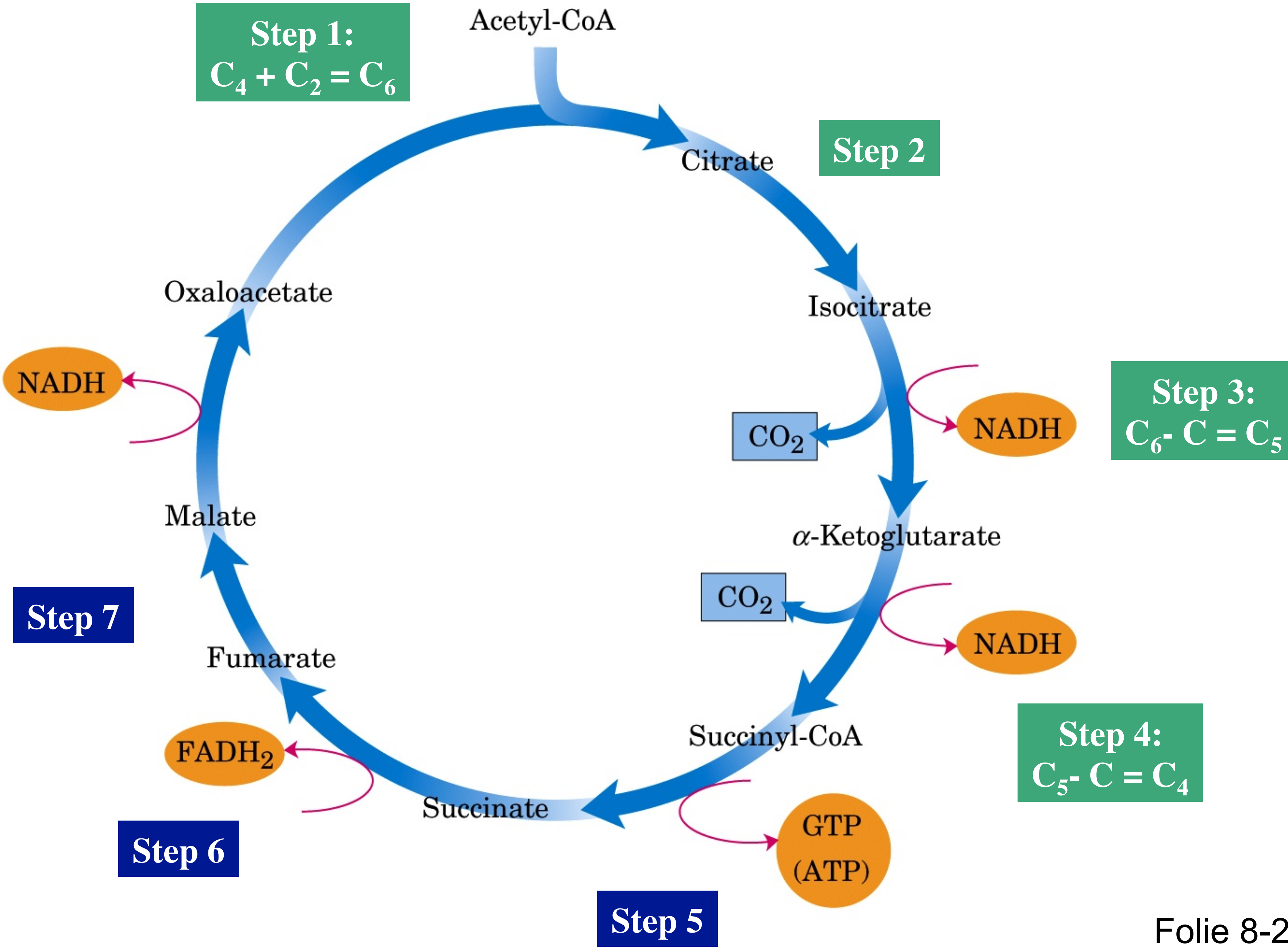
Succinate to Oxalacetate:
4 electrons must be removed.
Two oxidation steps are required, each removing 2 electrons.

Step 6

Oxidation of Succinate to Fumarate

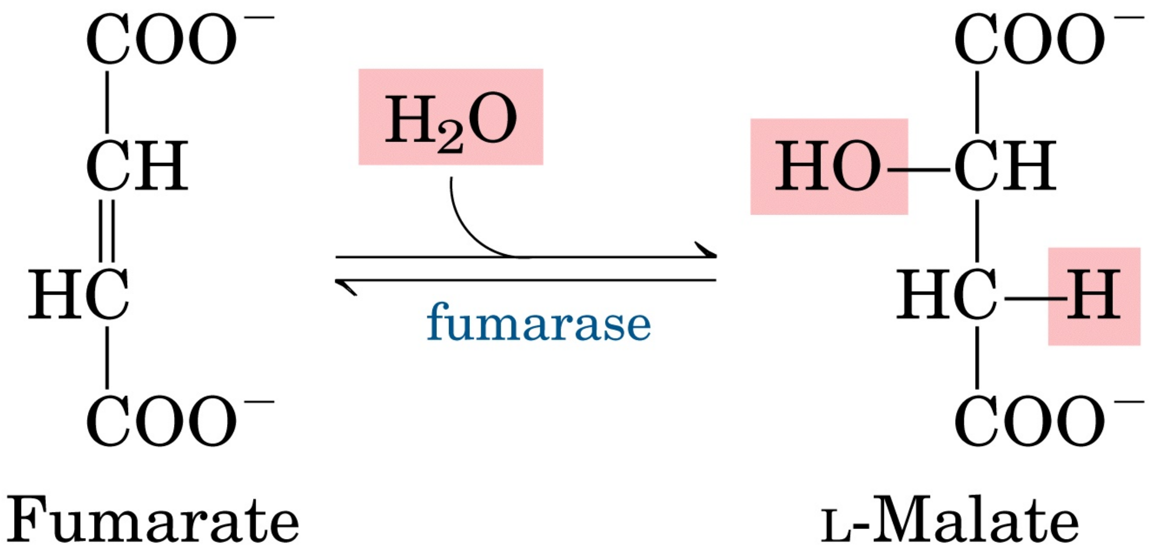


$$\Delta G'^{\circ} = 0 \text{ kJ/mol}$$

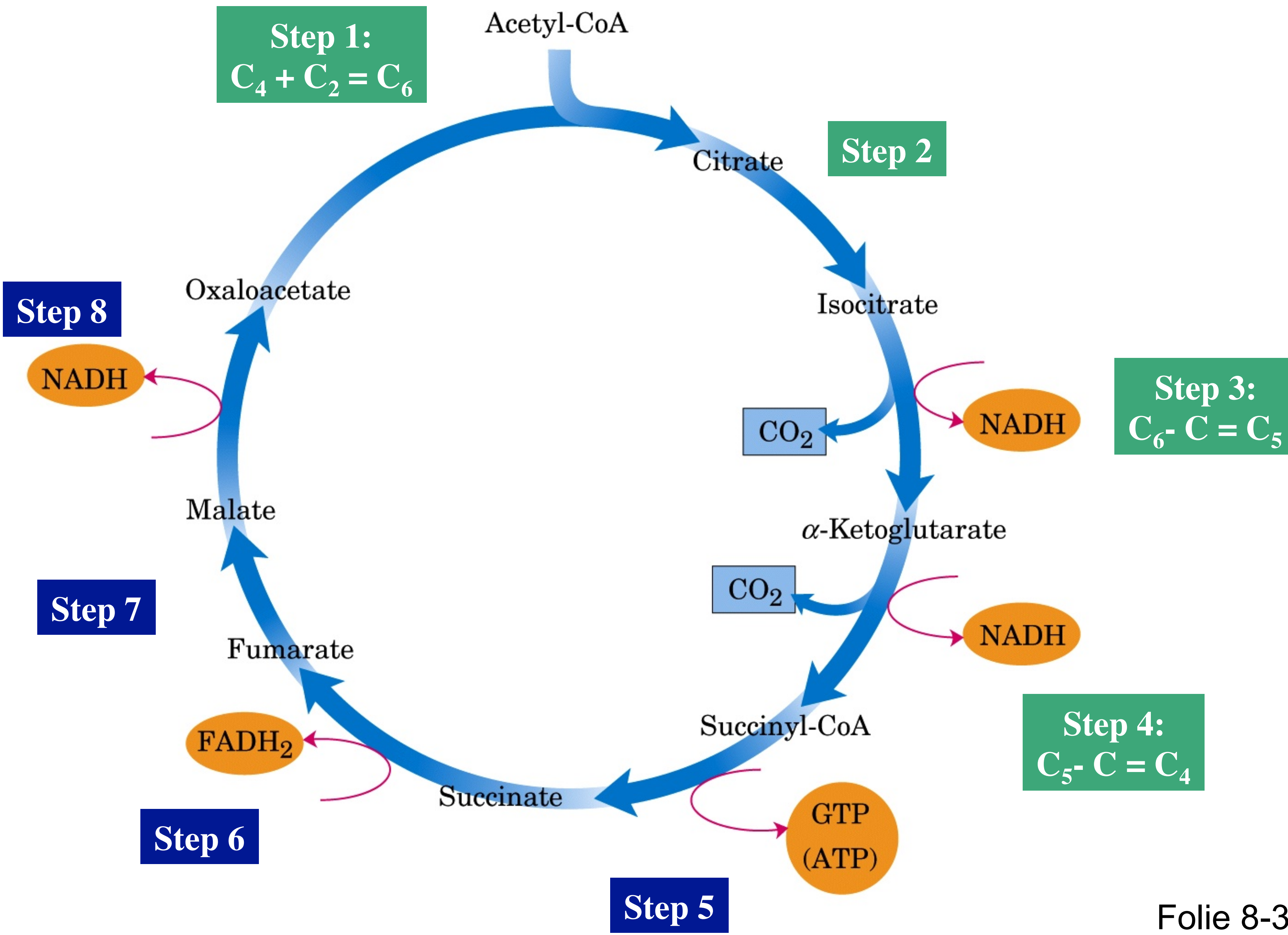


Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Step 5
Succinate
$FADH_2$
Step 6
Fumarate
Step 7
Malate
NADH
Oxaloacetate

Step 7

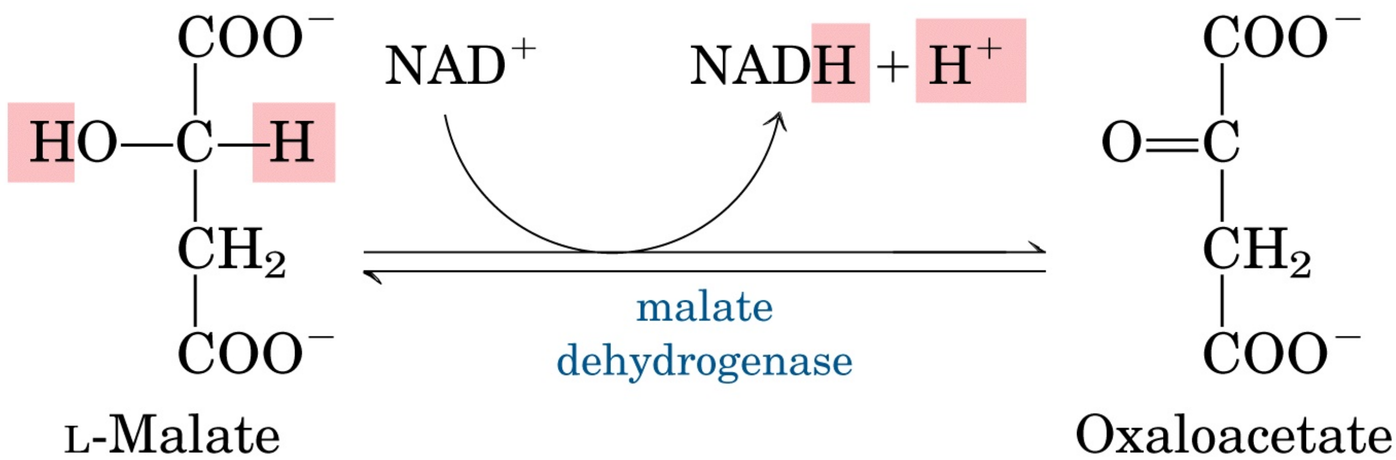


$$\Delta G'^{\circ} = -3.8\ \text{kJ/mol}$$



Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Step 5
Succinate
$FADH_2$
Step 6
Fumarate
Step 7
Malate
Oxaloacetate
Step 8
NADH

Step 8



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

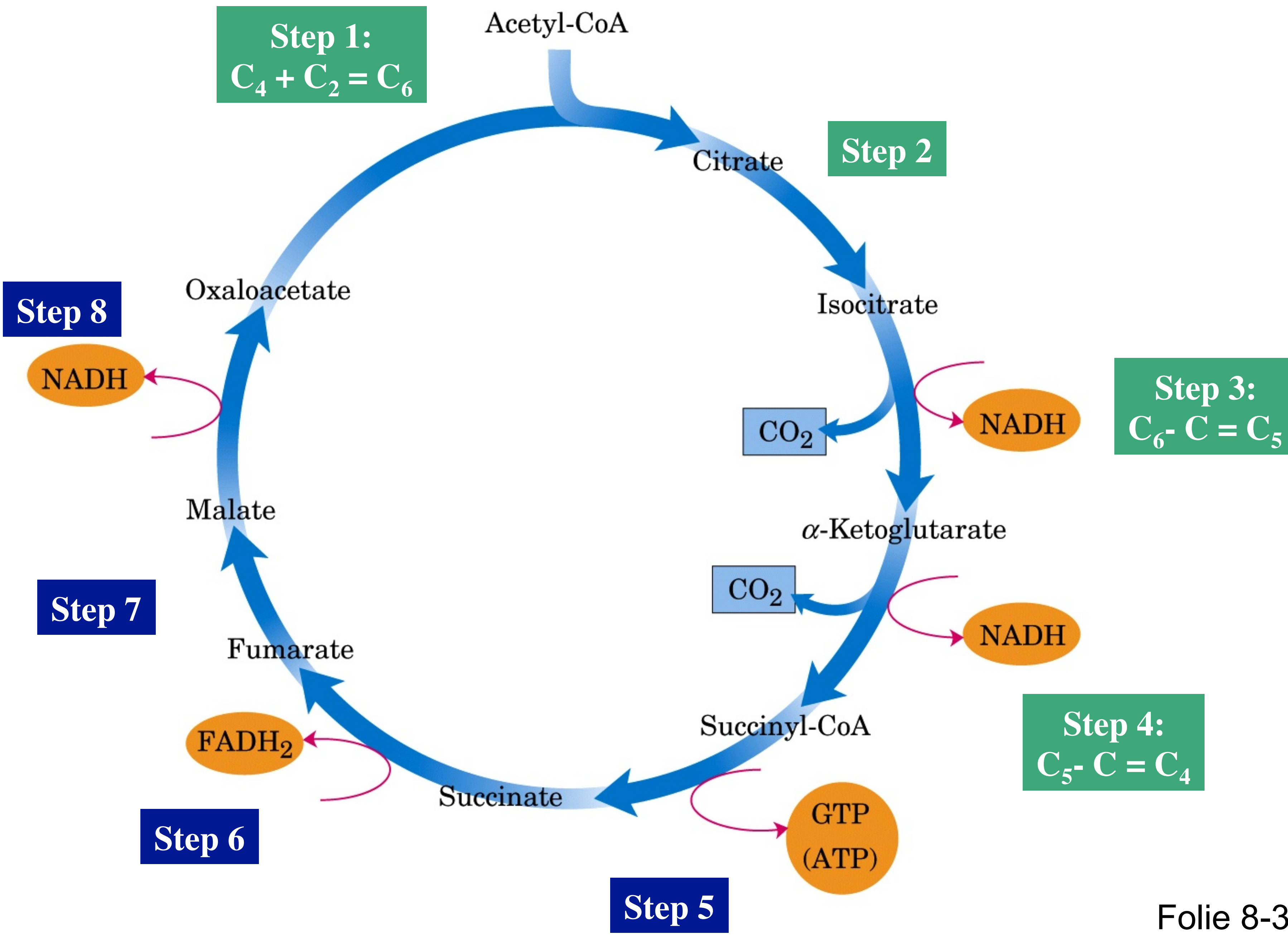

Step 1:
$C_4 + C_2 = C_6$
Acetyl-CoA
Citrate
Step 2
Isocitrate
CO_2
NADH
Step 3:
$C_6 - C = C_5$
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
Step 4:
$C_5 - C = C_4$
GTP
(ATP)
Step 5
Succinate
$FADH_2$
Step 6
Fumarate
Step 7
Malate
Oxaloacetate
Step 8
NADH

table 16–1

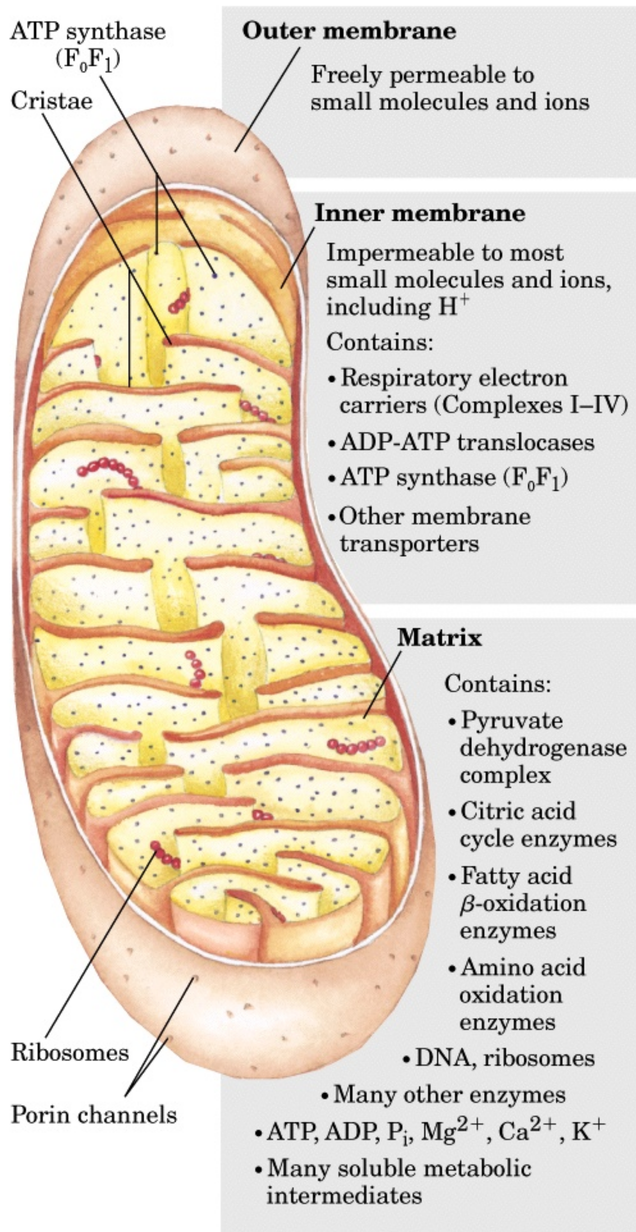
Stoichiometry of Coenzyme Reduction and ATP Formation in the Aerobic Oxidation of Glucose via Glycolysis, the Pyruvate Dehydrogenase Reaction, the Citric Acid Cycle, and Oxidative Phosphorylation

Reaction	Number of ATP or reduced coenzymes directly formed	
Glucose ⟶ glucose 6-phosphate	−1 ATP	
Fructose 6-phosphate ⟶ fructose 1,6-bisphosphate	−1 ATP	**Glycolysis**
2 Glyceraldehyde 3-phosphate ⟶ 2 1,3-bisphosphoglycerate	2 NADH	
2 1,3-Bisphosphoglycerate ⟶ 2 3-phosphoglycerate	2 ATP	
2 Phosphoenolpyruvate ⟶ 2 pyruvate	2 ATP	
2 Pyruvate ⟶ 2 acetyl-CoA	2 NADH	**Pyruvate**
2 Isocitrate ⟶ 2 α-ketoglutarate	2 NADH	**Dehydrogenase**
2 α-Ketoglutarate ⟶ 2 succinyl-CoA	2 NADH	**And**
2 Succinyl-CoA ⟶ 2 succinate	2 ATP (or 2 GTP)	**Citric Acid Cycle**
2 Succinate ⟶ 2 fumarate	2 $FADH_2$	
2 Malate ⟶ 2 oxaloacetate	2 NADH	
Total		

table 16–1

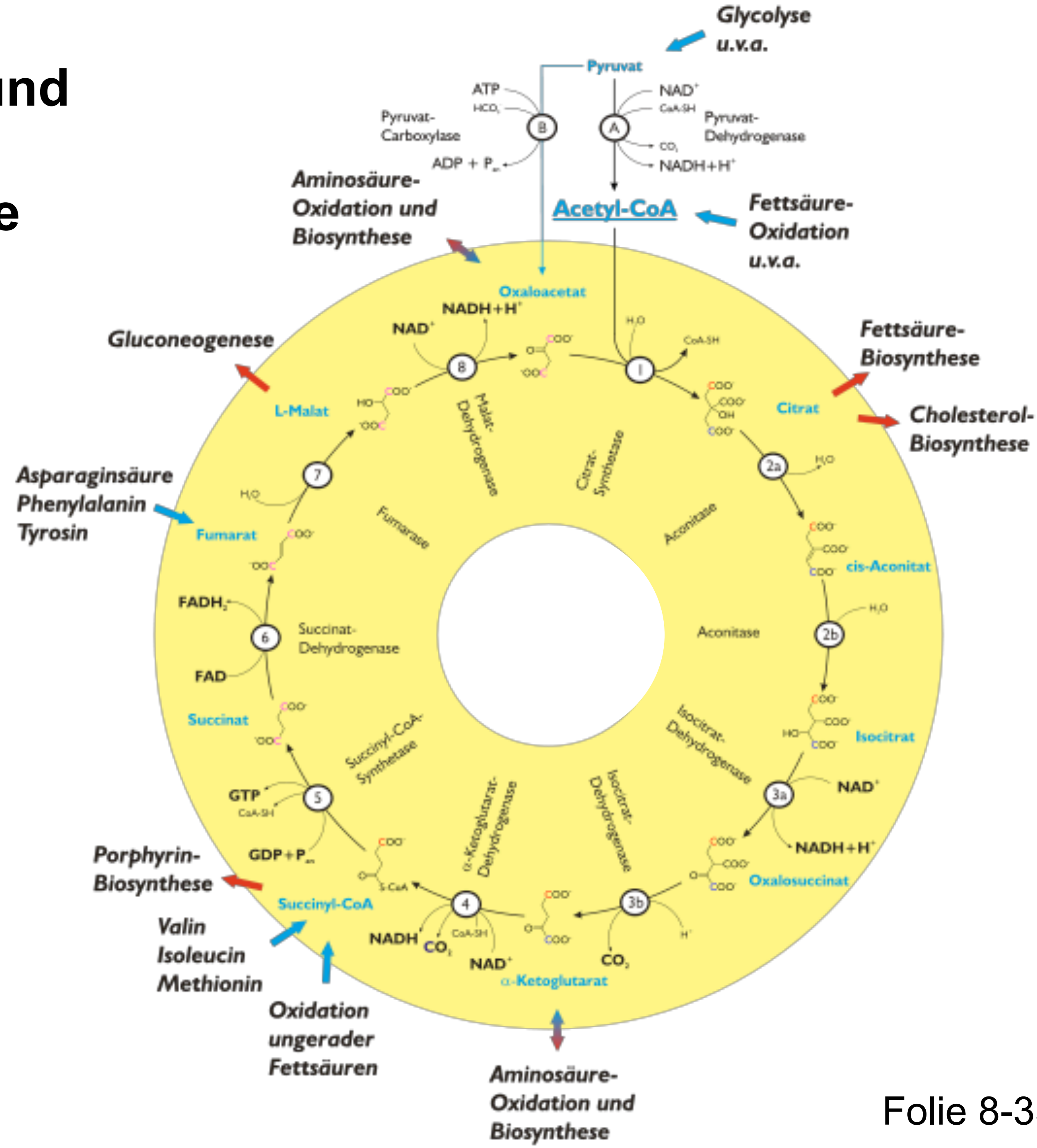
Stoichiometry of Coenzyme Reduction and ATP Formation in the Aerobic Oxidation of Glucose via Glycolysis, the Pyruvate Dehydrogenase Reaction, the Citric Acid Cycle, and Oxidative Phosphorylation

Reaction	Number of ATP or reduced coenzymes directly formed	Number of ATP ultimately formed*
Glucose $\longrightarrow$ glucose 6-phosphate	−1 ATP	−1
Fructose 6-phosphate $\longrightarrow$ fructose 1,6-bisphosphate	−1 ATP	−1
2 Glyceraldehyde 3-phosphate $\longrightarrow$ 2 1,3-bisphosphoglycerate	2 NADH	3–5
2 1,3-Bisphosphoglycerate $\longrightarrow$ 2 3-phosphoglycerate	2 ATP	2
2 Phosphoenolpyruvate $\longrightarrow$ 2 pyruvate	2 ATP	2
2 Pyruvate $\longrightarrow$ 2 acetyl-CoA	2 NADH	5
2 Isocitrate $\longrightarrow$ 2 α-ketoglutarate	2 NADH	5
2 α-Ketoglutarate $\longrightarrow$ 2 succinyl-CoA	2 NADH	5
2 Succinyl-CoA $\longrightarrow$ 2 succinate	2 ATP (or 2 GTP)	2
2 Succinate $\longrightarrow$ 2 fumarate	2 $FADH_2$	3
2 Malate $\longrightarrow$ 2 oxaloacetate	2 NADH	5
Total		30–32

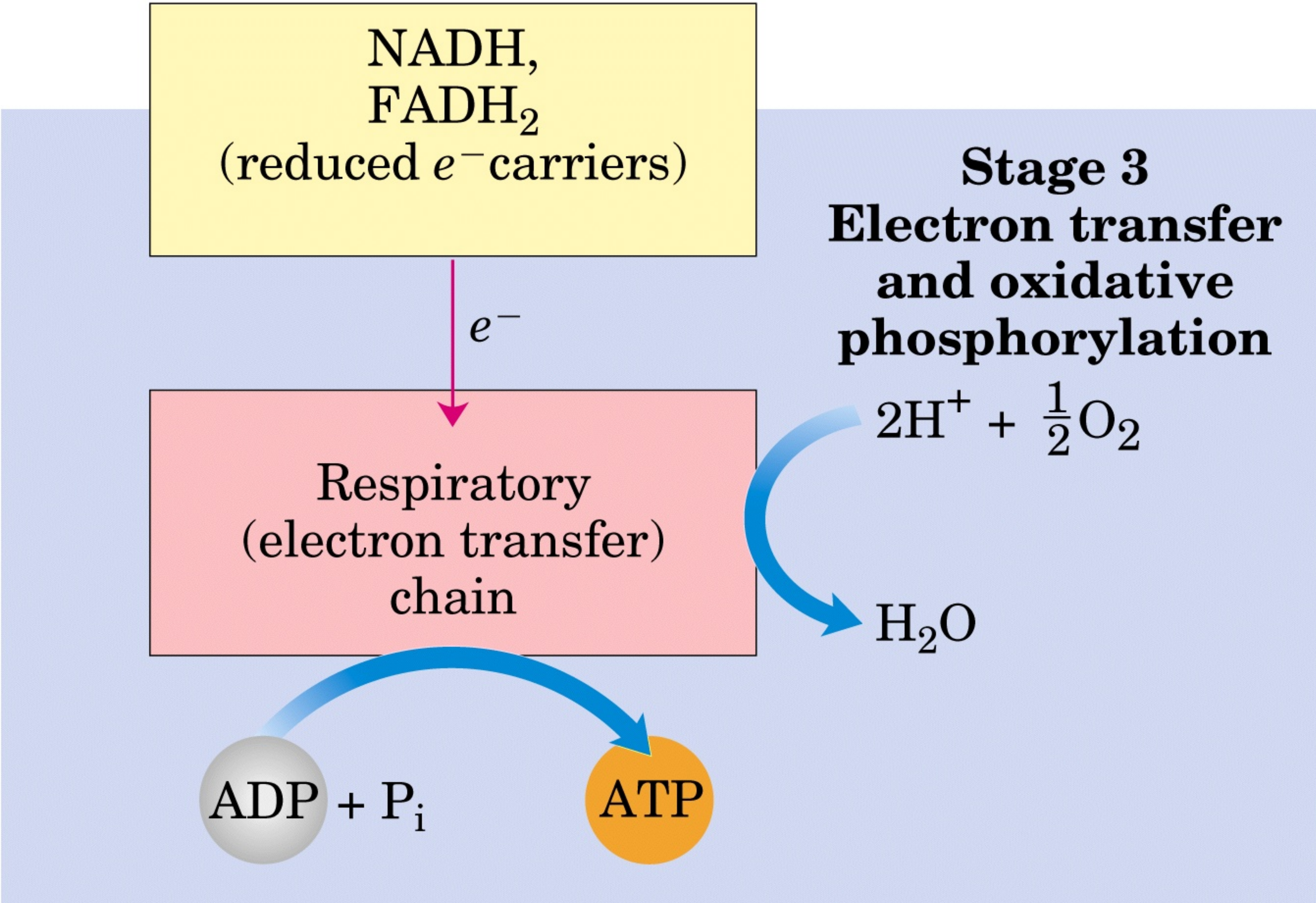


ATP synthase (F_0F_1)
Cristae
Outer membrane
Freely permeable to small molecules and ions
Inner membrane
Impermeable to most small molecules and ions, including H^+
Contains:
• Respiratory electron carriers (Complexes I–IV)
• ADP-ATP translocases
• ATP synthase (F_0F_1)
• Other membrane transporters
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
Ribosomes
Porin channels

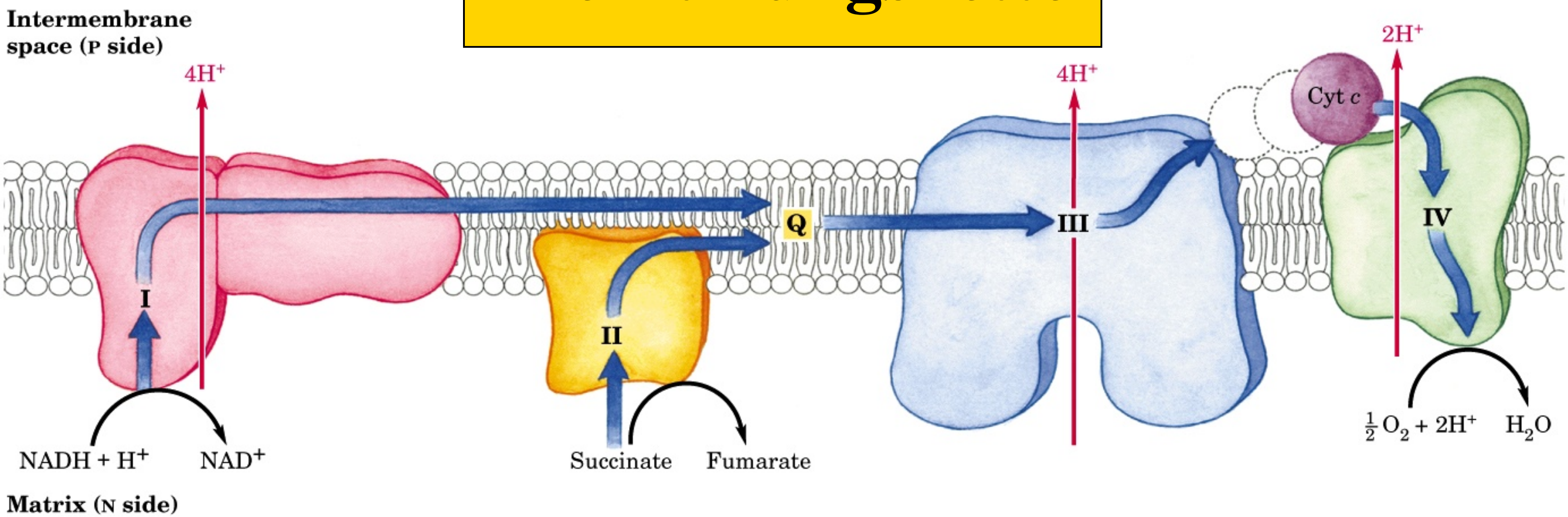
Cataplerotische und anaplerotische Stoffwechselwege



Atmungskette
F_1F_o-ATPase


NADH,
FADH2
(reduced e⁻ carriers)
Stage 3
Electron transfer
and oxidative
phosphorylation
e⁻
Respiratory
(electron transfer)
chain
2H+ + ½O2
H2O
ADP + Pi
ATP

Die Atmungskette



Elektronen werden in mehreren Schritten von NADH auf molekularen Sauerstoff übertragen.

Die Übertragung von Elektronen wird von Enzymkomplexen katalysiert, die in der mitochondrialen Innenmembran lokalisiert sind.

Die Übertragung von Elektronen ist an den Transport von Protonen über die Innenmembran gekoppelt.

Reduktion-Oxidations-Reaktionen

Reduktion: **Aufnahme von Elektronen**

Oxidation: **Abgabe von Elektronen**

Redoxreaktionen laufen gekoppelt ab.

$$NADH + H^+ \longrightarrow NAD^+ + 2H^+ + 2e^-$$

$$1/2O_2 + 2e^- + 2H^+ \longrightarrow OH^- + H^+ \longrightarrow H_20$$

$$NADH + H^+ + 1/2O_2 \longrightarrow NAD^+ + H_20$$

Änderung der freien Enthalpie bei Redoxreaktionen

Reduktionspotential und Fähigkeit elektrische Arbeit zu verrichten:

$$\Delta G_0{}' = -\, n\, F\, \Delta E_0{}'$$

n: Anzahl der pro Molekül übertragenen Elektronen

F: Faraday Konstante, 96,48 kJ V^{-1} mol^{-1}

Änderung der freien Enthalpie bei Redoxreaktionen

Reduktionspotential und Fähigkeit elektrische Arbeit zu verrichten:

$$\Delta G_0{}' = - n\, F\, \Delta E_0{}'$$

$1/2\ O_2 + 2H^+ + 2e^- \longrightarrow H_2O$ 0.816 V

$NAD^+ + 2H^+ + 2e^- \longrightarrow NADH + H^+$ - 0.320 V

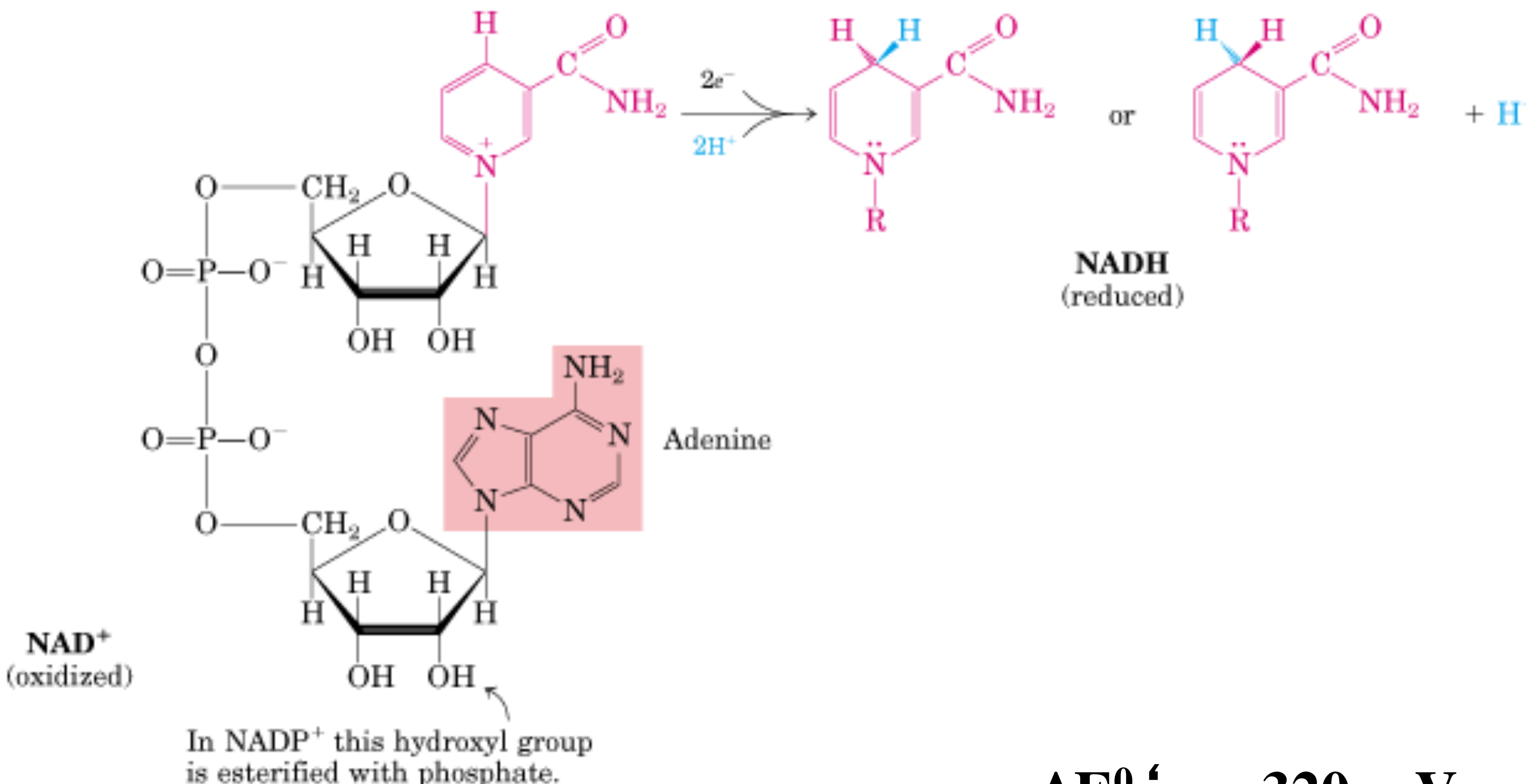
0.816 V - (- 0.320 V) = 1.136 V

$F = 96{,}48\ kJ\ V^{-1}\ mol^{-1}$

$$\Delta G_0{}' = - 2 \times 96{,}48\ kJ\ V^{-1}\ mol^{-1} \times 1.136\ V = - 219\ kJ\ mol^{-1}$$

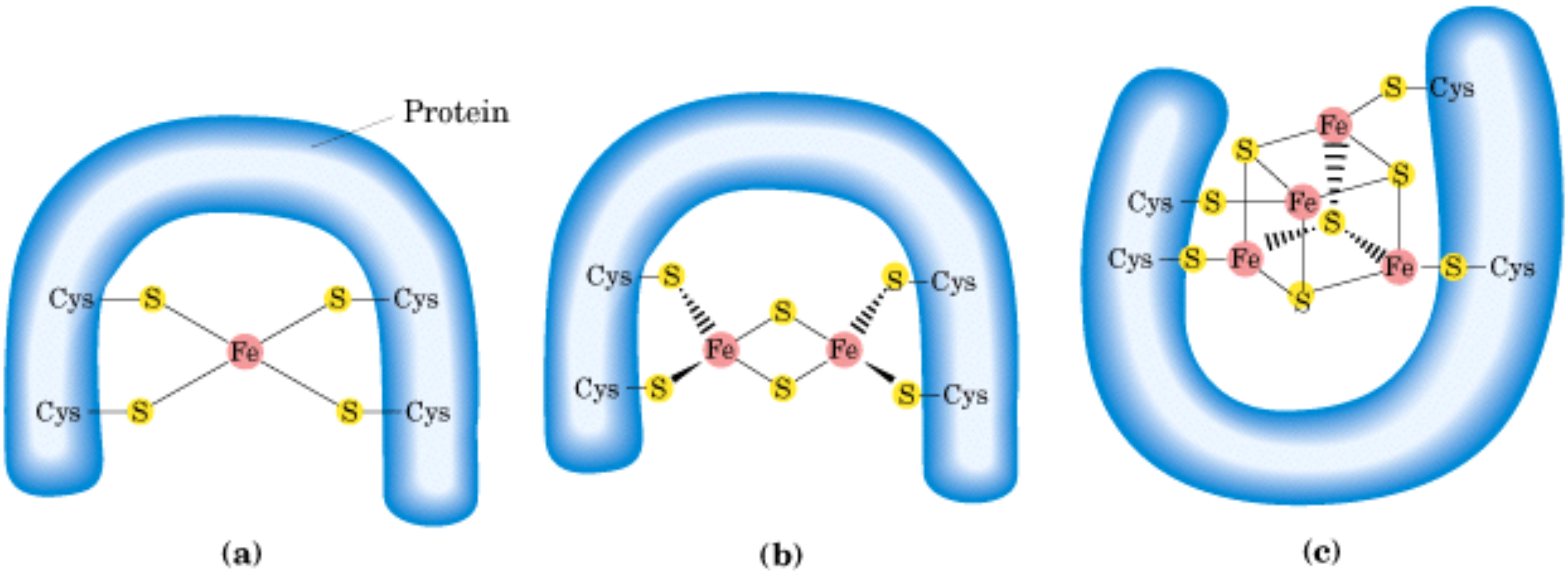
Elektronencarrier der Atmungskette

NADH



$\Delta E^{0\,\prime} = -\ 320\ \text{mV}$

FeS-Cluster are 1 Electron Carriers

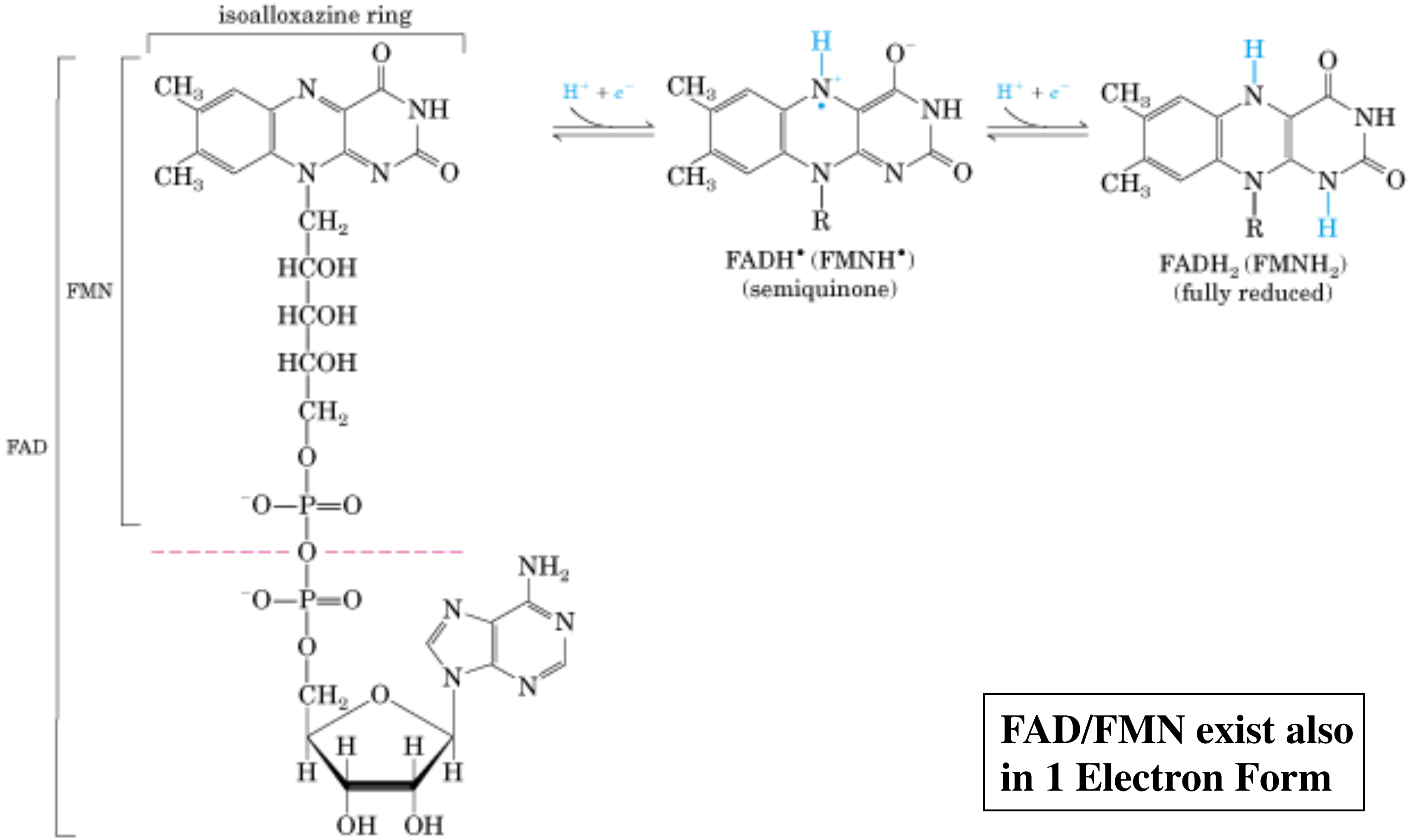


Fe-S Cluster in bacterial Complex II

2Fe-2S Cluster e.g. Complex I, II and Complex III (Rieske)

4Fe-4S Cluster e.g. Complex I and Complex II

FAD/FMN are 2 Electron Carriers

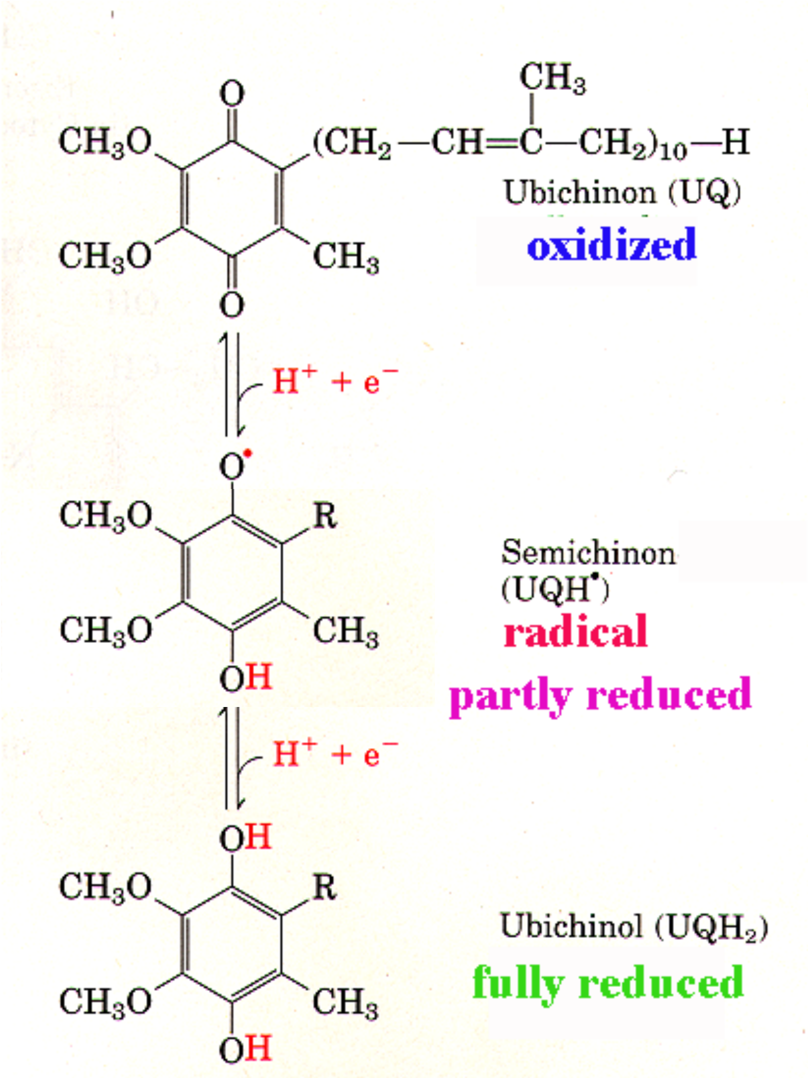


Flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN)

FAD/FMN exist also in 1 Electron Form

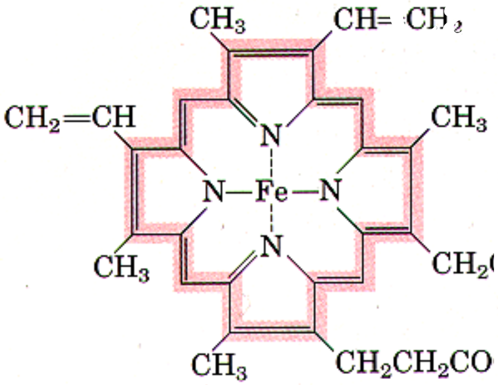
Ubiquinon is a 2 Electron/2 Proton Carri

UQ

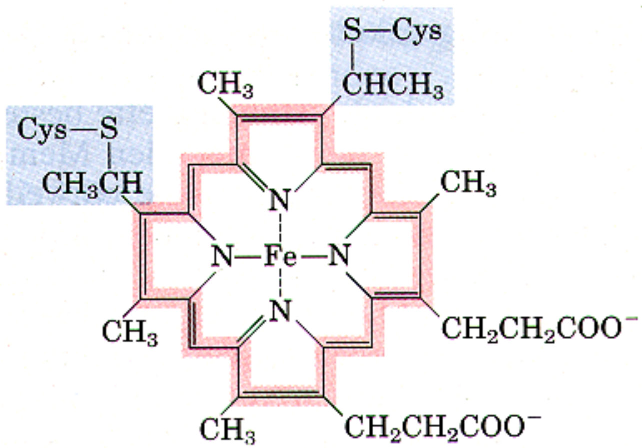


UQH_2

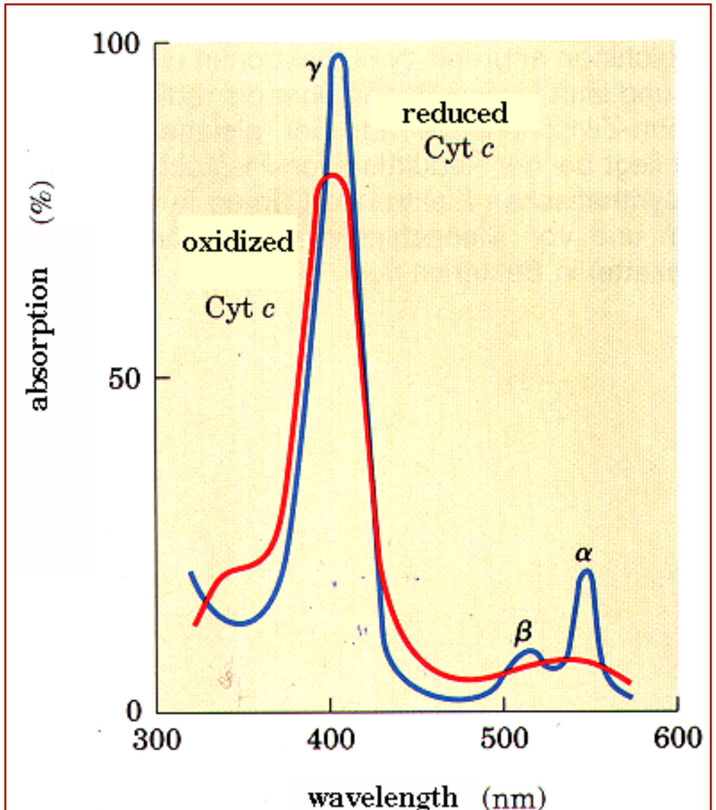
Cytochromes are 1 Electron

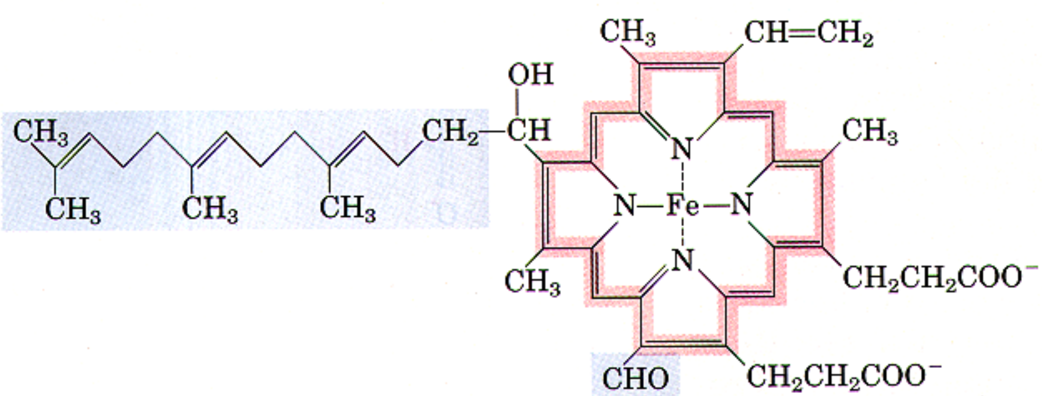


Iron-Protoporphyrin



Häm *C*
(in Cytochrom *c*)





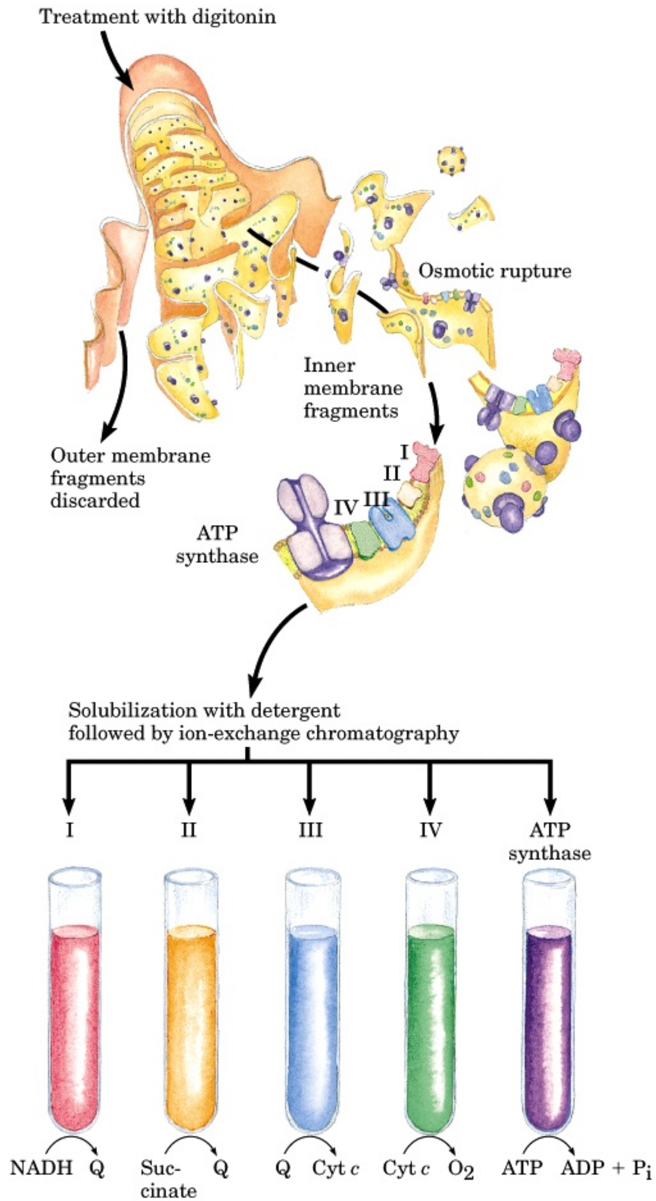
Häm *A*

Folie **9-7**

$$\mathrm{NADH} \xrightarrow{\text{rotenone}} \mathrm{Q} \longrightarrow \mathrm{Cyt}\ b \longrightarrow \mathrm{Cyt}\ c_1 \longrightarrow \mathrm{Cyt}\ c \longrightarrow \mathrm{Cyt}\ (a + a_3) \longrightarrow \mathrm{O}_2$$

$$\mathrm{NADH} \longrightarrow \mathrm{Q} \longrightarrow \mathrm{Cyt}\ b \xrightarrow{\text{antimycin A}} \mathrm{Cyt}\ c_1 \longrightarrow \mathrm{Cyt}\ c \longrightarrow \mathrm{Cyt}\ (a + a_3) \longrightarrow \mathrm{O}_2$$

$$\mathrm{NADH} \longrightarrow \mathrm{Q} \longrightarrow \mathrm{Cyt}\ b \longrightarrow \mathrm{Cyt}\ c_1 \longrightarrow \mathrm{Cyt}\ c \longrightarrow \mathrm{Cyt}\ (a + a_3) \xrightarrow{\mathrm{CN}^-\ \text{or CO}} \mathrm{O}_2$$



Reactions catalyzed by isolated fractions in vitro table 19–3

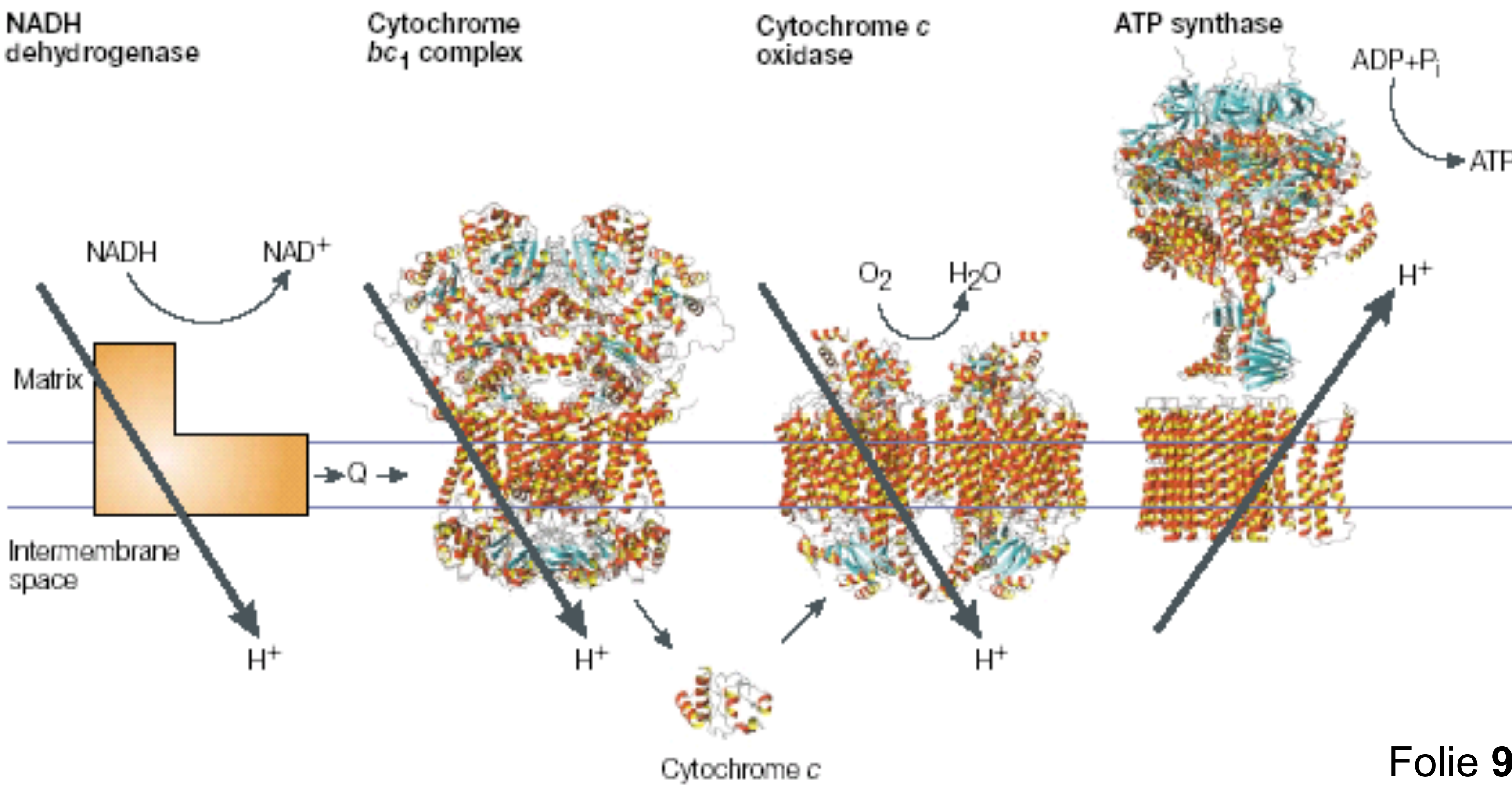
Protein Components of the Mitochondrial Electron-Transfer Chain

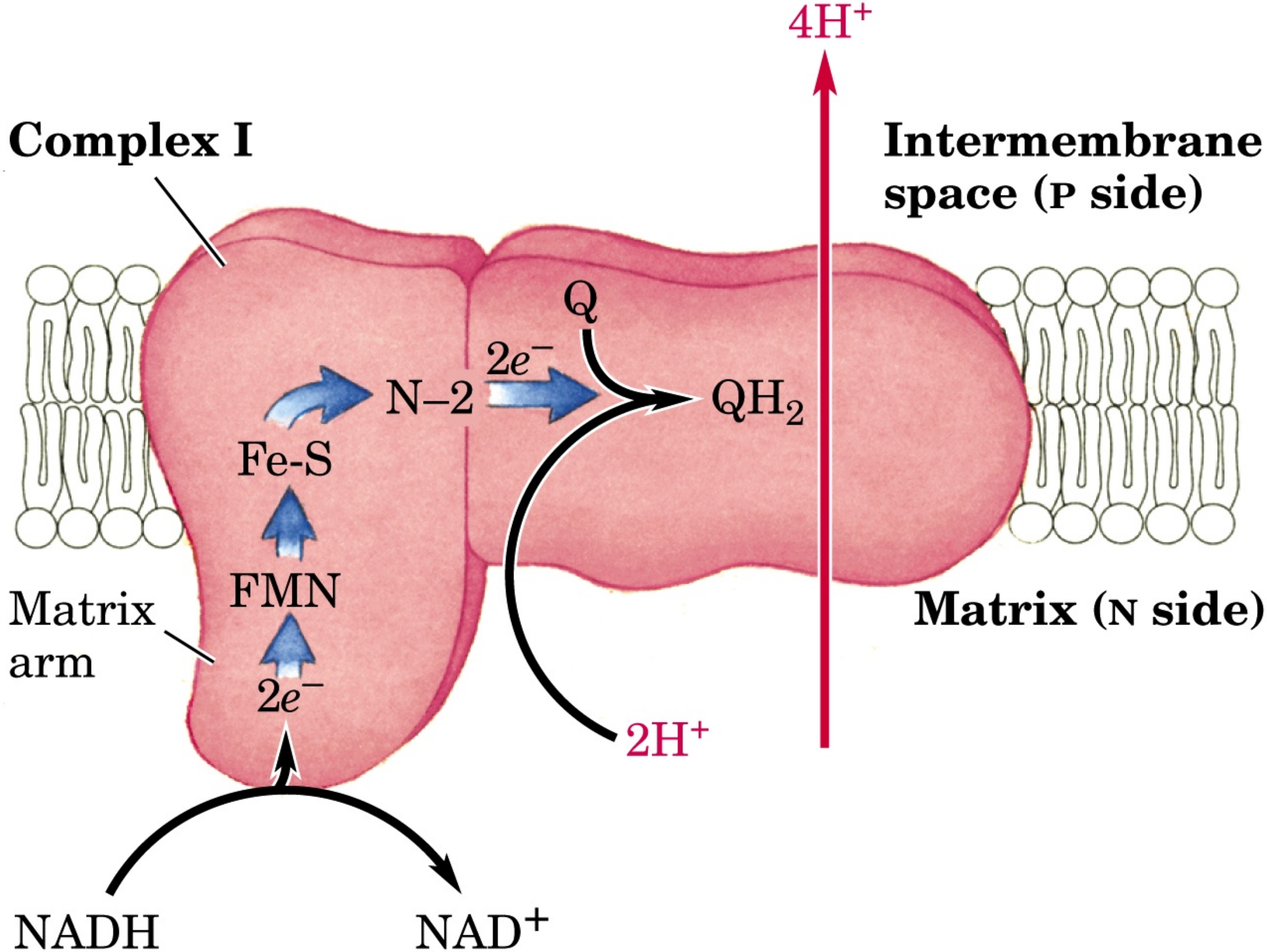
Enzyme complex	Mass (kDa)	Number of subunits*	Prosthetic group(s)
I NADH dehydrogenase	850	42 (14)	FMN, Fe-S
II Succinate dehydrogenase	140	5	FAD, Fe-S
III Ubiquinone: cytochrome *c* oxidoreductase	250	11	Hemes, Fe-S
Cytochrome *c*†	13	1	Heme
IV Cytochrome oxidase	160	13 (3–4)	Hemes; Cu_A, Cu_B

*Numbers of subunits in the bacterial equivalents in parentheses.

†Cytochrome *c* is not part of an enzyme complex; it moves between Complexes III and IV as a freely soluble protein.

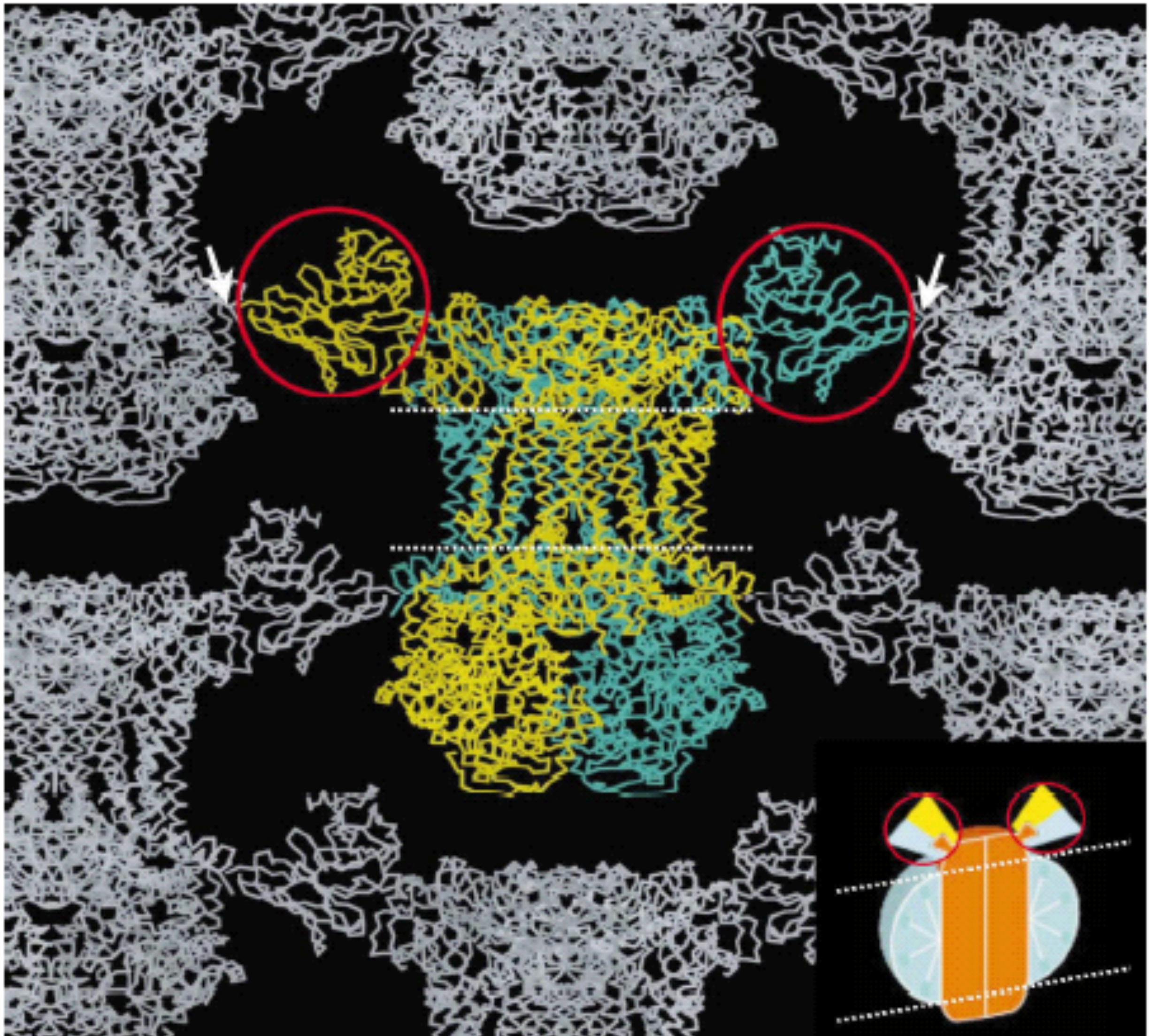
Die Atmungskette

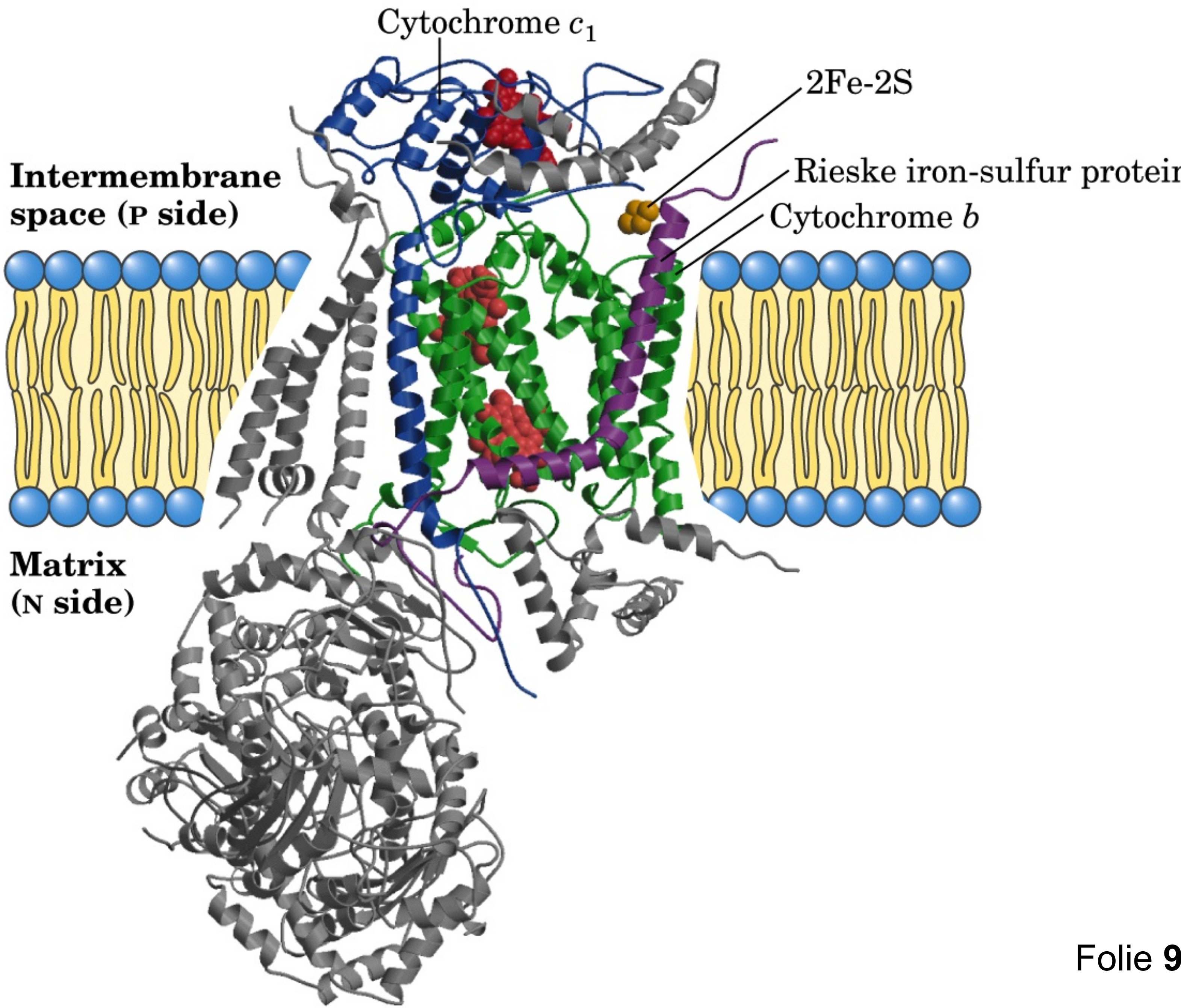




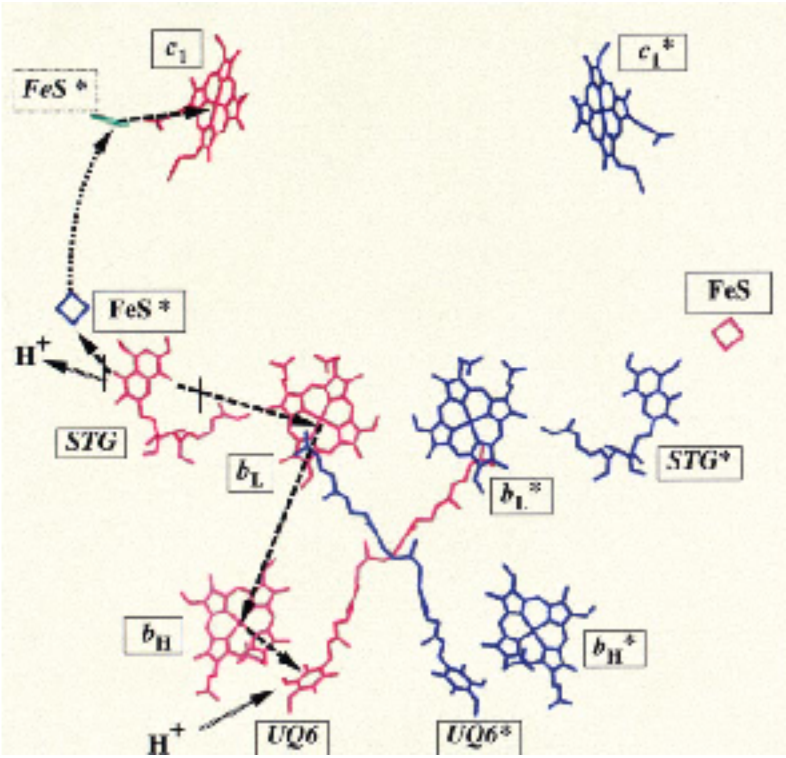
4H+
Complex I
Intermembrane space (P side)
Q
2e−
N–2
QH2
Fe-S
FMN
Matrix arm
Matrix (N side)
2e−
2H+
NADH
NAD+

Complex III




Cytochrome c_1
2Fe-2S
Rieske iron-sulfur protein
Cytochrome b
Intermembrane space (P side)
Matrix (N side)

Complex III

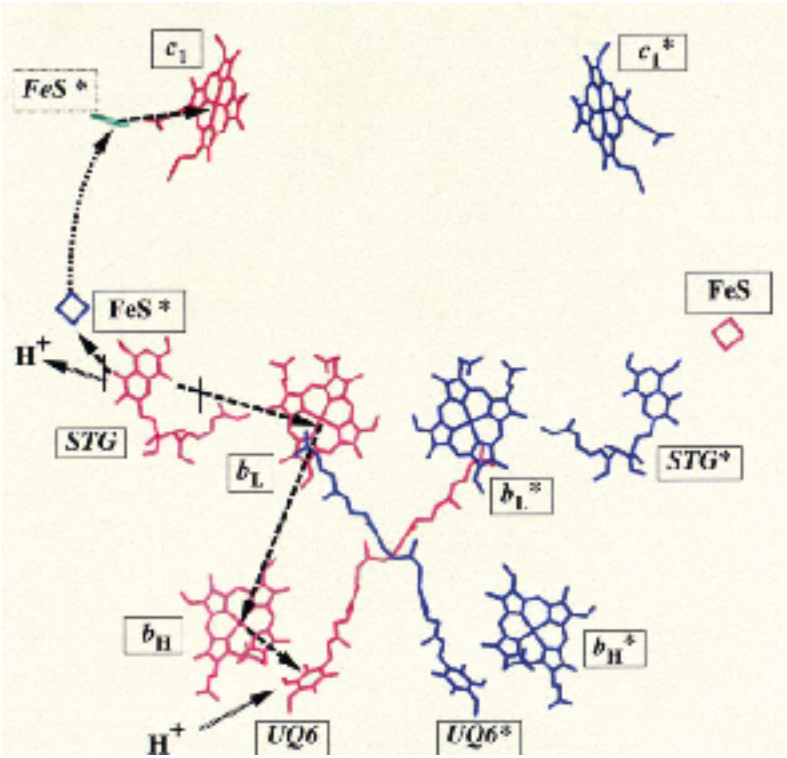


Stigmatellin

Ubiquimon

$$QH_2 + 2\ \text{Cyt c}(Fe^{3+}) \rightarrow Q + 2\ \text{Cyt c}(Fe^{2+}) + 2H_o^+$$

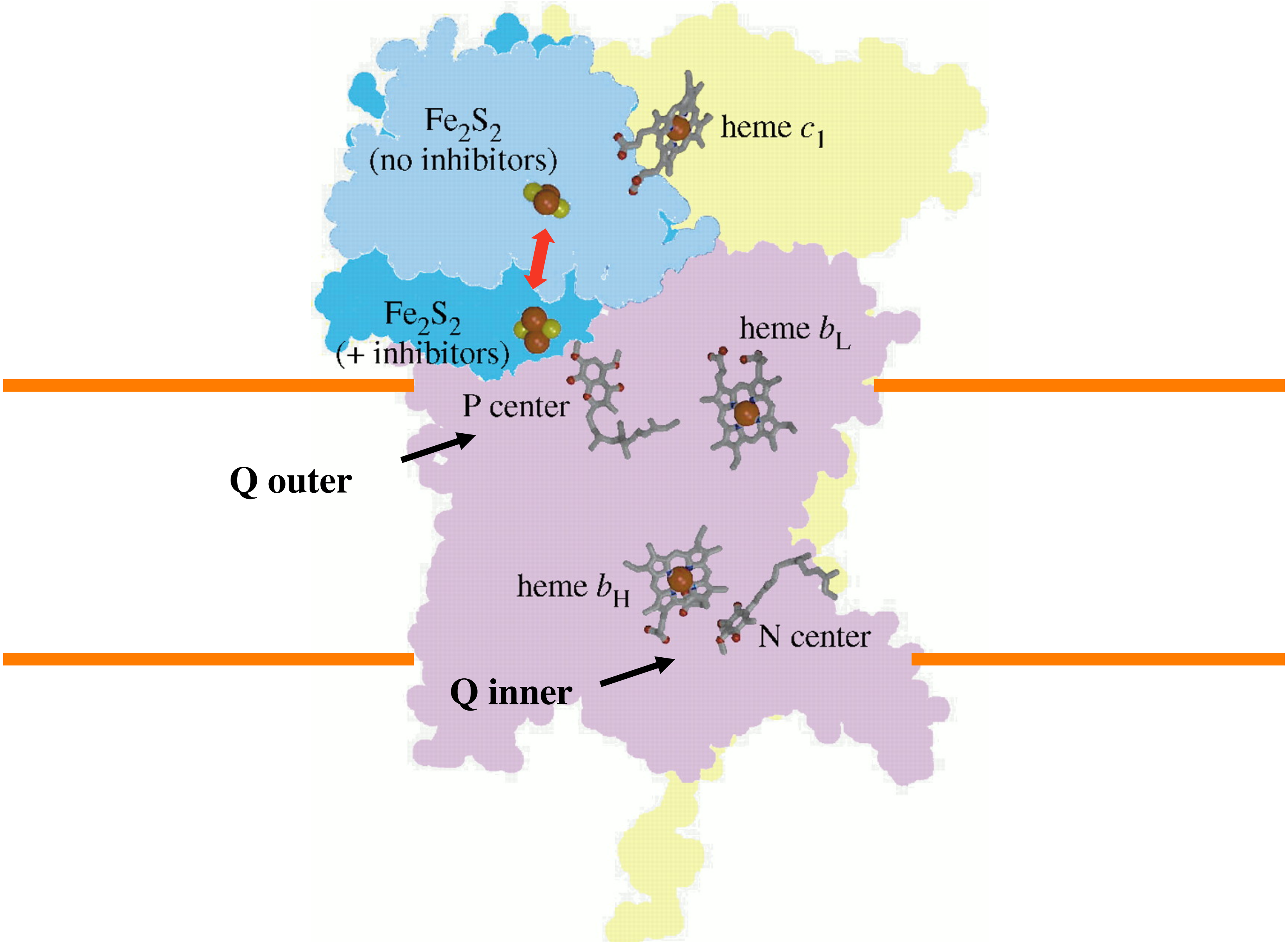
Complex III



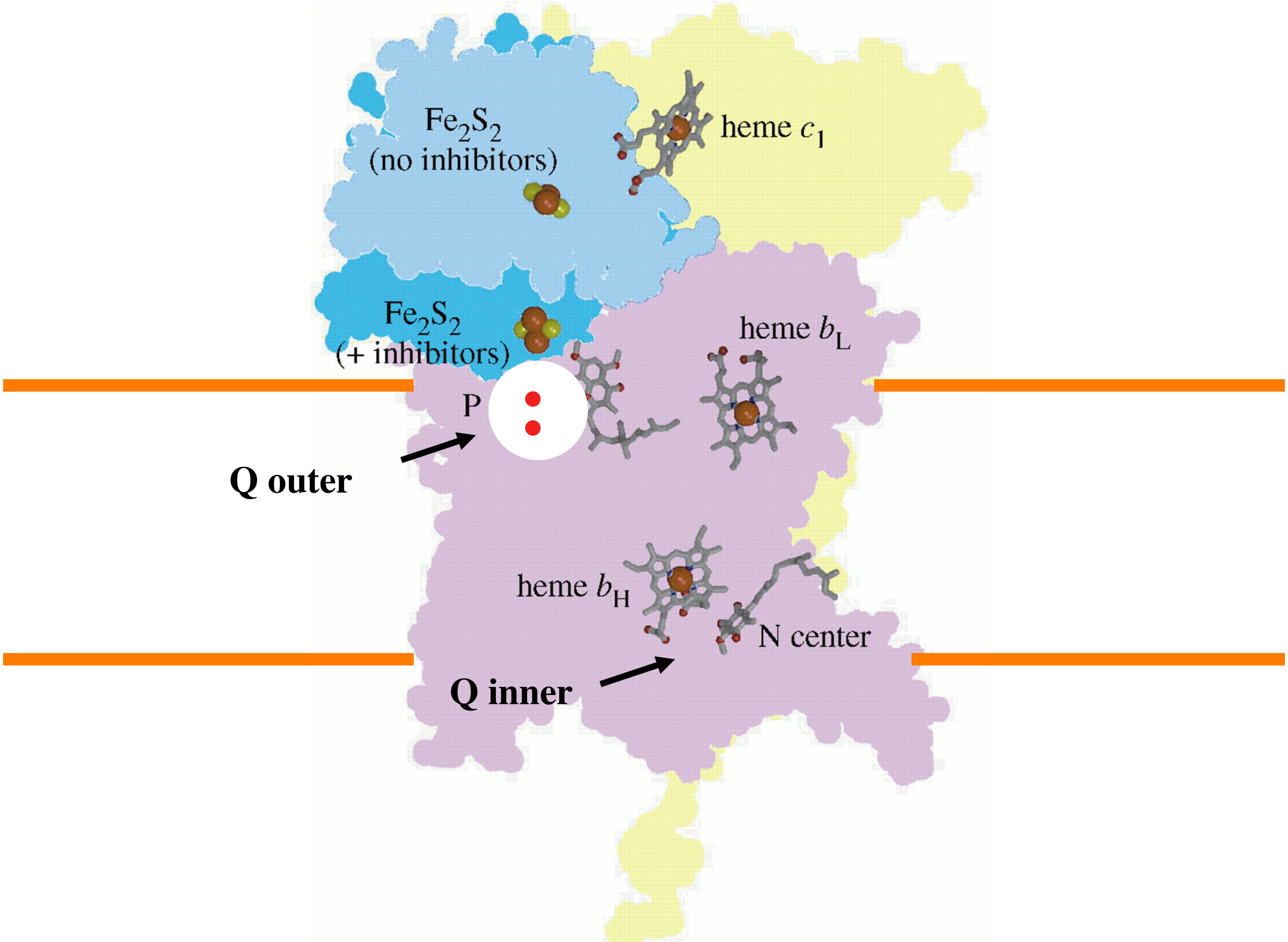
Stigmatellin

Ubiquimon

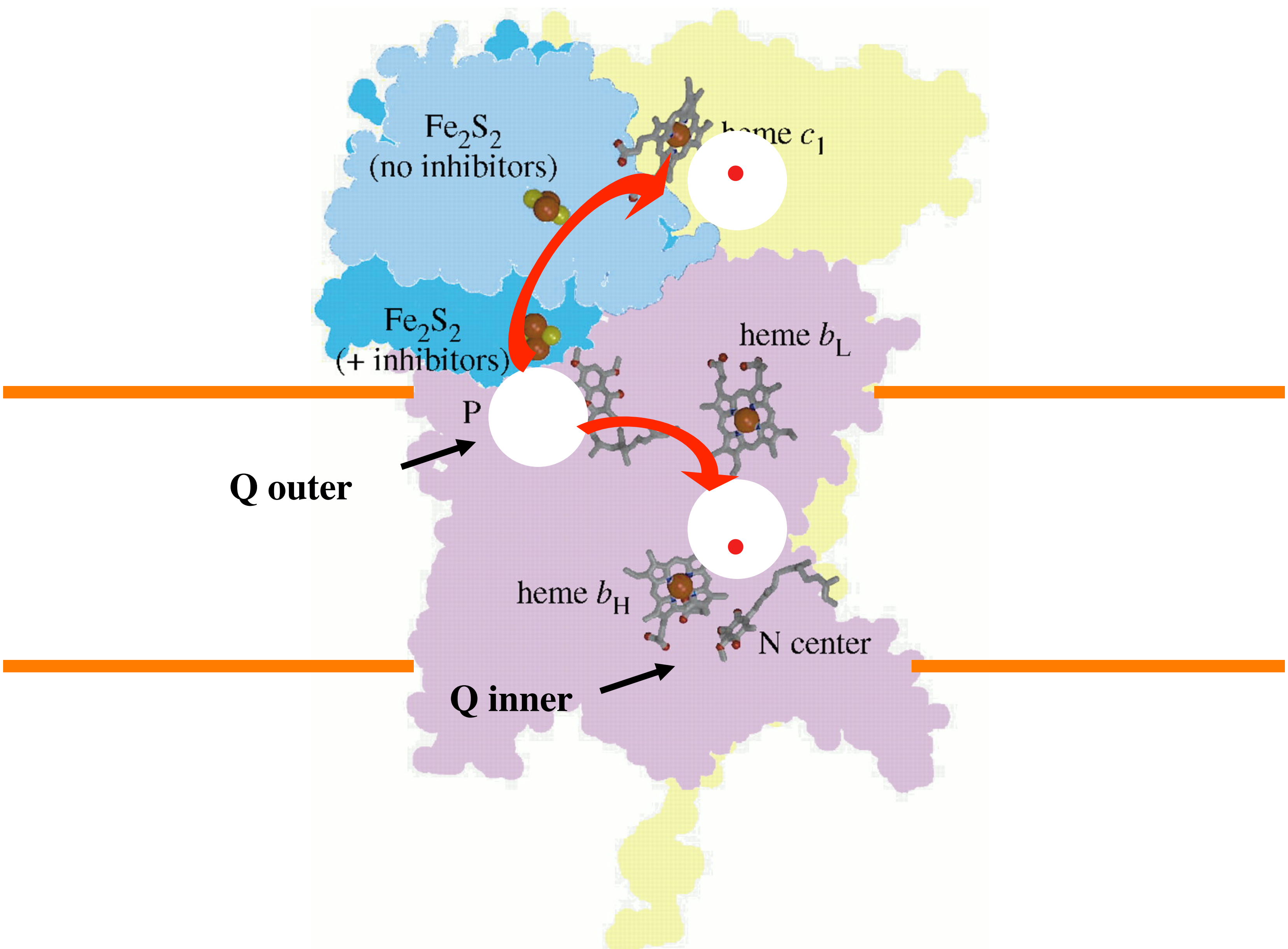
$$2QH_2 + Q + 2\ \text{Cyt c}(Fe^{3+}) + 2H_i^+ \longrightarrow 2Q + QH_2 + 2\ \text{Cyt c}(Fe^{2+}) + 4H_o^+$$

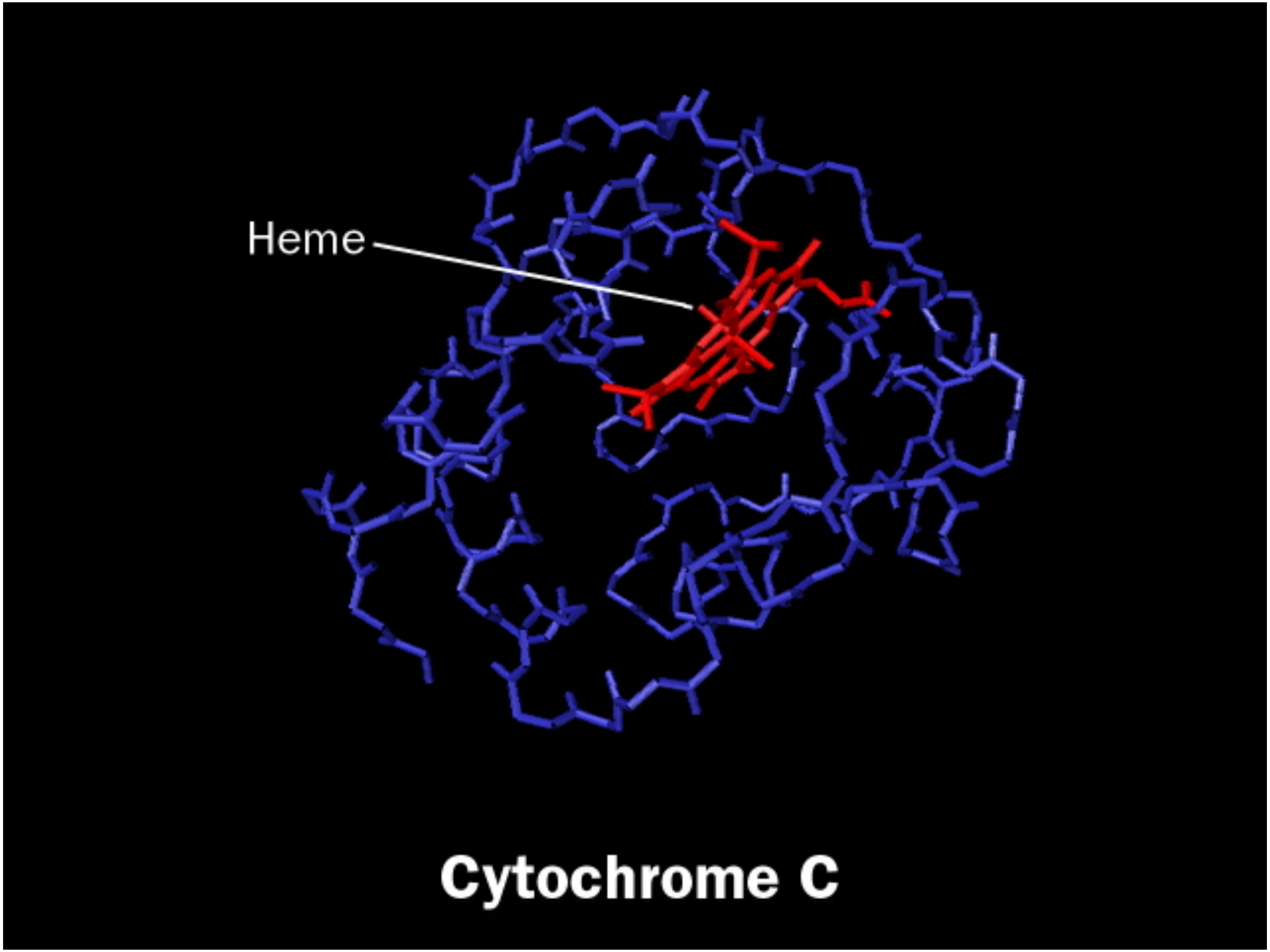


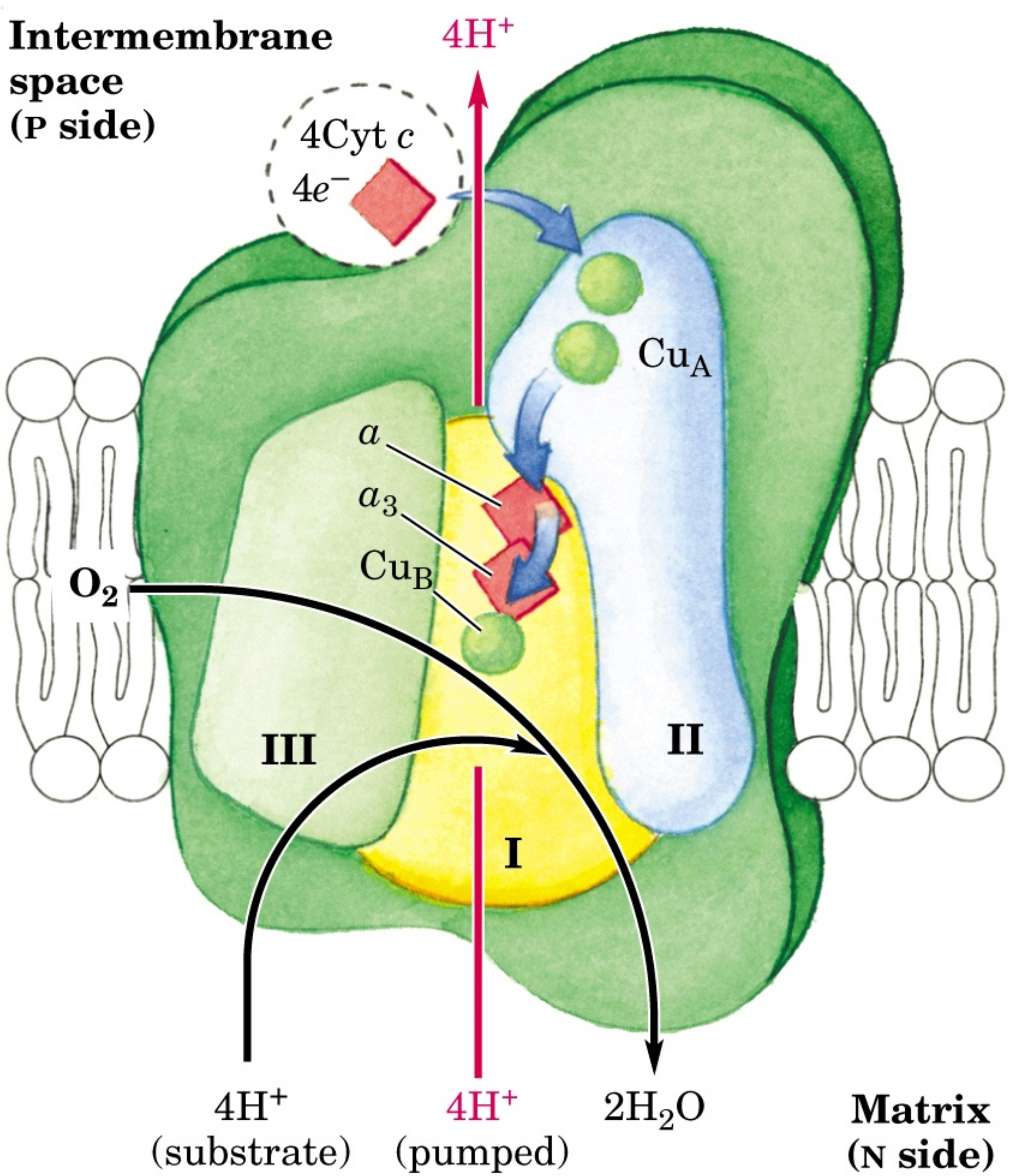
Fe_2S_2
(no inhibitors)
heme c_1
Fe_2S_2
(+ inhibitors)
heme b_L
P center
Q outer
heme b_H
N center
Q inner

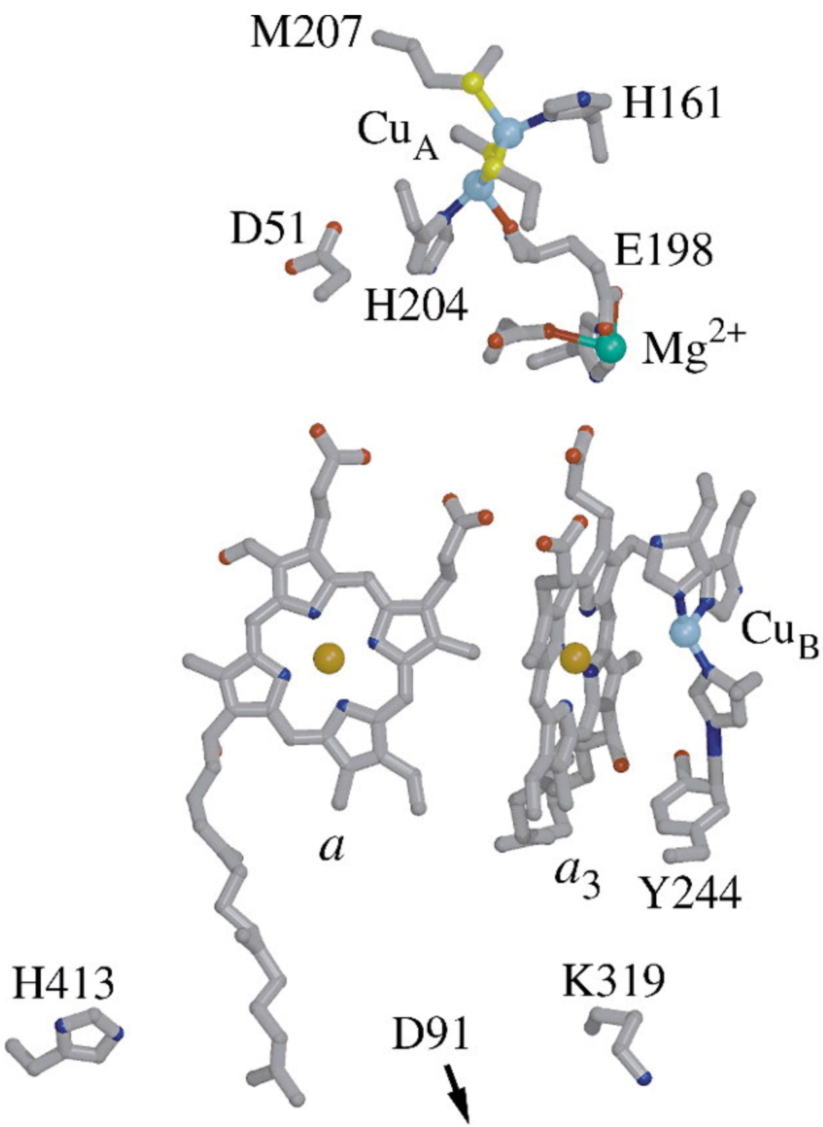


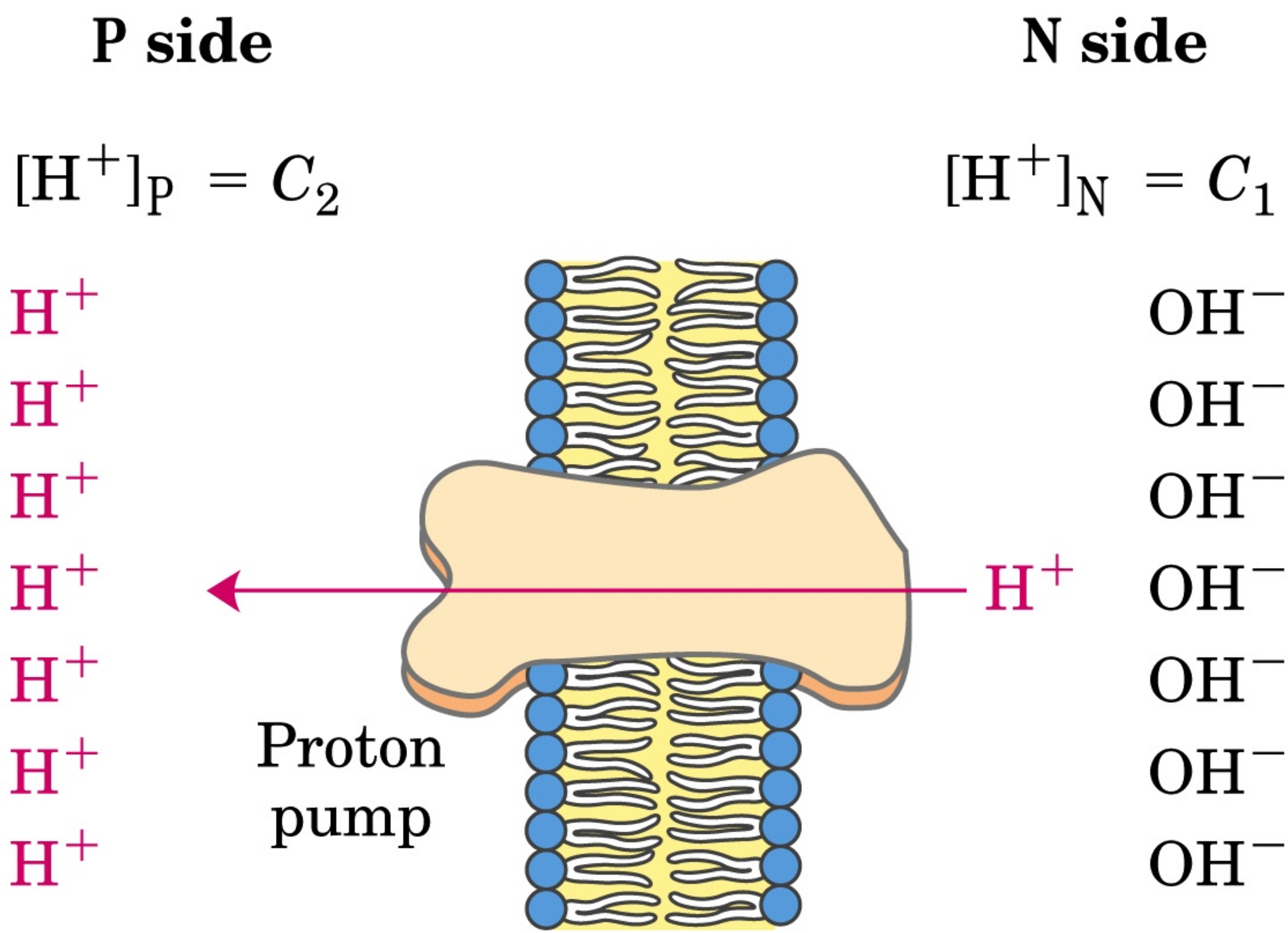
Fe_2S_2 (no inhibitors)
heme c_1
Fe_2S_2 (+ inhibitors)
heme b_L
P
Q outer
heme b_H
N center
Q inner


Fe_2S_2
(no inhibitors)
heme c_1
Fe_2S_2
(+ inhibitors)
heme b_L
P
Q outer
heme b_H
N center
Q inner

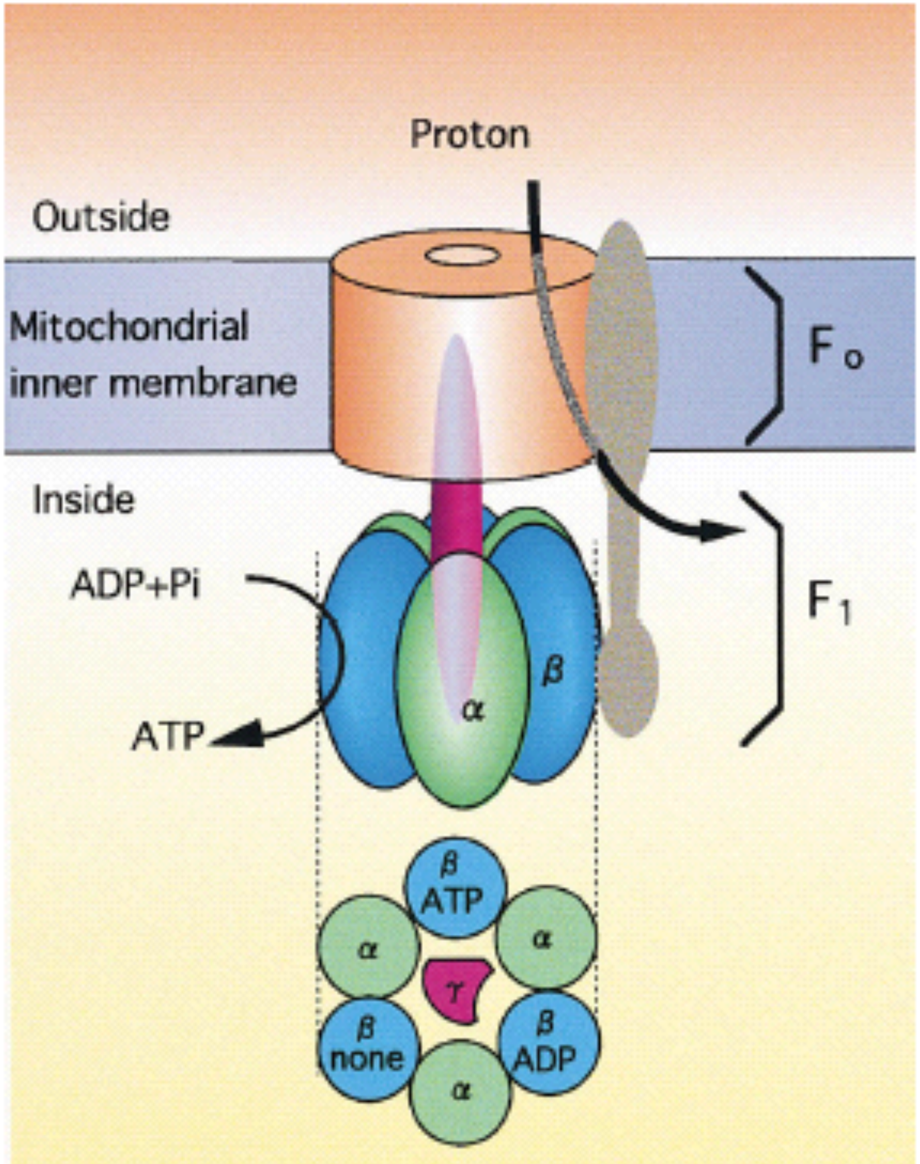

Heme
Cytochrome C

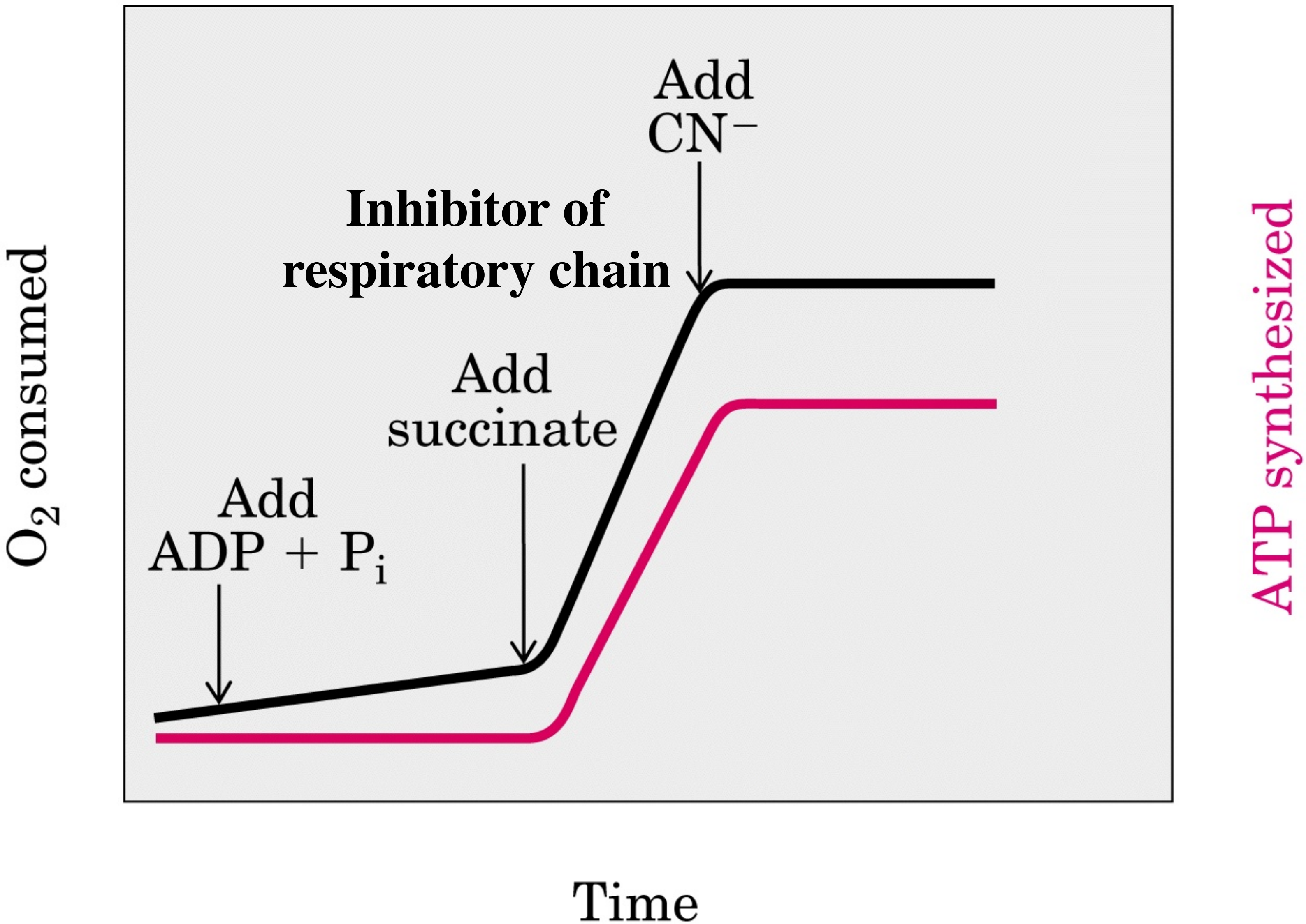

Intermembrane space (P side)
4H⁺
4Cyt c
4e⁻
Cu_A
a
a_3
Cu_B
O_2
III
II
I
4H⁺ (substrate)
4H⁺ (pumped)
2H_2O
Matrix (N side)


M207
H161
Cu_A
D51
E198
H204
Mg2+
Cu_B
a
a3
Y244
H413
K319
D91

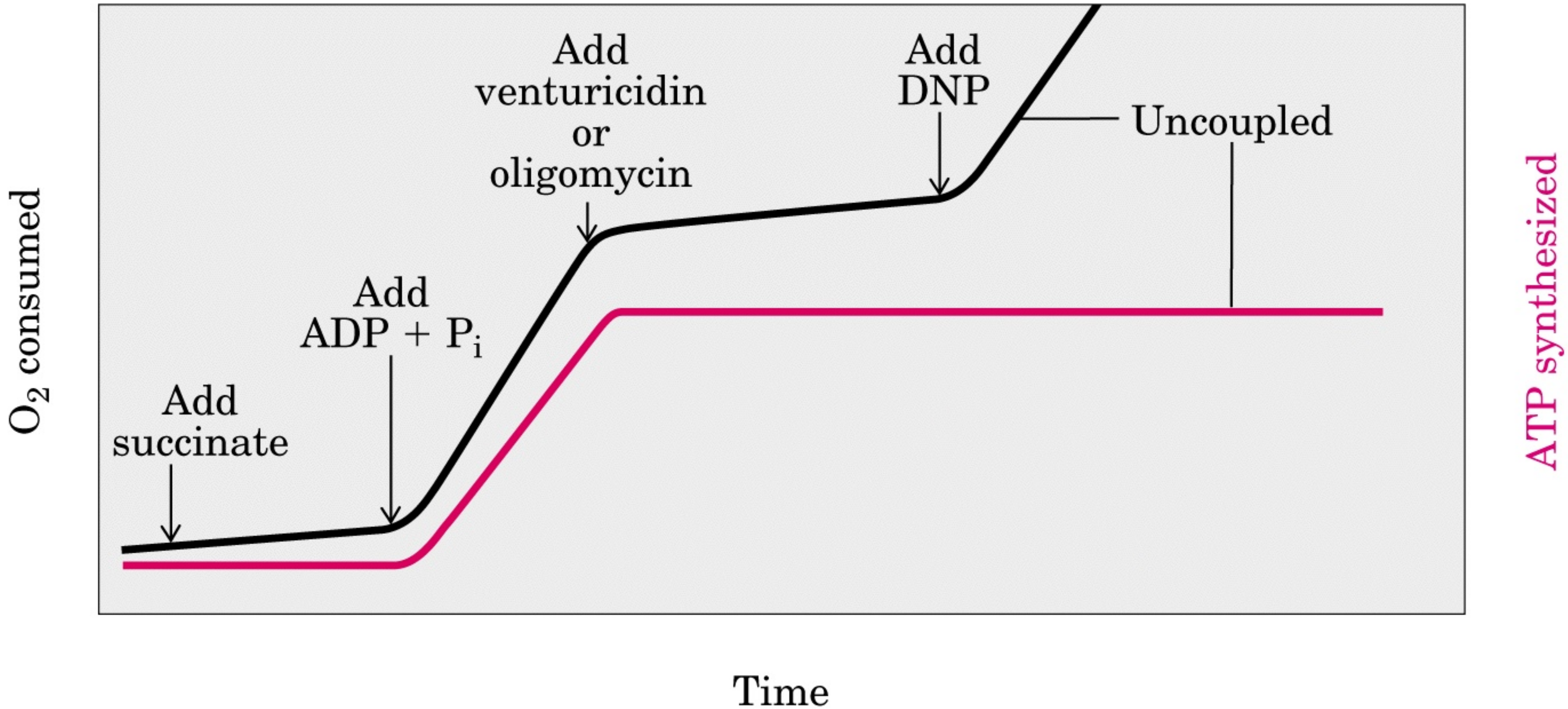


$$\Delta G = RT \ln (C_2/C_1) + Z\mathcal{F}\Delta\psi$$
$$= 2.3RT\,\Delta\text{pH} + \mathcal{F}\Delta\psi$$


Proton
Outside
Mitochondrial
inner membrane
Inside
ADP+Pi
ATP
α
β
F_o
F_1
β
ATP
α
α
γ
β
none
β
ADP
α

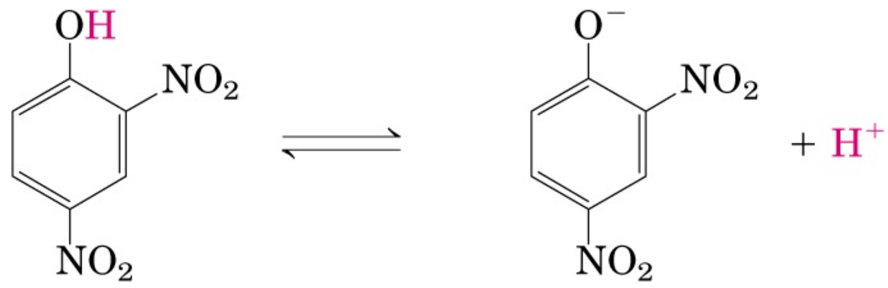


Add
CN^-
Inhibitor of
respiratory chain
Add
succinate
Add
ADP + P_i
O_2 consumed
ATP synthesized
Time

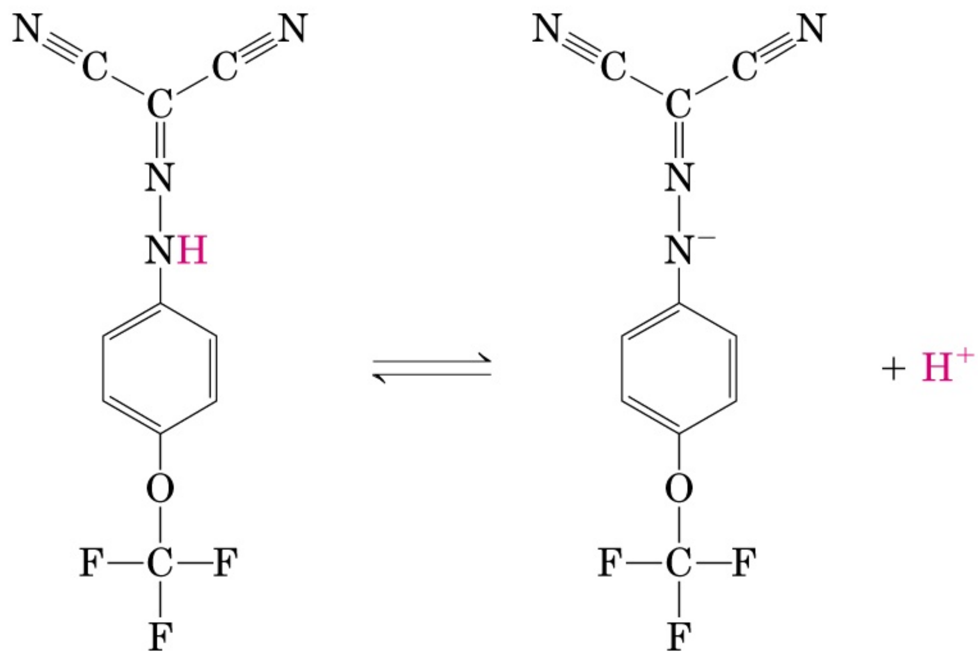


Add
venturicidin
or
oligomycin
Add
DNP
Uncoupled
Add
ADP + P_i
Add
succinate
O_2 consumed
ATP synthesized
Time

Uncoupler:

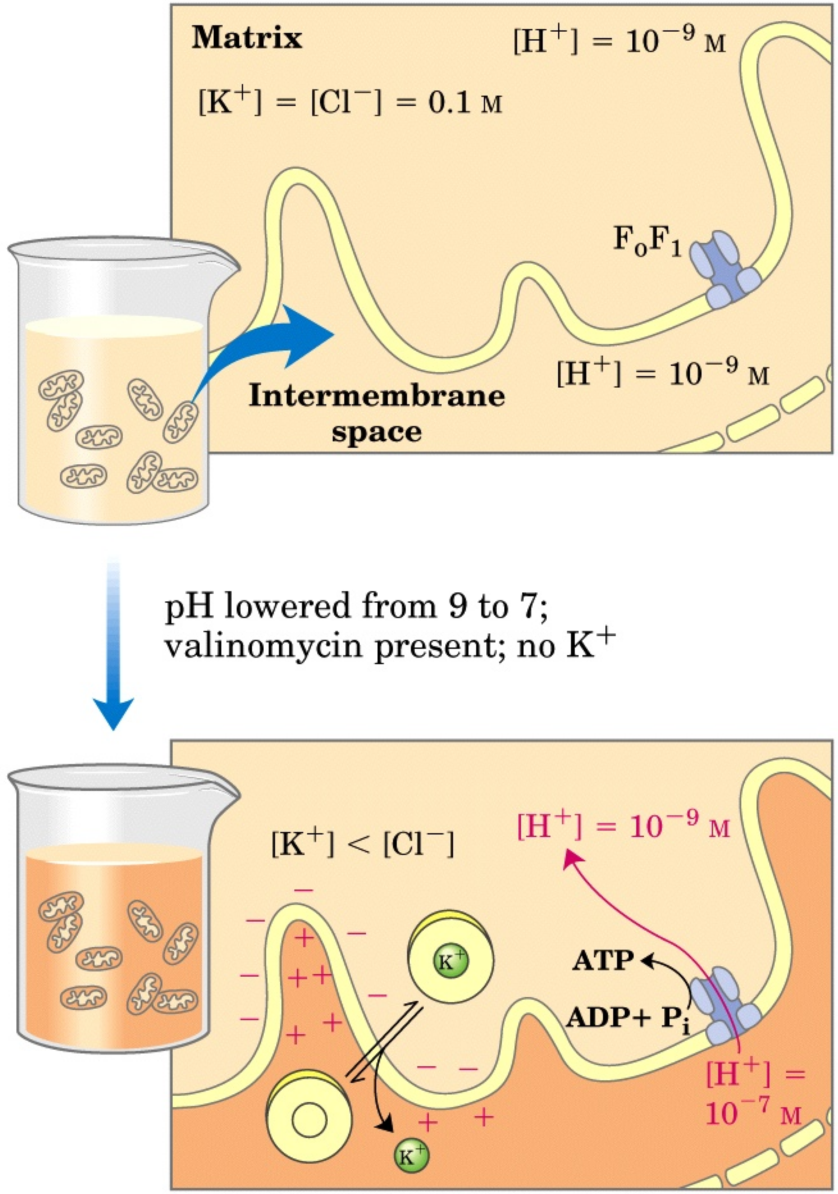


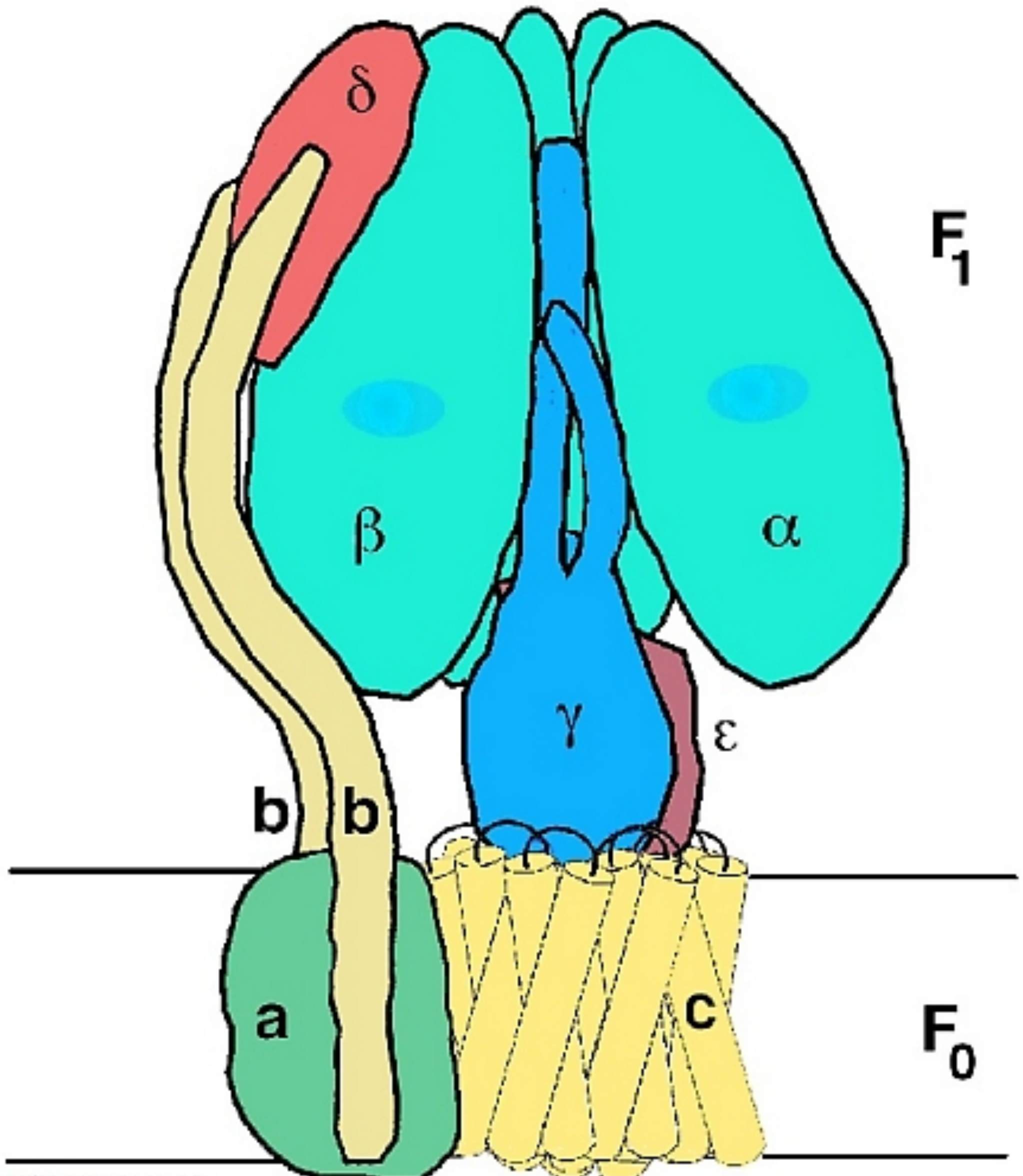
2,4-Dinitrophenol
(DNP)



Carbonylcyanide-*p*-
trifluoromethoxyphenylhydrazone
(FCCP)

ATP synthesis is coupled to proton flux into the matrix





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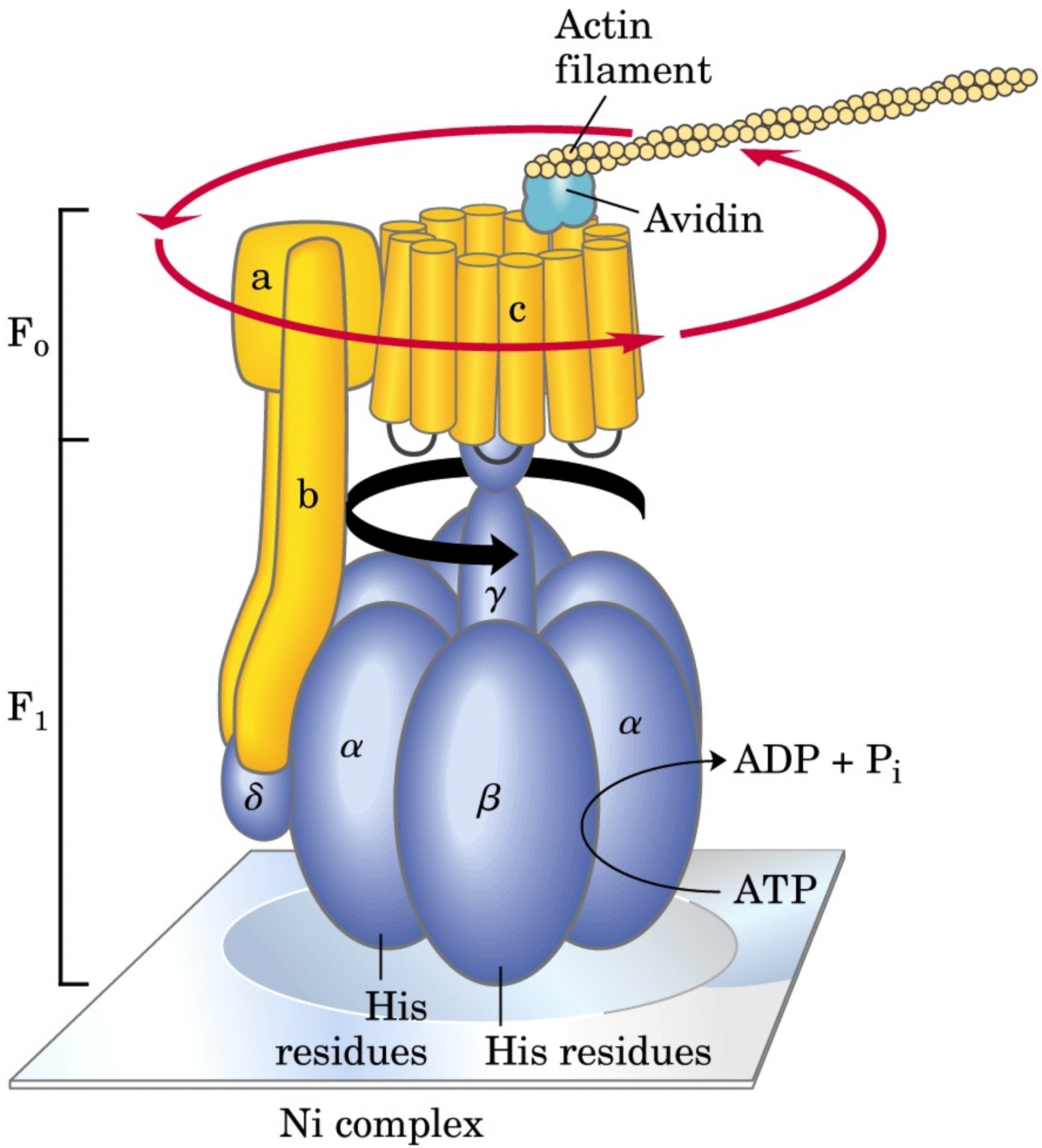
W. Junge, H. Lill & S. Engelbrecht
TIBS 22, 420 - 423 (1997)



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