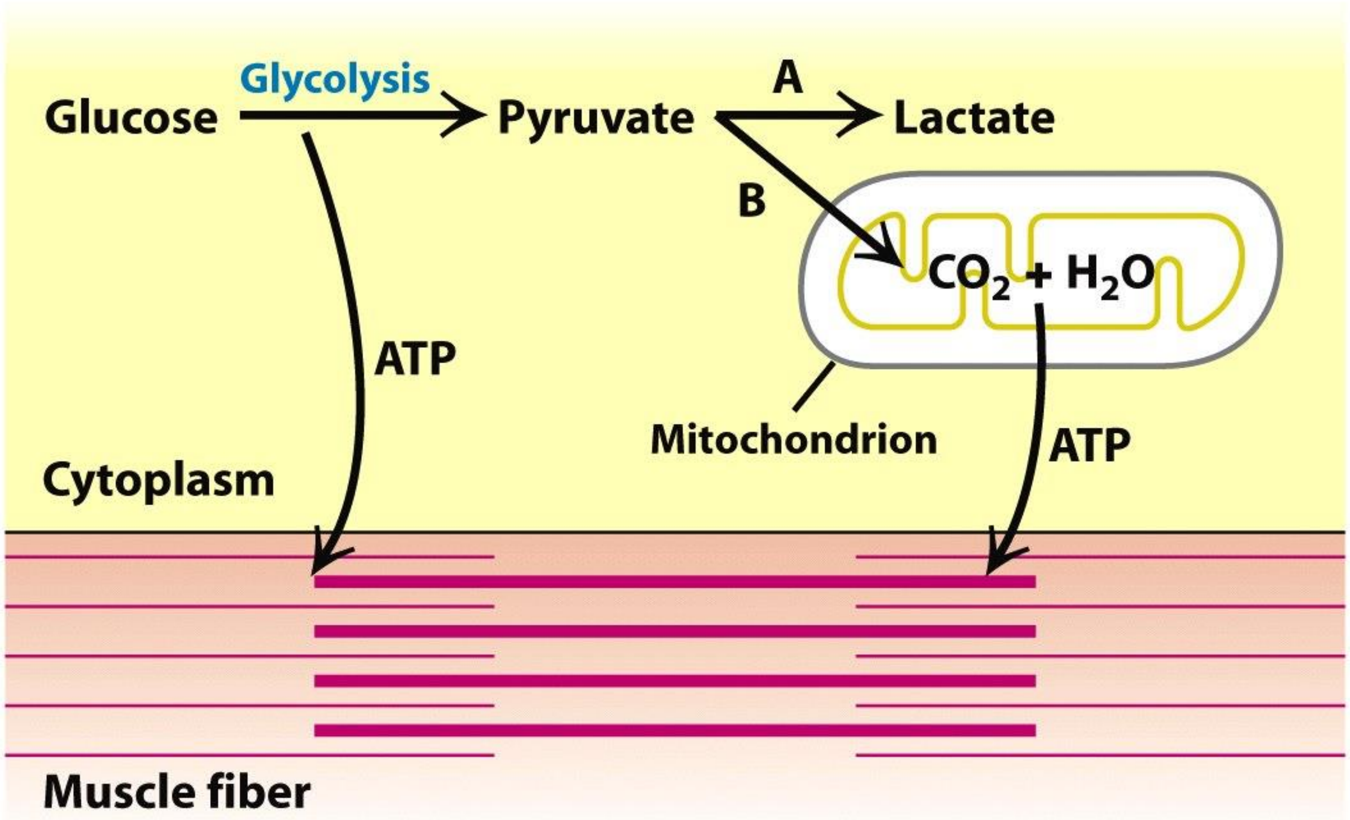
GLYCOLYSIS
AND
GLUCONEOGENESIS

Chapter 16 Opener part 1
Biochemistry, Sixth Edition



A. Low O_2
(last seconds of a sprint)

B. Normal
(long slow run)

Chapter 16 Opener part 2
Biochemistry, Sixth Edition

Glikolisis

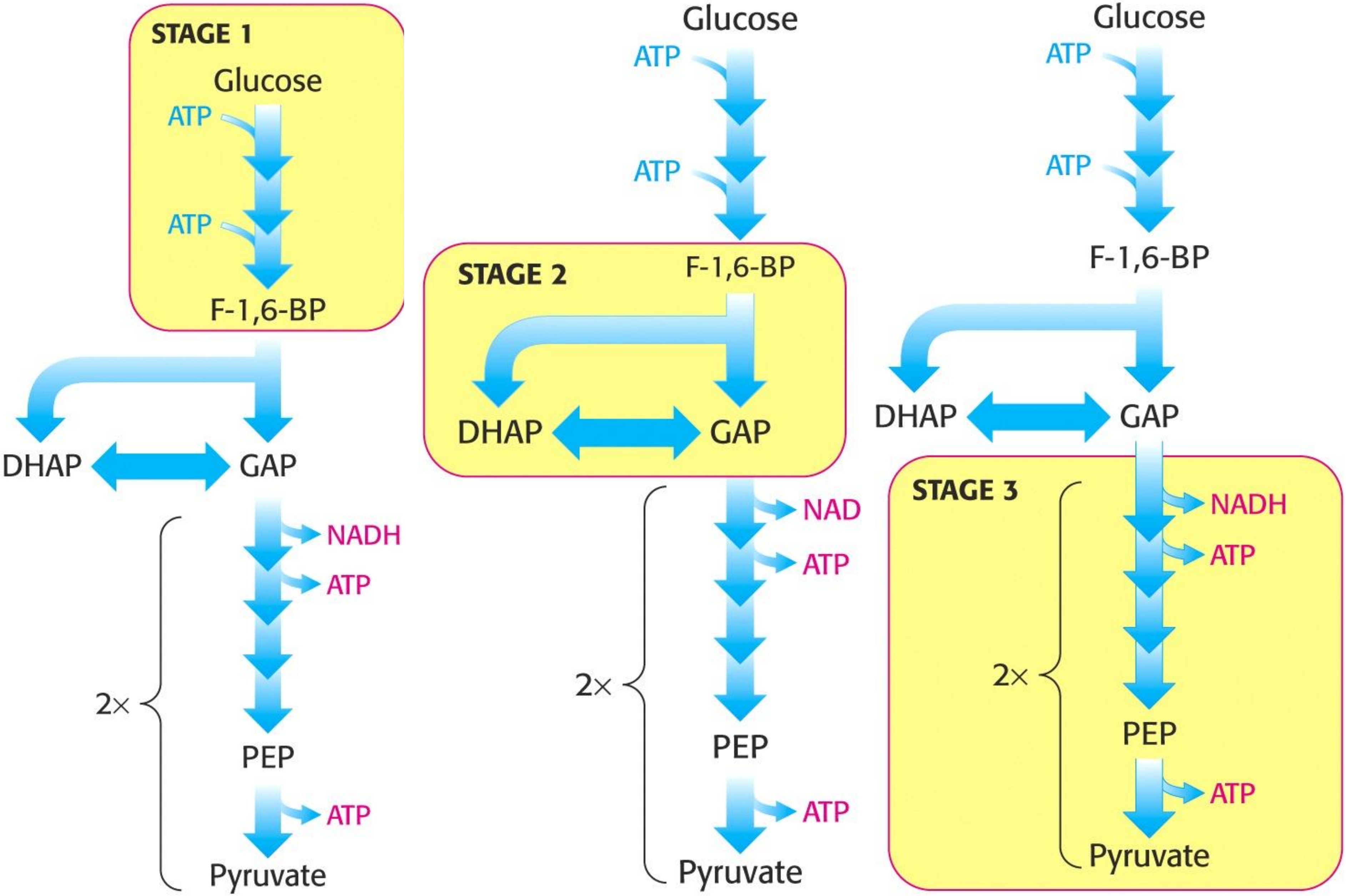
- Akar kata dari bahasa Yunani *glykys* (manis) dan *lysis* (penguraian)
- Urutan reaksi (10 tahap) penguraian satu molekul glukosa menghasilkan dua molekul piruvat
- Nama lain *Embden-Meyerhof Pathway* (EMP)
- Proses universal, hampir terjadi di semua sel hidup
- Proses berlangsung pada keadaan anaerob dan aerob

Gustav Embden
1874–1933

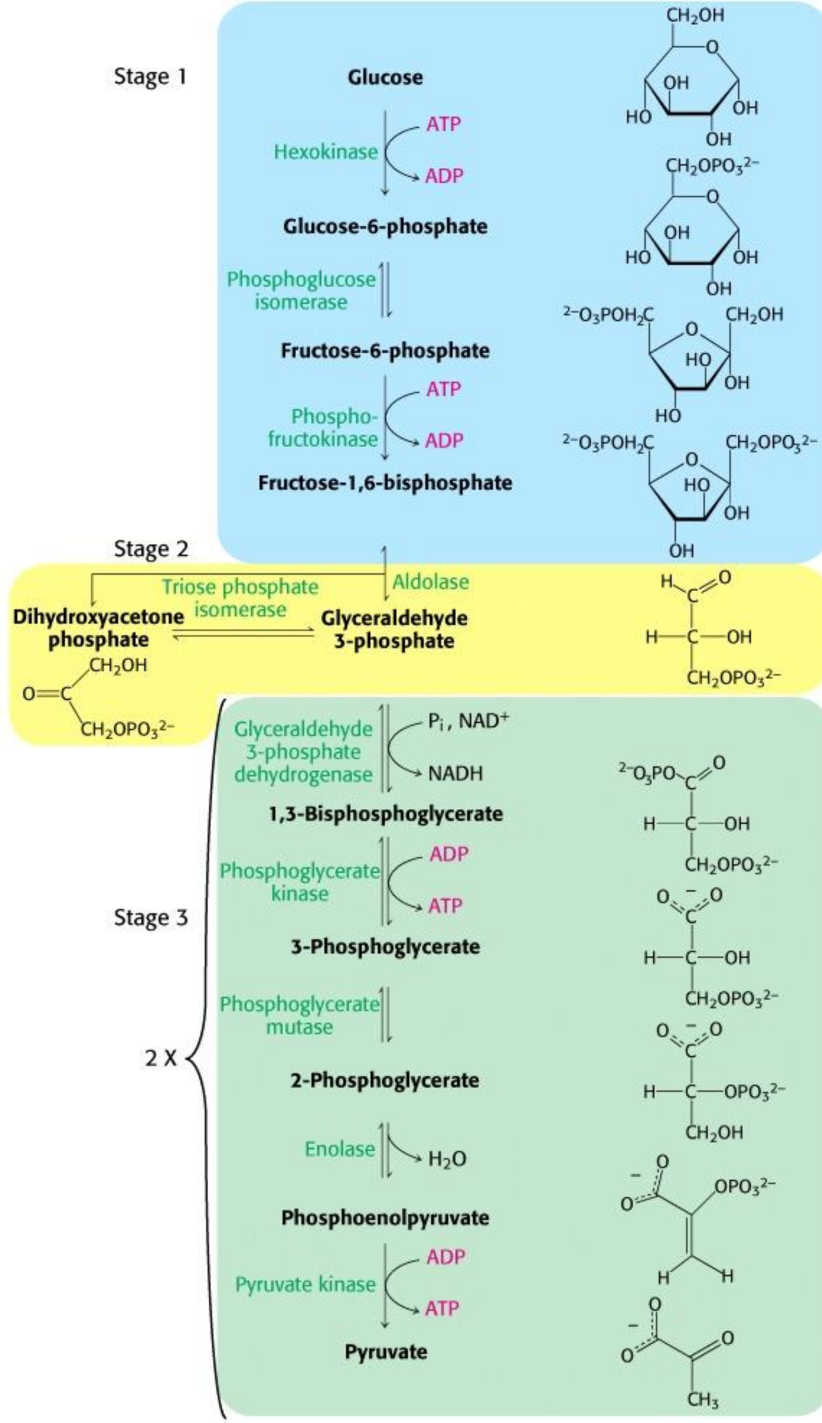
Otto Meyerhof
1884–1951

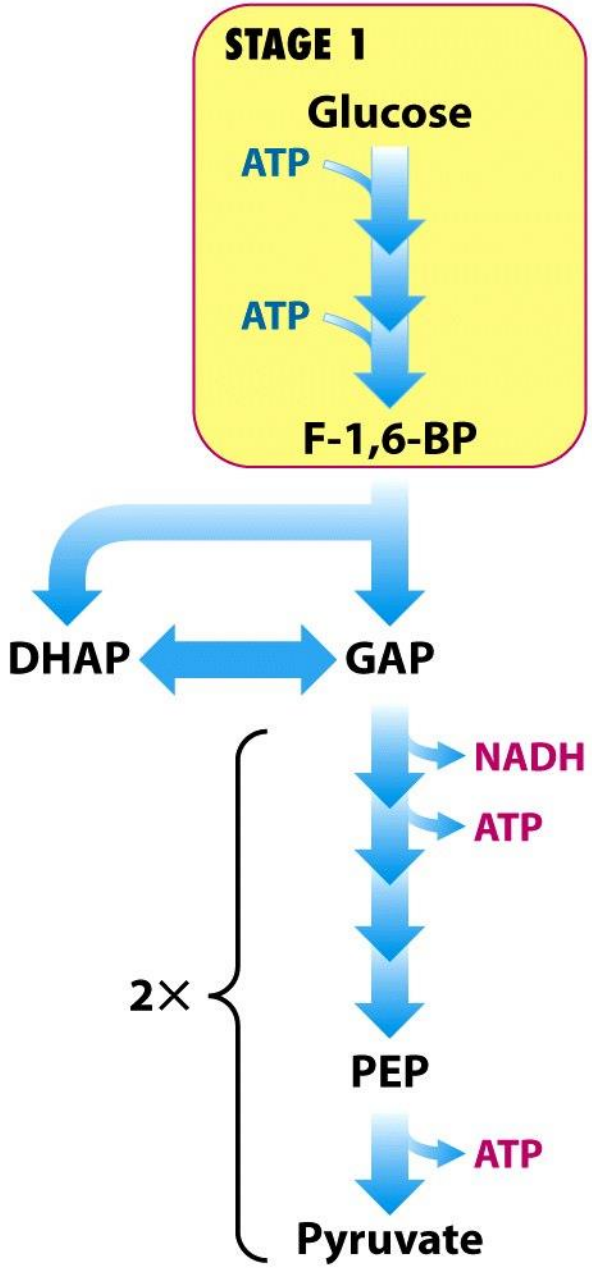
Tahap glikolisis

- Tahap 1: aktivasi molekul glukosa (fosforilasi) dan menjadi molekul fruktosa 1,6-bifosfat (reaksi 1 s.d. 3)
- Tahap 2: pemutusan menjadi 2 molekul triosa fosfat (reaksi 4 s.d. 5)
- Tahap 3: produksi energi dari dua molekul triosa fosfat menjadi 2 molekul piruvat (reaksi 6 s.d. 10)



STAGE 1
Glucose
ATP
ATP
F-1,6-BP
DHAP
GAP
NADH
ATP
2×
PEP
ATP
Pyruvate
Glucose
ATP
ATP
STAGE 2
F-1,6-BP
DHAP
GAP
NAD
ATP
2×
PEP
ATP
Pyruvate
Glucose
ATP
ATP
F-1,6-BP
DHAP
GAP
STAGE 3
NADH
ATP
2×
PEP
ATP
Pyruvate


Stage 1
Glucose
ATP
Hexokinase
ADP
Glucose-6-phosphate
Phosphoglucose isomerase
Fructose-6-phosphate
ATP
Phosphofructokinase
ADP
Fructose-1,6-bisphosphate
Stage 2
Aldolase
Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate
Stage 3
2 X
Glyceraldehyde 3-phosphate dehydrogenase
Pi, NAD+
NADH
1,3-Bisphosphoglycerate
Phosphoglycerate kinase
ADP
ATP
3-Phosphoglycerate
Phosphoglycerate mutase
2-Phosphoglycerate
Enolase
H2O
Phosphoenolpyruvate
Pyruvate kinase
ADP
ATP
Pyruvate



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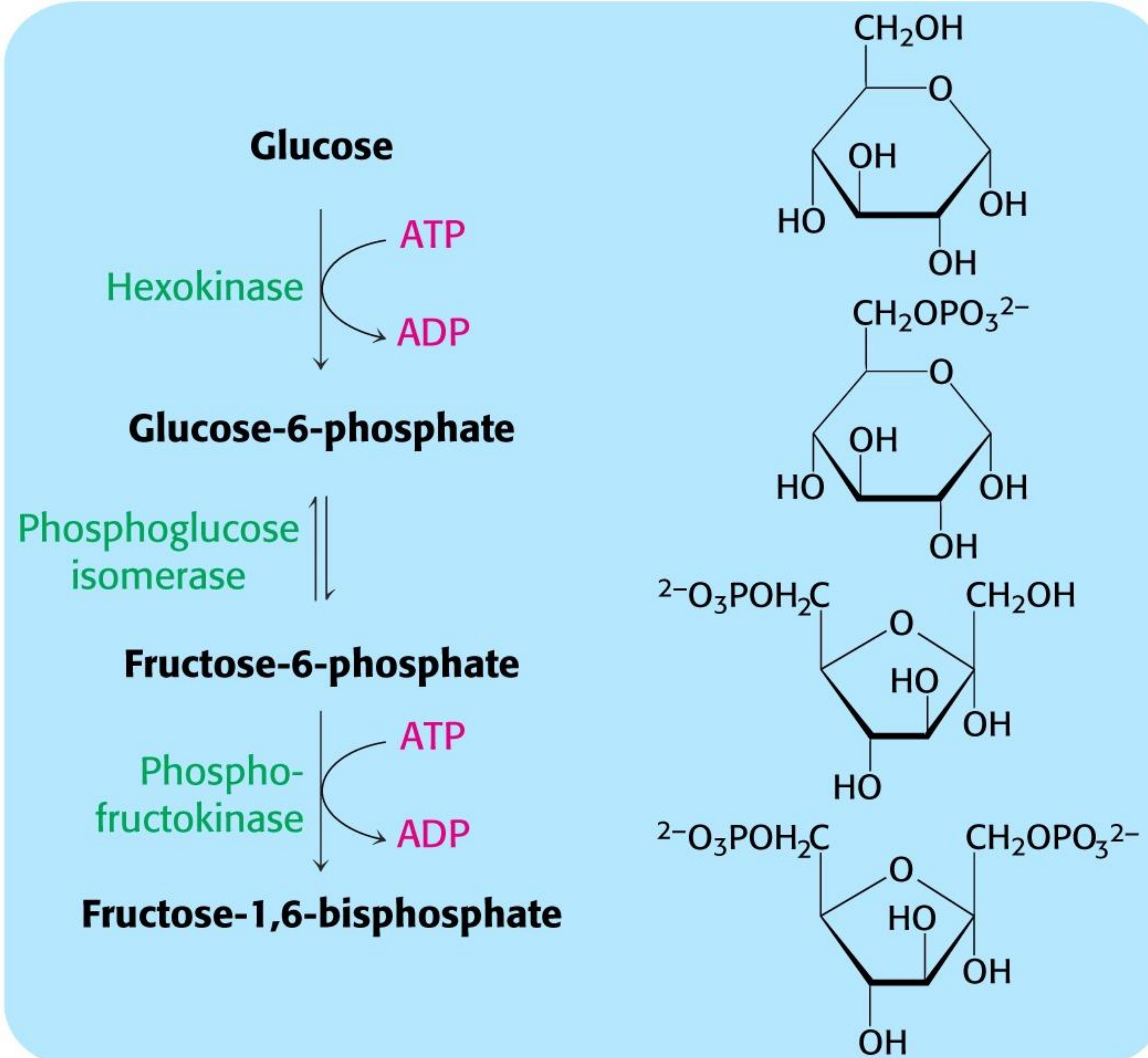
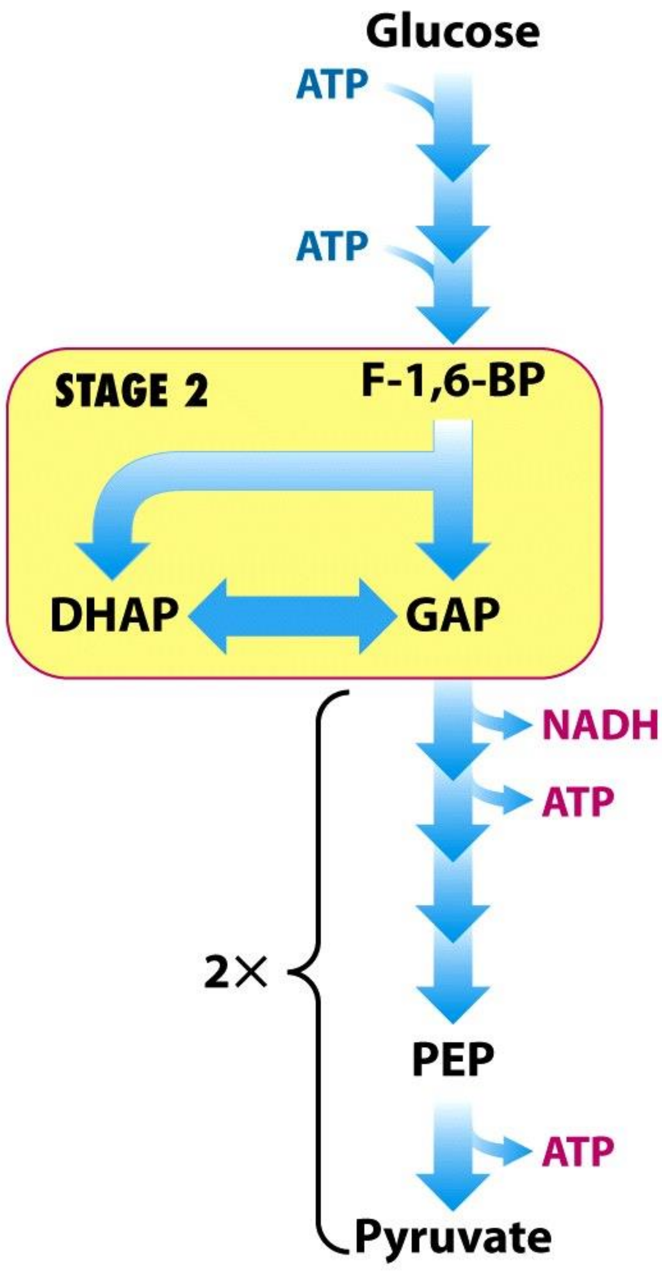
Stage 1



Glucose
ATP
Hexokinase
ADP
Glucose-6-phosphate
Phosphoglucose isomerase
Fructose-6-phosphate
ATP
Phospho-fructokinase
ADP
Fructose-1,6-bisphosphate
CH2OH
O
OH
HO
OH
OH
CH2OPO3 2−
2−O3POH2C
HO



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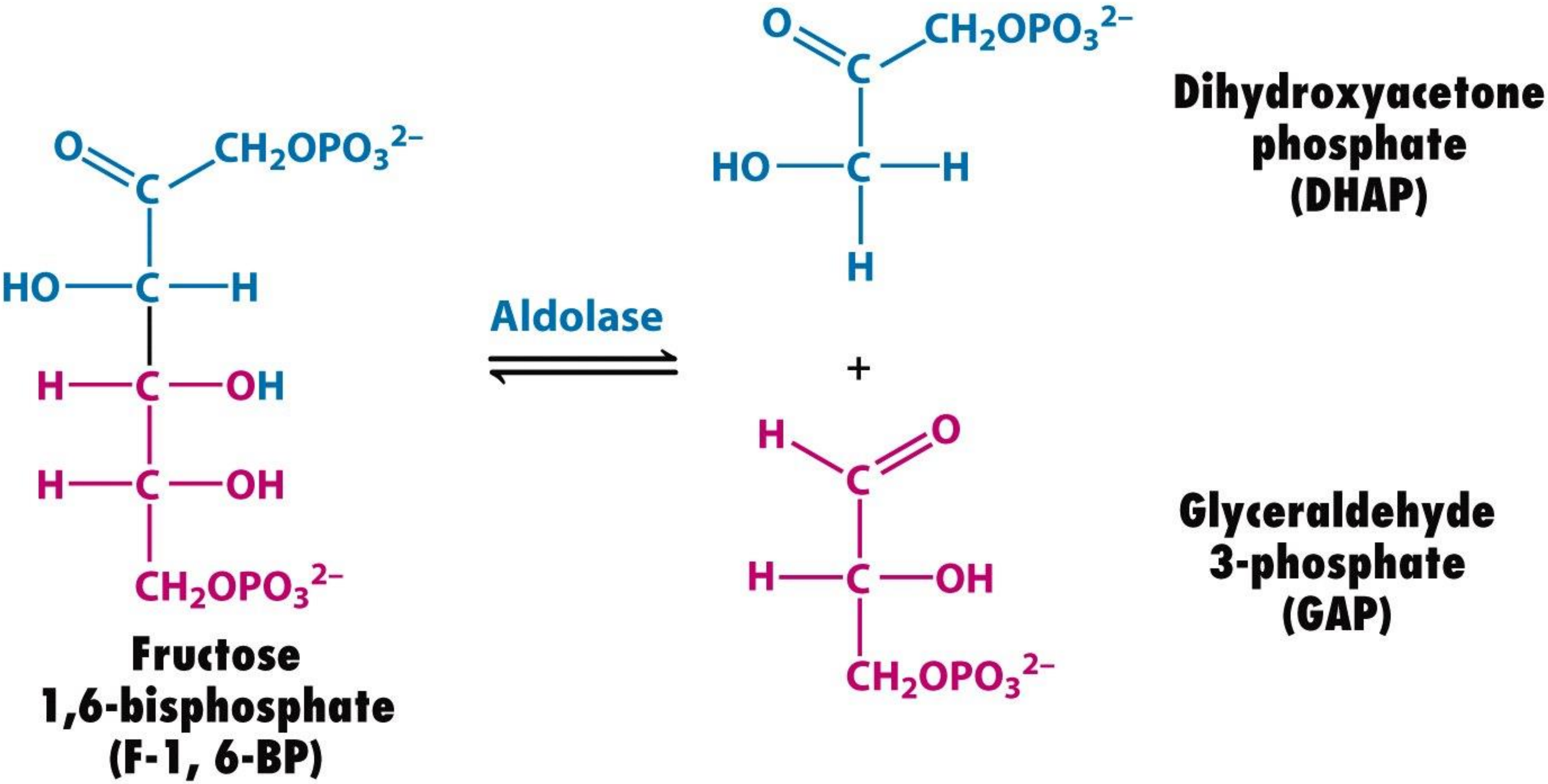

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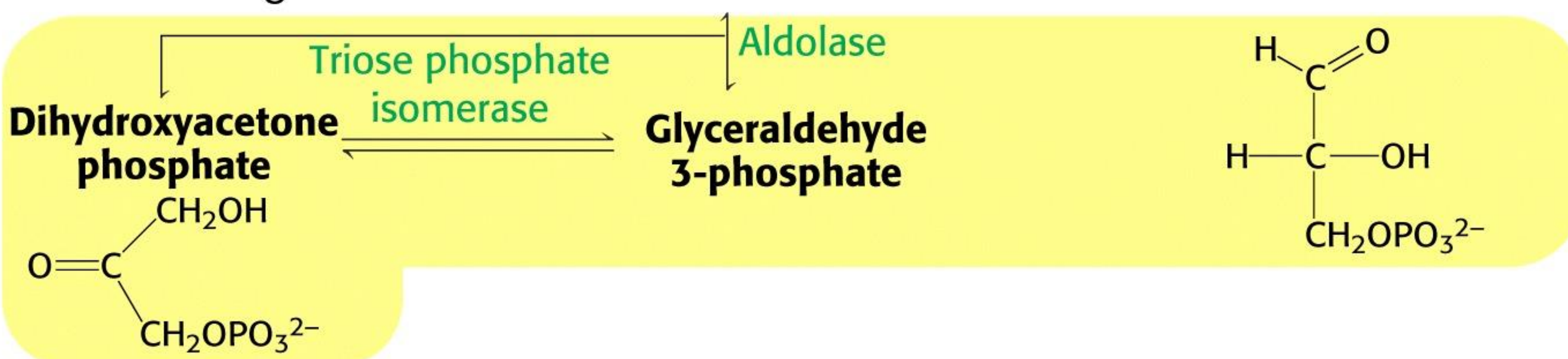
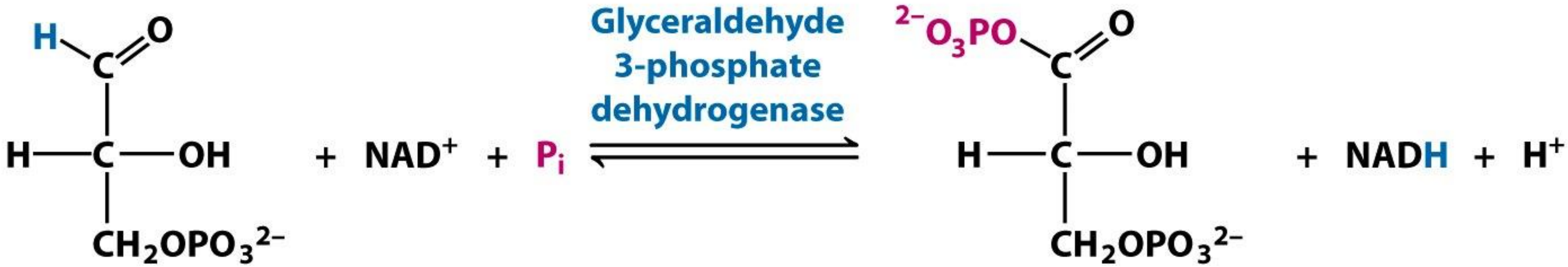
Stage 2


Aldolase
Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate
CH2OH
O=C
CH2OPO3 2−
H
O
C
H—C—OH
CH2OPO3 2−



Glyceraldehyde 3-phosphate (GAP)

1,3-Bisphosphoglycerate (1,3-BPG)

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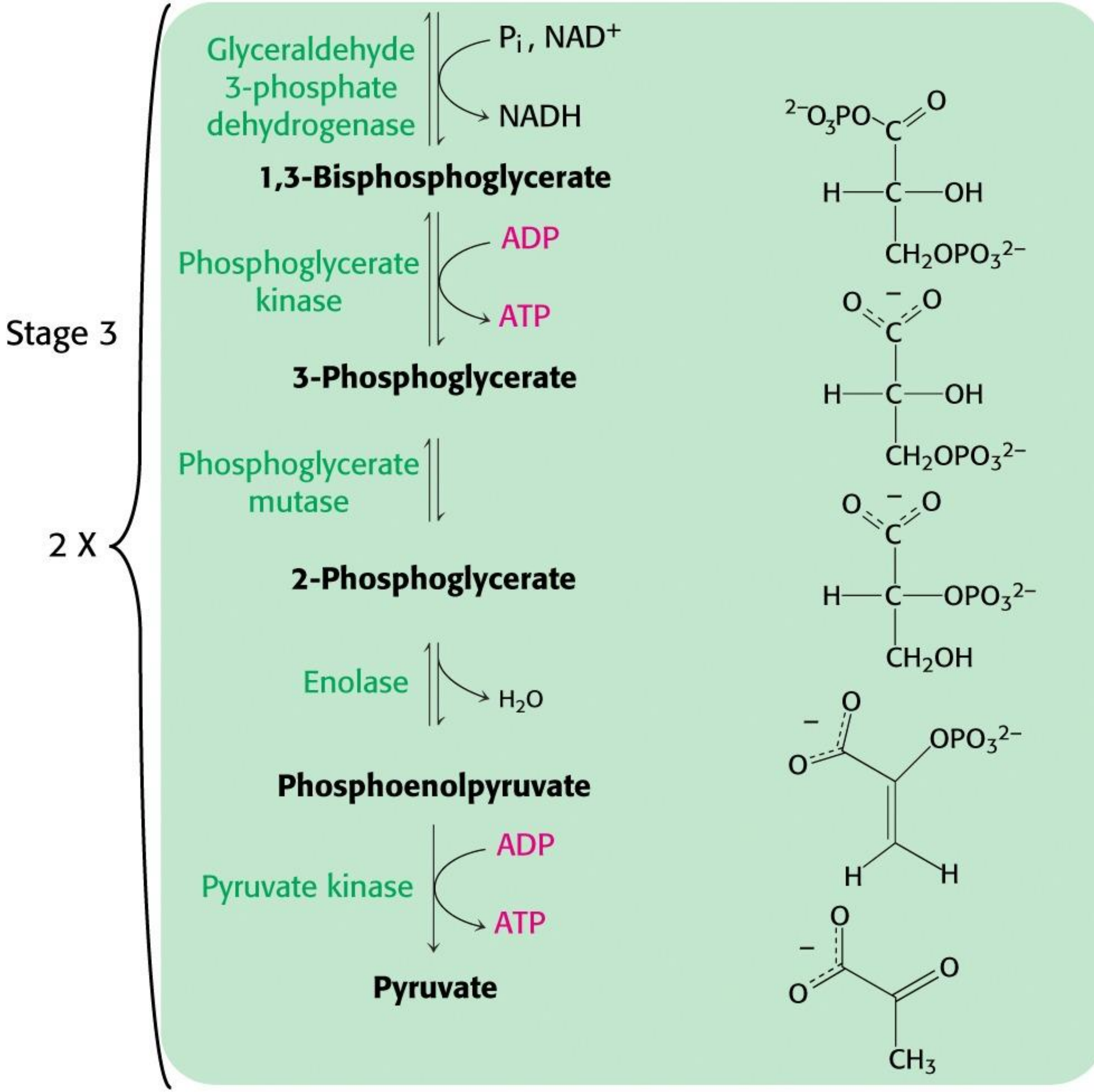
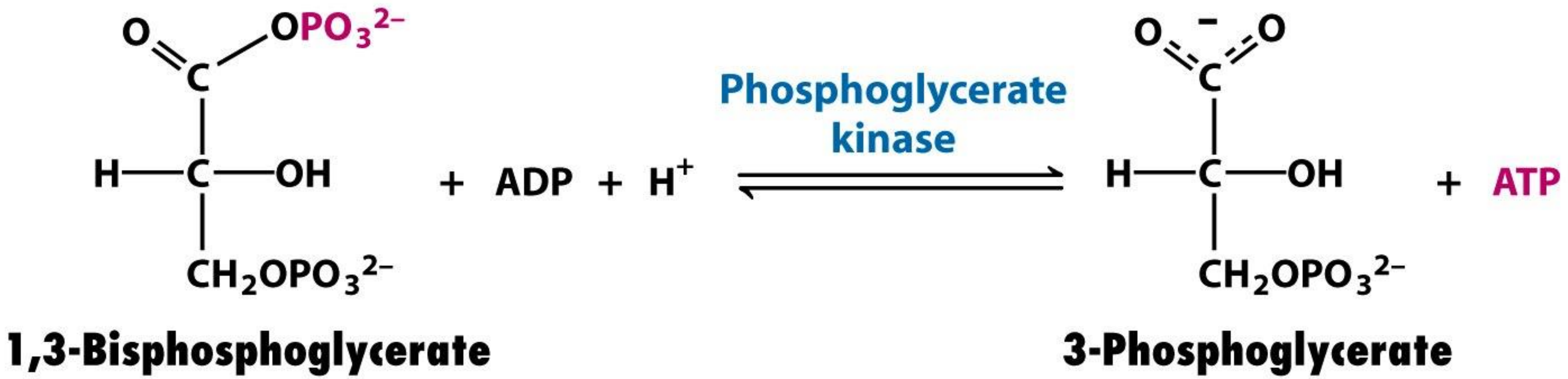


Stage 3
2 X
Glyceraldehyde 3-phosphate dehydrogenase
P_i, NAD^+
NADH
1,3-Bisphosphoglycerate
Phosphoglycerate kinase
ADP
ATP
3-Phosphoglycerate
Phosphoglycerate mutase
2-Phosphoglycerate
Enolase
H_2O
Phosphoenolpyruvate
Pyruvate kinase
ADP
ATP
Pyruvate



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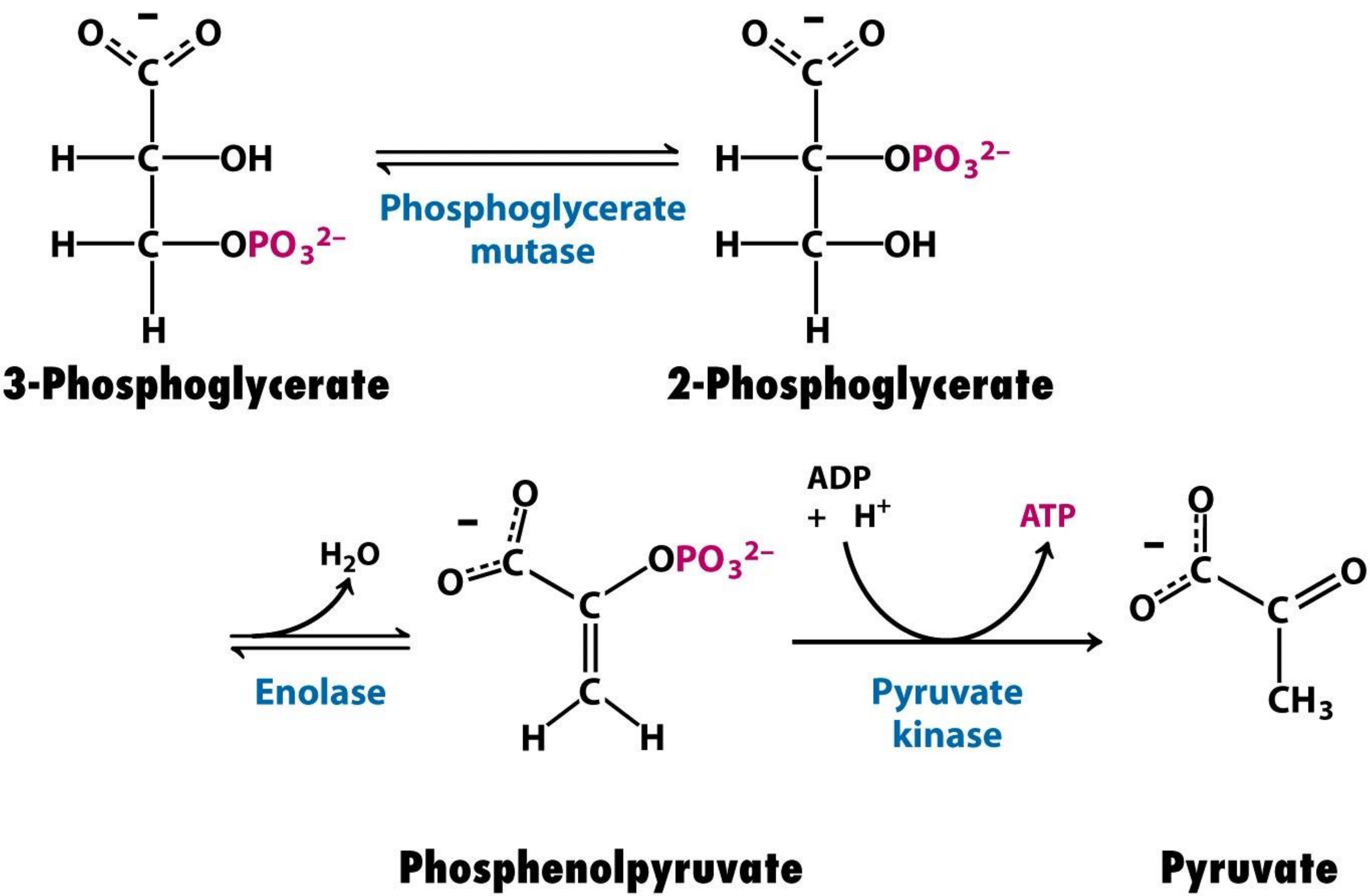

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TABLE 16.1 Reactions of glycolysis

Step	Reaction
1	Glucose + ATP $\rightarrow$ glucose 6-phosphate + ADP + H^+
2	Glucose 6-phosphate $\rightleftharpoons$ fructose 6-phosphate
3	Fructose 6-phosphate + ATP $\rightarrow$ fructose 1,6-bisphosphate + ADP + H^+
4	Fructose 1,6-bisphosphate $\rightleftharpoons$ dihydroxyacetone phosphate + glyceraldehyde 3-phosphate
5	Dihydroxyacetone phosphate $\rightleftharpoons$ glyceraldehyde 3-phosphate
6	Glyceraldehyde 3-phosphate + P_i + NAD^+ $\rightleftharpoons$ 1,3-bisphosphoglycerate + NADH + H^+
7	1,3-Bisphosphoglycerate + ADP $\rightleftharpoons$ 3-phosphoglycerate + ATP
8	3-Phosphoglycerate $\rightleftharpoons$ 2-phosphoglycerate
9	2-Phosphoglycerate $\rightleftharpoons$ phosphoenolpyruvate + H_2O
10	Phosphoenolpyruvate + ADP + H^+ $\rightarrow$ pyruvate + ATP

Note: ΔG, the actual free-energy change, has been calculated from $\Delta G^{\circ\prime}$ and known concentrations of reactants under typical physiological conditions. Glycolysis can proceed only if the ΔG values of all reactions are negative. The small positive ΔG values of three of the above reactions indicate that the concentrations of metabolites in vivo in cells undergoing glycolysis are not precisely known.

Table 16-1 part 1
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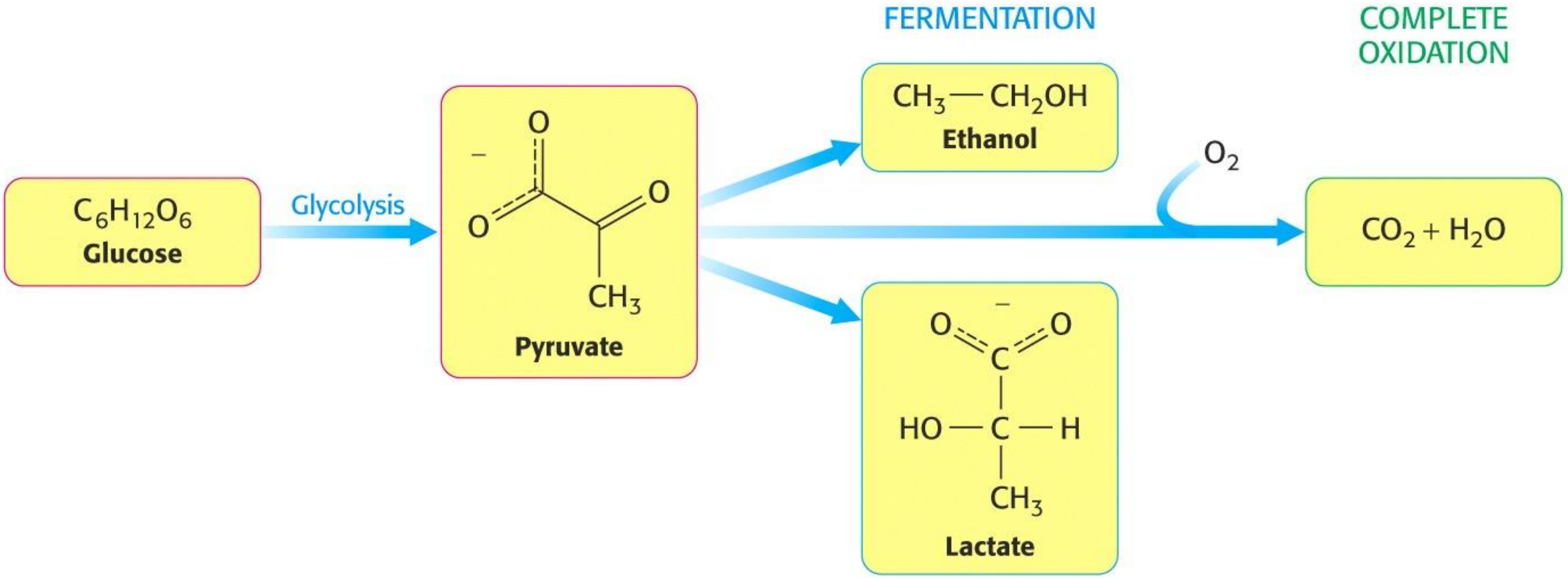
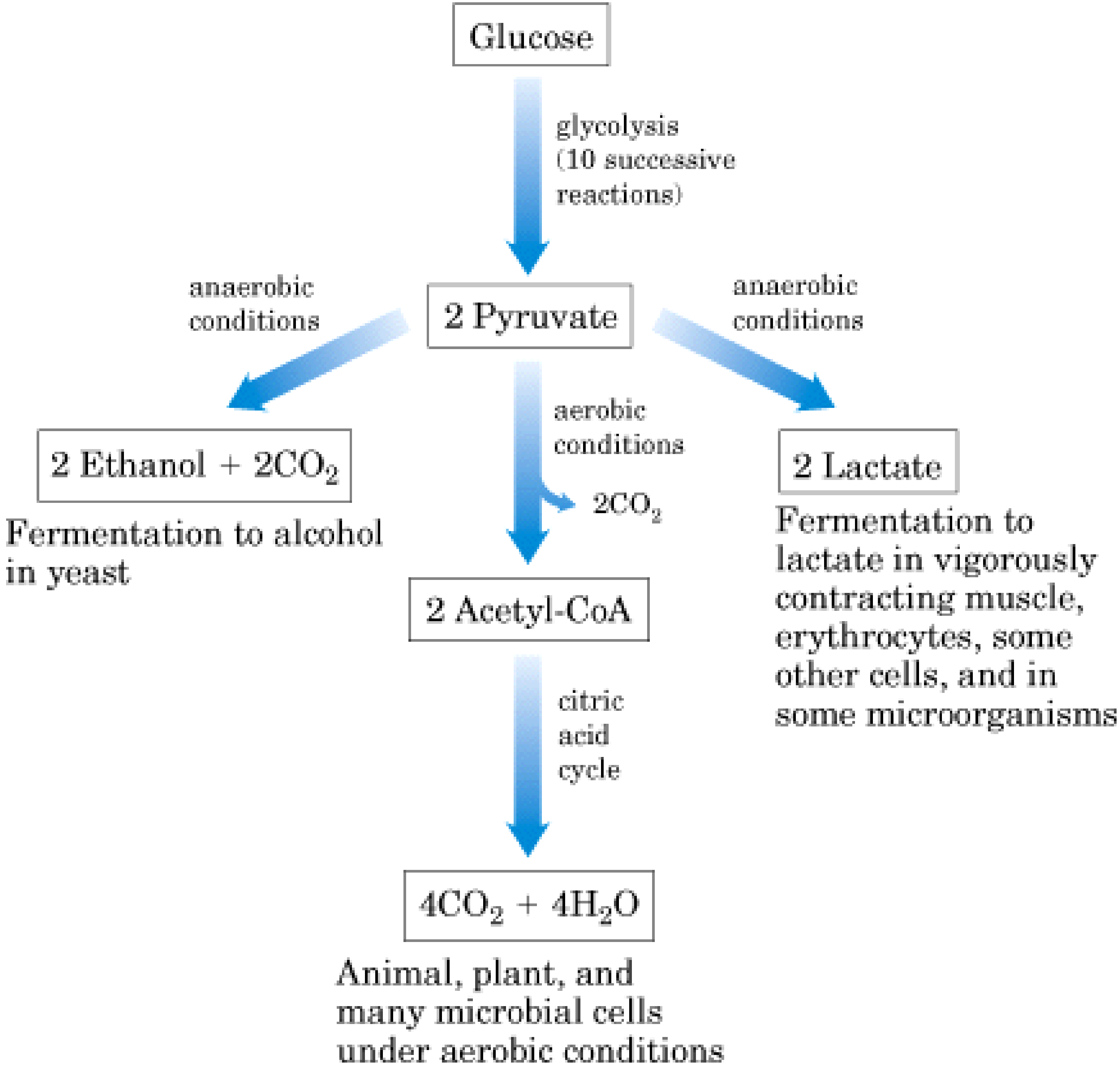
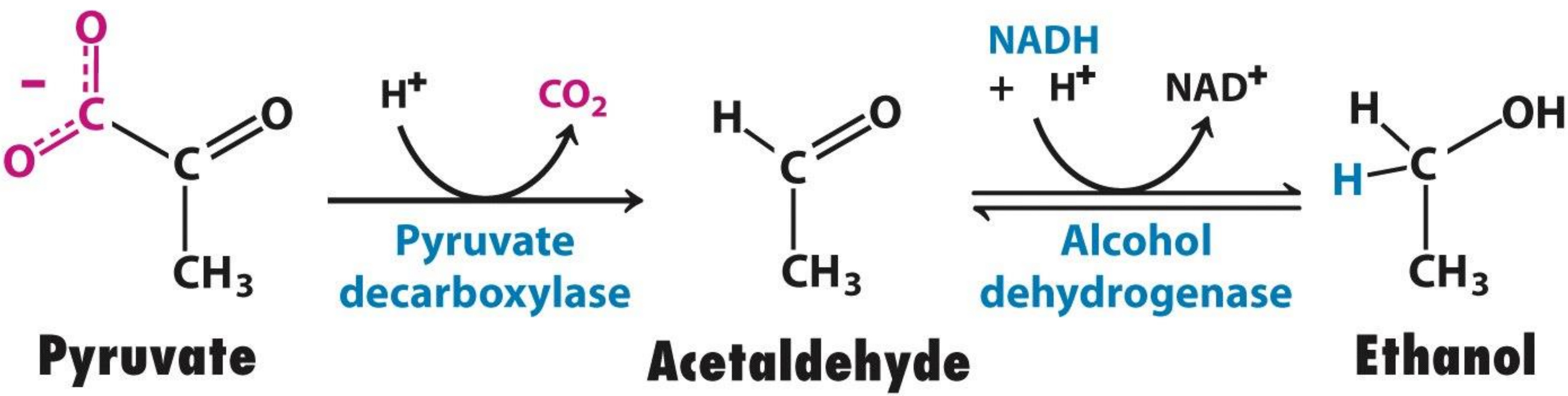
Fermentasi



Fermentasi: istilah umum untuk menyatakan proses degradasi glukosa atau nutrien organik lain secara anaerob menjadi berbagai produk untuk menghasilkan ATP (fermentasi alkohol atau fermentasi laktat)


Glucose
glycolysis
(10 successive
reactions)
anaerobic
conditions
2 Pyruvate
anaerobic
conditions
2 Ethanol + $2CO_2$
aerobic
conditions
$2CO_2$
2 Lactate
Fermentation to alcohol
in yeast
2 Acetyl-CoA
Fermentation to
lactate in vigorously
contracting muscle,
erythrocytes, some
other cells, and in
some microorganisms
citric
acid
cycle
$4CO_2 + 4H_2O$
Animal, plant, and
many microbial cells
under aerobic conditions



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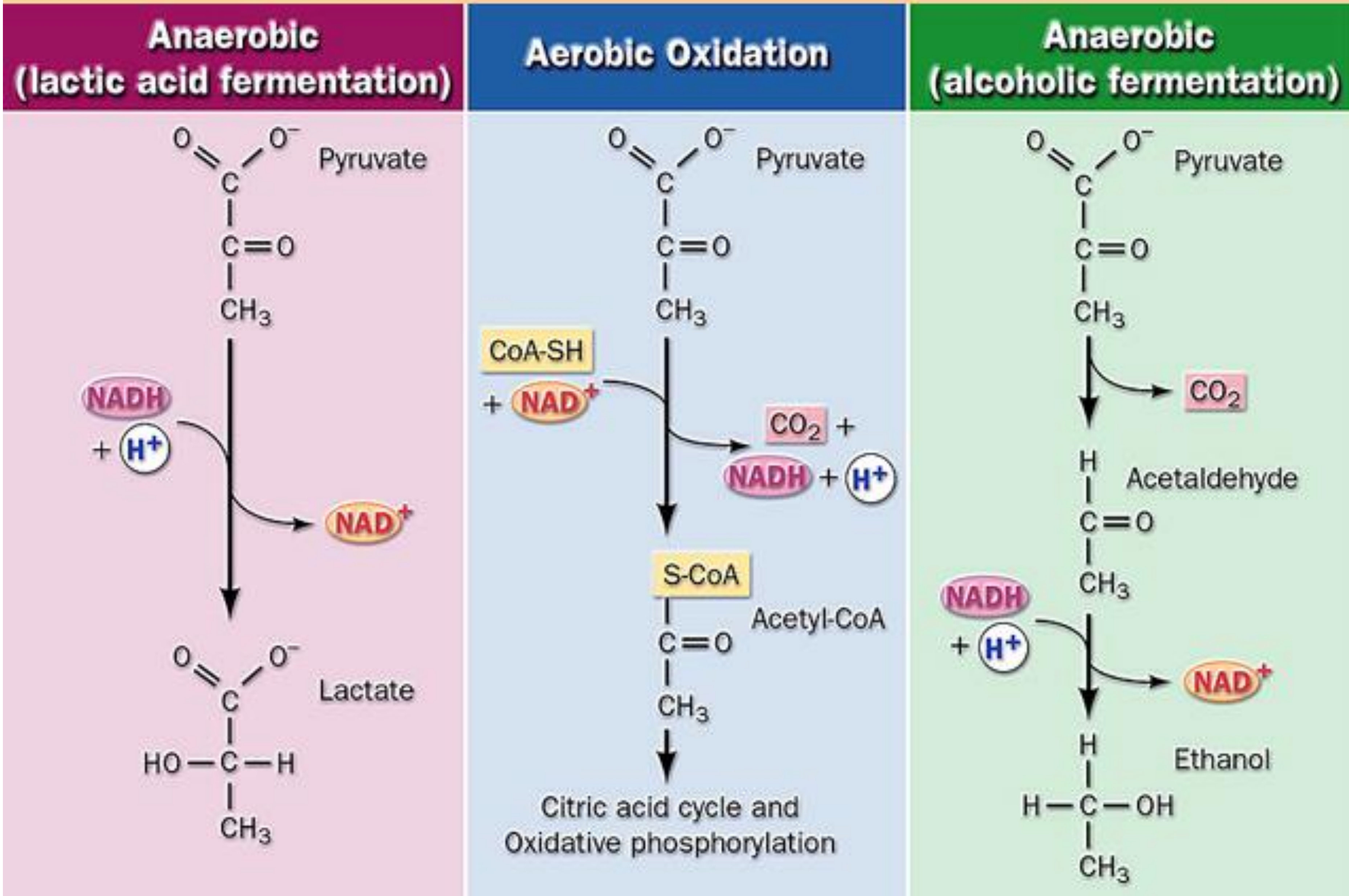
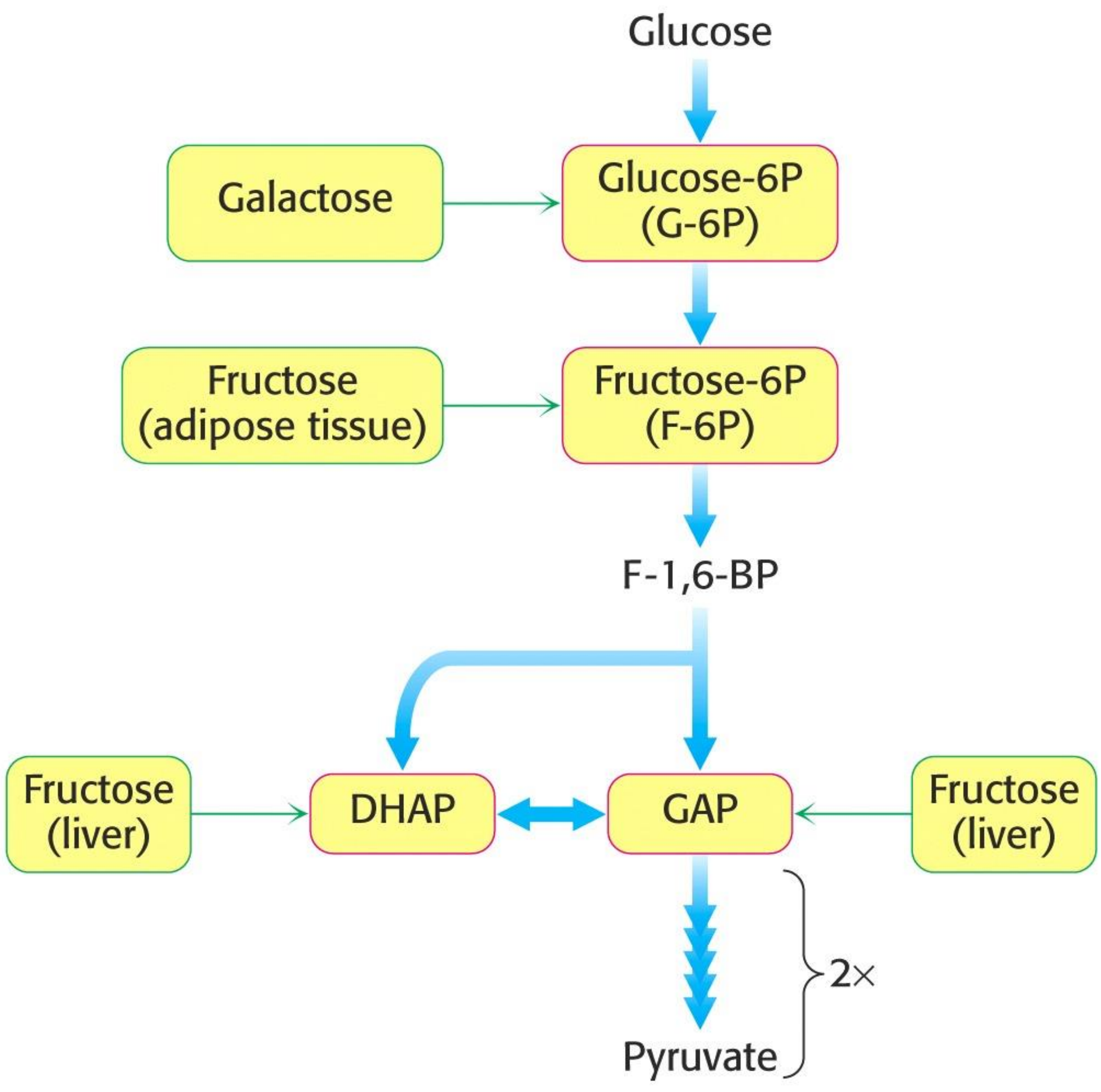
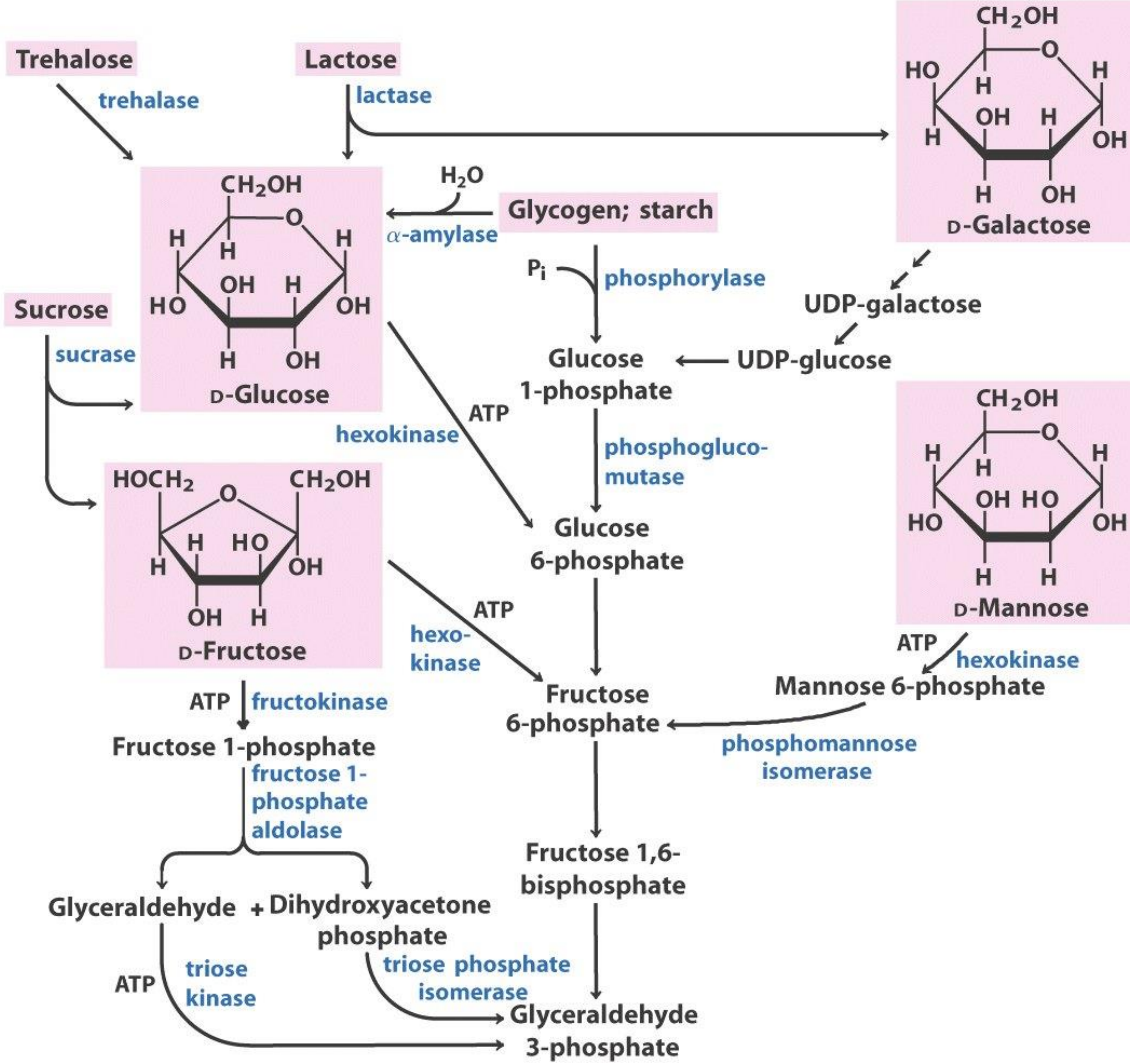
Three fates of pyruvate produced by glycolysis



Titik masuk glikolisis




Trehalose
trehalase
Lactose
lactase
CH2OH
HO
OH
H
D-Galactose
H2O
Glycogen; starch
α-amylase
D-Glucose
Sucrose
sucrase
Pi
phosphorylase
UDP-galactose
Glucose 1-phosphate
UDP-glucose
ATP
hexokinase
phosphoglucomutase
HOCH2
O
Glucose 6-phosphate
D-Mannose
D-Fructose
ATP
hexokinase
Mannose 6-phosphate
ATP
fructokinase
Fructose 6-phosphate
phosphomannose isomerase
Fructose 1-phosphate
fructose 1-phosphate aldolase
Fructose 1,6-bisphosphate
Glyceraldehyde
+ Dihydroxyacetone phosphate
triose phosphate isomerase
triose kinase
Glyceraldehyde 3-phosphate

Lactose Intolerance

- Suatu penyakit yang banyak dialami oleh orang dewasa karena tidak mampu mencerna susu yang mengandung laktosa
- Laktosa tidak mampu dicerna oleh tubuh karena tubuh tidak memiliki enzim yang dapat mengubah laktosa, yaitu lactase
- Gejala yang akan terjadi jika memiliki lactose intolerance adalah akan timbul diare dikarenakan laktosa yang ada akan difermentasi menjadi asam laktat. Asam laktat akan menghasilkan gas dan menyebabkan air masuk lebih banyak ke dalam usus sehingga menimbulkan diare.

Glukoneogenesis

- Produksi gula baru; biosintesis karbohidrat dari tiga- atau empat-karbon (umumnya bukan berasal dari karbohidrat)
- Prekursor/bahan baku: laktat (otot atau eritrosit), asam amino (alanin dari degradasi protein pada saat kelaparan), propionat (asam lemak dan asam amino), dan gliserol (degradasi lemak)

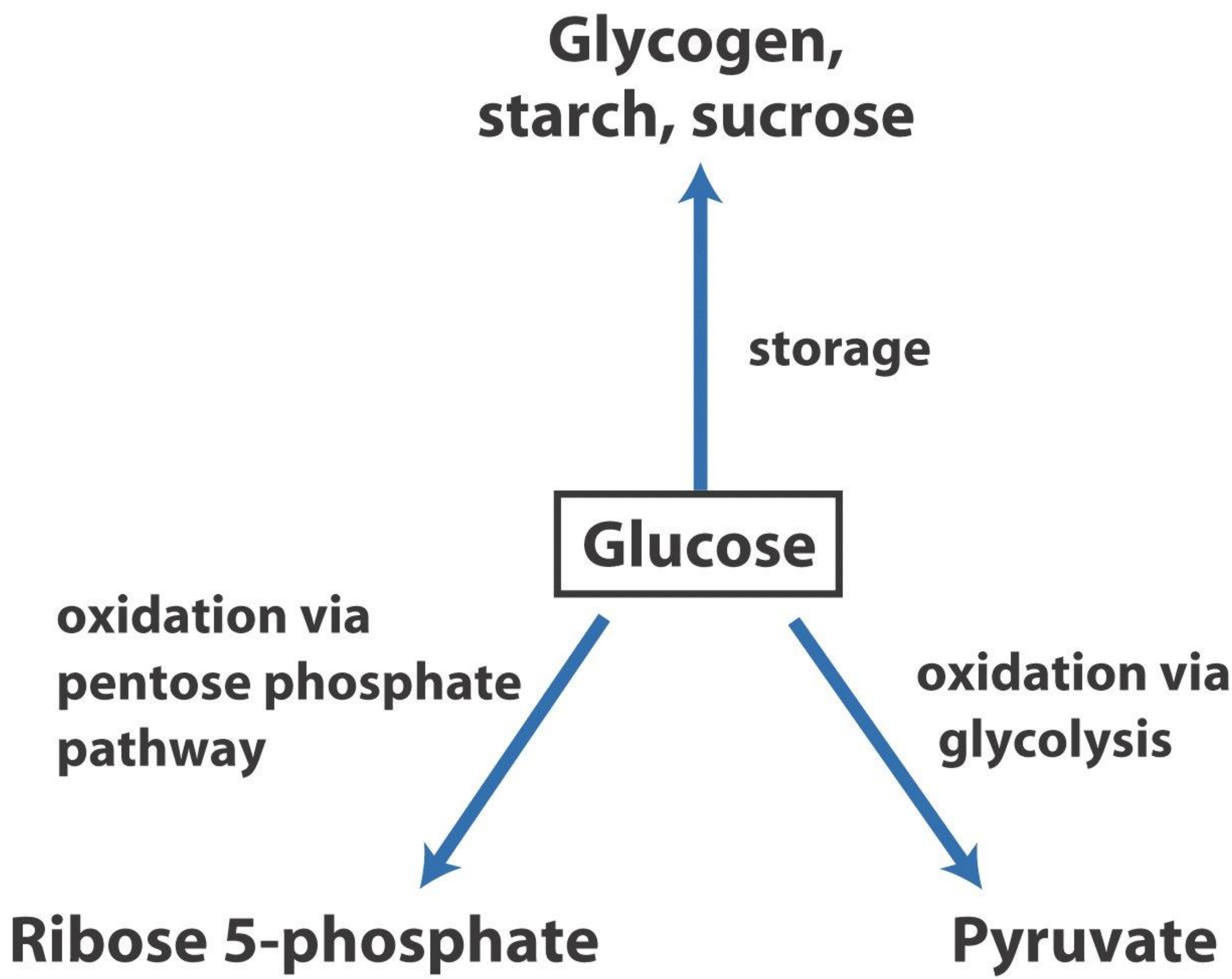

Glycogen,
starch, sucrose
storage
Glucose
oxidation via
pentose phosphate
pathway
oxidation via
glycolysis
Ribose 5-phosphate
Pyruvate

TABLE 14–3 Sequential Reactions in Gluconeogenesis Starting from Pyruvate

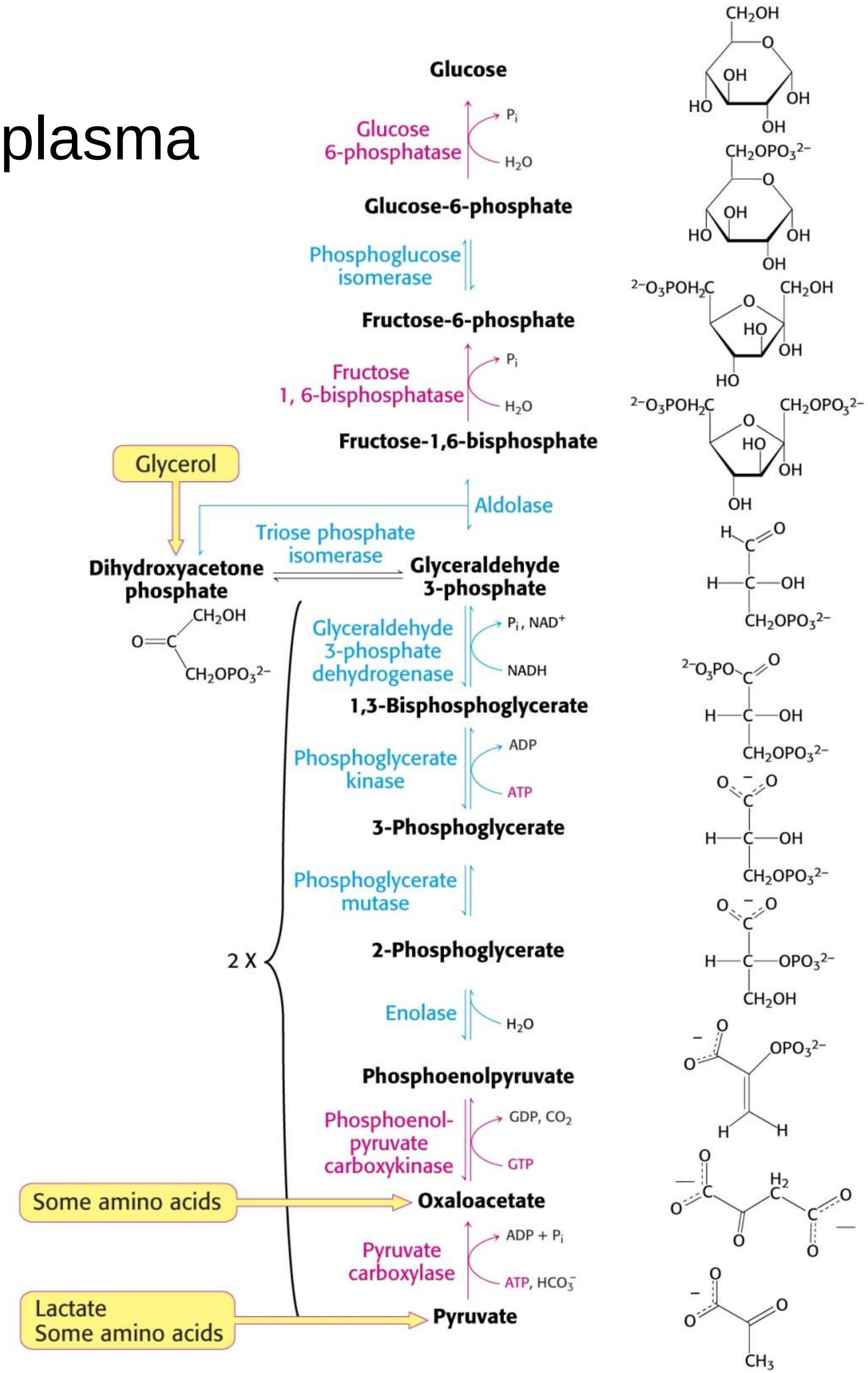
Pyruvate + HCO_3^- + ATP $\longrightarrow$ oxaloacetate + ADP + P_i	$\times 2$
Oxaloacetate + GTP $\rightleftharpoons$ phosphoenolpyruvate + CO_2 + GDP	$\times 2$
Phosphoenolpyruvate + H_2O $\rightleftharpoons$ 2-phosphoglycerate	$\times 2$
2-Phosphoglycerate $\rightleftharpoons$ 3-phosphoglycerate	$\times 2$
3-Phosphoglycerate + ATP $\rightleftharpoons$ 1,3-bisphosphoglycerate + ADP	$\times 2$
1,3-Bisphosphoglycerate + NADH + H^+ $\rightleftharpoons$ glyceraldehyde 3-phosphate + NAD^+ + P_i	$\times 2$
Glyceraldehyde 3-phosphate $\rightleftharpoons$ dihydroxyacetone phosphate	
Glyceraldehyde 3-phosphate + dihydroxyacetone phosphate $\rightleftharpoons$ fructose 1,6-bisphosphate	
Fructose 1,6-bisphosphate $\longrightarrow$ fructose 6-phosphate + P_i	
Fructose 6-phosphate $\rightleftharpoons$ glucose 6-phosphate	
Glucose 6-phosphate + H_2O $\longrightarrow$ glucose + P_i	
Sum: 2 Pyruvate + 4ATP + 2GTP + 2NADH + $2H^+$ + $4H_2O$ $\longrightarrow$ glucose + 4ADP + 2GDP + $6P_i$ + $2NAD^+$	

Note: The bypass reactions are in red; all other reactions are reversible steps of glycolysis. The figures at the right indicate that the reaction is to be counted twice, because two three-carbon precursors are required to make a molecule of glucose. The reactions required to replace the cytosolic NADH consumed in the glyceraldehyde 3-phosphate dehydrogenase reaction (the conversion of lactate to pyruvate in the cytosol or the transport of reducing equivalents from mitochondria to the cytosol in the form of malate) are not considered in this summary. Biochemical equations are not necessarily balanced for H and charge (p. 506).

Retikulum endoplasma

Sitosol

Mitokhondria



Glukoneogenesis

$$2\ Piruvat + 4\ ATP + 2\ GTP + 2\ NADH + 6\ H_2O \rightarrow$$
$$Glukosa + 2\ GDP + 6\ Pi + 4\ ADP + 2\ NAD^+ + 2\ H^+$$

Glikolisis

$$Glukosa + 2\ Pi + 2\ ADP + 2\ NAD^+ \rightarrow$$
$$2\ Piruvat + 2\ ATP + 2\ NADH + 2\ H^+ + 2\ H_2O$$

Pengendalian

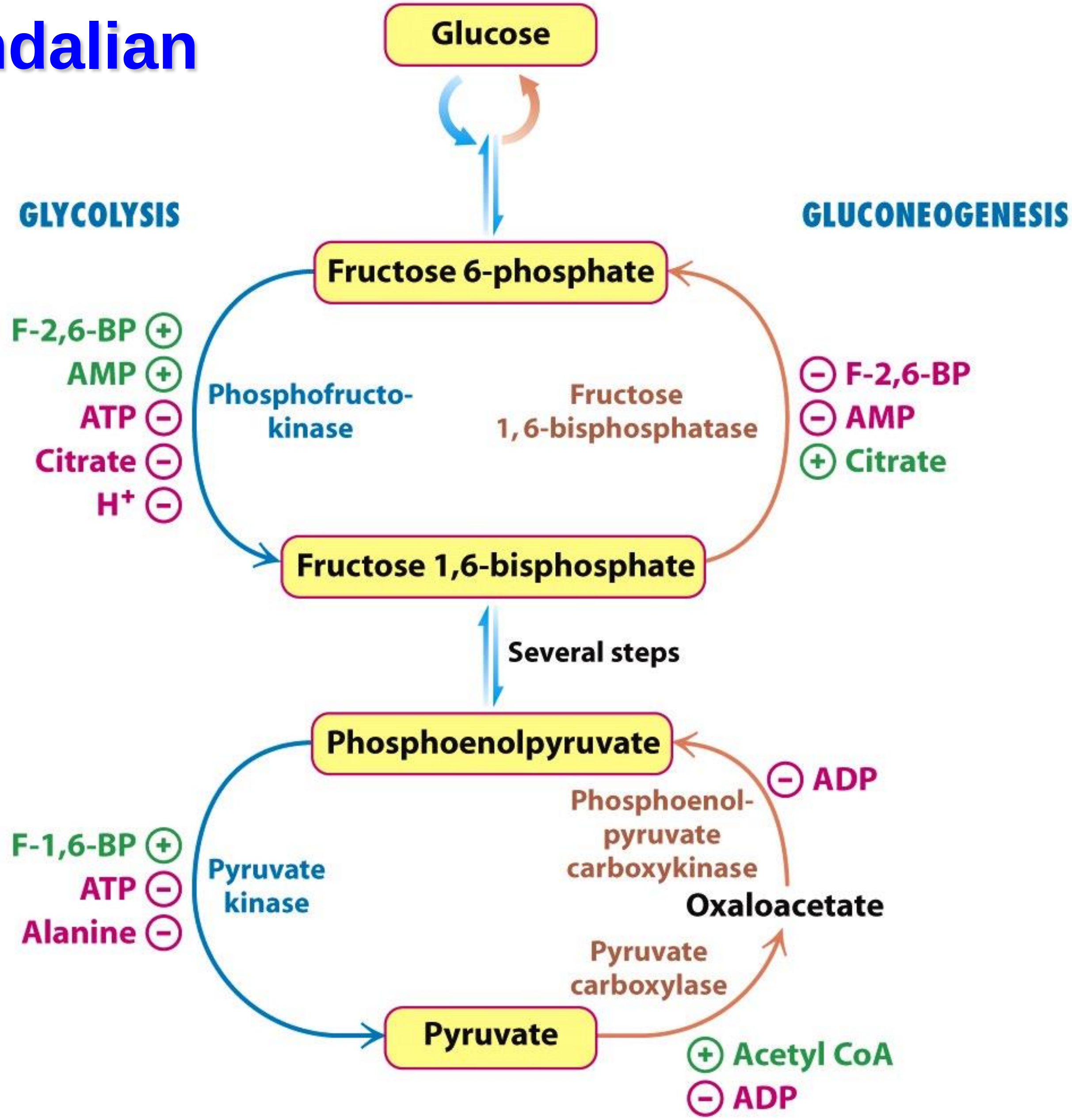


Figure 16-28
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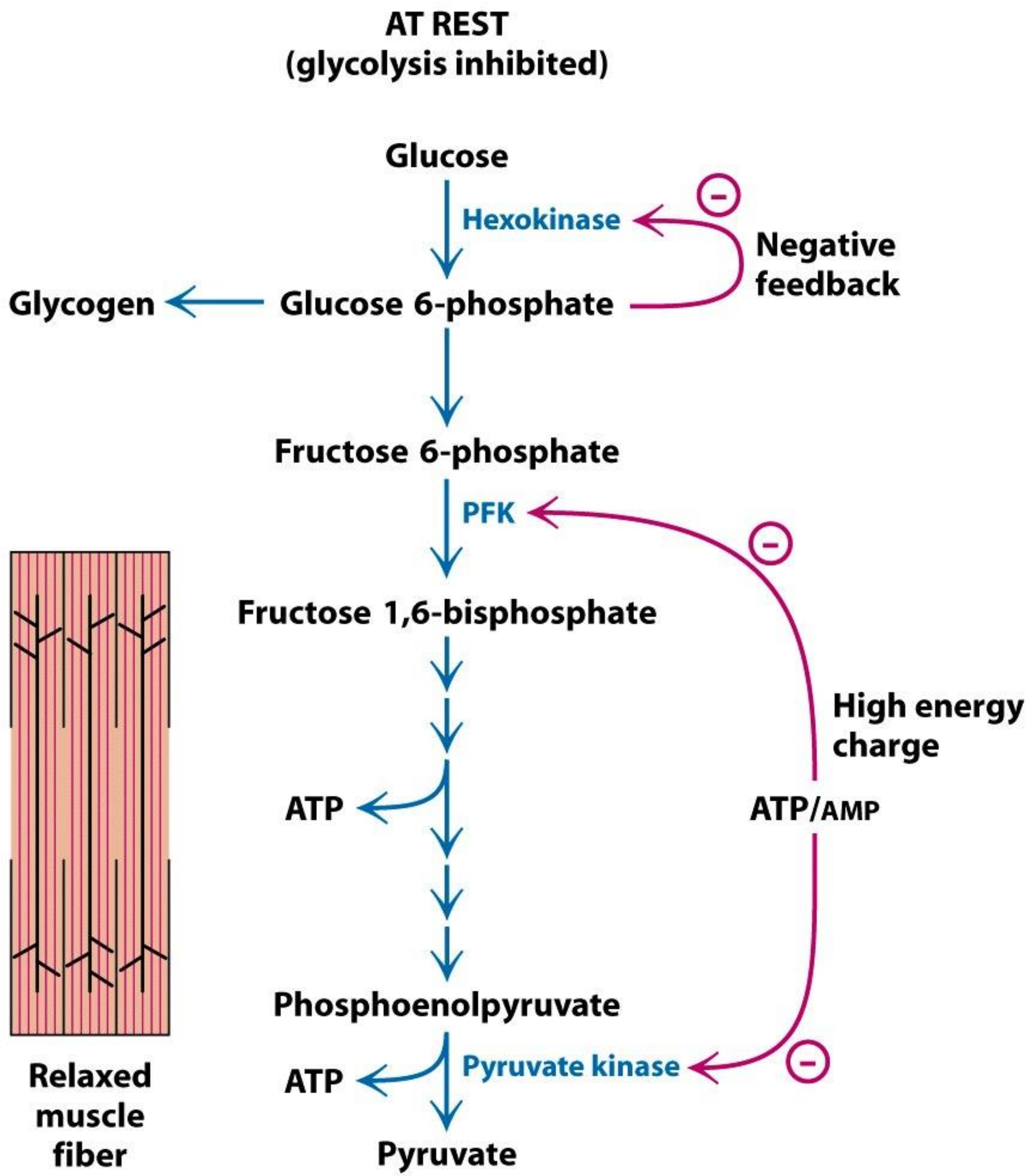


Figure 16-17 part 1
Biochemistry, Sixth Edition

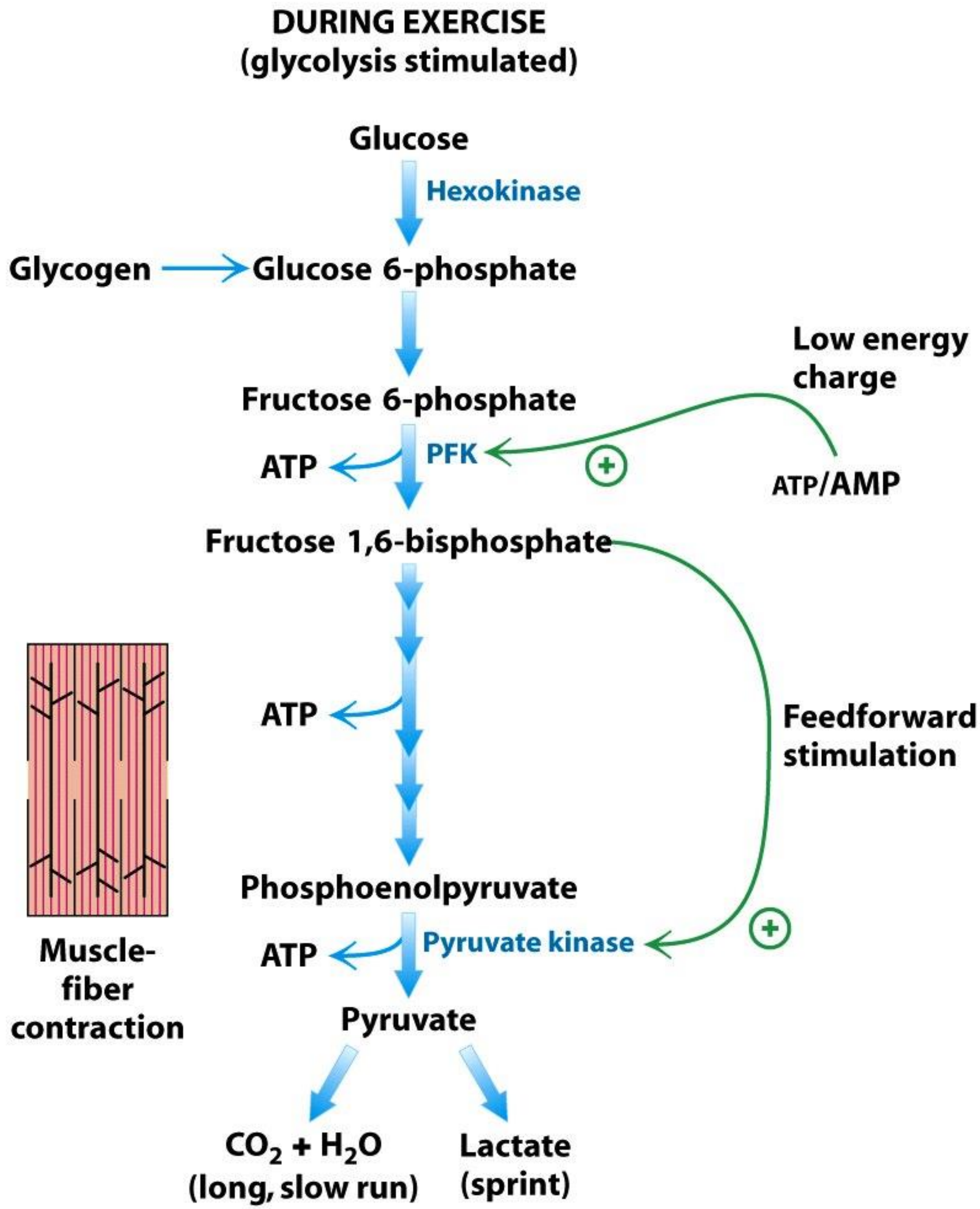
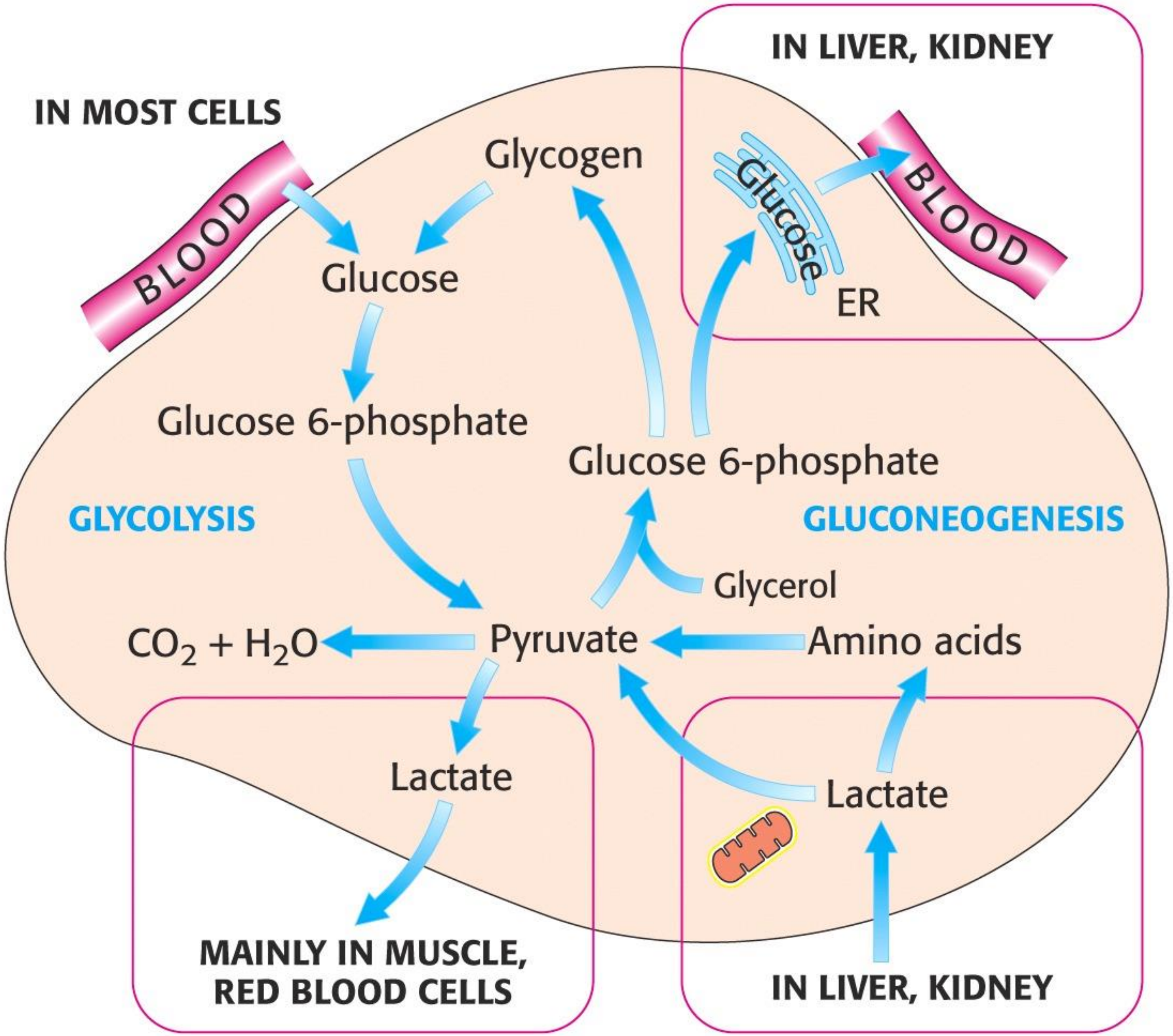
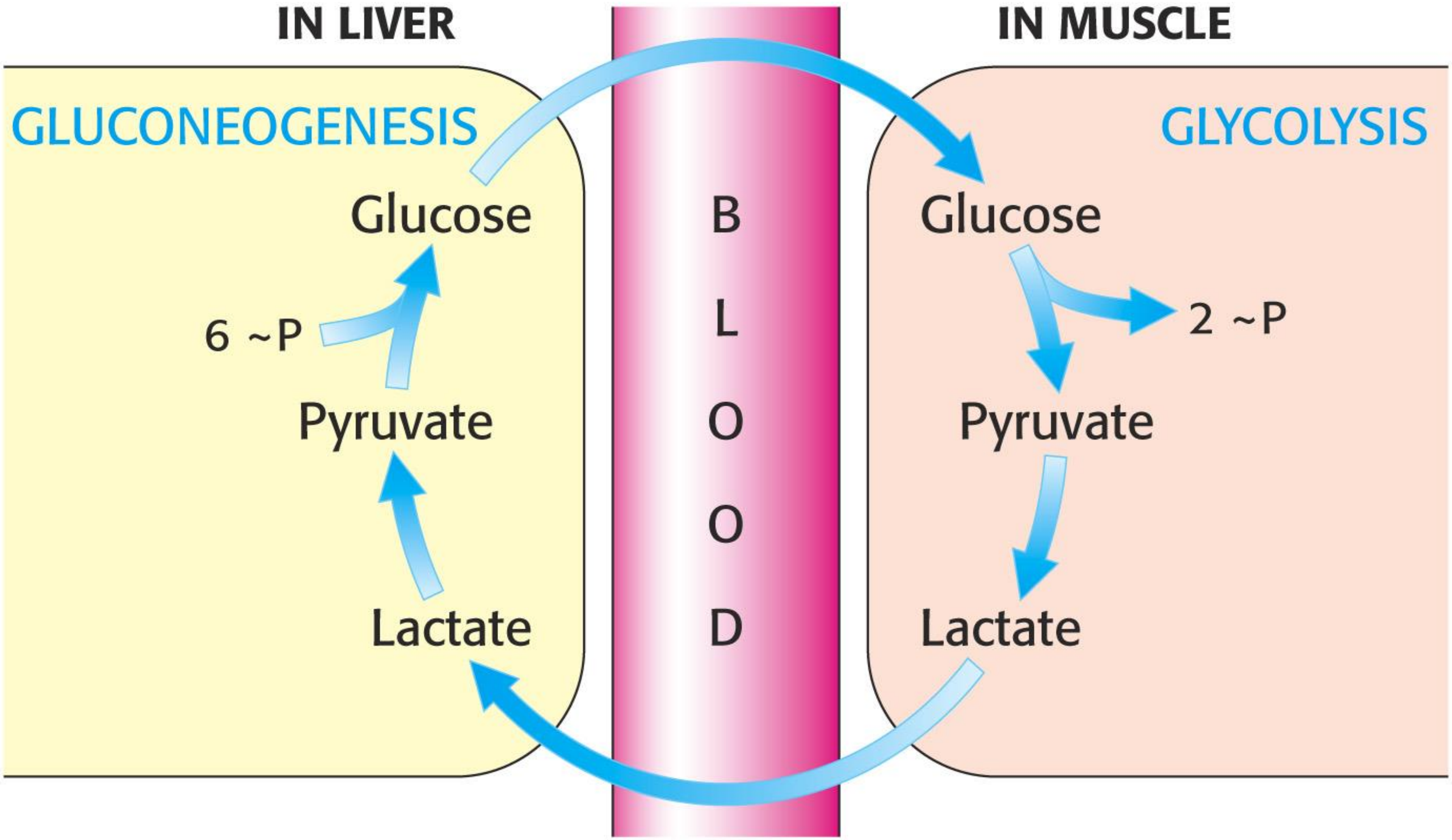
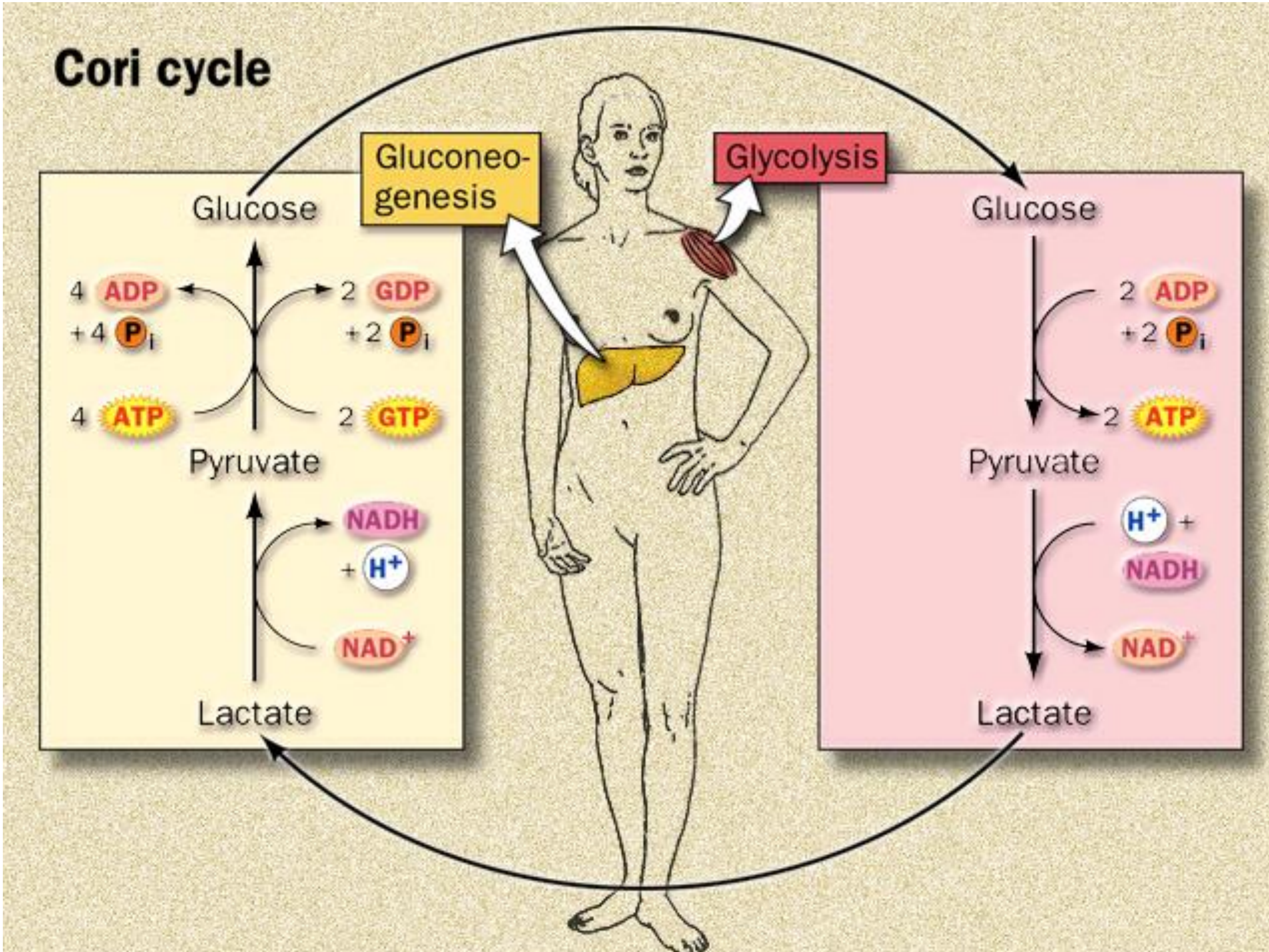


Figure 16-17 part 2
Biochemistry, Sixth Edition


IN LIVER, KIDNEY
IN MOST CELLS
Glycogen
Glucose
BLOOD
BLOOD
Glucose
ER
Glucose
Glucose 6-phosphate
Glucose 6-phosphate
GLYCOLYSIS
GLUCONEOGENESIS
Glycerol
$CO_2 + H_2O$
Pyruvate
Amino acids
Lactate
Lactate
MAINLY IN MUSCLE, RED BLOOD CELLS
IN LIVER, KIDNEY


IN LIVER
IN MUSCLE
GLUCONEOGENESIS
GLYCOLYSIS
Glucose
6 ~P
Pyruvate
Lactate
B
L
O
O
D
Glucose
2 ~P
Pyruvate
Lactate



Cori cycle
Gluconeo-
genesis
Glycolysis
Glucose
4 ADP
+4 Pi
2 GDP
+2 Pi
4 ATP
2 GTP
Pyruvate
NADH
+ H+
NAD+
Lactate
Glucose
2 ADP
+2 Pi
2 ATP
Pyruvate
H+ +
NADH
NAD+
Lactate

Siklus asam sitrat

Tahap awal respirasi/pernapasan sel

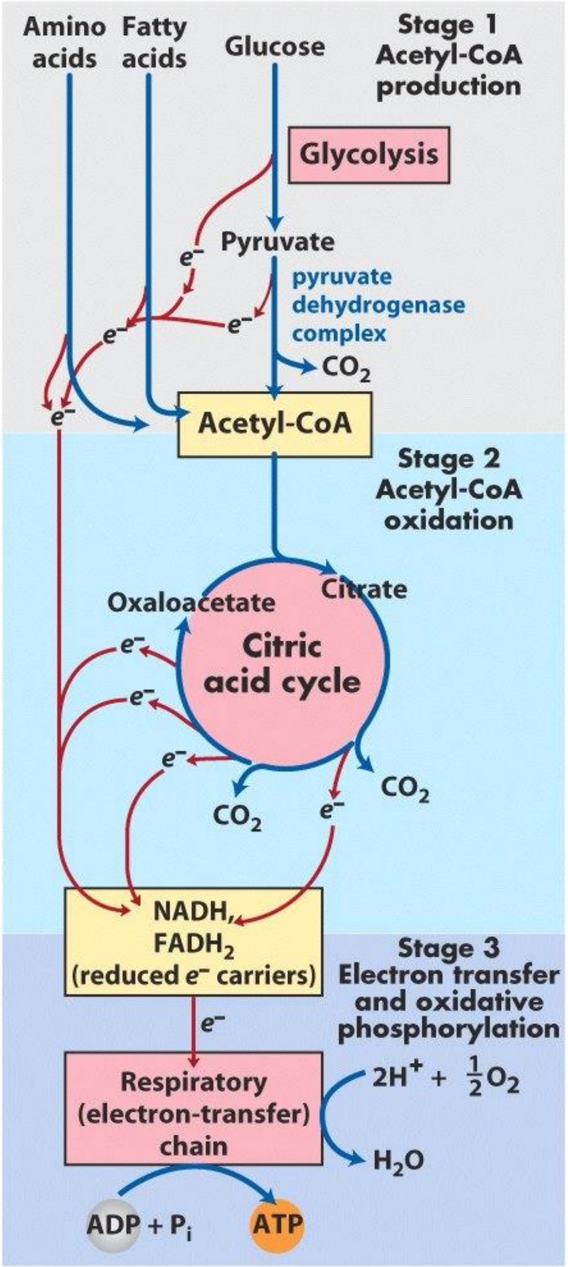
Jalur reaksi (8 tahap) untuk pengoksidasian semua bahan bakar metabolit

Diusulkan Krebs (1937), dari percobaan konsumsi oksigen pada cacahan otot dada merpati dengan asam trikarboksilat (sitrat, isositrat, cis akonitat)

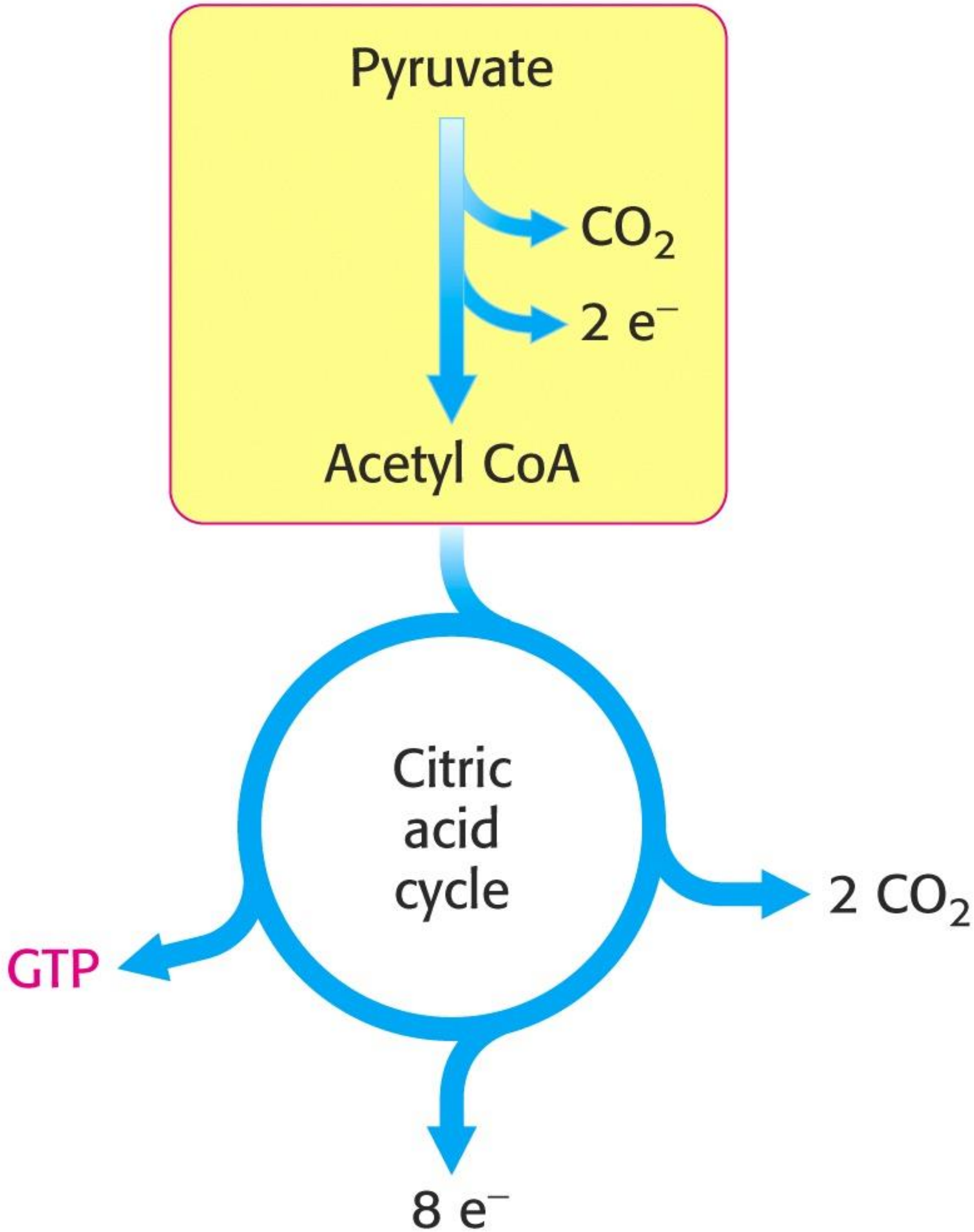
Fase 1: oksidasi asetil-CoA menjadi CO_2
(tahap 1 s.d. 4)

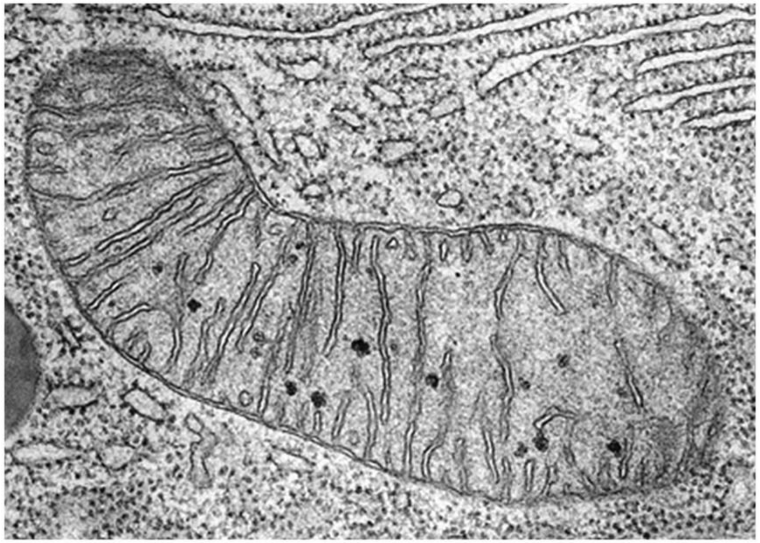
Fase 2: regenerasi oksaloasetat dari suksnil-CoA
(tahap 5 s.d. 8)

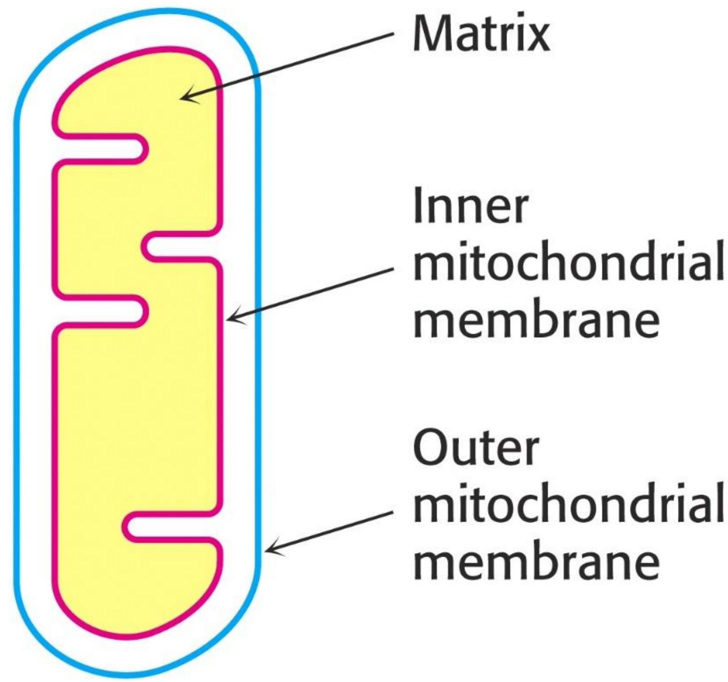
Hans Krebs, 1900–1981

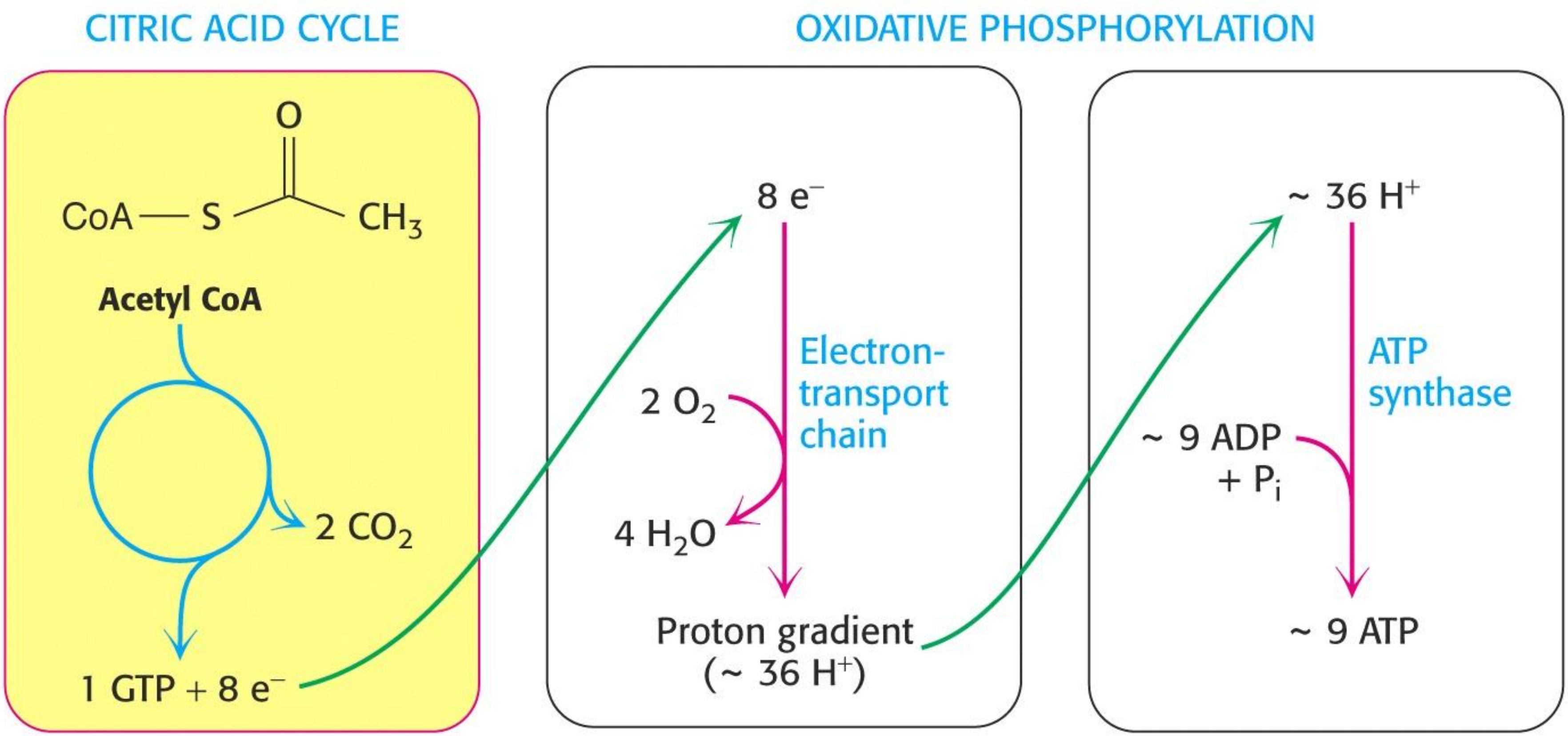


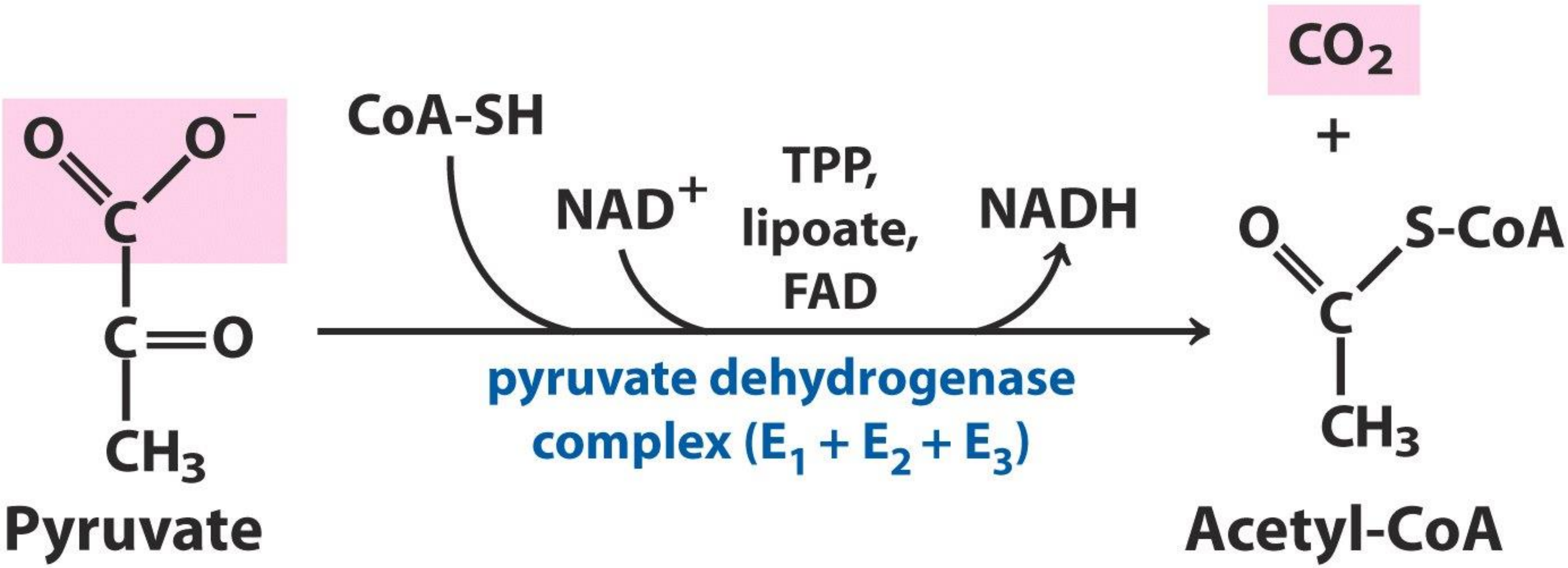
Amino acids
Fatty acids
Glucose
Stage 1 Acetyl-CoA production
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
CO_2
e^-
Acetyl-CoA
Stage 2 Acetyl-CoA oxidation
Citrate
Oxaloacetate
Citric acid cycle
CO_2
CO_2
NADH, $FADH_2$ (reduced e^- carriers)
Stage 3 Electron transfer and oxidative phosphorylation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


Pyruvate
CO_2
2 e⁻
Acetyl CoA
Citric acid cycle
2 CO_2
GTP
8 e⁻



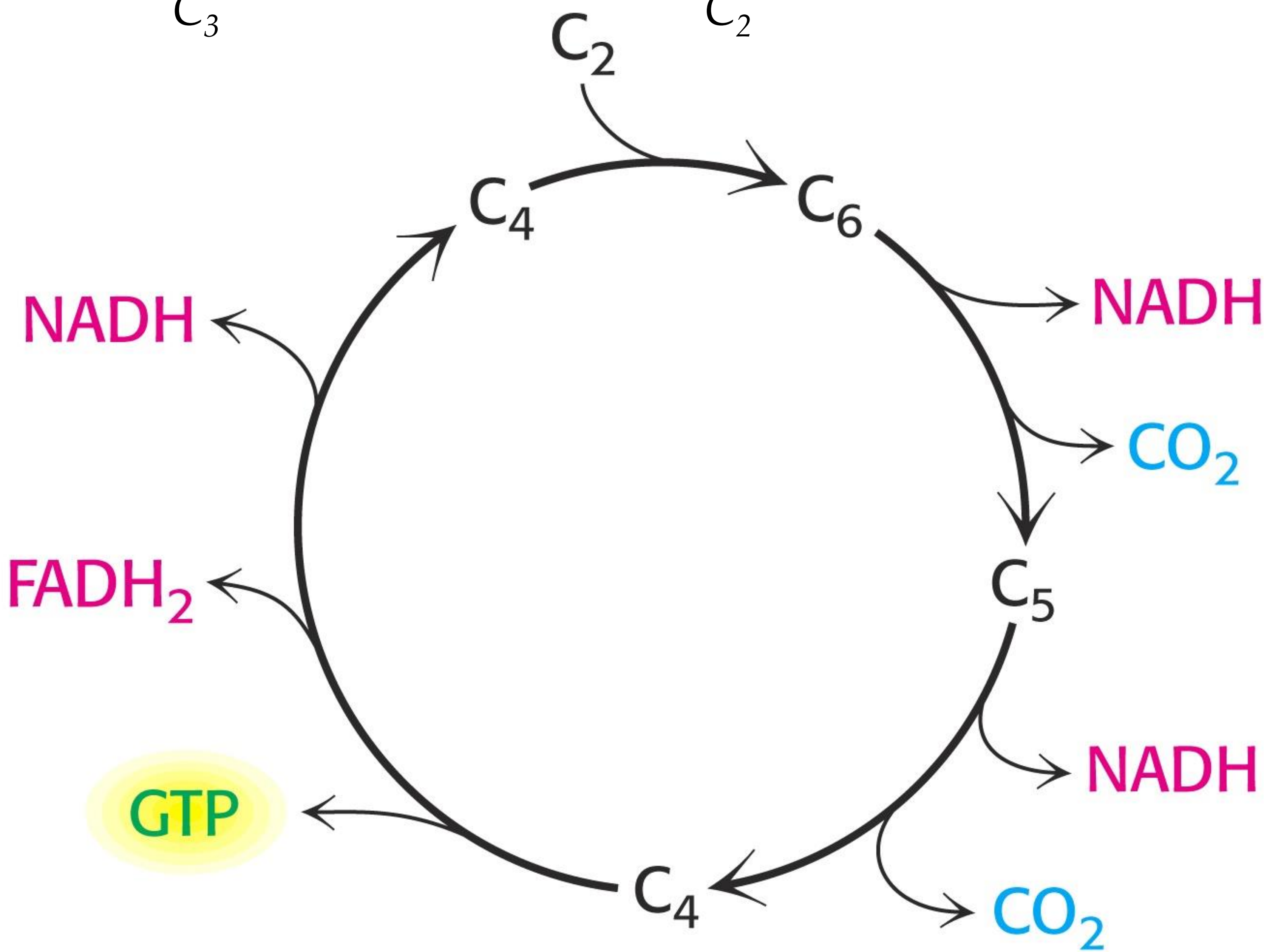

Matrix
Inner mitochondrial membrane
Outer mitochondrial membrane

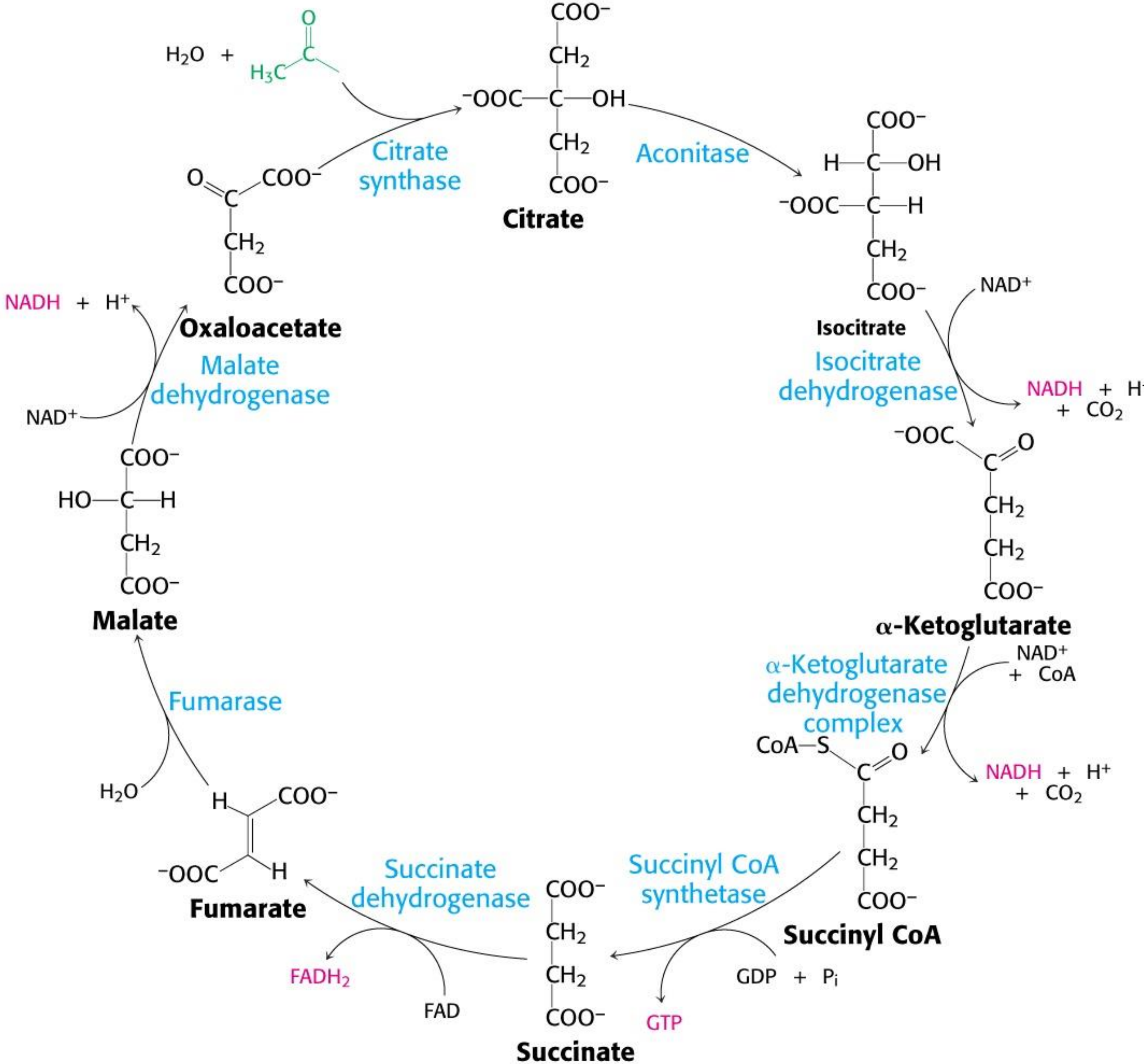

CITRIC ACID CYCLE
OXIDATIVE PHOSPHORYLATION
O
CoA — S — CH3
Acetyl CoA
2 CO2
1 GTP + 8 e−
8 e−
Electron-transport chain
2 O2
4 H2O
Proton gradient (~ 36 H+)
~ 36 H+
ATP synthase
~ 9 ADP + Pi
~ 9 ATP



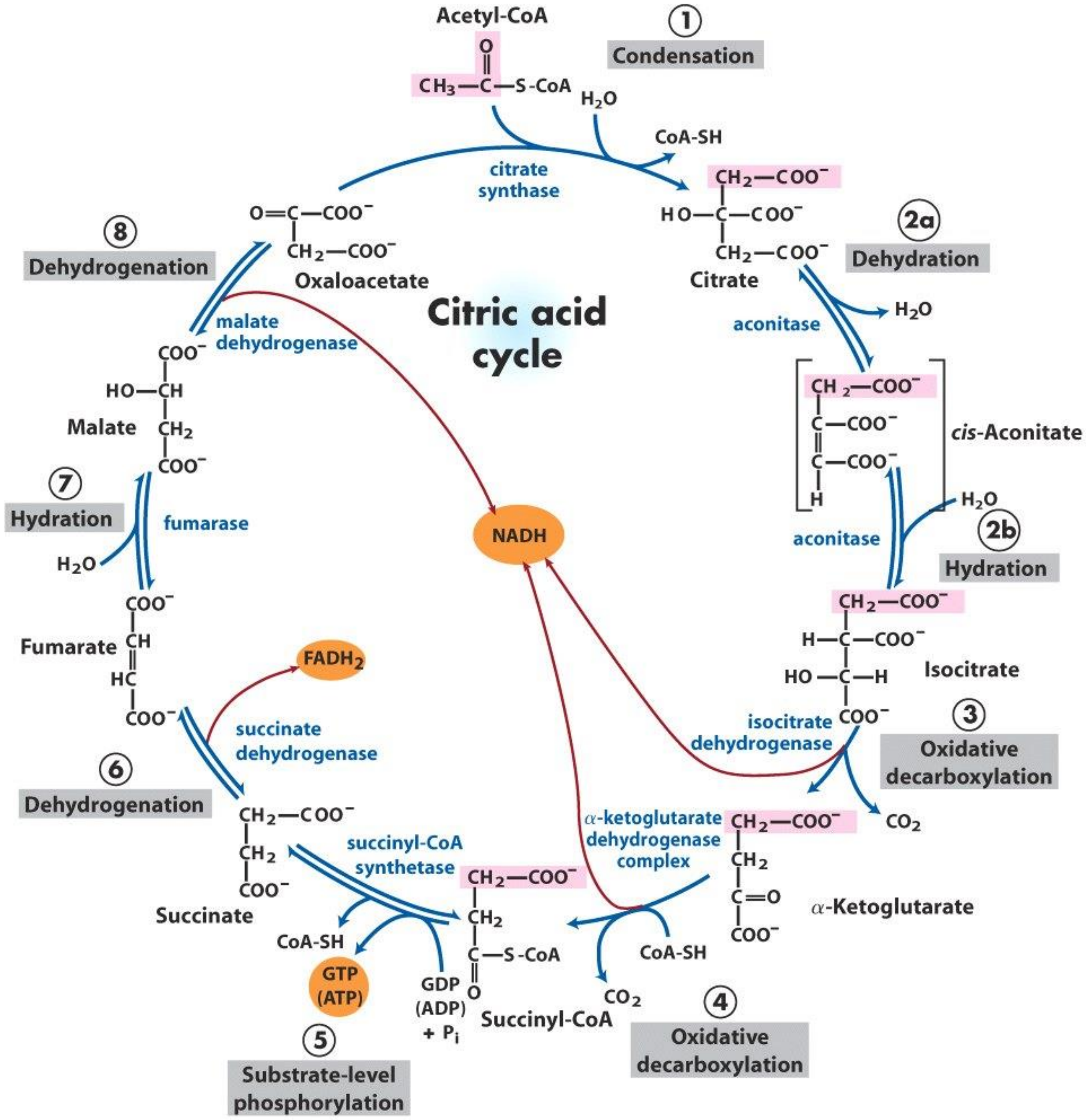
$$\Delta G'^{\circ} = -33.4 \text{ kJ/mol}$$

$$\underset{C_3}{Piruvat} + CoA + NAD^+ \rightarrow \underset{C_2}{Asetil\text{-}CoA} + CO_2 + NADH$$





Citrate
Isocitrate
α-Ketoglutarate
Succinyl CoA
Succinate
Fumarate
Malate
Oxaloacetate
Citrate synthase
Aconitase
Isocitrate dehydrogenase
α-Ketoglutarate dehydrogenase complex
Succinyl CoA synthetase
Succinate dehydrogenase
Fumarase
Malate dehydrogenase
H2O +
NAD+
NADH + H+ + CO2
NAD+ + CoA
NADH + H+ + CO2
GDP + Pi
GTP
FAD
FADH2
H2O
NAD+
NADH + H+



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

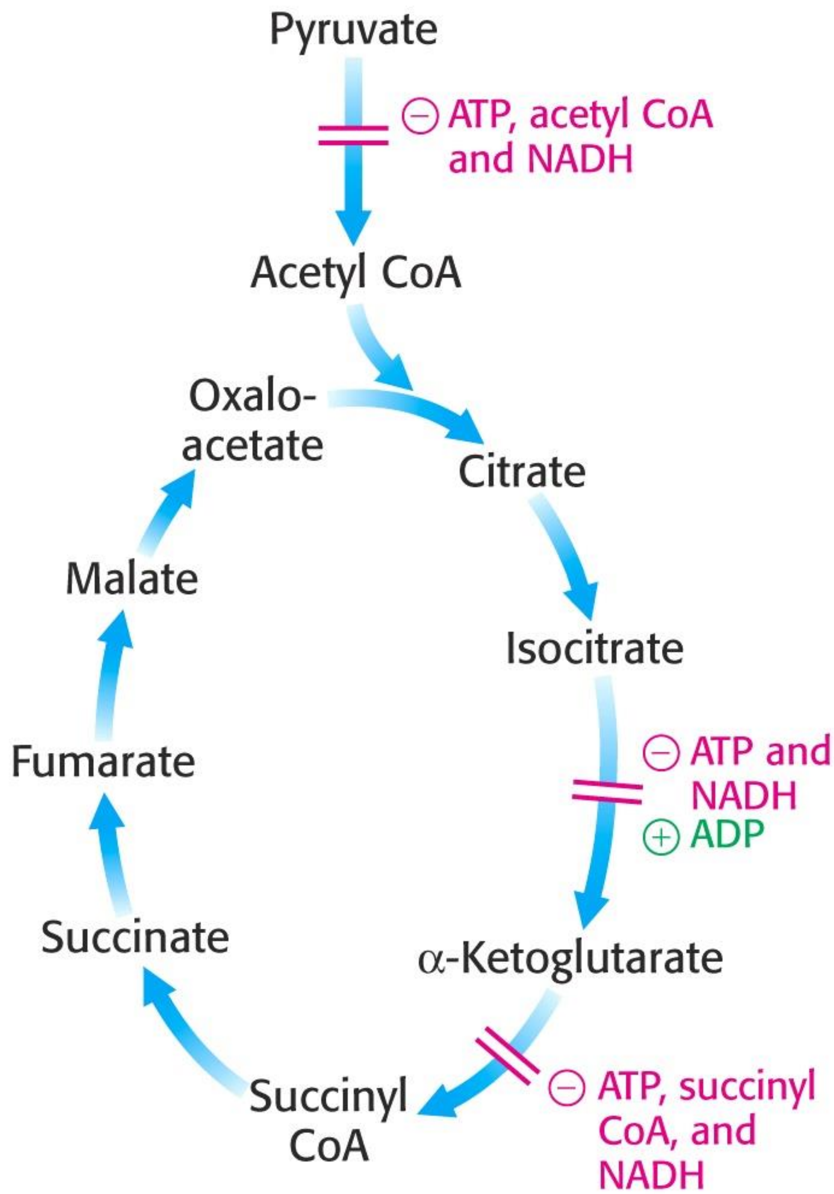
TABLE 17.2 **Citric acid cycle**

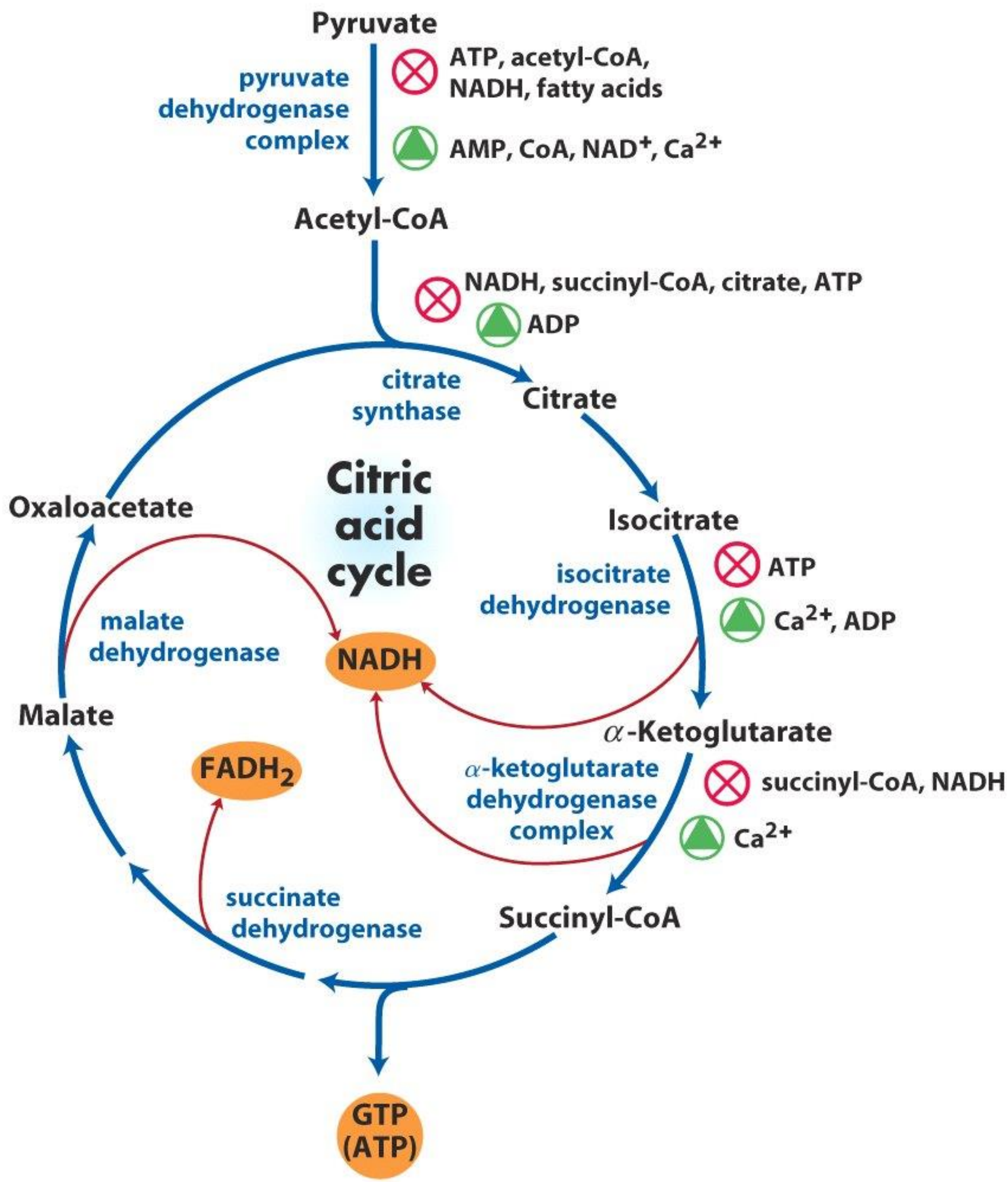
Step	Reaction	Enzyme	Prosthetic group	Type*	$\Delta G^{\circ\prime}$ kcal mol^{-1}	$\Delta G^{\circ\prime}$ kJ mol^{-1}
1	Acetyl CoA + oxaloacetate + $H_2O \longrightarrow$ citrate + CoA + H^+	Citrate synthase		a	−7.5	−31.4
2a	Citrate $\rightleftharpoons$ *cis*-aconitate + H_2O	Aconitase	Fe–S	b	+2.0	+8.4
2b	*cis*-Aconitate + $H_2O \rightleftharpoons$ isocitrate	Aconitase	Fe–S	c	−0.5	−2.1
3	Isocitrate + $NAD^+ \rightleftharpoons$ α-ketoglutarate + CO_2 + NADH	Isocitrate dehydrogenase		d + e	−2.0	−8.4
4	α-Ketoglutarate + NAD^+ + CoA $\rightleftharpoons$ succinyl CoA + CO_2 + NADH	α-Ketoglutarate dehydrogenase complex	Lipoic acid, FAD, TPP	d + e	−7.2	−30.1
5	Succinyl CoA + P_i + GDP $\rightleftharpoons$ succinate + GTP + CoA	Succinyl CoA synthetase		f	−0.8	−3.3
6	Succinate + FAD (enzyme-bound) $\rightleftharpoons$ fumarate + $FADH_2$ (enzyme-bound)	Succinate dehydrogenase	FAD, Fe–S	e	~0	0
7	Fumarate + $H_2O \rightleftharpoons$ L-malate	Fumarase		c	−0.9	−3.8
8	L-Malate + $NAD^+ \rightleftharpoons$ oxaloacetate + NADH + H^+	Malate dehydrogenase		e	+7.1	+29.7

*Reaction type: (a) condensation; (b) dehydration; (c) hydration; (d) decarboxylation; (e) oxidation; (f) substrate-level phosphorylation.

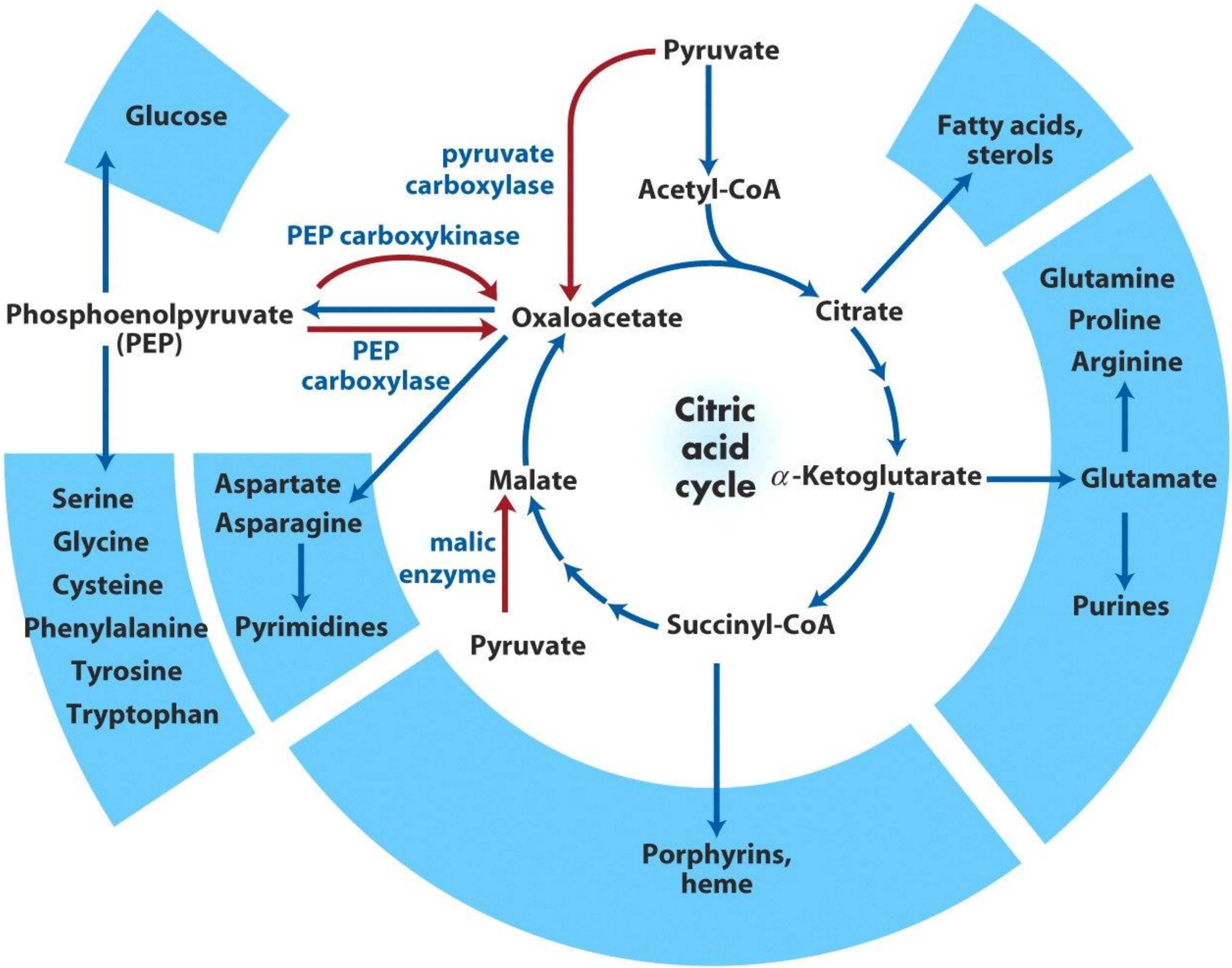
$$\textit{Asetil-SCoA} + NAD^+ + FAD + GDP + Pi + H_2O \rightarrow 2\,CO_2 + 3\,NADH + FADH_2 + GTP + 2\,H^+ + CoA$$

Pengendalian siklus





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
Citric acid cycle
Oxaloacetate
Isocitrate
isocitrate dehydrogenase
ATP
Ca2+, ADP
malate dehydrogenase
NADH
Malate
α-Ketoglutarate
FADH2
α-ketoglutarate dehydrogenase complex
succinyl-CoA, NADH
Ca2+
succinate dehydrogenase
Succinyl-CoA
GTP (ATP)


Pyruvate
pyruvate
carboxylase
Acetyl-CoA
Glucose
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