Bioenergetics of Metabolic Pathways

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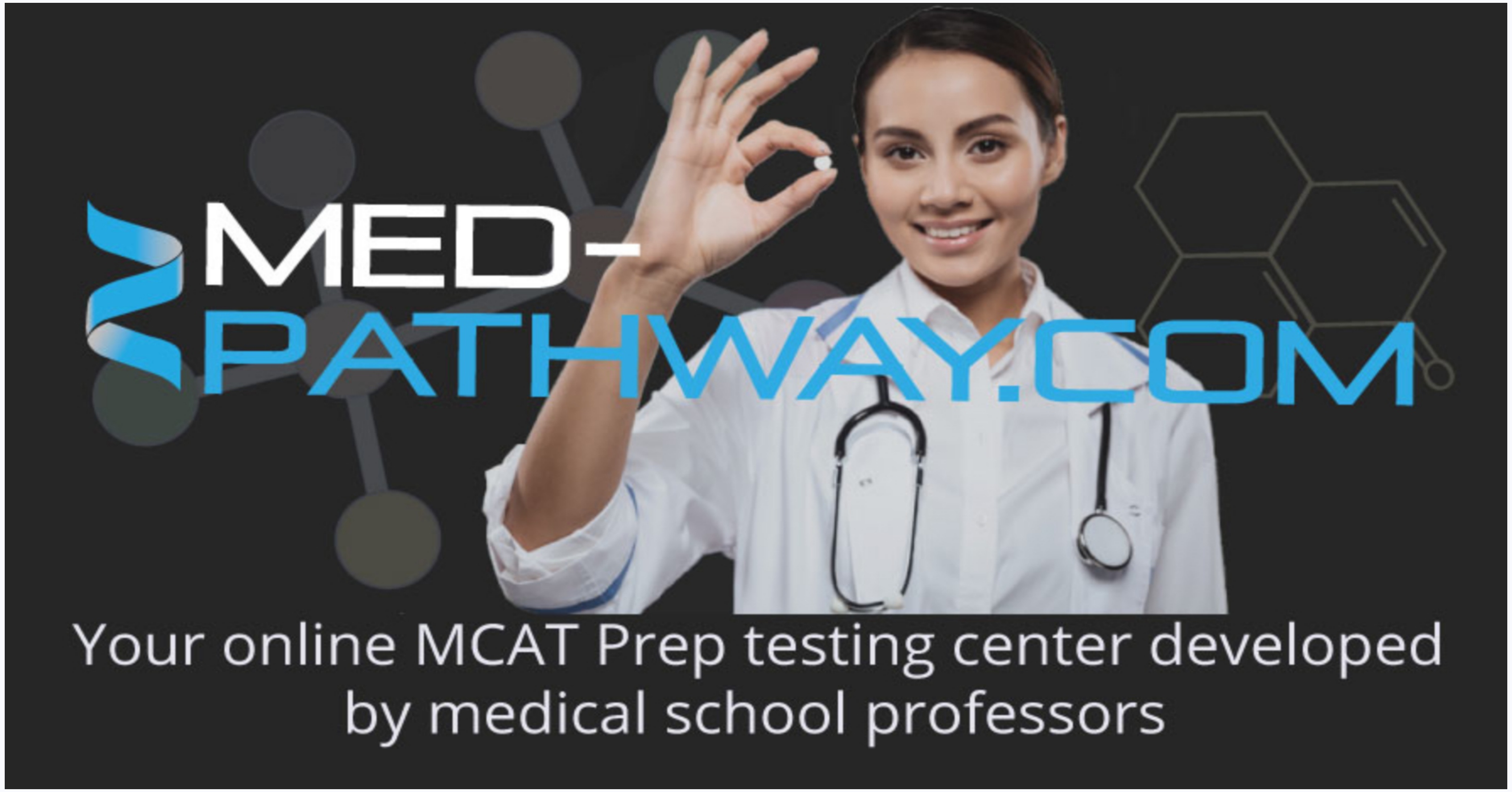

1st Law of Thermodynamics

Energy can neither be created nor destroyed,
but can be converted from one form to another.

$$U = \text{Energy} = Q - W$$

Work done *on* the system by the surroundings

Heat supplied to the system

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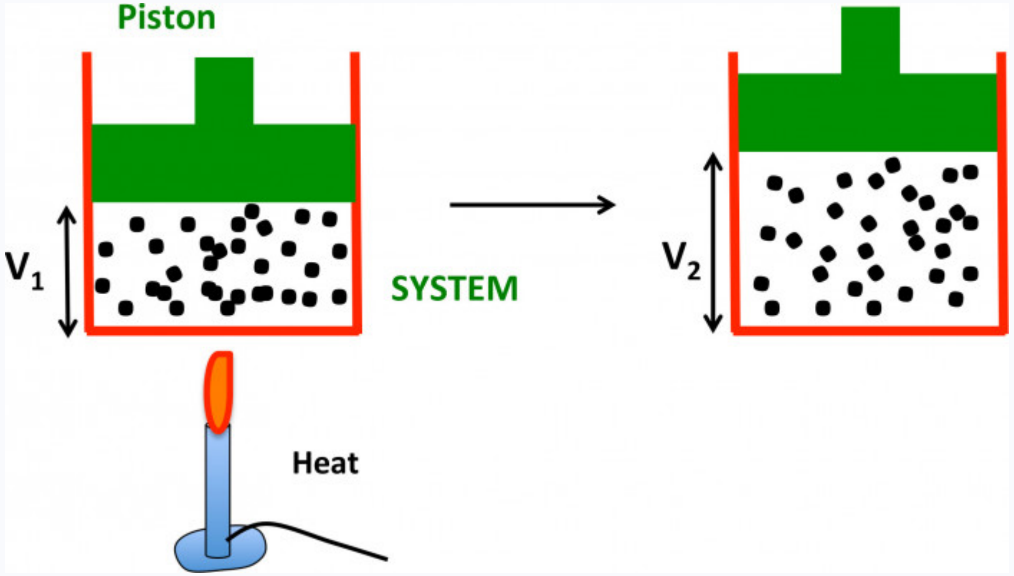
1st Law of Thermodynamics



1. Infused heat into system expands volume ($V_2 > V_1$)
2. Gas molecules (system) do work on surroundings
3. System loses energy in the form of work ($-\Delta W$).
4. Energy of heat is converted into the energy of work. $W = P\Delta V$

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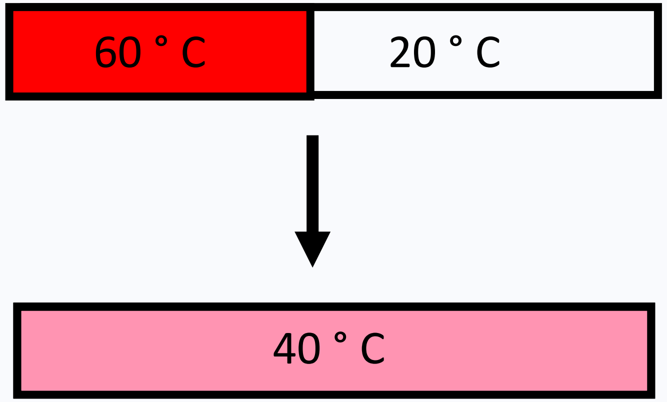
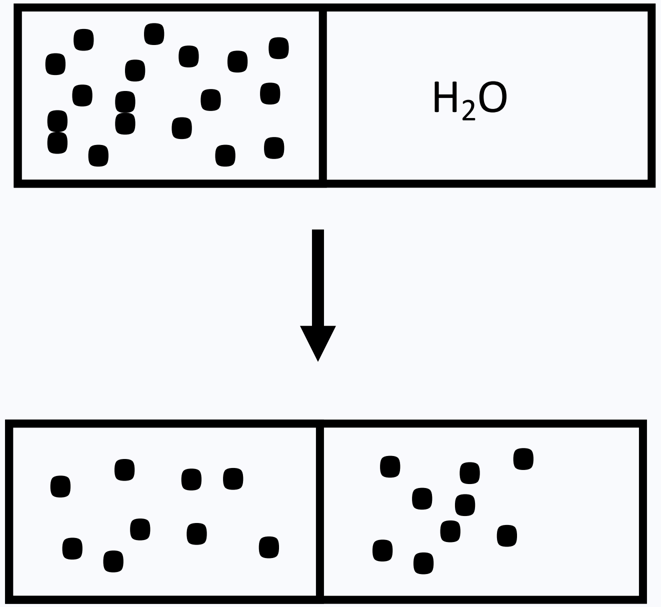
2^{nd} Law of Thermodynamics

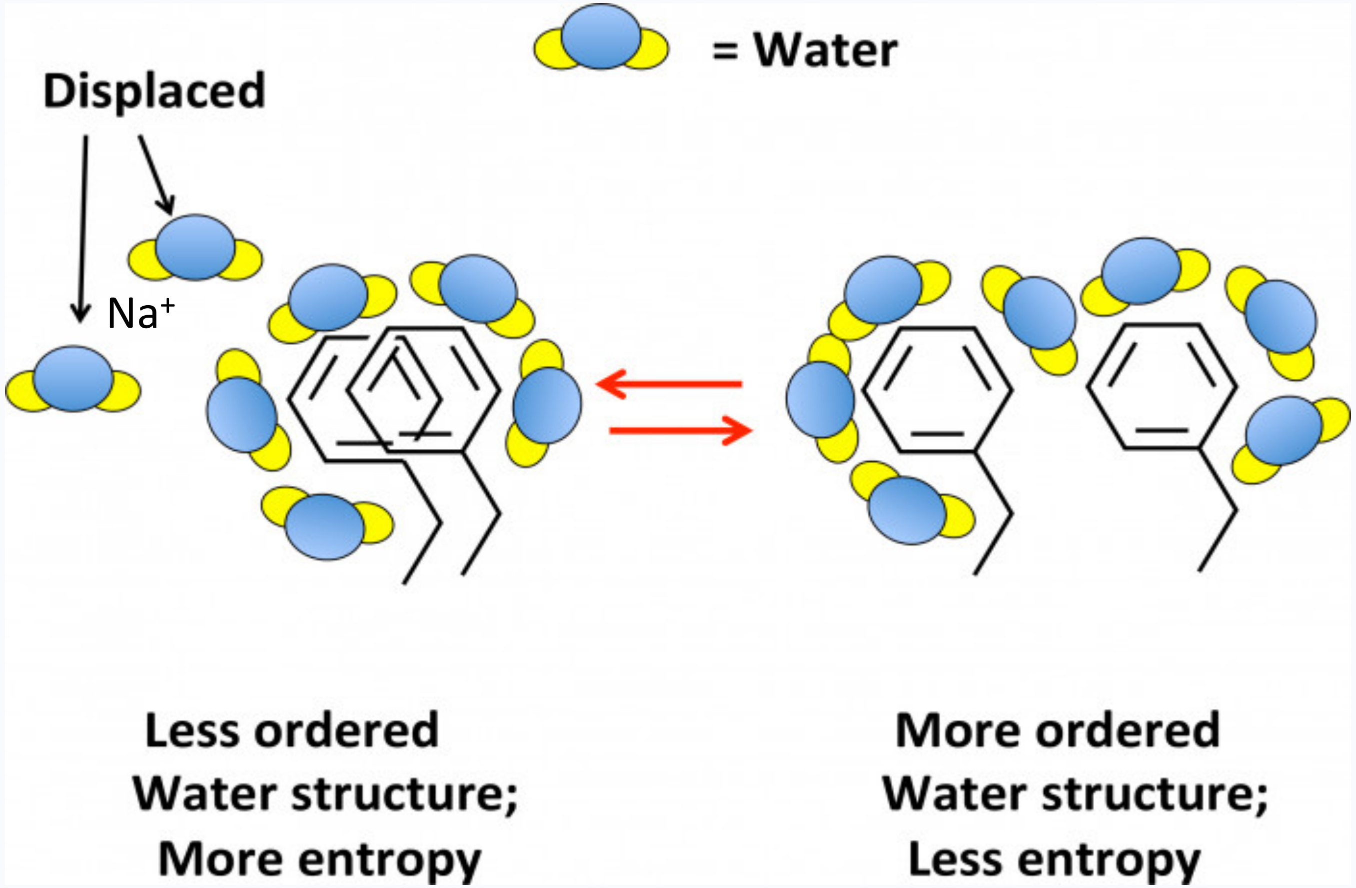
Spontaneity of chemical reactions

$$\Delta S_{System} + \Delta S_{Surroundings} > \textbf{Spontaneous Process}$$





Hydrophobic Effect and Entropy



Free Energy

Entropy is difficult to measure

$$\Delta G = \Delta H - T\,\Delta S$$

Gibbs Free Energy — Enthalpy — Temperature — Entropy

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Free Energy & Entropy

Entropy is difficult to measure

$$\Delta G = \Delta H - T\,\Delta S$$

Gibbs Free Energy · Enthalpy · Temperature · Entropy

$$\Delta G = \Delta G^{\circ} + (RT)(\ln K_{eq})$$

Free Energy & Entropy

Entropy is difficult to measure

$$\Delta G = \Delta H - T \Delta S$$

Gibbs Free Energy

Enthalpy

Temperature

Entropy

Actually occurs in cells

Gas Constant

$$K_{eq} = [\text{Reactants}]/[\text{Products}]$$

$$\Delta G = \Delta G° + (RT)(\ln K_{eq})$$

Standard (1.0 M reactants/products; pH = 8.0)

Temperature

Free Energy & Entropy

Entropy is difficult to measure

$$\Delta G = \Delta H - T\,\Delta S$$

Gibbs Free Energy

Enthalpy

Temperature

Entropy

Actually occurs in cells

Gas Constant

$\mathbf{K_{eq} = [Reactants]/[Products]}$

$$\mathbf{\Delta G = \Delta G^\circ + (RT)(\ln K_{eq})}$$

Standard (1.0 M reactants/products; pH = 8.0)

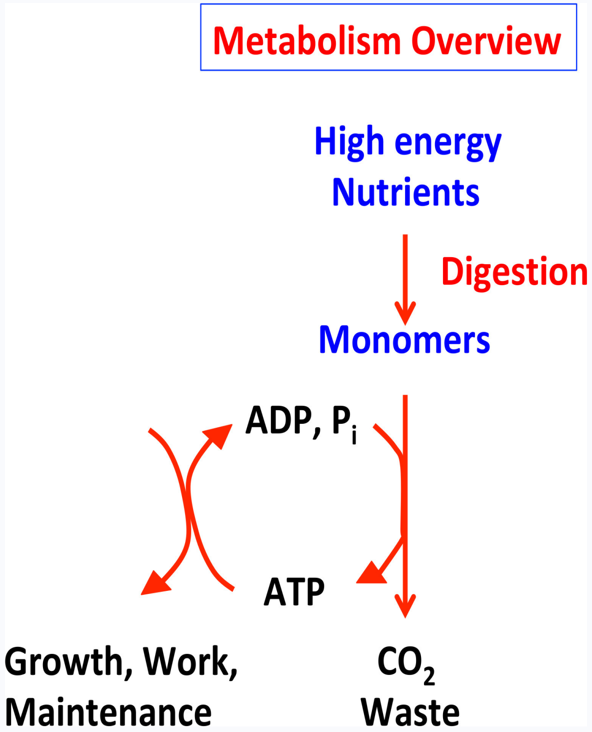
Temperature

$\Delta G = 0$ at equilibrium $\quad \Delta G = -RT\ln K_{eq}$

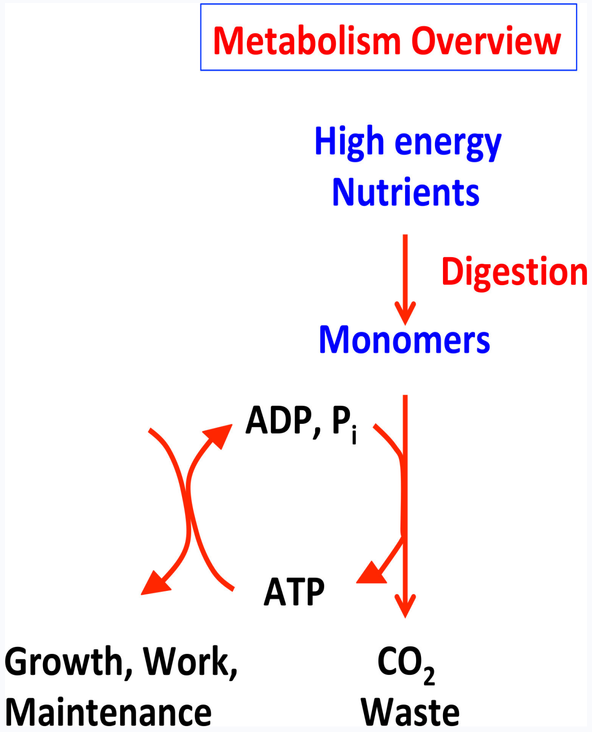
$\Delta G < 0$ for spontaneous processes

$\Delta G > 0$ for spontaneous processes

Energetics of Metabolism



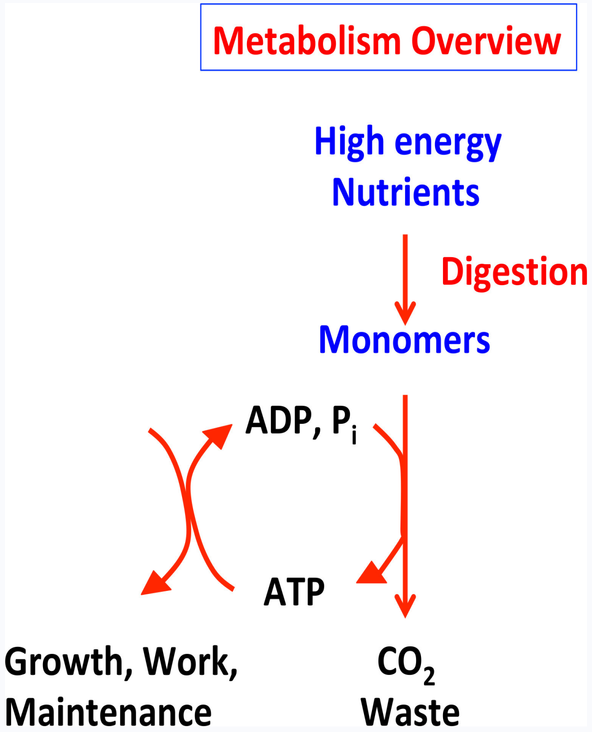
Energetics of Metabolism



BOND	Dissociation energy kJ/mol
C-H	400
C-O	350
C-C	350
O-H	450

Amount of energy released upon cleavage of bond (enthalpy **Δ**H or heat)

Energetics of Metabolism



BOND	Dissociation energy kJ/mol
C-H	400
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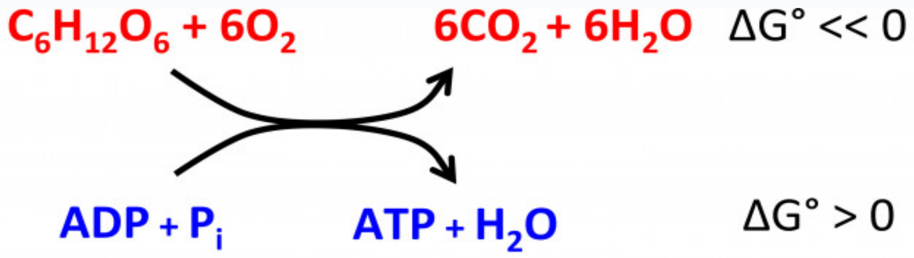
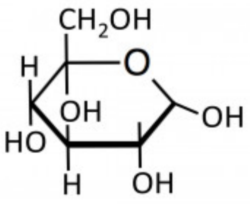
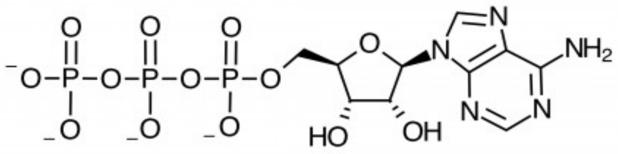
O-H	450

Amount of energy released upon cleavage of bond (enthalpy **Δ**H or heat)





Glucose



ATP

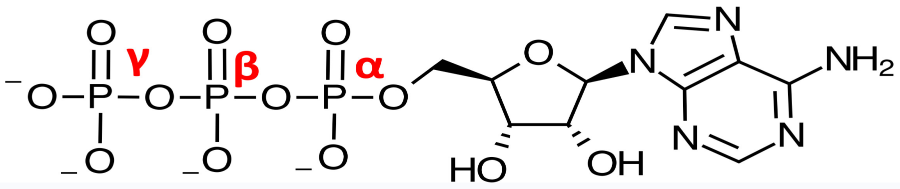
ATP hydrolysis

Phosphorylated Metabolite	ΔG° kcal/mol
PEP (phosphoenolpyruvate)	-15.0
Phosphocreatine	-10.0
ATP	-7.0
PP_i (Pyrophosphate)	-7.0
Glucose 6-Phosphate	-3.0

$ATP + H_2O \longleftrightarrow AMP + PP_I$ $\quad \Delta G° = -7.0$ kcal/mol

$PP_I + H_2O \longleftrightarrow 2P_I$ $\quad \Delta G° = -7.0$ kcal/mol

$ATP + 2\,H_2O \longrightarrow AMP + 2P_I$ $\quad \Delta G° = -14.0$ kcal/mol



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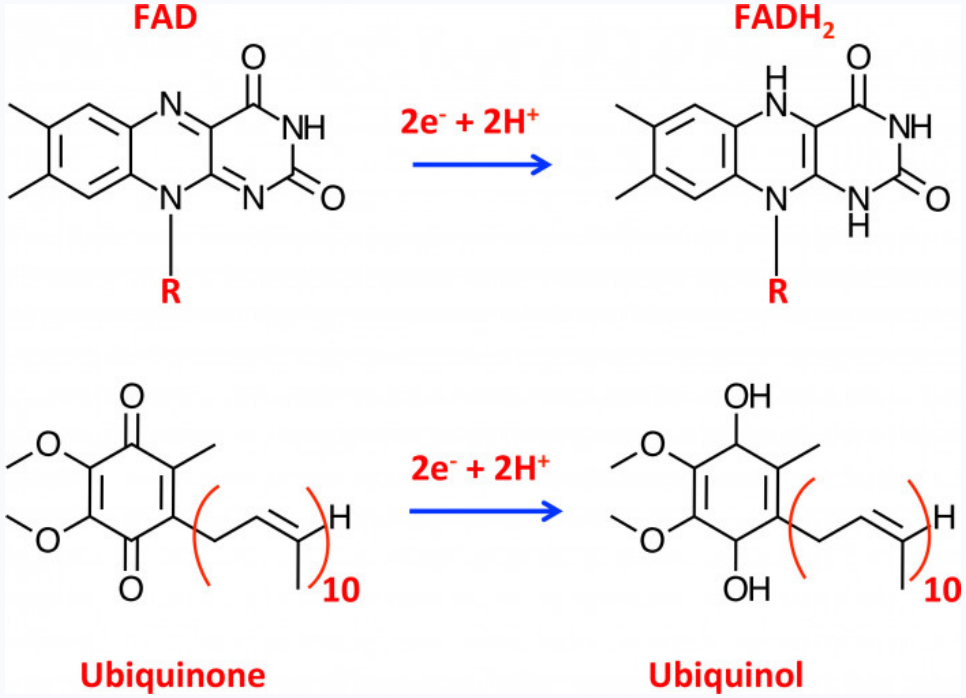
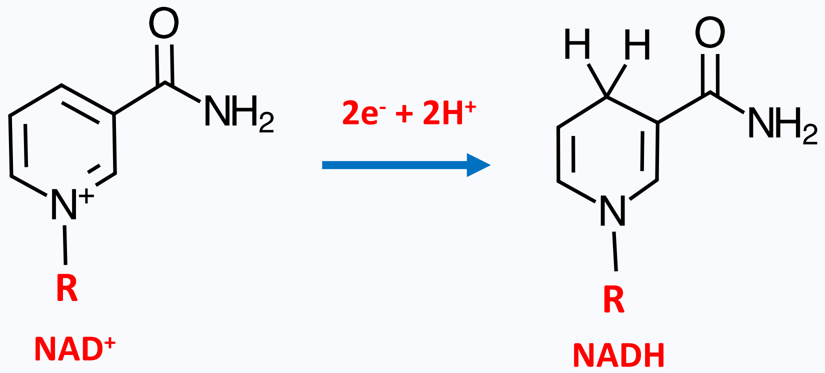
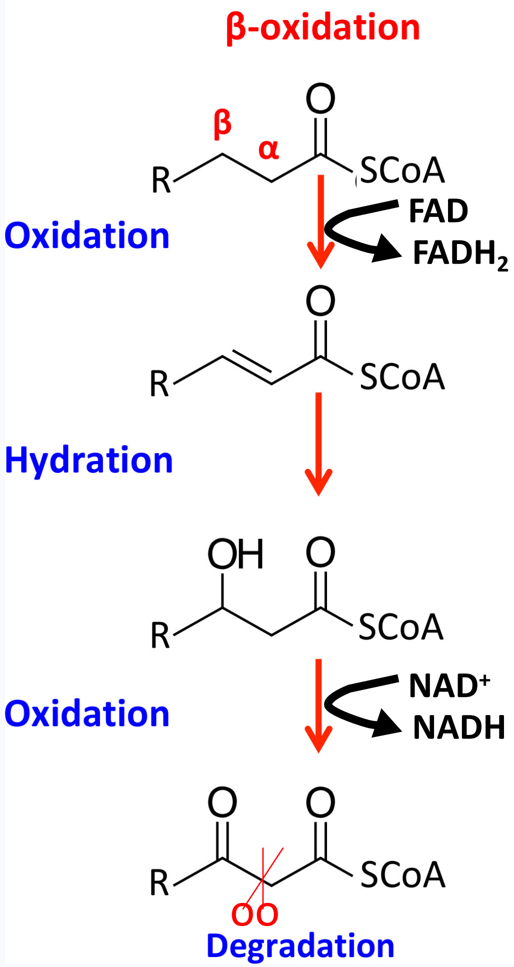
Electron transfer potential and synthesis of ATP

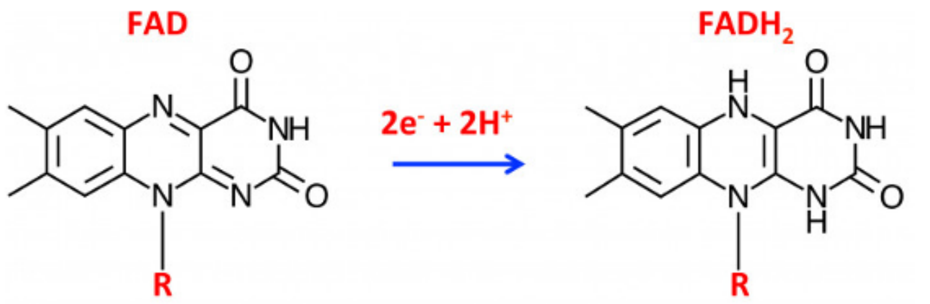


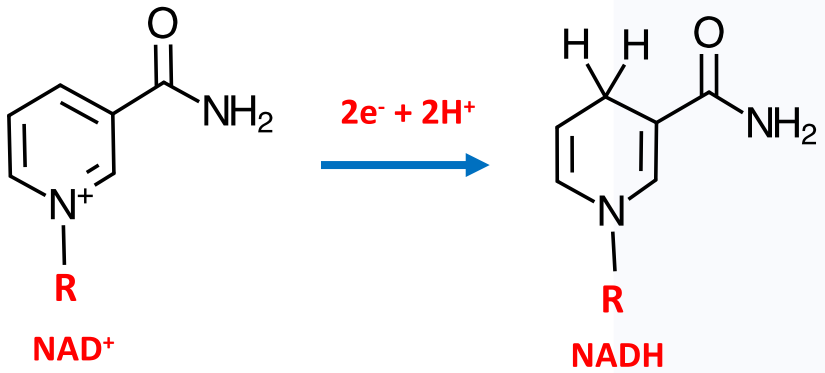


High Energy Carriers

Fatty Acid Oxidation







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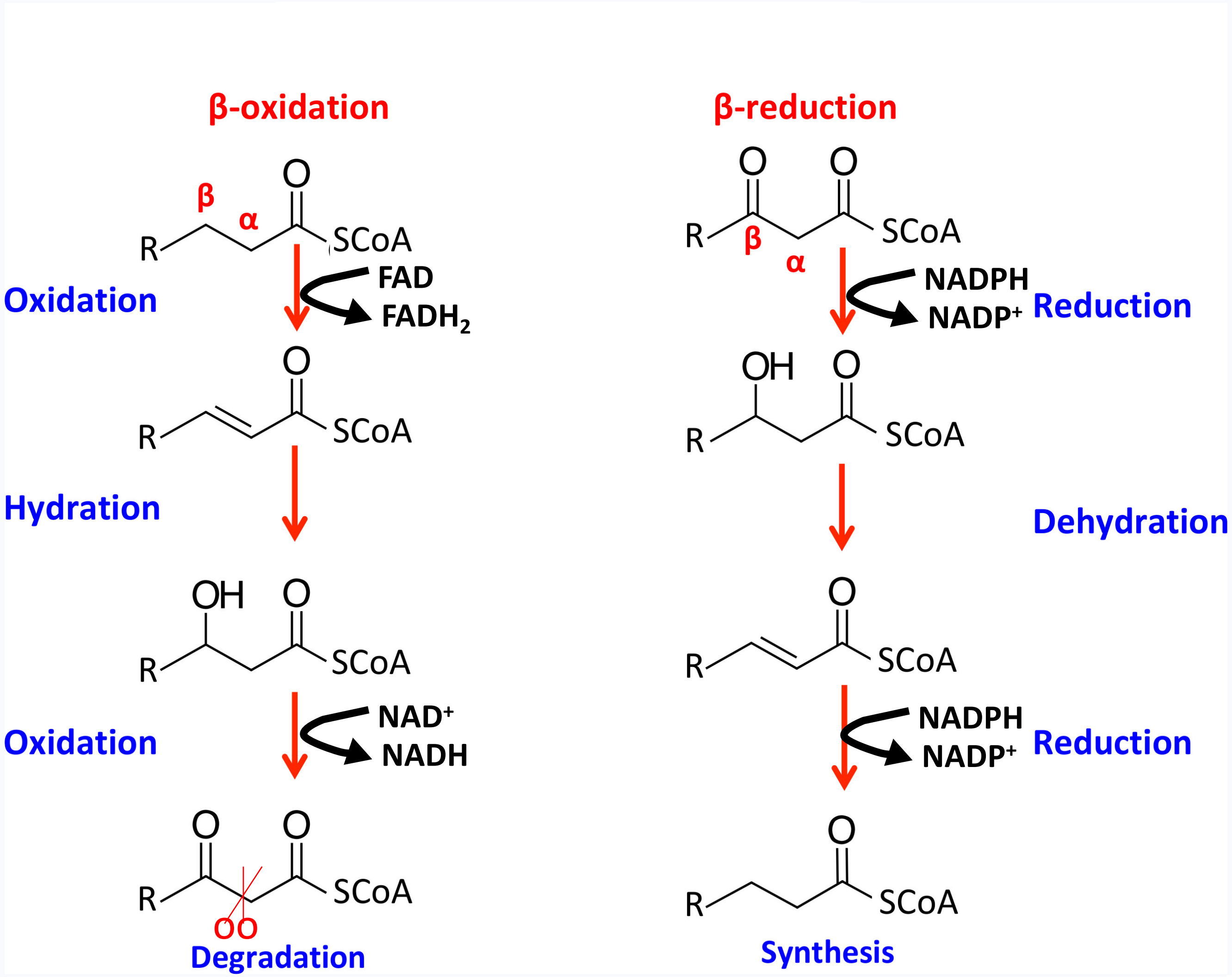
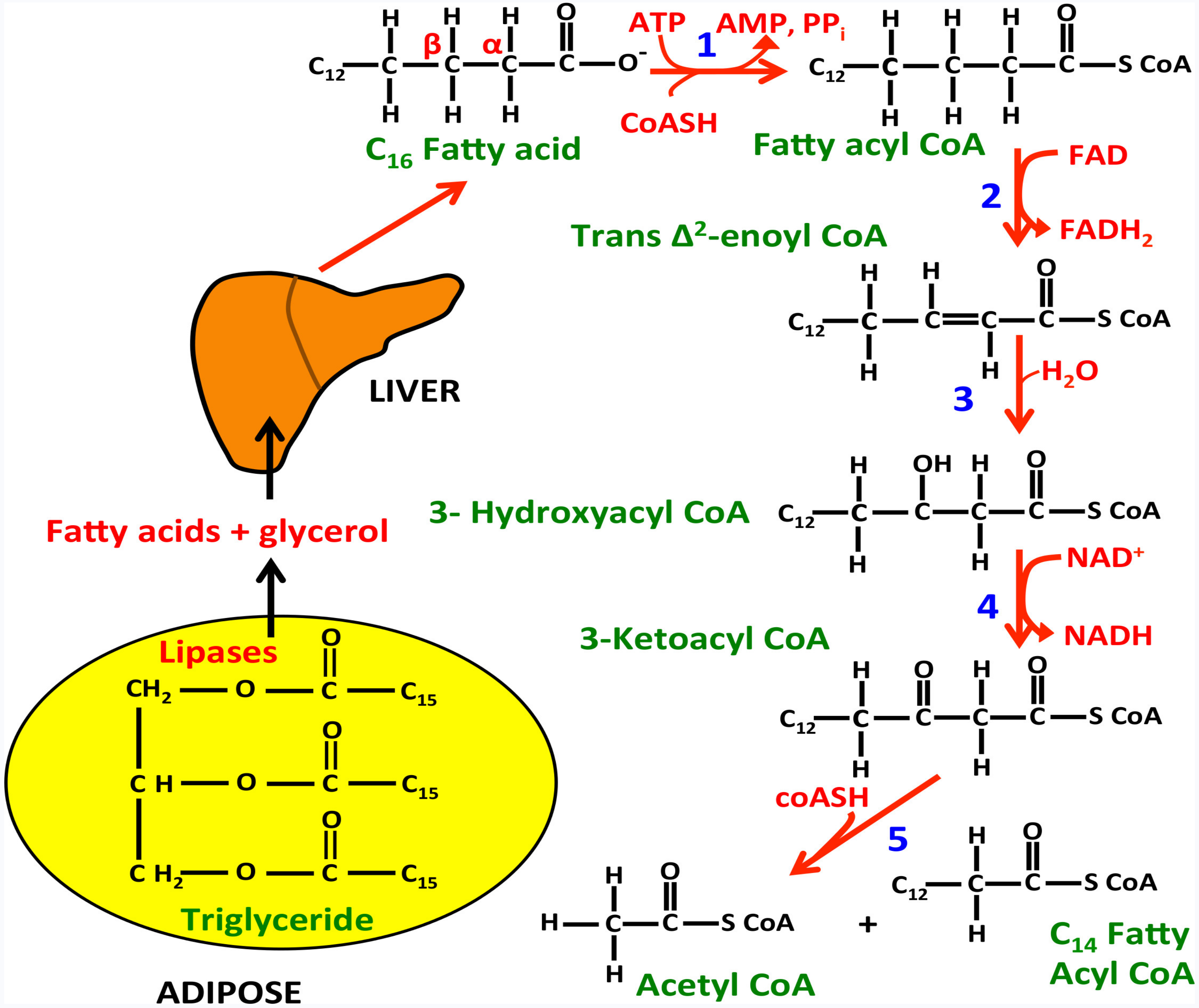
Fatty Acid Oxidation & Reduction



Fatty Acid Oxidation



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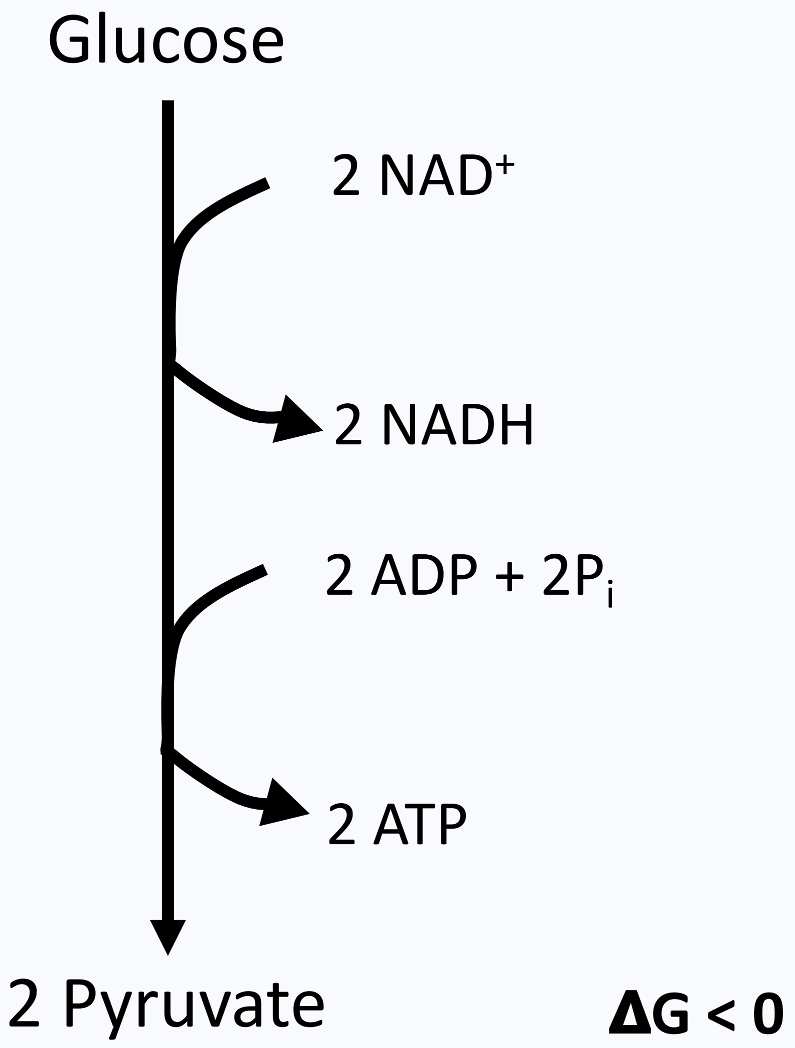
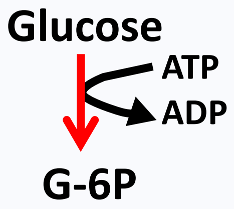
Partial Oxidation of Glucose in Glycolysis

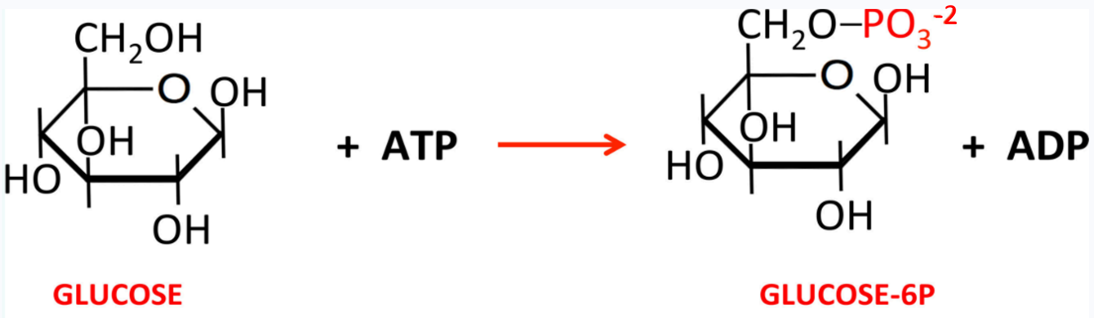


Energetics & Glycolysis

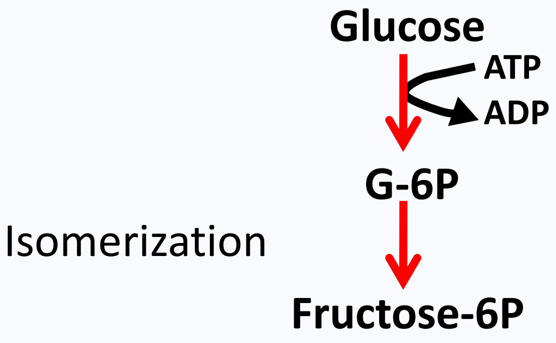
Hexokinase



ΔG = -8.0 kcal/mol



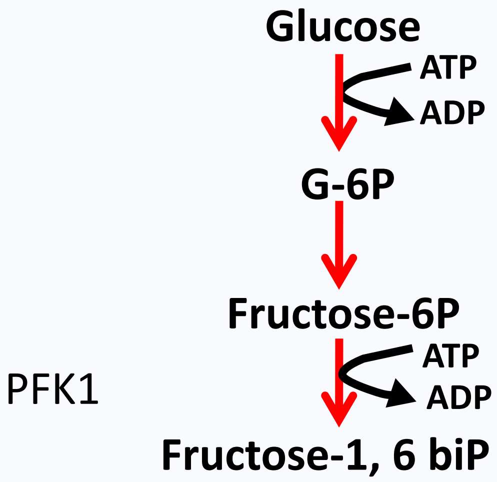
Energetics & Glycolysis



ΔG = -7.3 kcal/mol

ΔG = -.05 kcal/mol

Energetics & Glycolysis



ΔG = -8.0 kcal/mol

ΔG = -0.6 kcal/mol

ΔG = -5.3 kcal/mol

Energetics & Glycolysis

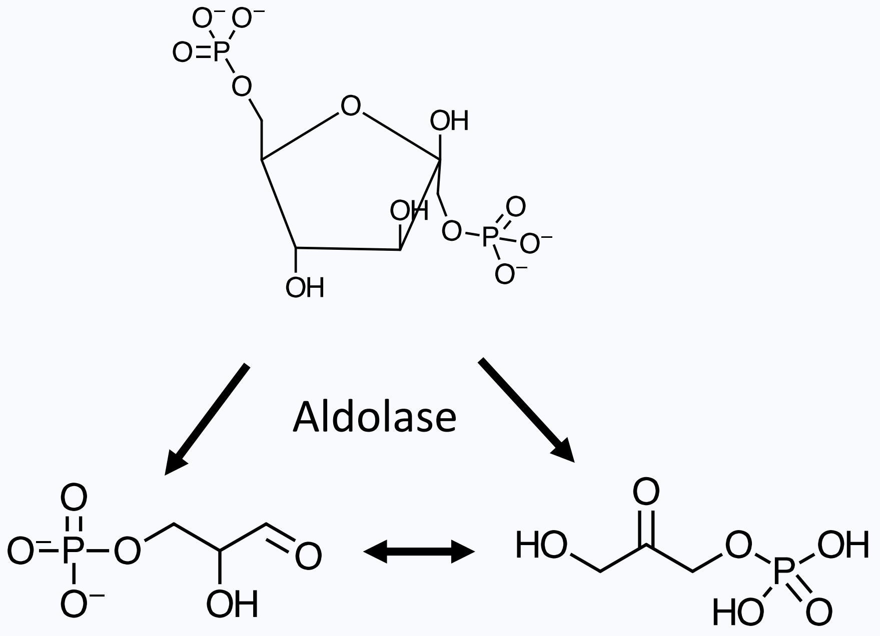
Glucose
ATP
ADP
G-6P
Fructose-6P
ATP
ADP
Fructose-1, 6 biP
Aldolase
G-3P + DHAP

ΔG = -8.0 kcal/mol

ΔG = -0.6 kcal/mol

ΔG = -5.3 kcal/mol

ΔG = -0.3 kcal/mol



G-3P

DHAP

Structural Isomers

Energetics & Glycolysis

Glucose

ATP → ADP

$\Delta G = -8.0$ kcal/mol

G-6P

$\Delta G = -0.6$ kcal/mol

Fructose-6P

ATP → ADP

$\Delta G = -5.3$ kcal/mol

Fructose-1, 6 biP

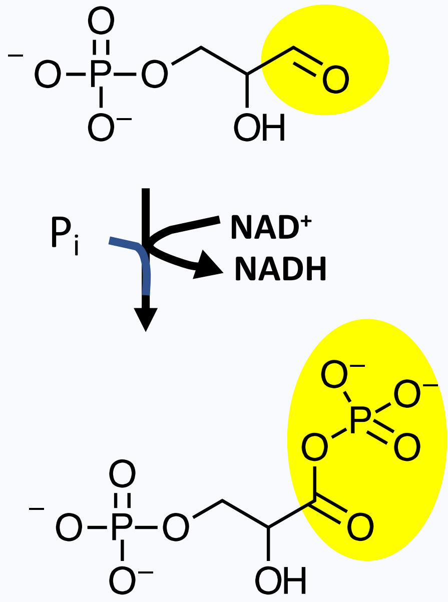
$\Delta G = -0.3$ kcal/mol

GAP + DHAP

P_i, NAD^+ → NADH

$\Delta G = -0.4$ kcal/mol

1, 3-Biphosphoglycerate

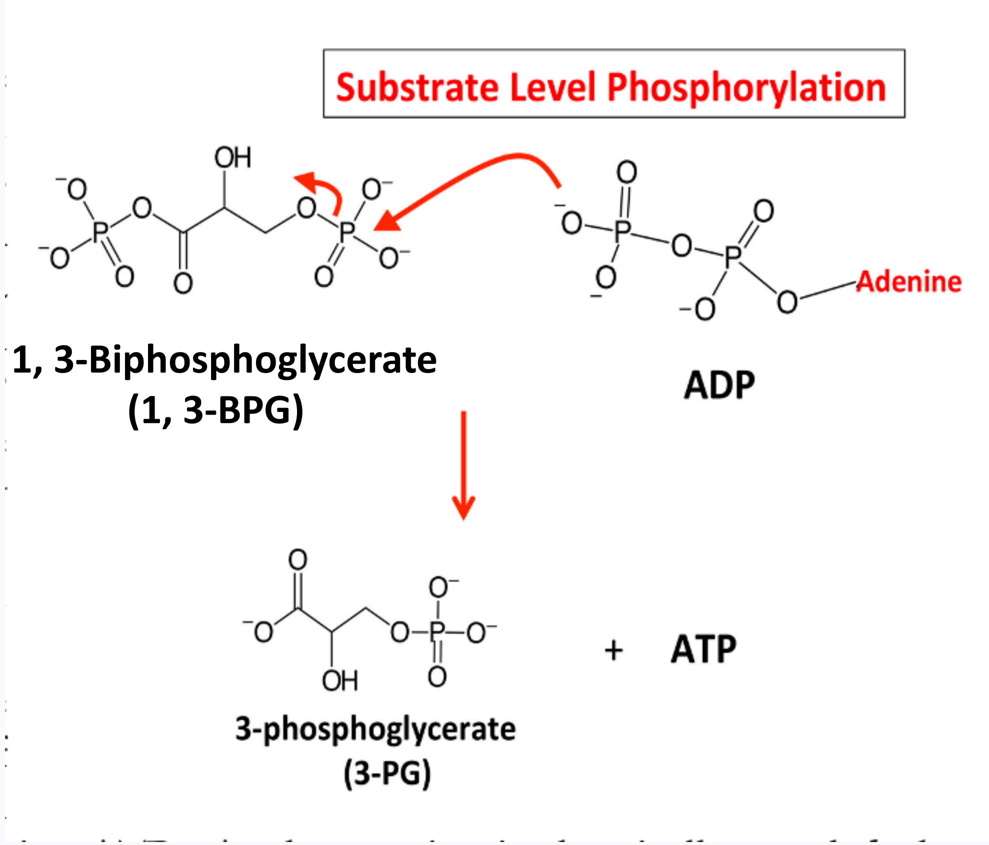


GAP

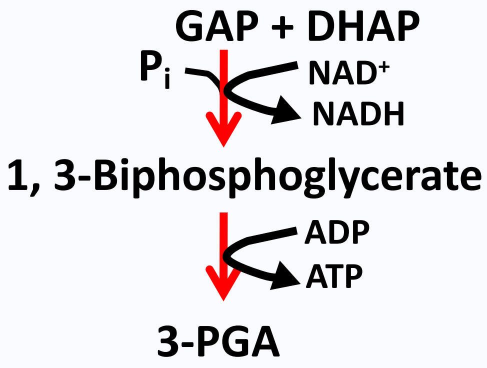
1, 3-BPG

Energetics & Glycolysis

Glucose
↓ ATP → ADP — ΔG = -8.0 kcal/mol
G-6P
↓ — ΔG = -0.6 kcal/mol
Fructose-6P
↓ ATP → ADP — ΔG = -5.3 kcal/mol
Fructose-1, 6 biP
↓ — ΔG = -0.3 kcal/mol
GAP + DHAP
↓ P_i, NAD^+ → NADH — ΔG = -0.4 kcal/mol
1, 3-Biphosphoglycerate
↓ ADP → ATP — ΔG = +0.3 kcal/mol
3-PGA



Coupling of Reactions



ΔG = -0.4 kcal/mol

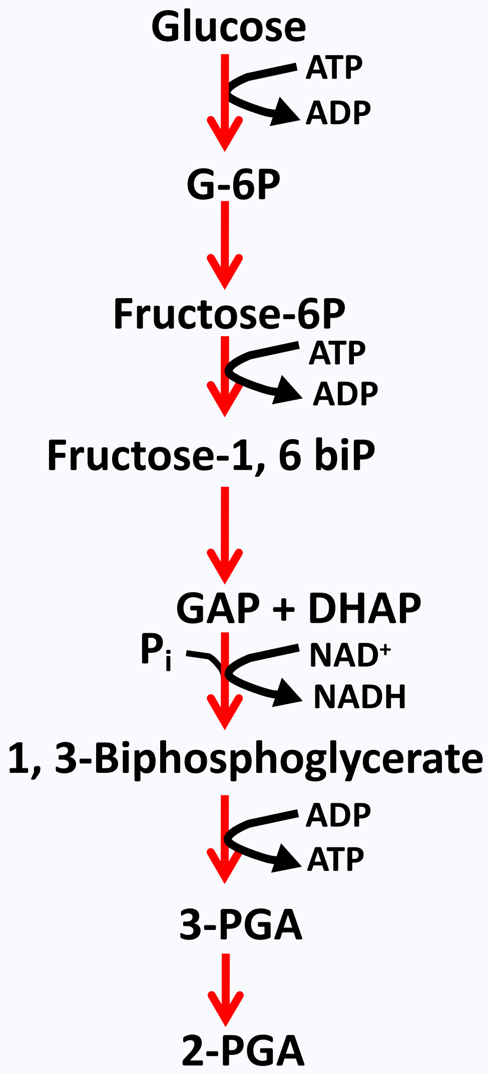
ΔG = +0.3 kcal/mol

I. GAP + NAD^+ + H_2O $\rightleftharpoons$ 3-Phosphoglyceric acid + NADH + H^+ **ΔG < 0**

II. 3-Phosphoglyceric acid + P_i $\rightleftharpoons$ 1, 3 BPG + H_2O **ΔG > 0**

NET GAP + NAD^+ + P_i $\rightleftharpoons$ 1, 3 BPG + NADH + H^+ **ΔG < 0**

Energetics & Glycolysis



ΔG = -8.0 kcal/mol

ΔG = -0.6 kcal/mol

ΔG = -5.3 kcal/mol

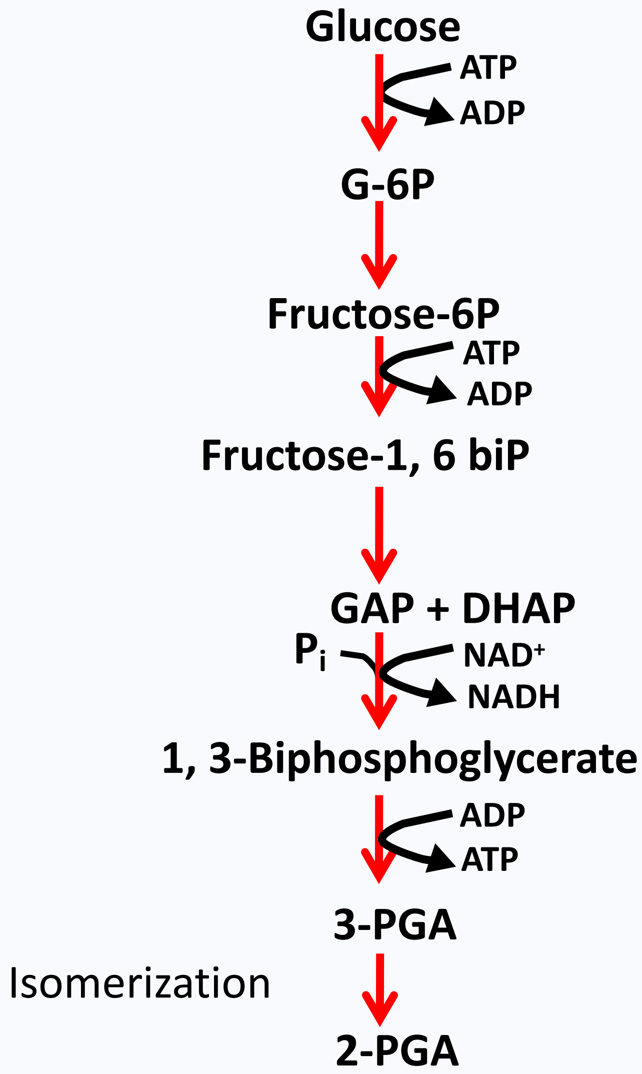
ΔG = -0.3 kcal/mol

ΔG = -0.4 kcal/mol

ΔG = +0.3 kcal/mol

ΔG = +0.2 kcal/mol

Energetics & Glycolysis



ΔG = -8.0 kcal/mol

ΔG = -0.6 kcal/mol

ΔG = -5.3 kcal/mol

ΔG = -0.3 kcal/mol

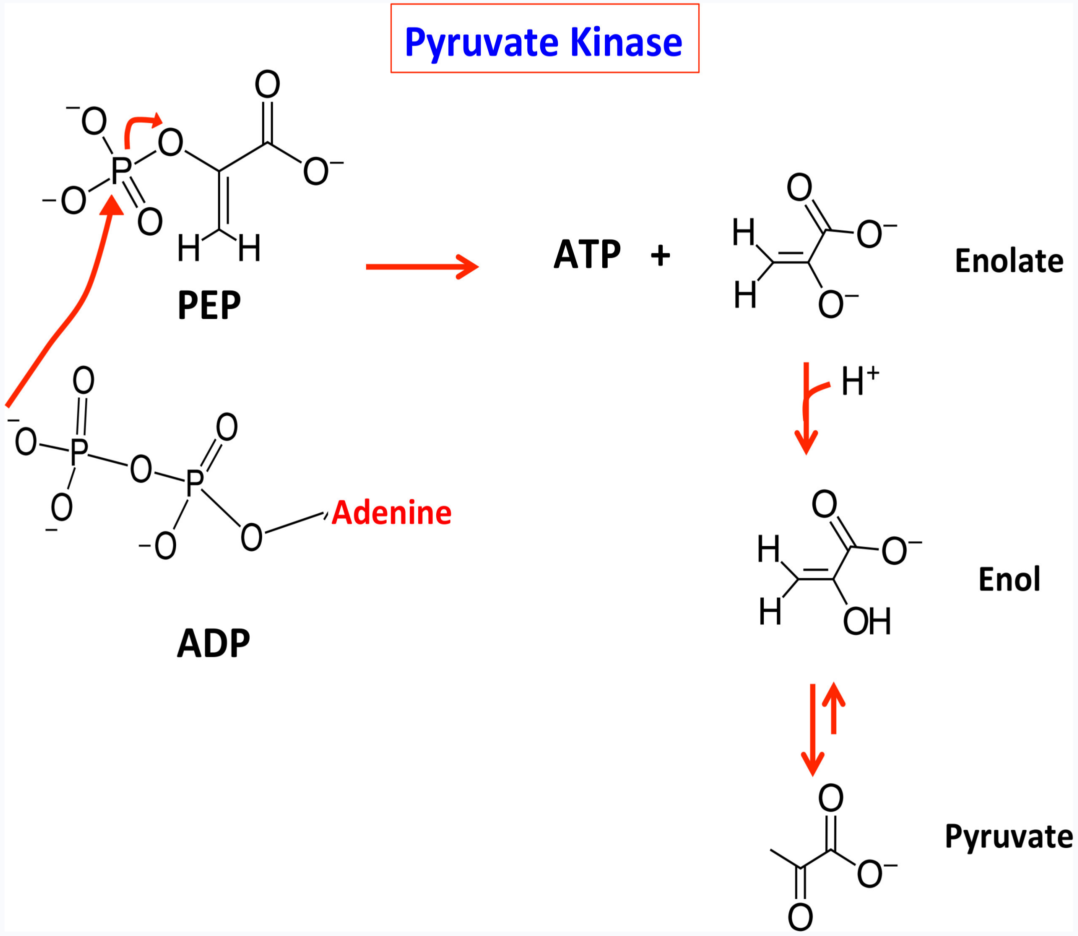
ΔG = -0.4 kcal/mol

ΔG = +0.3 kcal/mol

ΔG = +0.2 kcal/mol

Energetics & Glycolysis

Glucose → G-6P	ATP → ADP	ΔG = -7.3 kcal/mol
G-6P → Fructose-6P		ΔG = -.05 kcal/mol
Fructose-6P → Fructose-1, 6 biP	ATP → ADP	ΔG = -6.0 kcal/mol
Fructose-1, 6 biP → GAP + DHAP		ΔG = -0.2 kcal/mol
GAP + DHAP → 1, 3-Biphosphoglycerate	P_i; NAD^+ → NADH	ΔG = -0.4 kcal/mol
1, 3-Biphosphoglycerate → 3-PGA	ADP + P_i → ATP	ΔG = +0.3 kcal/mol
3-PGA → 2-PGA		ΔG = +0.2 kcal/mol
2-PGA → PEP		ΔG = -0.8 kcal/mol
PEP → Pyruvate (PK)	ADP + P_i → ATP	ΔG = -4.0 kcal/mol



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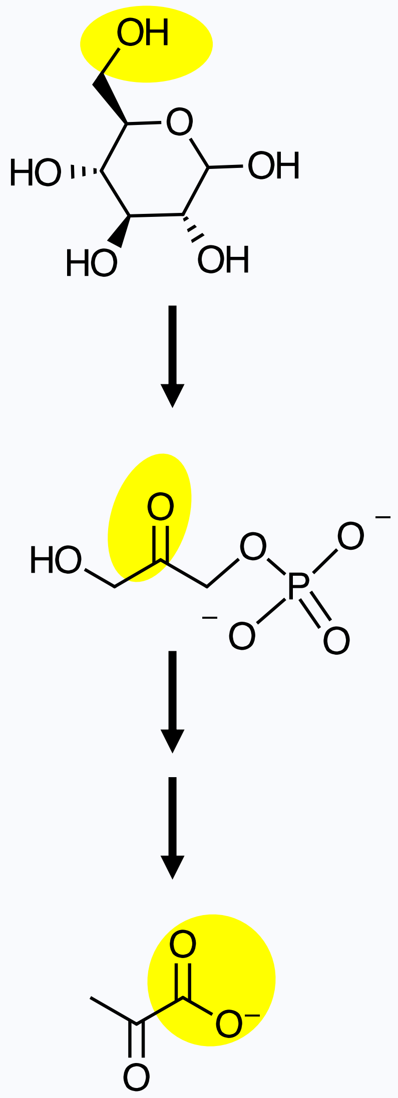
Energetics & Glycolysis

- Glucose → G-6P (ATP → ADP): ΔG = -8.0 kcal/mol
- G-6P → Fructose-6P: ΔG = -0.6 kcal/mol
- Fructose-6P → Fructose-1, 6 biP (ATP → ADP): ΔG = -5.3 kcal/mol
- Fructose-1, 6 biP → GAP + DHAP: ΔG = -0.3 kcal/mol
- GAP + DHAP → 1, 3-Biphosphoglycerate (P_i; NAD^+ → NADH): ΔG = -0.4 kcal/mol
- 1, 3-Biphosphoglycerate → 3-PGA (ADP → ATP): ΔG = +0.3 kcal/mol
- 3-PGA → 2-PGA: ΔG = +0.2 kcal/mol
- 2-PGA → PEP: ΔG = -0.8 kcal/mol
- PEP → Pyruvate (ADP + P_i → ATP): ΔG = -4.0 kcal/mol

ΔG = -18.9 kcal/mol



Glucose

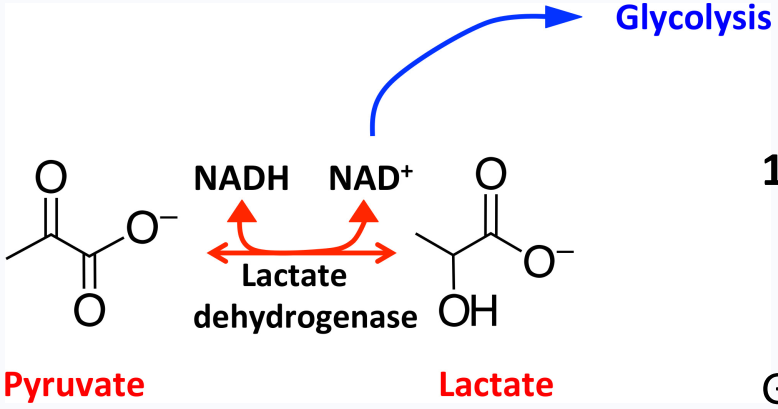
DHAP

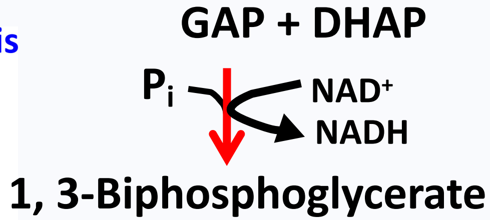
Pyruvate

$$\text{Glucose} + 2\text{ADP} + 2P_i + 2NAD^+ \longrightarrow 2\ \text{Pyruvate} + 2\text{ATP} + 2\text{NADH}$$

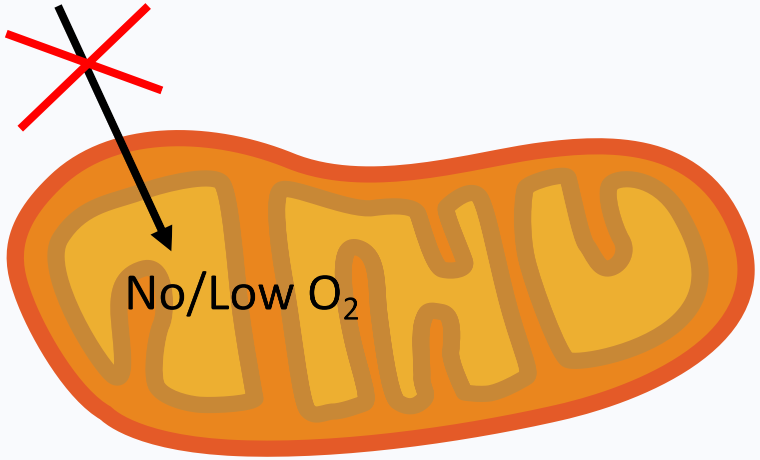
Anaerobic Respiration

Glycolysis is anerobic

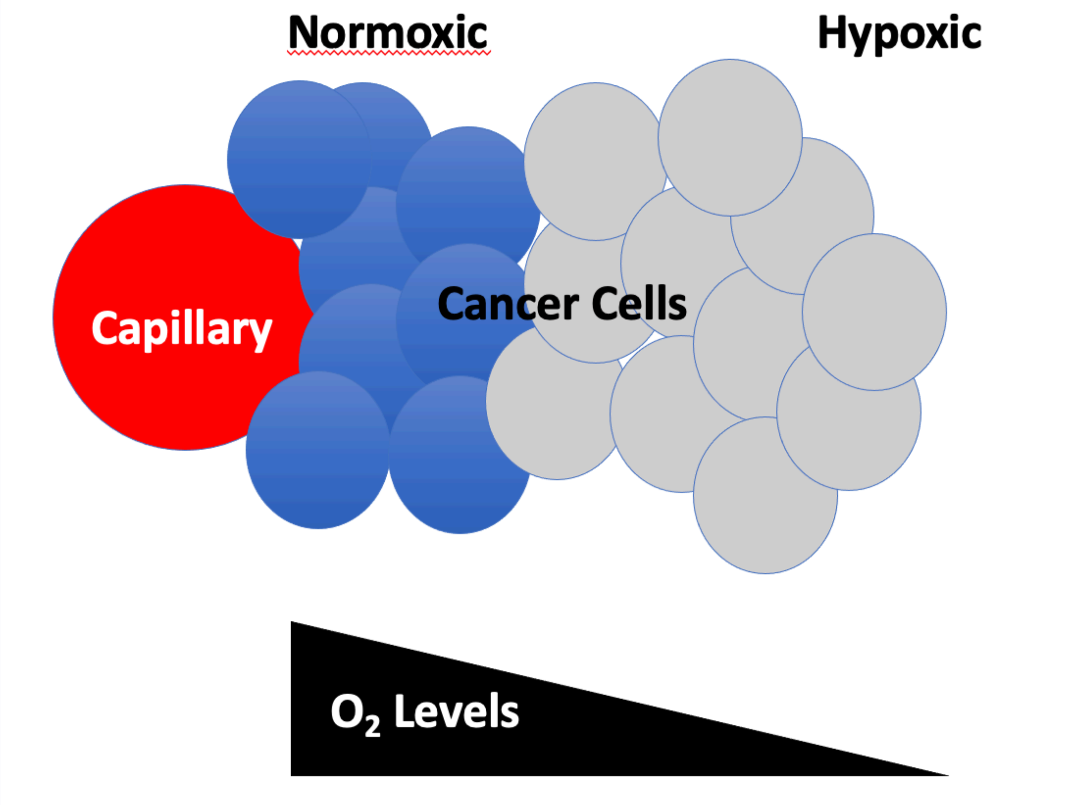


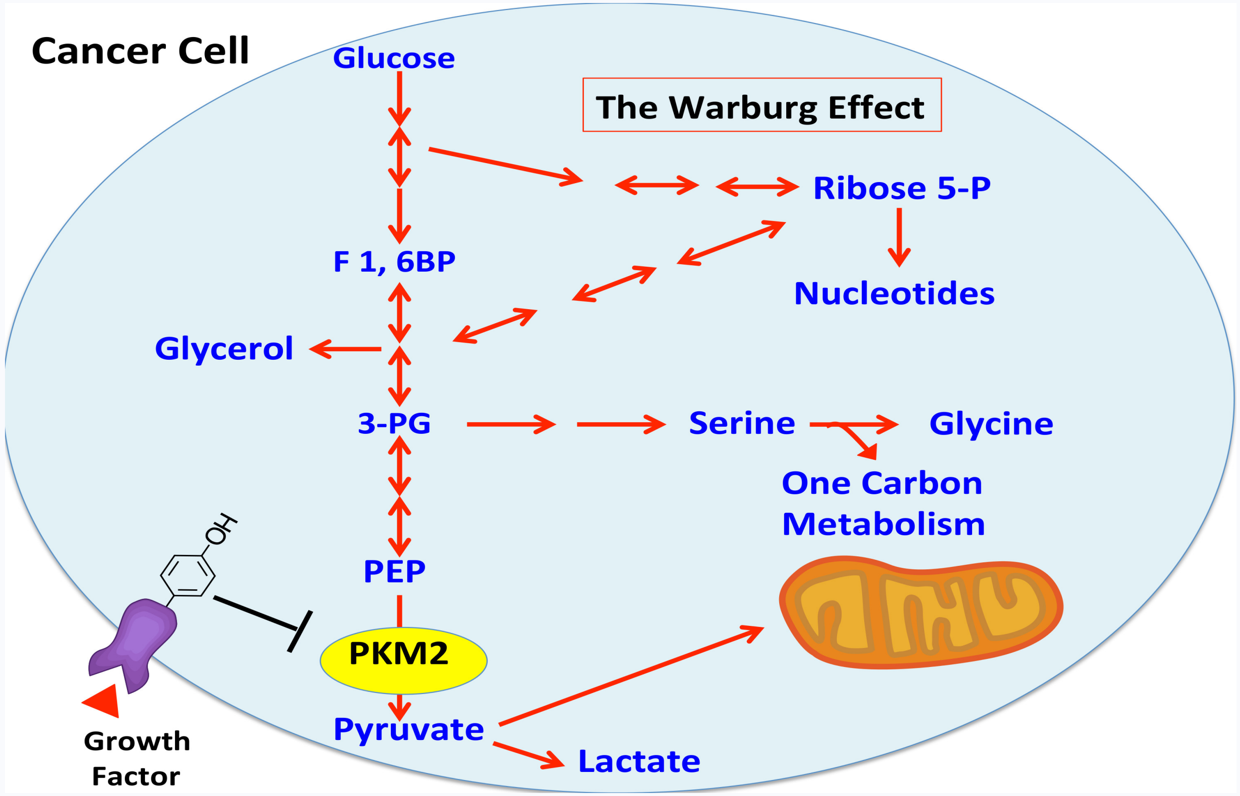


Glucose + 2ADP +2P_i $\longrightarrow$ 2 Lactate + 2TP



The Warburg Effect Aerobic Glycolysis



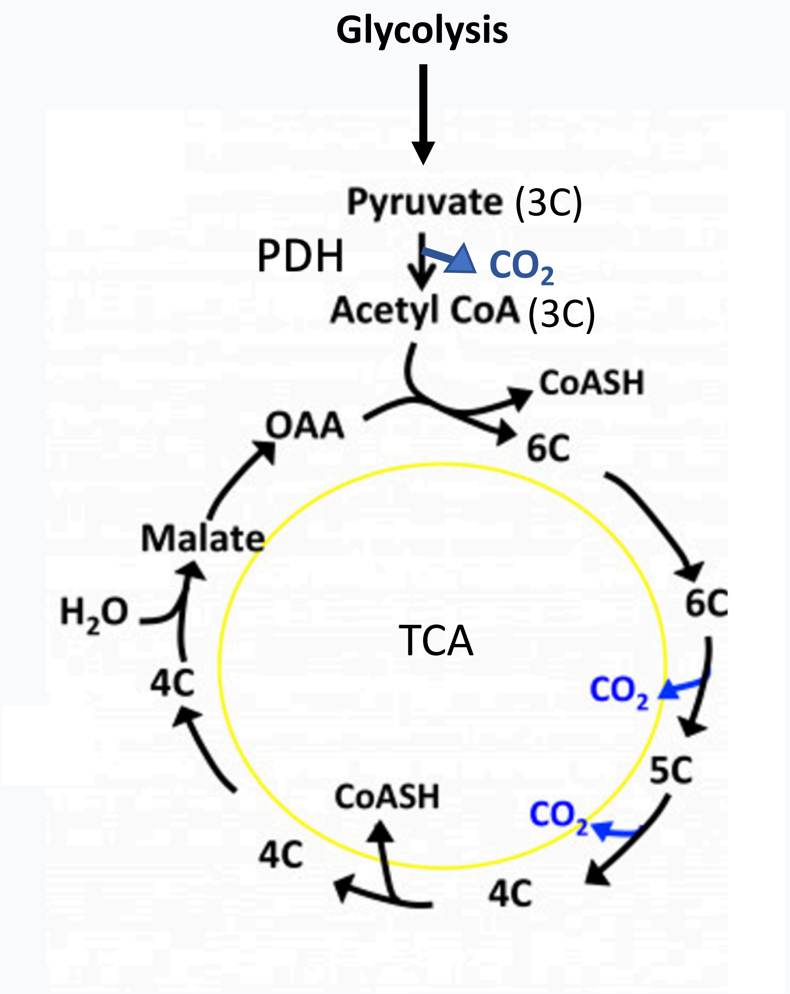


Pyruvate Dehydrogenase

Pyruvate + CoASH + NAD^+ ⟶ Acetyl CoA + CO_2 + NADH

TCA Cycle

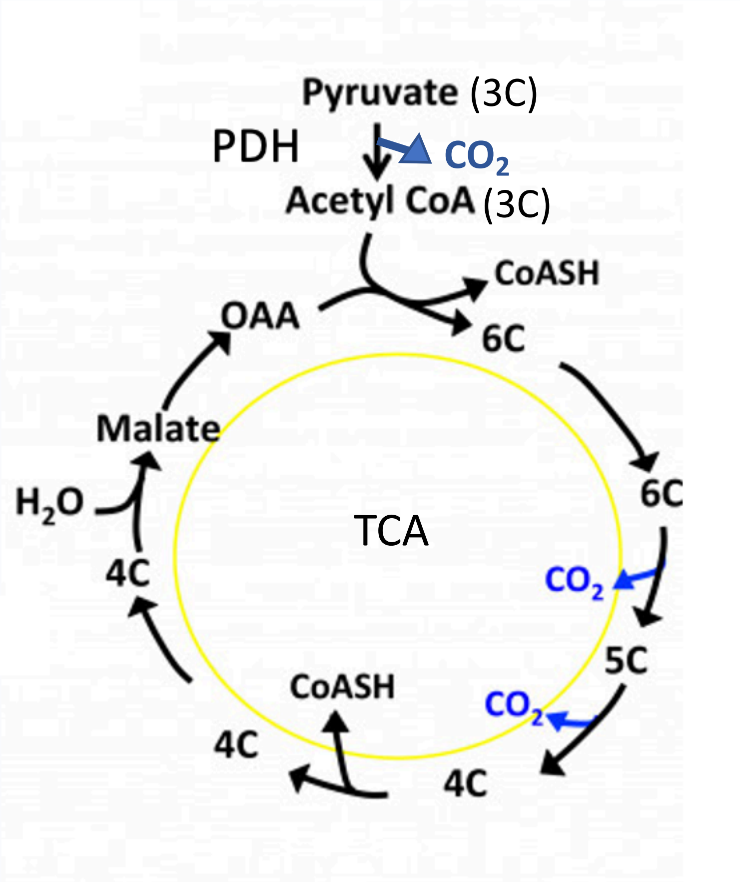
$2 + 4 = 6$



TCA Cycle

2 + 4 = 6

6 = 6

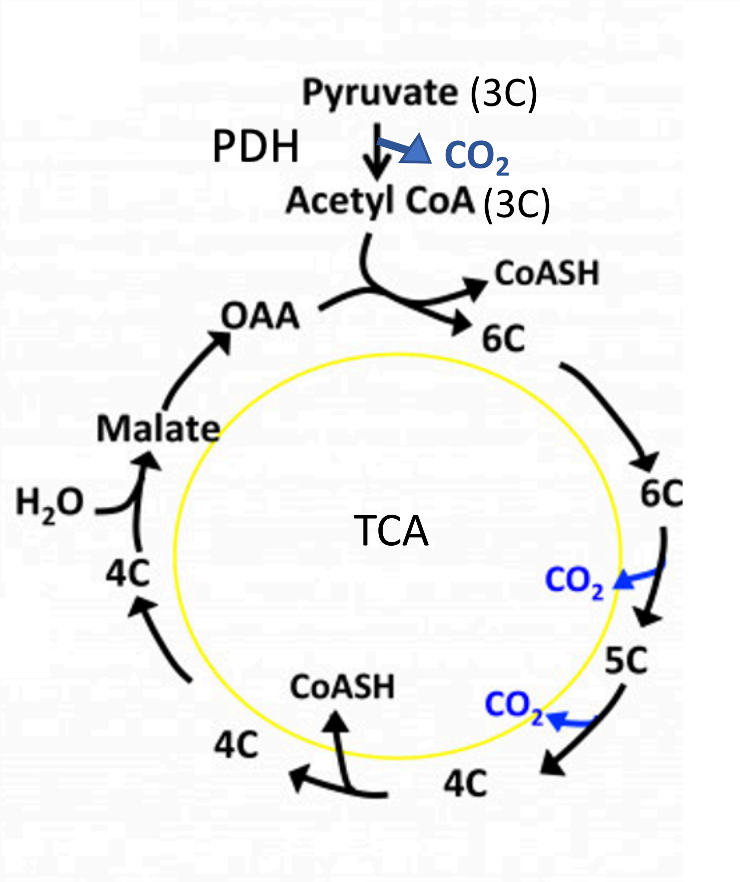


TCA Cycle

$2 + 4 = 6$

$6 = 6$

$6 - 1 = 5$



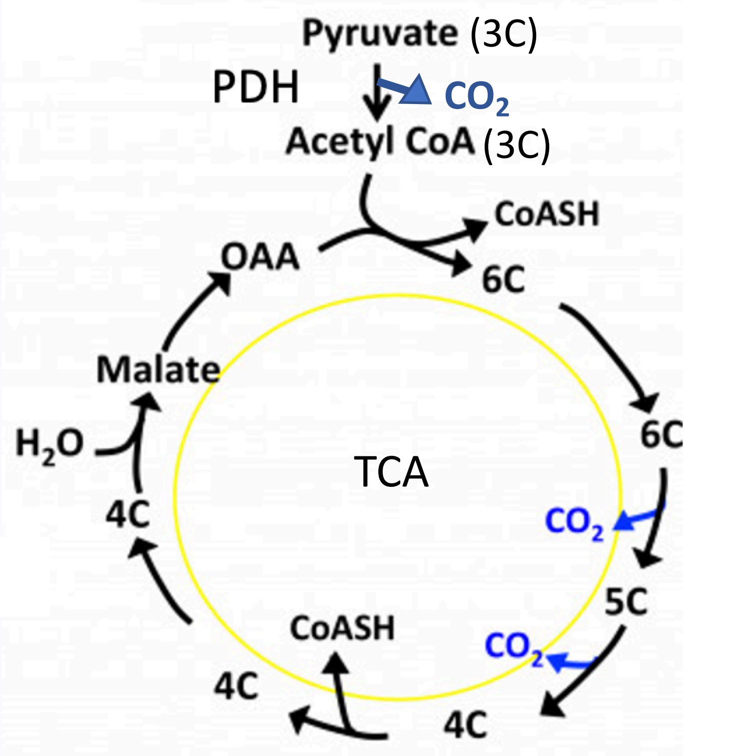
TCA Cycle

$2 + 4 = 6$

$6 = 6$

$6 - 1 = 5$

$5 - 1 = 4$



TCA Cycle

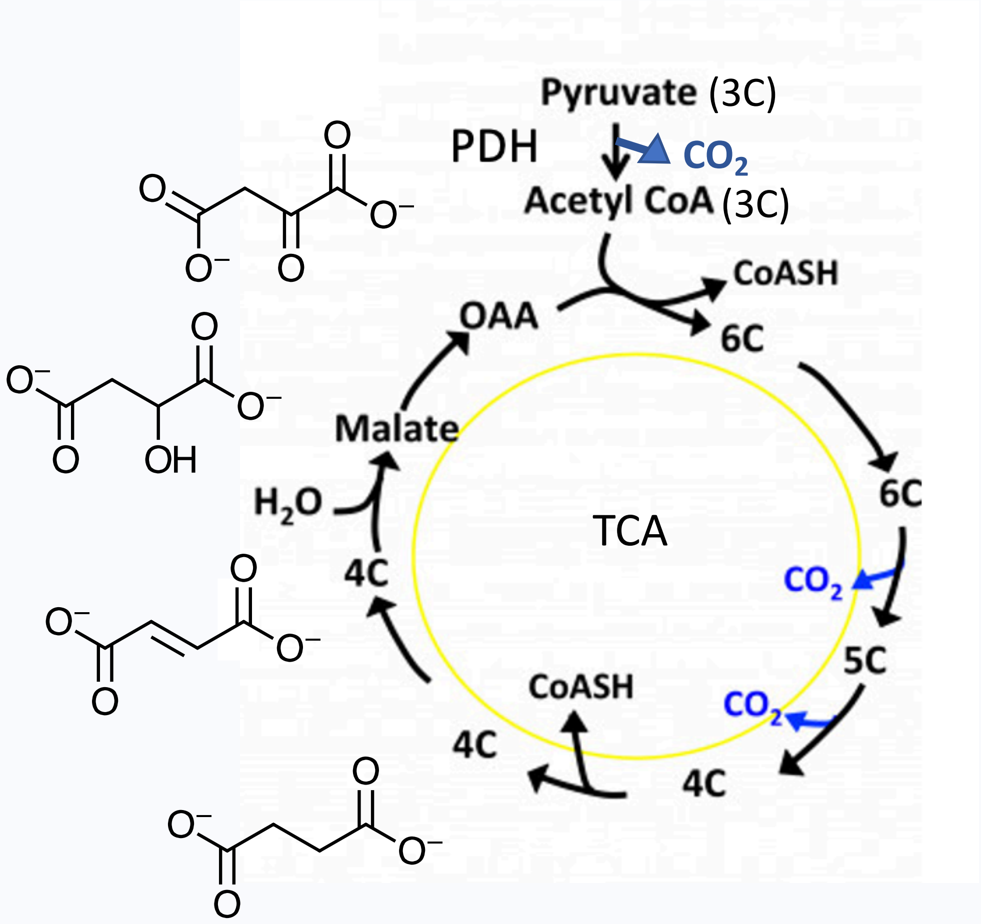
$2 + 4 = 6$

$6 = 6$

$6 - 1 = 5$

$5 - 1 = 4$

$4 = 4$



TCA Cycle

$2 + 4 = 6$

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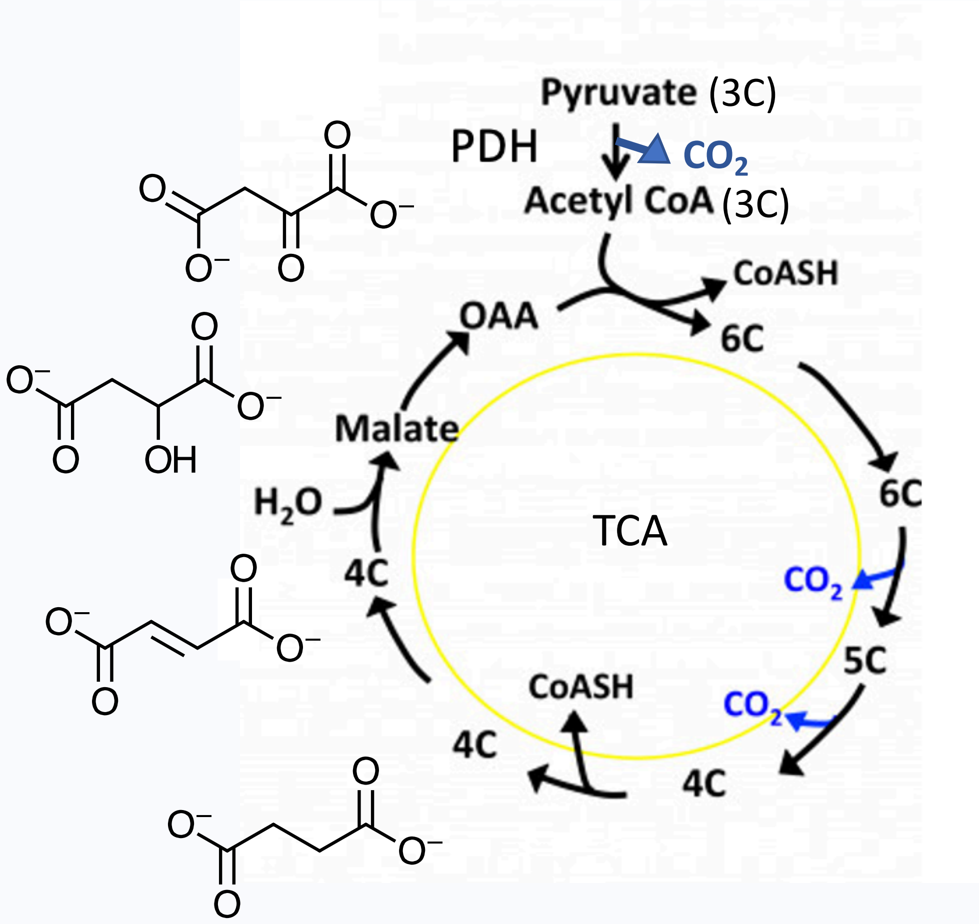
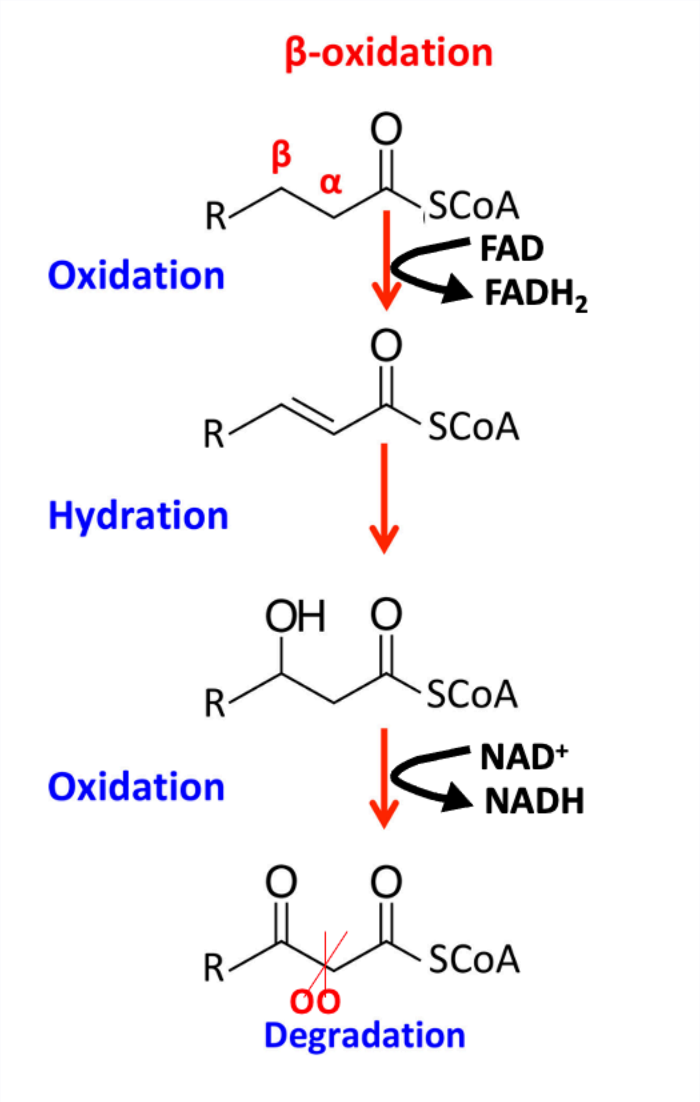
$6 - 1 = 5$

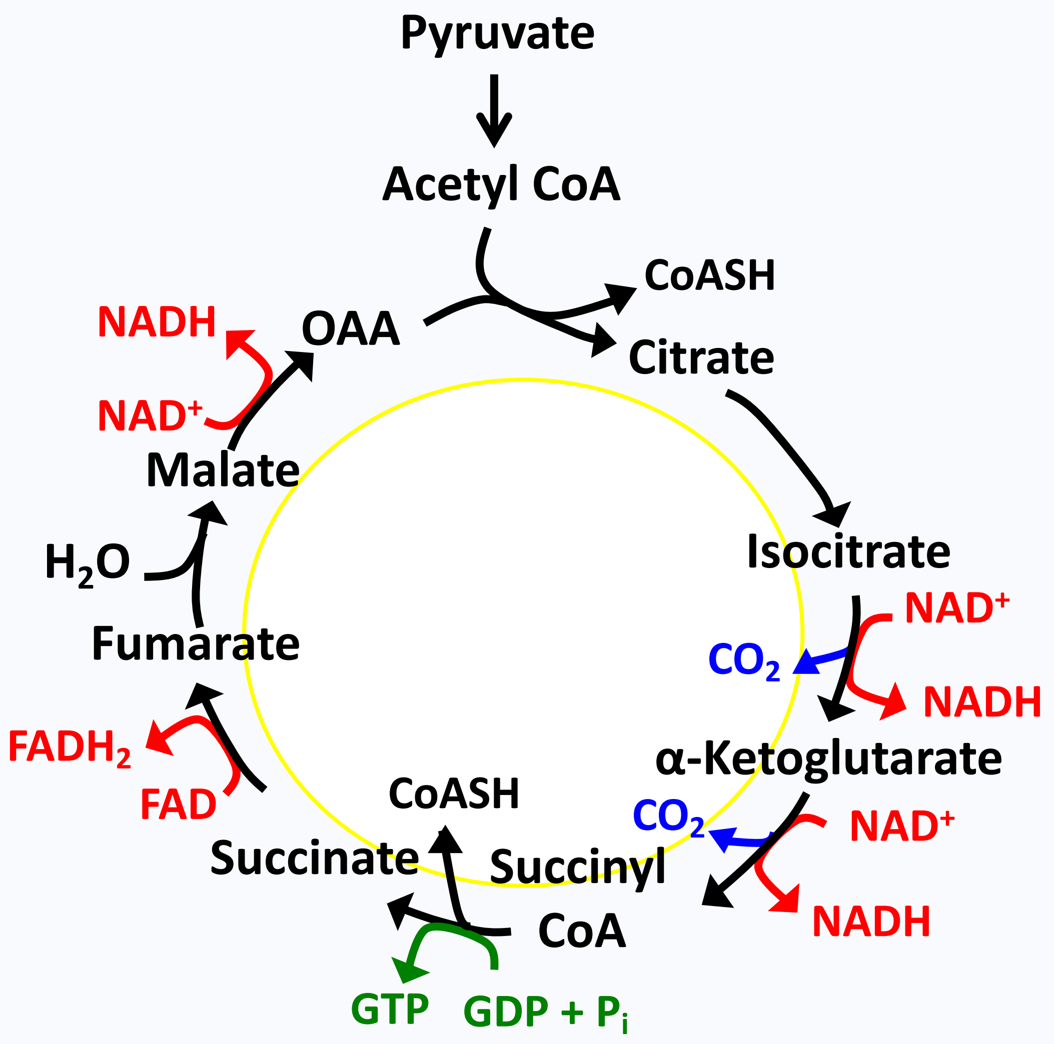
$5 - 1 = 4$

$4 = 4$





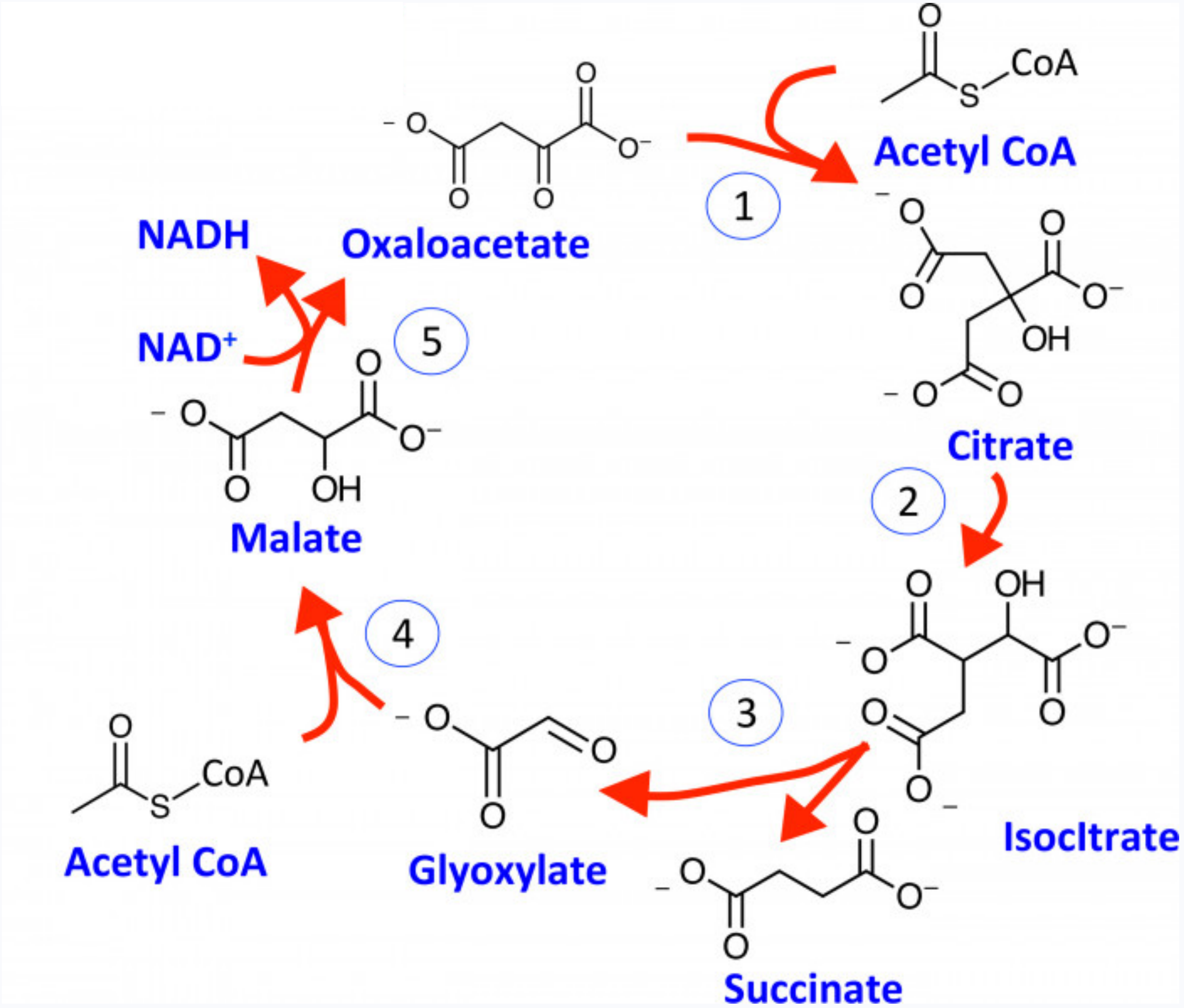
TCA Cycle



Oh My Such Good Apple Pie

$$\text{Acetyl CoA} + 3\ NAD^+ + FAD + GDP + P_i = 2\ CO_2 + 3\ NADH + FADH_2 + GTP + CoASH$$

Glyoxylate Cycle



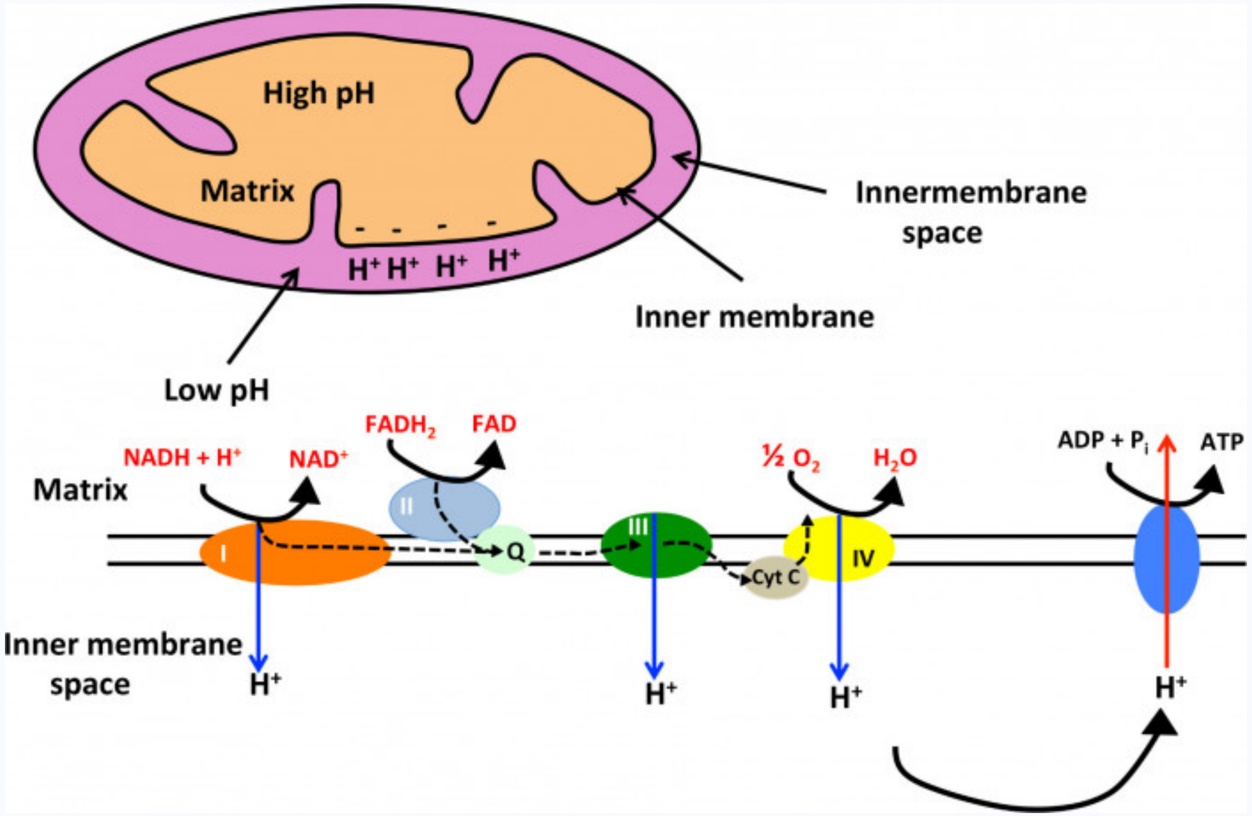
Occurs in bacteria, yeasts (fungi), and protists.

Involved in the synthesis of sugars through combining two molecules of acetyl CoA to generate succinate when other sugars such as glucose are unavailable.

Succinate is a precursor source for gluconeogenesis.

2 Acetyl CoA + NAD^+ + $2H_2O$ $\rightarrow$ **Succinate + 2 CoA + NADH + H+**

Electron Transport & Fate of Reducing Power

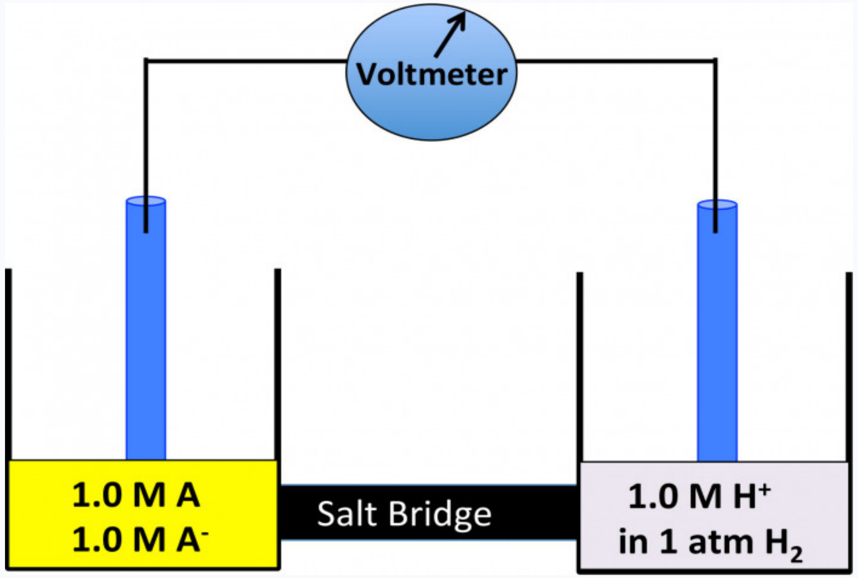


$H:^{-} = H^{+} + 2e^{-}$

Reaction Center	ENZYME	NOTES
1	NADH-Q OXIDOREDUCTASE	Lowest electron affinity in chain; uses NADH
2	SUCCINATE-Q OXIDOREDUCTASE	Enzyme is part of TCA cycle; uses $FADH_2$
3	Q-CYTOCHROME C OXIDOREDUCTASE	Oxidizes coenzyme Q and reduces cytochrome c
4	CYTOCHROME C OXIDASE	Catalyzes the reduction of O_2 to H_2O; Blocked by cyanide, carbon monoxide, azide

Standard Reduction Potentials

$\Delta G° = -nF\Delta E°$ where n = # electrons transferred; F = Faraday (23.0 kcal mol^{-1} V^{-1})



Standard Reduction Potentials (Half Reactions)

Oxidant	Reductant	# e⁻ transferred	E'ₒ (Volts)
$NAD^+ + H^+$	NADH	2	- 0.32
FAD	$FADH_2$	2	- 0.22
Pyruvate	Lactate	2	- 0.19
Fumarate	Succinate	2	+ 0.03
Fe^{+3}	Fe^{+2}	1	+ 0.77
½ $O_2 + 2H^+$	H_2O	2	+ 0.82

Lowest electron affinity

Highest electron affinity

E° represents the partial reaction:

Oxidant + e^- = Reductant

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Note that negative reduction potentials indicate that the oxidized form of the substance has a reduced affinity for electrons relative to the standard H_2.

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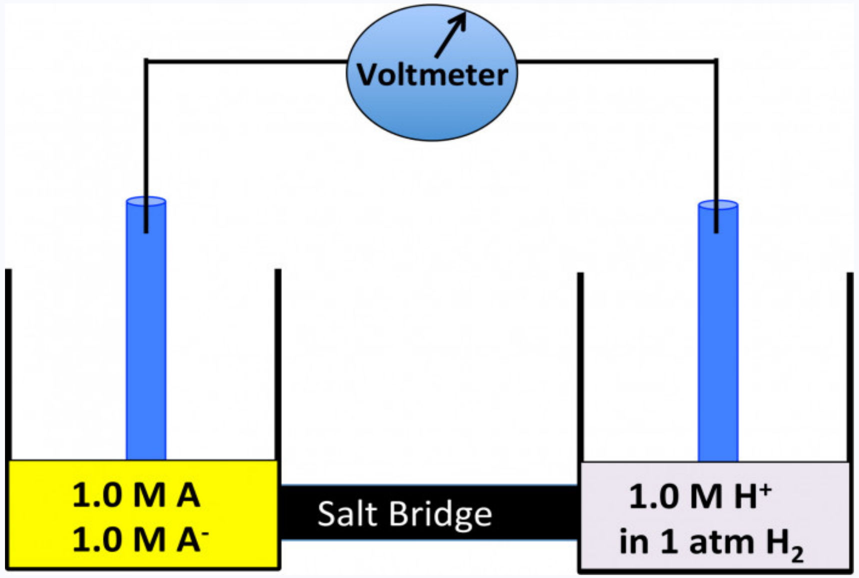

Standard Reduction Potentials

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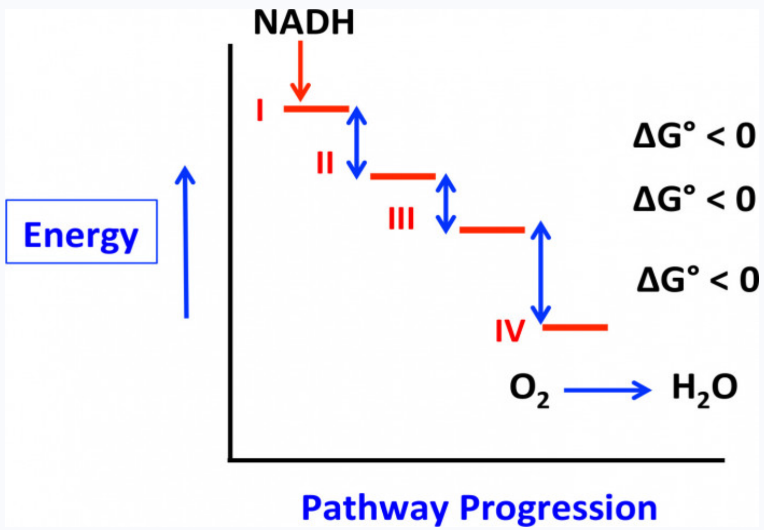

E'° represents the partial reaction:

Oxidant + e$^-$ = Reductant

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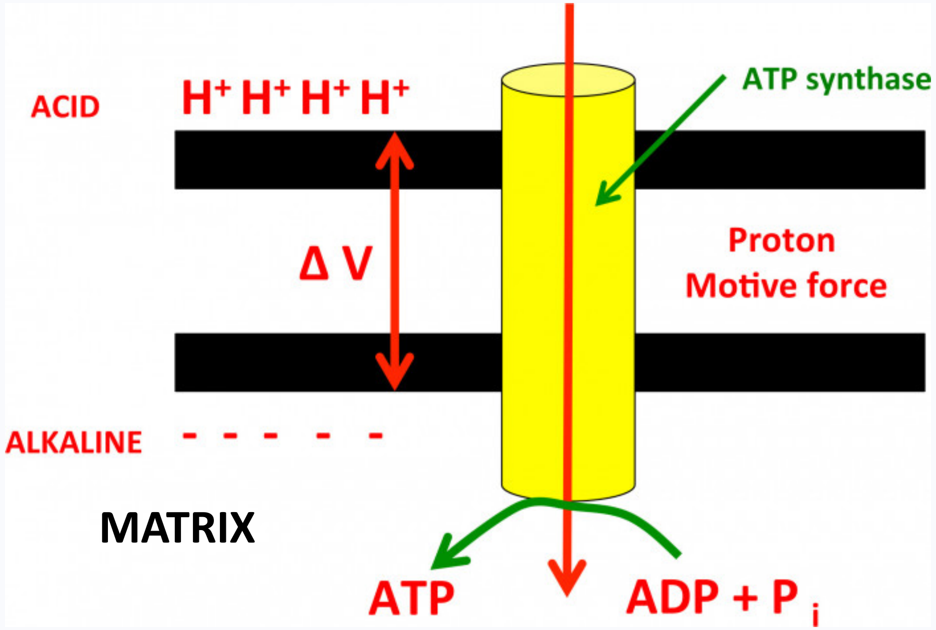
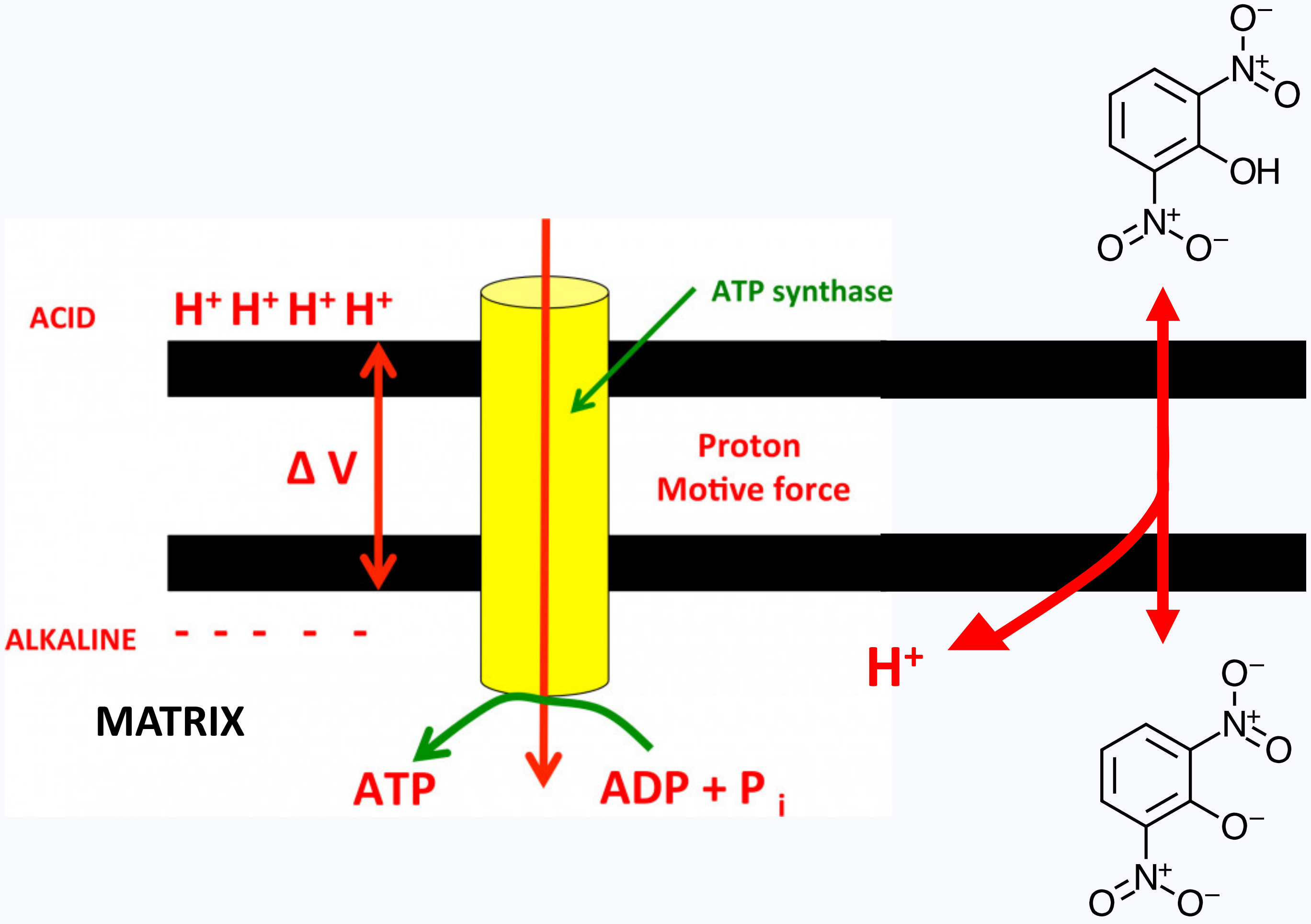
Note that negative reduction potentials indicate that the oxidized form of the substance has a reduced affinity for electrons relative to the standard H_2.

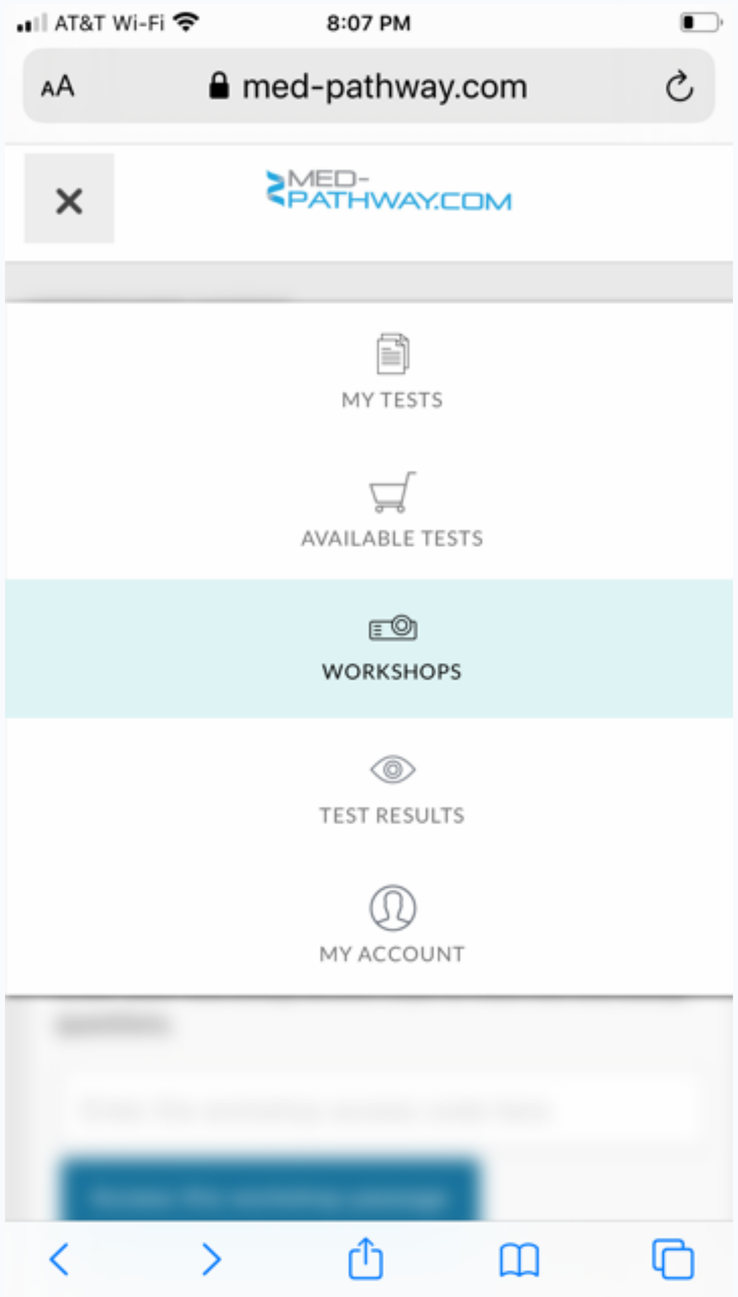
Chemiosmotic Synthesis of ATP



Uncoupling Chemiosmotic Synthesis of ATP



DNP: The Uncoupler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