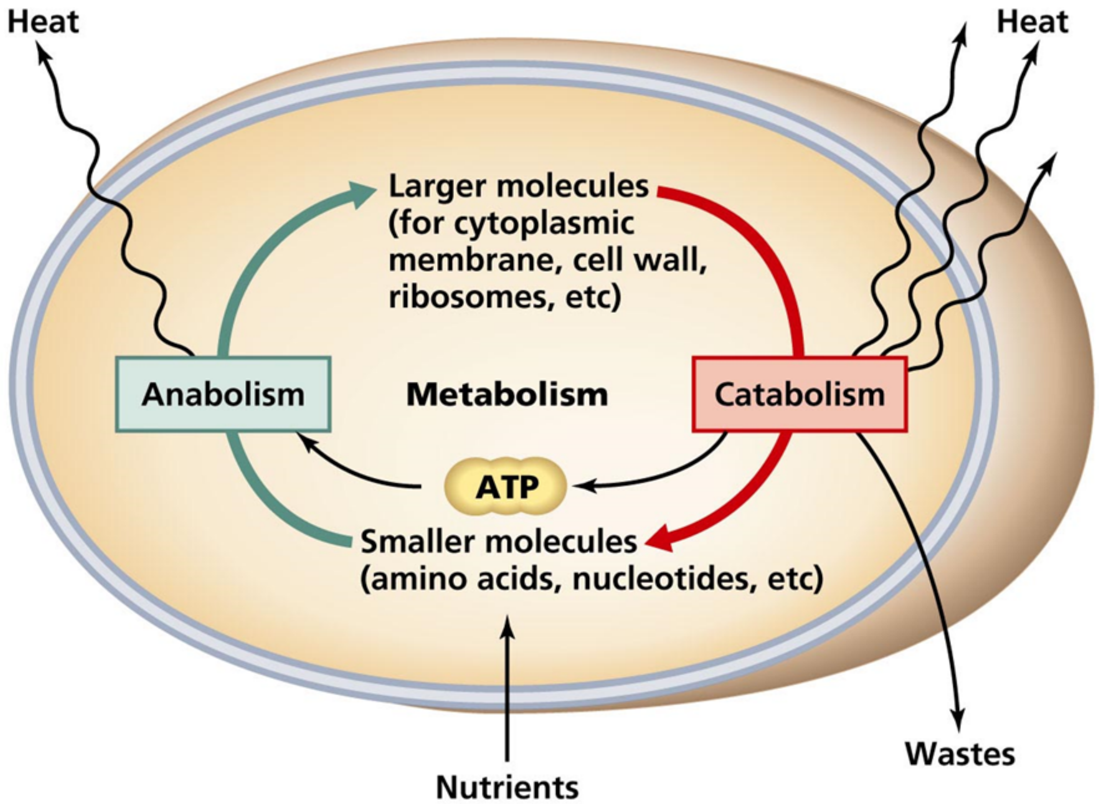
Metabolism I



Aim: understanding the basic concepts of metabolism, basic carbohydrate structure, glycolysis

Metabolism: overall chemical reactions in living cells

Catabolism *– energy-conserving reactions*

Anabolism *– synthesis of complex organic molecules (energy consumption)*

What are needed for a living cell?

Chemical work

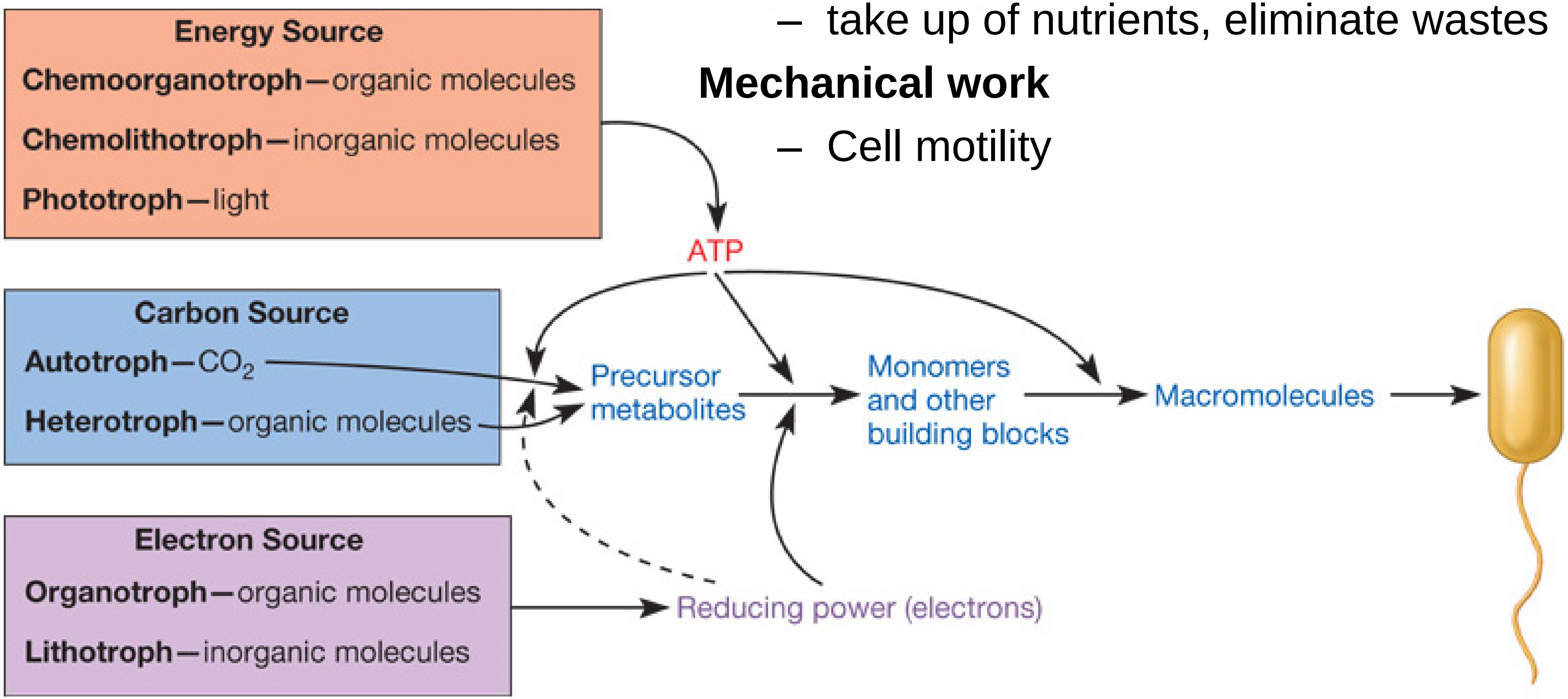
- synthesis of complex molecules

Transport work

- take up of nutrients, eliminate wastes

Mechanical work

- Cell motility



The 1st and 2nd law of thermodynamics

$$\mathbf{\Delta G = \Delta H - T \bullet \Delta S}$$

$\Delta G < 0$, spontaneous process

$\Delta G > 0$, non-spontaneous process

Oxidation-Reduction Reactions and Electron Carriers

- Many metabolic processes involve oxidation-reduction reactions (electron transfer)

- Electron carriers (e.g. NAD^+) are often used to transfer electrons from an electron donor to an electron acceptor

$$n\ e^{-1}$$

$$A_{ox} + B_{red} \rightleftharpoons A_{red} + B_{ox}$$

$$\Delta G = \Delta G_0^{'} + RT \ln \left(\frac{[A_{red}][B_{ox}]}{[A_{ox}][B_{red}]} \right)$$

$$\Delta G = - nF\, \Delta E$$

$$\Delta E = \Delta E_0^{'} - \frac{RT}{nF} \ln \left(\frac{[A_{red}][B_{ox}]}{[A_{ox}][B_{red}]} \right)$$

Standard Reduction Potential (E_0')

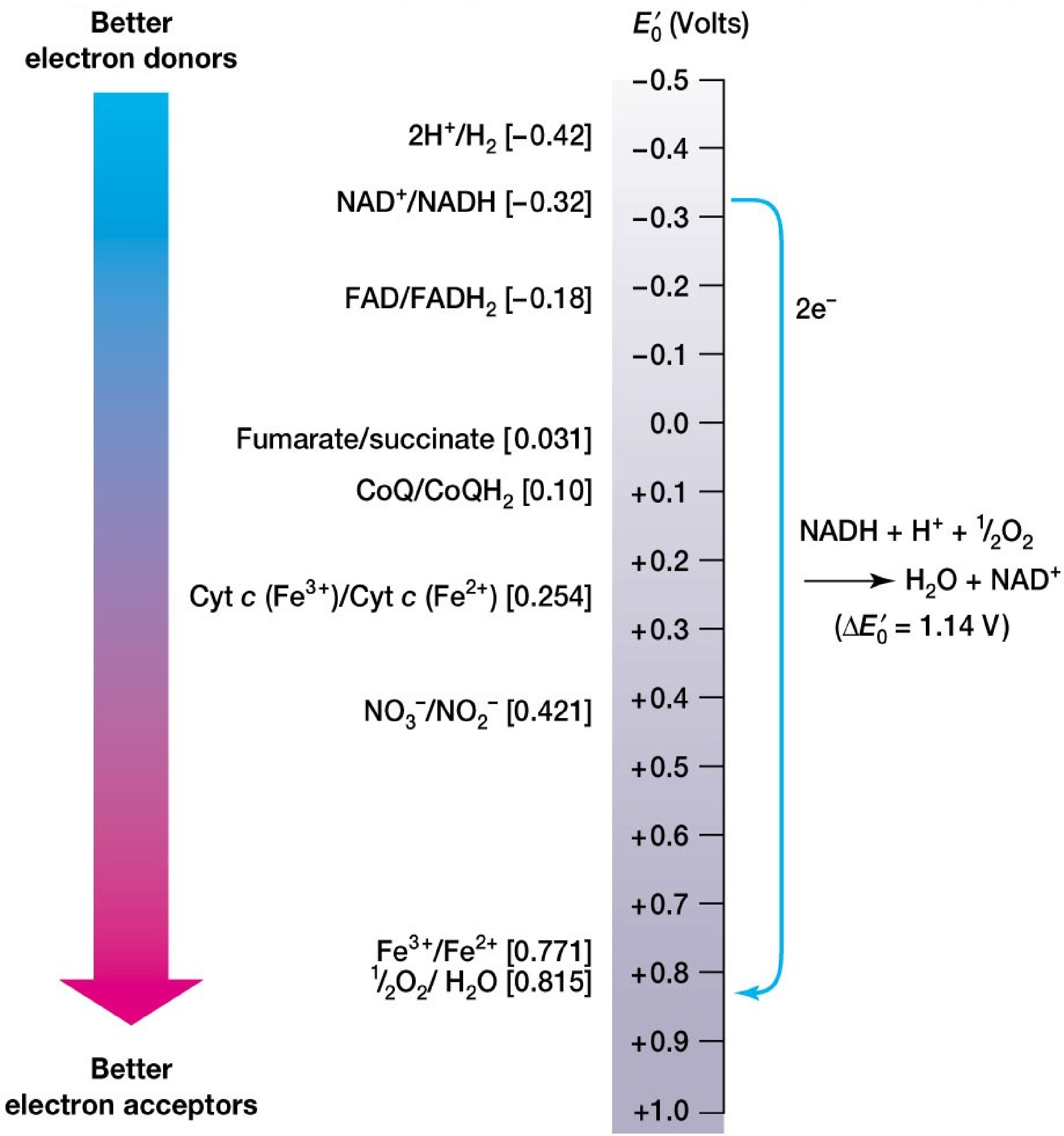
A measure of the tendency of a chemical species to accept electrons:

$$A_{ox} + n\, e^- \rightleftharpoons A_{red}$$

$$E_A = E'_{A0} - \frac{RT}{nF} \ln\left(\frac{[A_{red}]}{[A_{ox}]}\right)$$

more negative $E_0 \Rightarrow$ better electron donor

more positive $E_0 \Rightarrow$ better electron acceptor



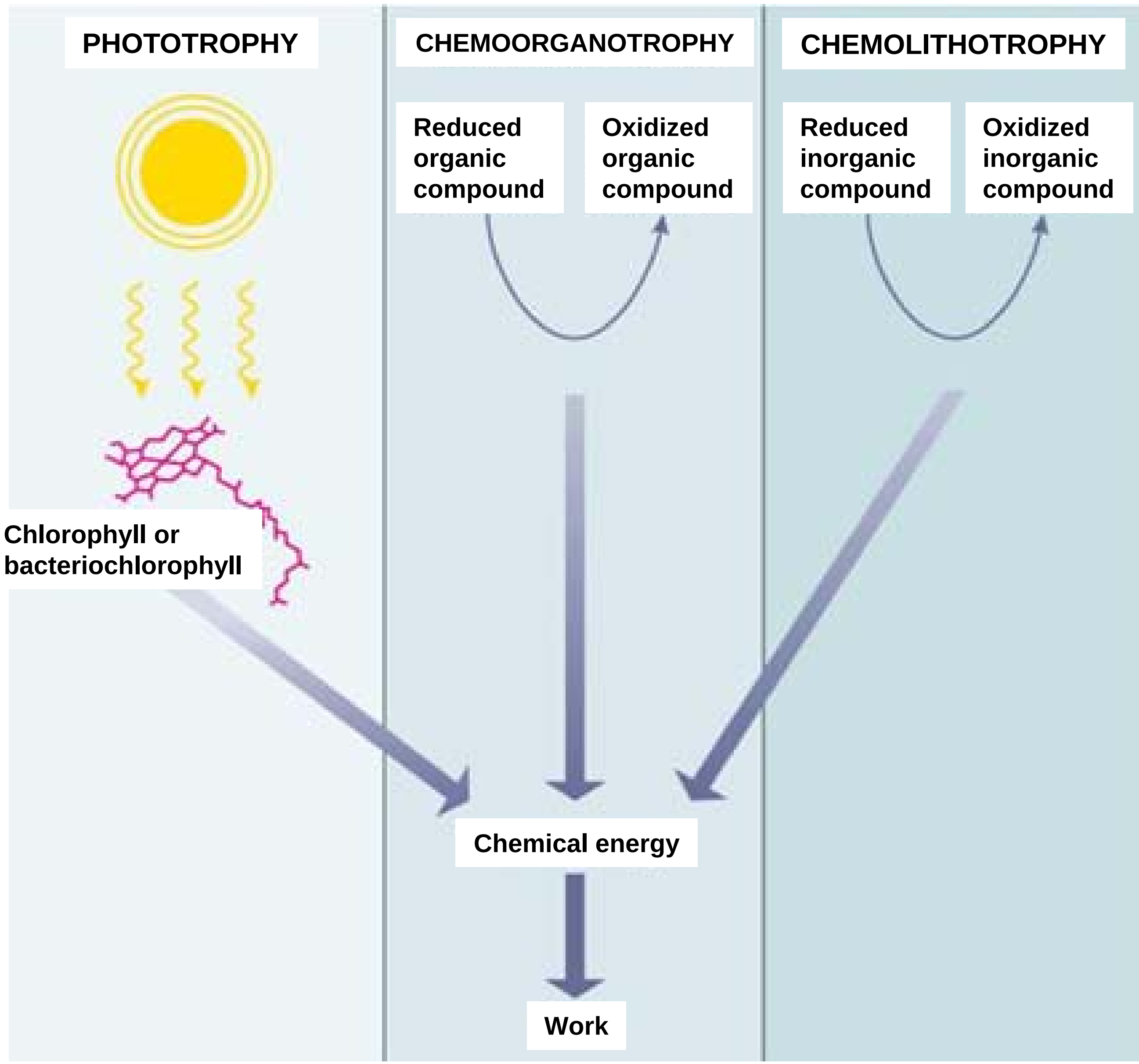
Better electron donors
Better electron acceptors
E_0' (Volts)
−0.5
−0.4
−0.3
−0.2
−0.1
0.0
+0.1
+0.2
+0.3
+0.4
+0.5
+0.6
+0.7
+0.8
+0.9
+1.0
$2H^+/H_2$ [−0.42]
$NAD^+/NADH$ [−0.32]
$FAD/FADH_2$ [−0.18]
Fumarate/succinate [0.031]
$CoQ/CoQH_2$ [0.10]
Cyt *c* (Fe^{3+})/Cyt *c* (Fe^{2+}) [0.254]
NO_3^-/NO_2^- [0.421]
Fe^{3+}/Fe^{2+} [0.771]
$\frac{1}{2}O_2/H_2O$ [0.815]
$2e^-$
$NADH + H^+ + \frac{1}{2}O_2 \longrightarrow H_2O + NAD^+$
($\Delta E_0' = 1.14$ V)

Sources of energy

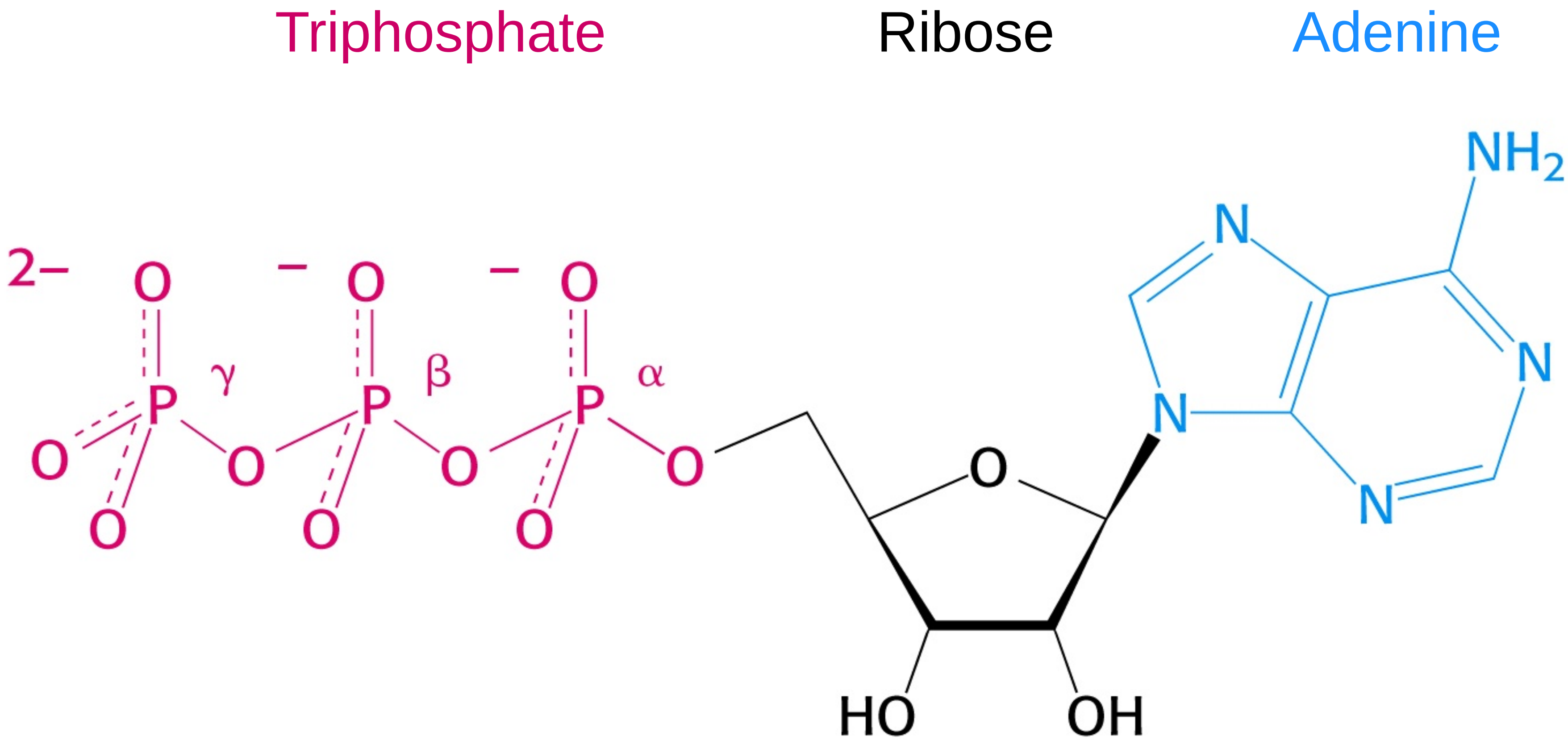
Most microorganisms use one of three energy sources:

- the sun
- reduced organic compounds
- reduced inorganic compounds

The chemical energy obtained can be used to do work

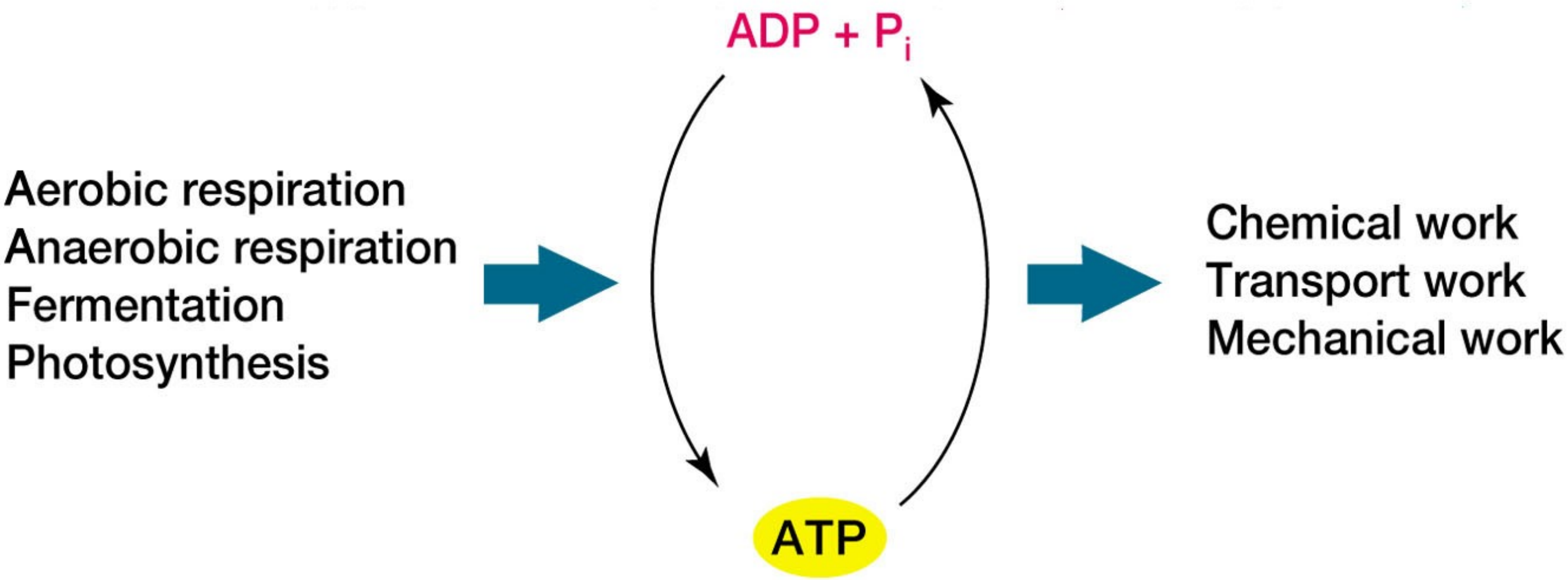


ATP is a universal energy currency

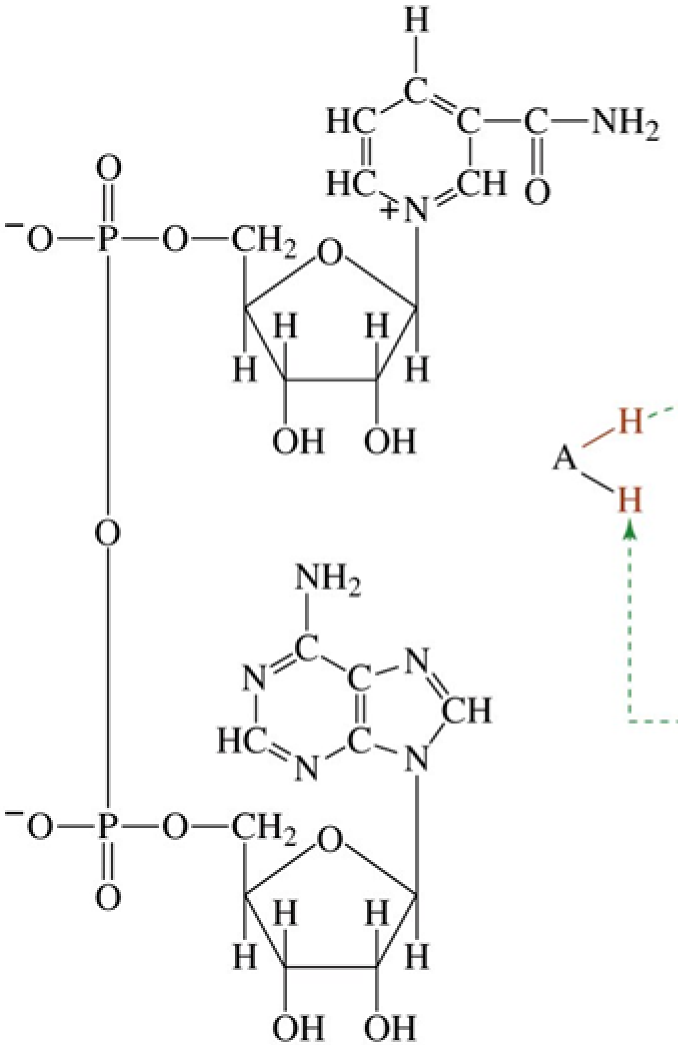


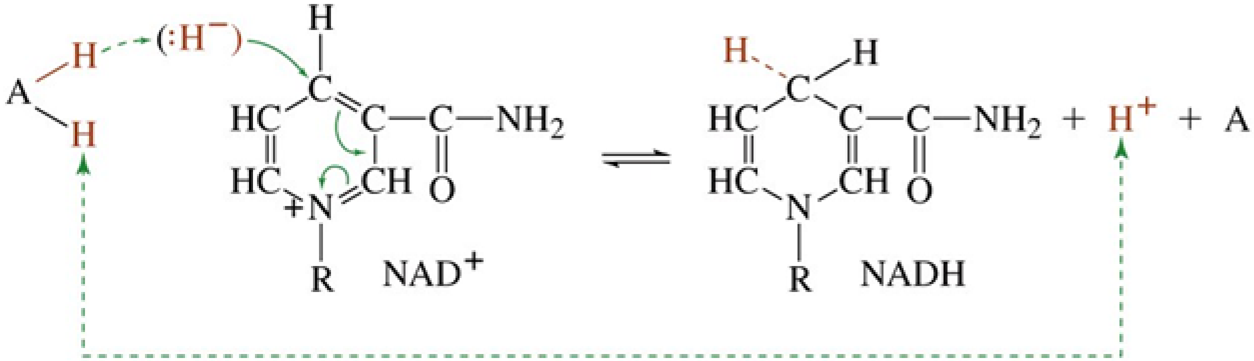
Adenosine triphosphate (ATP)

Cell’s energy cycle:



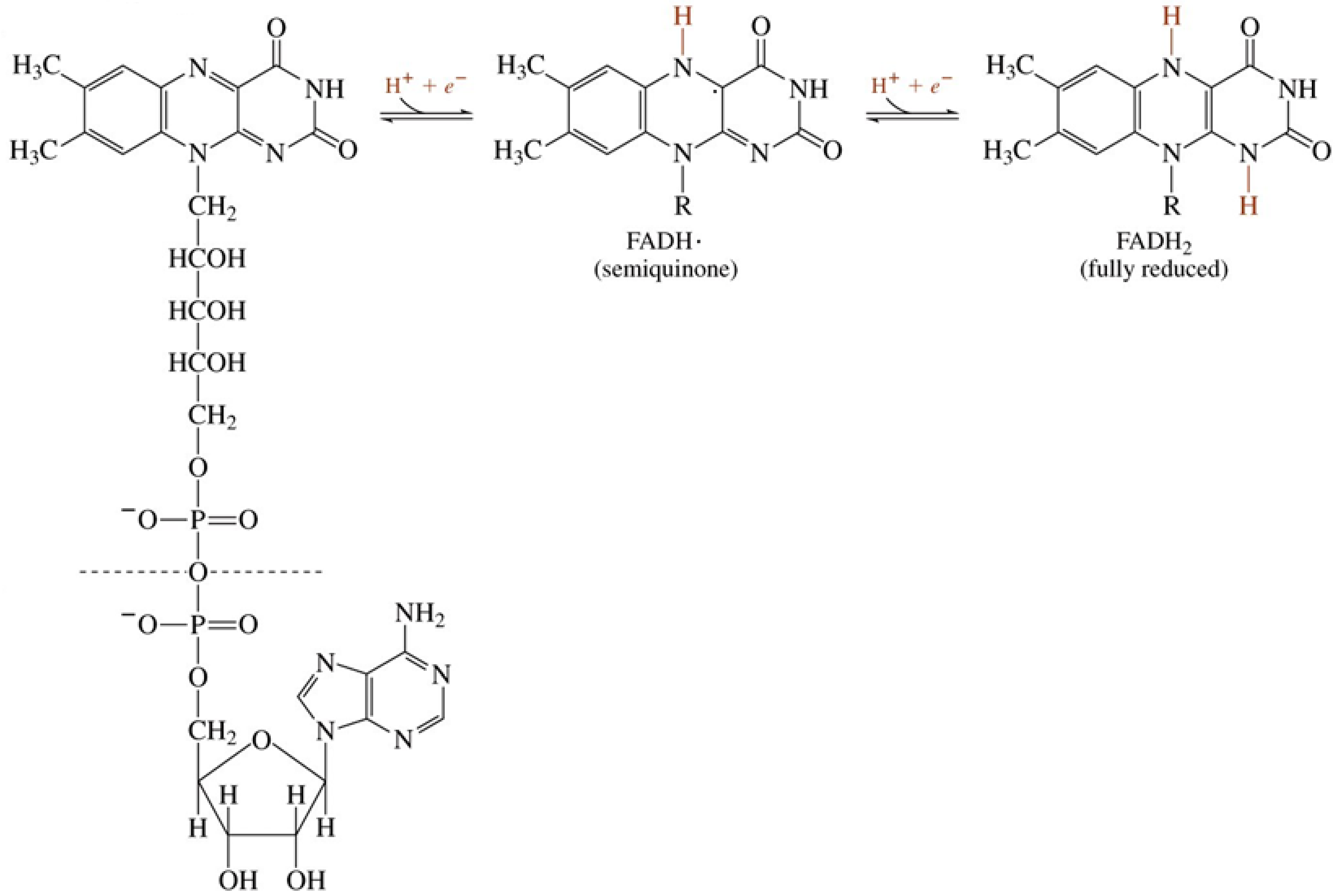
The electron carrier NAD$^+$





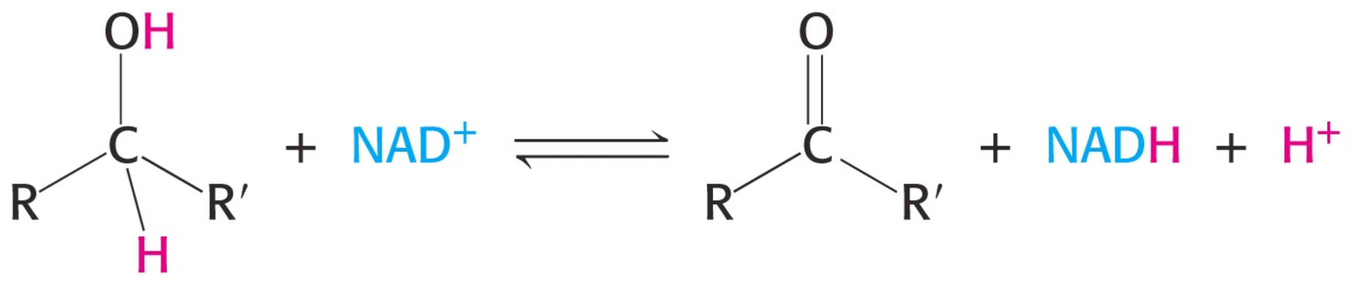
Nicotinamide adenine dinucleotide (NAD$^+$)

The electron carrier FAD

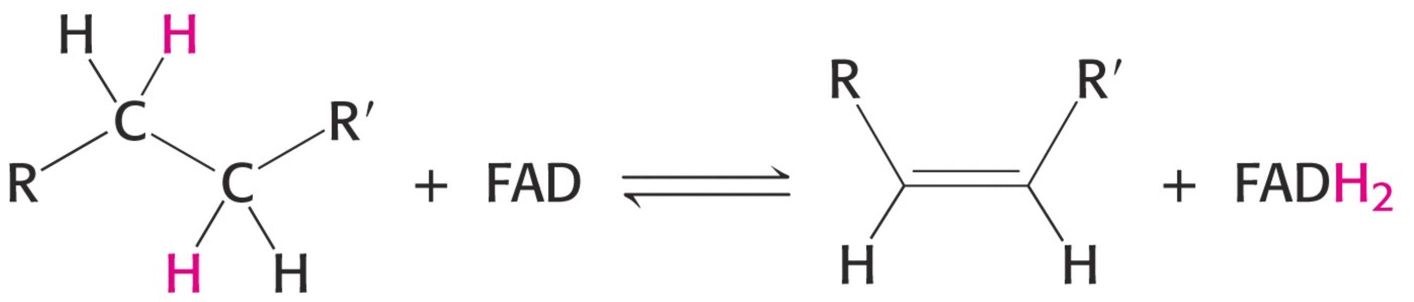


Flavin adenine dinucleotide (FAD)

NAD and FAD are used in different types of reactions

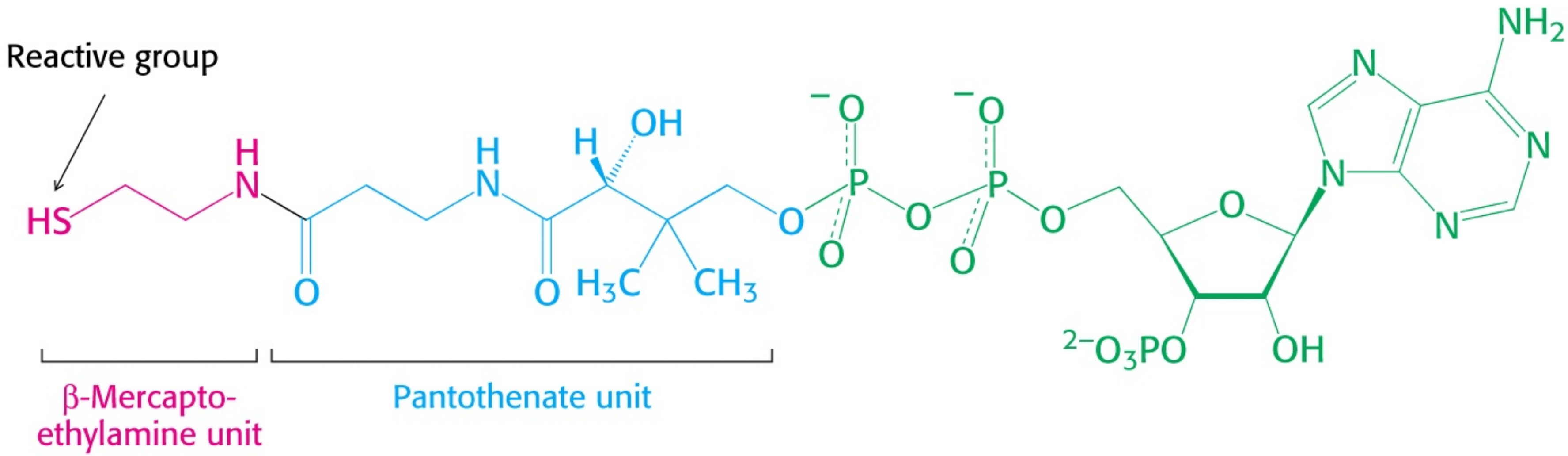


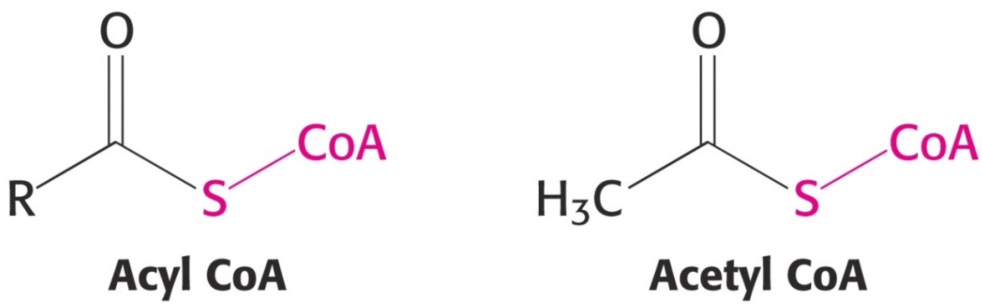
NAD is used in redox-reactions involving alcohols and ketones or aldehydes



FAD is used in redox-reactions involving saturated and unsaturated carbon-carbon bonds

CoA is a carrier for short and long acyl-groups





A few types of reactions can manage metabolism

Type of reaction	Description
Oxidation–reduction	Electron transfer
Ligation requiring ATP cleavage	Formation of covalent bonds (i.e., carbon–carbon bonds)
Isomerization	Rearrangement of atoms to form isomers
Group transfer	Transfer of a functional group from one molecule to another
Hydrolytic	Cleavage of bonds by the addition of water
Addition or removal of functional groups	Addition of functional groups to double bonds or their removal to form double bonds

The control of metabolism is important

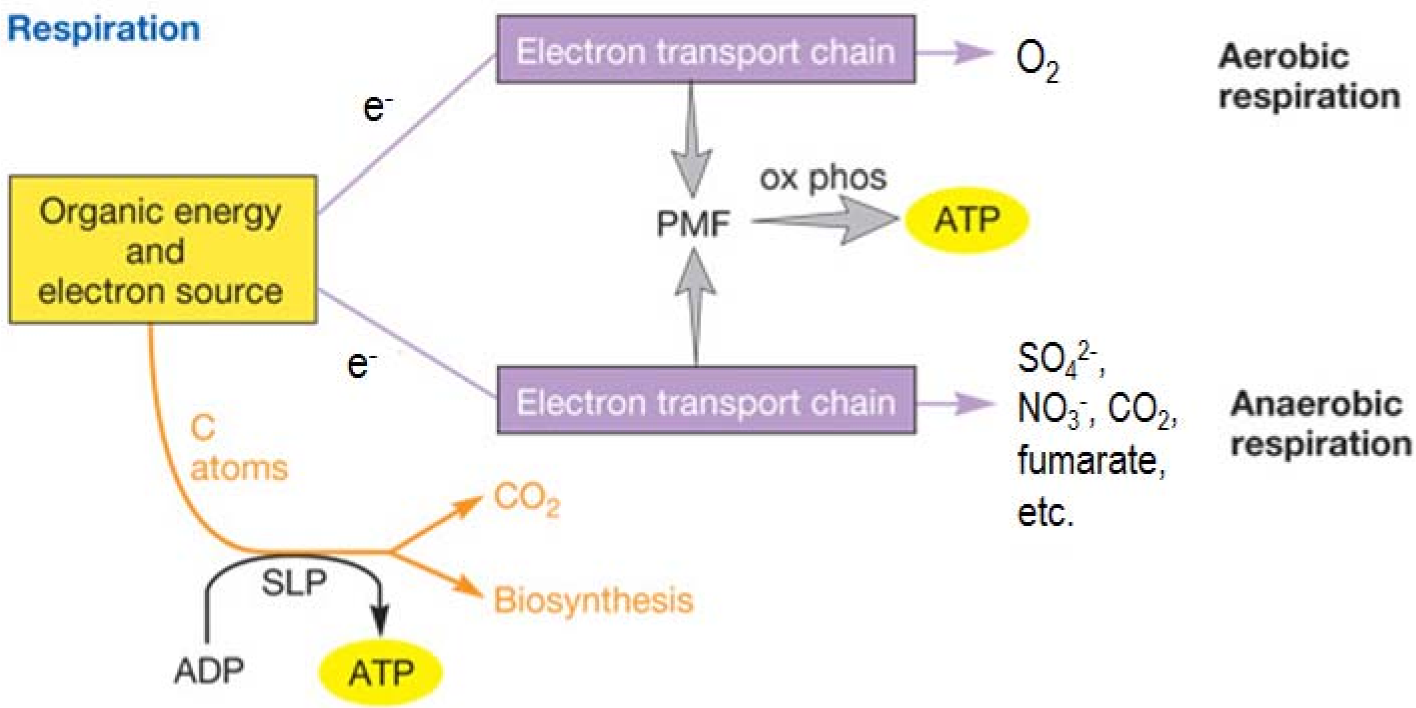
1. The amount of enzyme (Long Term)
2. The activity of enzyme (Short term)
   - Allosteric control
   - Covalent modification
   - Proteolytic cleavage
3. Substrate availability (compartmentalisation)

4. Hormones have an overall control function

Chemoorganic fueling processes - respiration

Most respiration involves use of electron transport chain

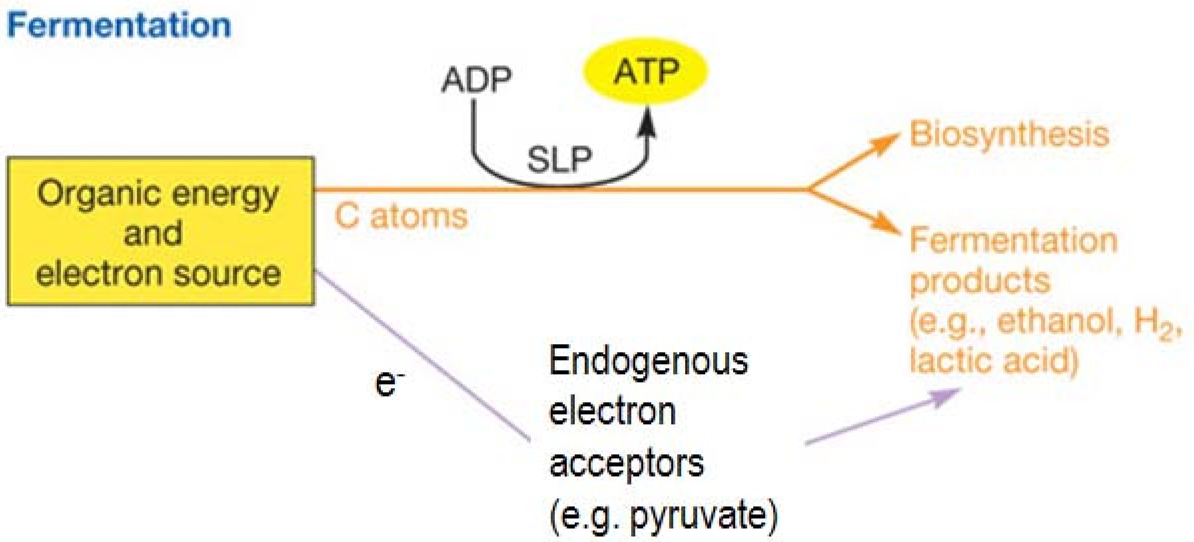
- *aerobic respiration: final electron acceptor is oxygen*
- *anaerobic respiration: final electron acceptor is different exogenous acceptor such as NO^{3-}, SO_4^{2-}, CO_2, Fe^{3+} or SeO_4^{2-}.*



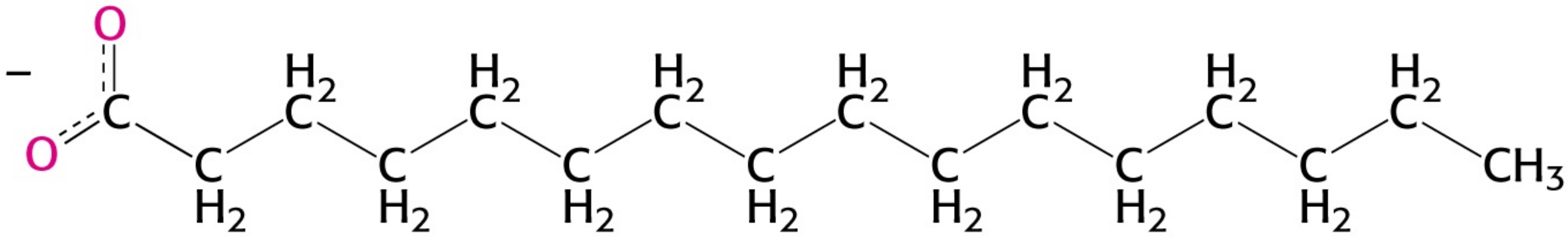
Chemoorganic fueling processes - fermentation

Uses an endogenous electron acceptor

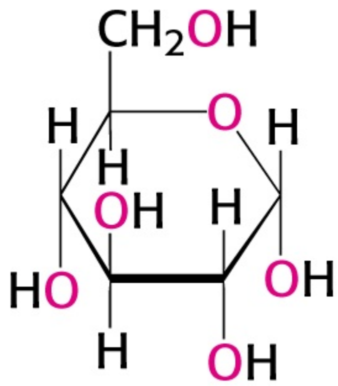
– *usually an intermediate of the pathway used to oxidize organic energy source (e.g. pyruvate)*



Common organic energy sources:



Fatty acid



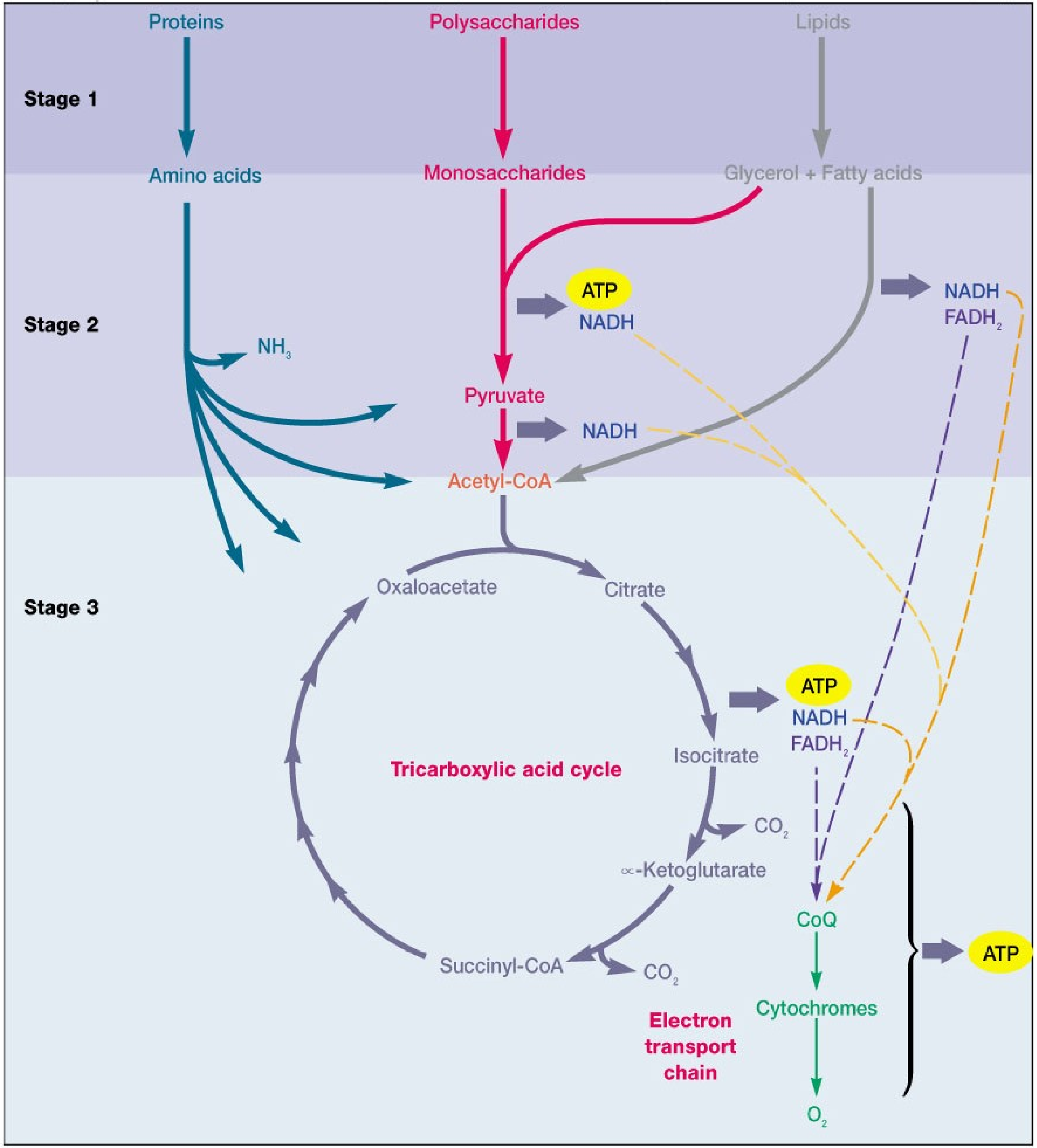
Glucose

When fatty acids and glucose are <u>oxidised</u>, energy can be generated in the form of ATP.

Overview of aerobic catabolism

Three-stage process:

- large molecules (polymers) $\rightarrow$ small molecules (monomers)
- initial oxidation and degradation of monomers to pyruvate
- oxidation and degradation of pyruvate by the tricarboxylic acid cycle (TCA cycle)



ATP made primarily by oxidative phosphory-lation

Carbohydrate metabolism

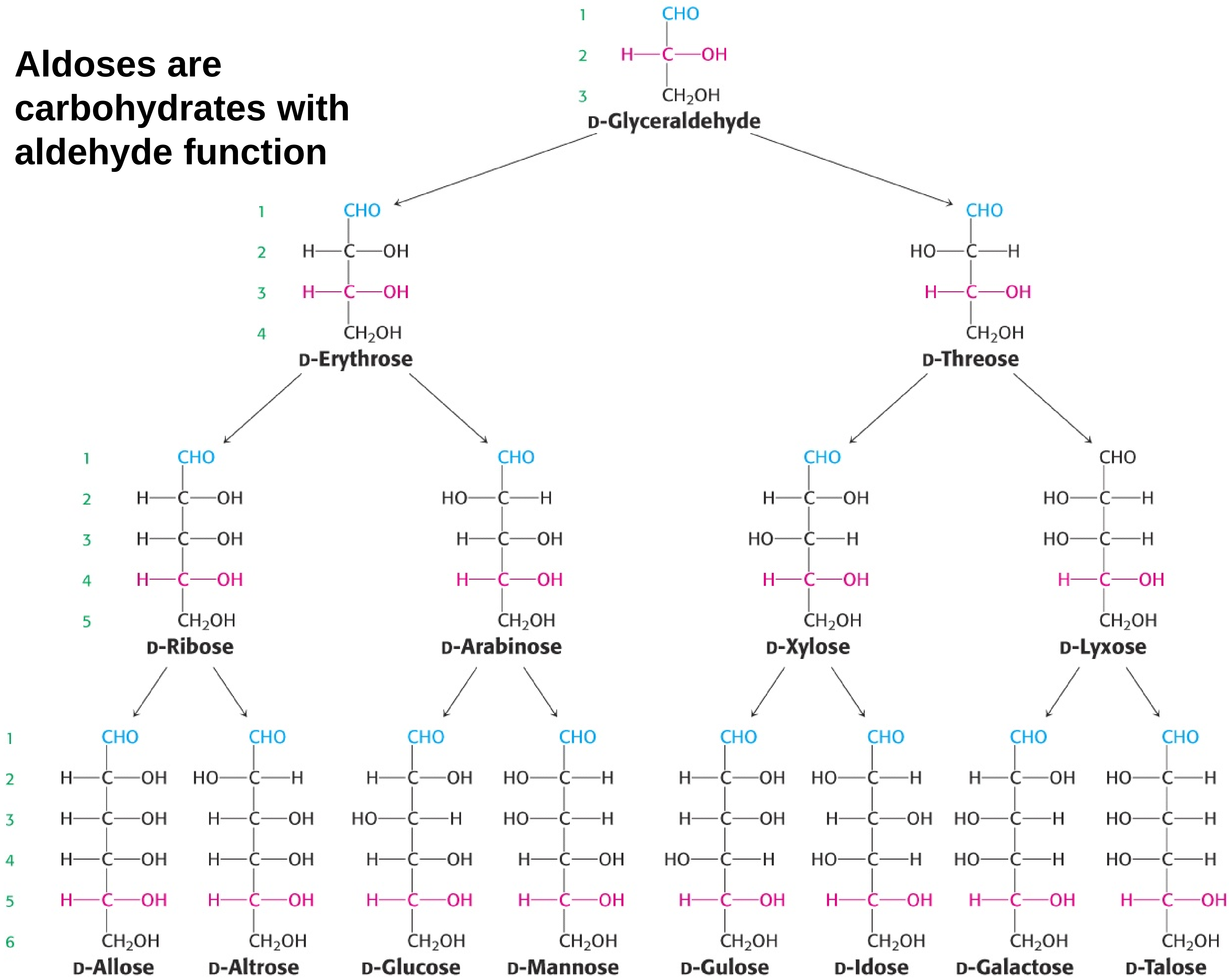
- Carbohydrates in the cell and their properties
- Glycolysis
- Metabolism of different sugars
- Control of glycolysis

Carbohydrates are aldehydes or ketones with many hydroxyl groups

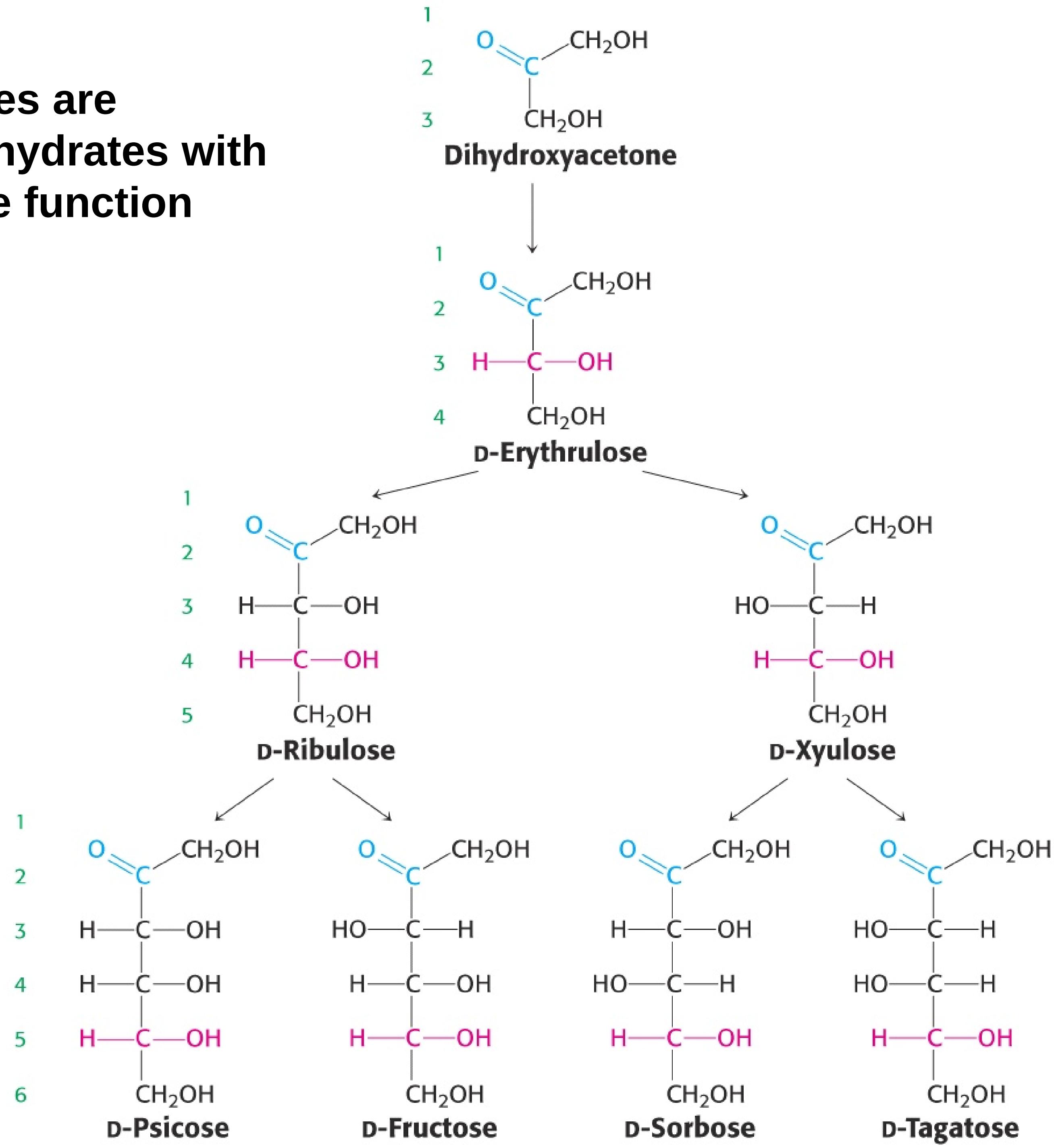
You can find carbohydrates as:

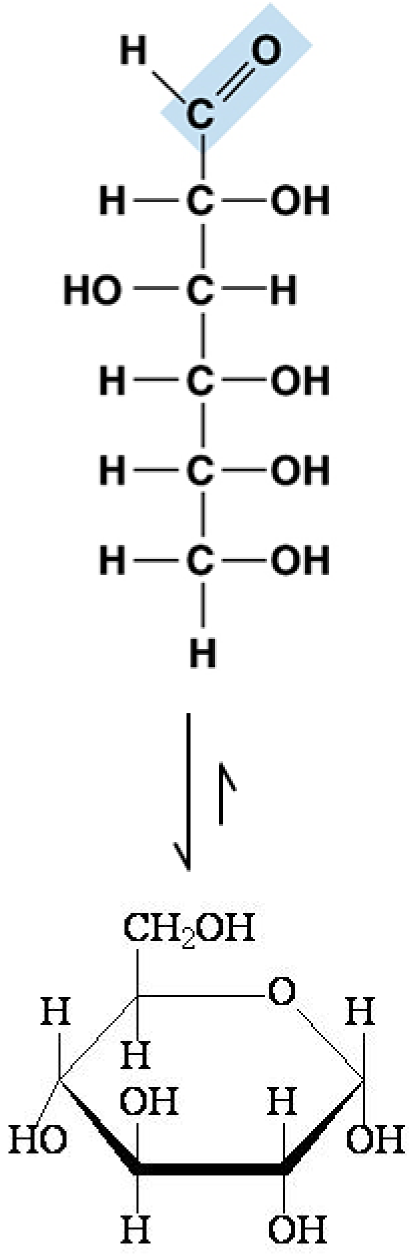
- Energy store, fuel and metabolite
- Parts of RNA and DNA
- Cell walls in bacteria and plants
- Oligosaccharides bound to proteins or lipids

Aldoses are carbohydrates with aldehyde function

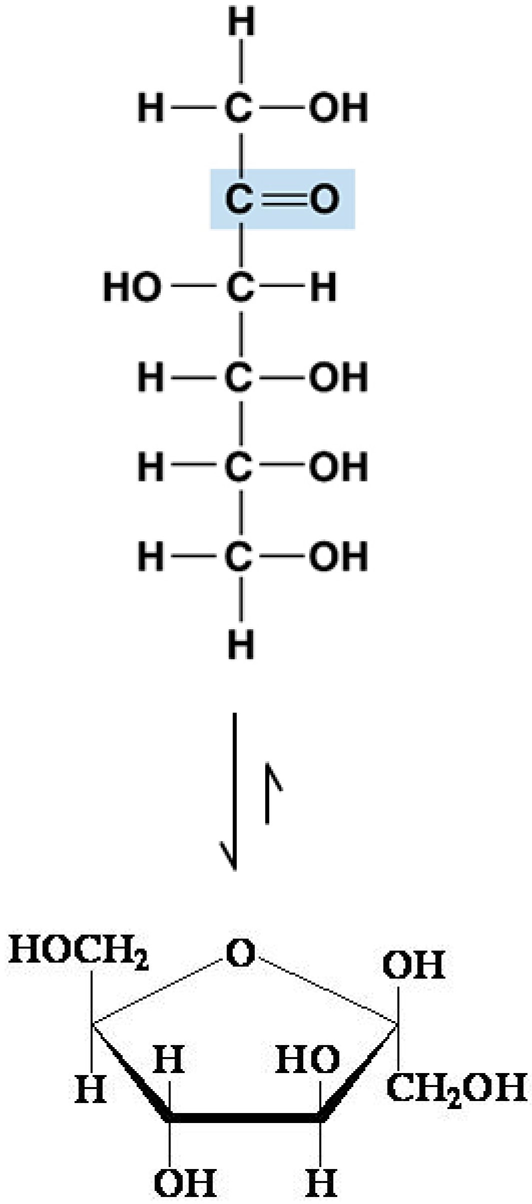


Ketoses are carbohydrates with ketone function

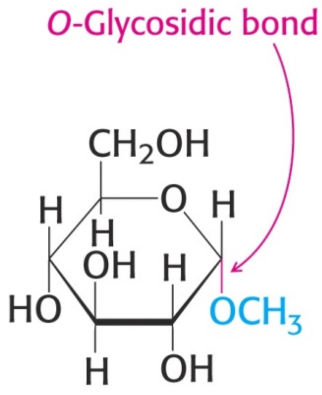




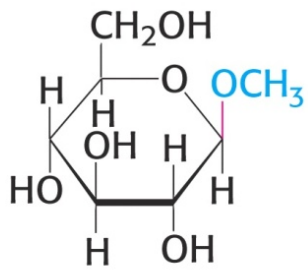
glucose



fructose



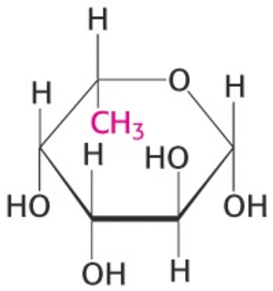
Methyl α-D-glucopyranoside



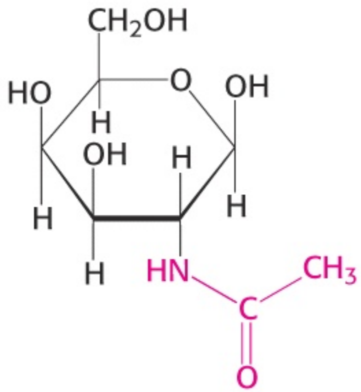
Methyl β-D-glucopyranoside

Glycosidic bonds connect different monosaccharides in e.g. disaccharides

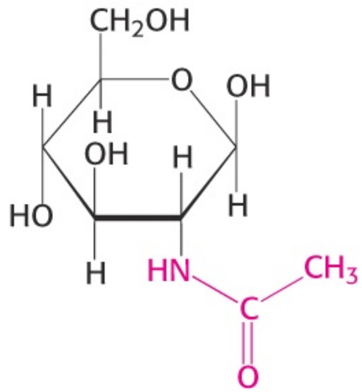
Modified sugars are common in oligosaccharides



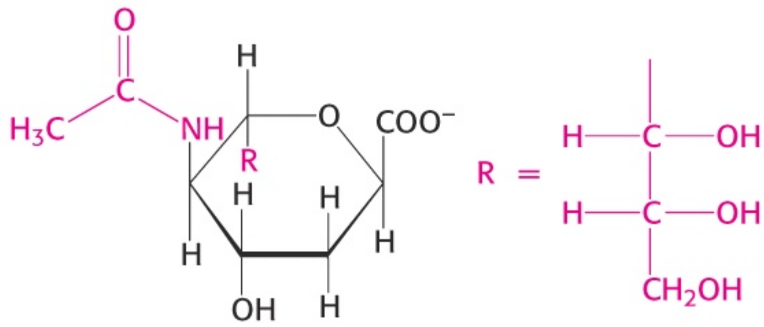
β-L-Fucose (Fuc)



β-D-Acetylgalactosamine (GalNAc)

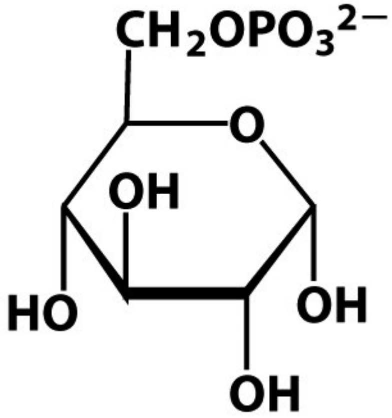


β-D-Acetylglucosamine (GlcNAc)

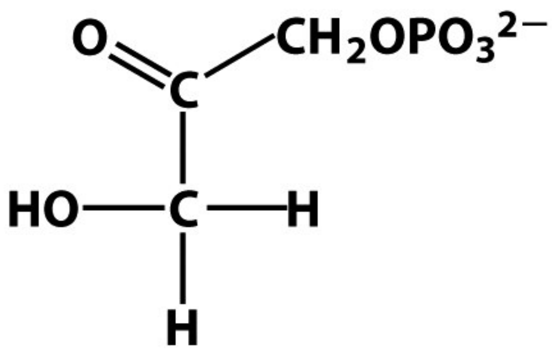


Sialic acid (Sia) (*N*-Acetylneuraminate)

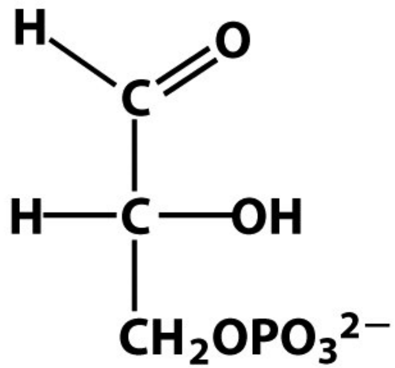
All monosaccharides in the cell are phosphorylated, which leads to increased solubility and allows them to remain in the cell



Glucose 6-phosphate
(G-6P)



Dihydroxyacetone phosphate
(DHAP)



Glyceraldehyde 3-phosphate
(GAP)

Common disaccharides in the food

Sucrose =

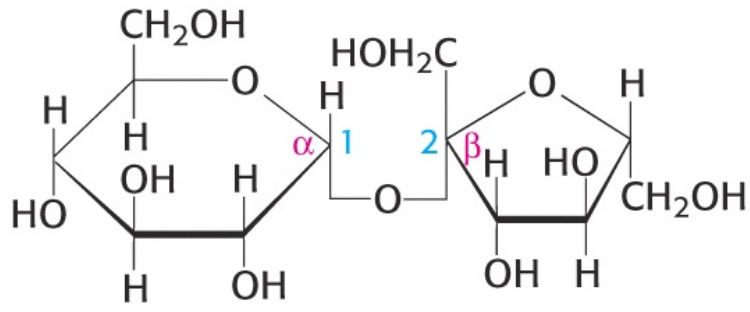
glucose + fructose

Lactose =

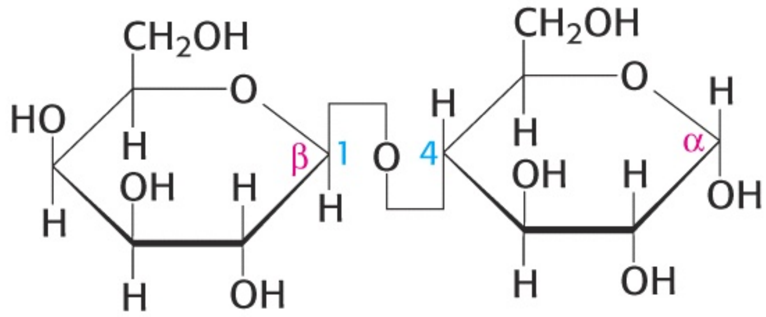
glucose + galactose

Maltose =

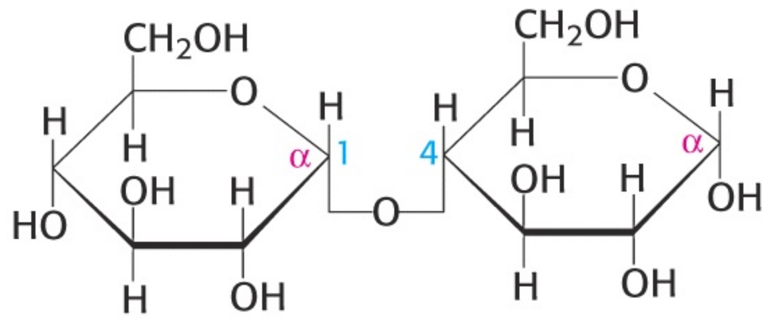
glucose + glucose



Sucrose
(α-D-Glucopyranosyl-(1→2)-β-D-fructofuranose



Lactose
(β-D-Galactopyranosyl-(1→4)-α-D-glucopyranose

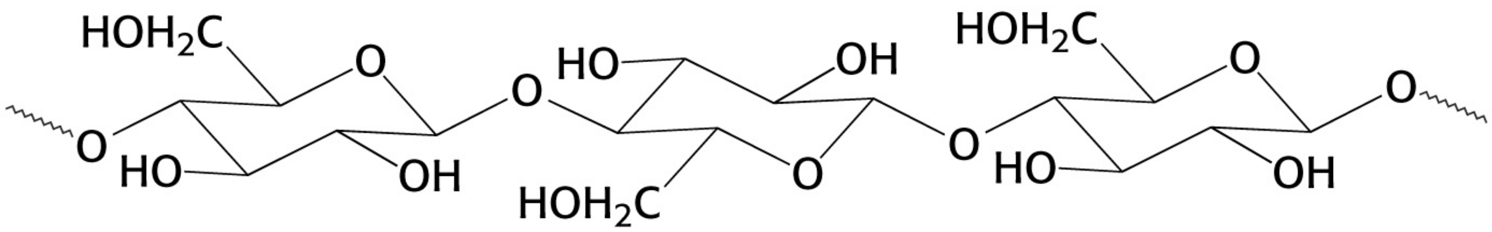


Maltose
(α-D-Glucopyranosyl-(1→4)-α-D-glucopyranose

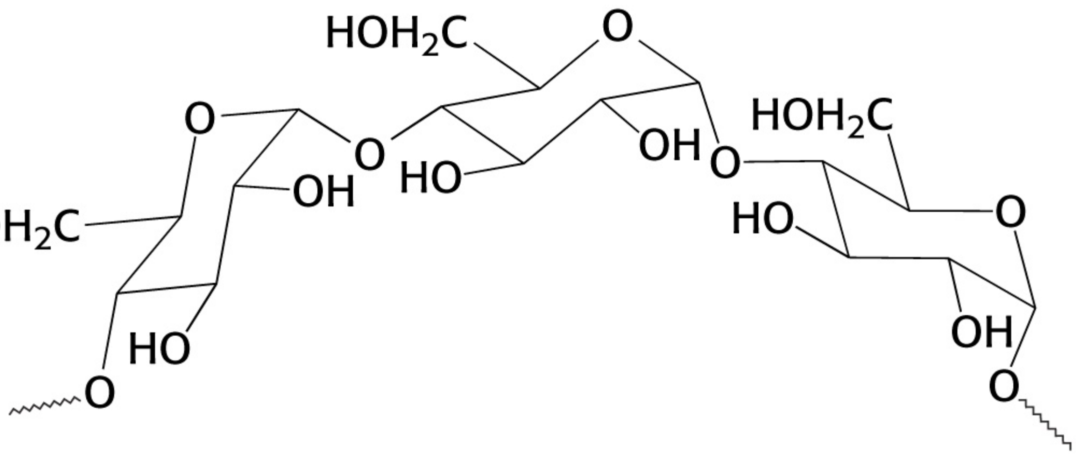
Polymeric carbohydrates

- Glycogen is a branched polymer of glucose
- Starch is a mixture of amylose (a linear glucose polymer) and amylopectin (a branched glucose polymer)
- Cellulose in plants is a linear glucose polymer

Both cellulose and starch are polymers of glucose



Cellulose
(β-1,4 linkages)



Starch and Glycogen
(α-1,4 linkages)

The difference between cellulose and starch is in the type of bonds between the glucose units, which promotes cellulose to form fibres and starch to form an open structure

The Breakdown of Glucose to Pyruvate

Three common routes:

- Embden-Meyerhof pathway
- *Pentose phosphate pathway*
- *Entner-Doudoroff pathway*

The Embden-Meyerhof Pathway

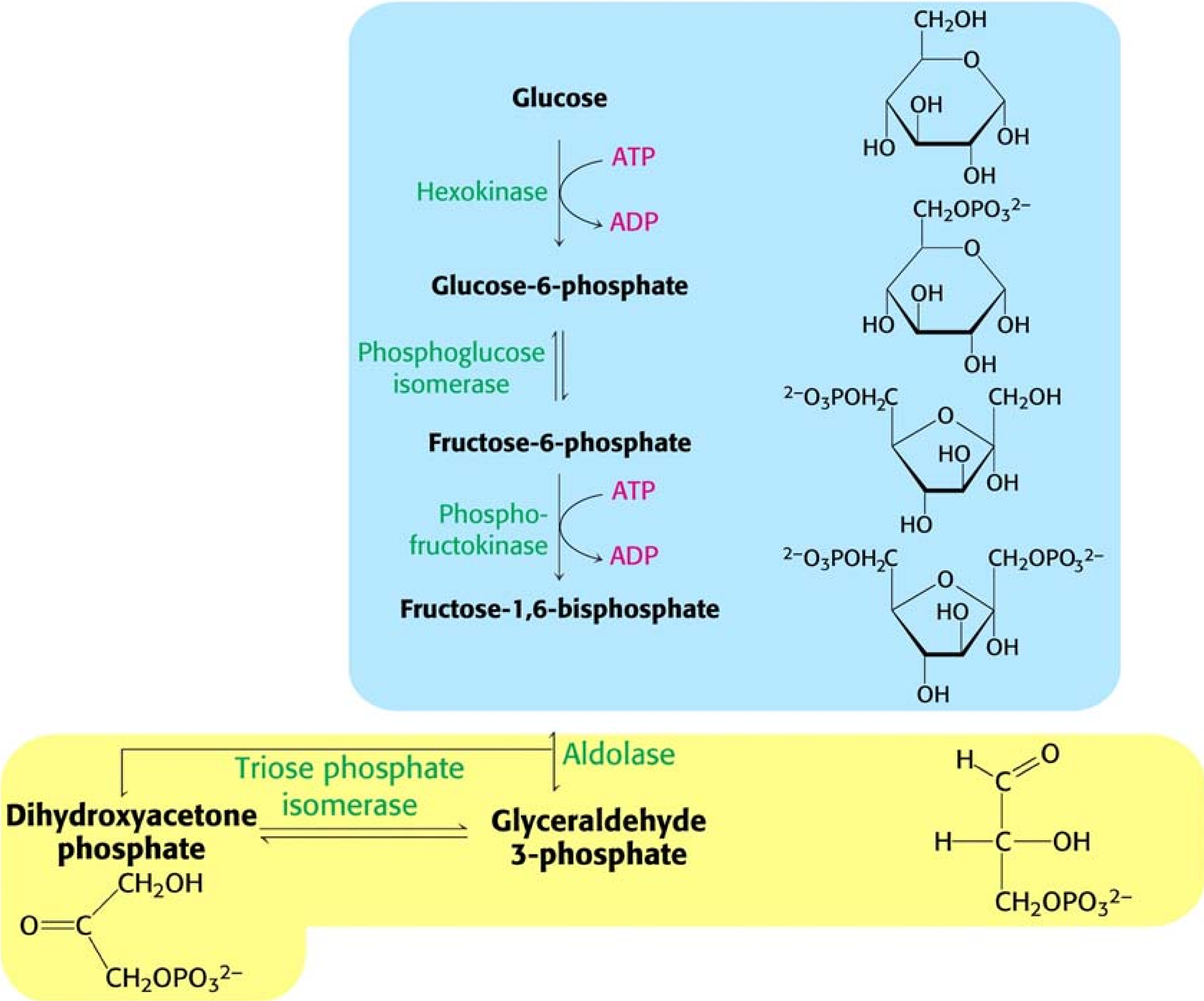
Occurs in cytoplasmic matrix of both procaryotes and eucaryotes

The most common pathway for glucose degradation to pyruvate in stage two of aerobic respiration

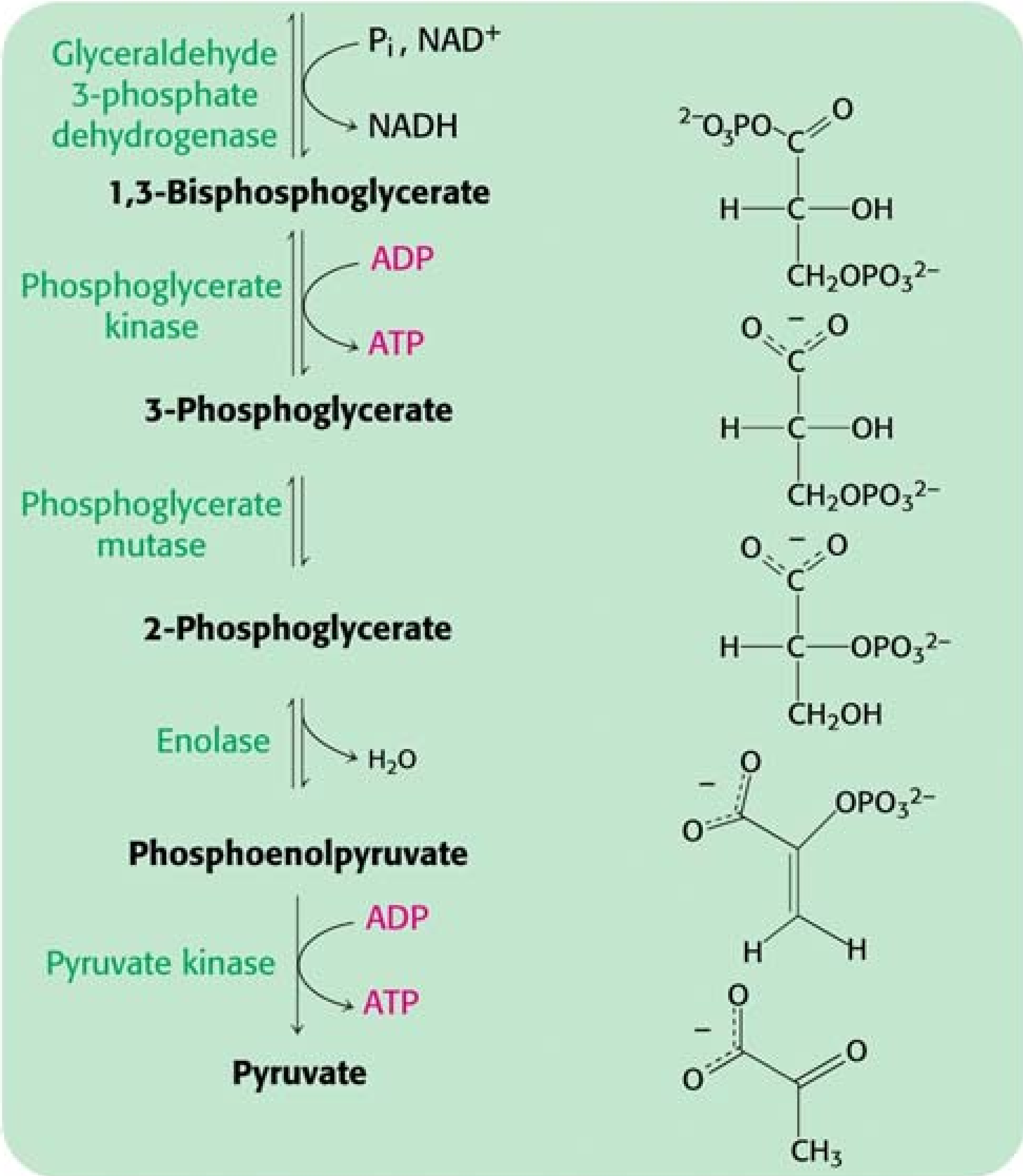
$$\textbf{Glucose + 2ADP + 2P}_i \textbf{ + 2NAD}^+$$

$$\downarrow$$

$$\textbf{2 Pyruvate + 2ATP + 2NADH + 2H}^+$$



Glucose
ATP
Hexokinase
ADP
Glucose-6-phosphate
Phosphoglucose isomerase
Fructose-6-phosphate
ATP
Phospho-fructokinase
ADP
Fructose-1,6-bisphosphate
Aldolase
Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate



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

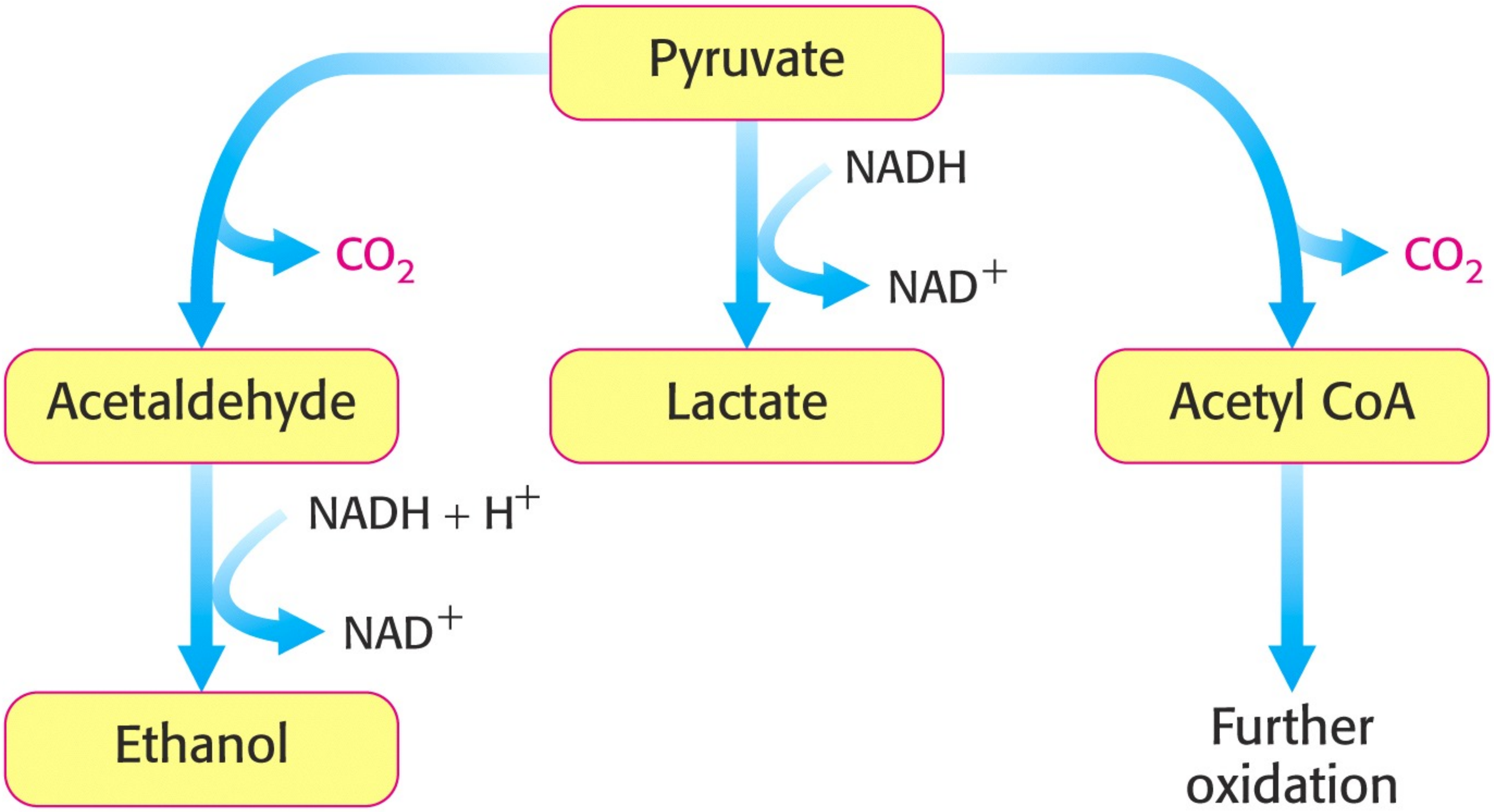
Overall result of glycolysis

$$\text{Glucose} + 2\text{ADP} + 2\text{P}_i + 2\text{NAD}^+$$

$$\downarrow$$

$$2\ \text{Pyruvate} + 2\text{ATP} + 2\text{NADH} + 2\text{H}^+$$

The availability of oxygen determines the fate of pyruvate

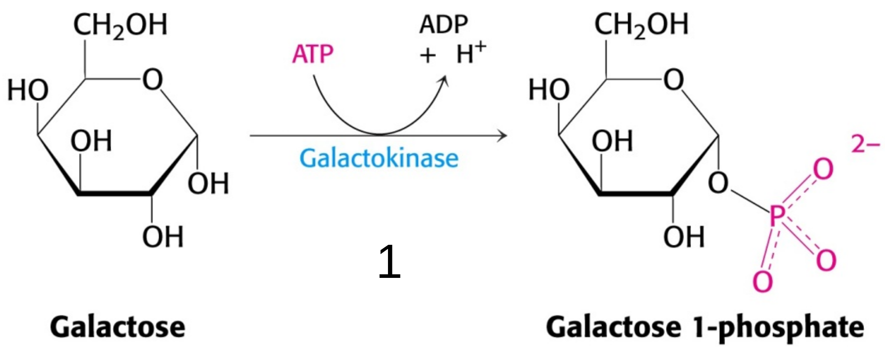


Anaerobic condition

Anaerobic condition

Aerobic condition

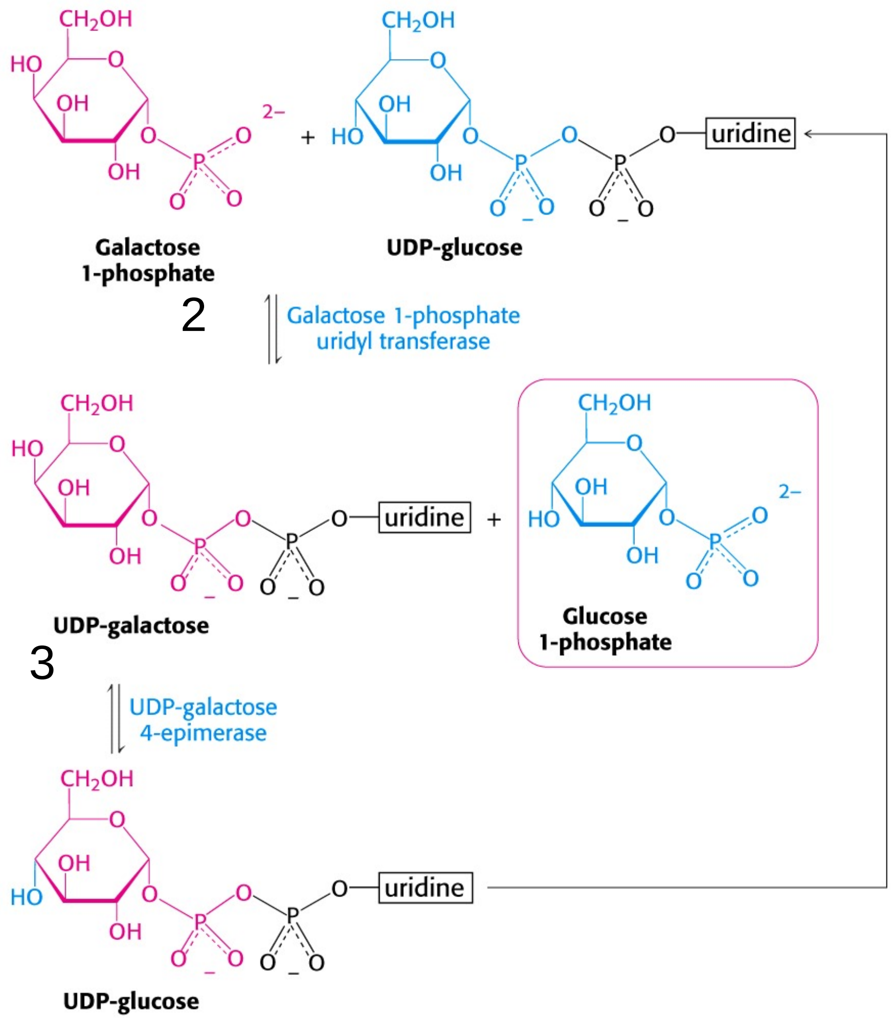
Fermentation



Galactose enters glycolysis

Galactose can be found in lactose (milk sugar)

1. Phosphorylation (activation)
2. Transferase reaction yields glucose 1-phosphate which is converted to glucose 6-phosphate entering glycolysis and UDP-galactose
3. UDP-galactose is epimerised and UDP-glucose is reformed



Fructose enters glycolysis

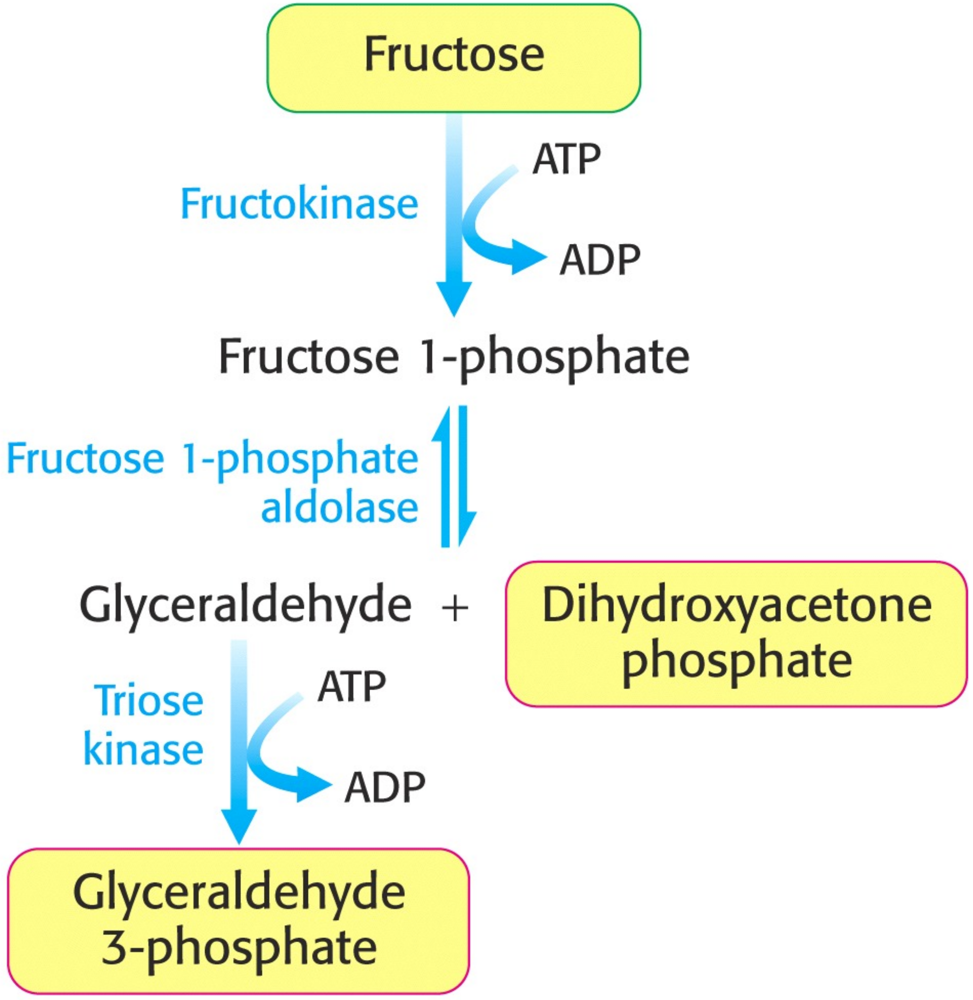
Fructose (mainly from sucrose) can enter glycolysis in two different ways

If plenty of glucose is present:

1. Phosphorylation (activation) to fructose 1-phosphate
2. Formation of dihydroxyacetone phosphate and glyceraldehyde by cleavage
3. Phosphorylation of glyceraldehyde to glyceraldehyde 3-phosphate

If glucose is scarce:

The fructose is phosphorylated directly to fructose 6-phosphate by Hexokinase



Summary

- General concepts in metabolism: thermodynamics, reduction potential, respiration, fermentation
- Basic structure of carbohydrates and lipids
- ATP act as energy currency
- Electron carrier (NAD^+)
- Glycolysis (ten steps, one redox reaction, substrate level phosphorylation)