Bioenergetics and Respiration

- https://www.khanacademy.org/test-prep/mcat/chemical-processes/bioenergetics/v/bioenergetics-the-transformation-of-free-energy-in-living-systems

- Food materials must undergo oxidation in order to yield biologically useful energy.
- **Bioenergetics** is the part of biochemistry concerned with the energy involved in making and breaking of chemical bonds in the molecules found in **biological** organisms. It can also be defined as the study of energy relationships and energy transformations and transductions in living organisms
- **Cellular respiration** is what cells do to break up sugars to get energy they can use. **Cellular respiration** takes in food and uses it to create ATP, a chemical which the cell uses for energy. Usually, this process uses oxygen, and is called aerobic **respiration**.

What is Bioenergetics?

- The study of energy in living systems (environments) and the organisms (plants and animals) that utilize them.

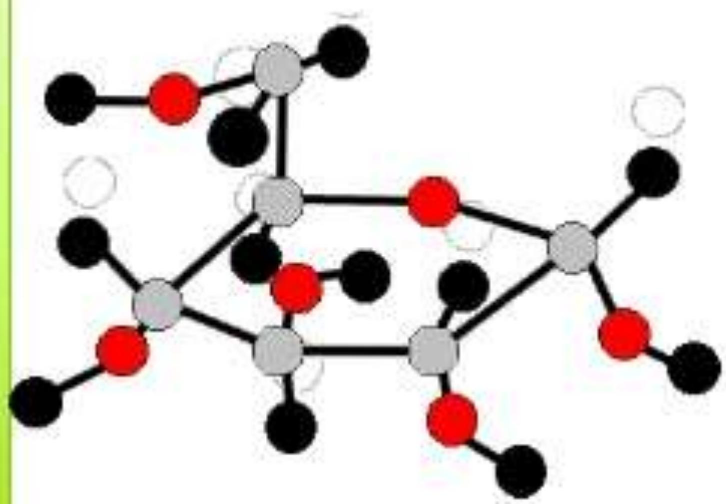
- *Energy*
  - **Required by all organisms**
  - **May be Kinetic or Potential energy**

Kinetic Energy

- Energy of Motion
- Heat and light energy are examples

Potential Energy

- Energy of position
- Includes energy stored in chemical bonds



Bioenergetics

- Bioenergetics is the part of biochemistry concerned with the energy involved in making and breaking of chemical bonds in the molecules found in biological organisms.
- Growth, development and metabolism are some of the central phenomena in the study of biological organisms. The role of energy is fundamental to such biological processes. The ability to harness energy from a variety of metabolic pathways is a property of all living organisms. Life is dependent on energy transformations; living organisms survive because of exchange of energy within and without.

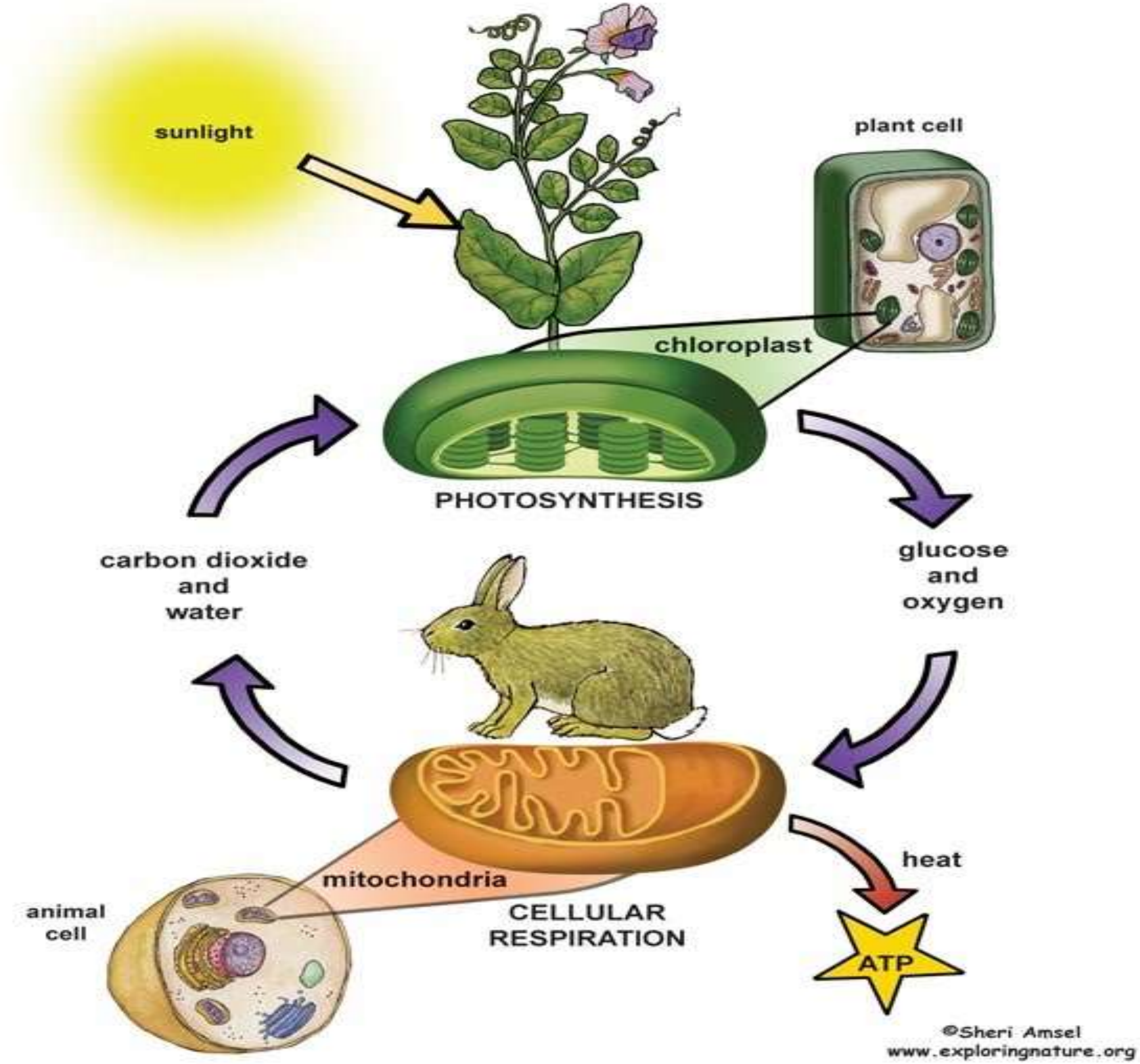
Bioenergetics

- In a living organism, chemical bonds are broken and made as part of the exchange and transformation of energy. Energy is available for work (such as mechanical work) or for other processes (such as chemical synthesis and anabolic processes in growth), when weak bonds are broken and stronger bonds are made. The production of stronger bonds allows release of usable energy.

Bioenergetics

- It is the quantitative study of the energy transductions that occur in living cells and of the nature and function of the chemical processes underlying these transductions.

Photosynthesis and Cellular Respiration



Law of Thermodynamics

- The laws of thermodynamics are important unifying principles of biology. These principles govern the chemical processes (metabolism) in all biological organisms.

Law of Thermodynamics

- The First Law of Thermodynamics, also know as the law of conservation of energy, states that energy can neither be created nor destroyed. It may change from one form to another, but the energy in a closed system remains constant.

- In any physical or chemical change, the total amount of energy in the universe remains constant, although the form of energy may change.

Law of Thermodynamics

- The Second Law of Thermodynamics states that when energy is transferred, law of entropy, there will be less energy available at the end of the transfer process than at the beginning. Due to entropy, which is the measure of disorder in a closed system, all of the available energy will not be useful to the organism. Entropy increases as energy is transferred.
- In all natural processes, the entropy of the universe increases.

Free energy change (Useful energy)

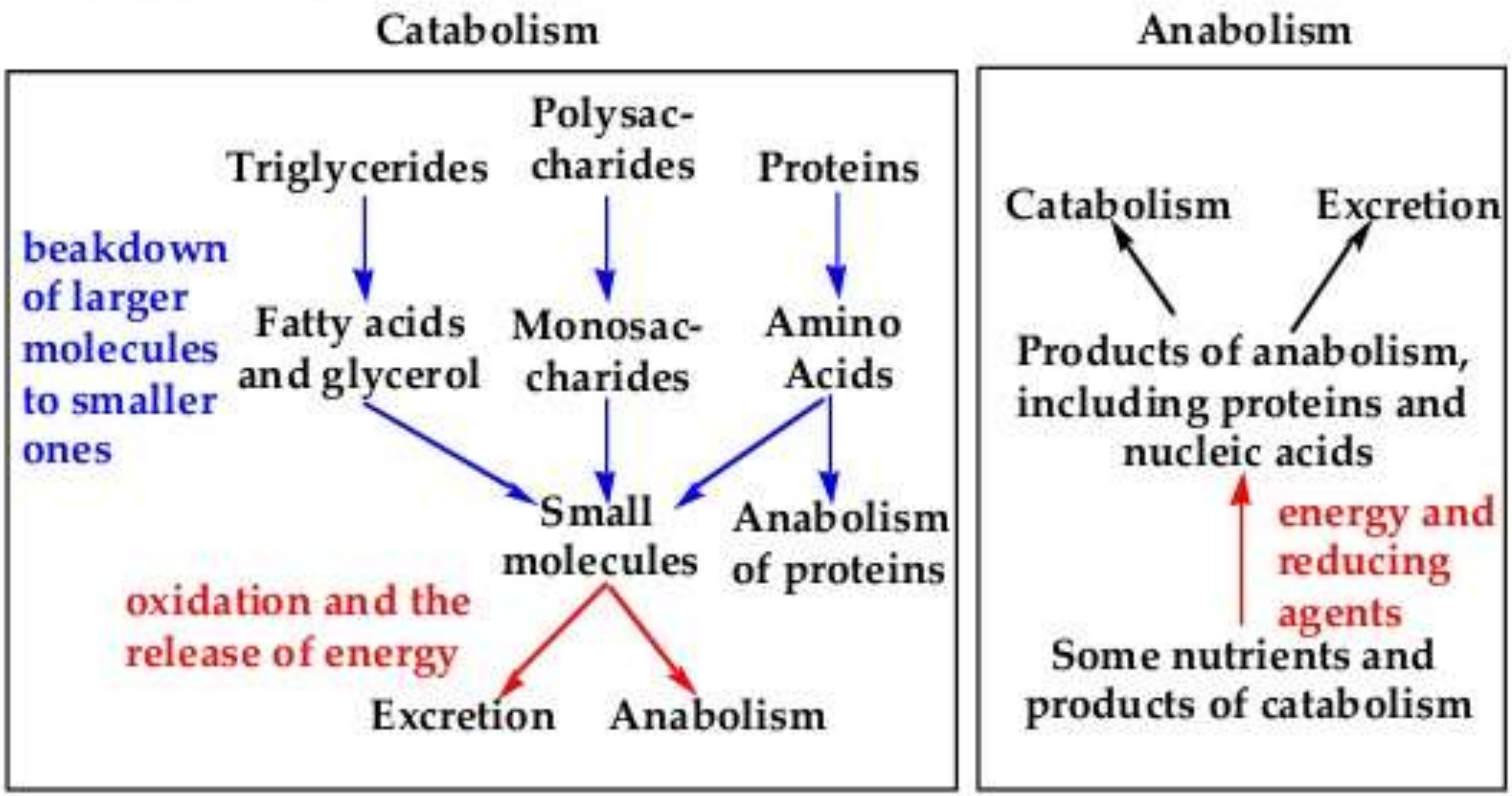
- Gibbs change in free energy (ΔG)is that portion of the total energy change in a system available for doing work. It is also known as the chemical potential .
- $\Delta G = \Delta H - T\Delta S$.
- Useful energy = change in Enthalpy – change in entropy
- Enthalpy – energy content
- Entropy - Randomness of the system

Metabolism

- **Metabolism:** the sum of all chemical reactions involved in maintaining the dynamic state of a cell or organism.
  - **Pathway:** a series of biochemical reactions.
  - **Catabolism:** the biochemical pathways that are involved in generating energy by breaking down large nutrient molecules into smaller molecules with the concurrent production of energy.
  - **Anabolism:** the pathways by which biomolecules are synthesized.

Metabolism

– Metabolism is the sum of catabolism and anabolism.



Energy relationships between catabolic and anabolic pathways

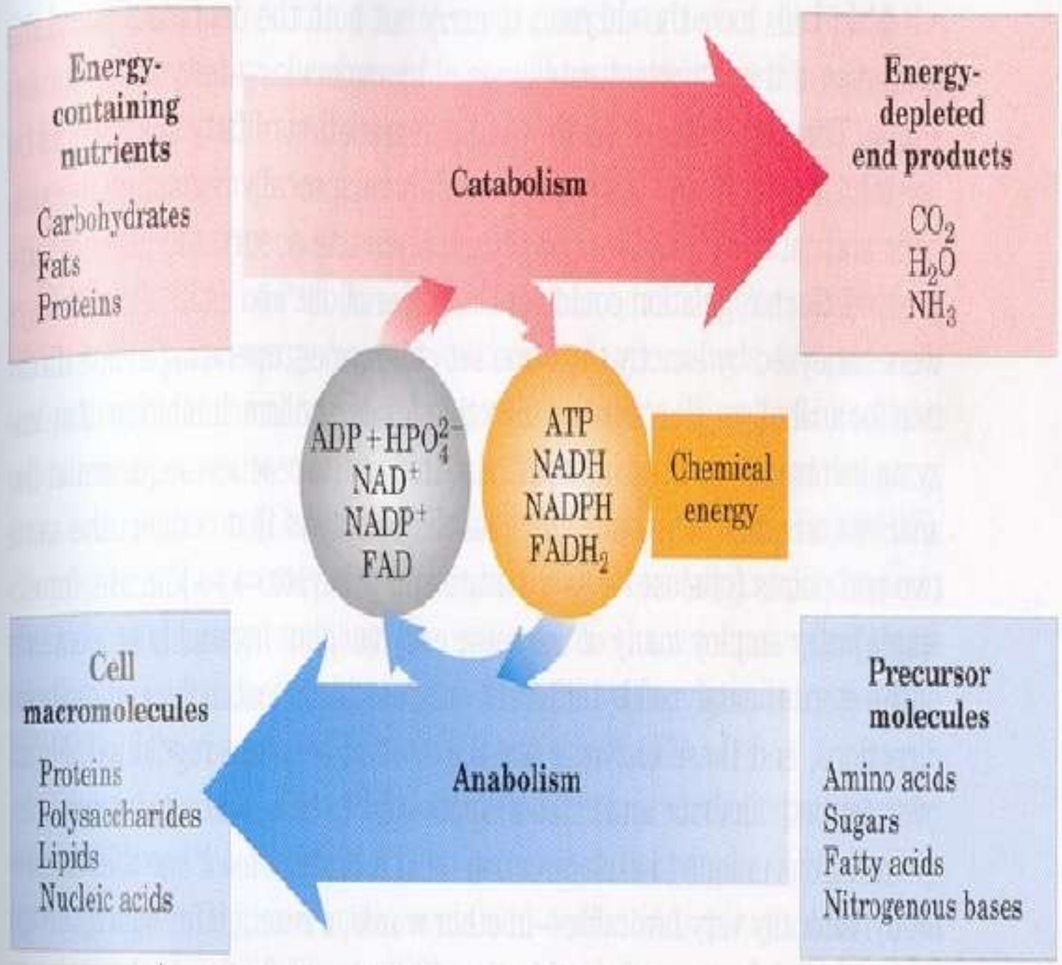


figure 3

Energy relationships between catabolic and anabolic pathways. Catabolic pathways deliver chemical energy in the form of ATP, NADH, NADPH, and $FADH_2$. These energy carriers are used in anabolic pathways to convert small precursor molecules into cell macromolecules.

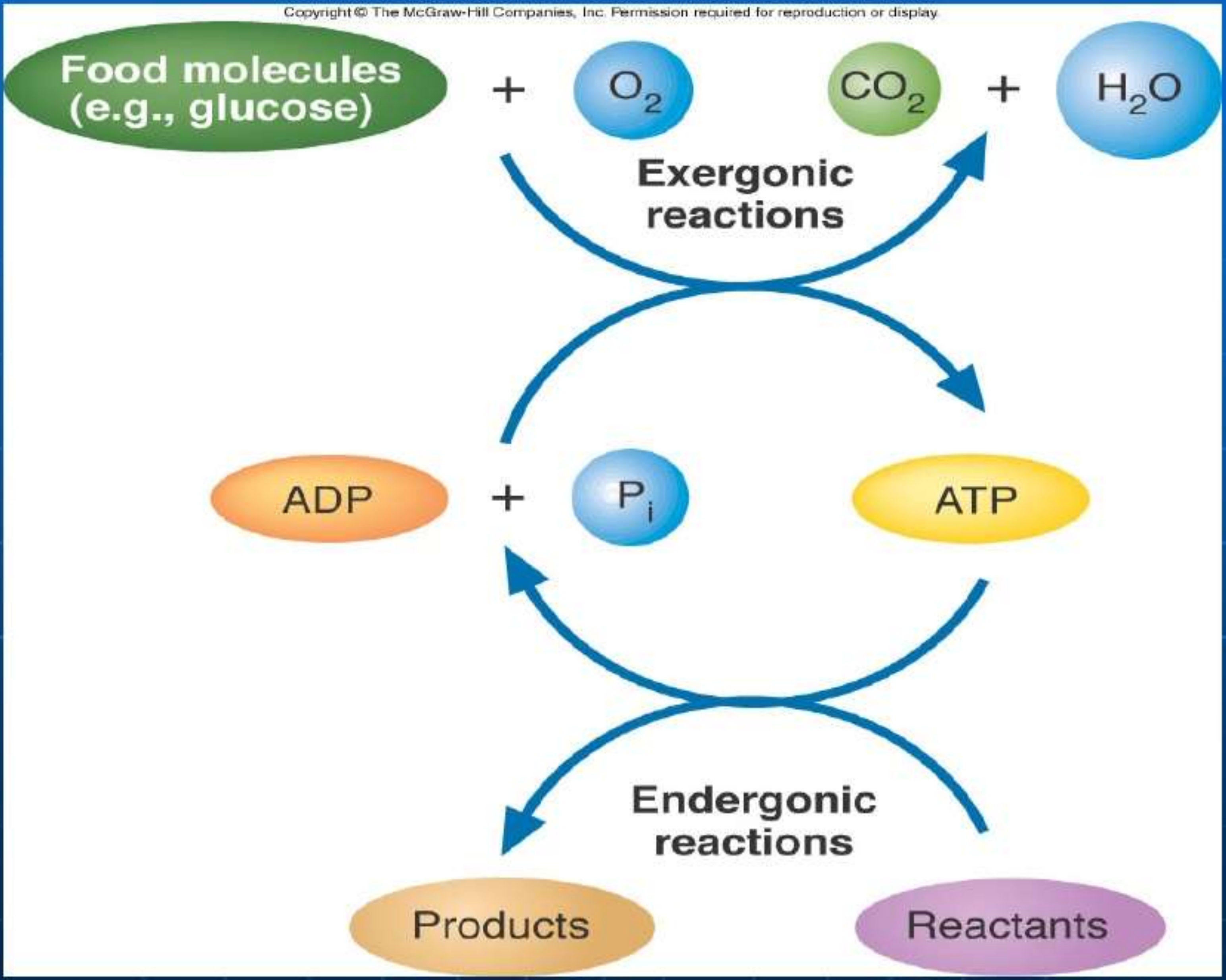
Two Groups of Metabolism

1. **Autotrophs** (自养生物，such as photosynthetic bacteria and higher plants) can use carbon dioxide from the atmosphere as their sole source of carbon, from which they construct all their carbon-containing biomolecules.
2. **Heterotrophs**（异养生物）cannot use atmospheric carbon dioxide and must obtain carbon from their environment in the form of relatively complex organic molecules, such as glucose, proteins.

Types of reactions

- Exergonic is a spontaneous reaction that releases energy. If the free energy change is negative ,this reaction is due to loss of energy from reactants, so it is called exergonic.

  E.g. catabolic reactions.
- Endergonic is an anabolic reaction that consumes energy. If the free energy change is positive, the reaction is called endergonic. E.g. synthetic reactions,
- But at equilibrium, it is zero
- The energy coupling occurs by coupling of Exergonic and endergonic reactions and liberation of heat.



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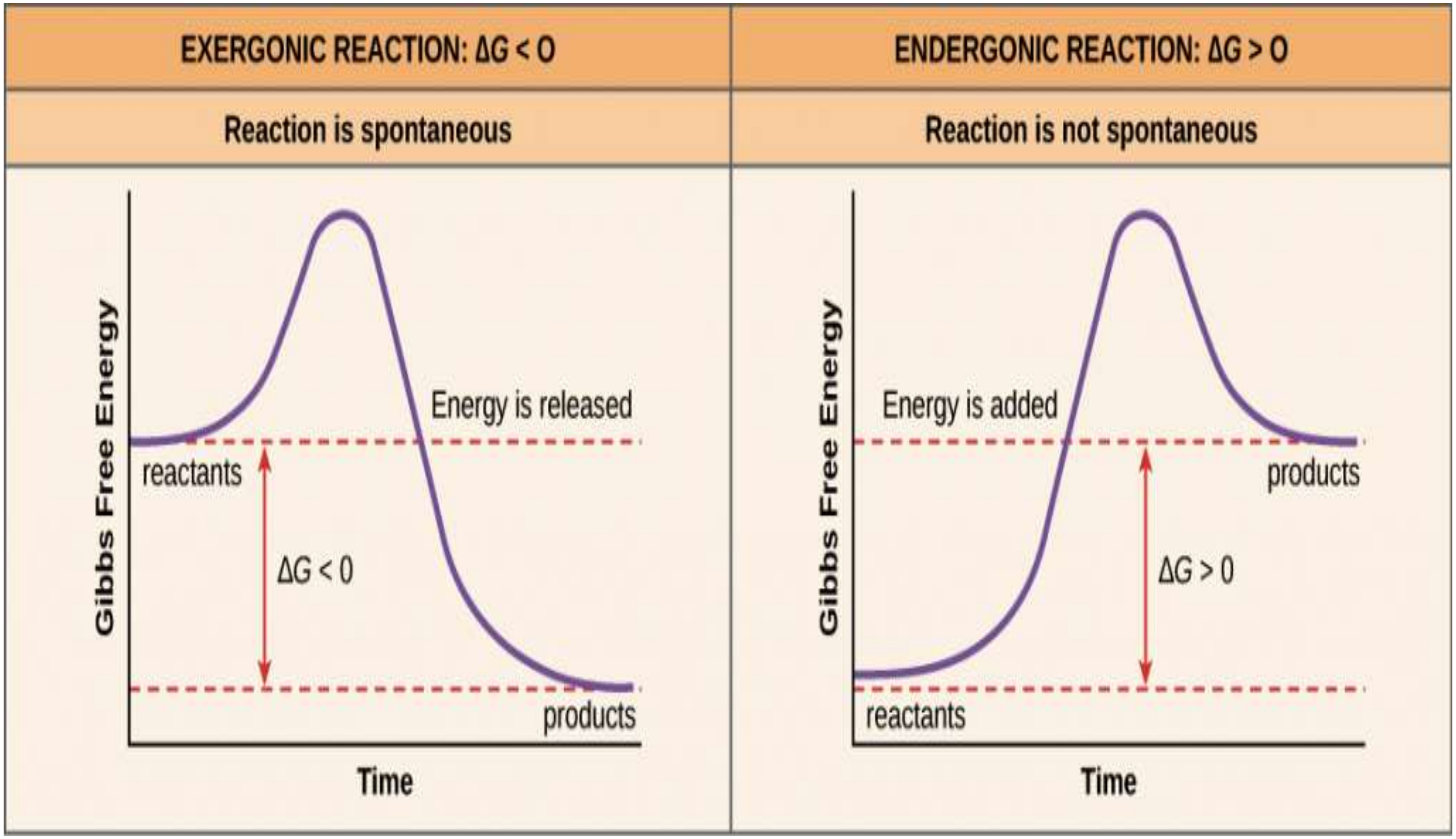
Food molecules (e.g., glucose)
+
O_2
CO_2
+
H_2O
Exergonic reactions
ADP
+
P_i
ATP
Endergonic reactions
Products
Reactants

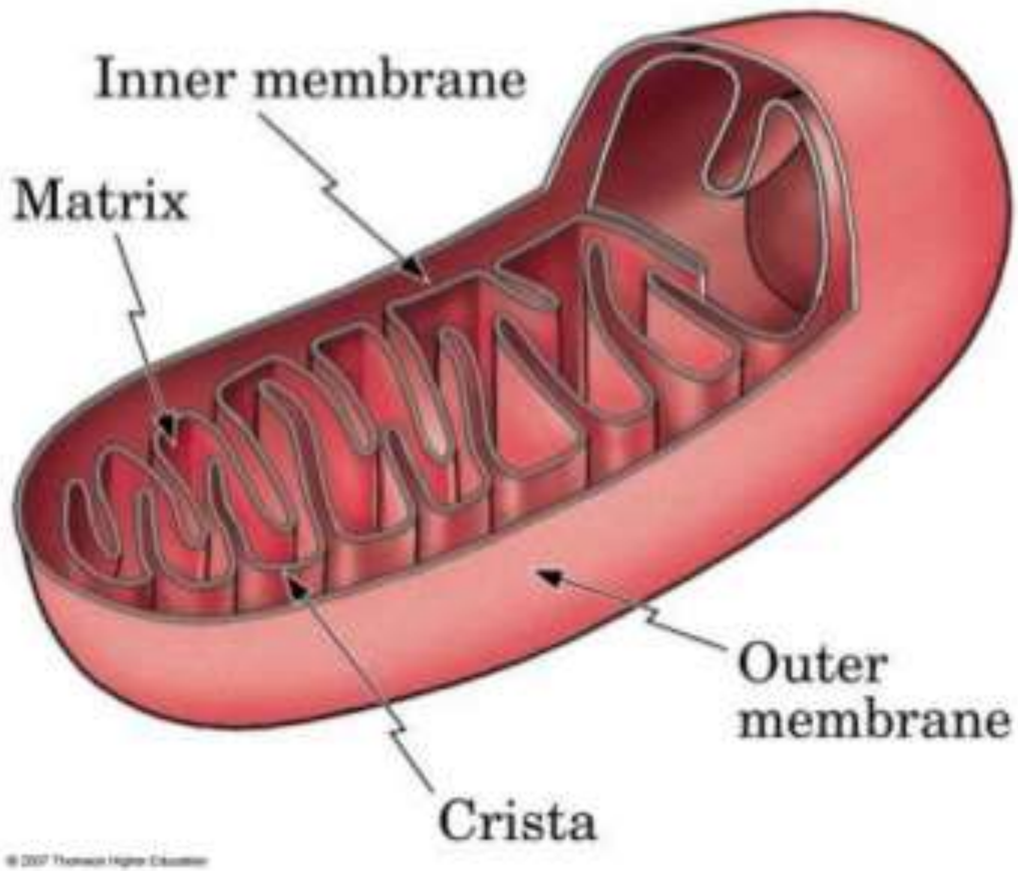

EXERGONIC REACTION: ΔG < O
Reaction is spontaneous
Gibbs Free Energy
Energy is released
reactants
ΔG < 0
products
Time
ENDERGONIC REACTION: ΔG > O
Reaction is not spontaneous
Gibbs Free Energy
Energy is added
products
ΔG > 0
reactants
Time

Four Functions of Metabolism:

1. To obtain chemical energy by capturing solar energy or by degradation of energy-rich nutrients from the environment .
2. To convert nutrient molecules into the cell's own characteristic molecules.
3. To polymerize monomeric precursors into macrobiomolecules (proteins, nucleic acids, lipids, polysaccharides).
4. To synthesize and degrade biomolecules required in specialized cellular functions.

A Mitochondrion

organelles in which the common catabolic pathway takes place in higher organisms; the purpose of this catabolic pathway is to convert the energy stored in food molecules into energy stored in molecules of ATP.



Common Catabolic Pathway

- The two parts to the common catabolic pathway:
  - The citric acid cycle, also called the tricarboxylic acid (TCA) or Krebs cycle.
  - Electron transport chain and phosphorylation, together called oxidative phosphorylation.
- Four principal compounds participating in the common catabolic pathway are:
  - AMP, ADP, and ATP
  - NAD^+/NADH
  - FAD/$FADH_2$
  - coenzyme A; abbreviated CoA or CoA-SH

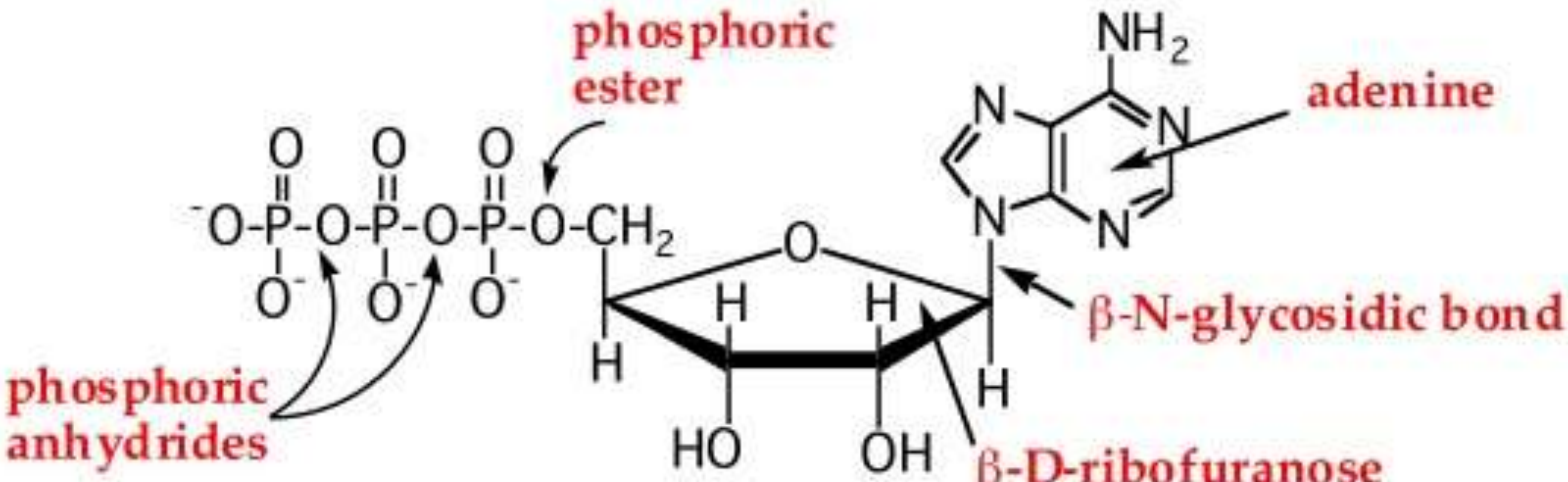
- Oxidation : it is defined as the removal of electrons
- Reduction : it is defined as the addition of electrons
- Eg. Fe^{++} is oxidized to Fe^{+++} **e^- removed**
- Fe^{+++} is reduced to Fe^{++} **e^- added**
- The affinity of an oxidation reduction system for electrons is referred to as oxidation – reduction potential (or) redox potential

ATP Production

- Before cells can use the energy of sunlight or energy /calories stored in carbohydrates, they must transfer the energy to molecules of ATP.

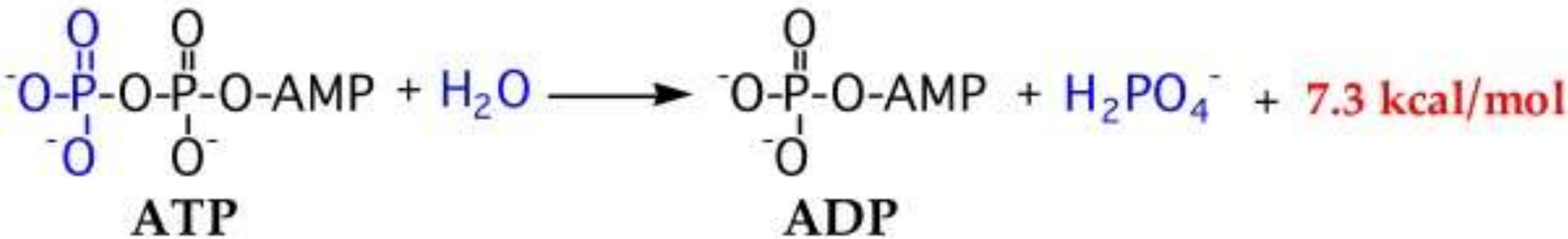
Adenosine Triphosphate

- **ATP** is the most important compound involved in the transfer of phosphate groups.
  - ATP contains two phosphoric anhydride bonds and one phosphoric ester bond.



ATP

– Hydrolysis of the terminal phosphate (anhydride) of ATP gives ADP, phosphate ion, and energy.



– Hydrolysis of a phosphoric anhydride liberates more energy than hydrolysis of a phosphoric ester.

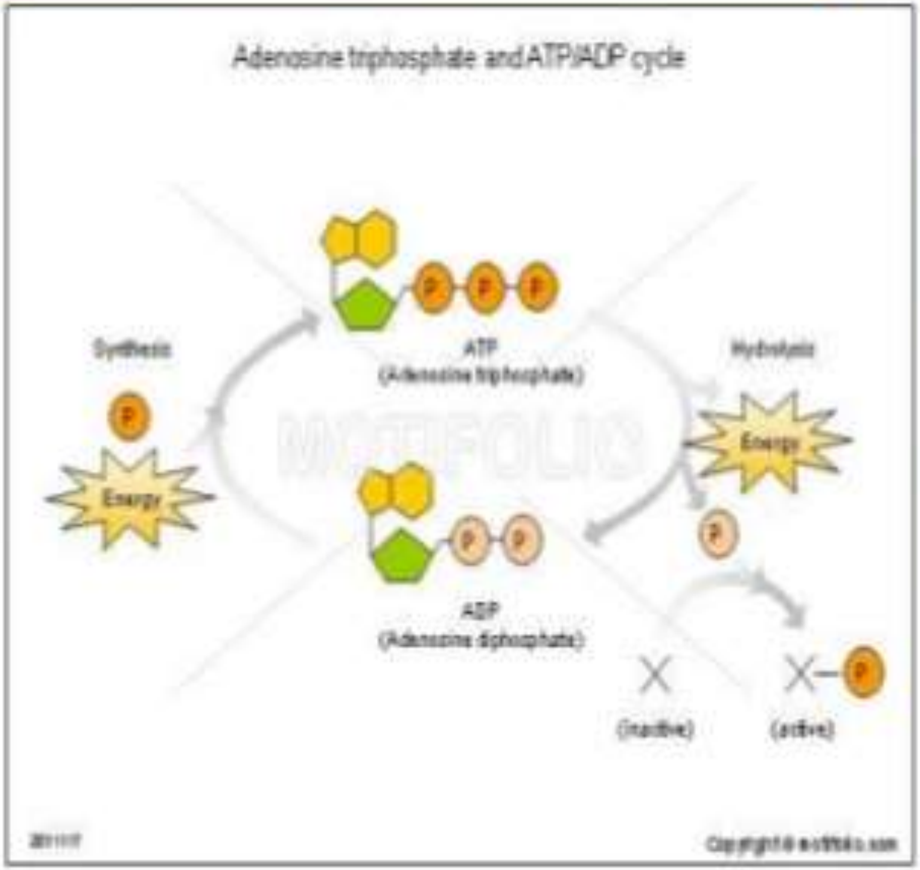
– We say that ATP and ADP contain two high-energy phosphoric anhydride bonds.

– ATP is a universal carrier of phosphate groups.

– ATP is also a common currency for the storage and transfer of energy.

ATP Production

- **<u>The ADP/ATP Cycle</u>**
- The ADP/ATP cycle is a method for renewing the supply of ATP that is constantly being used up in the cell.
- Energy input couples inorganic phosphate to ADP to form energized ATP.

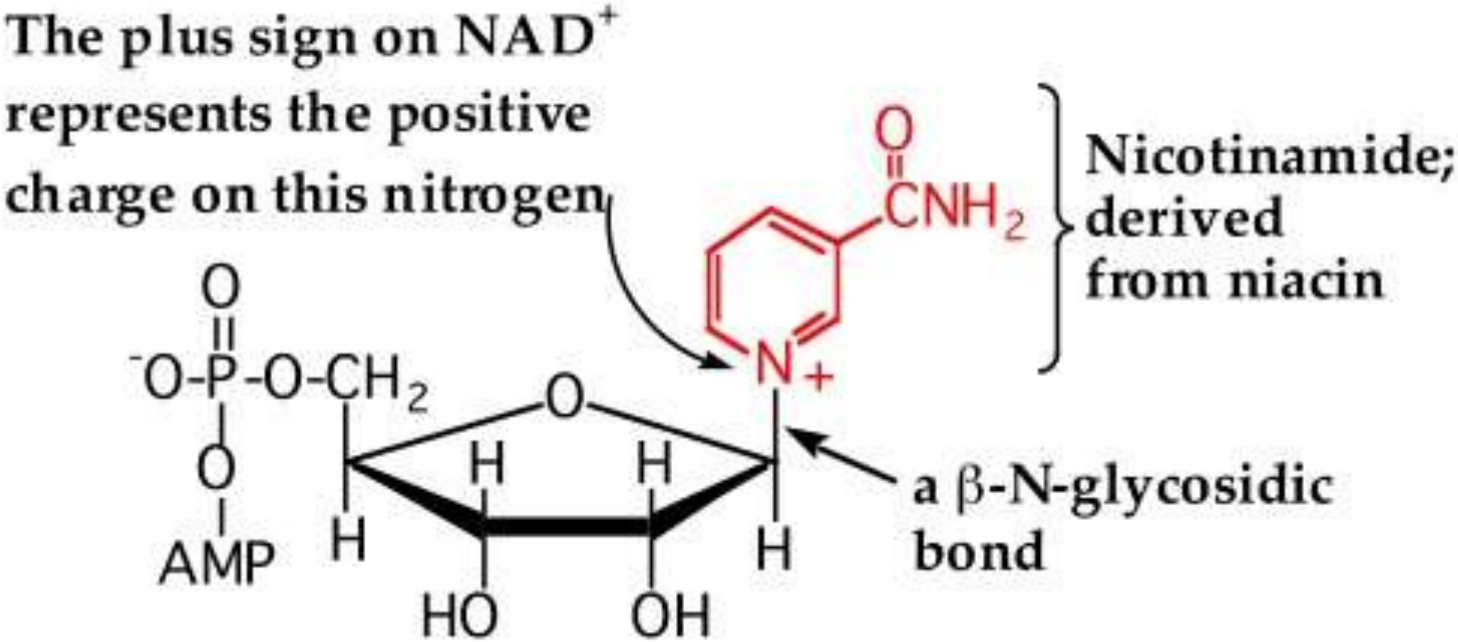


ATP Production

- Chemical Work- supplies energy needed to synthesize macromolecules that make up the cell.
- Transport Work- supplies the energy needed to pump substances across the plasma membrane.
- Mechanical Work- supplies the energy needed to permit muscle to contract, cilia and flagella to beat, chromosomes.

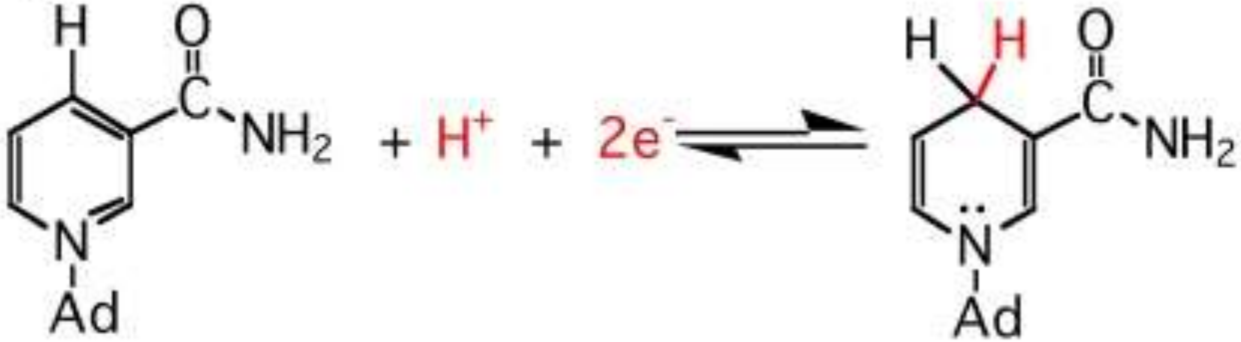
$NAD^+/NADH_2$

- **Nicotinamide adenine dinucleotide (NAD^+)** is a biological oxidizing agent.



NAD^+/NADH

- NAD^+ is a two-electron oxidizing agent, and is reduced to NADH.
- NADH is a two-electron reducing agent, and is oxidized to NAD^+.



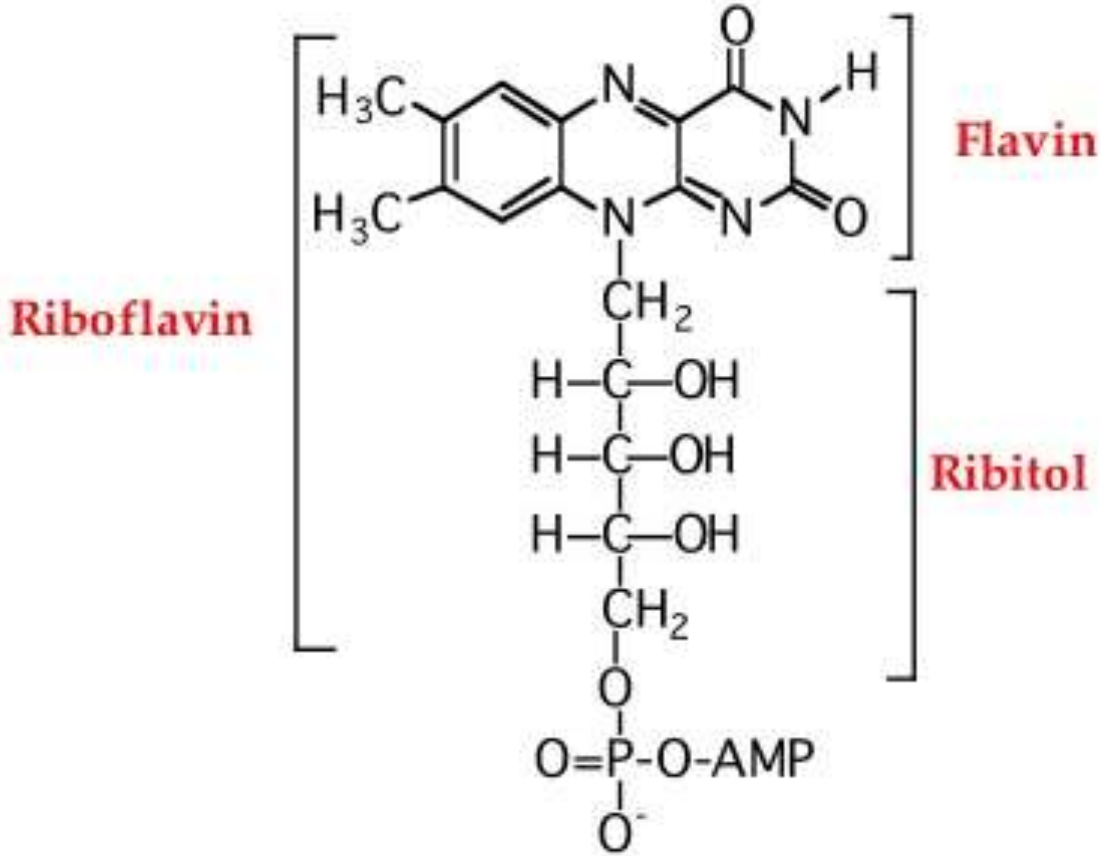
NAD^+
(oxidized form)

NADH
(reduced form)

- **NADH is an electron and hydrogen ion transporting molecule.**

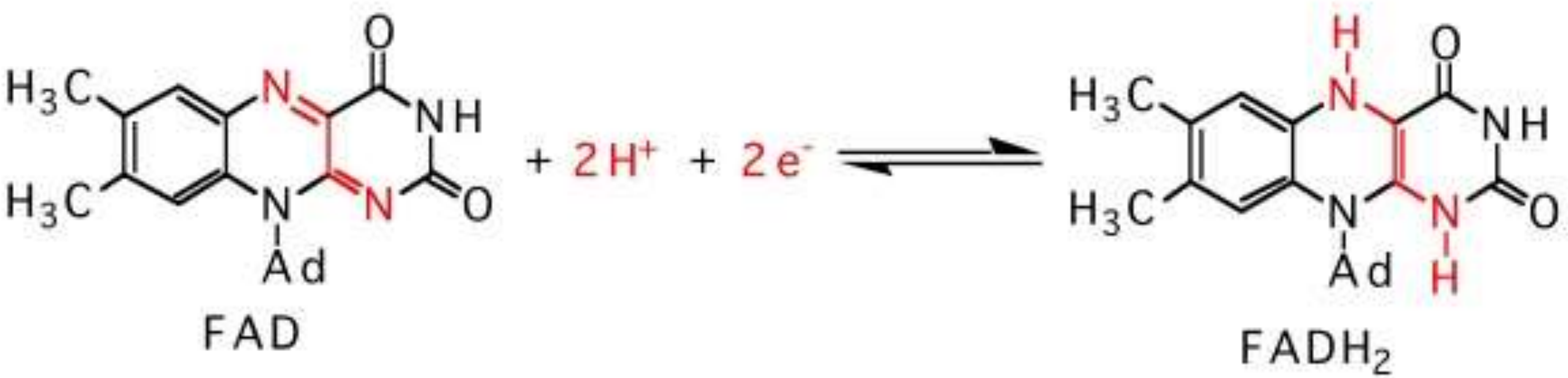
$FAD/FADH_2$

- **Flavin adenine dinucleotide (FAD)** is also a biological oxidizing agent.



FAD/$FADH_2$

- FAD is a two-electron oxidizing agent, and is reduced to $FADH_2$.
- $FADH_2$ is a two-electron reducing agent, and is oxidized to FAD.

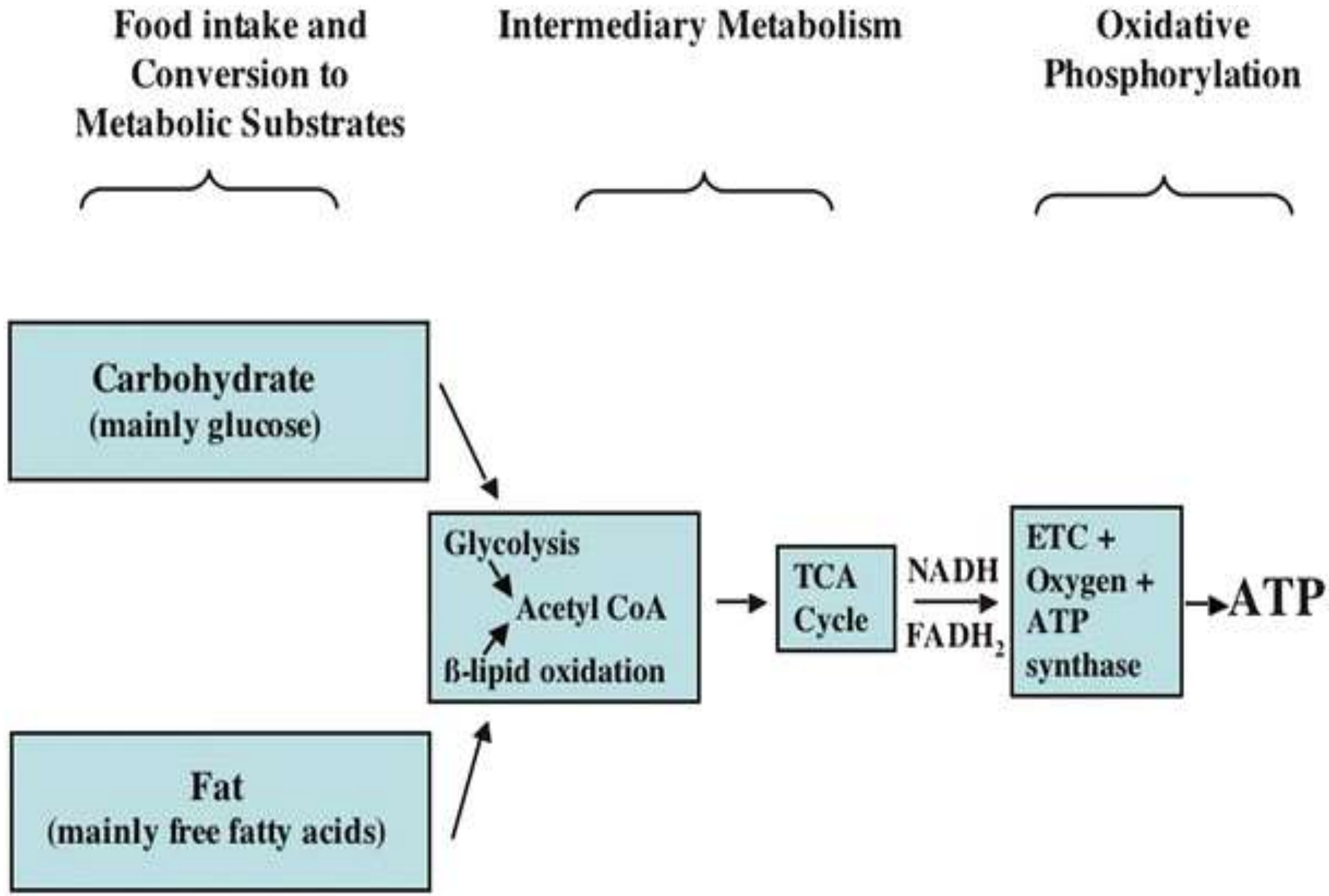


Coenzyme A

- **Coenzyme A (CoA)** is an acetyl-carrying group.
  - Like NAD^+ and FAD, coenzyme A contains a unit of ADP
  - CoA is often written **CoA-SH** to emphasize the fact that it contains a sulfhydryl group.
  - The vitamin part of coenzyme A is pantothenic acid.
  - The acetyl group of acetyl CoA is bound as a high-energy thioester.

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-S-CoA$$

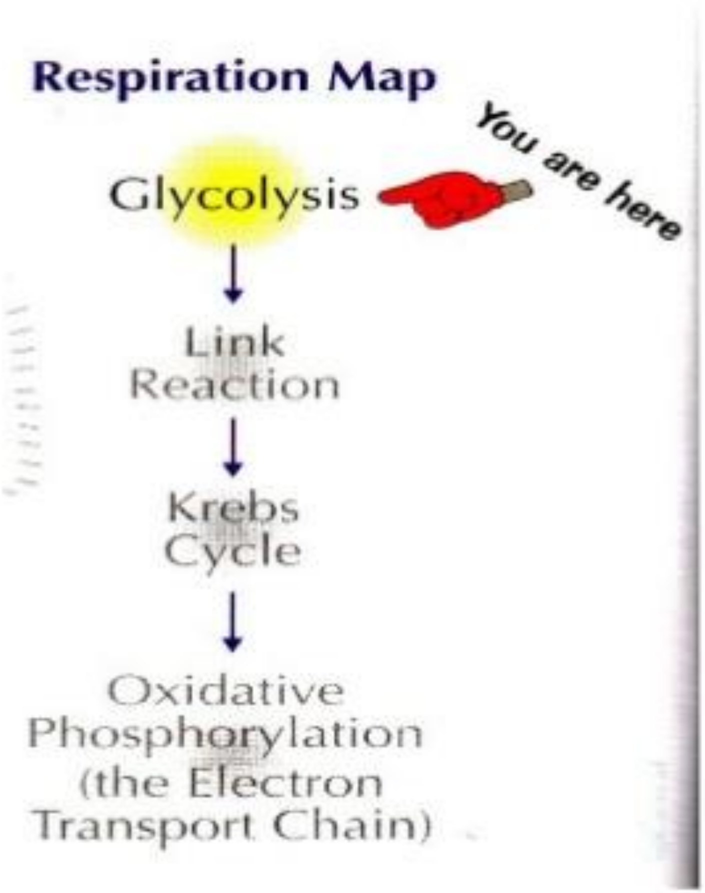
Acetyl coenzyme A
(An acyl CoA)


Food intake and
Conversion to
Metabolic Substrates
Intermediary Metabolism
Oxidative
Phosphorylation
Carbohydrate
(mainly glucose)
Fat
(mainly free fatty acids)
Glycolysis
Acetyl CoA
ß-lipid oxidation
TCA
Cycle
NADH
FADH2
ETC +
Oxygen +
ATP
synthase
ATP

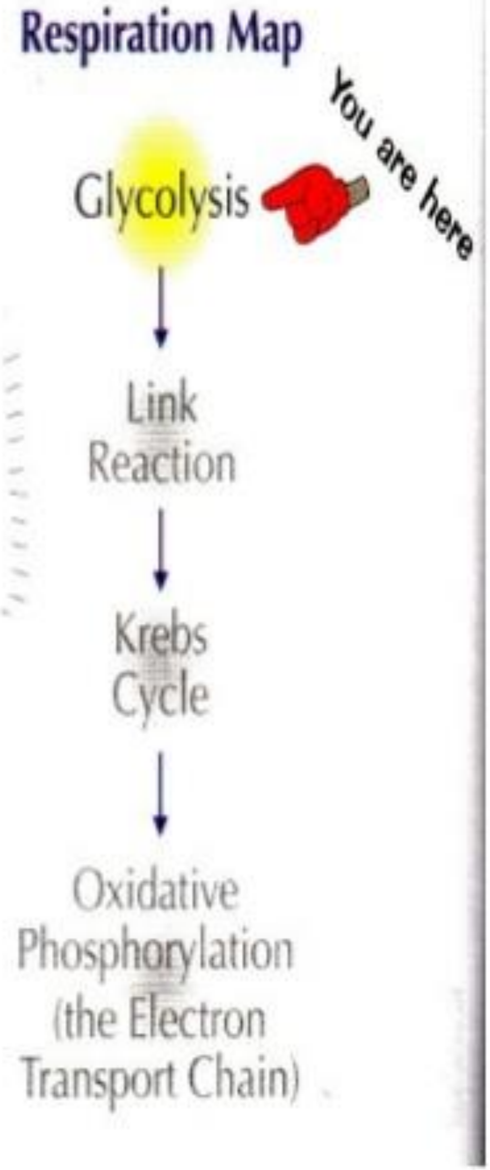
Glycolysis

The first stage of respiration

Respiration



- Process of respiration is split into four parts
- By breaking it into four parts we will have less to learn at any one stage



- It's the **first stage** of both aerobic and anaerobic respiration.
- It **doesn't need oxygen** to take place – so it's **anaerobic**

METABOLISM

- METABOLISM is a series of interconnected chemical reactions occurring within a cell and the chemical compounds involved in it are termed as METABOLITES.
- The enzymatic reactions are organized into discreet pathways which proceed in a stepwise manner, transforming substrates into end products through many specific chemical intermediates.

- Metabolic pathways can be of following types:

➢ **LINEAR (Eg. Glycolysis)**

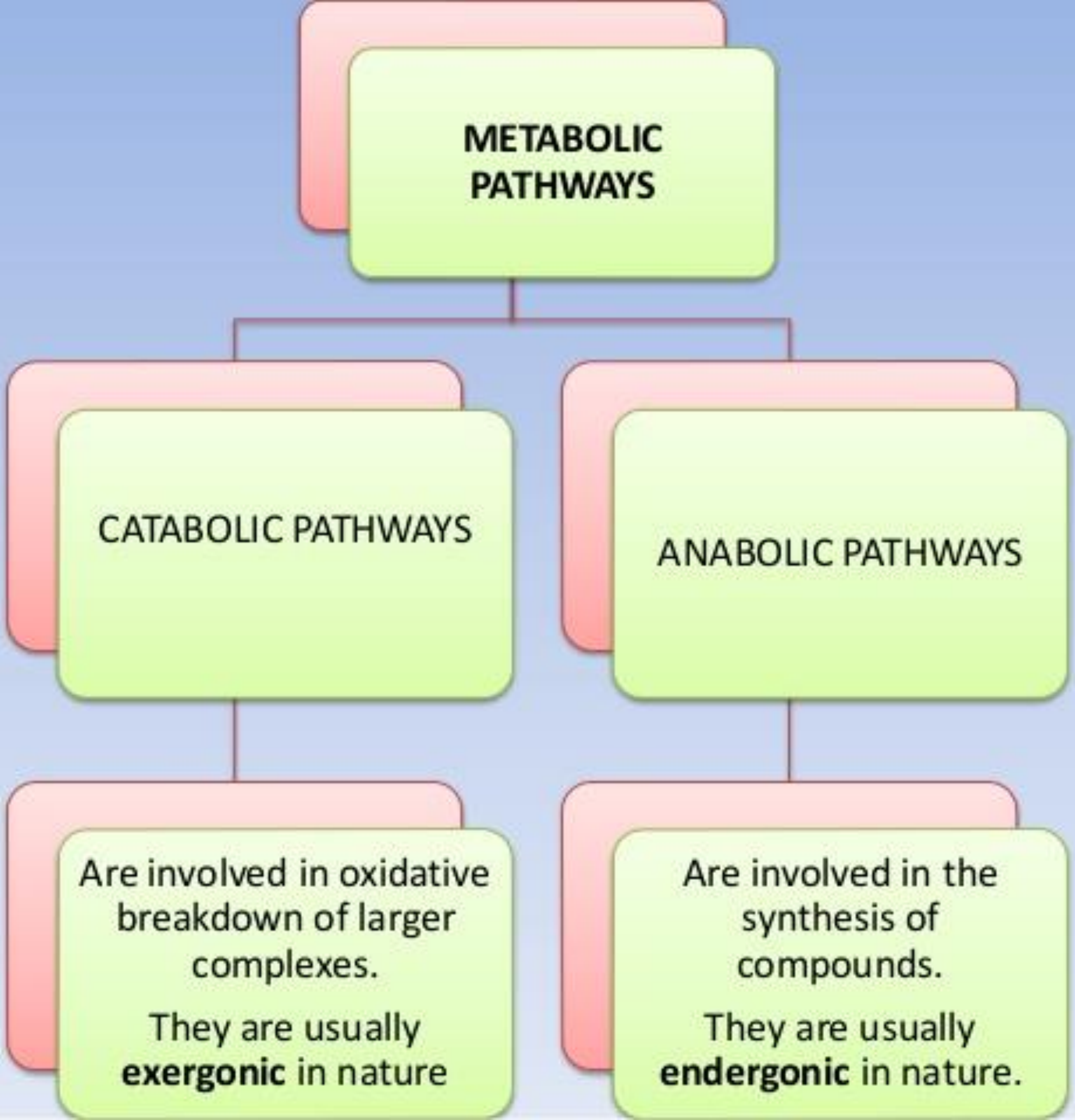
➢ **CYCLIC (Eg. Citric acid cycle)**

➢ **SPIRAL (Eg. Biosynthesis of Fatty Acids)**

- Metabolic pathways serve 2 functions:

➢ **Generation of energy to drive vital functions.**

➢ **Synthesis of biological molecules.**


METABOLIC PATHWAYS
CATABOLIC PATHWAYS
ANABOLIC PATHWAYS
Are involved in oxidative breakdown of larger complexes.
They are usually **exergonic** in nature
Are involved in the synthesis of compounds.
They are usually **endergonic** in nature.

CHARACTERISTICS OF METABOLISM

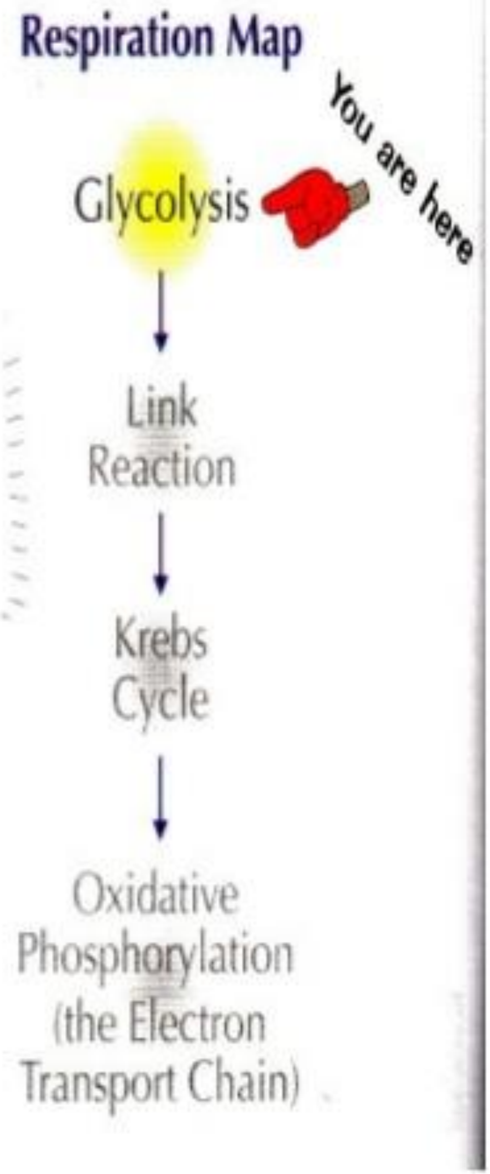
1. Metabolic pathways are irreversible
2. Every metabolic pathway has a committed first step.
3. All metabolic pathways are regulated.
4. Metabolic pathways in eukaryotic cells occur in specific cellular locations.

GLYCOLYSIS

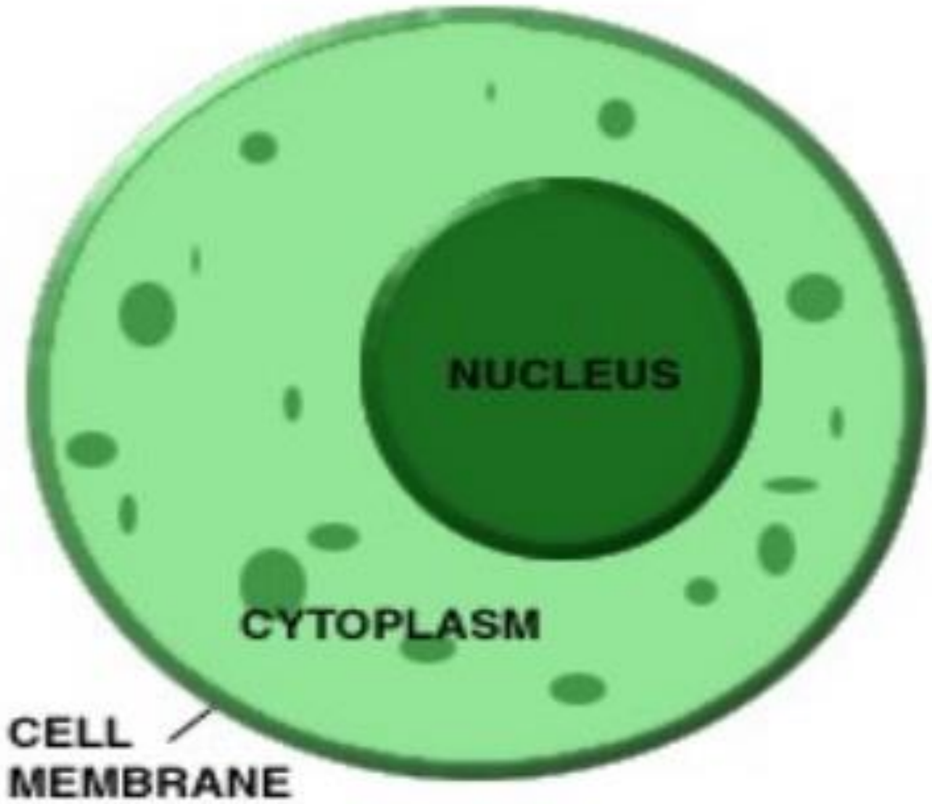
Glycolysis comes from a merger of two Greek words:

- **Glykys = sweet**
- **Lysis = breakdown/ splitting**

It is also known as Embden-Meyerhof-Parnas pathway or EMP pathway.



- Glycolysis takes place in the **cytoplasm** of cells.

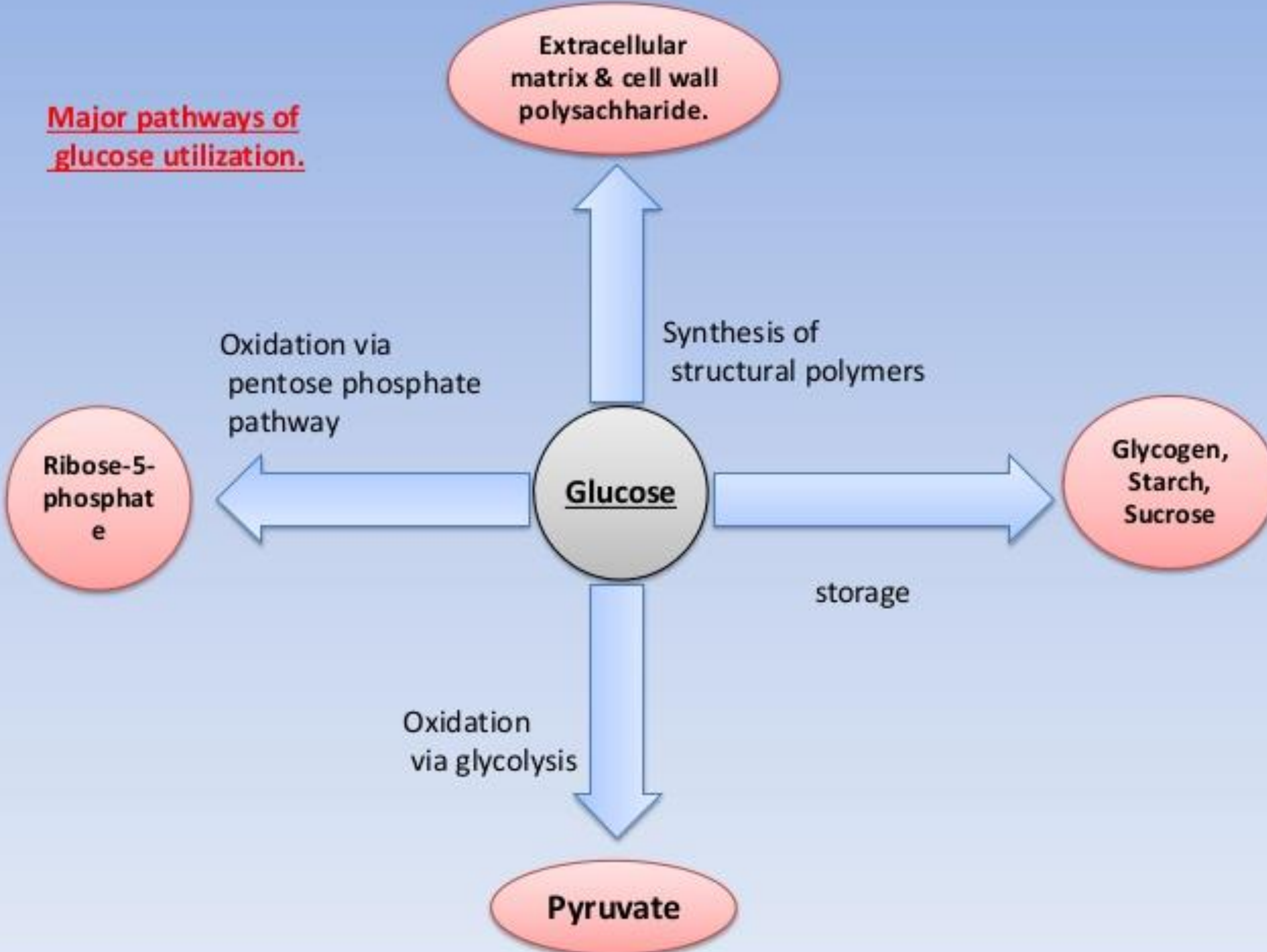


INTRODUCTION

- GLYCOLYSIS is the sequence of 10 enzyme-catalyzed reactions that converts glucose into pyruvate with simultaneous production on of ATP.
- In this oxidative process, 1mol of glucose is partially oxidised to 2 moles of pyruvate.
- This major pathway of glucose metabolism occurs in the cytosol of all cell.
- This unique pathway occurs **aerobically** as well as **anaerobically & doesn't involve molecular oxygen.**

- It also includes formation of Lactate from Pyruvate.
- The glycolytic sequence of reactions differ from species to species only in the mechanism of its regulation & in the subsequent metabolic fate of the pyruvate formed.
- In aerobic organisms, glycolysis is the prelude to Citric acid cycle and ETC.
- Glycolysis is the central pathway for Glucose catabolism.

Major pathways of glucose utilization.

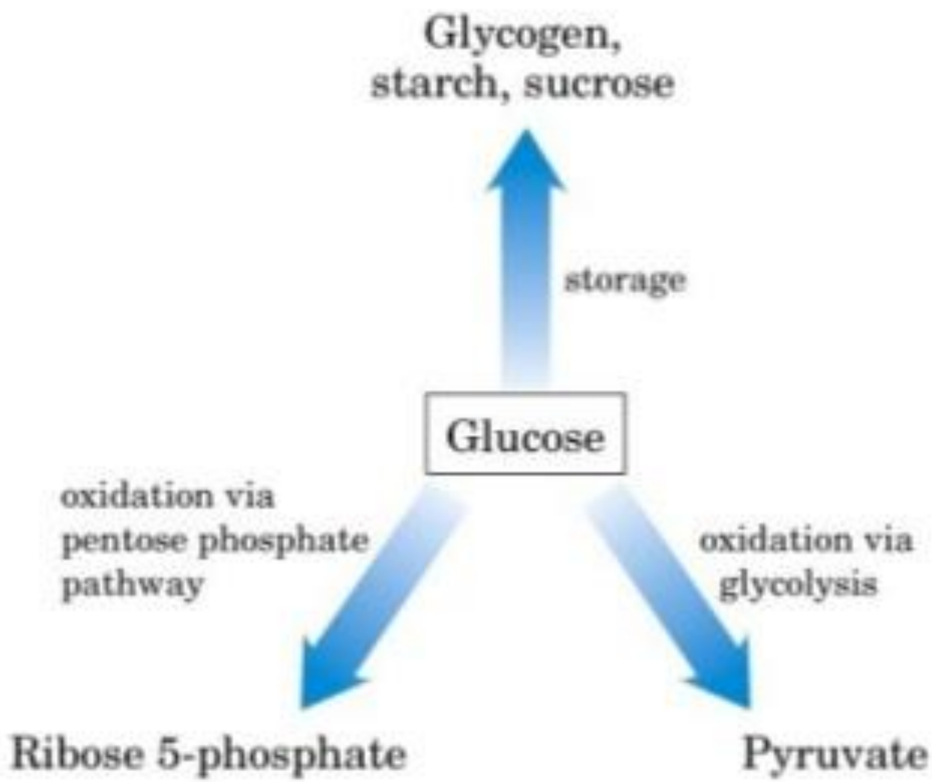


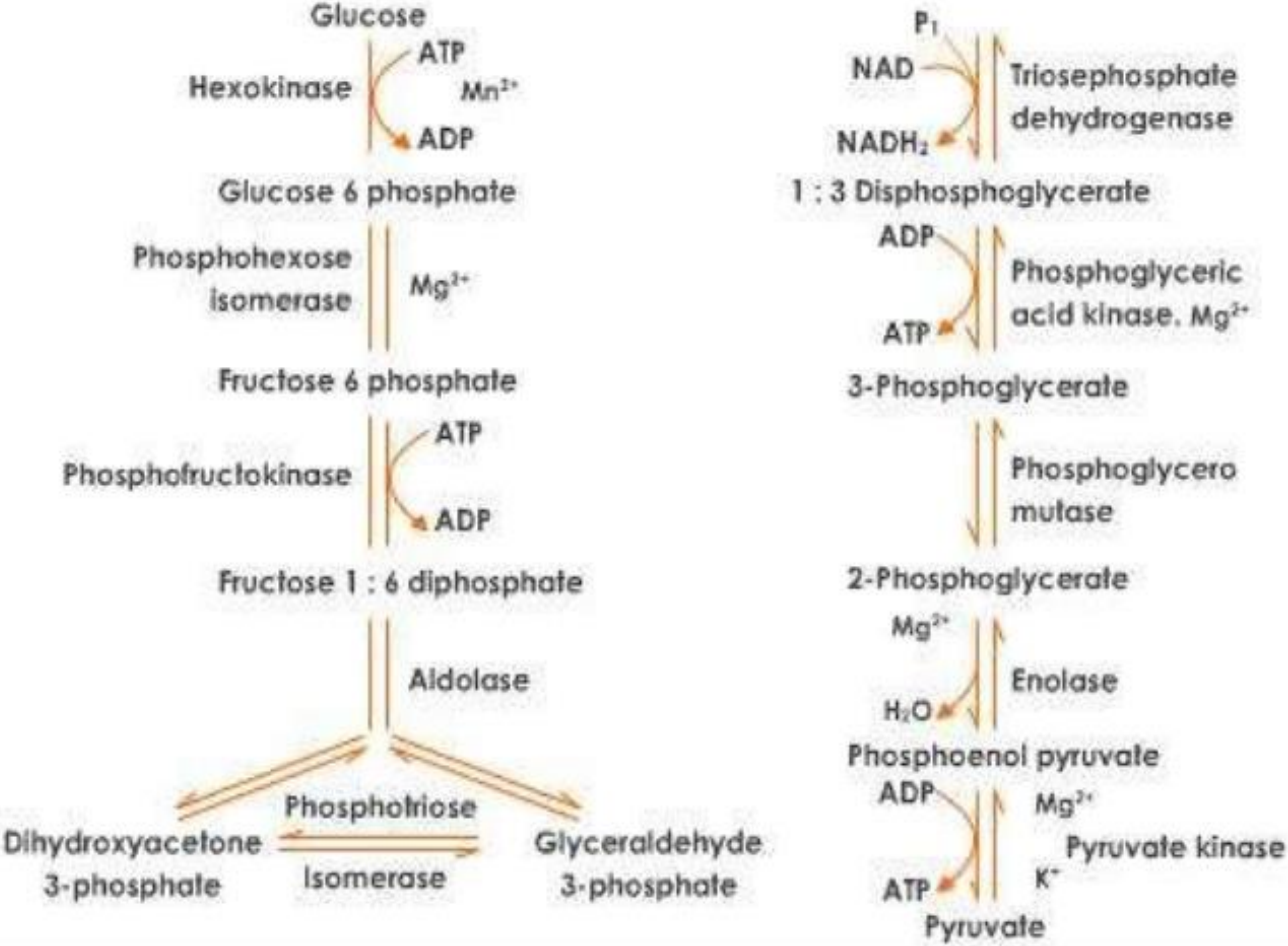
Fate of glucose in living systems

Glucose + $6O_2$ = $6CO_2$ + $6H_2O$ δG^o= -2840 kJ/mol

Glucose + $2NAD^+$ = 2Pyruvate + 2NADH + $2H^+$ δGo = -146 kJ/mol

5.2% of total free energy that can be released by glucose is released in glycolysis.




Glucose
ATP
Hexokinase
Mn2+
ADP
Glucose 6 phosphate
Phosphohexose
isomerase
Mg2+
Fructose 6 phosphate
ATP
Phosphofructokinase
ADP
Fructose 1 : 6 diphosphate
Aldolase
Phosphotriose
Dihydroxyacetone
3-phosphate
Isomerase
Glyceraldehyde
3-phosphate
P1
NAD
Triosephosphate
dehydrogenase
NADH2
1 : 3 Disphosphoglycerate
ADP
Phosphoglyceric
acid kinase, Mg2+
ATP
3-Phosphoglycerate
Phosphoglycero
mutase
2-Phosphoglycerate
Mg2+
Enolase
H2O
Phosphoenol pyruvate
ADP
Mg2+
Pyruvate kinase
K+
ATP
Pyruvate

TWO PHASES OF GLYCOLYSIS

- Glycolysis leads to breakdown of 6-C glucose into two molecules of 3-C pyruvate with the enzyme catalyzed reactions being bifurcated or categorized into 2 phases:

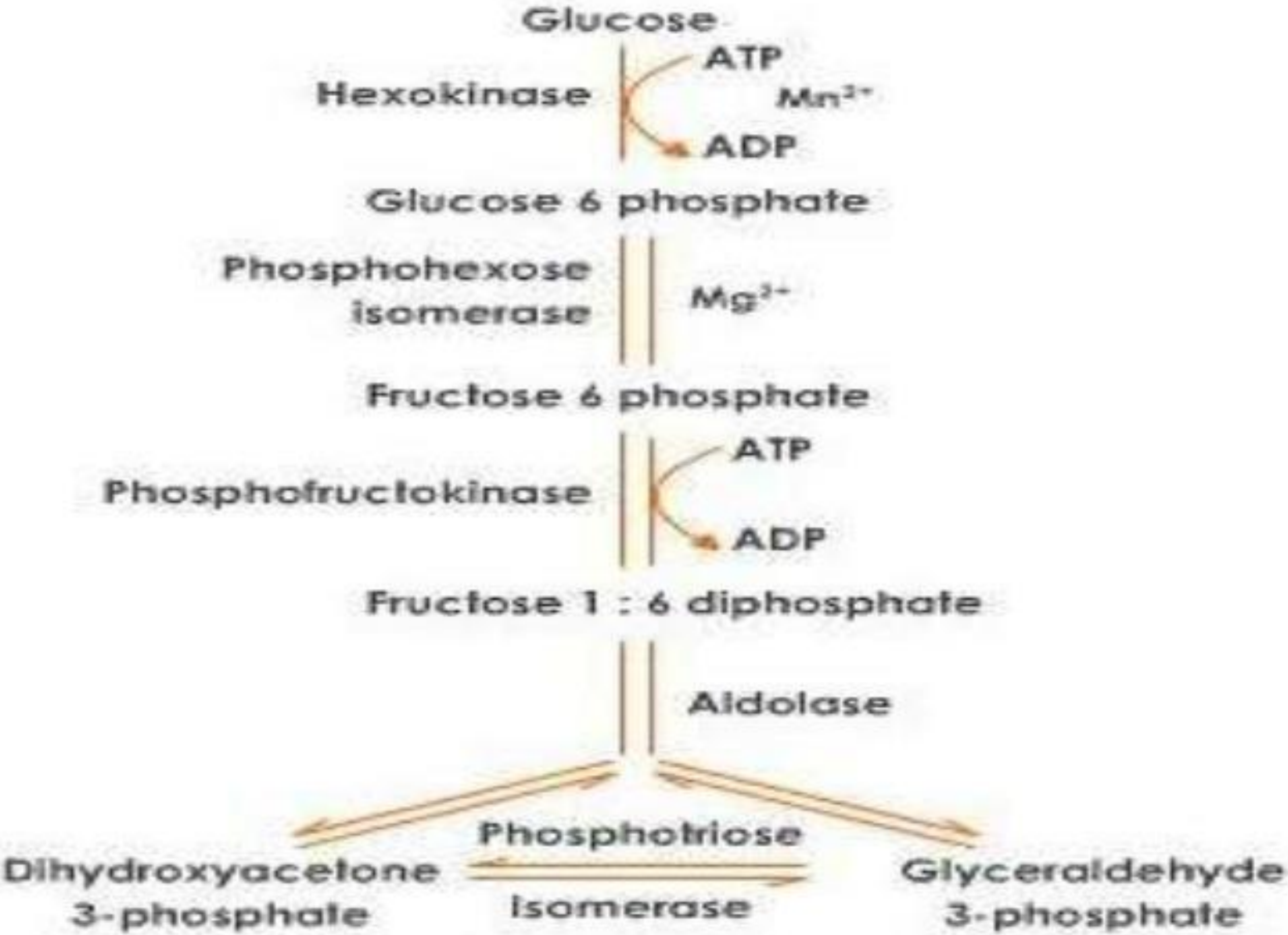
1. **Phase 1- preparatory phase**
2. **Phase 2- payoff phase.**

PREPARATORY PHASE

- It consists of the 1st 5 steps of glycolysis in which the glucose is enzymatically phosphorylated by ATP to yield Fructose-1,6-biphosphate.
- This fructuse-1,6-biphosphate is then split in half to yield 2 molecules of 3-carbon containing Glyceraldehyde-3-phosphate/ dihyroxyacteone phosphate.

- Thus the first phase **results in cleavage of the hexose chain.**

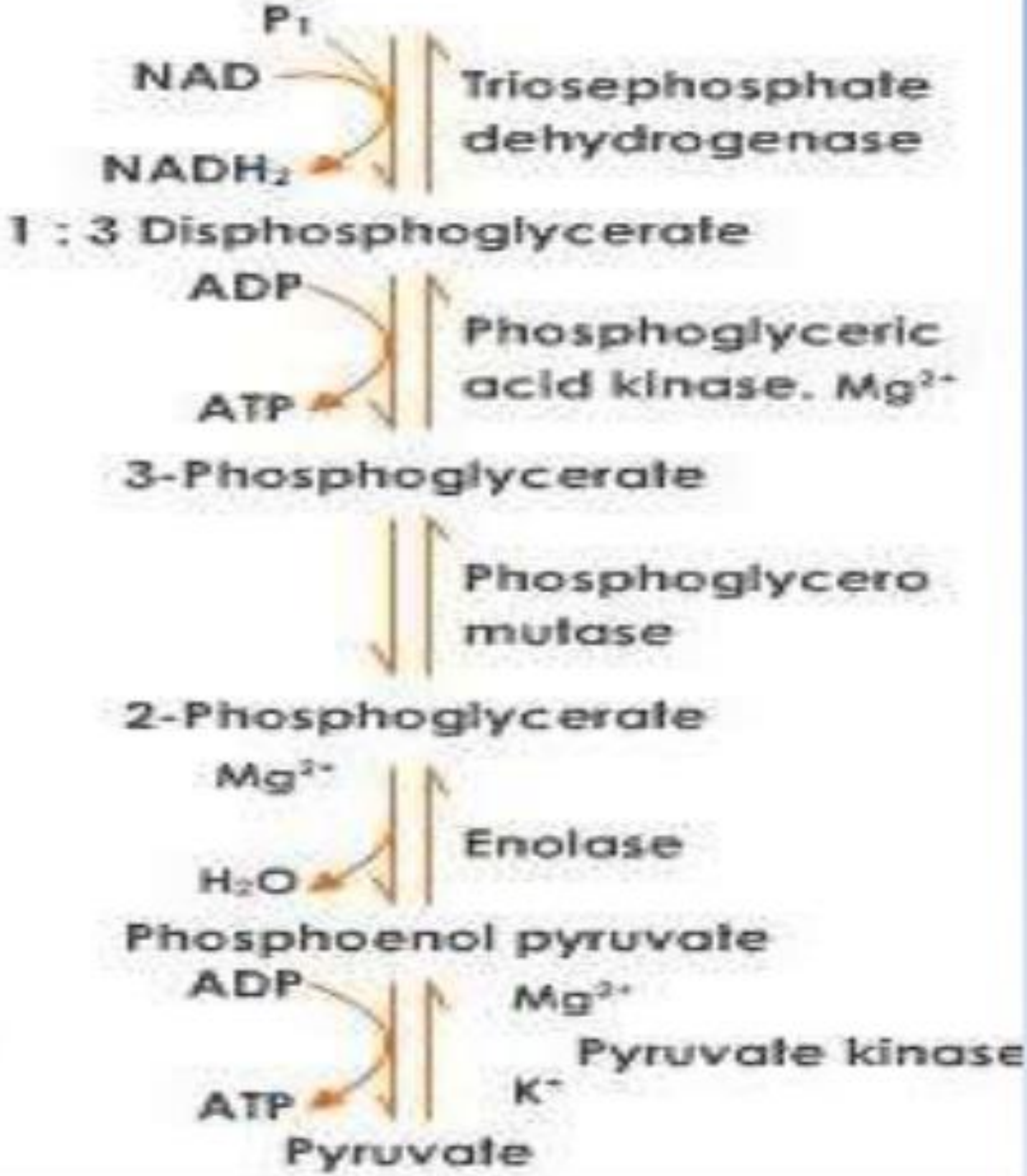
- This cleavage requires an investment of 2 ATP molecules to activate the glucose mole and prepare it for its cleavage into 3-carbon compound.



Glucose
ATP
Hexokinase
Mn2+
ADP
Glucose 6 phosphate
Phosphohexose
isomerase
Mg2+
Fructose 6 phosphate
ATP
Phosphofructokinase
ADP
Fructose 1 : 6 diphosphate
Aldolase
Phosphotriose
Dihydroxyacetone
3-phosphate
isomerase
Glyceraldehyde
3-phosphate

PAYOFF PHASE

- This phase constitutes the last 5 reactions of Glycolysis.
- This phase marks the release of ATP molecules during conversion of Glyceraldehyde-3-phosphtae to 2 moles of Pyruvate.
- Here 4 moles of ADP are phosphorylated to ATP. Although 4 moles of ATP are formed, the net result is only 2 moles of ATP per mole of Glucose oxidized, since 2 moles of ATP are utilized in Phase 1.



P1
NAD
NADH2
Triosephosphate dehydrogenase
1 : 3 Disphosphoglycerate
ADP
ATP
Phosphoglyceric acid kinase. Mg2+
3-Phosphoglycerate
Phosphoglycero mutase
2-Phosphoglycerate
Mg2+
H2O
Enolase
Phosphoenol pyruvate
ADP
ATP
Mg2+
Pyruvate kinase
K+
Pyruvate

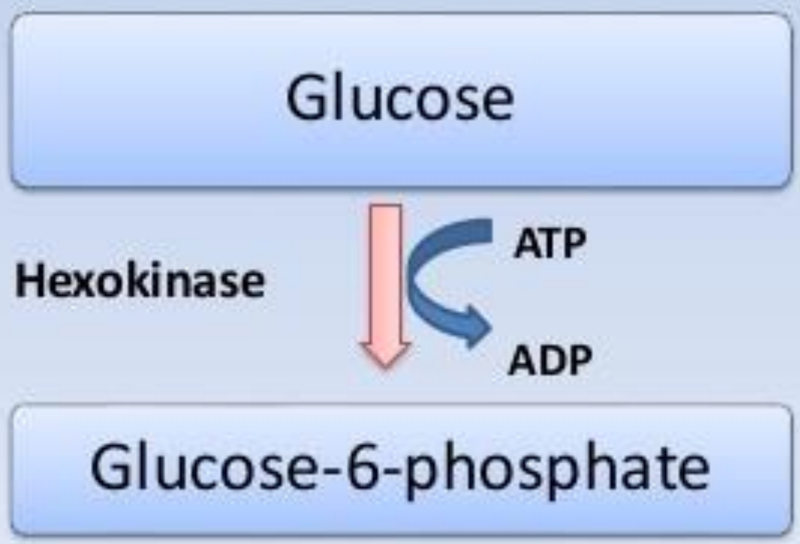
STEPWISE EXPLAINATION OF GLYCOLYSIS

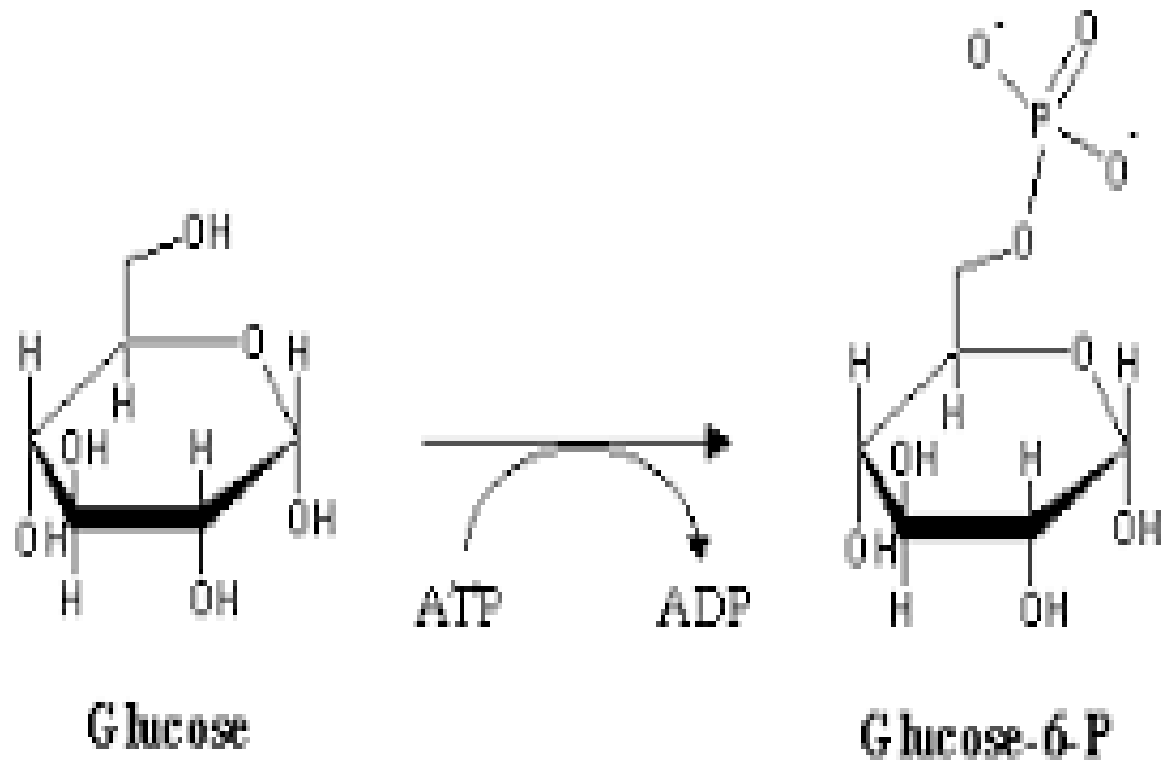
Steps for glycolysis

- Step 1: Phosphorylation of glucose
- Step 2: Isomerization of Glucose-6-phosphate
- Step 3: Phosphorylation of fructose-6-phosphate
- Step 4: cleavage of fructose 1,6-diphosphate
- Step 5: isomerization of dihydroxyacetone phosphate
- Step 6: oxidative phosphorylation of Glyceraldehyde 3-phosphate
- Step 7: Transfer of phosphate from 1,3-diphosphoglycerate to ADP
- Step 8: Isomerization of 3-phophoglycerate
- Step 9: Dehydration of 2-phosphoglycerate
- Step 10:Transfer of phosphate from phosphoenolpyruvate

STEP 1: PHOSPHORYLATION

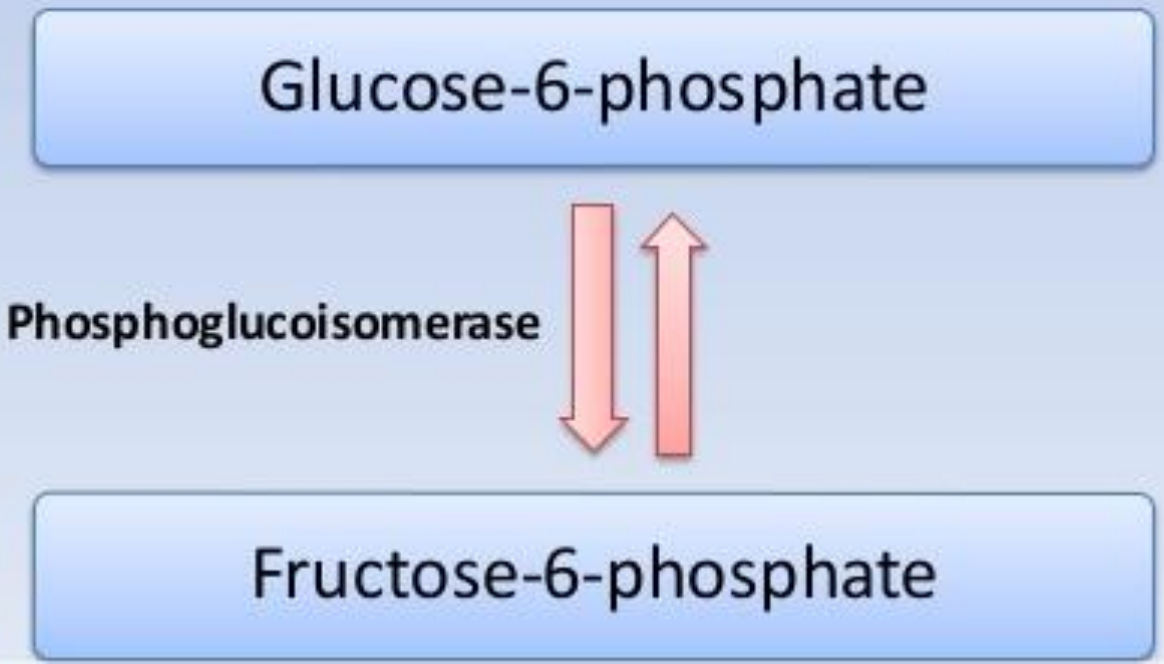
- Glucose is phosphorylated by ATP to form sugar phosphate.
- This is an irreversible reaction & is catalyzed by ***hexokinase.***
- Thus the reaction can be represented as follows:

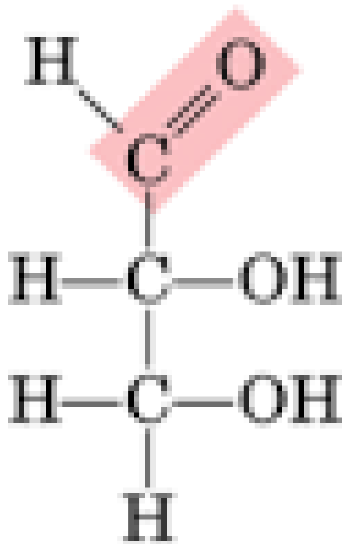



ATP
ADP
Glucose
Glucose-6-P

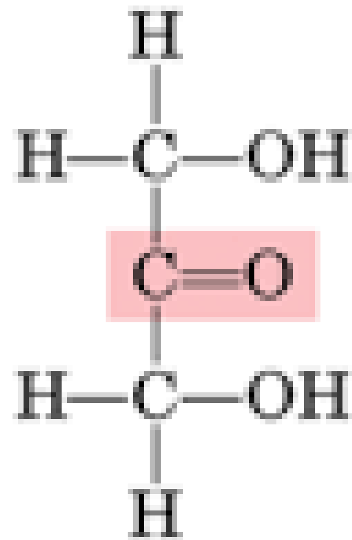
STEP 2: ISOMERIZATION

- It is a reversible rearrangement of chemical structure of carbonyl oxygen from C1 to C2, forming a Ketose from the Aldose.
- Thus, isomerization of the aldose Glucose6-phosphate gives the ketose, Fructose-6-phoshphate.





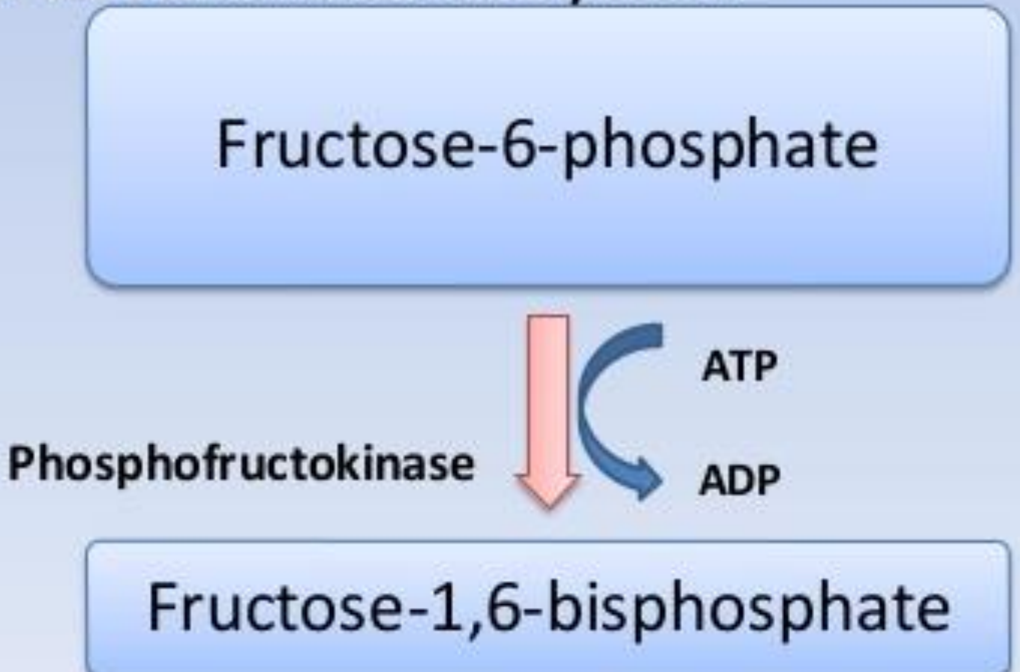
Aldose

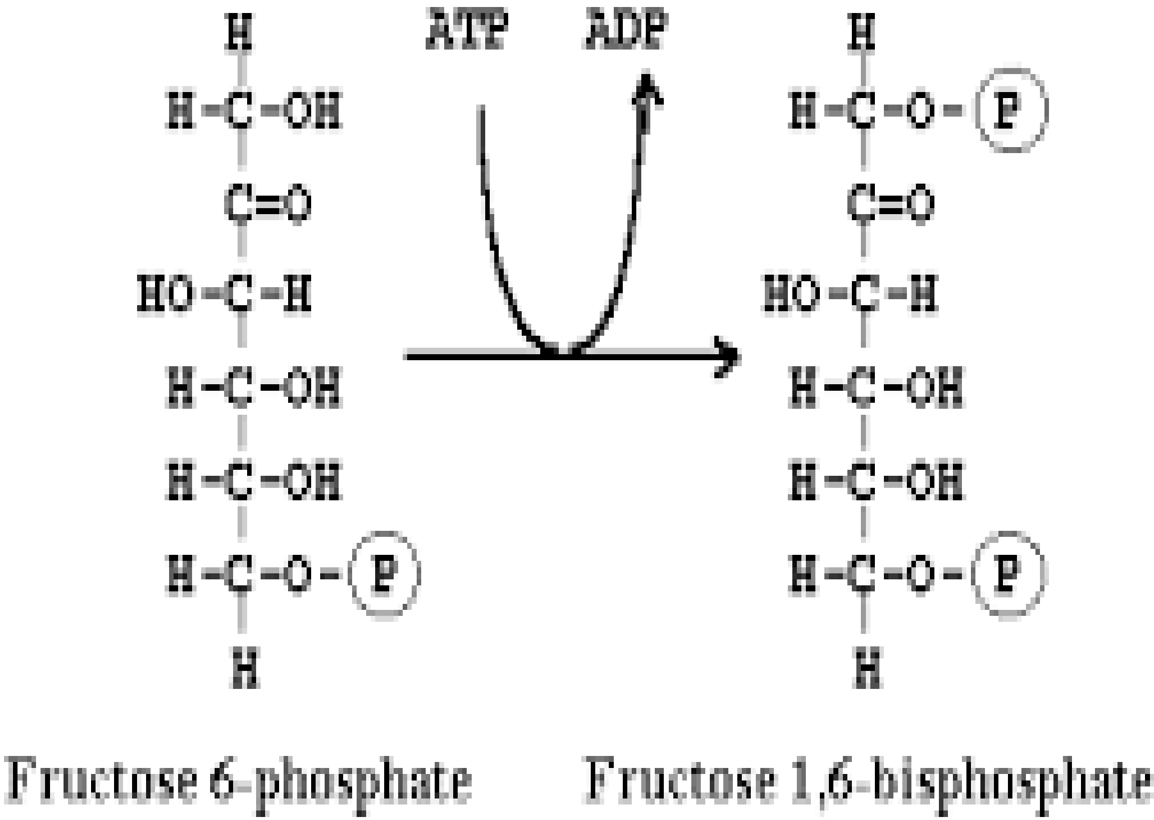


Ketose

STEP 3: PHOPHORYLATION

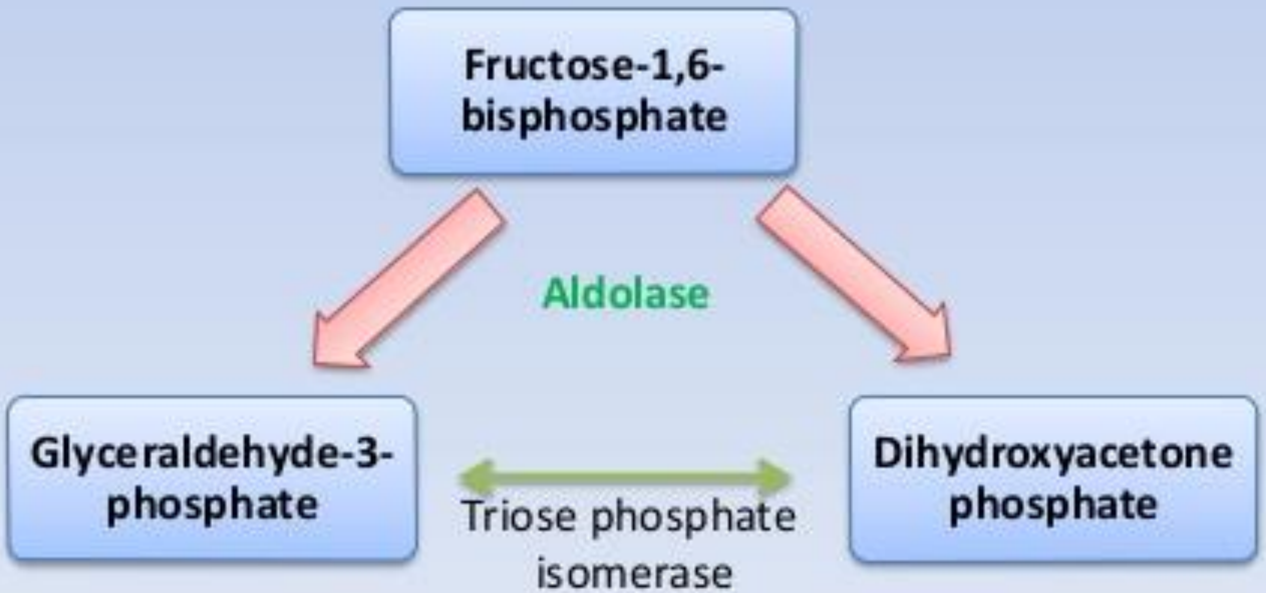
- Here the ***Fructose-6-phosphate*** is phosphorylated by ATP to ***fructose-1,6-bisphosphate.***
- This is an ***irreversible reaction*** and is catalyzed by ***phosphofructokinase*** enzyme.

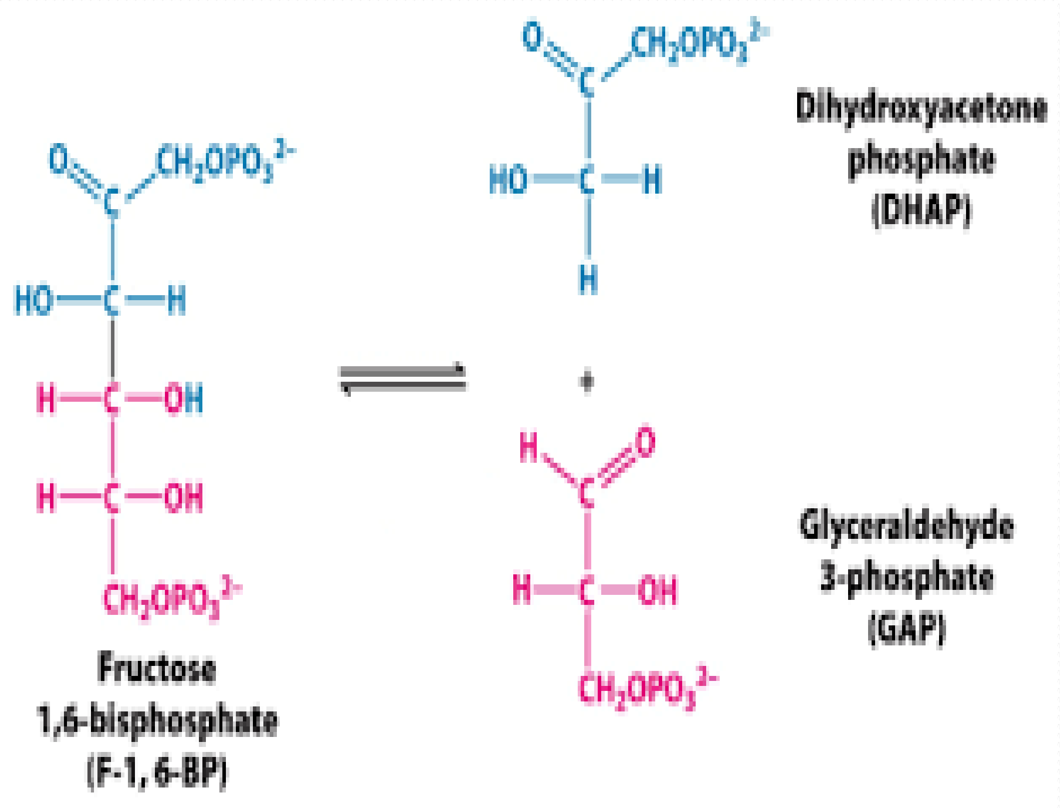



ATP
ADP
H
H-C-OH
C=O
HO-C-H
H-C-OH
H-C-OH
H-C-O-P
H
H
H-C-O-P
C=O
HO-C-H
H-C-OH
H-C-OH
H-C-O-P
H
Fructose 6-phosphate
Fructose 1,6-bisphosphate

STEP 4: BREAKDOWN

- This six carbon sugar is cleaved to produce two 3-C molecules: ***glyceradldehyde-3-phosphate (GAP)*** & ***dihydroxyacetone phosphate(DHAP).***
- This reaction is catalyzed by ***Aldolase.***

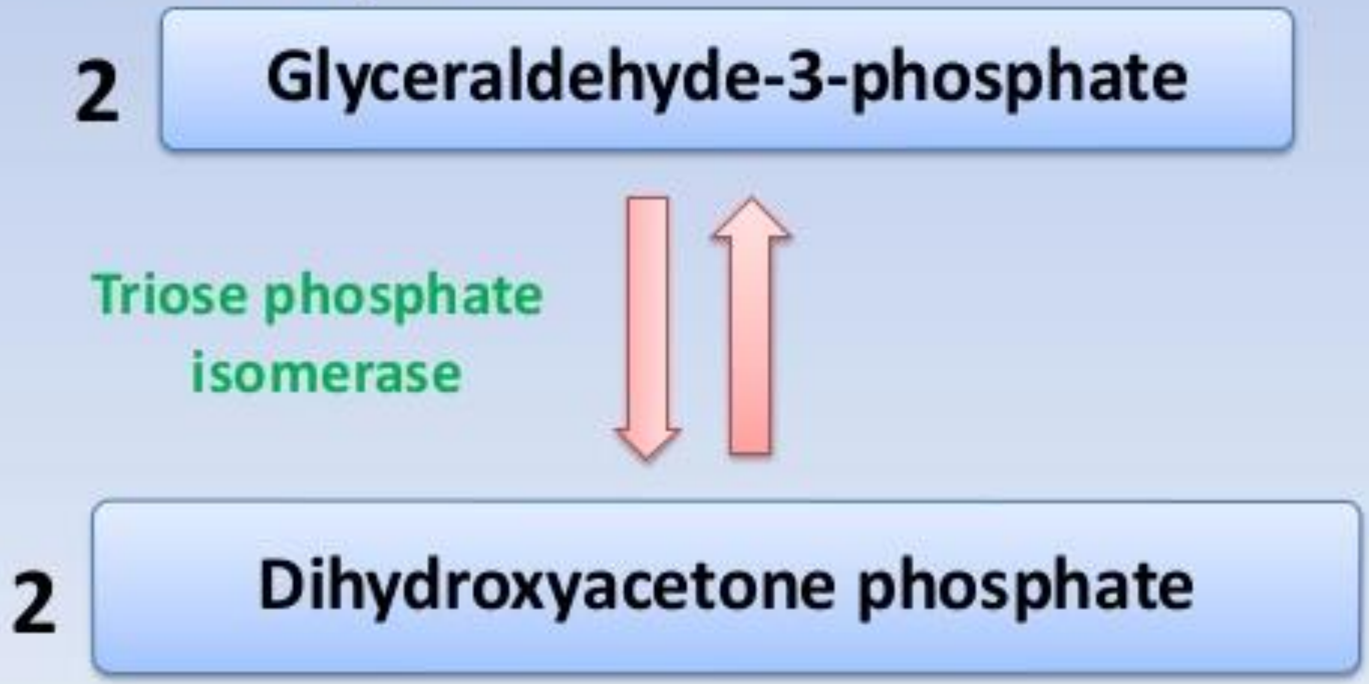


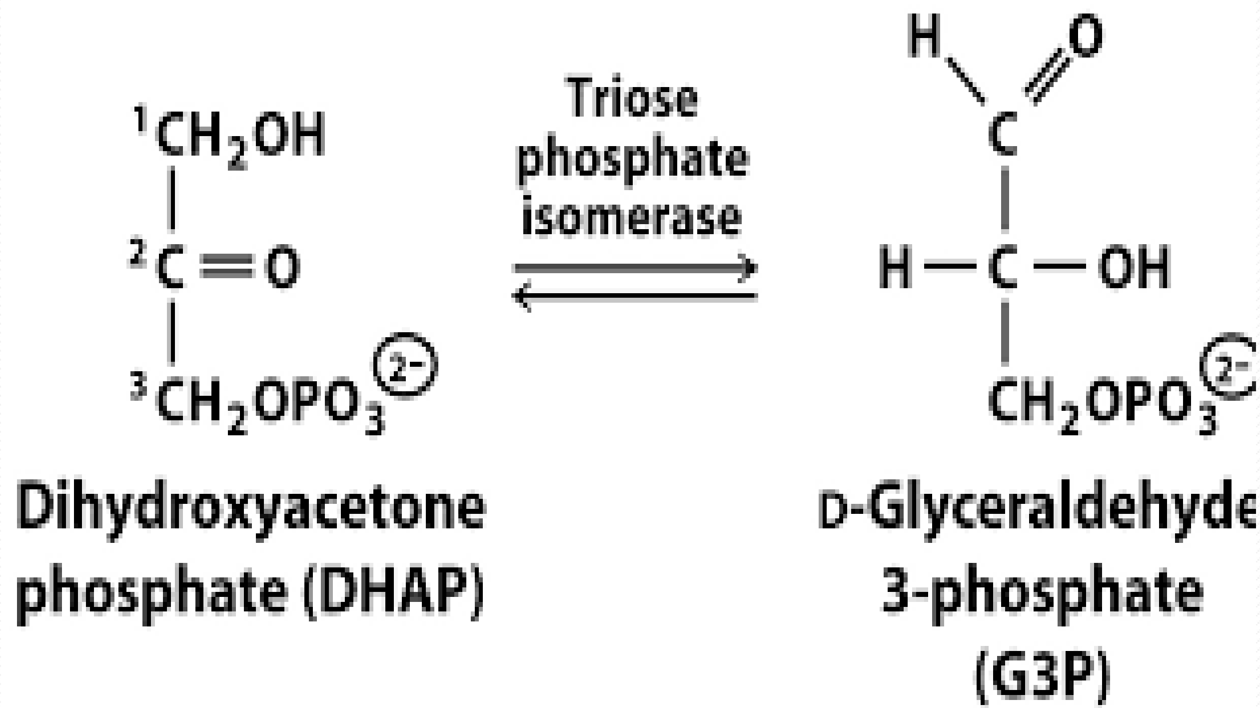


Fructose
1,6-bisphosphate
(F-1, 6-BP)
Dihydroxyacetone
phosphate
(DHAP)
Glyceraldehyde
3-phosphate
(GAP)

STEP 5: ISOMERIZATION

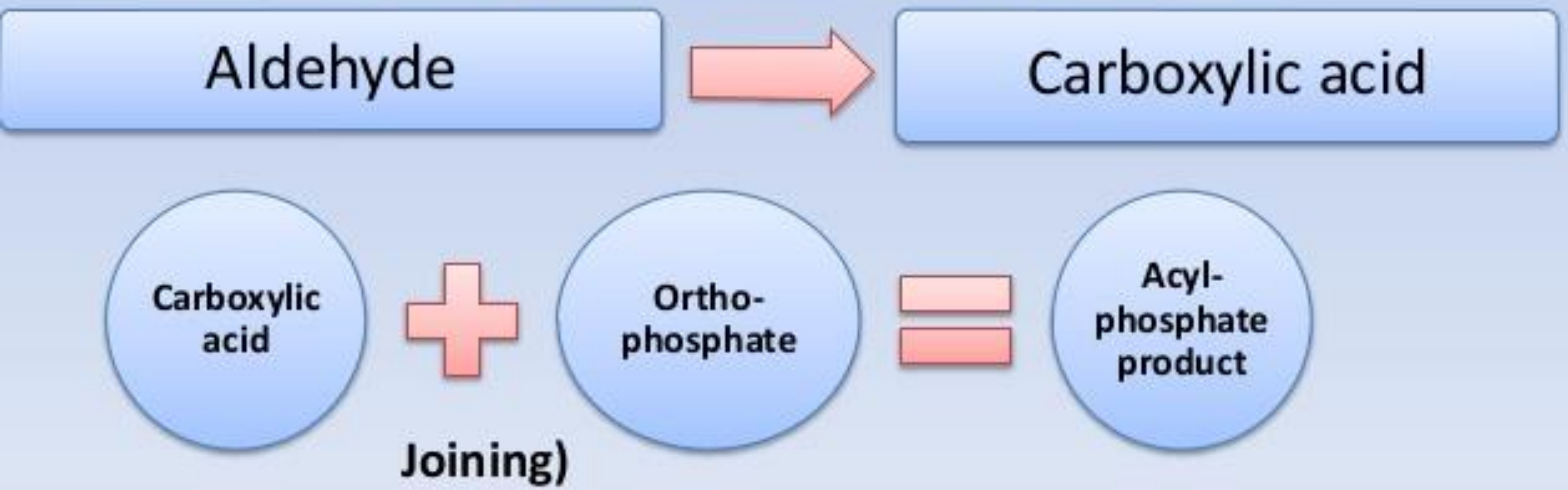
- Dihydroxyacetone phosphate is oxidized to form Glyceraldehyde-3-phosphate.
- This reaction is catalyzed by ***triose phosphate isomerase*** enzyme.



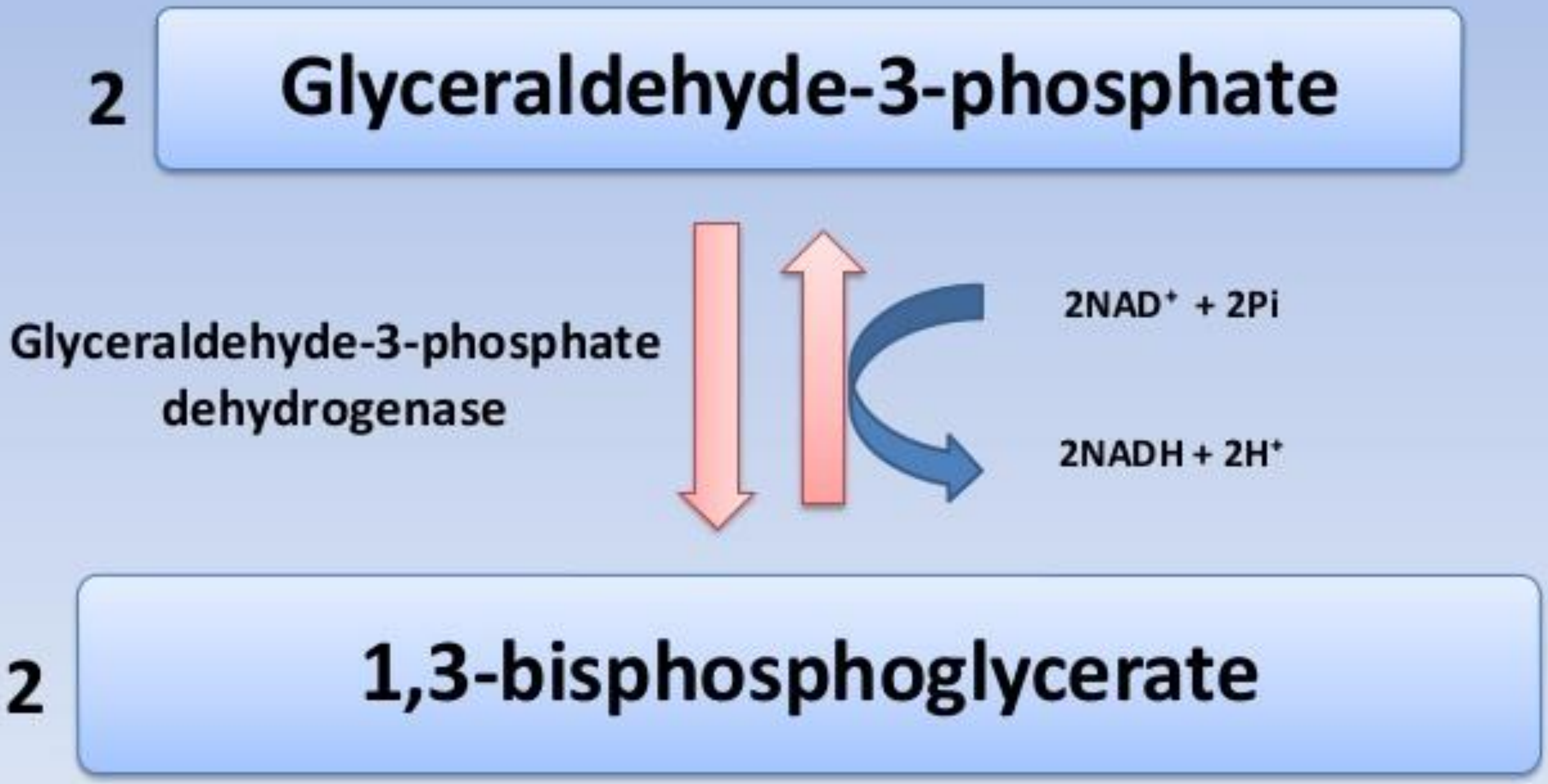

1 CH2OH
2 C=O
3 CH2OPO3 2-
Dihydroxyacetone phosphate (DHAP)
Triose phosphate isomerase
H
O
C
H—C—OH
CH2OPO3 2-
D-Glyceraldehyde 3-phosphate (G3P)

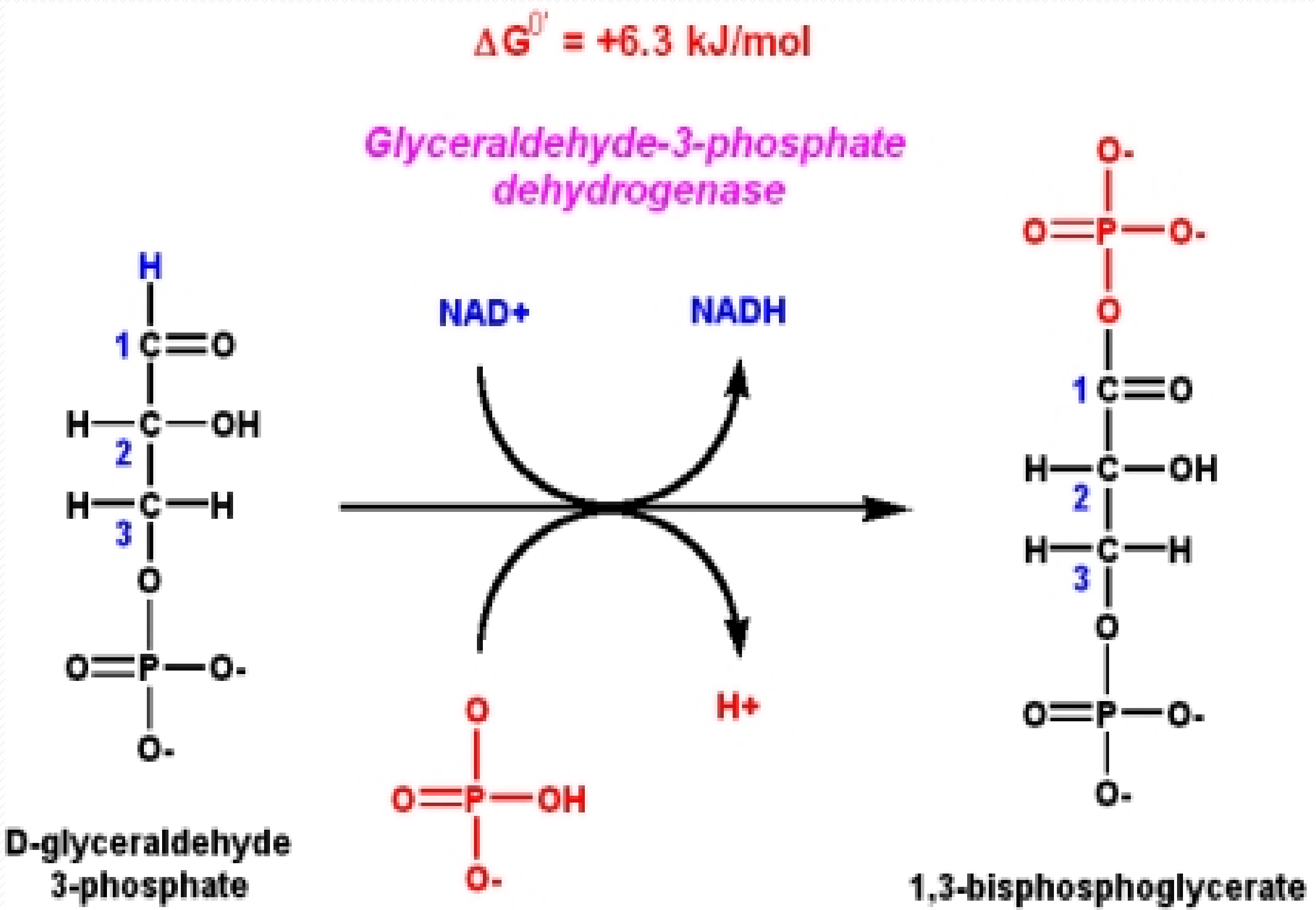
STEP 6

- 2 molecules of Glyceraldehyde-3-phosphate are oxidized.
- ***Glyceraldehyde-3-phosphate dehydrogenase*** catalyzes the conversion of Glyceraldehyde3-phosphate into ***1,3-bisphosphoglycerate.***



Resultant reaction





ΔG°' = +6.3 kJ/mol
Glyceraldehyde-3-phosphate dehydrogenase
NAD+
NADH
H+
D-glyceraldehyde 3-phosphate
1,3-bisphosphoglycerate

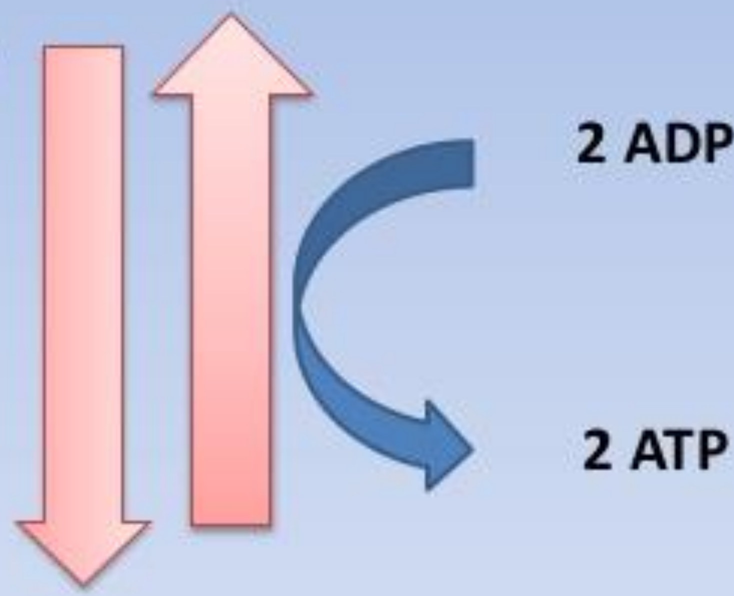
STEP 7

- The transfer of high-energy phosphate group that was generated earlier to ADP, form ATP.
- This phosphorylation i.e. addition of phosphate to ADP to give ATP is termed as ***substrate level phosphorylation*** as the phosphate donor is the substrate ***1,3-bisphosphoglycerate (1,3-BPG).***
- The product of this reaction is 2 molecules of ***3-phosphoglycerate.***

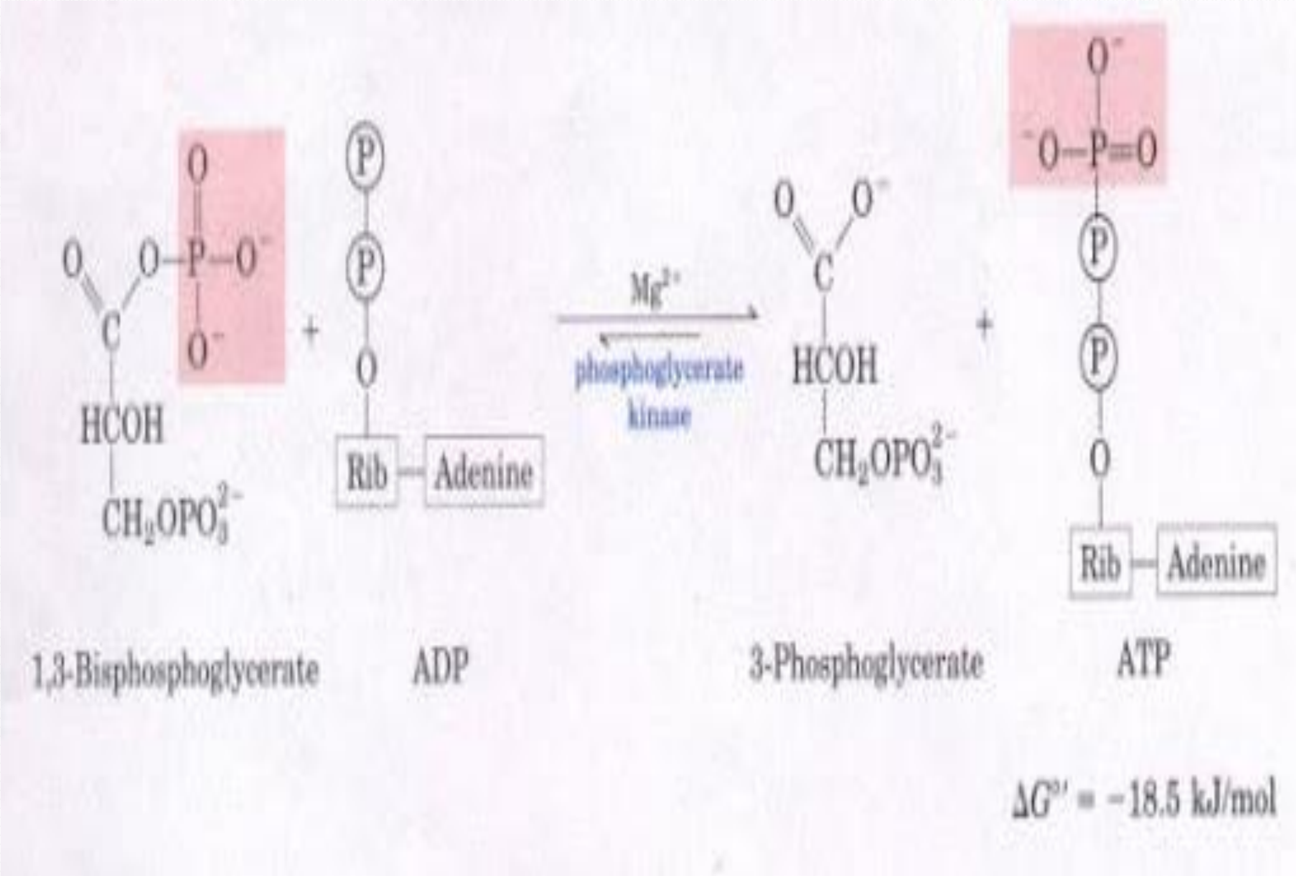
2 **1,3-bisphosphoglycerate**

Phosphoglycerate kinase

FIRST SUBSTRATE LEVEL PHOSPHORYLATION



2 **3-phosphoglycerate**


Mg2+
phosphoglycerate kinase
HCOH
Rib
Adenine
1,3-Bisphosphoglycerate
ADP
3-Phosphoglycerate
ATP
ΔG°' = −18.5 kJ/mol

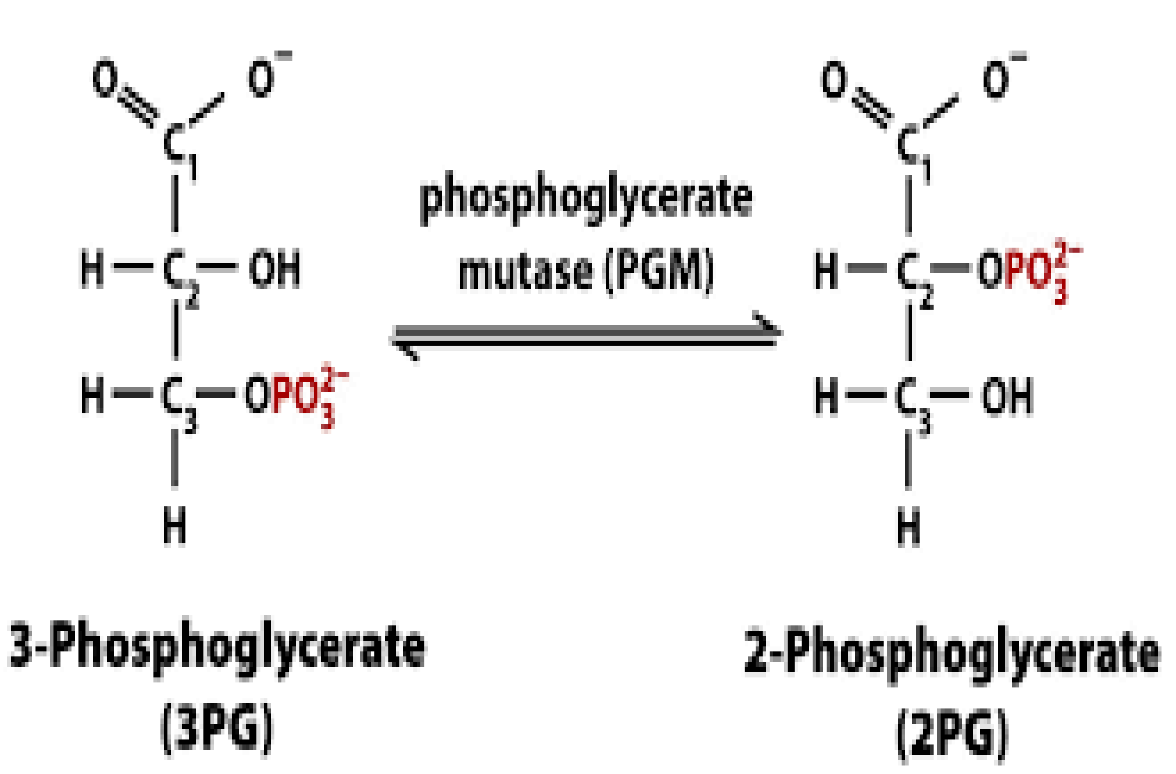
STEP 8

- The remaining phosphate-ester linkage in 3-phosphoglycerate, is moved from carbon 3 to carbon 2 ,because of relatively low free energy of hydrolysis, to form ***2-phosphoglycerate*****(2-PG).**

2 **3-phosphoglycerate**

Phosphoglycerate mutase ⇅

2 **2-phosphoglycerate**

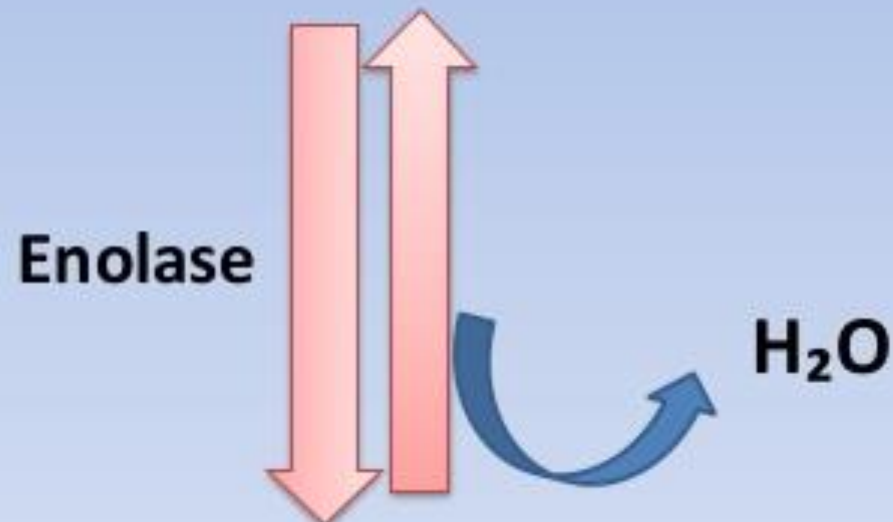


phosphoglycerate
mutase (PGM)
3-Phosphoglycerate
(3PG)
2-Phosphoglycerate
(2PG)

STEP 9: DEHYDRATION OF 2-PG

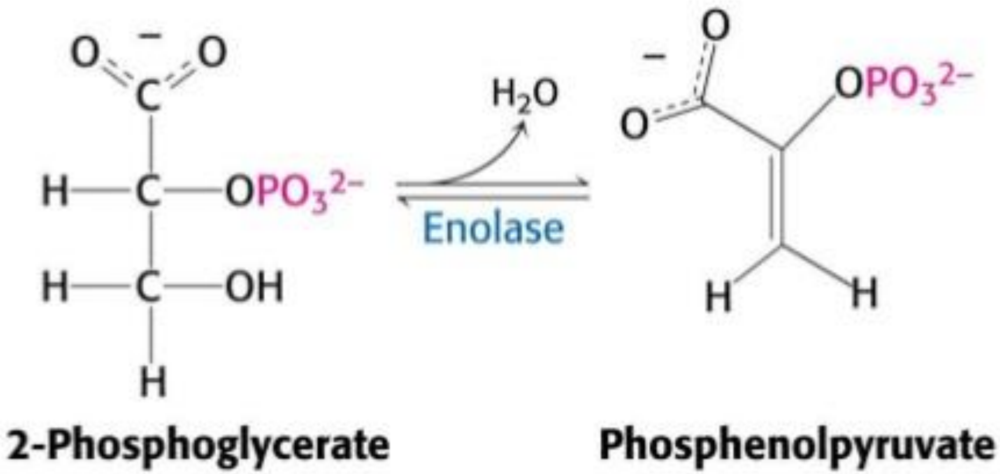
- This is the second reaction in glycolysis where a high-energy phosphate compound is formed.
- The 2-phosphoglycerate is dehydrated by the action of ***enolase*** to ***phosphoenolpyruvate(PEP)***. This compound is the phosphate ester of the enol tautomer of pyruvate.
- This is a reversible reaction.

2 2-phosphoglycerate



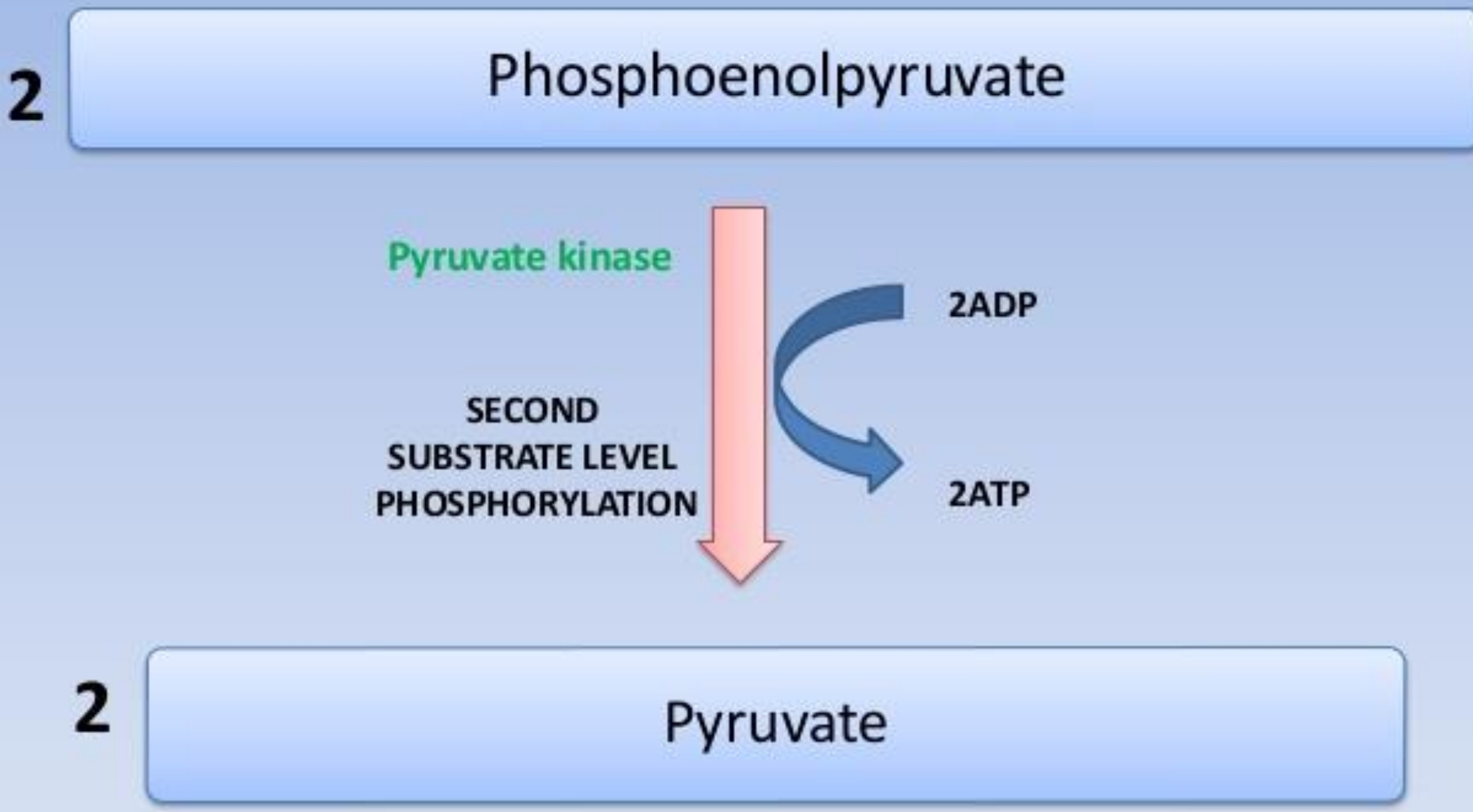
2 Phosphoenol pyruvate

9.DEHYDRATION OF 2-PHOSPHOGLYCERATE

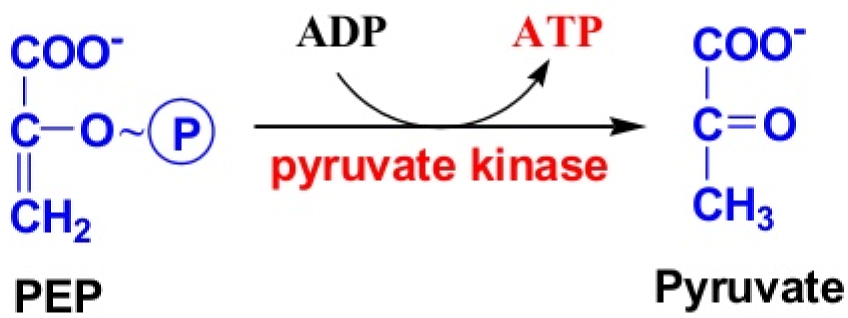


STEP 10: TRANSFER OF PHOSPHATE FROM PEP to ADP

- This last step is the irreversible transfer of high energy phosphoryl group from phosphoenolpuruvate to ADP.
- This reaction is catalyzed by ***pyruvate kinase.***
- This is the ***2nd substrate level phosphorylation*** reaction in glycolysis which yields ATP.
- This is a non-oxidative phosphorylation reaction.


2
Phosphoenolpyruvate
Pyruvate kinase
SECOND
SUBSTRATE LEVEL
PHOSPHORYLATION
2ADP
2ATP
2
Pyruvate

(10) PEP →pyruvate



- Second substrate level phosphorylation
- irreversible

OVERALL BALANCE SHEET OF GLYCOLYSIS

- Each molecule of glucose gives 2 molecules of Glyceraldehyde-3-phosphate. Therefore , the total input of all 10 reactions can be summarized as:

$$\text{Glucose} + 2\text{ATP} + 2\text{Pi} + 2\text{NAD}^+ + 2\text{H}^+ + 4\text{ADP}$$

$$\downarrow$$

$$2\text{Pyruvate} + 2\text{H}^+ + 4\text{ATP} + 2\text{H}_2\text{O} + 2\text{NADH} + 2\text{ADP}$$

On cancelling the common terms from the above equation, we get the net equation for Glycolysis:

$$\text{Glucose} + 2\text{Pi} + 2\text{ADP} + 2\text{NAD}^+ \downarrow 2\text{Pyruvate} + 2\text{NADH} + 2\text{ATP} + 2\text{H}^+ + 2\text{H}_2\text{O}$$

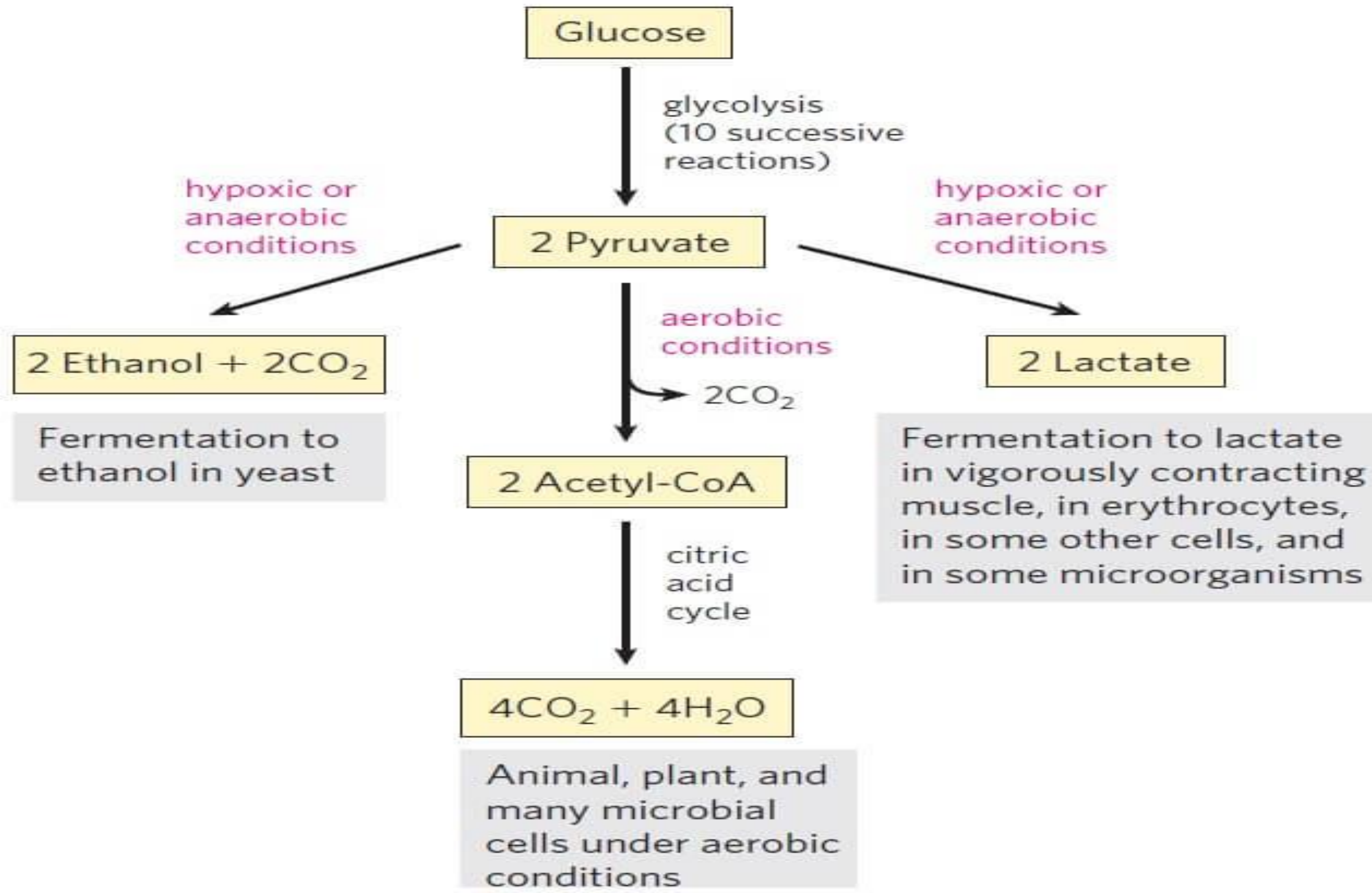
THUS THE SIMULTANEOUS REACTIONS INVOLVED IN GLYCOLYSIS ARE:

- ***Glucose is oxidized to Pyruvate***
- ***NAD^+ is reduced to NADH***
- ***ADP is phosphorylated to ATP***

- **ENERGY YIELD IN GLYCOLYSIS:**

STEP NO.	REACTION	CONSUMPTION of ATP	GAIN of ATP
1	Glucose → glucose-6-phosphate	1	-
3	Fructose-6-phosphate → fructose-1,6-biphosphate	1	-
7	1,3-diphosphoglycerate → 3-phosphoglycerate	-	1x2=2
10	Phosphoenolpyruvate → pyruvate	-	1x2=2
		2	4
		Net gain of ATP=4-2= 2	

Fate of pyruvate

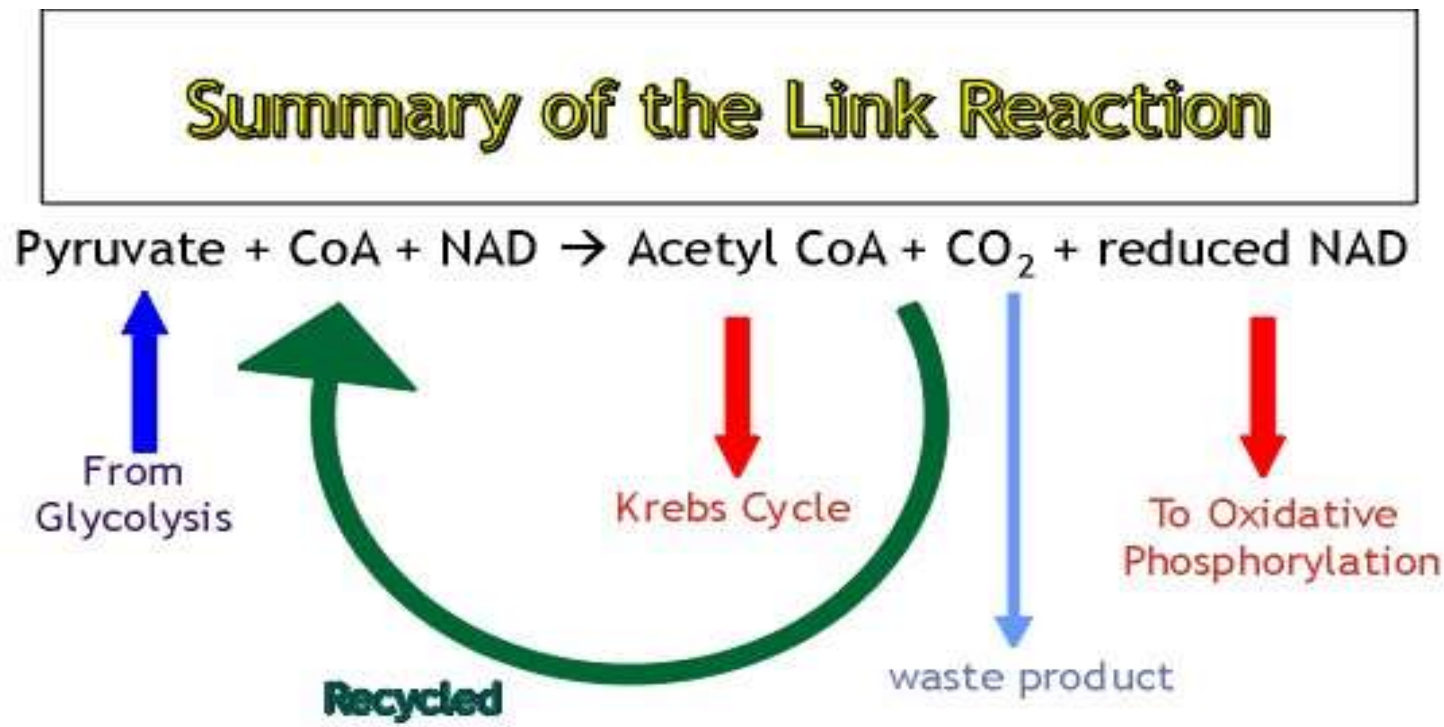


Significance of glycolysis

- Glycolysis is present in nearly all living organisms. Glucose is the source of almost all energy used by cells.
- It is the principle route for glucose metabolism and the metabolism of other hexoses (fructose, galactose)
- Its ability to function under anaerobic condition is of significance, as it allows skeletal muscle to function and survive under anoxic episodes by providing ATP
- Glycolysis is the main way to produce ATP in some tissues, even though the oxygen supply is sufficient, such as RBC, retina, testis, skin, medulla of kidney
- Hexokinase deficiency and pyruvate kinase deficiency causes hemolytic anemia

Tricarboxylic acid cycle/Citric acid cycle/Kreb's cycle

Oxidative Decarboxylation of pyruvate to acetyl coA



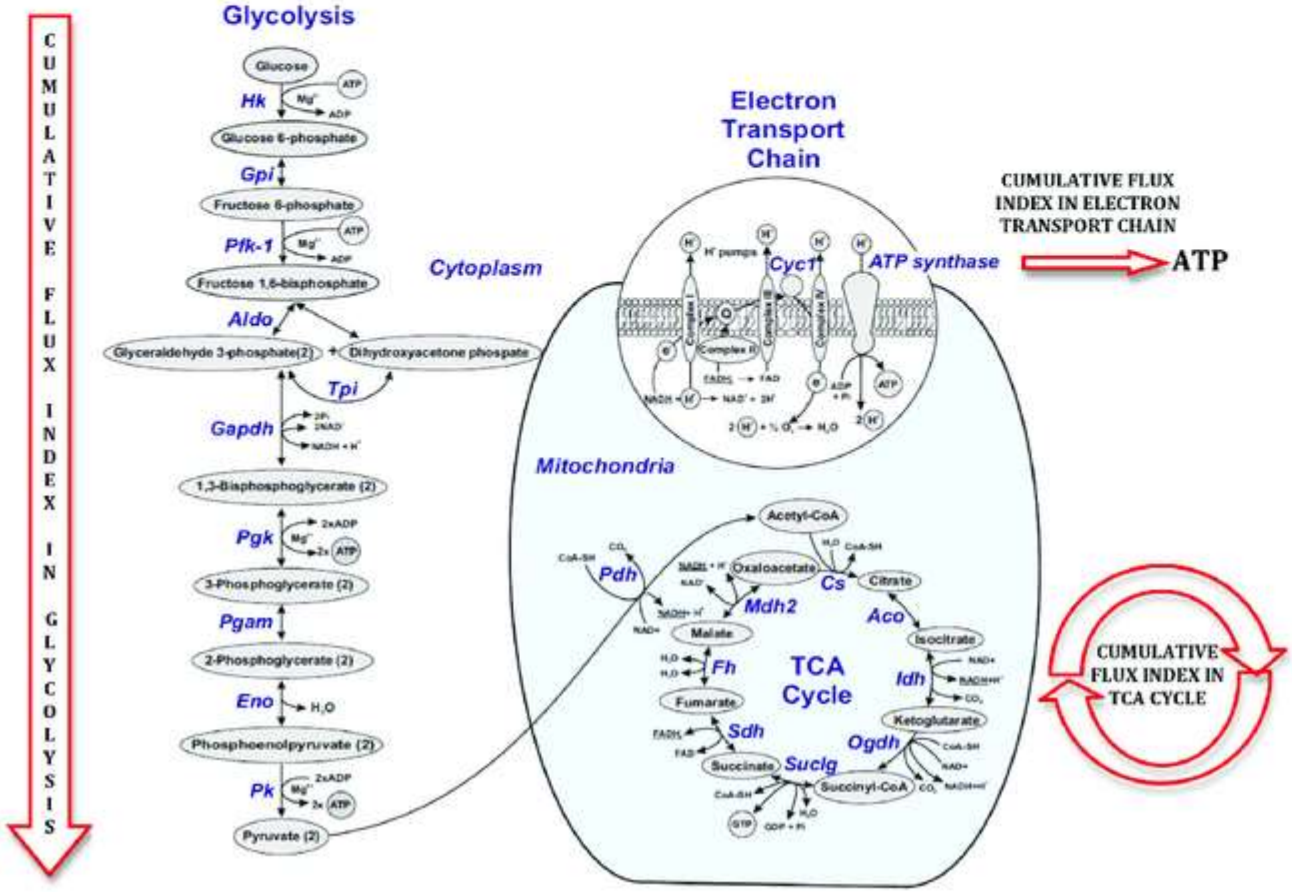
One NADH are formed from a molecule of pyruvate in the oxidative decarboxylation of pyruvate to Acetyl CoA.

TCA CYCLE

- **Definition:-**

✓ The tricarboxylic acid cycle (TCA CYCLE) is a series of enzyme catalyzed chemical reactions that form a key part of aerobic respiration in cells.

✓ This cycle is also called the Kreb's cycle and the Citric acid cycle.



CUMULATIVE FLUX INDEX IN GLYCOLYSIS
Glycolysis
Glucose
Hk
ATP
ADP
Glucose 6-phosphate
Gpi
Fructose 6-phosphate
Pfk-1
ATP
ADP
Fructose 1,6-bisphosphate
Aldo
Glyceraldehyde 3-phosphate(2)
Dihydroxyacetone phospate
Tpi
Gapdh
NADH + H
1,3-Bisphosphoglycerate (2)
Pgk
2xADP
ATP
3-Phosphoglycerate (2)
Pgam
2-Phosphoglycerate (2)
Eno
Phosphoenolpyruvate (2)
Pk
2xADP
ATP
Pyruvate (2)
Cytoplasm
Electron Transport Chain
H pumps
Cyc1
ATP synthase
Complex I
Complex II
Complex III
Complex IV
ATP
CUMULATIVE FLUX INDEX IN ELECTRON TRANSPORT CHAIN
ATP
Mitochondria
Acetyl-CoA
Pdh
CoA-SH
NAD+
Oxaloacetate
Cs
Citrate
Mdh2
Aco
Malate
Isocitrate
Fh
TCA Cycle
Idh
Fumarate
Ketoglutarate
Sdh
Ogdh
Succinate
Suclg
Succinyl-CoA
GTP
CUMULATIVE FLUX INDEX IN TCA CYCLE

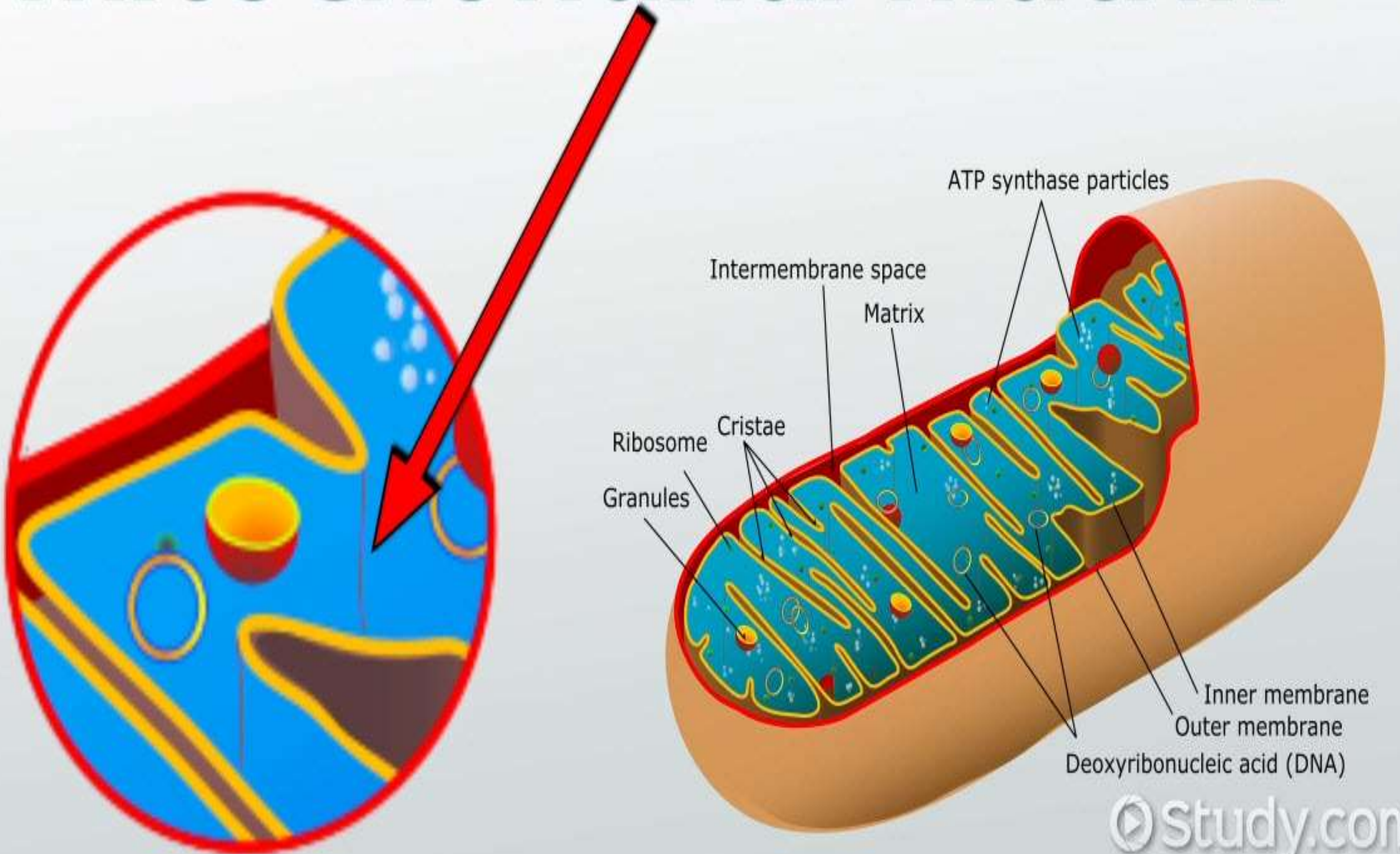
INTRODUCTION

- ✓ The citric acid cycle was discovered by Hans Kreb's in 1937 and was also called tricarboxylic acid (TCA) cycle.
- ✓ Kreb's received the Nobel prize in physiology or medicine in 1953 for his discovery.

- ✓ The TCA cycle Occupies a central position in metabolism and meet most of cell energy Requirement by complete oxidation of acetyl-Co A a key product in the catabolism of Carbohydrates ,Fatty acid and amino acid to carbon dioxide and chemical energy in the form of guanosine-triphosphate(GTP).

- ✓ In addition, the cycle provides precursors of Certain amino acids as well as the reducing agent NADH that is used in numerous other biochemical Reactions.

mitochondrial matrix



- ✓ The cycle consumes acetate(in the form of acetyl-CoA) and water, reduces NAD± to NADH and produces Co_2 as a waste by product. The NADH generated by the TCA cycle is fed into the oxidative phosphorylation (electron transport) pathway.

- ✓ In eukaryotic cells, the citric acid cycle occurs in the matrix of the mitochondrion.

- The citric acid cycle in eukaryotes takes place in the mitochondria while in prokaryotes, it takes place in the cytoplasm.
- The pyruvate formed in the cytoplasm (from glycolysis) is brought into the mitochondria where further reactions take place.
- The different enzymes involved in the citric acid cycle are located either in the inner membrane or in the matrix space of the mitochondria.

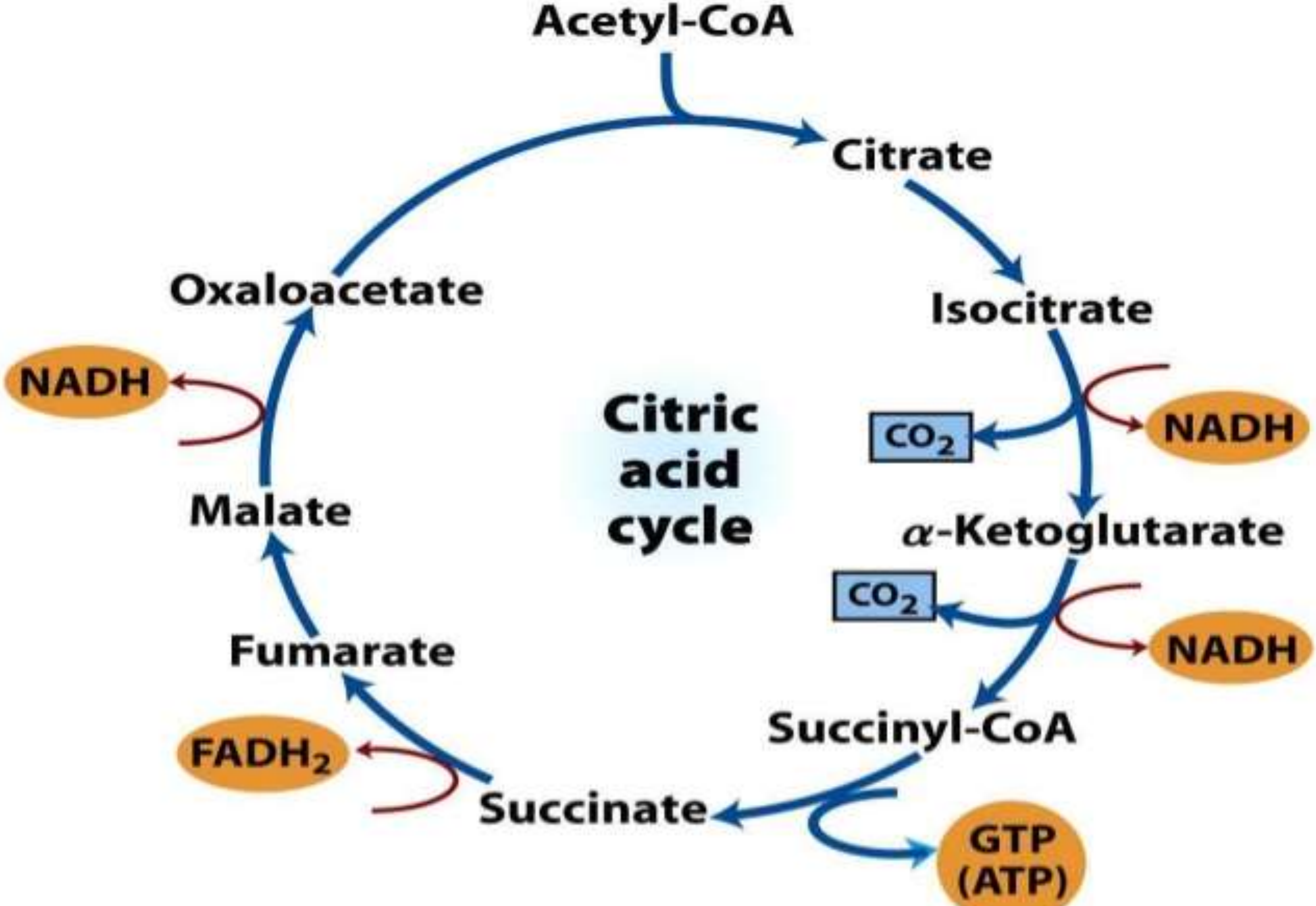


Figure 16-13
Lehninger Principles of Biochemistry, Fifth Edition

TCA cycle enzymes

- In eukaryotic cells, the enzymes that catalyze the reactions of the citric acid cycle are present in the matrix of the mitochondria except for succinate dehydrogenase and aconitase, which are present in the inner mitochondrial membrane.

- One common characteristic in all the enzymes involved in the citric acid cycle is that nearly all of them require Mg2+

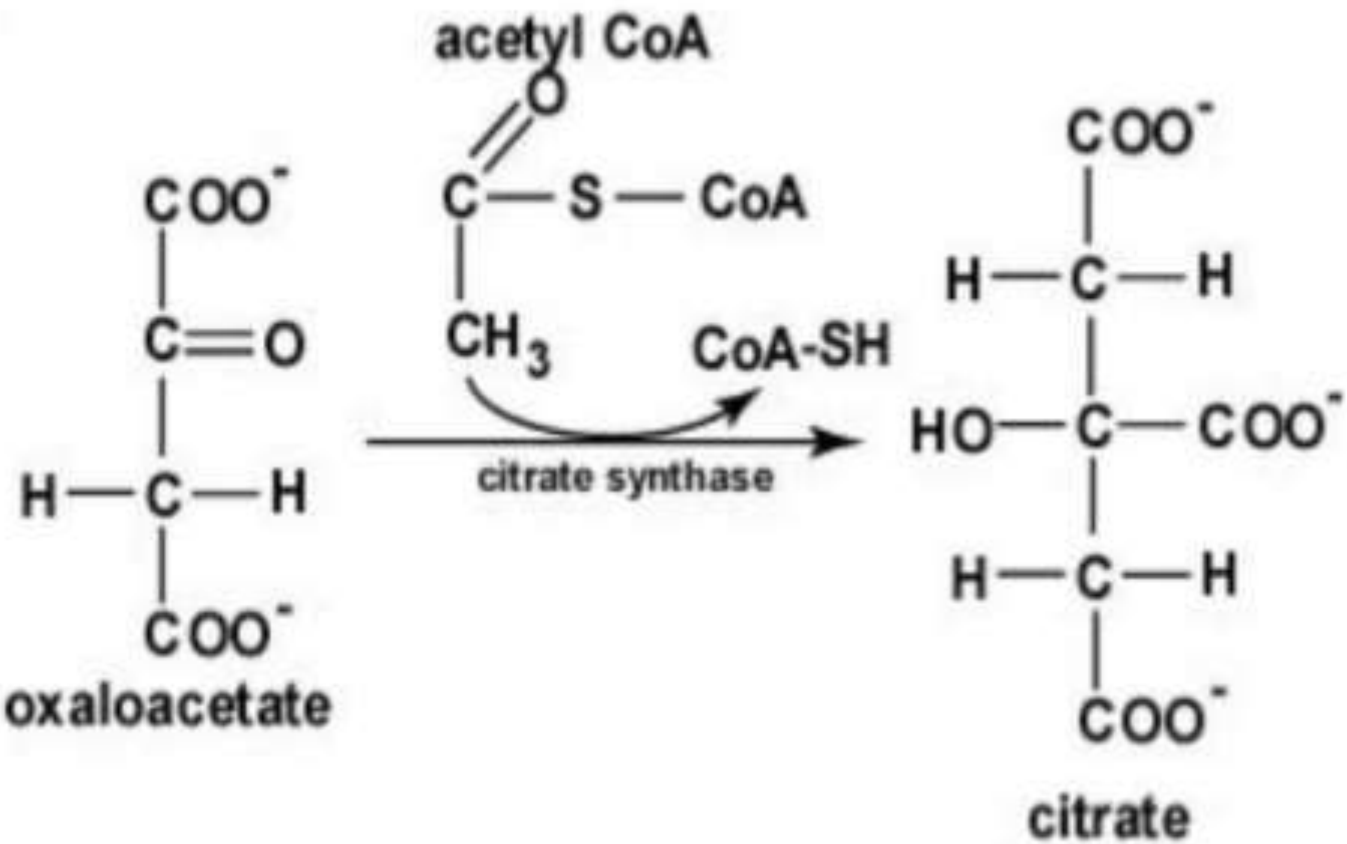
- The following are the enzymes that catalyze different steps throughout the process of the citric acid cycle:

1. Citrate synthase
2. Aconitase
3. Isocitrate dehydrogenase
4. α-ketoglutarate
5. Succinyl-CoA synthetase
6. Succinate dehydrogenase
7. Fumarase
8. Malate dehydrogenase

Step 1: **Condensation of acetyl CoA with oxaloacetate**

REACTION OF CITRIC ACID CYCLE

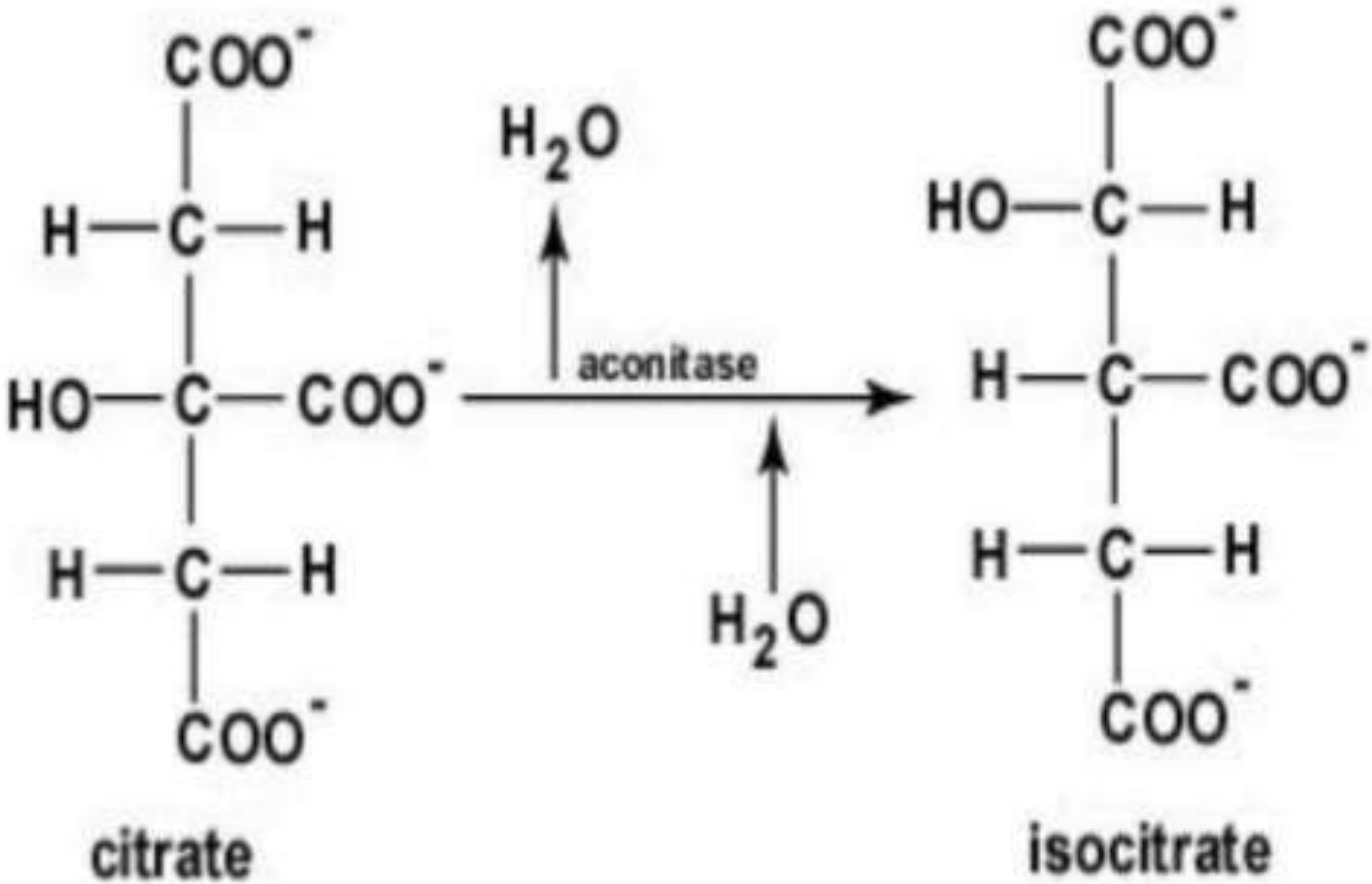
1) Citrate synthase :- Formation of citroyl CoA intermediate.



- The first step is a condensation step, combining the two-carbon acetyl group (from acetyl CoA) with a four-carbon oxaloacetate molecule to form a six-carbon molecule of citrate.

Step 2: Isomerization of citrate into isocitrate

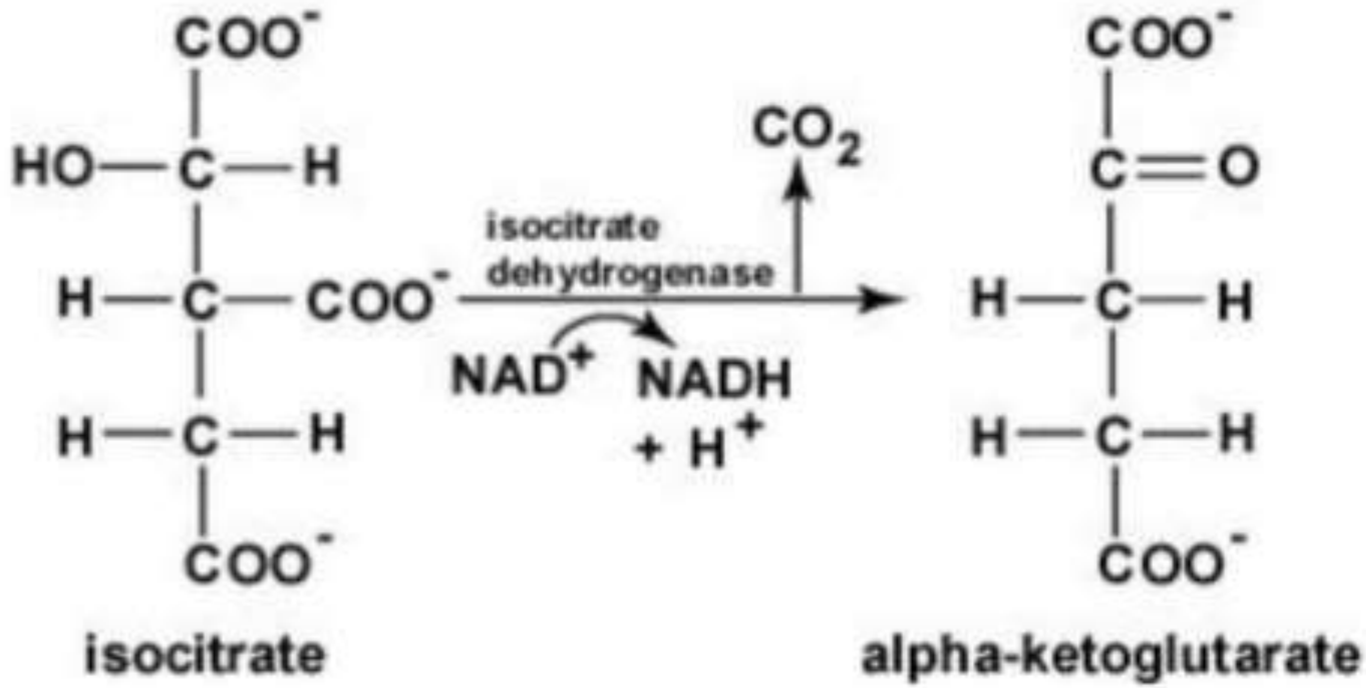
2) <u>Aconitase</u> :- **This enzyme catalyses the isomerization reaction by removing and then adding back the water to yield isocitric acid.**



- In the second step, citrate is converted into its isomer, isocitrate. This is actually a two-step process, involving first the removal and then the addition of a water molecule

Step 3: Oxidative decarboxylations of isocitrate

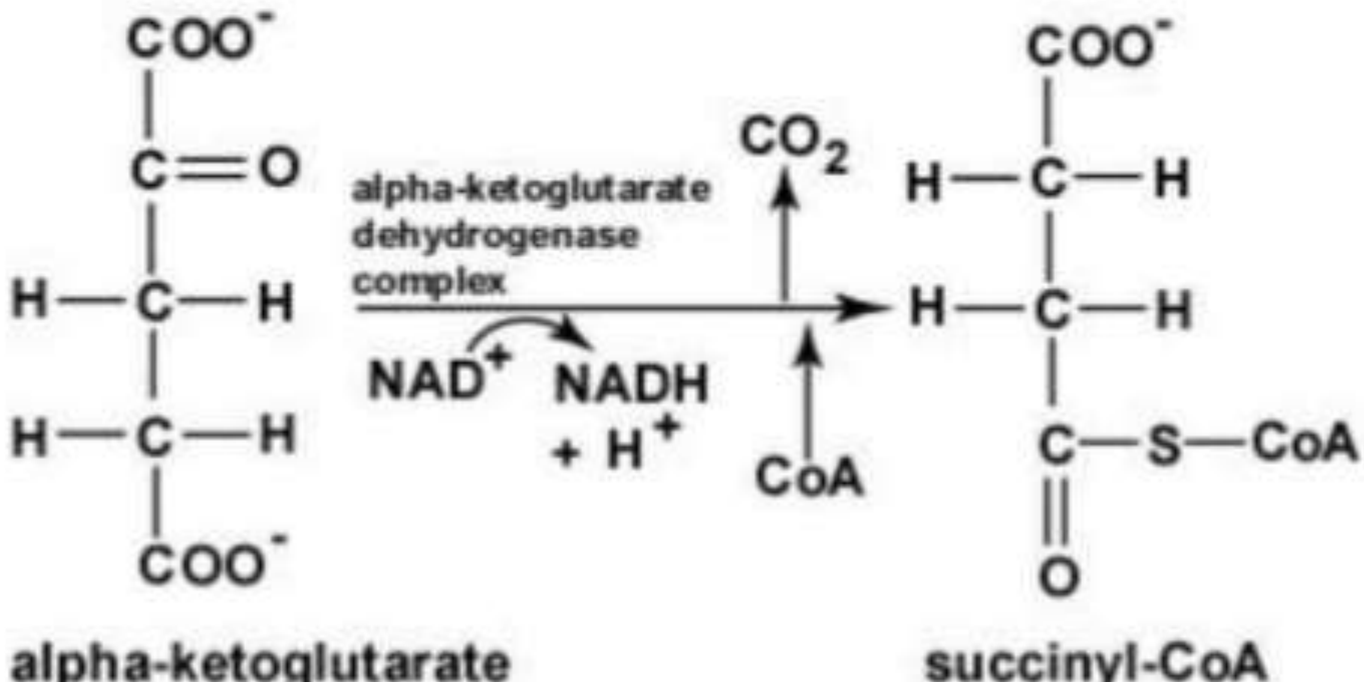
3) Isocitrate dehydrogenase :- In the first oxidation Step of the krebs cycle isocitric acid is oxidatively Decarboxylated to ∝-ketoglutaric acid.



- In the third step, isocitrate is oxidized and releases a molecule of carbon dioxide, leaving behind a five-carbon molecule—α-ketoglutarate. During this step, NAD^+ is reduced to form NADH
- The enzyme catalyzing this step, isocitrate dehydrogenase, is important in regulating the speed of the citric acid cycle.

Step 4: Oxidative decarboxylation of α-ketoglutarate

4) ∝-Ketoglutarate dehydrogenase :- **This is a complex Of different enzymatic activities similar to the Pyruvate dehydrogenase.**

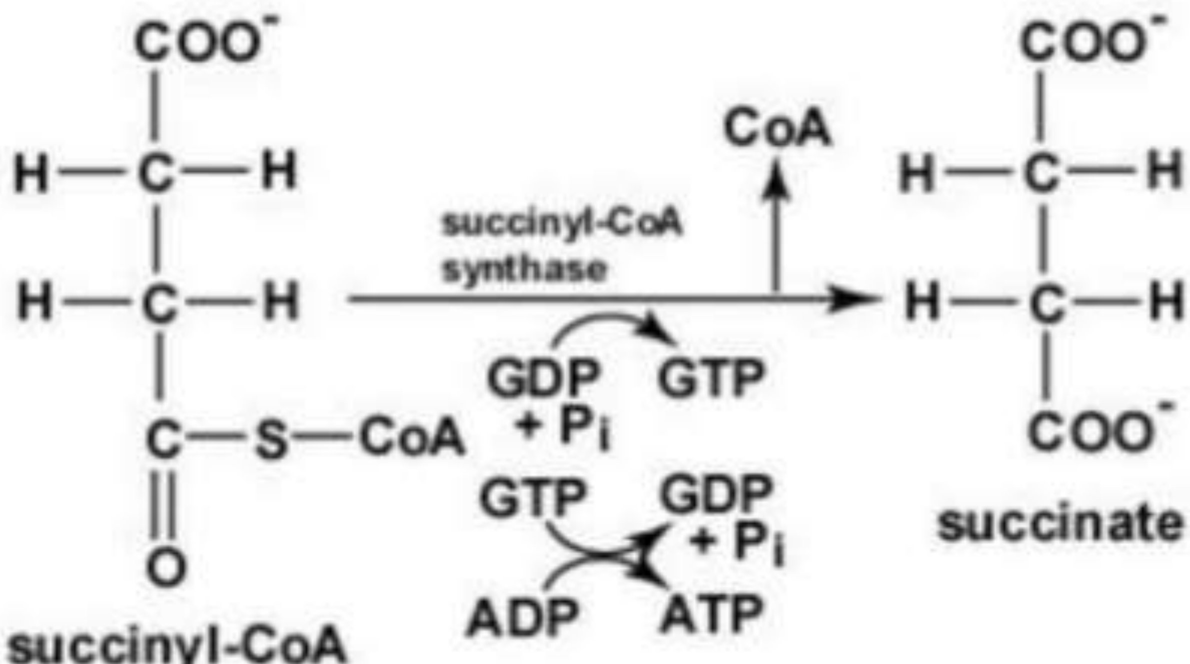


- The fourth step is similar to the third. In this case, it's α-ketoglutarate that's oxidized, reducing NAD+ and releasing a molecule of carbon dioxide in the process. The remaining four-carbon molecule picks up Coenzyme A, forming the unstable compound Succinyl CoA. The enzyme catalyzing this step, α-ketoglutarate dehydrogenase, is also important in regulation of the citric acid cycle.

Step 5: Conversion of succinyl-CoA into succinate

5) Succinyl CoA synthatase :- succinyl CoA like acetyl CoA has a thioester bond with very negative free energy of hydrolysis.

GTP + ADP ----> GDP + ATP.

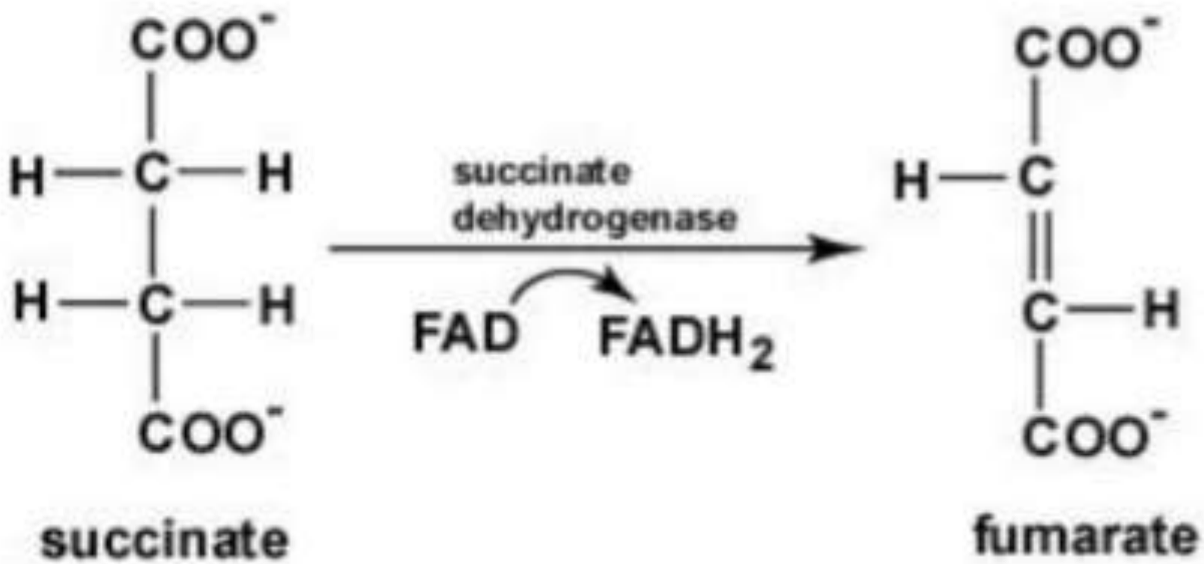


- In step five, the CoA is replaced by a phosphate group, which is then transferred ADP to ATP. In some cells, GDP(guanosine diphosphate)—is used instead of ADP and converted to GTP(guanosine triphosphate)—as a product. The four-carbon molecule produced in this step is called succinate.

Step 6: Dehydration of succinate to fumarate

6) <u>Succinate Dehydrogenase</u> :- oxidation of succinate to fumarate. This is the only citric acid cycle enzyme that is tightly bound to the inner mitochondrial membrane.

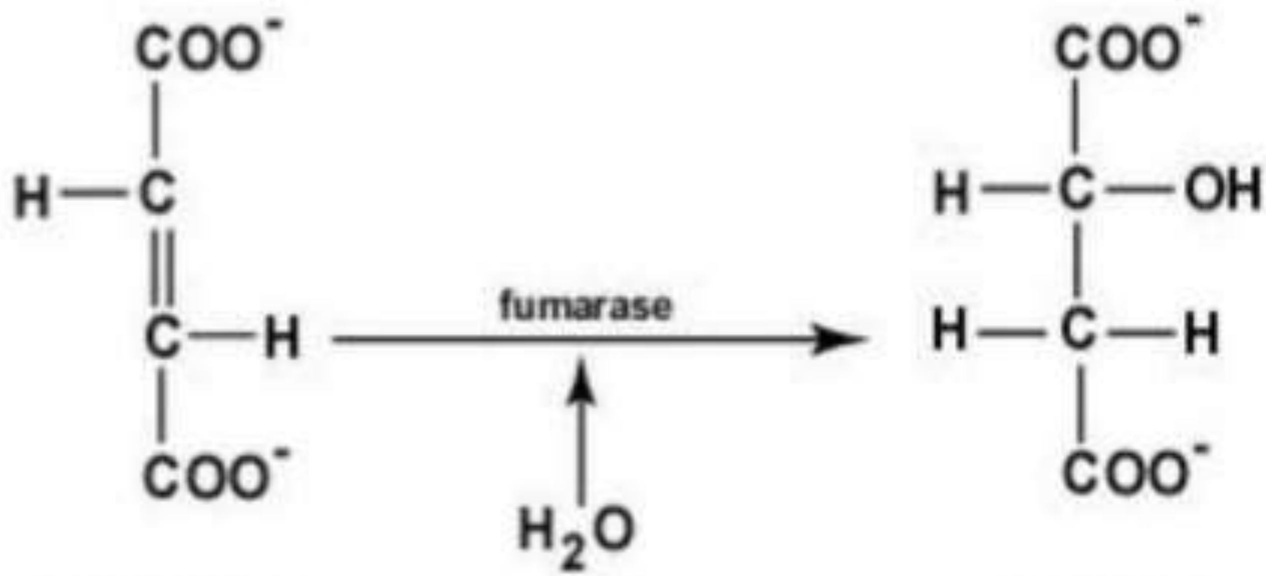
✓ It is an FAD dependent enzyme.



- In step six, succinate is oxidized, forming another four-carbon molecule called fumarate. In this reaction, two hydrogen atoms-with their electrons-are transferred to FAD, producing FADH2. The enzyme that carried out this step is embedded in the inner membrane of the mitochondrion, so FADH2 can transfer its electrons directly into electron transport chain

Step 7: Hydration of fumarate to malate

7) <u>Fumarase</u> :- The fumaric acid reacts with molecule of water to form malic acid in the presence of the enzyme fumarase .



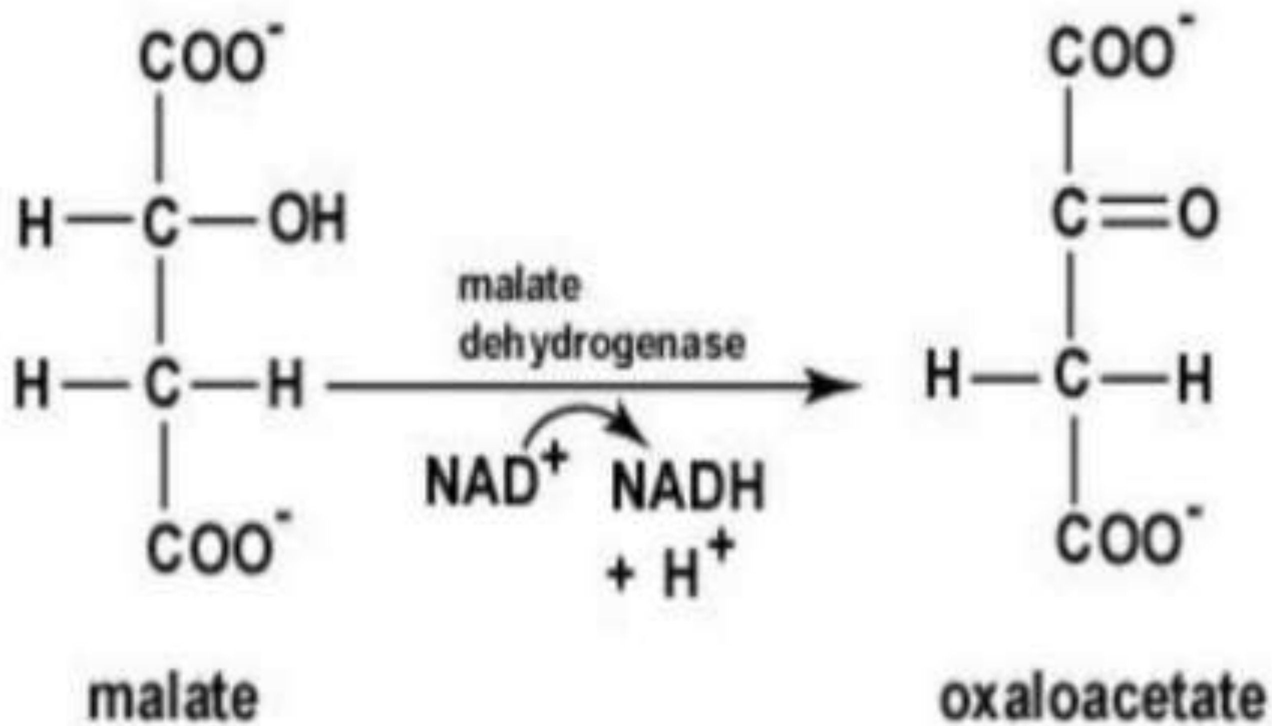
fumarate

malate

- In step seven, water is added to the four-carbon molecule fumarate, converting it into another four-carbon molecule called malate

Step 8: Dehydrogenation of L-malate to oxaloacetate

8) L-Malate dehydrogenase :- Oxidation of malate to oxaloacetate. It is an NAD+ dependent enzyme.



- In the last step of of the citric acid cycle, oxaloacetate the starting four carbon compound is regenerated by oxidation of malate. Another molecule of NAD+ is reduced to NADH in the process

Products of citric acid cycle

- Fate of carbons that enter the cycle and counting the reduced electron carriers NADH, FADH2 and ATP produced
- In a single turn of the cycle
- Two carbons enter from acetyl coA, and two molecules of carbon dioxide are released
- Three molecules of NADH and one molecule of FADH2 are generated and
- One molecule of ATP or GTP is produced

- These figures are for one turn of the cycle, corresponding to molecule of acetyl coA. Each glucose produces two acetyl coA molecules, so we need to multiply these numbers by 2 if we want per glucose yield

- The overall reaction/ equation of the citric acid cycle is:

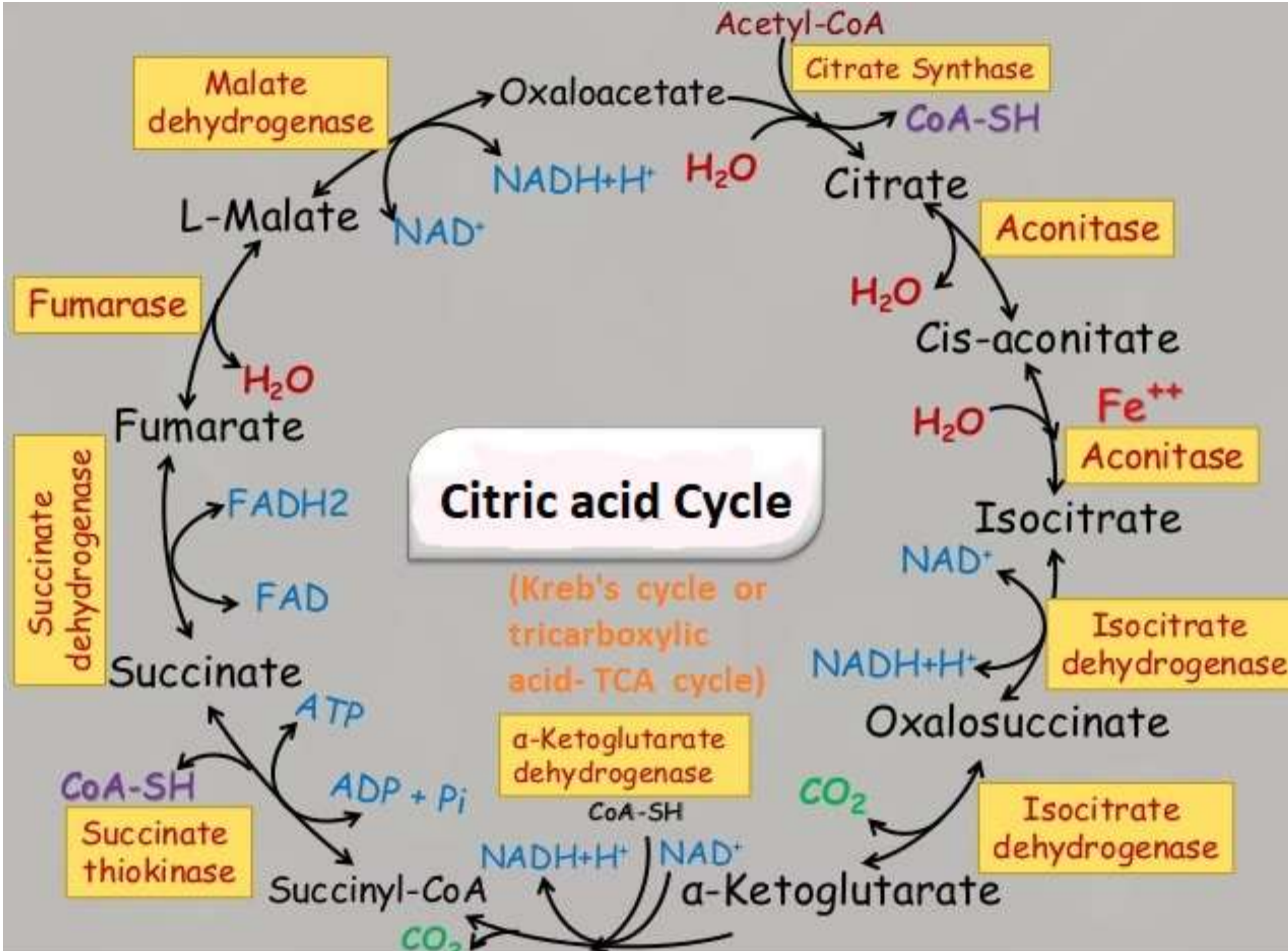
Acetyl CoA + 3 NAD^+ + 1 FAD + 1 ADP + 1 Pi → 2 CO_2 + 3 NADH + 3 H^+ + 1 $FADH_2$ + 1 ATP

- In words, the equation is written as:

Acetyl CoA + Nicotinamide adenine dinucleotide + Flavin adenine dinucleotide + Adenosine diphosphate + Phosphate → Pyruvate + Water + Adenosine triphosphate + Nicotinamide adenine dinucleotide + Hydrogen ions

At each turn of the cycle,

3 NADH, 1 $FADH_2$, 1 GTP (or ATP), 2 CO_2



Citric acid Cycle
(Kreb's cycle or tricarboxylic acid- TCA cycle)
Acetyl-CoA
Citrate Synthase
Oxaloacetate
$CoA-SH$
H_2O
Citrate
Aconitase
H_2O
Cis-aconitate
Fe^{++}
H_2O
Aconitase
Isocitrate
NAD^+
Isocitrate dehydrogenase
$NADH+H^+$
Oxalosuccinate
CO_2
Isocitrate dehydrogenase
α-Ketoglutarate
α-Ketoglutarate dehydrogenase
CoA-SH
$NADH+H^+$
NAD^+
Succinyl-CoA
CO_2
Succinate thiokinase
CoA-SH
ADP + Pi
ATP
Succinate
Succinate dehydrogenase
FADH2
FAD
Fumarate
Fumarase
H_2O
L-Malate
Malate dehydrogenase
$NADH+H^+$
NAD^+

SIGNIFICANCE OF TCA CYCLE

1. Intermediate compounds formed during Krebs cycle are used for the synthesis of biomolecules like amino acids, nucleotides, chlorophyll, cytochromes and fats etc.
2. Intermediate like succinyl CoA takes part in the formation of chlrophyll.
3. Amino Acids are formed from α-Ketoglutaric acid, pyruvic acid and oxaloacetic acid.
4. Krebs cycle releases plenty of energy required for various metabolic activities of cell.
5. By this cycle, carbon skeleton are got, which are used in process of growth and for maintaining the cells.

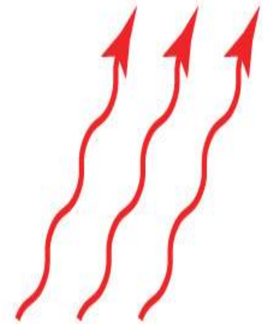
- https://www.youtube.com/watch?v=ubzw64PQPqM

Cellular respiration

Cellular respiration

Cellular respiration, the process by which organisms combine oxygen with foodstuff molecules, diverting the chemical energy in these substances into life-sustaining activities and discarding, as waste products, carbon dioxide and water.

The release of energy during cellular respiration



energy released

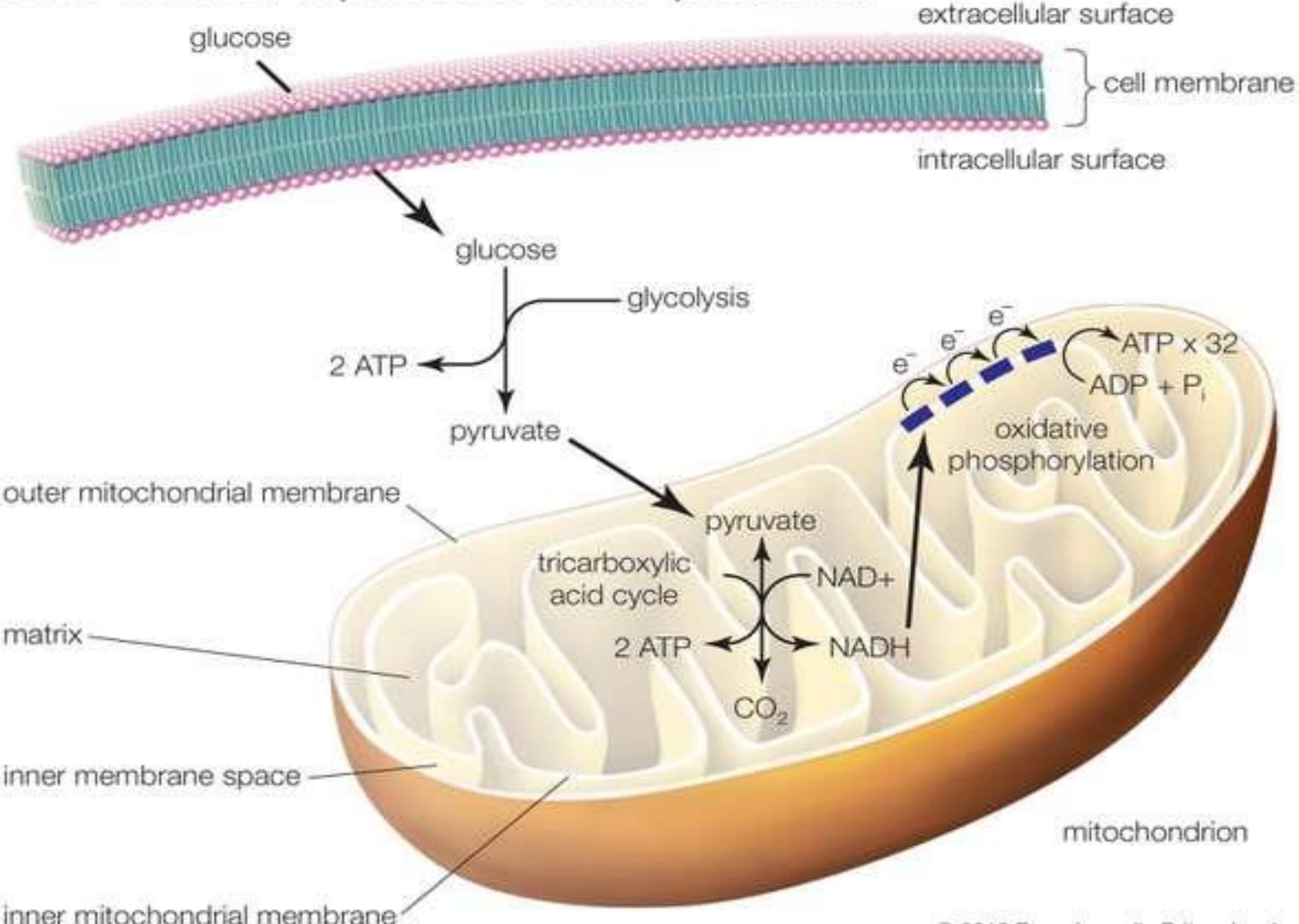
glucose + oxygen ⟶ carbon dioxide + water

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O$$

Role Of Mitochondria

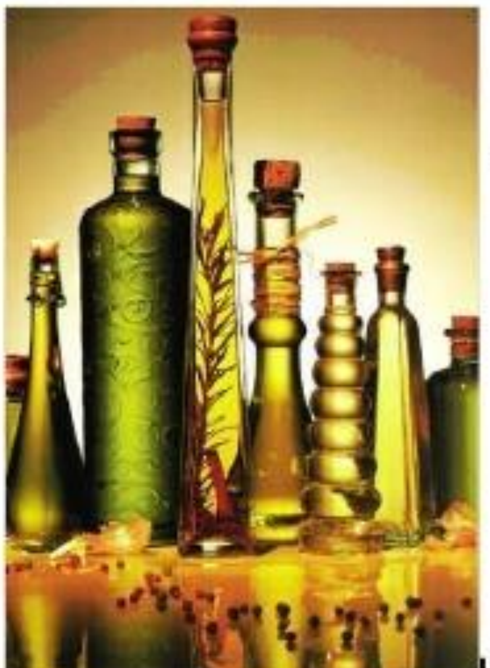
- One objective of the degradation of foodstuffs is to convert the energy contained in chemical bonds into the energy-rich compound adenosine triphosphate (ATP), which captures the chemical energy obtained from the breakdown of food molecules and releases it to fuel other cellular processes. In eukaryotic cells (that is, any cells or organisms that possess a clearly defined nucleus and membrane-bound organelles) the enzymes that catalyze the individual steps involved in respiration and energy conservation are located in highly organized rod-shaped compartments called mitochondria.

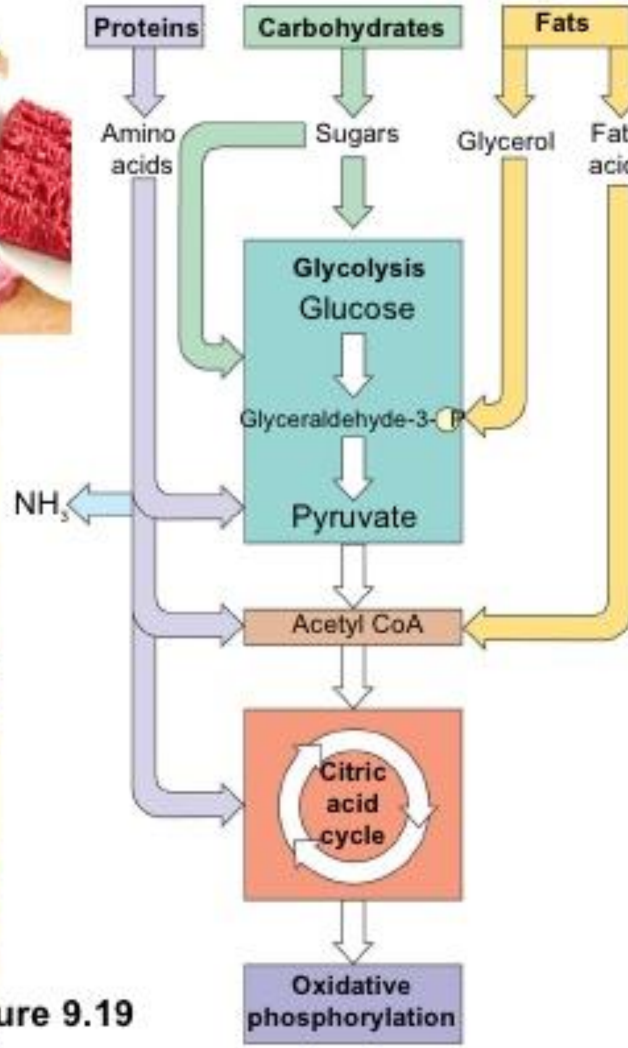
Basic overview of processes of ATP production



Carbohydrates not only source of Energy Use

- The catabolism of various molecules from food





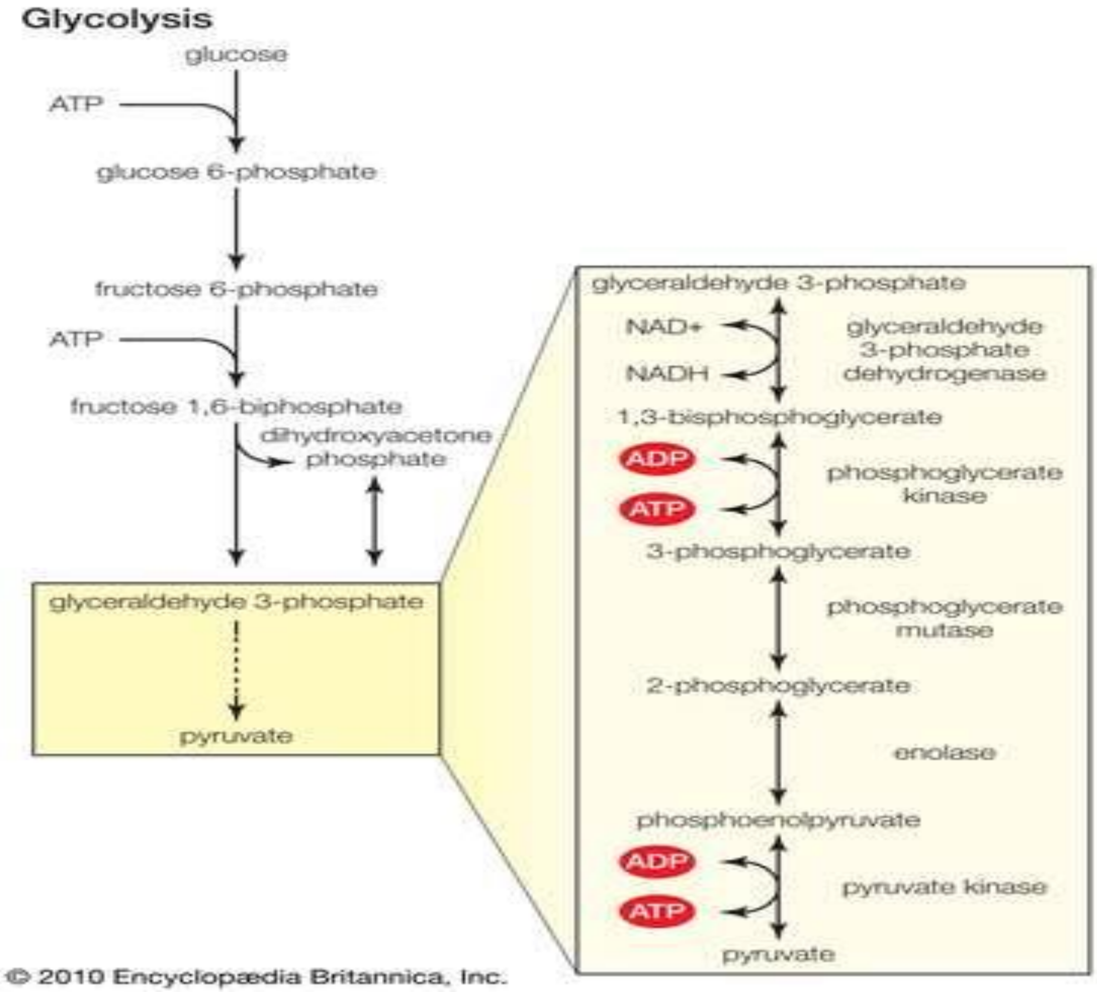
ure 9.19

Main Metabolic Processes

- Biologists differ somewhat with respect to the names, descriptions, and the number of stages of cellular respiration. The overall process, however, can be distilled into three main metabolic stages or steps: glycolysis, the tricarboxylic acid cycle (TCA cycle), and oxidative phosphorylation (respiratory-chain phosphorylation).

Glycolysis

- Glycolysis (which is also known as the glycolytic pathway or the Embden-Meyerhof-Parnas pathway) is a sequence of 10 chemical reactions taking place in most cells that breaks down a glucose molecule into two pyruvate (pyruvic acid) molecules. Energy released during the breakdown of glucose and other organic fuel molecules from carbohydrates, fats, and proteins during glycolysis is captured and stored in ATP. In addition, the compound nicotinamide adenine dinucleotide (NAD+) is converted to NADH during this step (see below). Pyruvate molecules produced during glycolysis then enter the mitochondria, where they are each converted into a compound known as acetyl coenzyme A, which then enters the TCA cycle.

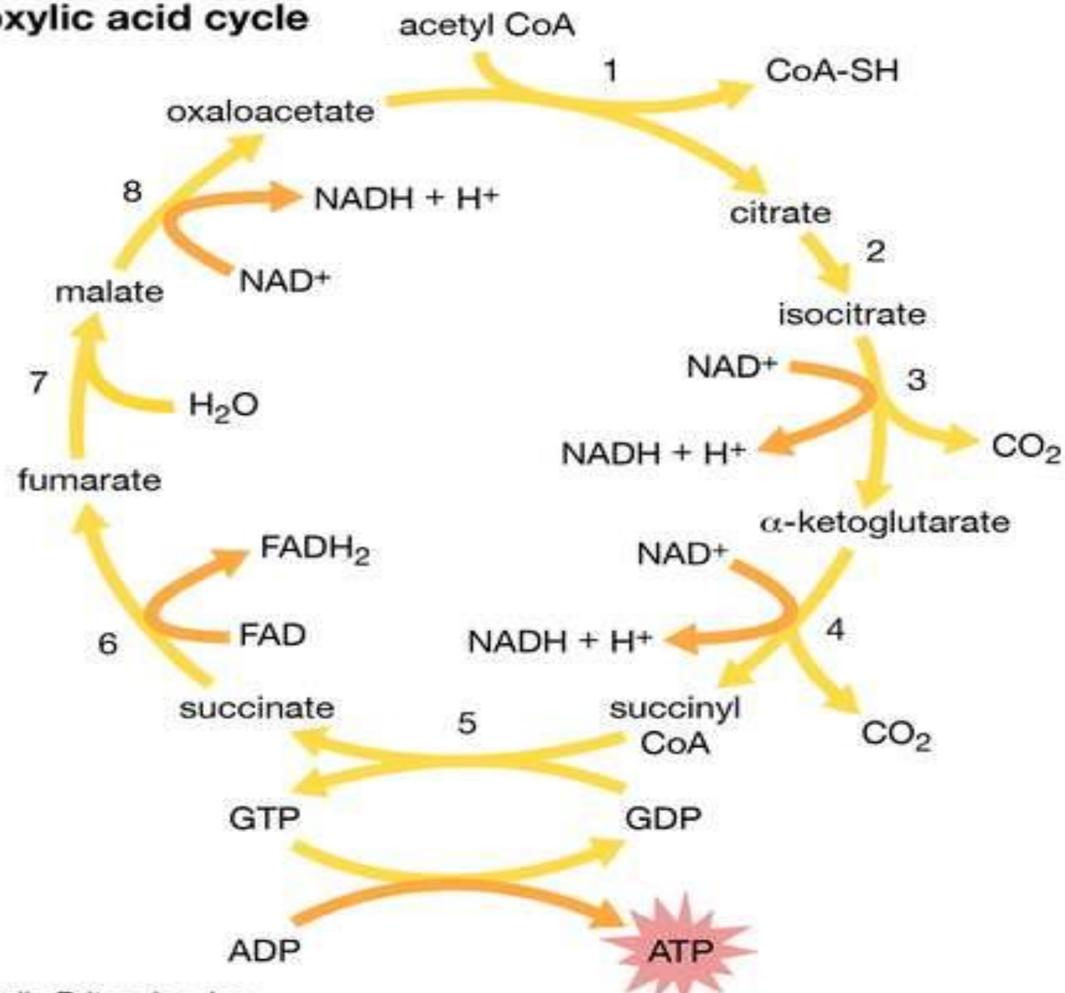


Glycolysis
glucose
ATP
glucose 6-phosphate
fructose 6-phosphate
ATP
fructose 1,6-biphosphate
dihydroxyacetone phosphate
glyceraldehyde 3-phosphate
pyruvate
glyceraldehyde 3-phosphate
NAD+
NADH
glyceraldehyde 3-phosphate dehydrogenase
1,3-bisphosphoglycerate
ADP
ATP
phosphoglycerate kinase
3-phosphoglycerate
phosphoglycerate mutase
2-phosphoglycerate
enolase
phosphoenolpyruvate
ADP
ATP
pyruvate kinase
pyruvate

Tricarboxylic acid cycle

- The TCA cycle (which is also known as the Krebs, or citric acid cycle) plays a central role in the breakdown, or catabolism, of organic fuel molecules. The cycle is made up of eight steps catalyzed by eight different enzymes that produce energy at several different stages. Most of the energy obtained from the TCA cycle, however, is captured by the compounds NAD+ and flavin adenine dinucleotide (FAD) and converted later to ATP. The products of a single turn of the TCA cycle consist of three NAD+ molecules, which are reduced (through the process of adding hydrogen, H+) to the same number of NADH molecules, and one FAD molecule, which is similarly reduced to a single $FADH_2$ molecule. These molecules go on to fuel the third stage of cellular respiration, whereas carbon dioxide, which is also produced by the TCA cycle, is released as a waste product.

Tricarboxylic acid cycle



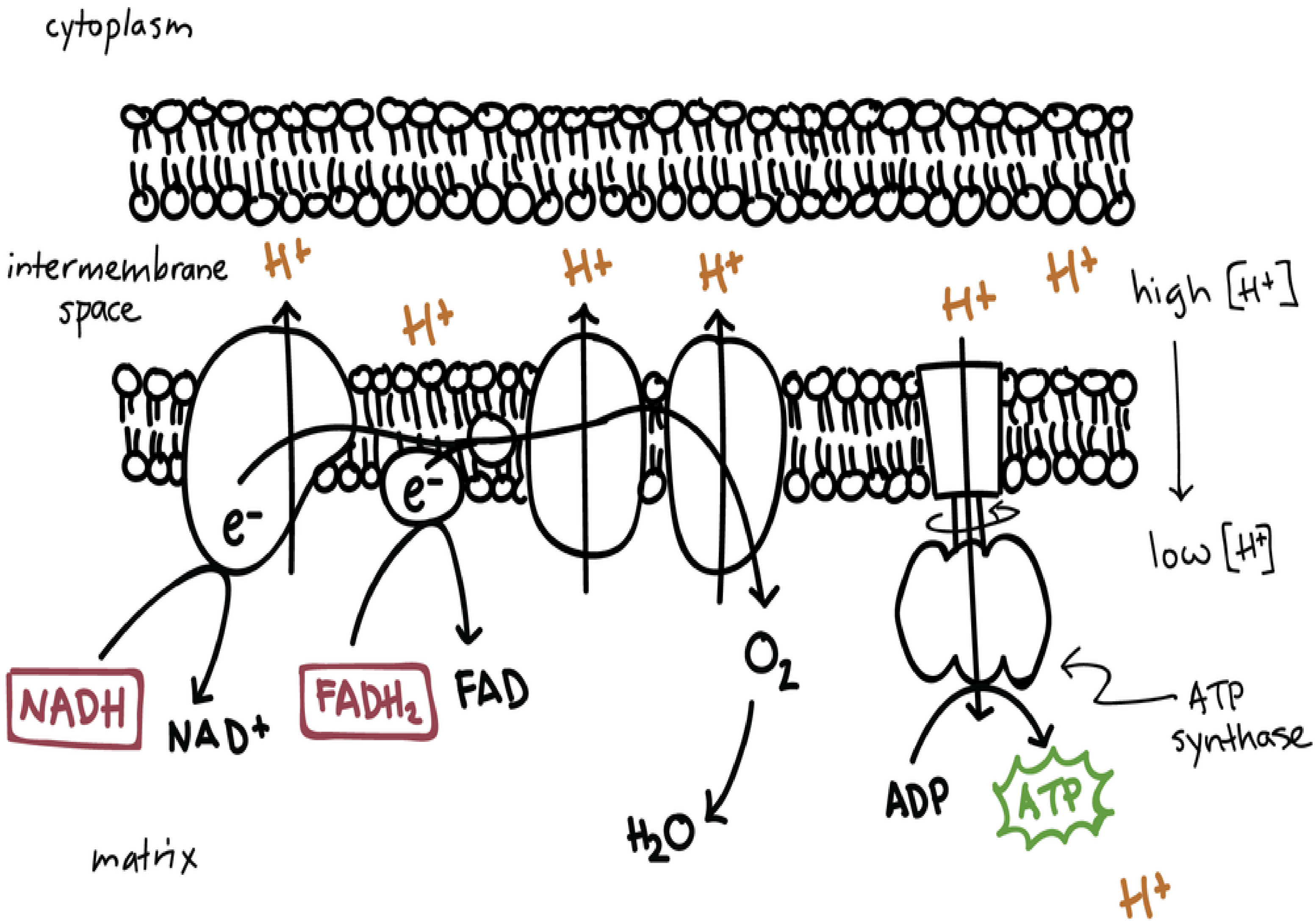
Why do we need oxygen?

- As it turns out, the reason you need oxygen is so your cells can use this molecule during oxidative phosphorylation, the final stage of cellular respiration. Oxidative phosphorylation is made up of two closely connected components: the electron transport chain and chemiosmosis. In the electron transport chain, electrons are passed from one molecule to another, and energy released in these electron transfers is used to form an electrochemical gradient. In chemiosmosis, the energy stored in the gradient is used to make ATP.
- So, where does oxygen fit into this picture? Oxygen sits at the end of the electron transport chain, where it accepts electrons and picks up protons to form water. If oxygen isn't there to accept electrons (for instance, because a person is not breathing in enough oxygen), the electron transport chain will stop running, and ATP will no longer be produced by chemiosmosis. Without enough ATP, cells can't carry out the reactions they need to function, and, after a long enough period of time, may even die.

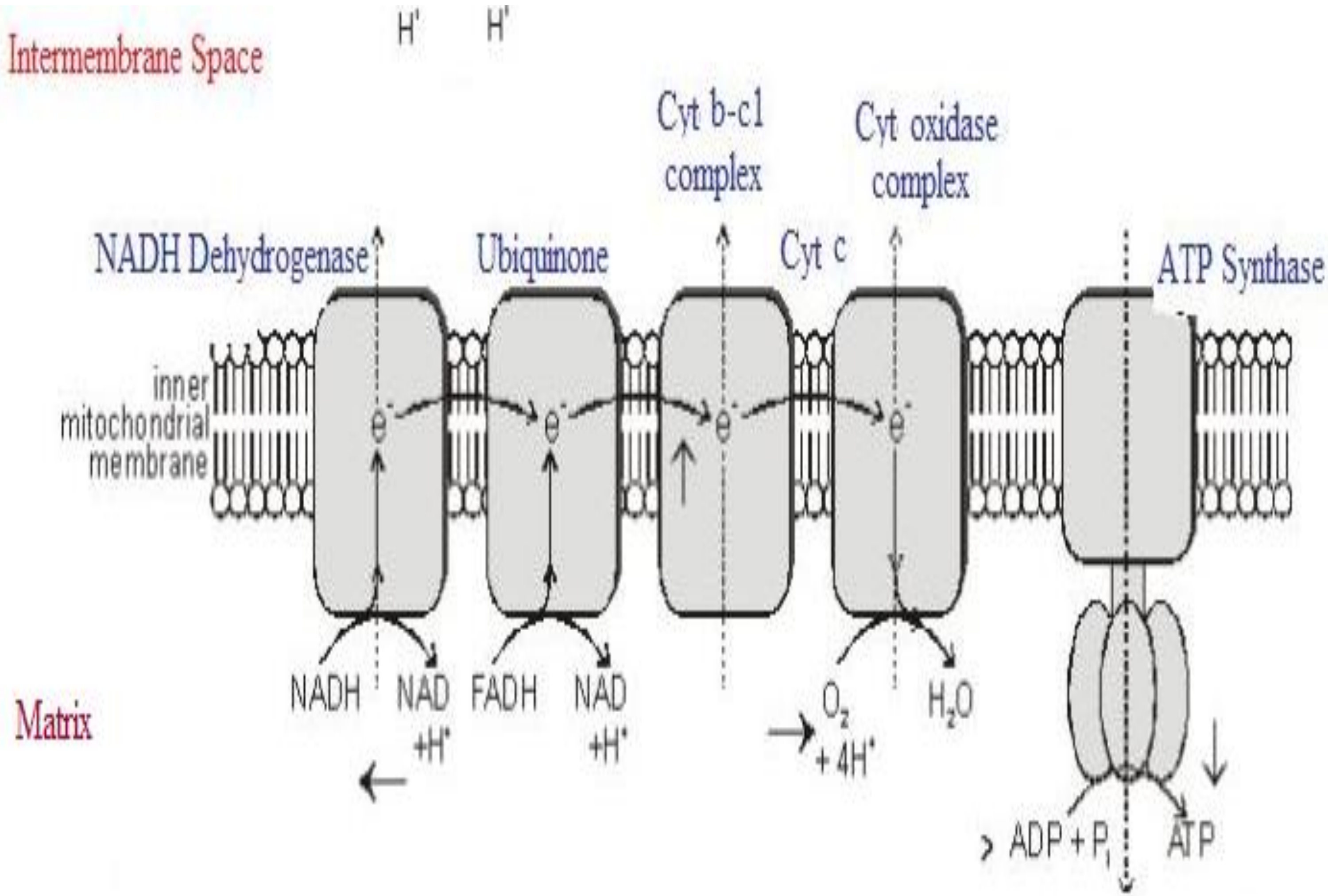
ETC & Oxidative phosphorylation

ETC

- The electron transport chain is a series of proteins and organic molecules found in the inner membrane of the mitochondria. Electrons are passed from one member of the transport chain to another in a series of redox reactions. Energy released in these reactions is captured as a proton gradient, which is then used to make ATP in a process called chemiosmosis. Together, the electron transport chain and chemiosmosis make up oxidative phosphorylation.



cytoplasm
intermembrane space
H+
H+
H+
H+
H+
H+
H+
high [H+]
low [H+]
e-
e-
NADH
NAD+
FADH2
FAD
O2
H2O
ADP
ATP
ATP synthase
matrix
H+



Oxidative ADP Phosphorylation

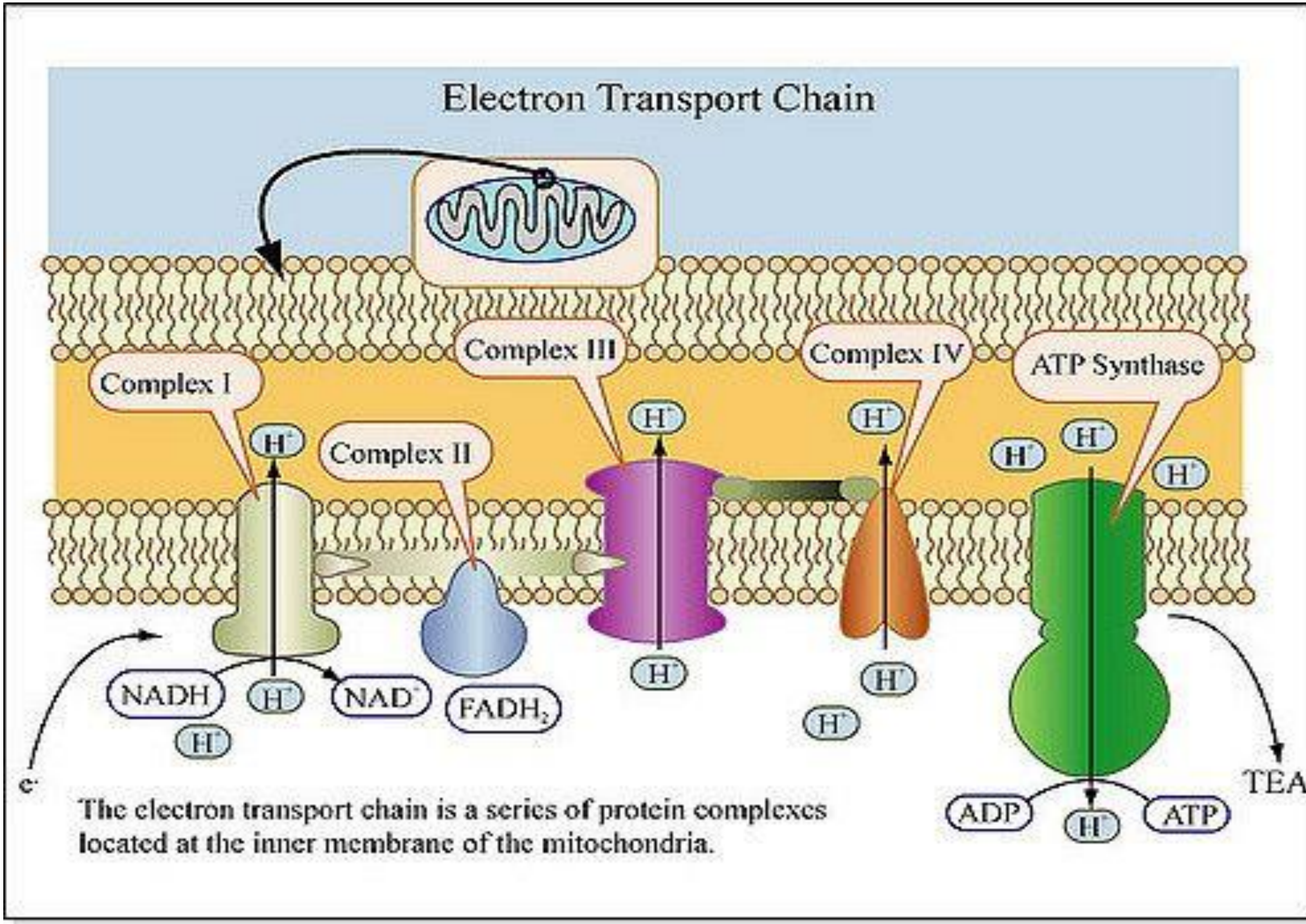
- The electron transport chain is a collection of membrane-embedded proteins and organic molecules, most of them organized into four large complexes labeled I to IV. In eukaryotes, many copies of these molecules are found in the inner mitochondrial membrane. In prokaryotes, the electron transport chain components are found in the plasma membrane.
- As the electrons travel through the chain, they go from a higher to a lower energy level, moving from less electron-hungry to more electron-hungry molecules. Energy is released in these “downhill” electron transfers, and several of the protein complexes use the released energy to pump protons from the mitochondrial matrix to the intermembrane space, forming a proton gradient.

- **Complex I - NADH-Q oxidoreductase**

- **Complex II - Succinate dehydrogenase**

- **Complex III -Q-cytochrome c oxidoreductase**

- **Complex IV- Cytochrome c oxidase**


Electron Transport Chain
Complex I
Complex II
Complex III
Complex IV
ATP Synthase
H+
NADH
NAD+
FADH2
e-
TEA
ADP
ATP
The electron transport chain is a series of protein complexes located at the inner membrane of the mitochondria.

Oxidative phosphorylation

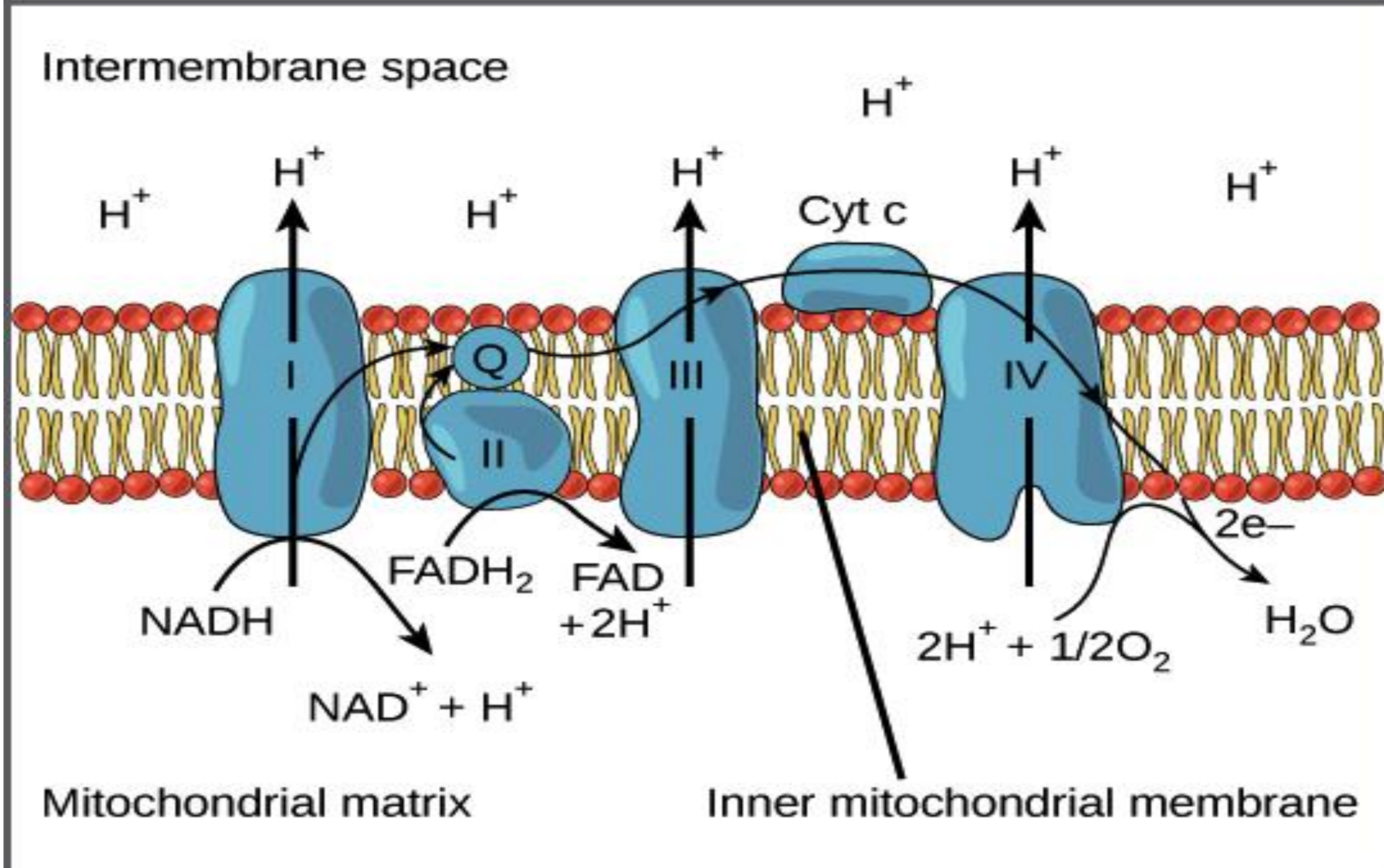
Oxidative phosphorylation is the process where energy is harnessed through a series of protein complexes embedded in the inner-membrane of mitochondria (called the electron transport chain and ATP synthase) to create ATP.

Oxidative phosphorylation can be broken down into two parts

1. Oxidation of NADH and $FADH_2$
2. Phosphorylation

- All of the electrons that enter the transport chain come from NADH and $FADH_2$ molecules produced during earlier stages of cellular respiration: glycolysis, pyruvate oxidation, and citric acid cycle
- NADH is very good at donating electrons in redox reactions (that is, its electrons are at a high energy level), so it can transfer its electrons directly to complex I, turning back into NAD+. As electrons move through complex I in a series of redox reactions, energy is released, and the complex uses this energy to pump protons from the matrix into intermembrane space
- $FADH_2$ is not as good at donating electrons as NADH (that is, its electrons are at a lower energy level), so it cannot transfer its electrons to complex I. Instead, it feeds them into the transport chain through complex II, which does not pump protons across the membrane.
- Because of this bypass, each $FADH_2$ molecule causes fewer protons to be pumped than an NADH

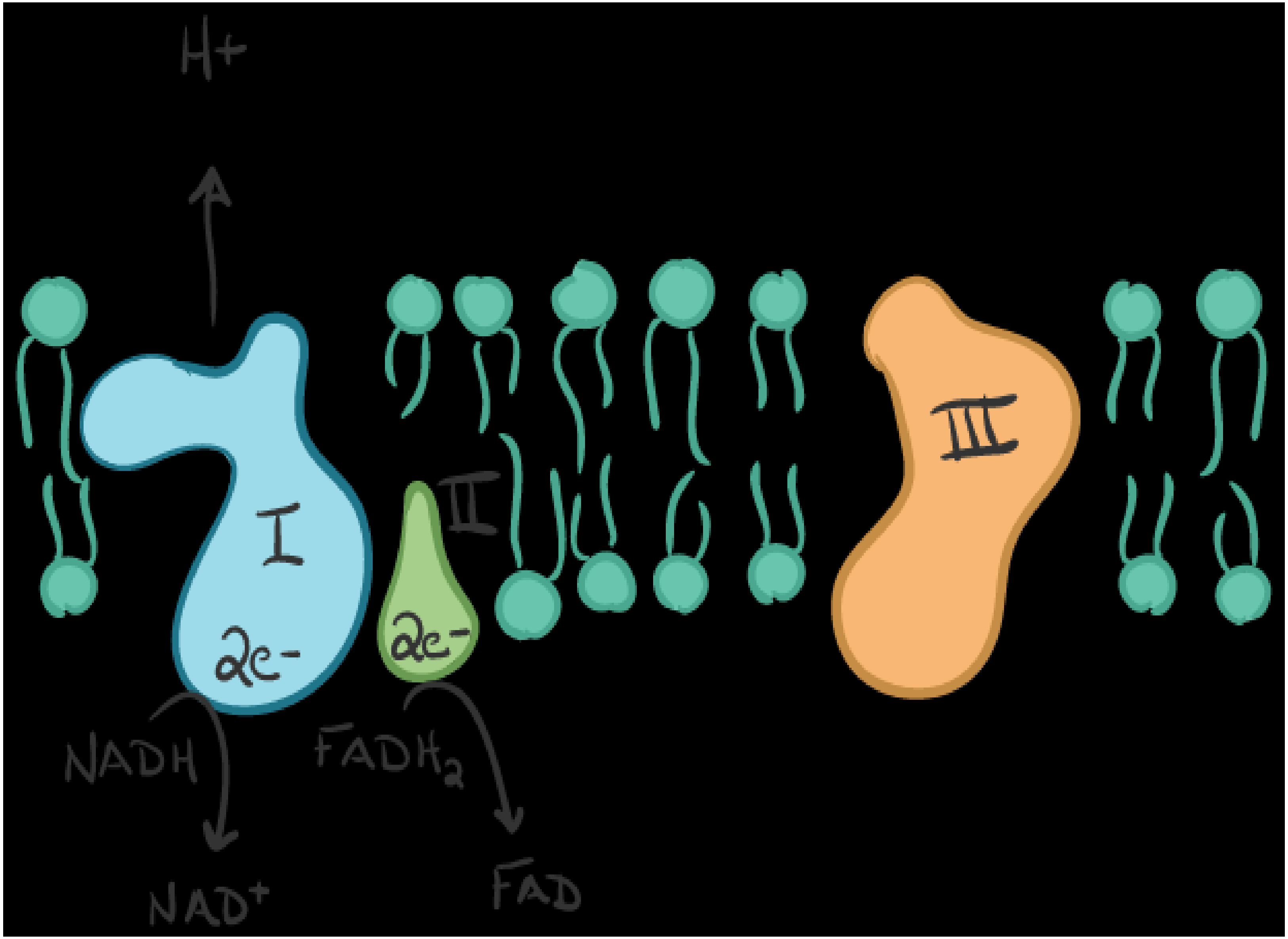
Electron Transport Chain



Oxidation of NADH and FADH2- losing electrons via high energy molecules

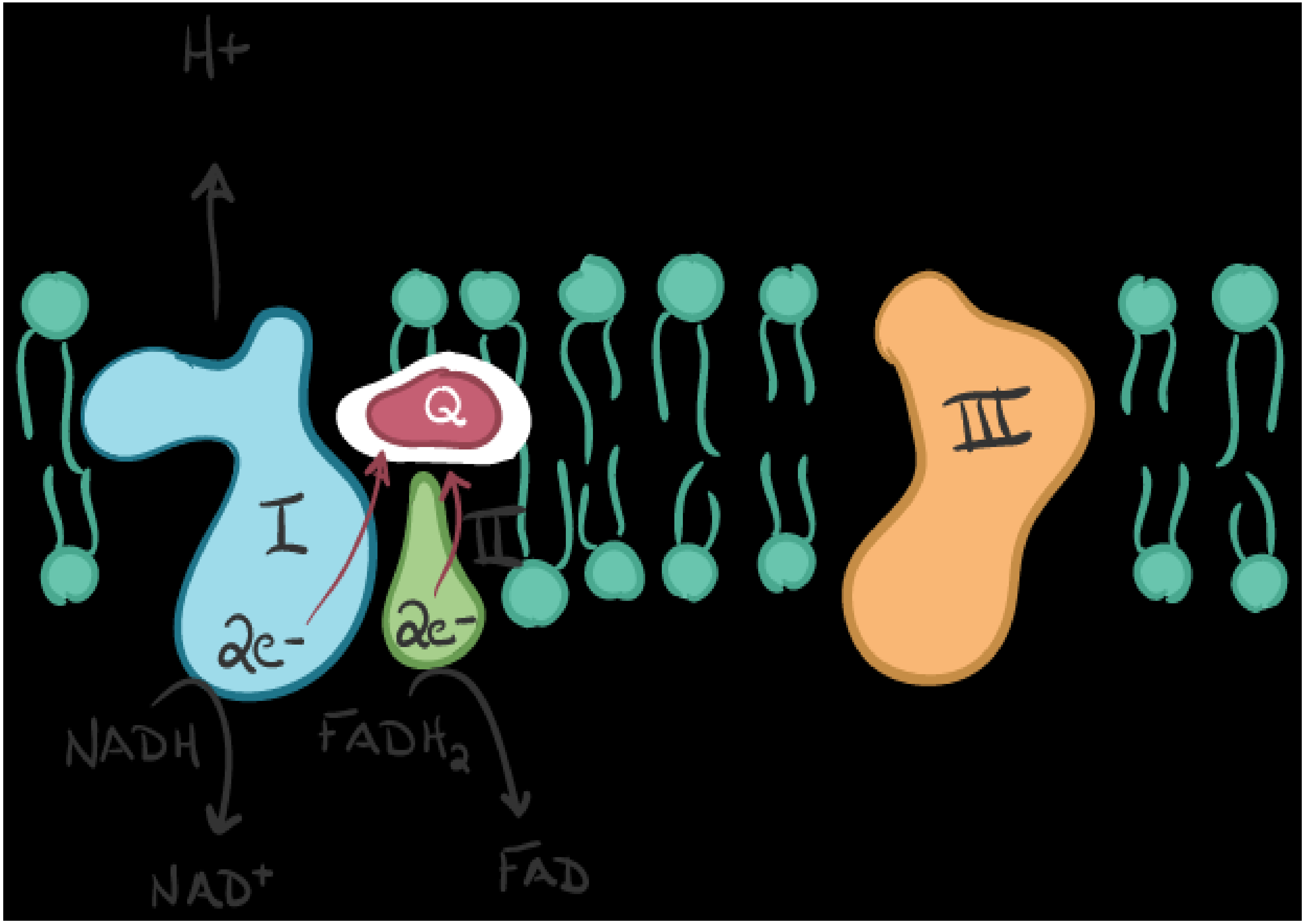
Step 1

- Oxidative phosphorylation starts with the arrival of 3 NADH and 1 $FADH_2$ from the TCA cycle, which shuttle high energy molecules to ETC. NADH transfers its high energy molecules to protein complex I, while $FADH_2$ transfers its high energy molecules to protein complex II. Shuttling high energy molecules causes a loss of electrons from NADH and $FADH_2$, called as oxidation


H+
I
2e-
II
2e-
III
NADH
NAD+
FADH2
FAD

Step 2

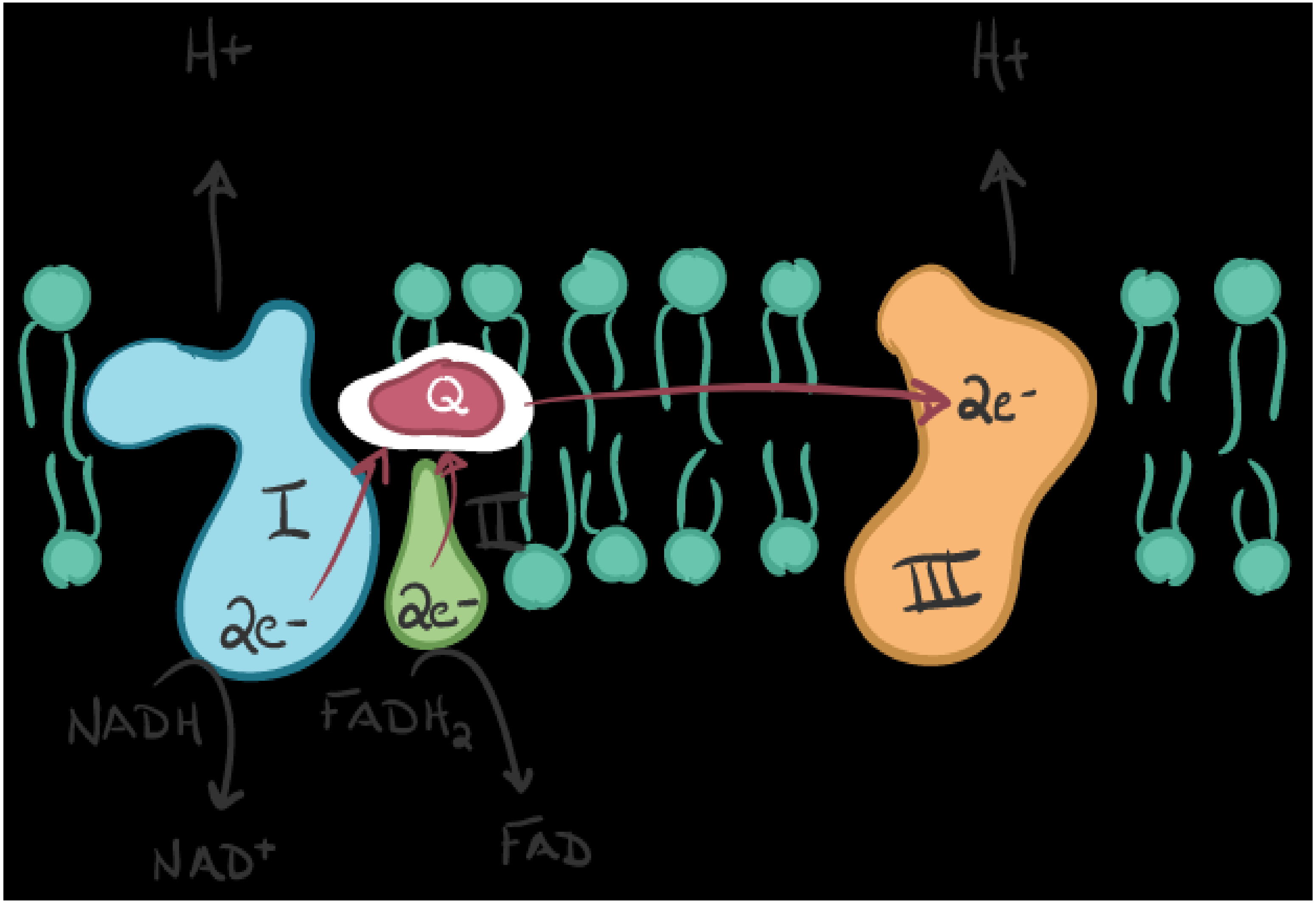
- The process of NADH oxidation leads to the pumping of protons through protein complex I from the matrix to the intermembrane space. The electrons that were received by protein complex I are given to another membrane bound electron carrier called ubiquinone or Q
- As this action is repeated, protons will accumulate in the intermembrane space. This accumulation of protons is how the cell temporarily stored transformed energy
- $FADH_2$ has a slightly different route than NADH. After its arrival at protein complex II, its high energy electrons are directly transferred to Q, to form reduced Q or QH_2. there is no hydrogen pumping for the exchange of the $FADH_2$ electrons here.



H+
Q
I
2e-
2e-
II
III
NADH
NAD+
FADH2
FAD

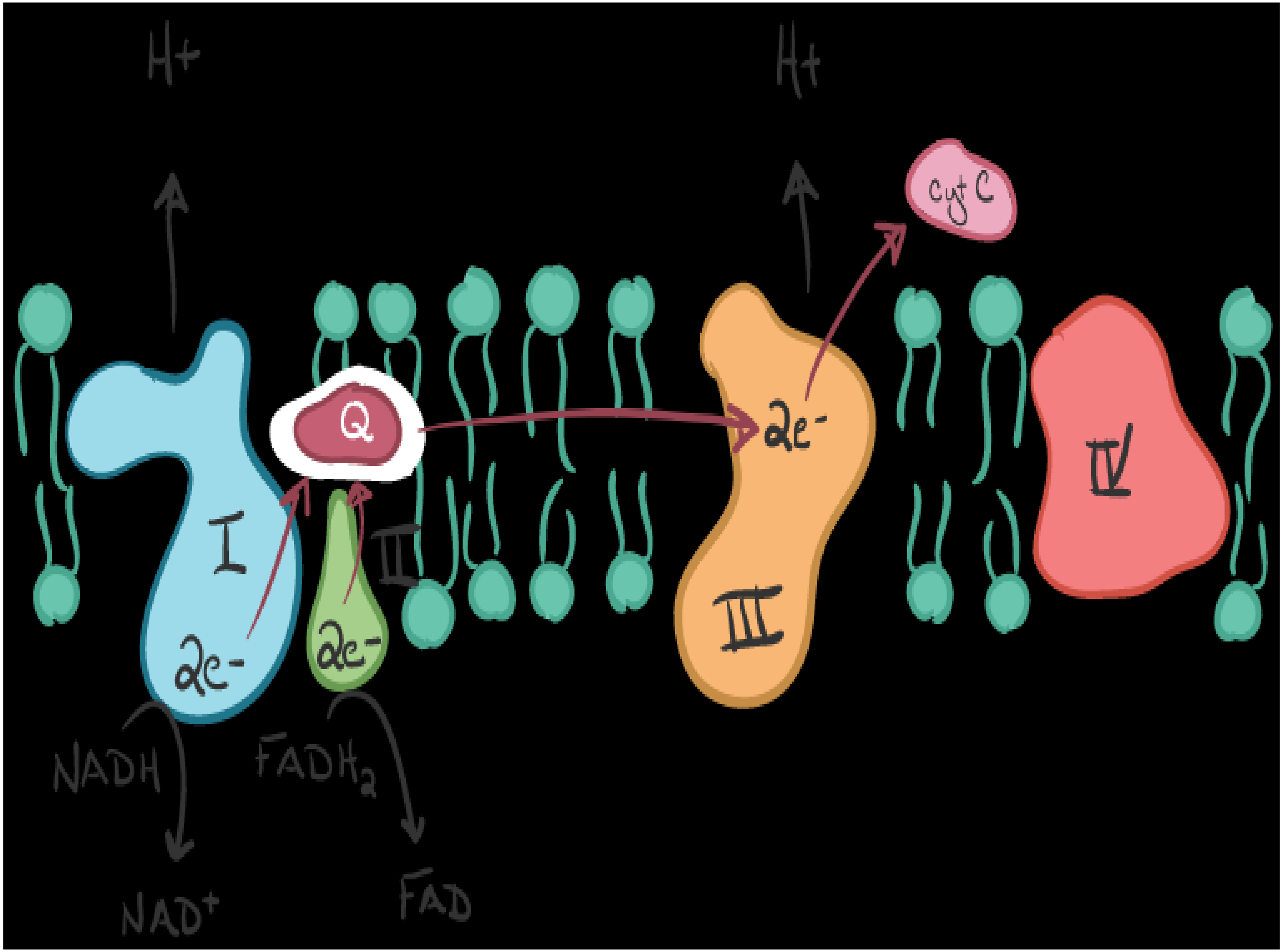
Step 3

- The rest of the steps are now the same for the high energy molecules from NADH and $FADH_2$ in earlier steps. Inside the nonpolar region of the phospholipid bilayer, UQH_2 transports the electrons to protein complex III. UQH_2 also carries protons. When UQH_2 delivers electrons to protein complex III, it also donates its protons to be pumped
- Complex III pumps protons through the membrane and passes its electrons to cytochrome C for transport to the fourth complex of proteins and enzymes.


H+
H+
Q
2e-
I
2e-
2e-
II
III
NADH
NAD+
FADH2
FAD

Step 4

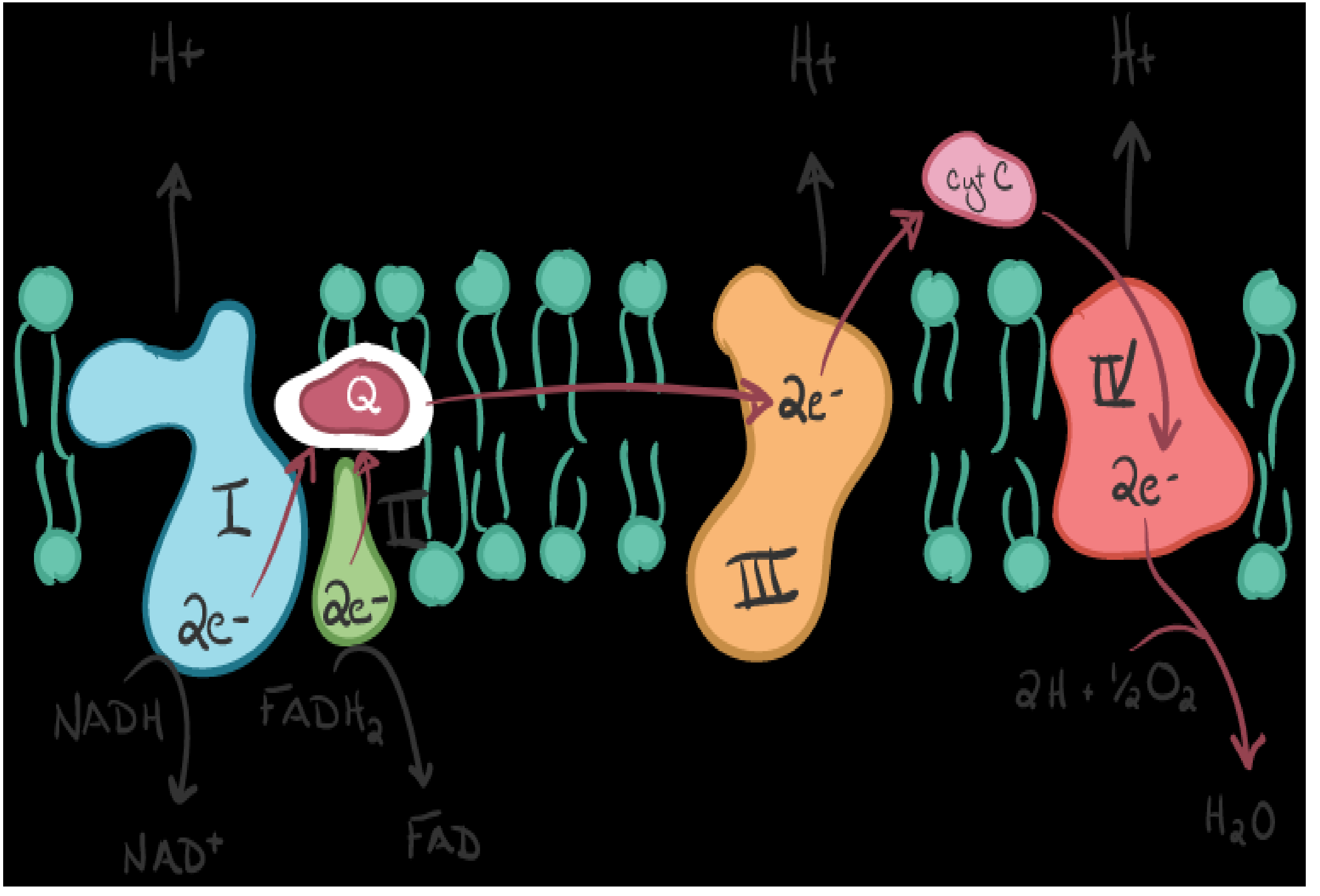
- The third complex is composed of cytochrome b, another Fe-S protein, Rieske center (2Fe-2S center), and cytochrome c proteins; this complex is also called cytochrome oxidoreductase.
- The electrons that arrived at the protein complex III are picked up by cytochrome C or (cyt C), the last electron carrier. This action also causes protons to be pumped into the intermembrane space
- Cytochrome proteins have a prosthetic heme group. The heme molecule is similar to the heme in hemoglobin, but it carries electrons, not oxygen.



H+
H+
cyt C
Q
2e-
I
2e-
2e-
II
III
IV
NADH
NAD+
FADH2
FAD

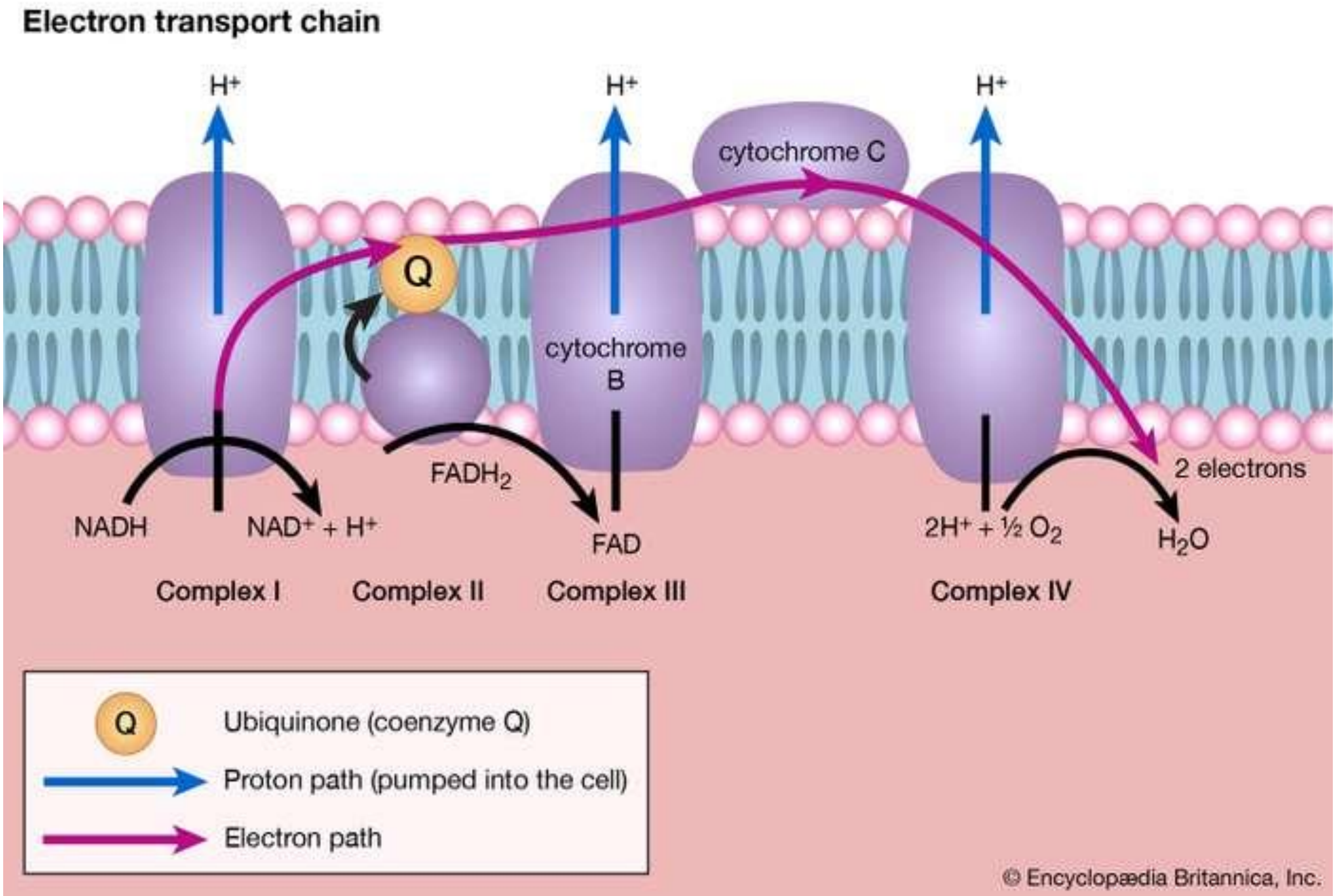
Step 5

- The fourth complex is composed of cytochrome proteins c, a, and a_3. This complex contains two heme groups (one in each of the cytochromes a and a_3) and three copper ions (a pair of Cu_A and one Cu_B in cytochrome a_3). The cytochromes hold an oxygen molecule very tightly between the iron and copper ions until the oxygen is completely reduced. The reduced oxygen then picks up two hydrogen ions from the surrounding medium to produce water (H_2O). The removal of the hydrogen ions from the system also contributes to the ion gradient used in the process of chemiosmosis.
- Cytochrome C carries the electrons to the final protein complex, protein IV. Once again, energy released via electron shuttling allows for another proton to be pumped into the intermembrane space. The electrons are then drawn to oxygen, which is the final electron acceptor. Water is formed as oxygen receives the electrons from protein complex IV, and combines with protons on the inside of the cell.


H+
H+
H+
cyt C
Q
2e-
IV
I
II
2e-
III
2e-
2e-
NADH
FADH2
2H + ½O2
NAD+
FAD
H2O

Summary

- Beyond the first two complexes, electrons from NADH and $FADH_2$ travel exactly the same route. Both complex I and complex II pass their electrons to a small, mobile electron carrier called **ubiquinone** (**Q**), which is reduced to form QH_2 and travels through the membrane, delivering the electrons to complex III. As electrons move through complex III, more H+ ions are pumped across the membrane, and the electrons are ultimately delivered to another mobile carrier called **cytochrome C** (**cyt C**). Cyt C carries the electrons to complex IV, where a final batch of H+ ions is pumped across the membrane. Complex IV passes the electrons to O_2 , which splits into two O_2 atoms and accepts protons from the matrix to form water. Four electrons are required to reduce each molecule of oxygen and two water molecules are formed in the process.

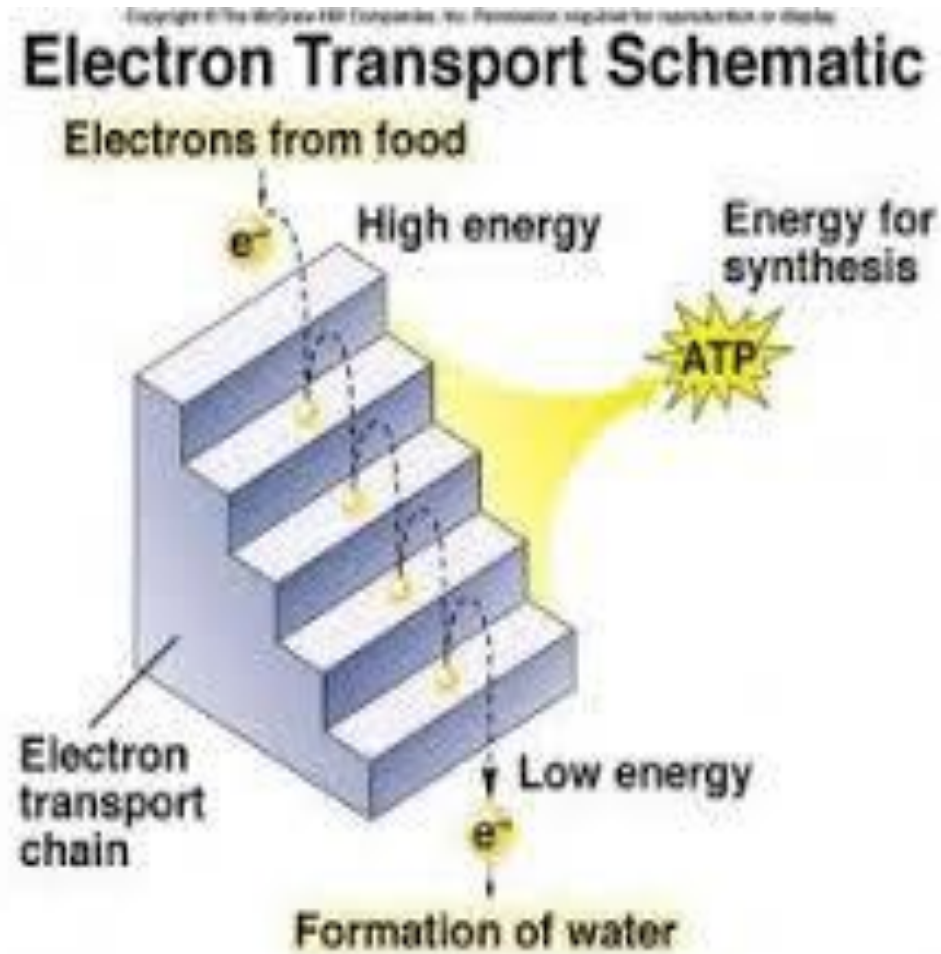


Electron transport chain
H+
H+
H+
cytochrome C
Q
cytochrome
B
NADH
NAD+ + H+
FADH2
FAD
2H+ + ½ O2
H2O
2 electrons
Complex I
Complex II
Complex III
Complex IV
Q
Ubiquinone (coenzyme Q)
Proton path (pumped into the cell)
Electron path
© Encyclopædia Britannica, Inc.

- Overall, what does the electron transport chain do for the cell? It has two important functions:
- **Regenerates electron carriers:** NADH and $FADH_2$ pass their electrons to the electron transport chain, turning back into NAD+ and FAD. This is important because the oxidized forms of these electron carriers are used in glycolysis and the citric acid cycle and must be available to keep these processes running
- **Makes a proton gradient:** The transport chain builds a proton gradient across the inner mitochondrial membrane, with a higher concentration of H+ in the intermembrane space and a lower concentration in the matrix. This gradient represents a stored form of energy, and as well it can be used to make ATP

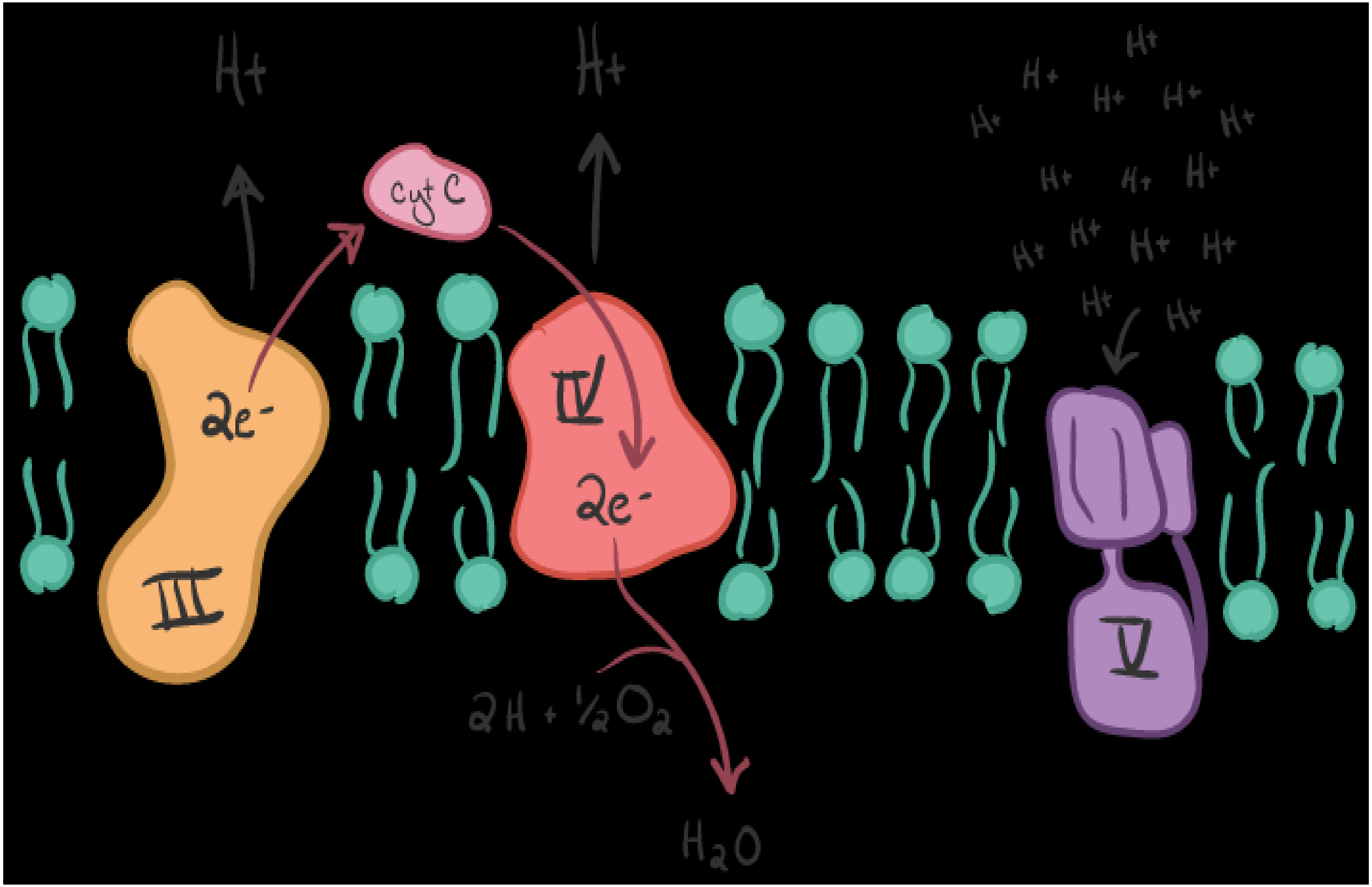
Step 6: Phosphorylation-the production of ATP

- Complexes I, III and IV of the electron transport chain are proton pumps. As electrons move energetically downhill, the complexes capture the released energy and use it to pump H+ ions from the matrix to the intermembrane space. This pumping forms an elecrochemical gradient across the inner mitochondrial membrane. The gradient is sometimes called the proton-motive force, and you can think of it as a form of stored energy, kind of like a battery
- In the inner mitochondrial membrane, H+ ions have just one channel available: a membrane-spanning protein known as ATP synthase. Conceptually, ATP synthase is a lot like a turbine in a hydroelectric power plant. Instead of being turned by water, its turned by the flow of H+ ions moving down their electrochemical gradient. As ATP synthase turns, it catalyzes the addition of a phosphate to ADP, capturing energy from the proton gradient as ATP.


Electron Transport Schematic
Electrons from food
e⁻
High energy
Energy for synthesis
ATP
Electron transport chain
Low energy
e⁻
Formation of water

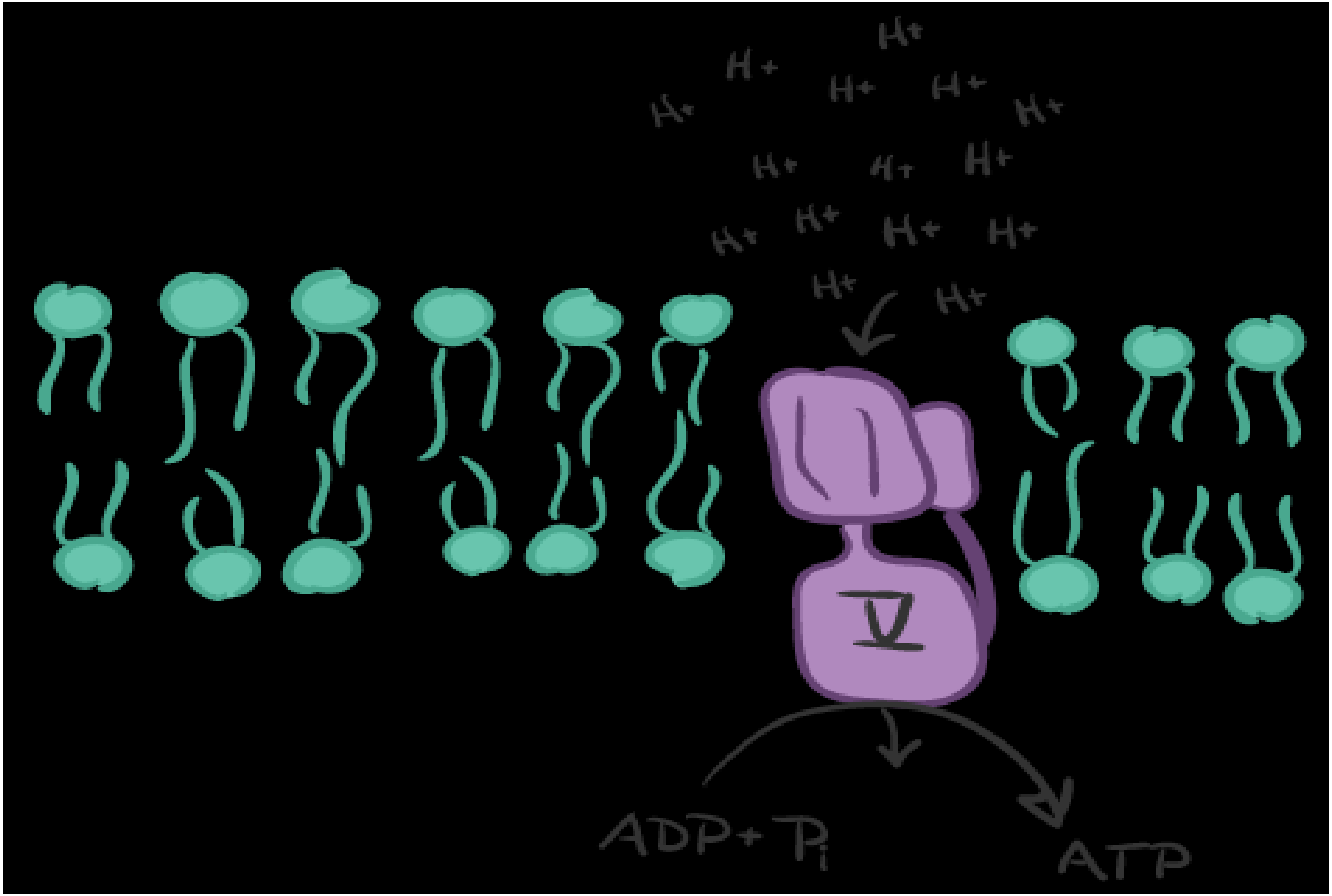
Electrochemical gradient

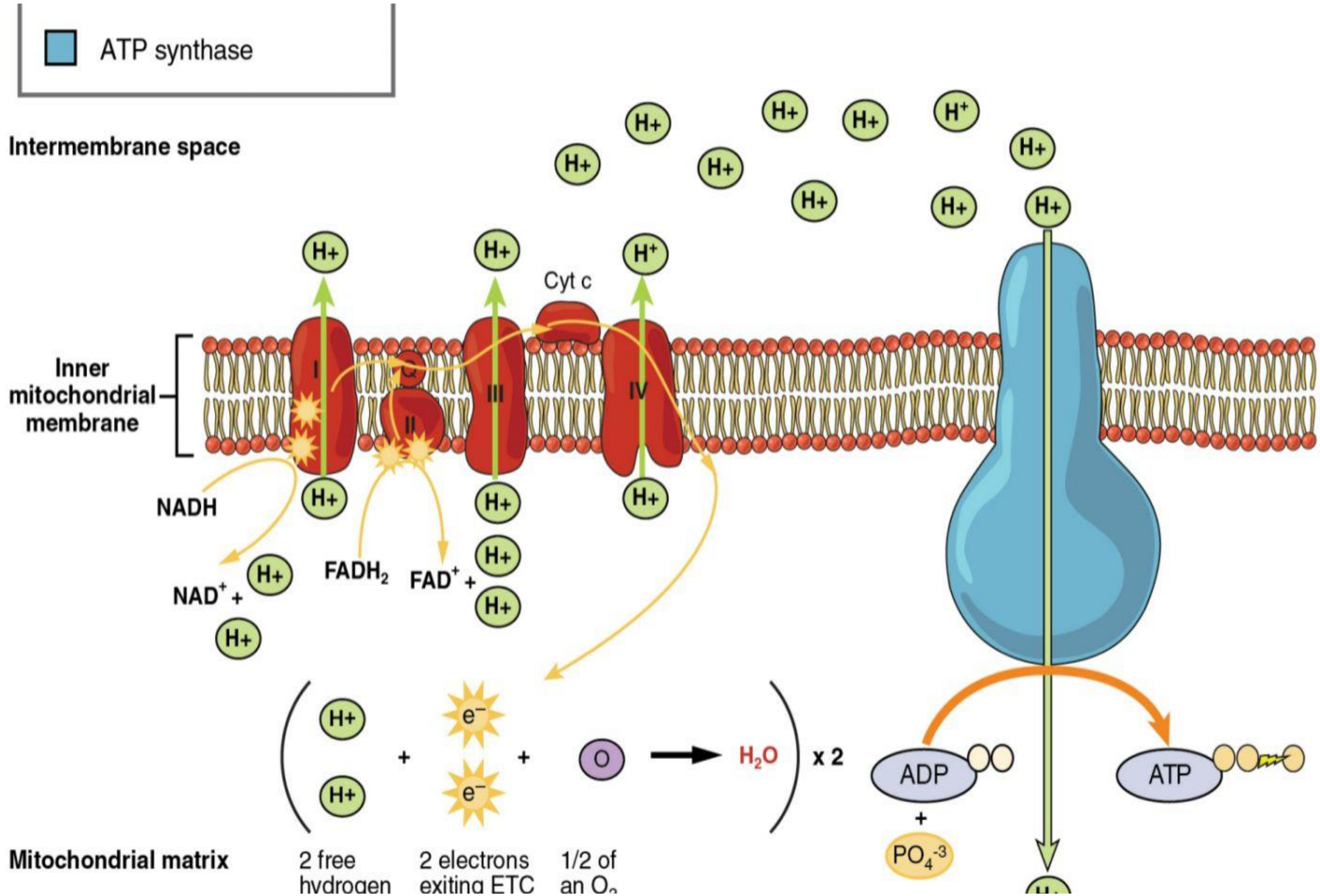
- The outside, or exterior, of the mitochondrial membrane is positive because of the accumulation of the protons (H+)
- and the inside is negative due to the loss of the protons. A chemical concentration gradient has also developed on either side of the membrane. The electrochemical gradient is how the cell transfers the stored energy from the reduced NADH and $FADH_2$


H+
cyt C
H+
2e-
III
IV
2e-
V
2H + ½O2
H2O

Step 7:

- When there is a high concentration of protons on the outside of the mitochondrial membrane, protons are pushed through ATP synthase. This movement of protons causes ATP synthase to spin, and bind ADP and Pi, producing ATP. Finally, ATP is made


H+
ADP + Pi
ATP



ATP synthase
Intermembrane space
H+
Cyt c
Inner mitochondrial membrane
I
II
III
IV
Q
NADH
NAD+ +
FADH2
FAD+ +
H+ + e− + e− + O → H2O x 2
ADP
+
PO4-3
ATP
Mitochondrial matrix
2 free hydrogen
2 electrons exiting ETC
1/2 of an O2

- This process, in which energy from a proton gradient is used to make ATP, is called chemiosmosis. More broadly, chemiosmosis can refer to any process in which energy stored in a proton gradient is used to do work. Although chemiosmosis accounts for over 80% of ATP made during glucose breakdown in cellular respiration, it’s not unique to cellular respiration. For instance, chemiosmosis is also involved in the light reactions of photosynthesis.
- What would happen to the energy stored in the proton gradient if it weren't used to synthesize ATP or do other cellular work? It would be released as heat, and interestingly enough, some types of cells deliberately use the proton gradient for heat generation rather than ATP synthesis. This might seem wasteful, but it's an important strategy for animals that need to keep warm. For instance, hibernating mammals (such as bears) have specialized cells known as brown fat cells. In the brown fat cells, uncoupling proteins are produced and inserted into the inner mitochondrial membrane. These proteins are simply channels that allow protons to pass from the intermembrane space to the matrix without traveling through ATP synthase. By providing an alternate route for protons to flow back into the matrix, the uncoupling proteins allow the energy of the gradient to be dissipated as heat.

ATP yield

- How many ATP do we get per glucose in cellular respiration
- 30-32 ATP
- 2 net ATP are made in glycolysis
- 2 ATP are made in TCA cycle
- Remaining all ATP from ETC
- Based on experimental work, is appears that four H+ ions must flow back into matrix through ATP synthase to power the synthesis of one ATP molecule
- When electrons from NADH move the ETC, about 10 H+ are pumped from the matrix to the intermembrane space, so each NADH yields about 2.5 ATP.
- Eletrons from $FADH_2$, which enter the chain at a later stage, drive pumping of only 6 H+, leading to production of about 1.5 ATP.

Stage	Direct products (net)	Ultimate ATP yield (net)
Glycolysis	2 ATP	2 ATP
	2 NADH	3-5 ATP
Pyruvate oxidation	2 NADH	5 ATP
Citric acid cycle	2 ATP/GTP	2 ATP
	6 NADH	15 ATP
	2 $FADH_2$	3 ATP
Total		**30-32 ATP**

Electron transport chain 4

- The overall reaction of the electron transport chain:

$$10NADH + 2FADH_2 + 6O_2$$

$$\downarrow$$

$$10NAD + 2FAD + 12H_2O$$

- During this oxidative reaction, ATP is produced by <u>oxidative phosphorylation</u>

Consider the following

- In oxidative phosphorylation, oxygen must be present to receive electrons from the protein complexes. This allows for more electrons and high energy molecules to be passed along, and maintains the hydrogen pumping that produces ATP. What happens if we run out of oxygen? How do we break down our food to make energy? The body has a plan B for this situation called fermentation. It happens all the time in athletes, like runners, when they use all their oxygen and produce lactic acid. Fermentation starts after glycolysis, replacing the citric acid cycle and oxidative phosphorylation. During glycolysis, only two ATP molecules are produced. NADH is then oxidized to transform the pyruvates made in glycolysis into lactic acid.

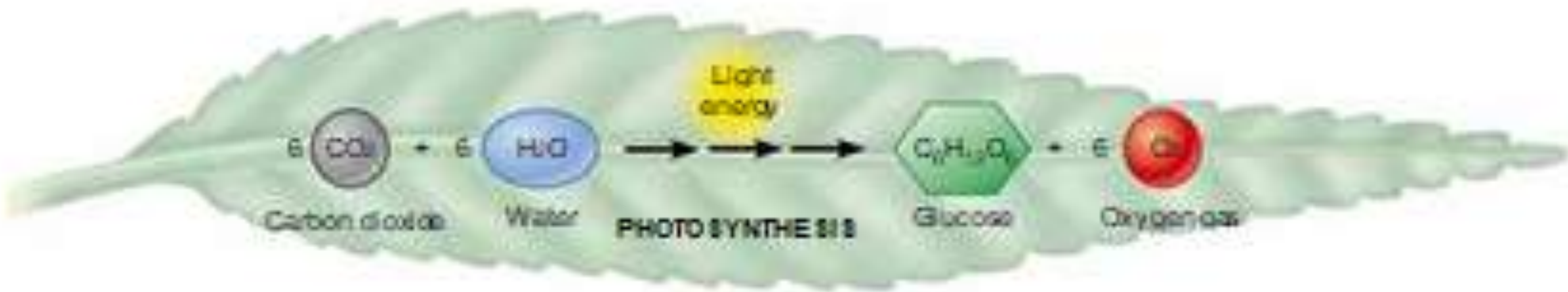
- https://www.youtube.com/watch?v=nkdXZUHUyE0

Photosynthesis

Photosynthesis, the process by which green plants and certain other organisms transform light energy into chemical energy. During photosynthesis in green plants, light energy is captured and used to convert water, carbon dioxide, and minerals into oxygen and energy-rich organic compounds.

What is Photosynthesis?

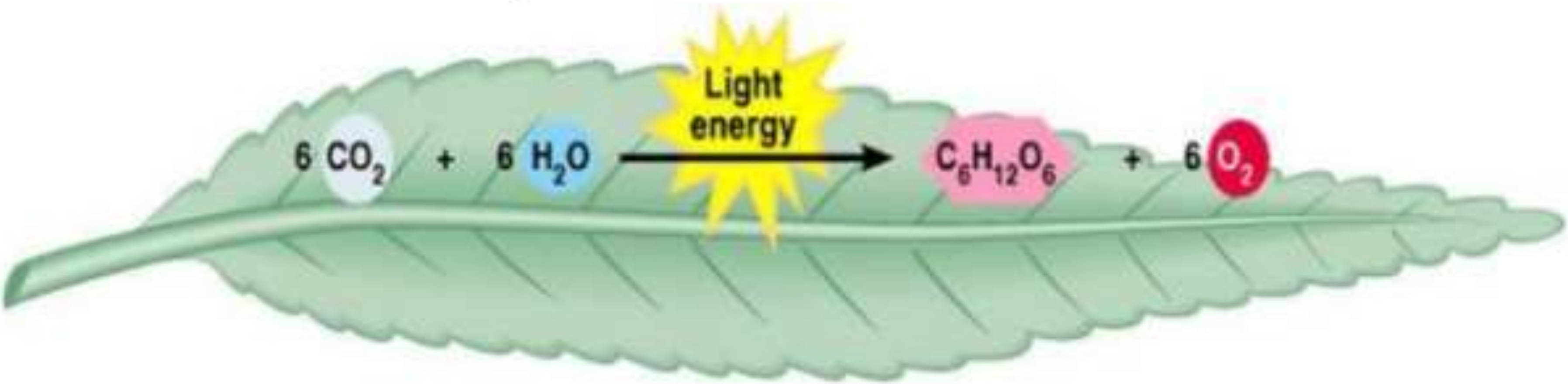
The process of converting light energy (kinetic) into energy stored in the covalent bonds of glucose molecules (potential).



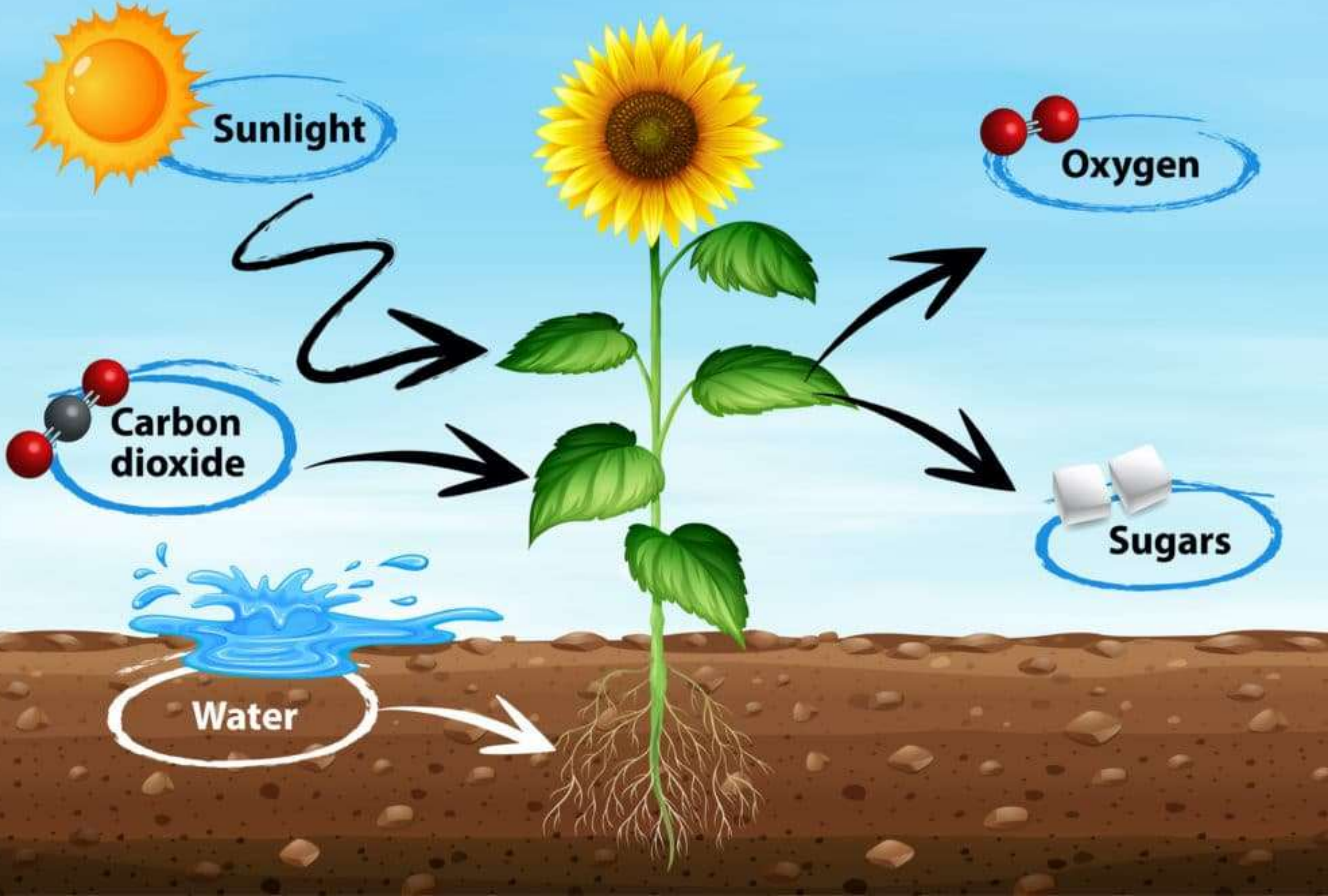
- carried out by photo<u>autotrophs</u>
  - <u>plants</u>, phytoplankton, cyanobacteria (any photosynthetic organism)
- the basis of almost all ecosystems
  - all “food energy” ultimately comes from the sun
  - source of all atmospheric oxygen (O_2)

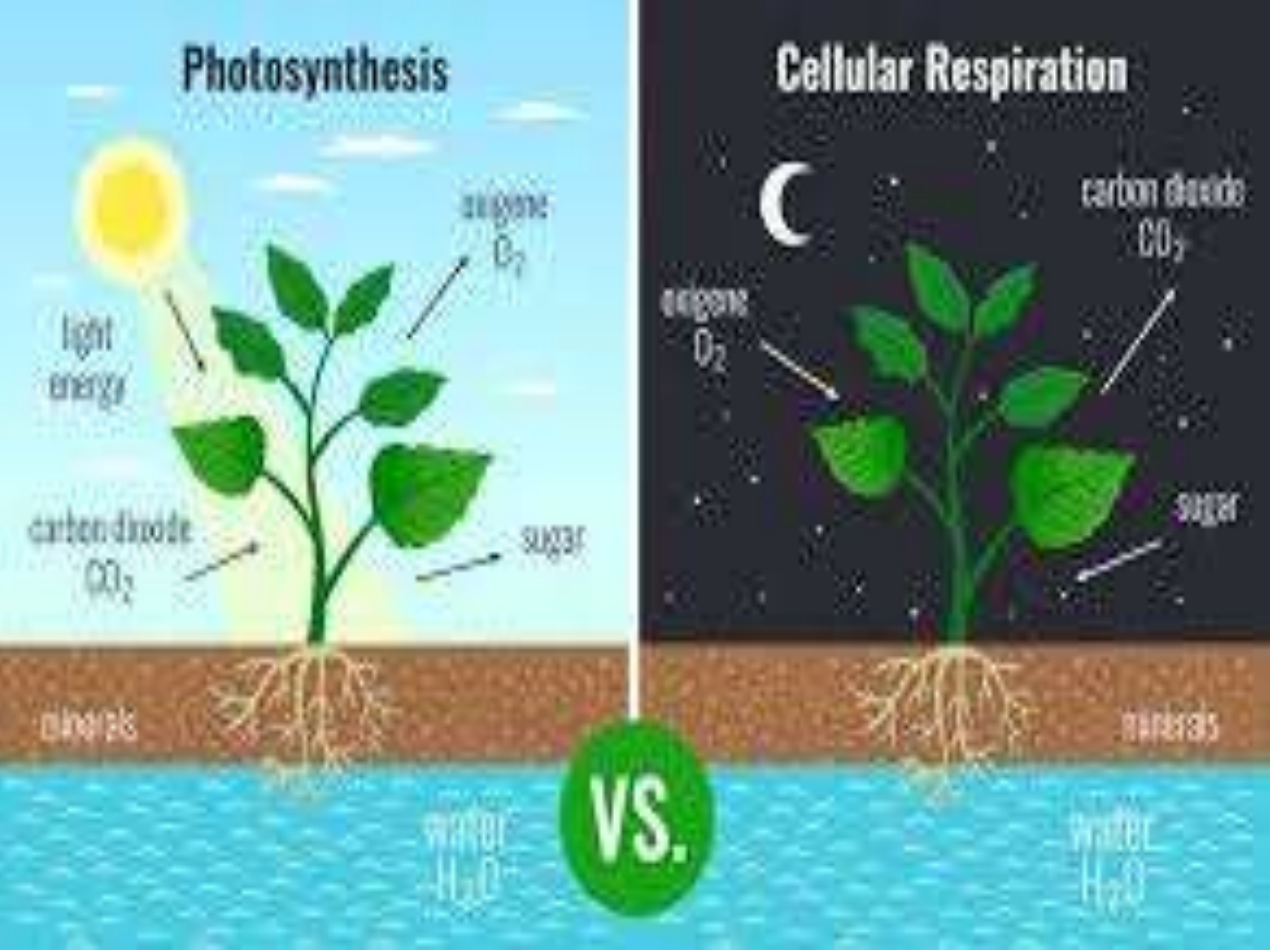
DEFINITION OF PHOTOSYNTHESIS

- Is the process by which autotrophic organisms use light energy to make sugar and oxygen gas from carbon dioxide and water.
- Occurs in plants, algae and some prokaryotes
- Anabolic (small molecules combined)
- Endergonic (stores energy)
- Stored as carbohydrate in their bodies.

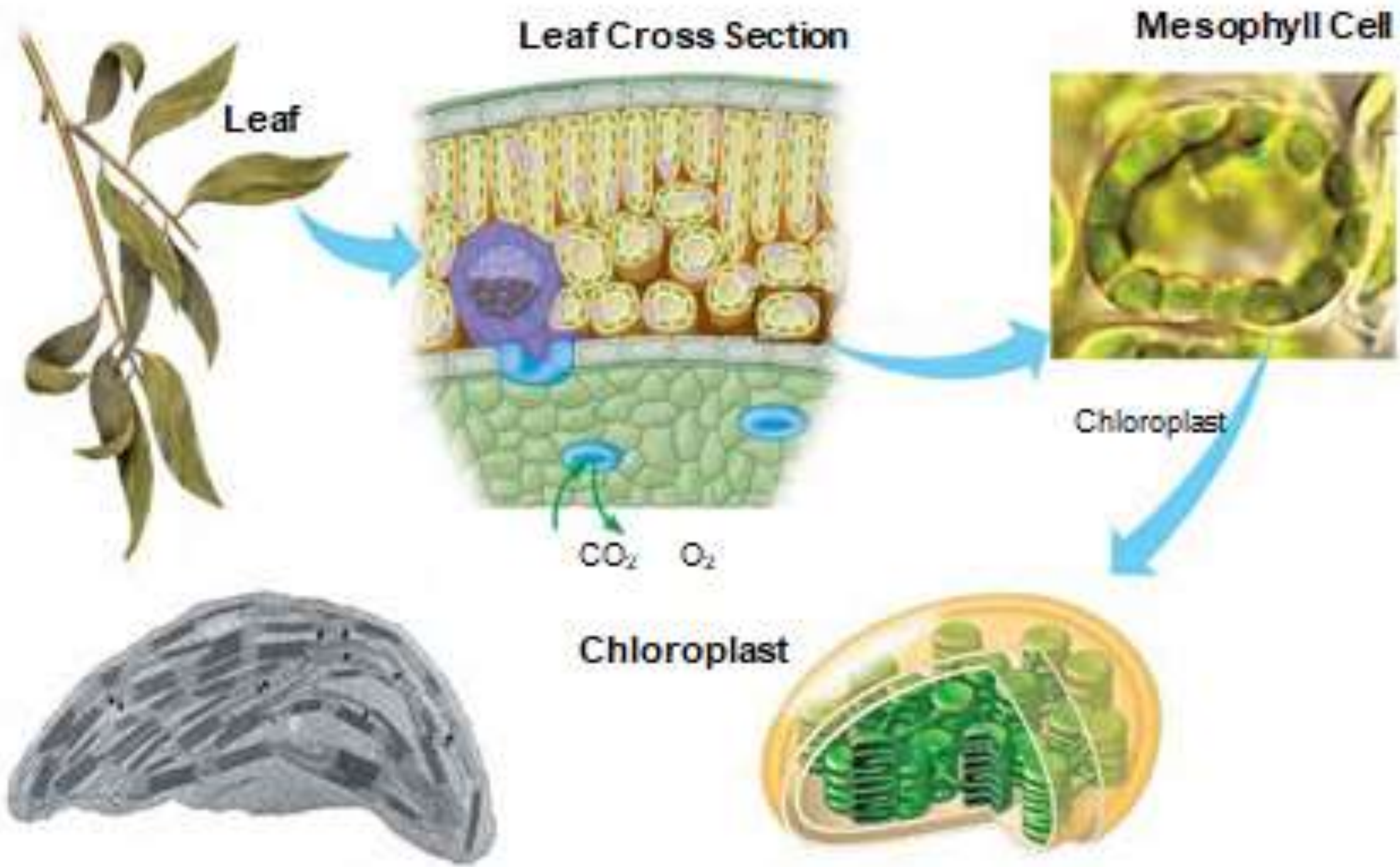


Process of Photosynthesis

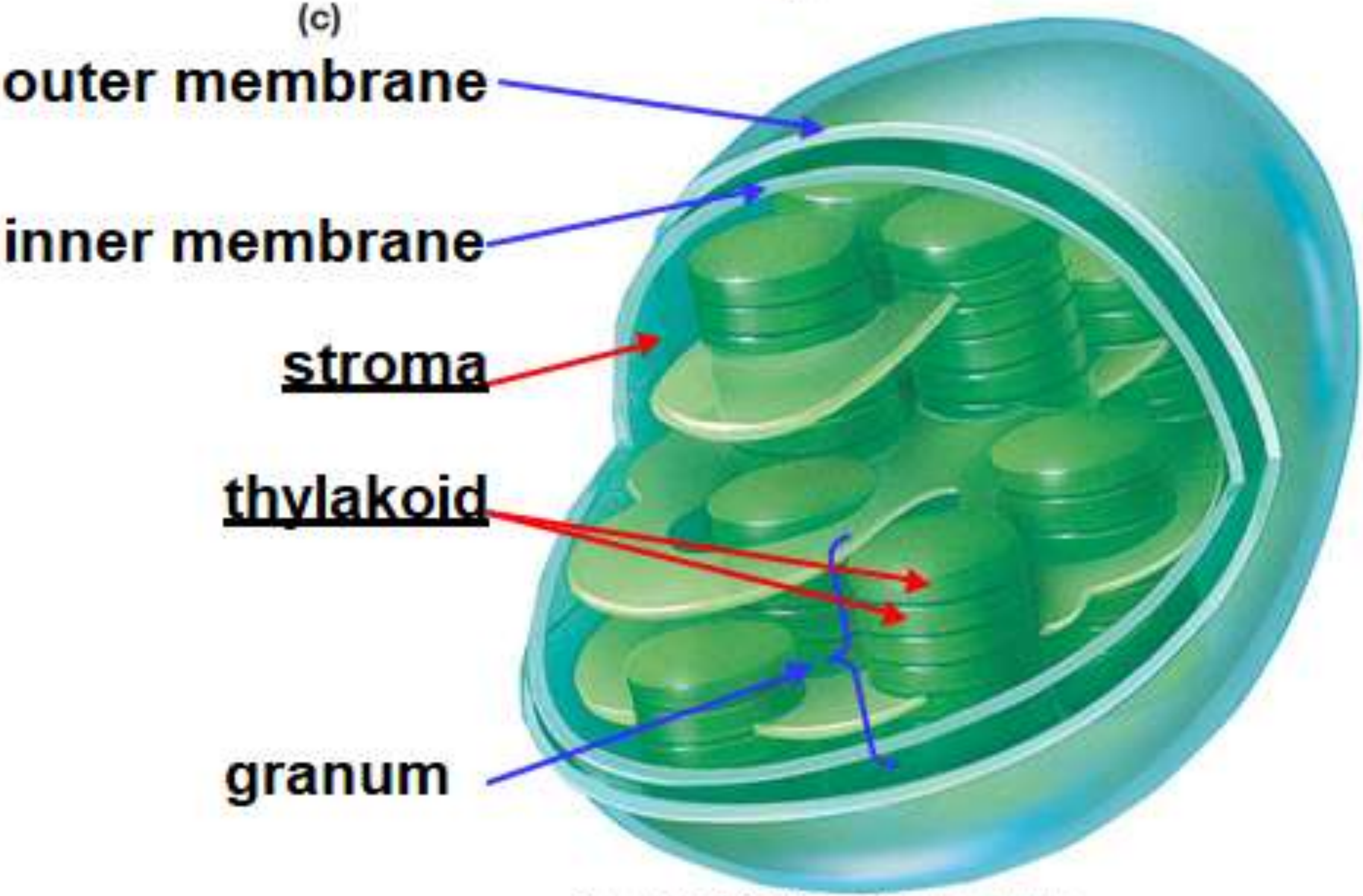



Photosynthesis
Cellular Respiration
light energy
O_2
carbon dioxide
CO_2
sugar
water
H_2O
VS.

Photosynthesis occurs in Chloroplasts



The Chloroplast



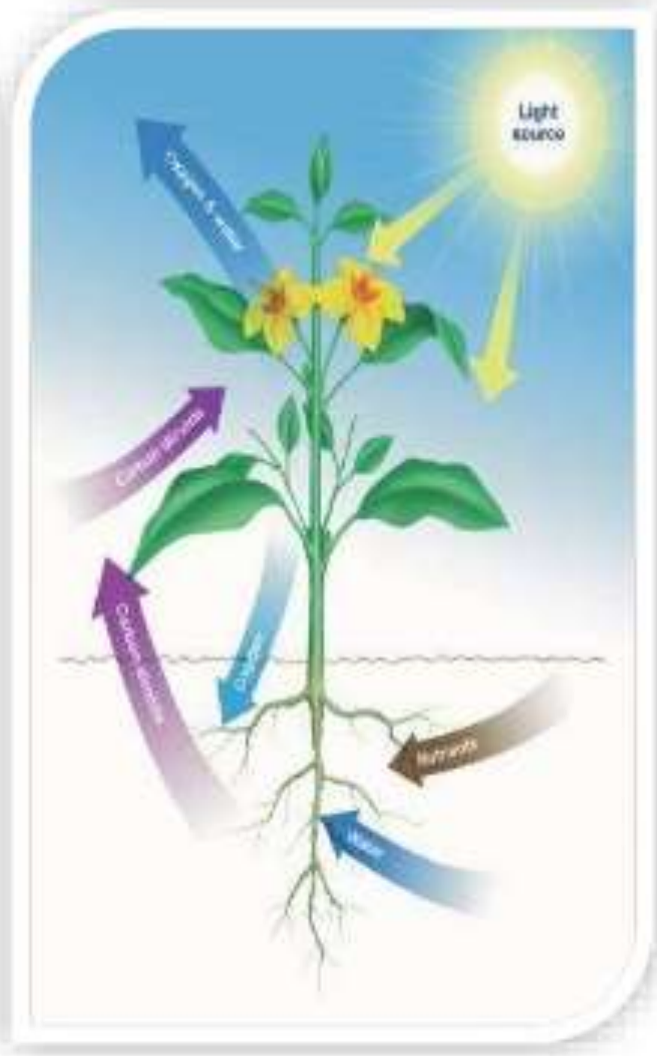
Why photosynthesis?

- Photosynthesis is critical for the existence of the vast majority of life on Earth.
- It is the way in which virtually all energy in the biosphere becomes available to living things.
- As primary producers, photosynthetic organisms form the base of Earth's food webs and are consumed directly or indirectly by all higher life-forms.
- Additionally, almost all the oxygen in the atmosphere is due to the process of photosynthesis.
- If photosynthesis ceased, there would soon be little food or other organic matter on Earth, most organisms would disappear, and Earth's atmosphere would eventually become nearly devoid of gaseous oxygen.

IMPORTANCE OF PHOTOSYNTHESIS

<u>Photosynthesis and Sun Energy:</u>

- Harnesses the sun's energy into utilizable forms of energy on earth.
- A process that most biological organisms are unable to perform.
- ATP is used to power these processes.
- Converts light energy into chemical energy in the form of glucose.
- Then the process of cellular respiration converts energy in glucose to energy in the form of ATP which is used to power biological processes.



IMPORTANCE OF PHOTOSYNTHESIS

Photosynthesis and Carbon Dioxide Removal:

- Converts carbon dioxide into oxygen.
- During photosynthesis, carbon dioxide leaves the atmosphere and enters the plant and leaves as oxygen.
- A process which is ecologically and environmentally important in nature.

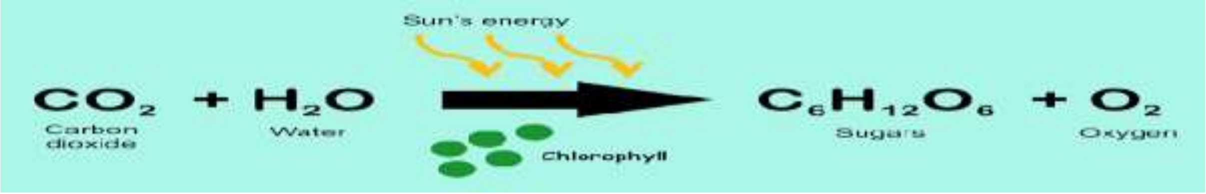
IMPORTANCE OF PHOTOSYNTHESIS

Photosynthesis and the Ecosystem:

- The energy produced by photosynthesis forms the basis of virtually all terrestrial and aquatic food chains.
- As a result, photosynthesis is the ultimate source of carbon in the organic molecules found in most organisms.
- The high oxygen concentration in the atmosphere is derived directly from the light reactions of photosynthesis.
- Prior to the evolution of photosynthesis on earth, the atmosphere was anoxic.

Overall reaction of photosynthesis

- In chemical terms, photosynthesis is a light-energized oxidation–reduction process.
- In plant photosynthesis, the energy of light is used to drive the oxidation of water (H_2O), producing oxygen gas (O_2), hydrogen ions (H^+), and electrons.
- Most of the removed electrons and hydrogen ions ultimately are transferred to carbon dioxide (CO_2), which is reduced to organic products. Other electrons and hydrogen ions are used to reduce nitrate and sulfate to amino and sulfhydryl groups in amino acids, which are the building blocks of proteins.
- In most green cells, carbohydrates—especially starch and the sugar sucrose—are the major direct organic products of photosynthesis. The overall reaction in which carbohydrates—represented by the general formula (CH_2O)—are formed during plant photosynthesis can be indicated by the following equation:



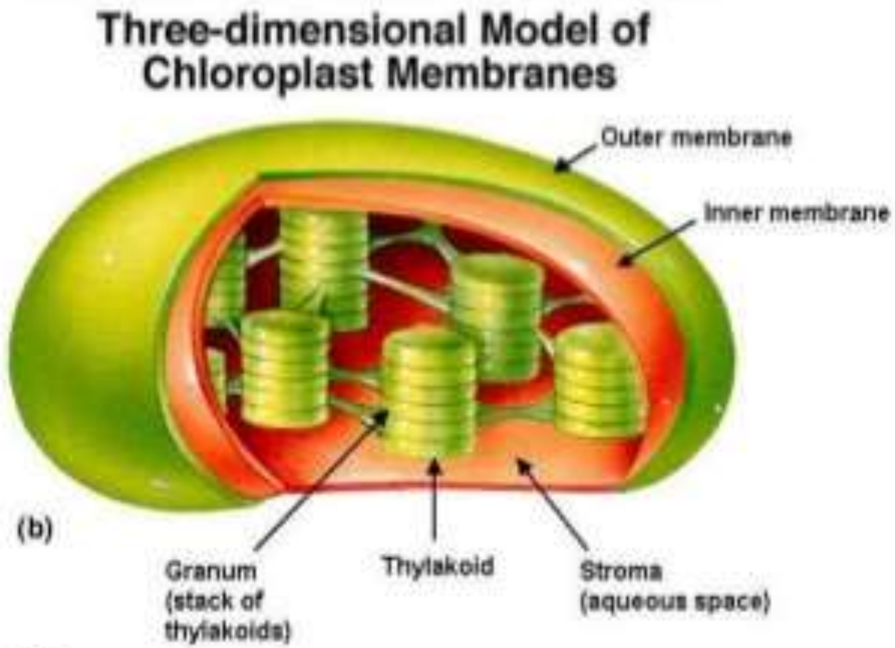
- This equation is merely a summary statement, for the process of photosynthesis actually involves numerous reactions catalyzed by enzymes (organic catalysts).
- These reactions occur in two stages: the “light” stage, consisting of photochemical (i.e., light-capturing) reactions; and the “dark” stage, comprising chemical reactions controlled by enzymes.
- During the first stage, the energy of light is absorbed and used to drive a series of electron transfers, resulting in the synthesis of ATP and the electron-donor-reduced nicotine adenine dinucleotide phosphate (NADPH).
- During the dark stage, the ATP and NADPH formed in the light-capturing reactions are used to reduce carbon dioxide to organic carbon compounds. This assimilation of inorganic carbon into organic compounds is called carbon fixation.

Sites of Photosynthesis

- Photosynthesis occurs in chloroplasts, organelles in certain plants
- All green plant parts have chloroplasts and carry out photosynthesis
- The leaves have the most chloroplasts
- The green colour comes from chlorophyll in the chloroplasts
- The pigments absorb light energy

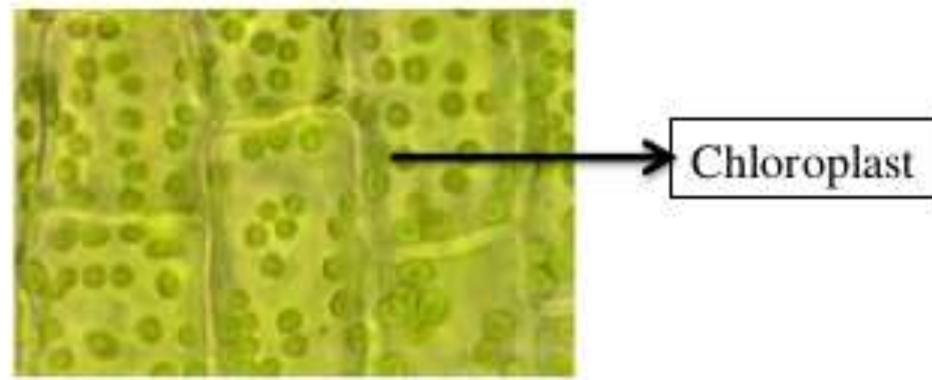
Sites of Photosynthesis

- A chloroplast contains:
  - stroma, a fluid
  - grana, stacks of thylakoids
- The thylakoids contain chlorophyll
  - Chlorophyll is the green pigment that captures light for photosynthesis

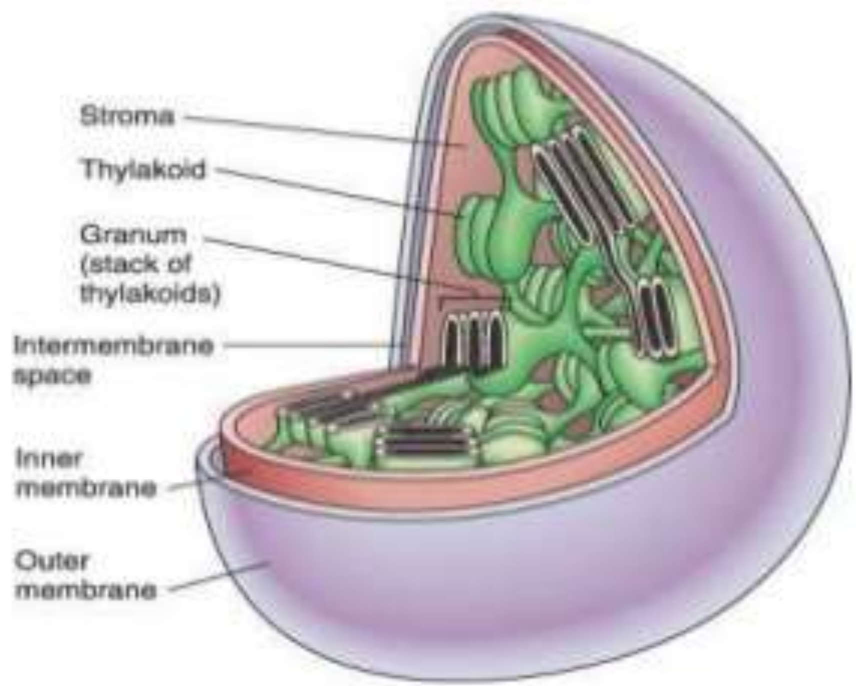


WHY ARE PLANTS GREEN?

- Plant cells have green chloroplast.



- The thylakoid membrane of the chloroplast is impregnated with photosynthetic pigments (chlorophylls, carotenoids).

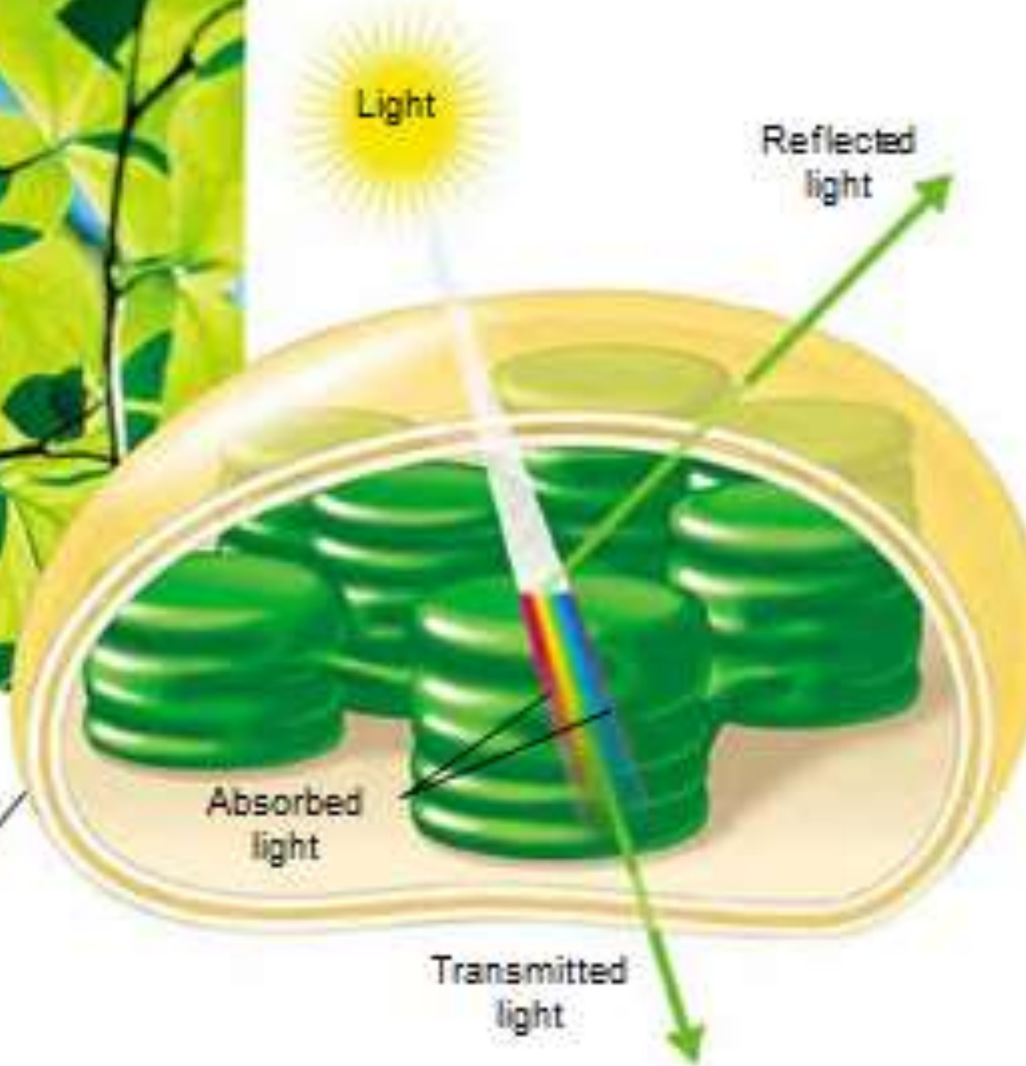


WHY ARE PLANTS GREEN?

- Chlorophyll is located in the thylakoid membranes.
- Chlorophyll have Mg+ in the centre.
- Chlorophyll pigments harvest energy (photons) by absorbing certain wavelengths

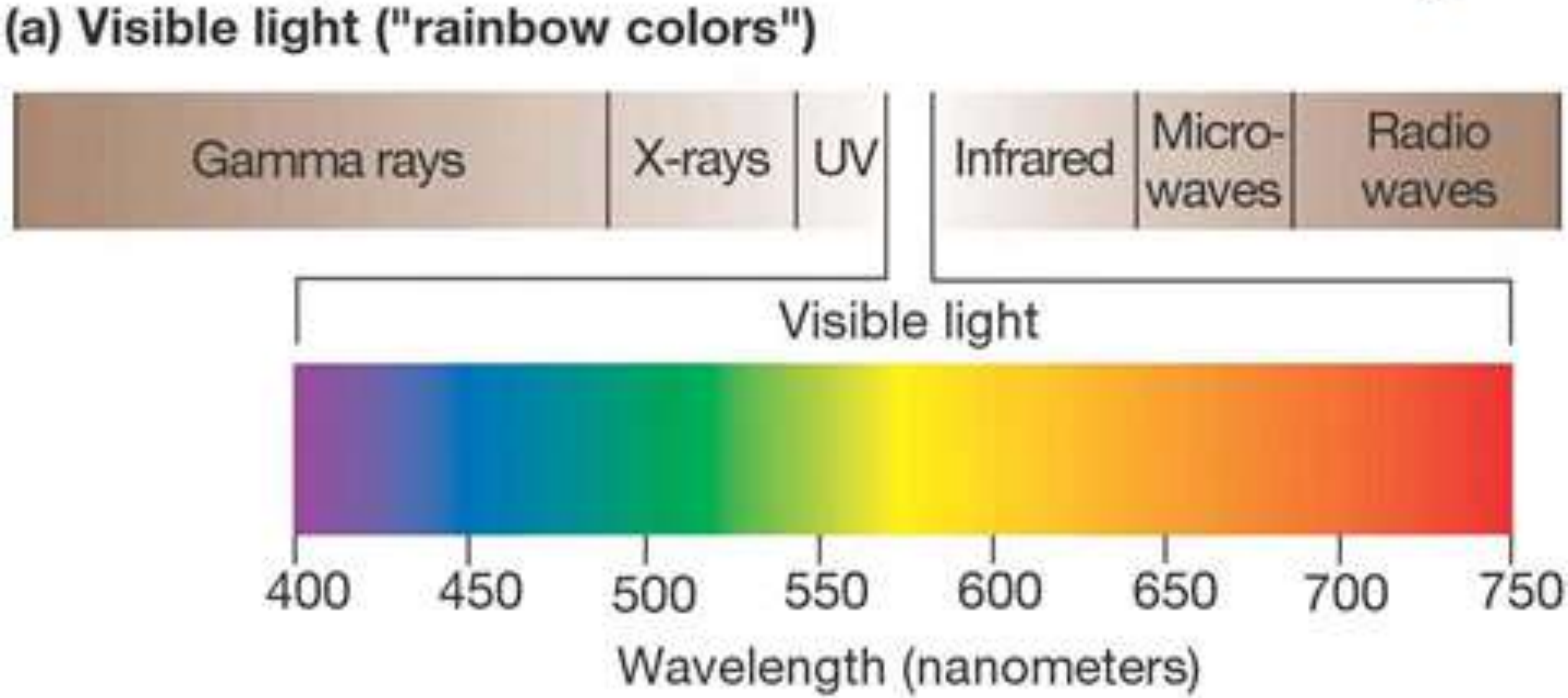
  (blue-420 nm and red-660 nm are most important).
- Plants are green because the green wavelength is reflected, not absorbed.

Chlorophyll absorbs "non-green" light energy



- green light passes on through or is reflected, causing the leaves to appear green

The Pigments absorb "Visible" Light



Chlorophyll a & b:

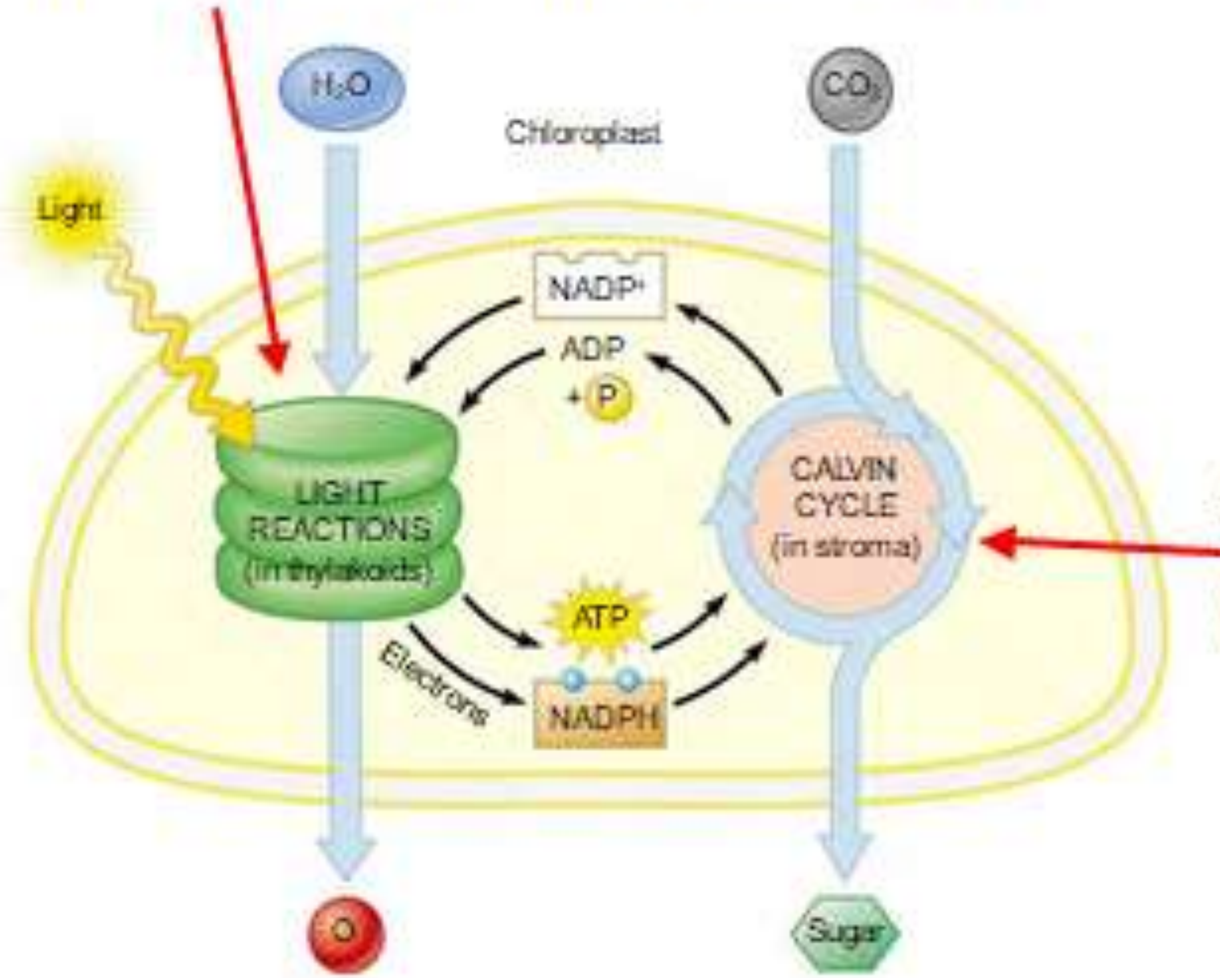
- the major pigments (<u>absorb</u> red, blue…, <u>reflect</u> green)

Carotenoids (e.g., β-carotene)

- accessory pigments (<u>absorb</u> green, blue, <u>reflect</u> red, yellow)

Photosynthesis consists of 2 sets of Reactions

The light-dependent or "Light" Reactions:

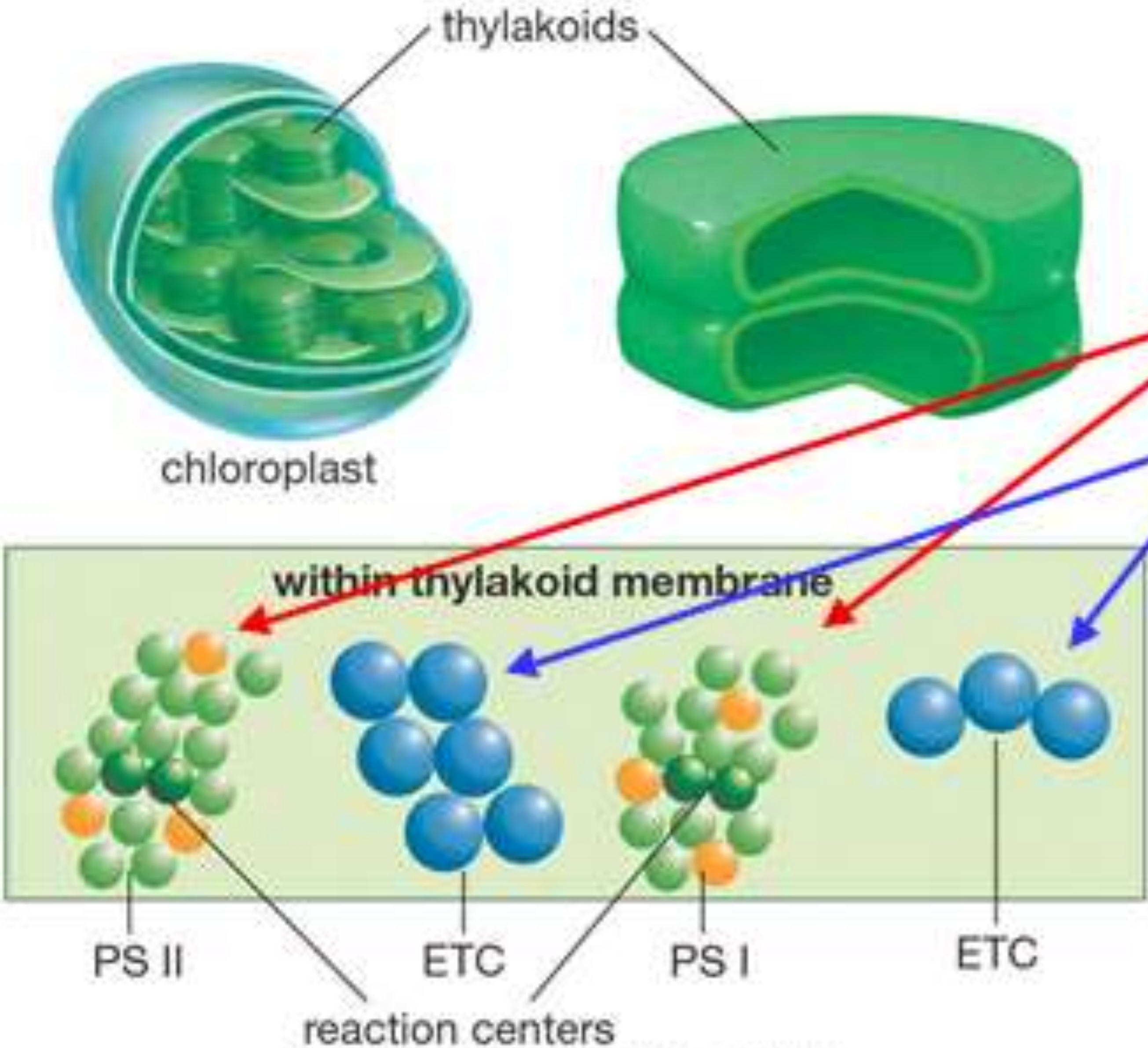


- convert sunlight energy into chemical energy (stored in ATP & NADPH)

"Dark" Reactions (Calvin cycle):

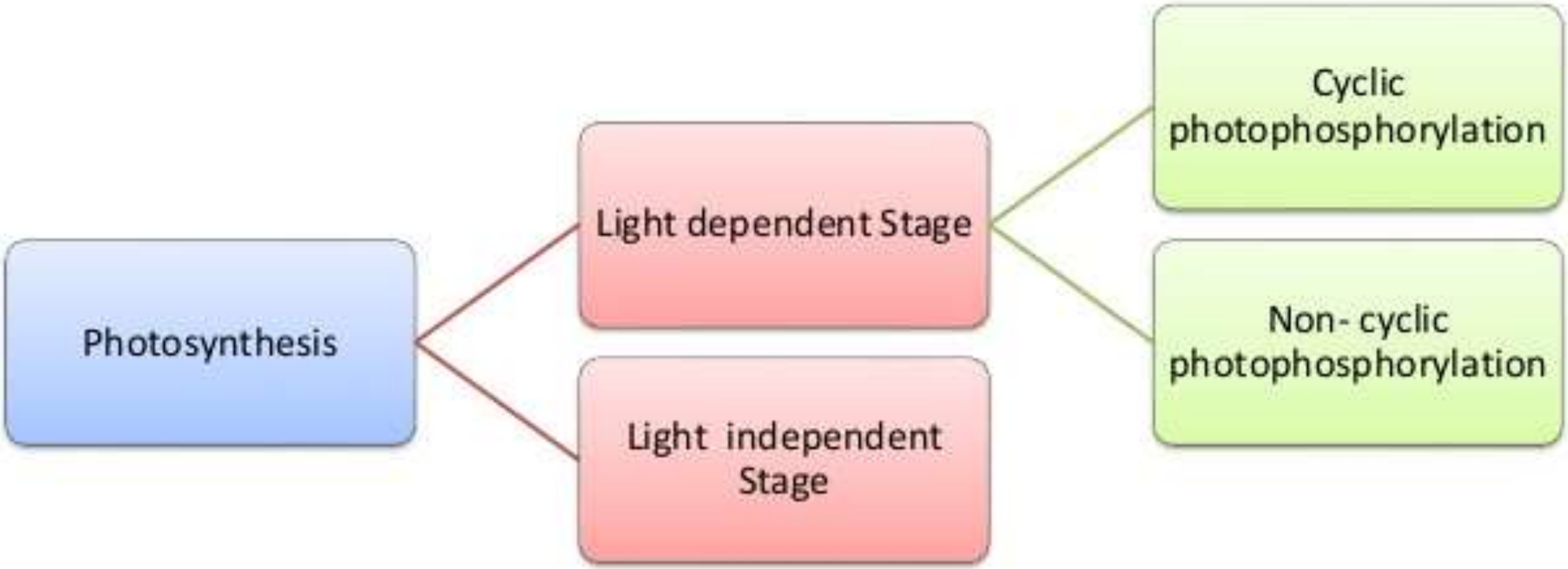
- use chemical energy from light reactions to make glucose

Light Reactions occur in Thylakoids



A variety of light-absorbing **pigments** & **electron transport proteins** are embedded within the thylakoid membrane

Photosynthesis



- Plants and other photosynthetic organisms are experts at collecting solar energy, thanks to the light-absorbing pigment molecules in their leaves.
- But what happens to the light energy that is absorbed? We don’t see plant leaves glowing like light bulbs, but we also know that energy can't just disappear (thanks to the First Law of Thermodynamics).
- As it turns out, some of the light energy absorbed by pigments in leaves is converted to a different form: chemical energy. Light energy is converted to chemical energy during the first stage of photosynthesis, which involves a series of chemical reactions known as the light-dependent reactions.

Light Energy absorbed by Pigments Fuels 4 General Steps of the “Light Reactions”:

1) H_2O split to O, 2 H^+ & 2 high energy e^- ($*e^-$) in PSII

$$H_2O \xrightarrow{\text{sunlight}} O_2 + H^+ + *e^-$$

2) Energy released by a series of $*e^-$ transfers is used to generate H^+ gradient
   - H^+ accumulates inside the thylakoid membrane

3) H^+ gradient used to make ATP (chemiosmosis)

4) $*e^-$ “re-energized” in PS I, passed on to $NADP^+$
   - $*e^-$ ends up in NADPH (an electron carrier)

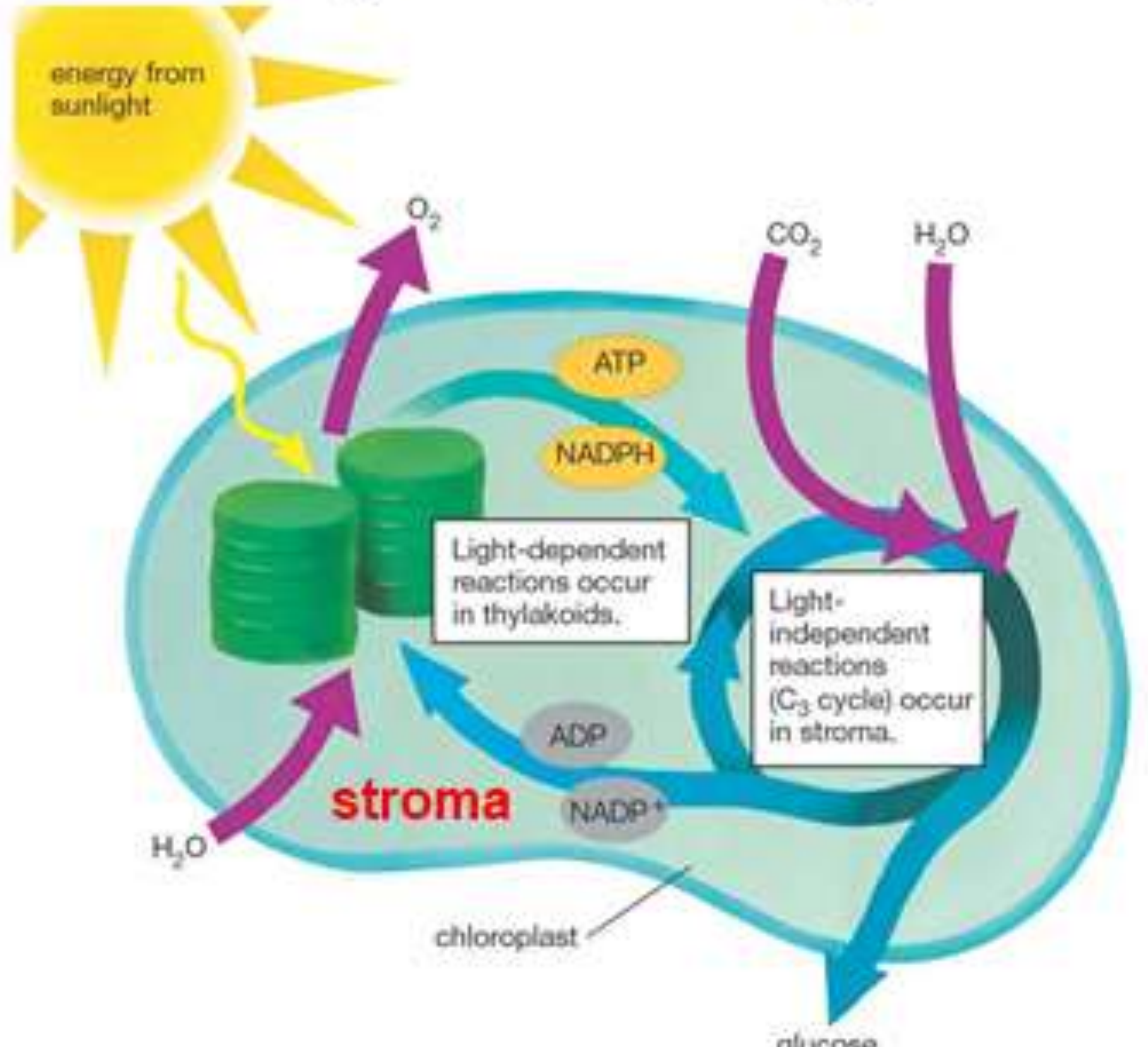
The "Dark" Reactions

A series of reactions called the Calvin cycle that synthesize glucose from CO_2 and H_2O:

$$CO_2 + H_2O \xrightarrow{\text{ATP, NADPH}} C_6H_{12}O_6 \text{ (glucose)}$$

- uses energy stored in ATP and NADPH
  - produced by the light reactions
- can occur in dark (doesn't require light directly)
  - also occurs during daylight!
- takes place in the stroma of chloroplasts
  - outside the thylakoids

Summary of Photosynthesis



What is a photosystem?

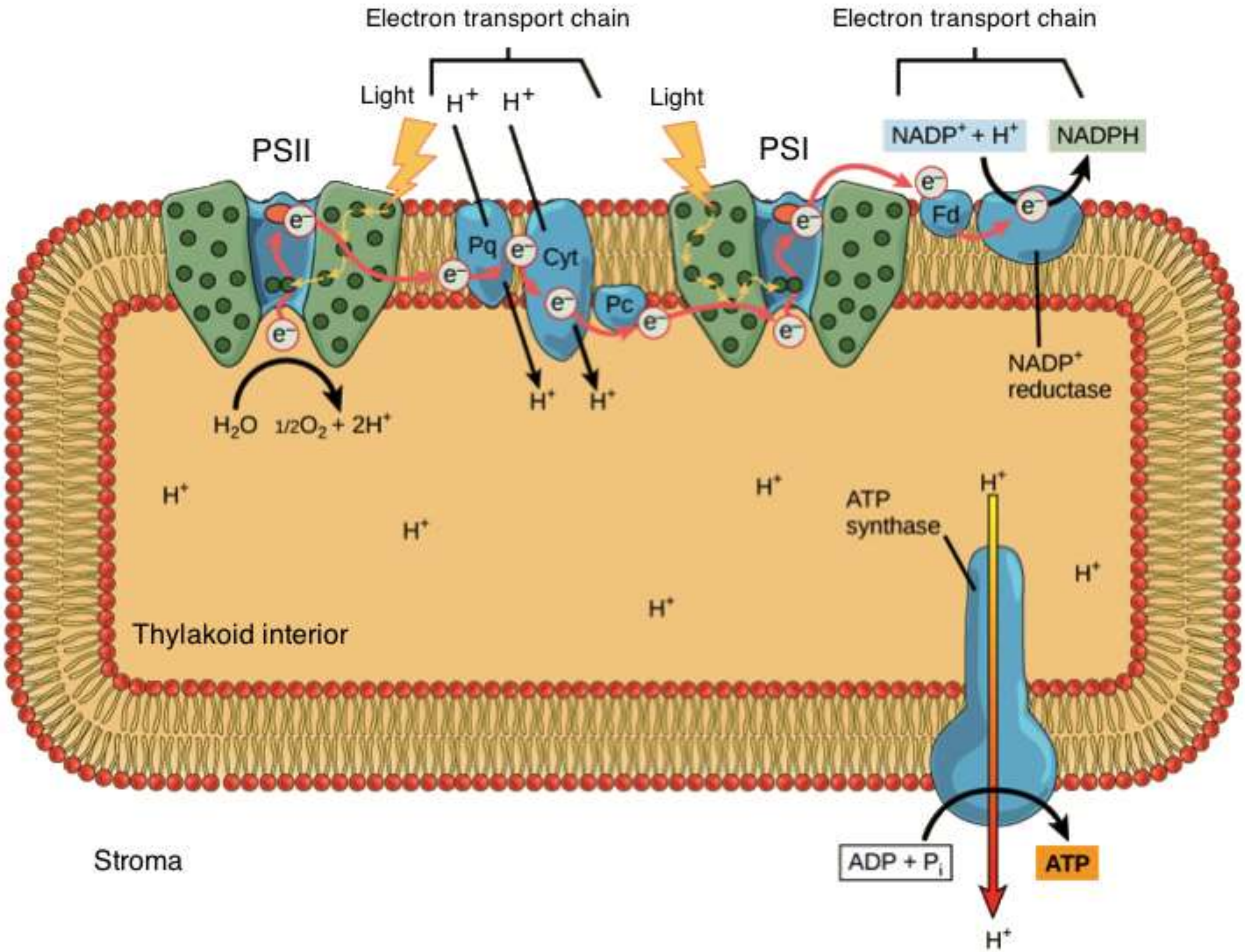
- Photosynthetic pigments, such as chlorophyll *a*, chlorophyll *b*, and carotenoids, are light-harvesting molecules found in the thylakoid membranes of chloroplasts. As mentioned above, pigments are organized along with proteins into complexes called **photosystems**.
- **Photosystems**, large complexes of proteins and pigments (light-absorbing molecules) that are optimized to harvest light, play a key role in the light reactions. There are two types of photosystems: photosystem I (PSI) and photosystem II (PSII).
- Both photosystems contain many pigments that help collect light energy, as well as a special pair of chlorophyll molecules found at the core (reaction center) of the photosystem. The special pair of **photosystem I** is called **P700**, while the special pair of **photosystem II** is called **P680**.

- There are two types of photosystems in the light-dependent reactions, **photosystem II (PSII)** and **photosystem I (PSI)**. PSII comes first in the path of electron flow, but it is named as second because it was discovered after PSI.

Photosystem II

When the P680 special pair of photosystem II absorbs energy, it enters an excited (high-energy) state. Excited P680 is a good electron donor and can transfer its excited electron to the primary electron acceptor, pheophytin. The electron will be passed on through the first leg of the photosynthetic **electron transport chain** in a series of redox, or electron transfer, reactions.

- After the special pair gives up its electron, it has a positive charge and needs a new electron. This electron is provided through the splitting of water molecules, a process carried out by a portion of PSII called the manganese center. The positively charged P680 can pull electrons off of water (which doesn't give them up easily) because it's extremely "electron-hungry."
- When the manganese center splits water molecules, it binds two at once, extracting four electrons, releasing four H+, and producing a molecule of O2. About 10 percent of the oxygen is used by mitochondria in the leaf to support oxidative phosphorylation. The remainder escapes to the atmosphere where it is used by aerobic organisms to support respiration.

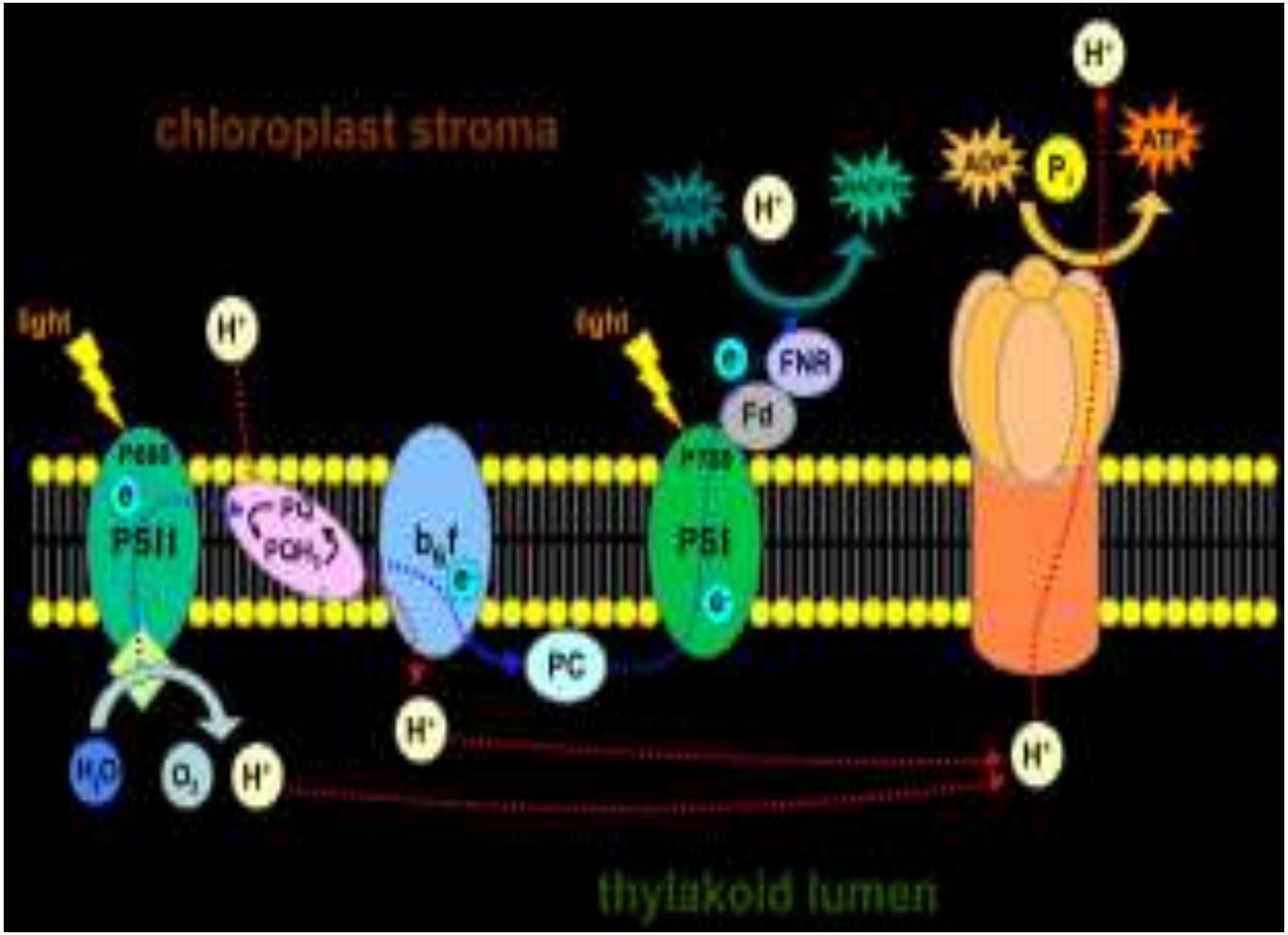


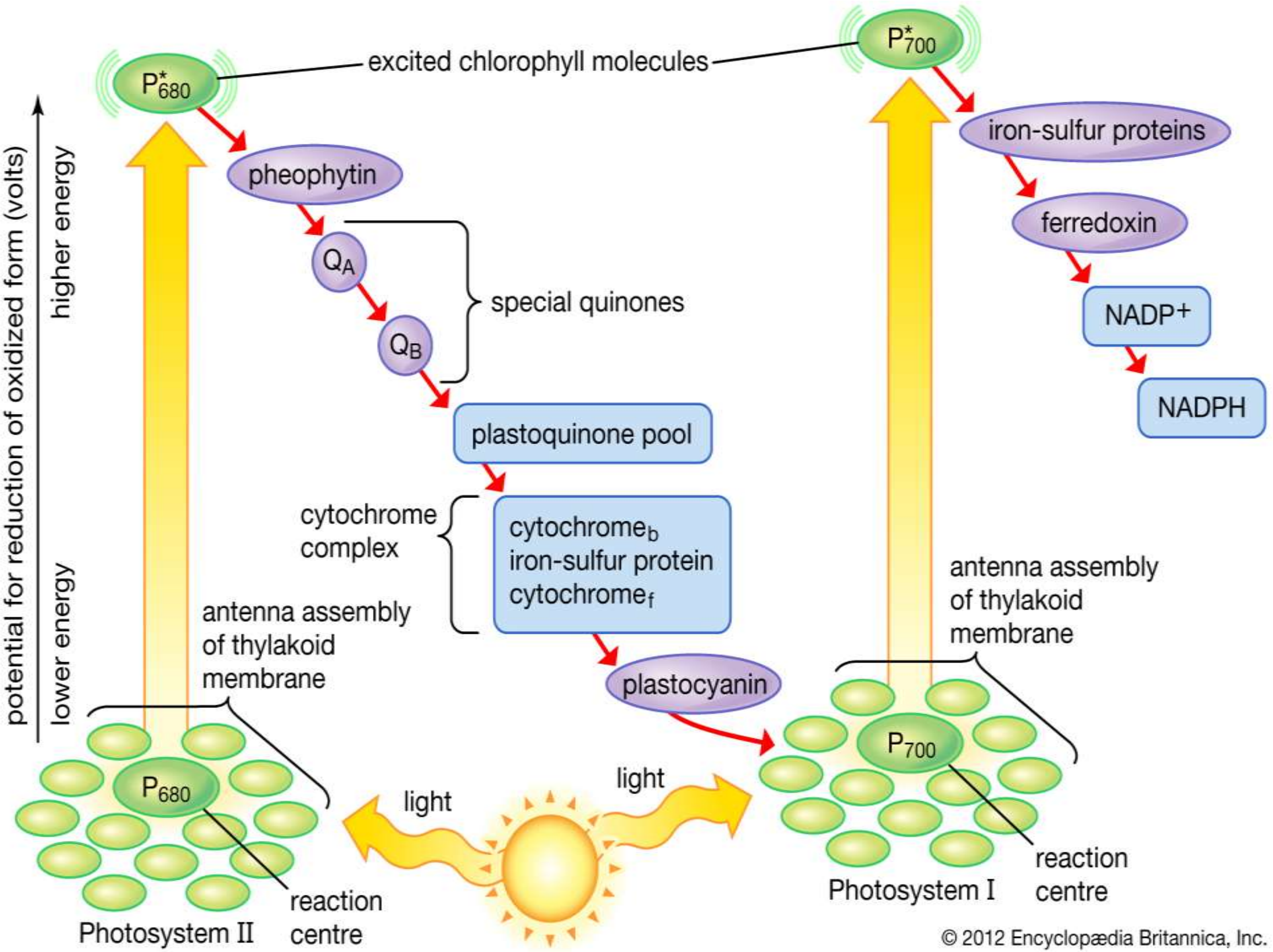
Electron transport chain
Electron transport chain
Light
H+
H+
Light
PSII
PSI
NADP+ + H+
NADPH
e−
Pq
Cyt
Pc
Fd
H+
H+
H2O
1/2O2 + 2H+
NADP+
reductase
H+
H+
H+
H+
H+
ATP
synthase
H+
Thylakoid interior
Stroma
ADP + Pi
ATP
H+

Electron transport chains and photosystem I

- When an electron leaves PSII, it is transferred first to a small organic molecule (plastoquinone, Pq), then to a cytochrome complex (Cyt), and finally to a copper-containing protein called plastocyanin (Pc). As the electron moves through this electron transport chain, it goes from a higher to a lower energy level, releasing energy. Some of the energy is used to pump protons from the stroma (outside of the thylakoid) into the thylakoid interior.
- This transfer of H+, along with the release of H+ from the splitting of water, forms a proton gradient that will be used to make ATP (as we'll see shortly).

- Once an electron has gone down the first leg of the electron transport chain, it arrives at PSI, where it joins the chlorophyll *a* special pair called P700. Because electrons have lost energy prior to their arrival at PSI, they must be re-energized through absorption of another photon.
- Excited P700 is a very good electron donor, and it sends its electron down a short electron transport chain. In this series of reactions, the electron is first passed to a protein called ferredoxin (Fd), then transferred to an enzyme called NADP+ reductase. NADP+ reductase transfers electrons to the electron carrier NADP+ to make NADPH. NADPH will travel to the Calvin cycle, where its electrons are used to build sugars from carbon dioxide.


chloroplast stroma
light
H+
P680
e
PSII
PQ
PQH2
b6f
e
PC
light
P700
PSI
e
Fd
FNR
ADP
Pi
ATP
H2O
O2
thylakoid lumen



excited chlorophyll molecules
P^*_{680}
P^*_{700}
potential for reduction of oxidized form (volts)
higher energy
lower energy
pheophytin
Q_A
Q_B
special quinones
plastoquinone pool
cytochrome complex
$cytochrome_b$
iron-sulfur protein
$cytochrome_f$
plastocyanin
iron-sulfur proteins
ferredoxin
$NADP^+$
NADPH
antenna assembly of thylakoid membrane
antenna assembly of thylakoid membrane
P_{680}
P_{700}
light
light
reaction centre
reaction centre
Photosystem II
Photosystem I

- The other ingredient needed by the Calvin cycle is ATP, and this too is provided by the light reactions. As we saw above, H+ ions build inside the thylakoid interior and make a concentration gradient. Protons "want" to diffuse back down the gradient and into the stroma, and their only route of passage is through the enzyme **ATP synthase**.
- ATP synthase harnesses the flow of protons to make ATP from ADP and phosphate (Pi). This process of making ATP using energy stored in a chemical gradient is called **chemiosmosis**.

Some electrons flow cyclically

- The pathway above is sometimes called **linear photophosphorylation**. That's because electrons travel in a line from water through PSII and PSI to NADPH. (*Photophosphorylation* = light-driven synthesis of ATP.)
- In some cases, electrons break this pattern and instead loop back to the first part of the electron transport chain, repeatedly cycling through PSI instead of ending up in NADPH. This is called **cyclic photophosphorylation**.
- After leaving PSI, cyclically flowing electrons travel back to the cytochrome complex (Cyt) or plastoquinone (Pq) in the first leg of the electron transport chain. The electrons then flow down the chain to PSI as usual, driving proton pumping and the production of ATP. The cyclic pathway does not make NADPH, since electrons are routed away from NADP+ reductase.

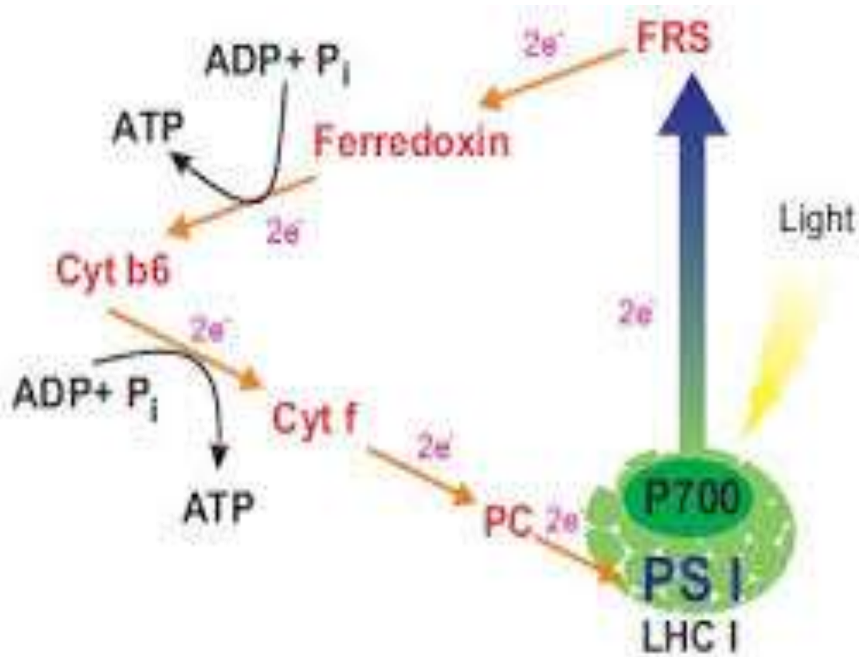
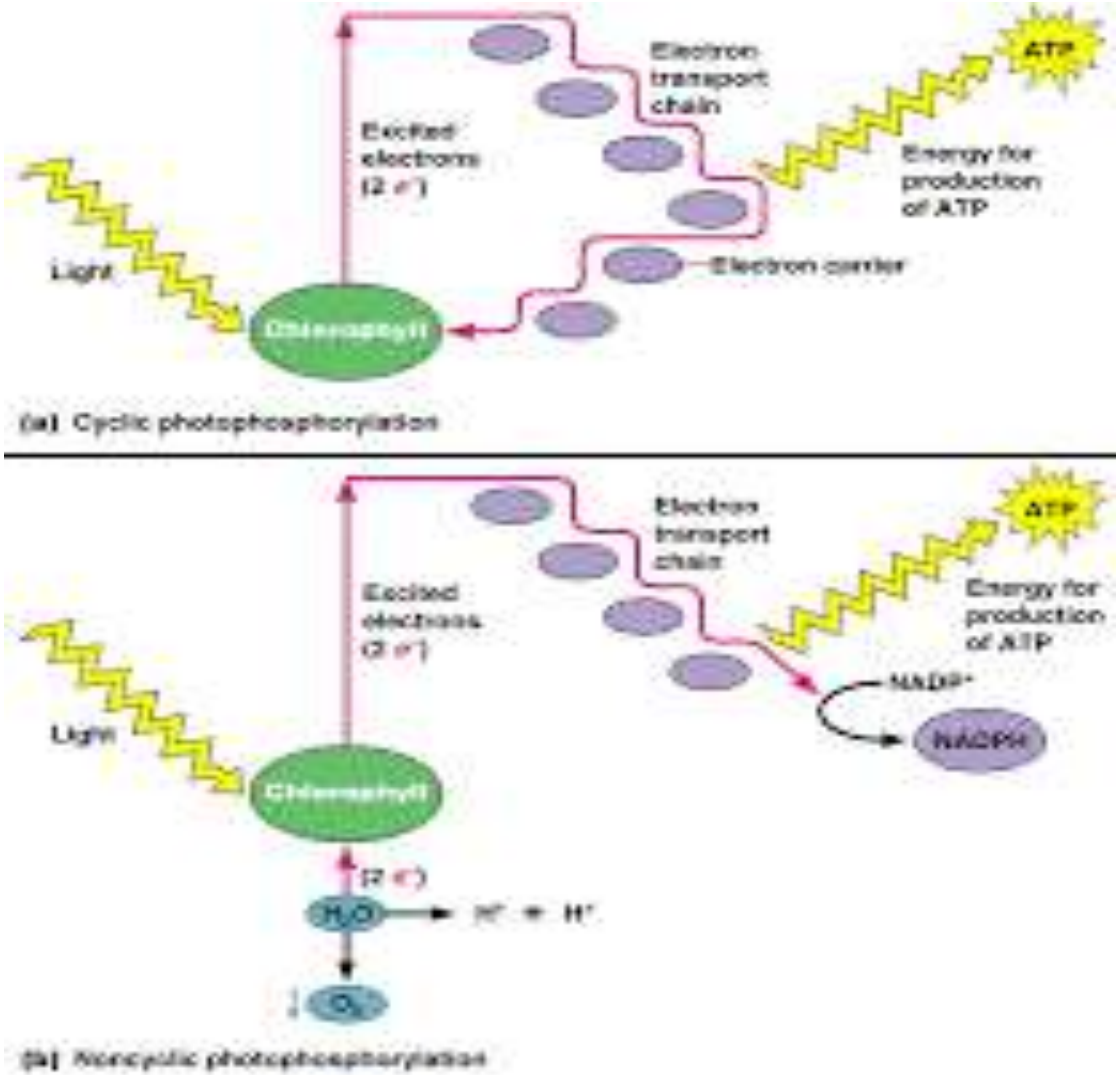


Figure 13.15: Cyclic Photophosphorylation

- Why does the cyclic pathway exist? At least in some cases, chloroplasts seem to switch from linear to cyclic electron flow when the ratio of NADPH to $NADP^+$ is too high (when too little $NADP^+$ is available to accept electrons).
- In addition, cyclic electron flow may be common in photosynthetic cell types with especially high ATP needs (such as the sugar-synthesizing bundle-sheath cells of plants that carry out photosynthesis).
- Finally, cyclic electron flow may play a photoprotective role, preventing excess light from damaging photosystem proteins and promoting repair of light-induced damage

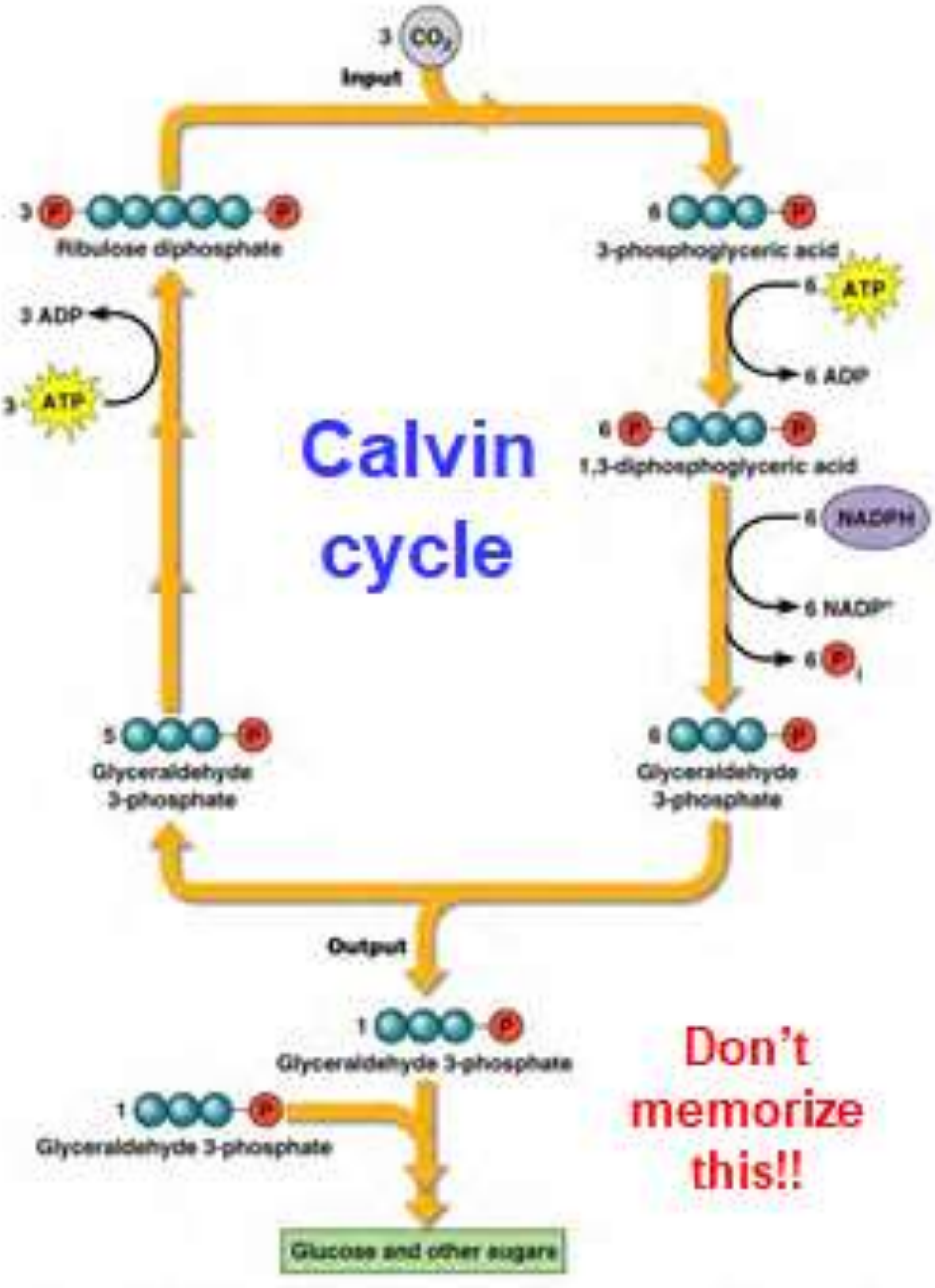

Electron transport chain
ATP
Excited electrons (2 e⁻)
Energy for production of ATP
Light
Electron carrier
Chlorophyll
(a) Cyclic photophosphorylation
Electron transport chain
ATP
Excited electrons (2 e⁻)
Energy for production of ATP
NADP⁺
NADPH
Light
Chlorophyll
(2 e⁻)
H₂O
H⁺ + H⁺
O₂
(b) Noncyclic photophosphorylation

Calvin cycle/C3 cycle

- The Calvin cycle is the cycle of chemical reactions performed by plants to "fix" carbon from CO_2 into three-carbon sugars.
- Later, plants and animals can turn these three-carbon compounds into amino acids, nucleotides, and more complex sugars such as starches.
- This process of "carbon fixation" is how most new organic matter is created. The sugars created in the Calvin cycle are also used by plants for long-term energy storage, unlike ATP which is used up quickly after it is created.
- These plant sugars can also become a source of energy for animals who eat the plants, and predators who eat those herbivores.
- The Calvin cycle is also sometimes referred to as the "light independent" reactions of photosynthesis, since it is not powered directly by photons from the Sun. Instead, the Calvin cycle is powered by ATP and NADPH, which are created by harnessing the energy from photons in the light-dependent reactions.

- **light-independent reaction**: chemical reactions during photosynthesis that convert carbon dioxide and other compounds into glucose, taking place in the stroma
- **Rubisco**: (Ribulose bisphosphate carboxylase) a plant enzyme which catalyzes the fixing of atmospheric carbon dioxide during photosynthesis by catalyzing the reaction between carbon dioxide and RuBP
- **Ribulose bisphosphate**: an organic substance that is involved in photosynthesis, reacts with carbon dioxide to form 3-PGA

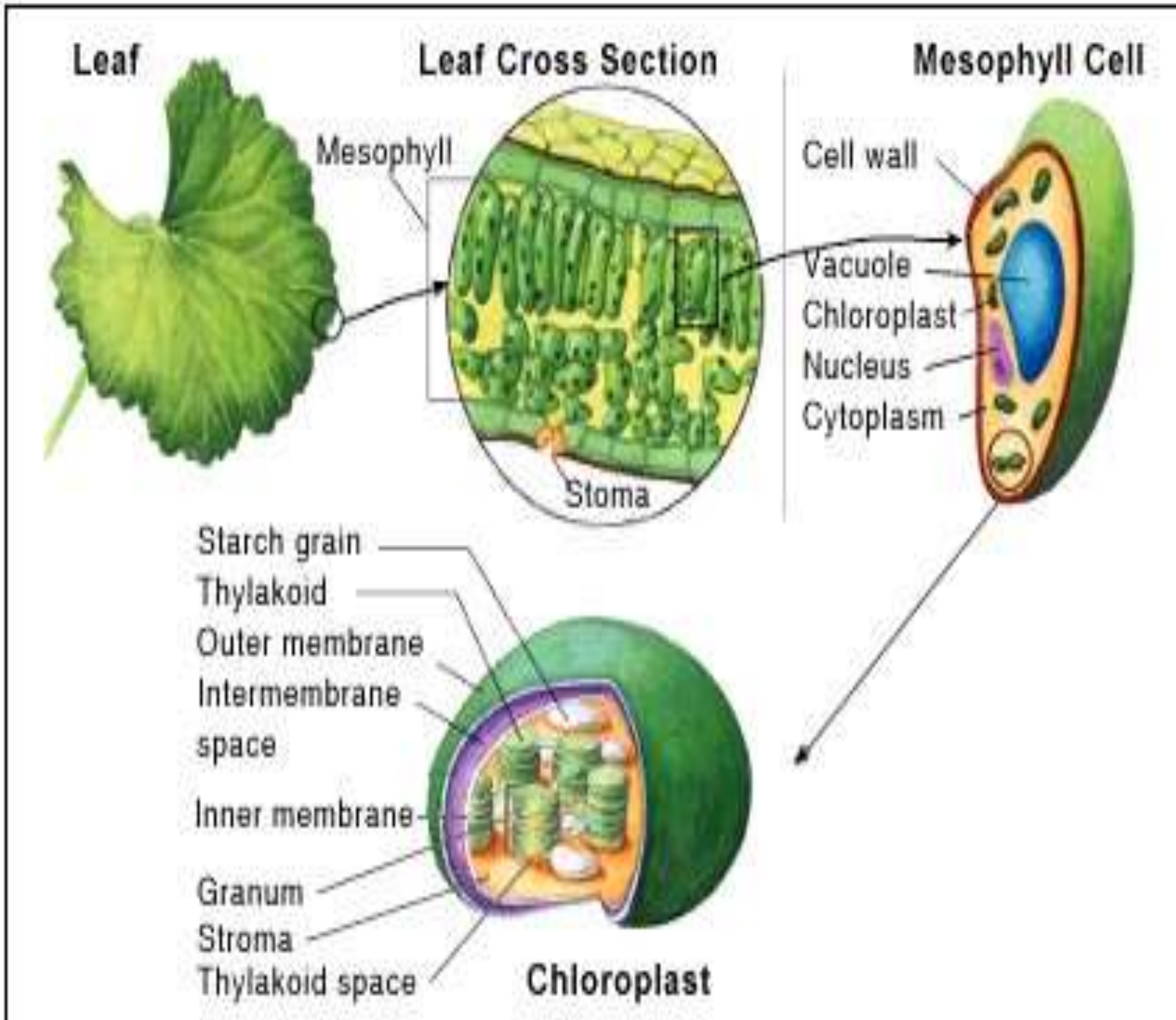
"Dark" Reactions



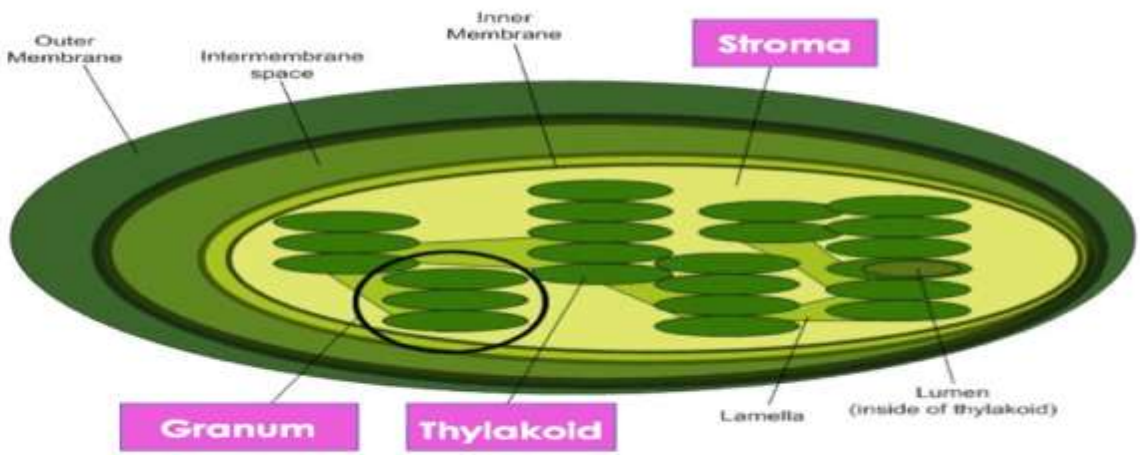
Involves an anabolic pathway known as the Calvin cycle:

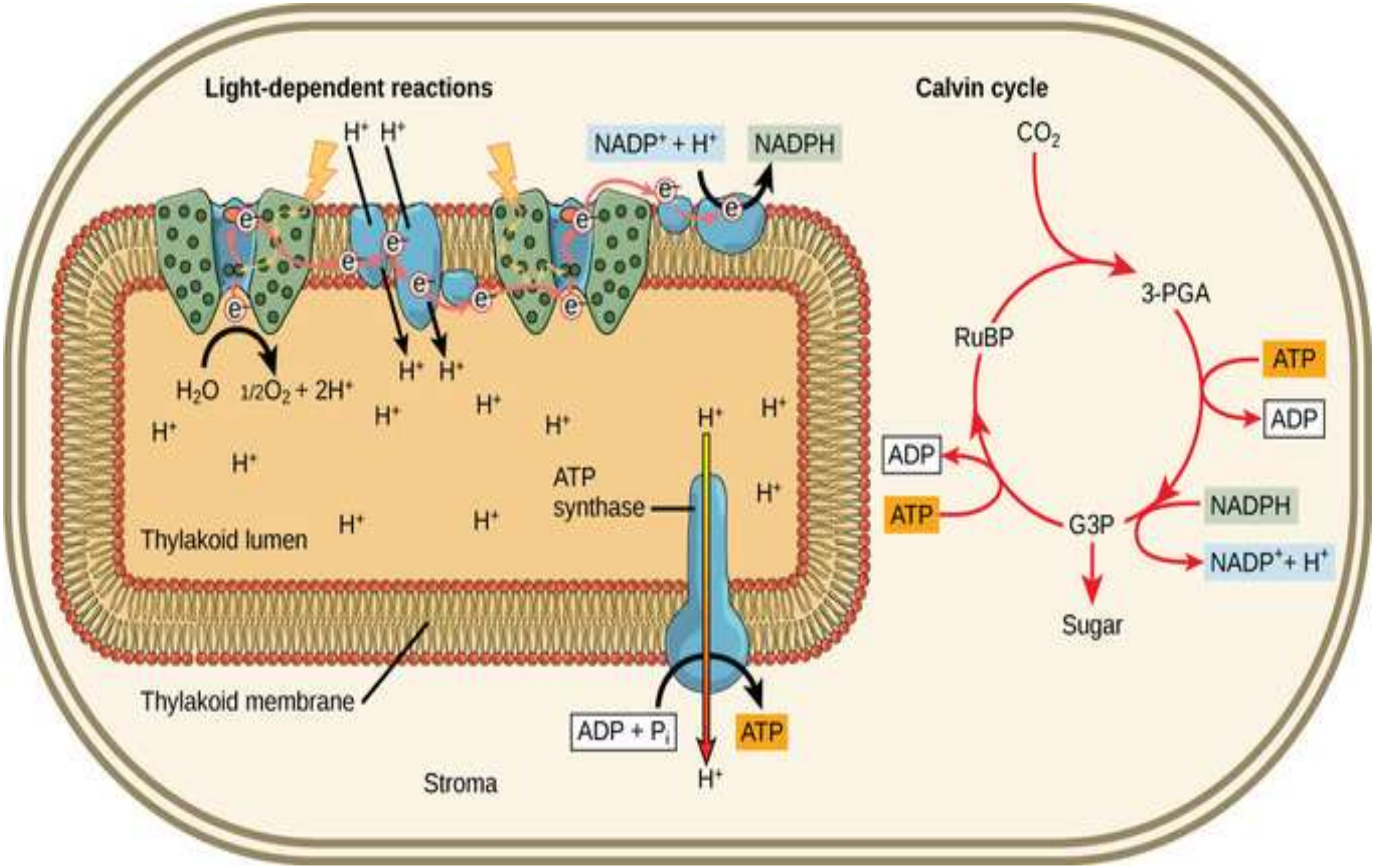
- endergonic reactions of this pathway are fueled by ATP & NADPH from the "light" reactions
- resulting sugars can be used as a source of energy or to build other organic molecules

- **The Calvin Cycle**
- In plants, carbon dioxide (CO_2) enters the leaves through stomata, where it diffuses over short distances through intercellular spaces until it reaches the mesophyll cells.
- Once in the mesophyll cells, CO_2 diffuses into the stroma of the chloroplast, the site of light-independent reactions of photosynthesis.
- These reactions actually have several names associated with them. Other names for light-independent reactions include the Calvin cycle, the Calvin-Benson cycle, and dark reactions.
- The most outdated name is dark reactions, which can be misleading because it implies incorrectly that the reaction only occurs at night or is independent of light, which is why most scientists and instructors no longer use it.


Leaf
Leaf Cross Section
Mesophyll Cell
Mesophyll
Stoma
Cell wall
Vacuole
Chloroplast
Nucleus
Cytoplasm
Starch grain
Thylakoid
Outer membrane
Intermembrane
space
Inner membrane
Granum
Stroma
Thylakoid space
Chloroplast

- The dark reaction occurs in the stroma of the chloroplast
- In the light-independent reactions, the plant uses carbon dioxide (CO2) and the ATP and NADPH from the light-dependent reactions to produce a sugar called **glucose**.
- Glucose (C6H12O6) can then be converted by the plant into other molecules that the cell needs. It can also be used in cellular respiration.





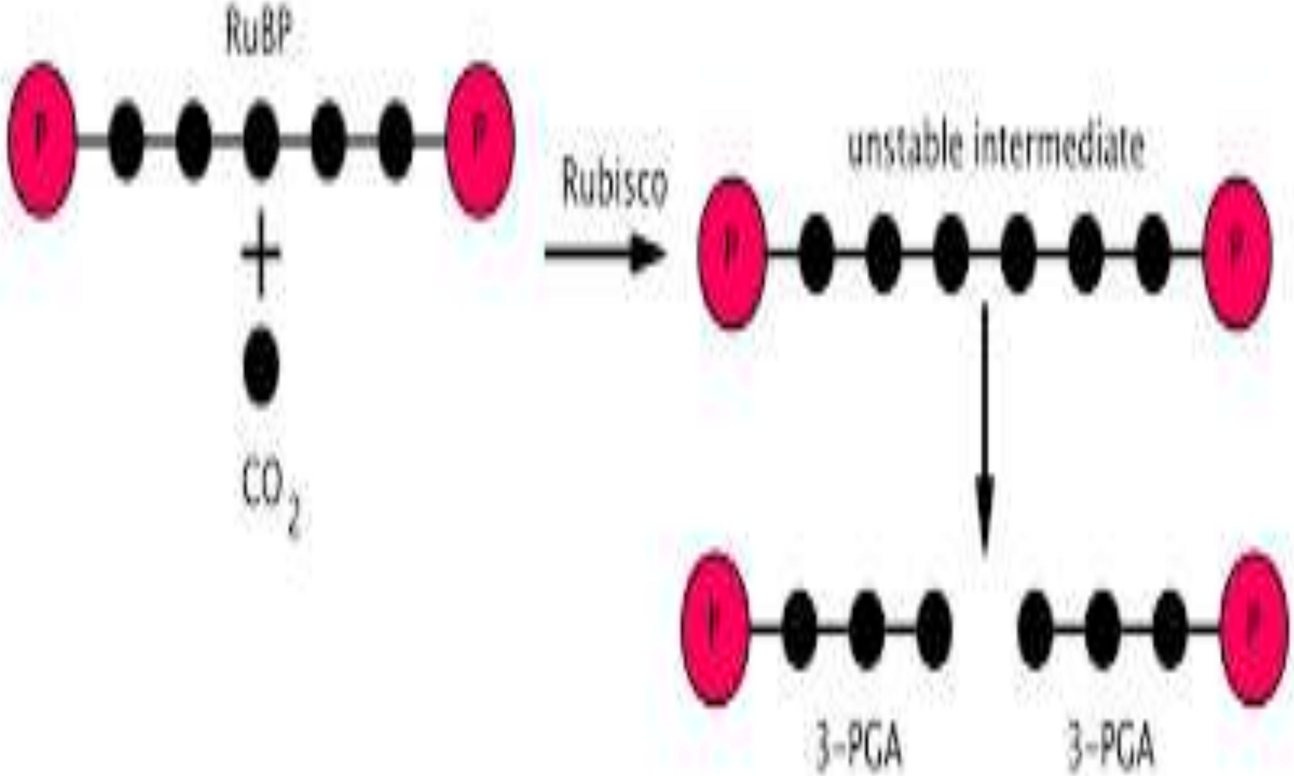
Light-dependent reactions
Calvin cycle
H⁺ H⁺
NADP⁺ + H⁺
NADPH
CO2
3-PGA
RuBP
ATP
ADP
ADP
ATP
G3P
NADPH
NADP⁺+ H⁺
Sugar
H2O
1/2O2 + 2H⁺
H⁺ H⁺
ATP synthase
Thylakoid lumen
Thylakoid membrane
ADP + Pi
ATP
Stroma

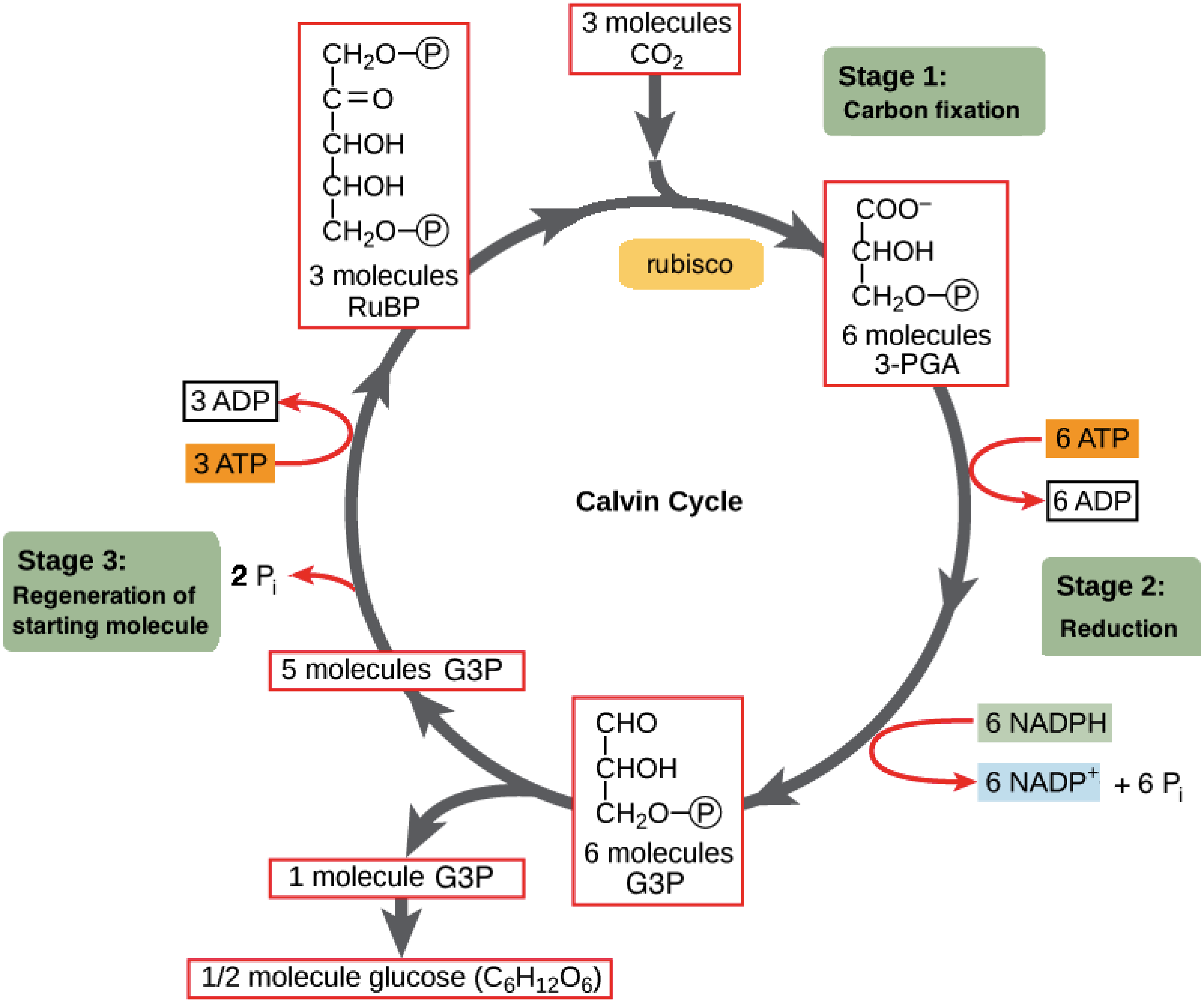
The light-independent reactions of the Calvin cycle can be organized into three basic stages:

- Fixation,
- Reduction, and
- Regeneration.

Stage 1: Fixation

- In the stroma, in addition to CO_2, two other components are present to initiate the light-independent reactions: an enzyme called Ribulose Bisphosphate Carboxylase (RuBisCO) and three molecules of Ribulose 1,5-bisphosphate (RuBP).
- RuBP has five atoms of carbon, flanked by two phosphates. RuBisCO catalyzes a reaction between CO_2 and RuBP. For each CO_2 molecule that reacts with one RuBP, two molecules of 3-phosphoglyceric acid (3-PGA) form. 3-PGA has three carbons and one phosphate.
- Each turn of the cycle involves only one RuBP and one carbon dioxide and forms two molecules of 3-PGA. The number of carbon atoms remains the same, as the atoms move to form new bonds during the reactions (3 atoms from $3CO_2$ + 15 atoms from 3RuBP = 18 atoms in 3 atoms of 3-PGA).
- This process is called carbon fixation because CO_2 is “fixed” from an inorganic form into organic molecules.

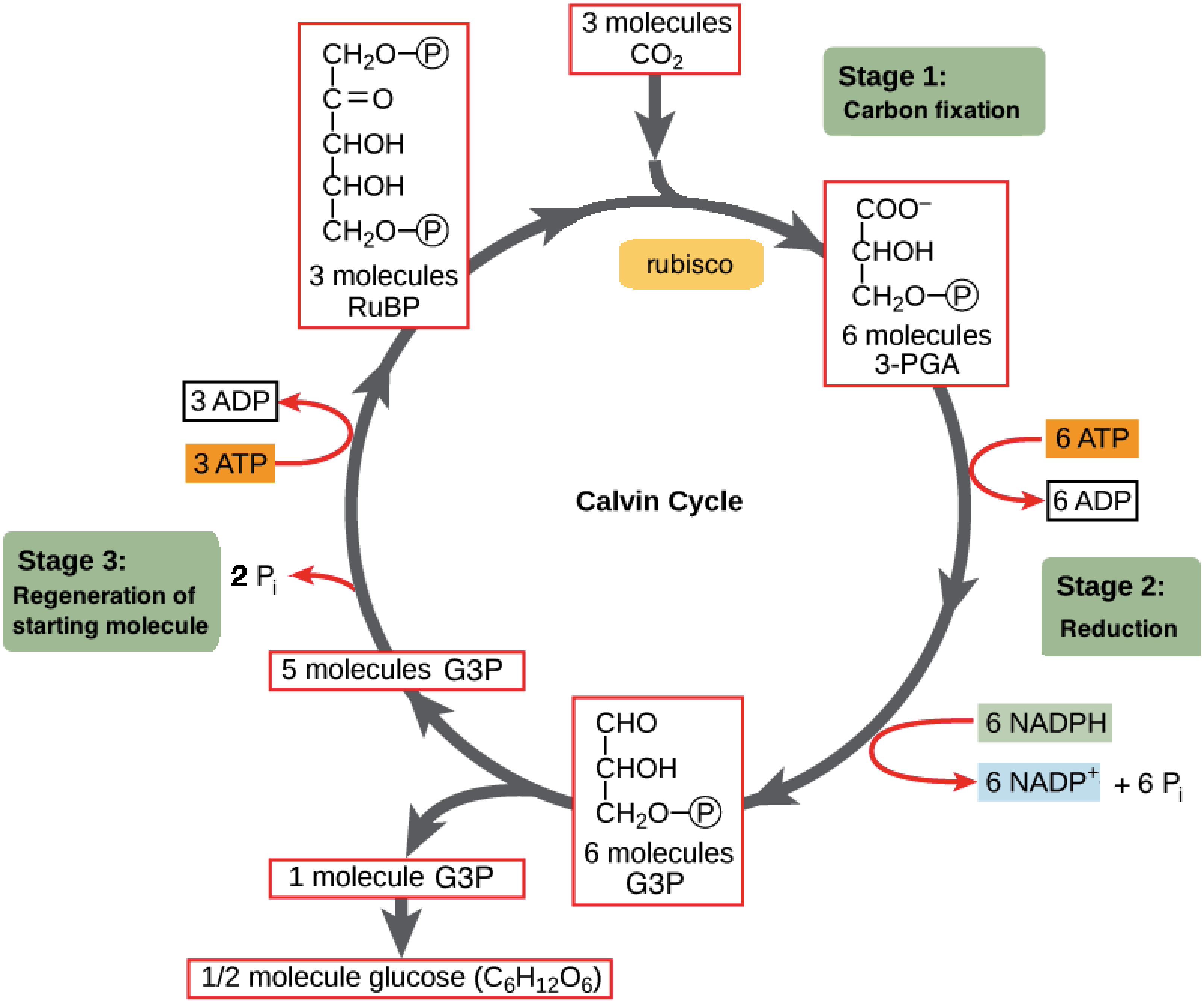

RuBP
CO2
Rubisco
unstable intermediate
3-PGA
3-PGA



3 molecules CO_2
Stage 1: Carbon fixation
$CH_2O-Ⓟ$
$C=O$
CHOH
CHOH
$CH_2O-Ⓟ$
3 molecules RuBP
rubisco
COO^-
CHOH
$CH_2O-Ⓟ$
6 molecules 3-PGA
3 ADP
3 ATP
6 ATP
6 ADP
Calvin Cycle
Stage 3: Regeneration of starting molecule
2 P_i
Stage 2: Reduction
5 molecules G3P
CHO
CHOH
$CH_2O-Ⓟ$
6 molecules G3P
6 NADPH
6 $NADP^+$ + 6 P_i
1 molecule G3P
1/2 molecule glucose ($C_6H_{12}O_6$)

Stage 2: Reduction

- ATP and NADPH are used to convert the six molecules of 3-PGA into six molecules of a chemical called glyceraldehyde 3-phosphate (G3P).
- This is a reduction reaction because it involves the gain of electrons by 3-PGA. Recall that a reduction is the gain of an electron by an atom or molecule. Six molecules of both ATP and NADPH are used.
- For ATP, energy is released with the loss of the terminal phosphate atom, converting it to ADP; for NADPH, both energy and a hydrogen atom are lost, converting it into $NADP^+$. Both of these molecules return to the nearby light-dependent reactions to be reused and reenergized.


3 molecules CO2
Stage 1: Carbon fixation
CH2O–P
C=O
CHOH
CHOH
CH2O–P
3 molecules RuBP
rubisco
COO−
CHOH
CH2O–P
6 molecules 3-PGA
6 ATP
6 ADP
Stage 2: Reduction
6 NADPH
6 NADP+ + 6 Pi
CHO
CHOH
CH2O–P
6 molecules G3P
Calvin Cycle
3 ADP
3 ATP
Stage 3: Regeneration of starting molecule
2 Pi
5 molecules G3P
1 molecule G3P
1/2 molecule glucose (C6H12O6)

Calvin cycle: reduction of PGA into PGAL

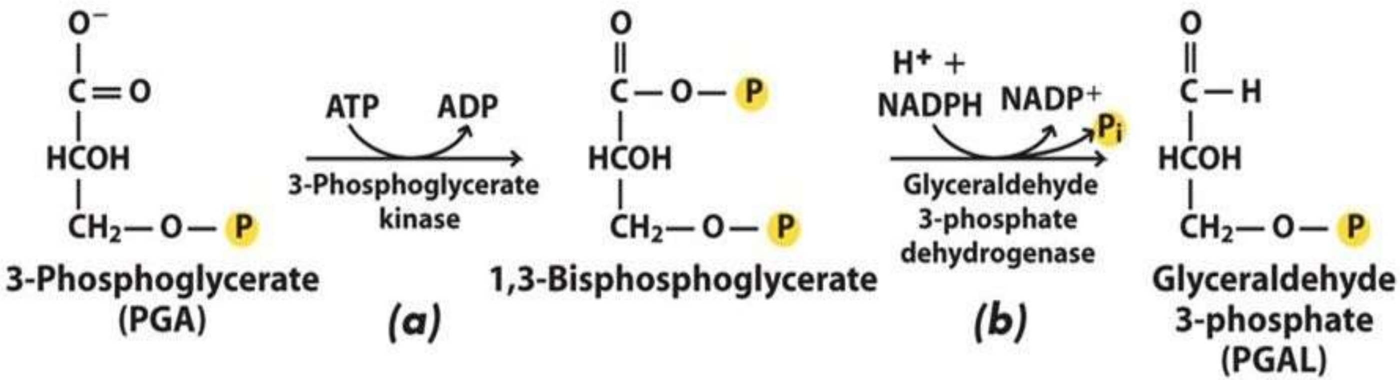
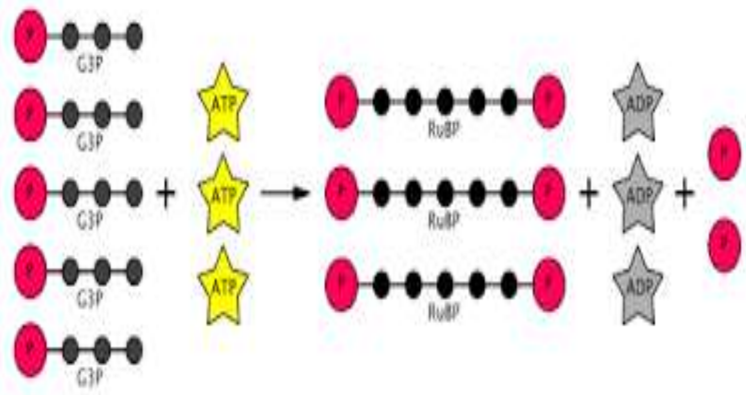


Figure 7-17
Biology of Plants, Seventh Edition

Stage 3: Regeneration

- At this point, only one of the G3P molecules leaves the Calvin cycle and is sent to the cytoplasm to contribute to the formation of other compounds needed by the plant.
- Because the G3P exported from the chloroplast has three carbon atoms, it takes three “turns” of the Calvin cycle to fix enough net carbon to export one G3P. But each turn makes two G3Ps, thus three turns make six G3Ps.
- One is exported while the remaining five G3P molecules remain in the cycle and are used to regenerate RuBP, which enables the system to prepare for more CO_2 to be fixed. Three more molecules of ATP are used in these regeneration reactions.

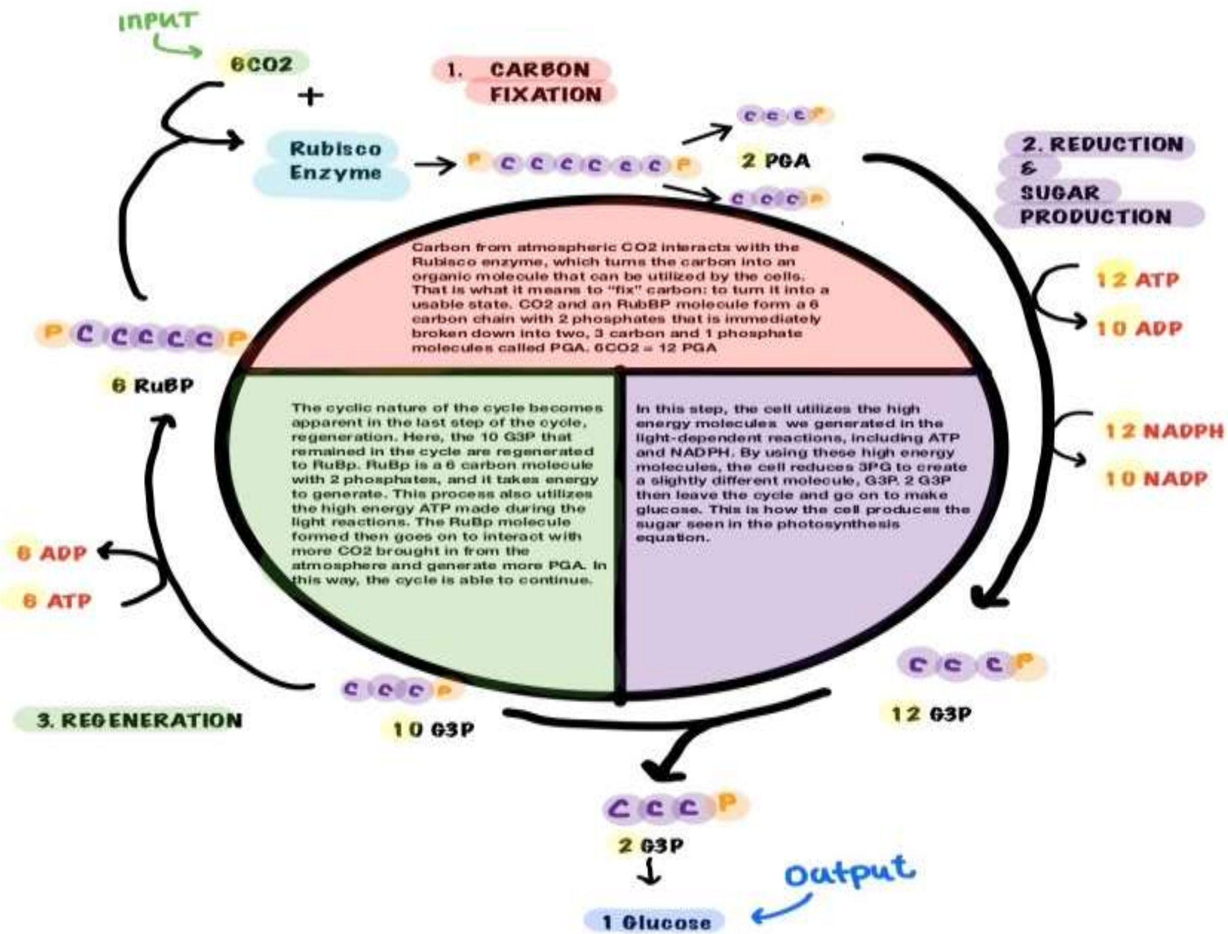


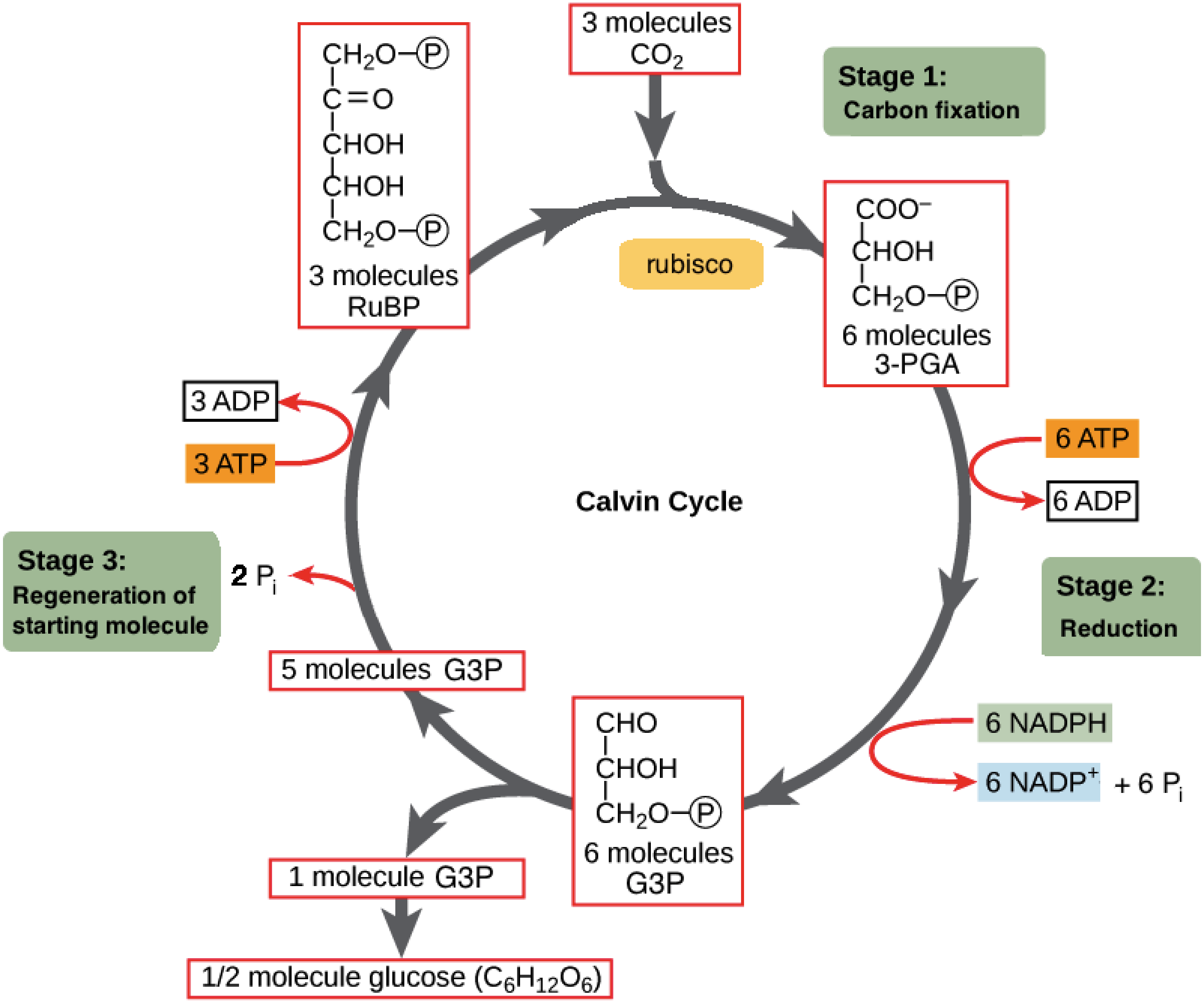
P
G3P
ATP
RuBP
ADP

At the end of the light reactions, we have generated NADPH, ATP, and oxygen. Oxygen is a waste product of the electron transport chain, while ATP and NADPH move onto the **Calvin Cycle**

$$6CO_2 + 6H_2O \longrightarrow \text{Glucose} + 6O_2$$

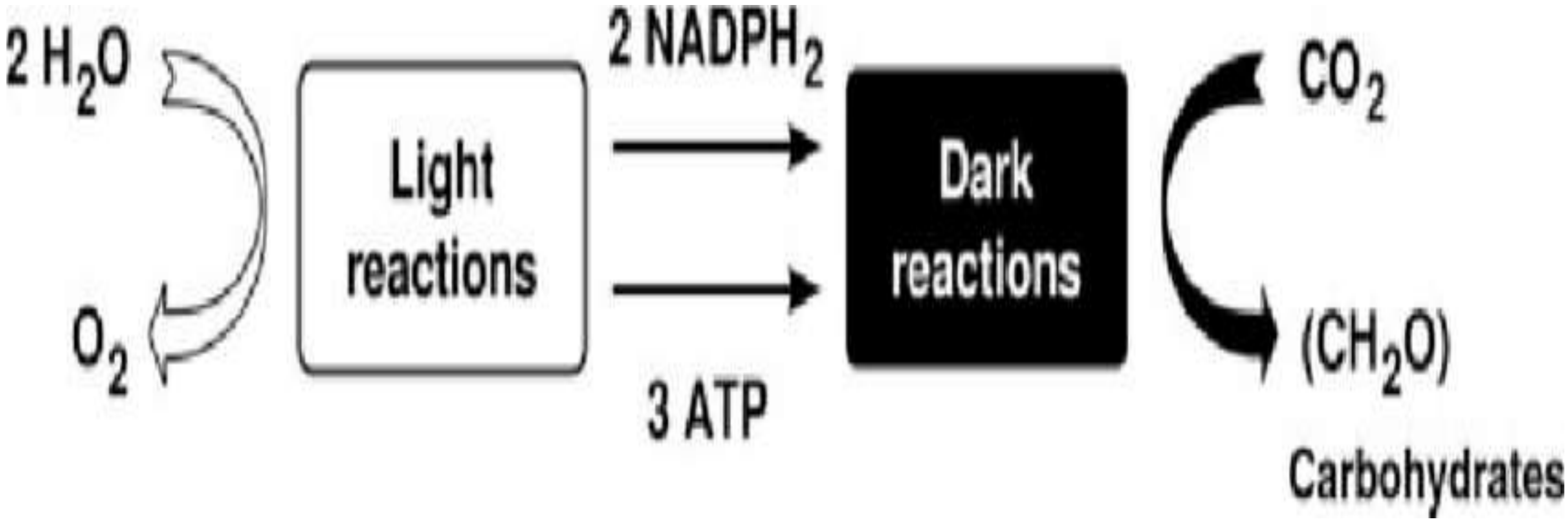
Input of Calvin cycle | Input of light-dependent reactions | Product of Calvin Cycle | Waste product of light-dependent reactions




3 molecules CO2
Stage 1: Carbon fixation
CH2O–P
C=O
CHOH
CHOH
CH2O–P
3 molecules RuBP
rubisco
COO−
CHOH
CH2O–P
6 molecules 3-PGA
6 ATP
6 ADP
Stage 2: Reduction
6 NADPH
6 NADP+ + 6 Pi
3 ADP
3 ATP
Calvin Cycle
Stage 3: Regeneration of starting molecule
2 Pi
5 molecules G3P
CHO
CHOH
CH2O–P
6 molecules G3P
1 molecule G3P
1/2 molecule glucose (C6H12O6)

Calvin Cycle Products

- Each turn of the Calvin cycle “fixes” one molecule of carbon that can be used to make sugar.
- It takes three turns of the Calvin cycle to create one molecule of glyceraldehyde-3 phosphate.
- After six turns of the Calvin cycle, two molecules of glyceraldehyde-3 phosphate can be combined to make a glucose molecule.
- Each turn of the Calvin cycle also uses up 3 ATP and 2 NADPH in the processes of reducing (adding electrons to) 3-phosphoglyceric acid to produce glyceraldehyde-3 phosphate, and regenerating RuBP so that they can accept a new atom of carbon from CO2 from the air.
- This means that to produce a single molecule of glucose, 18 ATP and 12 NADPH are consumed.


2 H2O
O2
Light reactions
2 NADPH2
3 ATP
Dark reactions
CO2
(CH2O)
Carbohydrates

Youtube links

Dark reaction

- https://www.youtube.com/watch?v=ZnXpppgSWhY

Light reaction

- https://www.youtube.com/watch?v=SnnmmKApT-c

Travel inside a leaf animation

- https://www.youtube.com/watch?v=pwymX2LxnQs

Human physiology

What is human physiology?

Human physiology is the branch of science that deals with the study of the functionality of the organ systems of the human body. The complexity of the human body is understood as well as explored when you enter the world of human physiology.

Organ systems

An **organ system** is a group of **organs** that work together as a biological **system** to perform one or more functions. Each **organ** does a particular job in the body, and is made up of distinct tissues.

Organ system	Function	Organs, tissues, and structures involved
Cardiovascular	Transports oxygen, nutrients, and other substances to the cells and transports wastes, carbon dioxide, and other substances away from the cells; it can also help stabilize body temperature and pH	Heart, blood, and blood vessels
Lymphatic	Defends against infection and disease and transfers lymph between tissues and the blood stream	Lymph, lymph nodes, and lymph vessels
Digestive	Processes foods and absorbs nutrients, minerals, vitamins, and water	Mouth, salivary glands, esophagus, stomach, liver, gall bladder, exocrine pancreas, small intestine, and large intestine

Endocrine	**Provides communication within the body via hormones and directs long-term change in other organ systems to maintain homeostasis**	**Pituitary, pineal, thyroid, parathyroids, endocrine pancreas, adrenals, testes, and ovaries.**
Integumentary	Provides protection from injury and fluid loss and provides physical defense against infection by microorganisms; involved in temperature control	Skin, hair, nails, exocrine glands
Muscular	Provides movement, support, and heat production	Skeletal, cardiac, and smooth muscles
Nervous	Collects, transfers, and processes information and directs short-term change in other organ systems	Brain, spinal cord, nerves, and sensory organs—eyes, ears, tongue, skin, and nose

Reproductive	**Produces gametes—sex cells—and sex hormones; ultimately produces offspring**	**Fallopian tubes, uterus, vagina, ovaries, mammary glands (female), testes, vas deferens, seminal vesicles, prostate, and penis (male)**
Respiratory	Delivers air to sites where gas exchange can occur	Mouth, nose, pharynx, larynx, trachea, bronchi, lungs, and diaphragm
Skeletal	Supports and protects soft tissues of the body; provides movement at joints; produces blood cells; and stores minerals	Bones, cartilage, joints, tendons, and ligaments
Urinary	Removes excess water, salts, and waste products from the blood and body and controls pH	Kidneys, ureters, urinary bladder, and urethra
Immune	Defends against microbial pathogens—disease-causing agents—and other diseases	Leukocytes, tonsils, adenoids, thymus, and spleen

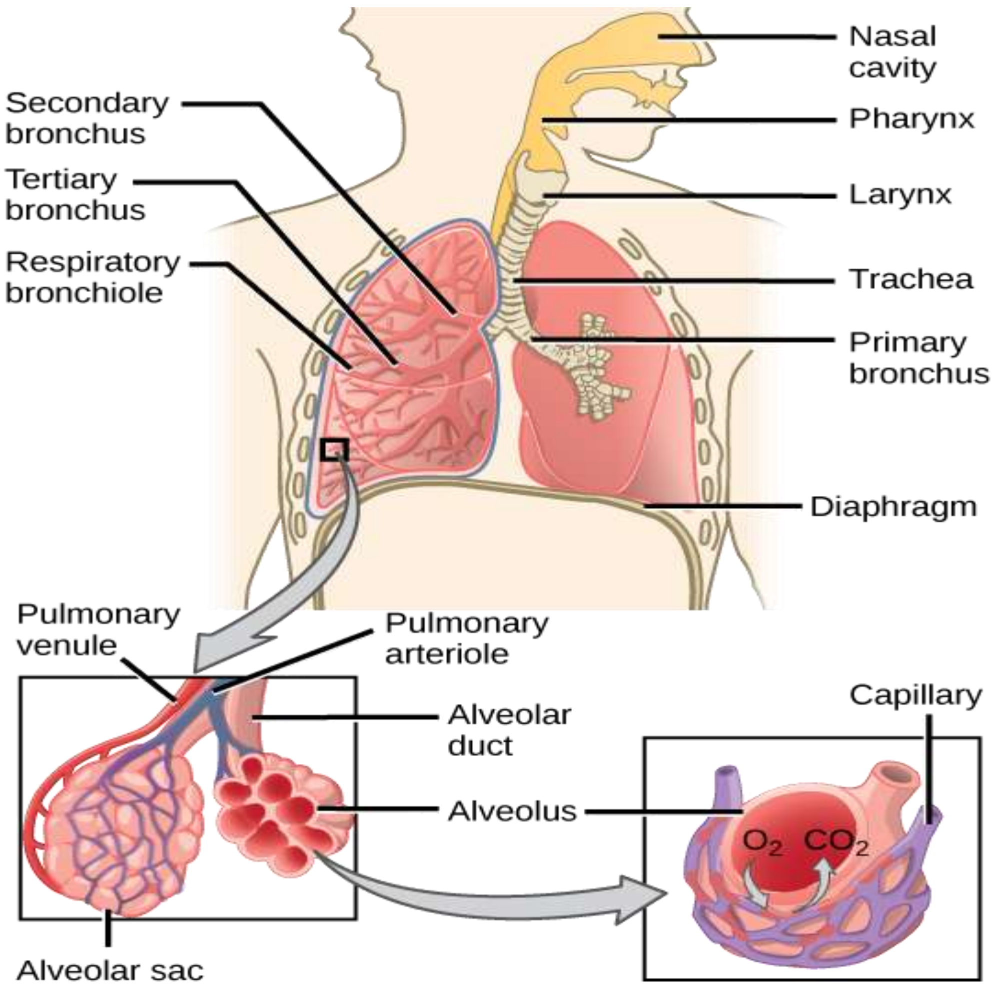
Respiratory system

- The process of physiological respiration includes two major parts: external respiration and internal respiration. **External respiration**, also known as breathing, involves both bringing air into the lungs (inhalation) and releasing air to the atmosphere (exhalation). During **internal respiration**, oxygen and carbon dioxide are exchanged between the cells and blood vessels.
- The third type of respiration is cellular respiration

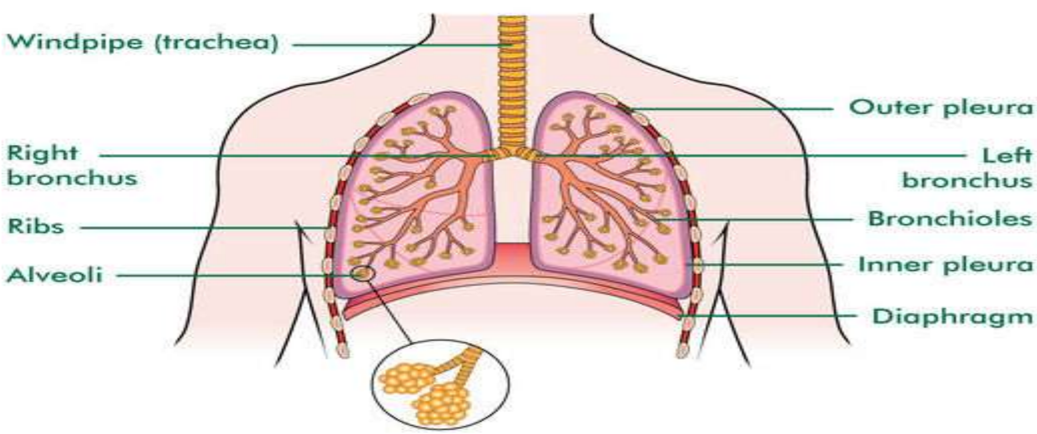
Key terms

Term	Meaning
Respiratory system	The body system responsible for gas exchange between the body and the external environment
Pharynx (throat)	Tube connected the nose/mouth to the esophagus
Larynx (voice box)	Tube forming a passage between the pharynx and trachea
Trachea	Tube connecting the larynx to the bronchi of the lungs
Bronchi	Branches of tissue stemming from the trachea
Bronchiole	Airway that extends from the bronchus
Alveoli	Structures of the lung where gas exchange occurs
Diaphragm	Thoracic muscle that lays beneath the lungs and aids in inhalation/exhalation

Respiratory system

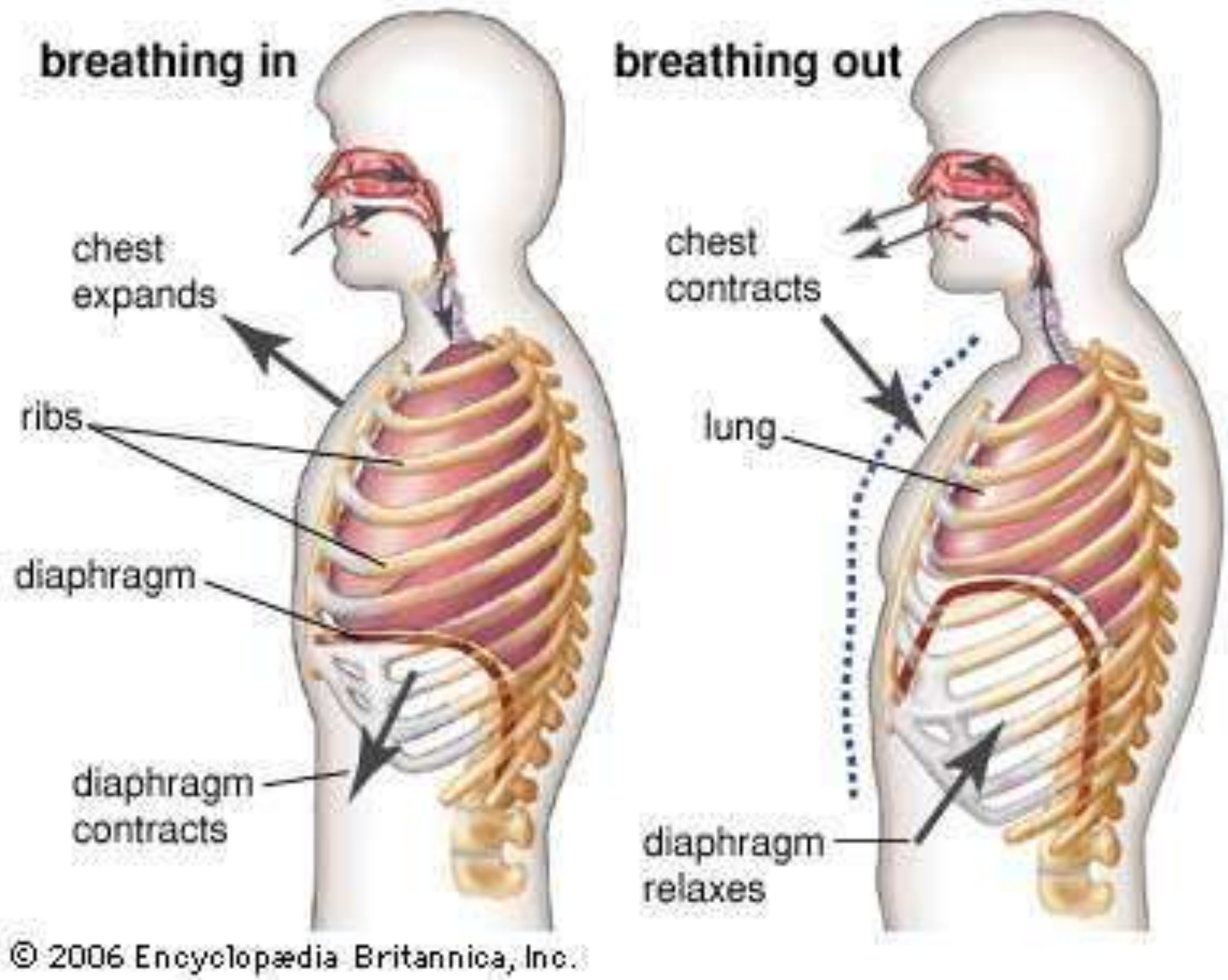


- Respiration begins at the nose or mouth, where oxygenated air is brought in before moving down the **pharynx**, **larynx**, and the **trachea**. The trachea branches into two **bronchi**, each leading into a lung. Each bronchus divides into smaller bronchi, and again into even smaller tubes called **bronchioles**. At the end of the bronchioles are air sacs called **alveoli**, and this is where gas exchange occurs.



The **lungs** are found in the chest on the right and left side. At the **front** they extend from just above the collarbone (clavicle) at the top of the chest to about the sixth rib down. At the **back** of the chest the **lungs** finish around the tenth rib.

- An important structure of respiration is the **diaphragm**. When the diaphragm contracts, it flattens and the lungs expand, drawing air into the lungs. When it relaxes, air flows out, allowing the lungs to deflate.
- The **diaphragm** is the primary muscle used in respiration, which is the process of breathing. This dome-shaped muscle is located just below the lungs and heart. It contracts continually as you breathe in and out


breathing in
chest
expands
ribs
diaphragm
diaphragm
contracts
breathing out
chest
contracts
lung
diaphragm
relaxes
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The Nose

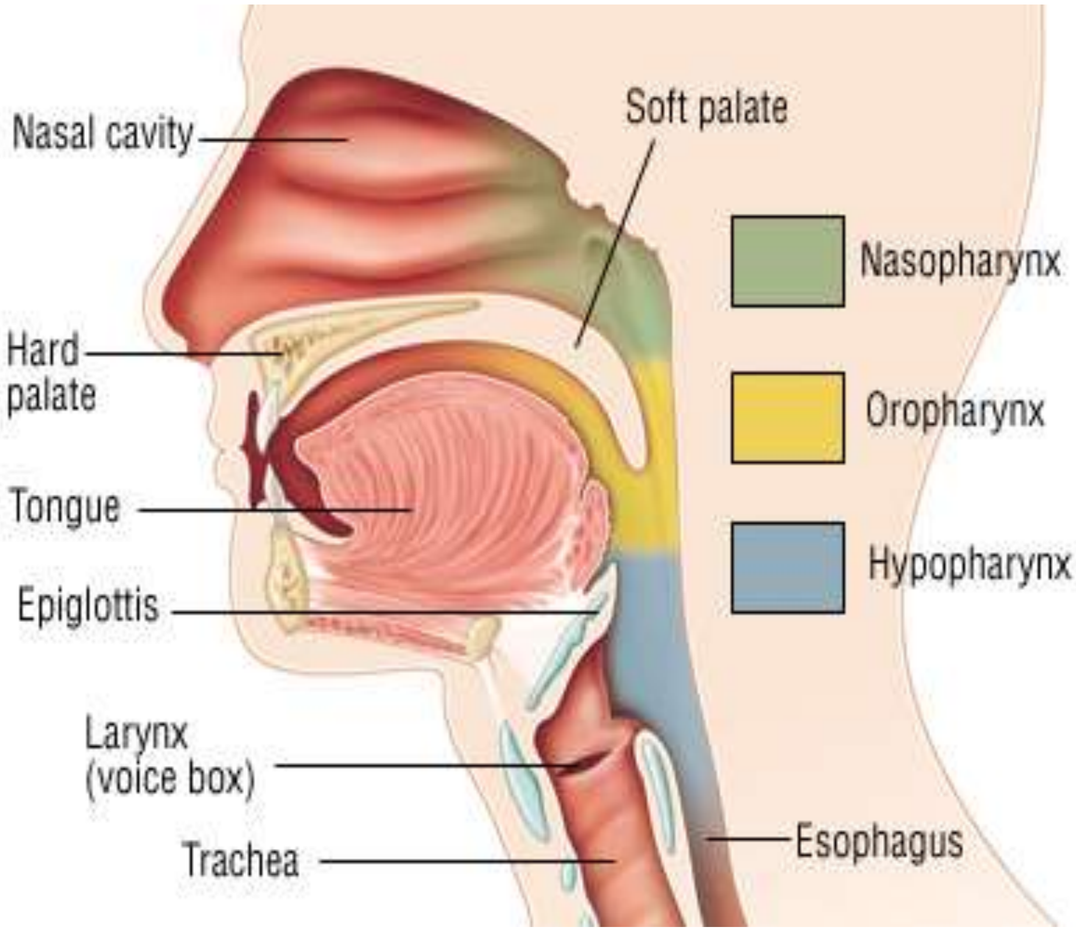
- The only externally visible part of the respiratory system
- Air enters the nose through the external nares (nostrils)
- The interior of the nose consists of a nasal cavity divided by a nasal ***septum***

Nasal Cavity

- Lateral walls have projections called ***conchae***
- Nasal cavity is separated from the oral cavity by the ***hard*** & ***soft palates***
- Olfactory receptors are located in the mucosa on the superior surface
- Cavity is lined with respiratory ***mucosa***
  - Moistens air
  - Traps incoming foreign particles

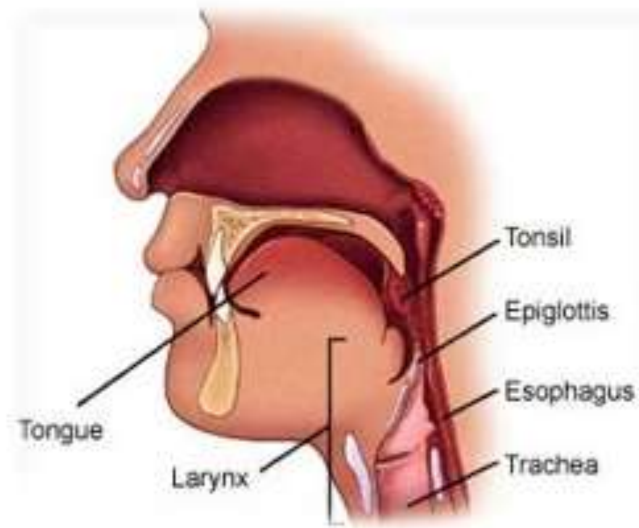
Pharynx (Throat)

- Muscular passage from nasal cavity to larynx
- Three regions of the pharynx:
  - Nasopharynx – superior region behind nasal cavity
  - Oropharynx – middle region behind mouth
  - Laryngopharynx – inferior region attached to larynx
- Oropharynx & laryngopharynx are the passageways for air & food


Nasal cavity
Soft palate
Nasopharynx
Hard palate
Oropharynx
Tongue
Hypopharynx
Epiglottis
Larynx (voice box)
Trachea
Esophagus

Larynx

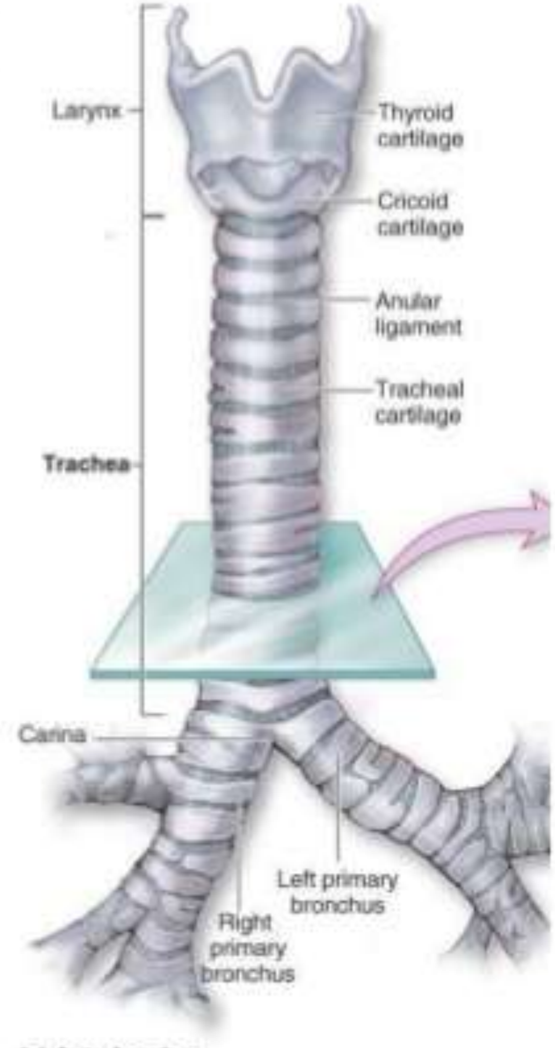
- Vocal cords (vocal folds)
- Glottis – opening between vocal cords
- Thyroid cartilage
  - Largest hyaline cartilage
  - “Adam’s apple”



- Epiglottis
  - Superior opening of the larynx
  - Routes food to the larynx and air toward the trachea

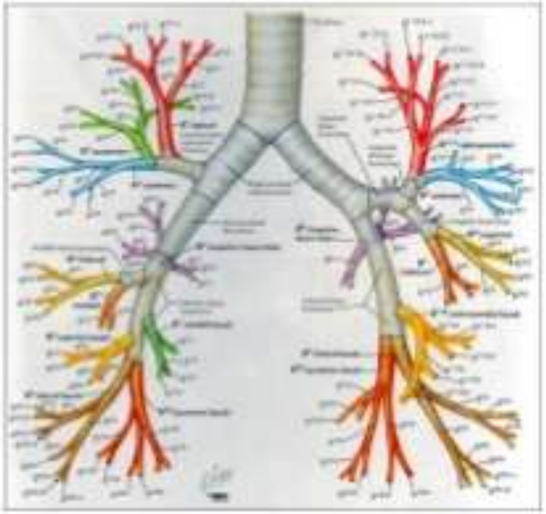
Trachea (Windpipe)

- Connects larynx with bronchi
- Lined with ciliated mucosa
  - Beat continuously in the opposite direction of incoming air
  - Expel mucus loaded with dust and other debris away from lungs
- Walls are reinforced with C-shaped hyaline cartilage



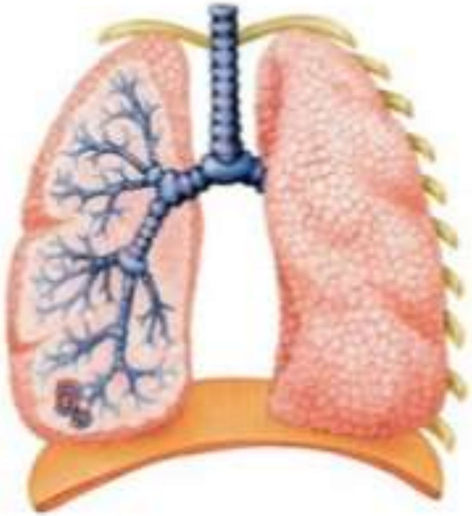
Primary Bronchi

- Formed by division of the trachea
- Enters the lung at the hilus (medial depression)
- Right bronchus is wider, shorter, and straighter than the left
- Bronchi subdivide into smaller and smaller branches



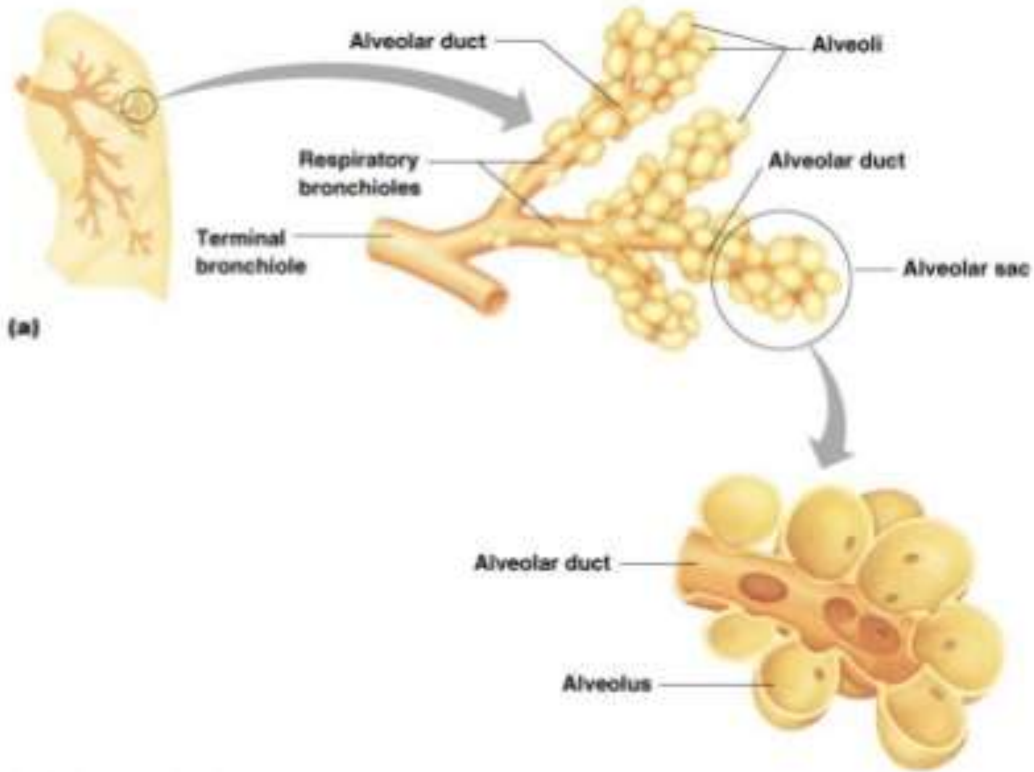
Lungs

- Site of gas exchange
- Occupy most of the thoracic cavity
  - Apex is near the clavicle (superior portion)
    - Base rests on the diaphragm (inferior portion)
  - Each lung is divided into lobes
    - Left lung – two lobes
    - Right lung – three lobes



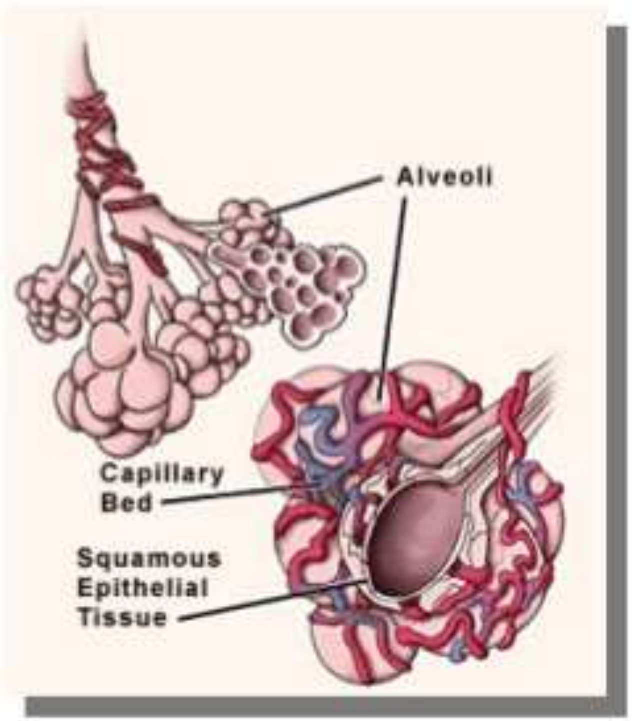
Bronchioles

- Smallest branches of the bronchi
- Terminal bronchioles end in alveoli
- All but the smallest branches have reinforcing cartilage



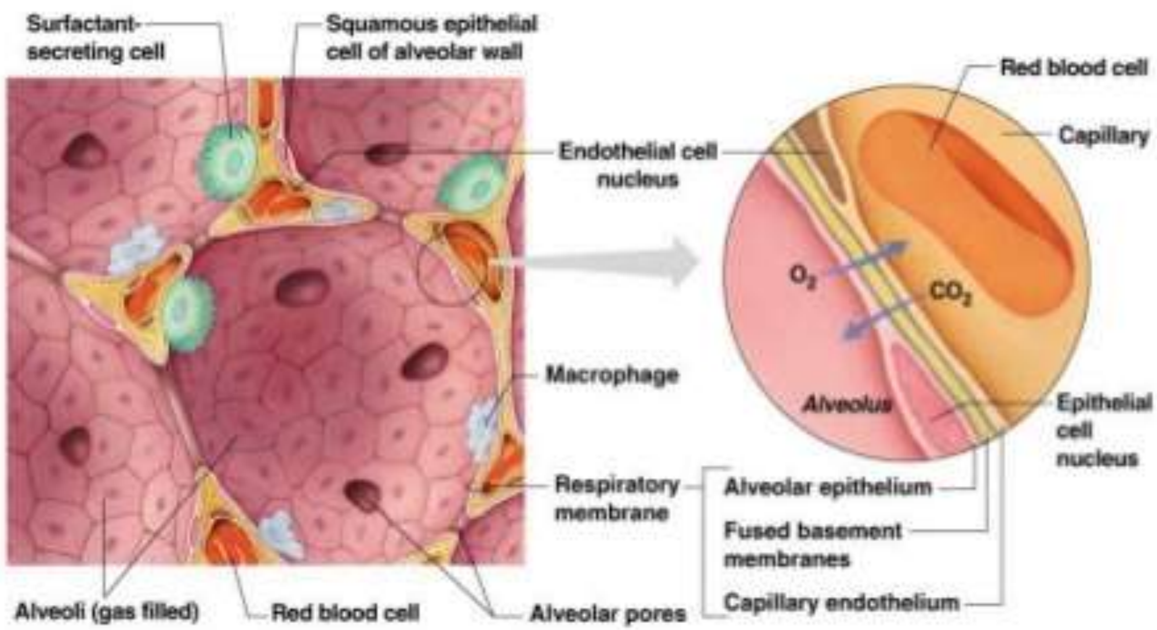
Alveoli

- Gas exchange takes place within the alveoli in the respiratory membrane
- Tiny blood capillaries surround alveoli and allow for simple diffusion of O_2 & CO_2



Coverings of the Lungs

- Pulmonary ***Pleura*** covers the lung surface
- ***Pleural fluid*** fills the area between layers
- Macrophages add protection
- ***Surfactant*** coats gas-exposed alveolar surfaces



Mechanics of Breathing

Inspiration

- ***Diaphragm*** and ***intercostal*** muscles contract
- The size of the thoracic cavity increases
- External air is pulled into the lungs due to an increase increased volume

Exhalation

- As muscles relax, air is pushed out of the lungs
- Forced expiration can occur mostly by contracting internal intercostal muscles to depress the rib cage

- **Lungs**
- Human lungs are composed of approximately 300 million alveoli. Red blood cells pass through the capillaries in single file, and oxygen from each alveolus enters the red blood cells and binds to the hemoglobin. In addition, carbon dioxide contained in the plasma and red blood cells leaves the capillaries and enters the alveoli when a breath is taken. Most carbon dioxide reaches the alveoli as bicarbonate ions, and about 25 percent of it is bound loosely to hemoglobin.
- When a person inhales, the rib muscles and diaphragm contract, thereby increasing the volume of the chest cavity. This increase leads to reduced air pressure in the chest cavity, and air rushes into the alveoli, forcing them to expand and fill. The lungs passively obtain air from the environment by this process. During exhalation, the rib muscles and diaphragm relax, the chest cavity volume diminishes, and the internal air pressure increases. The compressed air forces the alveoli to close, and air flows out.

Common mistakes and misconceptions

- **Physiological respiration and cellular respiration are not the same**. People sometimes use the word "respiration" to refer to the process of cellular respiration, which is a cellular process in which carbohydrates are converted into energy. The two are related processes, but they are not the same.

- **We do not breathe in *only* oxygen or breathe out *only* carbon dioxide.** Often the terms "oxygen" and "air" are used interchangeably. It is true that the air we breathe in has more oxygen than the air we breathe out, and the air we breathe out has more carbon dioxide than the air that we breathe in. However, oxygen is just one of the gases found in the air we breathe. (In fact, the air has more nitrogen than oxygen!)

- **The respiratory system does not work alone in transporting oxygen through the body.** The respiratory system works directly with the circulatory system to provide oxygen to the body. Oxygen taken in from the respiratory system moves into blood vessels that then circulate oxygen-rich blood to tissues and cells.

Youtube links

- https://www.youtube.com/watch?v=GjfD55C9v38
- https://www.youtube.com/watch?v=k9BWCnnXOG8&pbjreload=101