How a cell gets energy

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Content of the present lecture

1) Chemical processes in live systems
2) Enzymes
3) Control of metabolism
4) Cell respiration
5) Photosynthesis

Chemical processes in live systems

Chemical processes in live systems

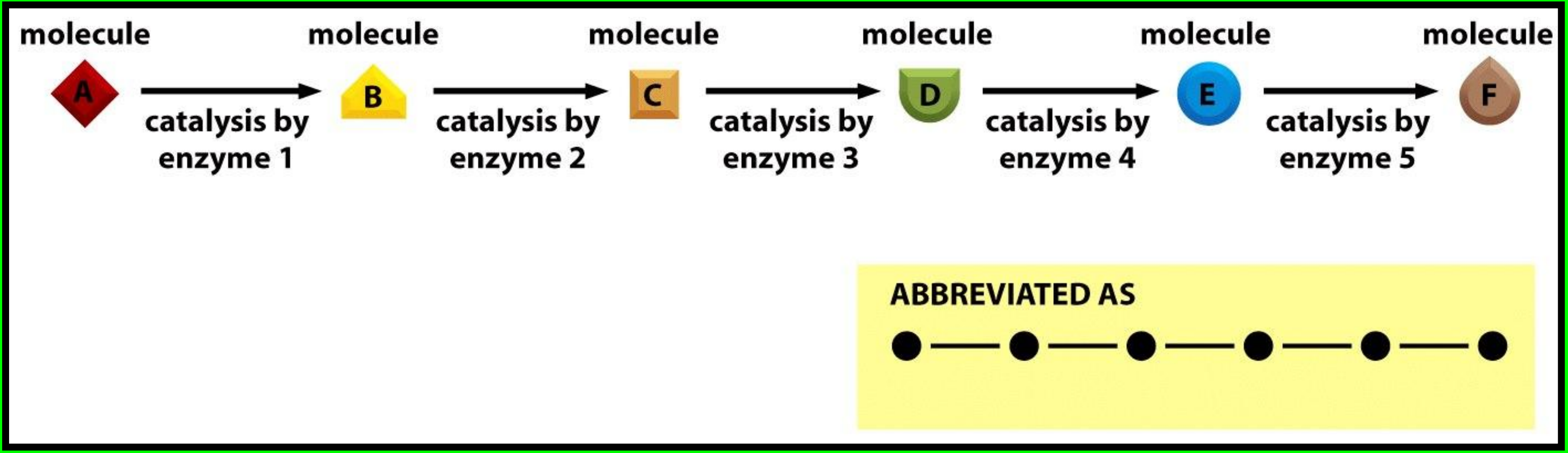
Living things are different from nonliving matter

- create and maintain order
- perform never-ending stream of chemical reactions
- small organic molecules (AA, sugars, nucleotides, lipids) are modified to supply many other small molecules
- their are used to construct macromolecules that endow living systems with all of their most distinctive properties

Cell is tiny chemical factory performs many millions of reactions every second

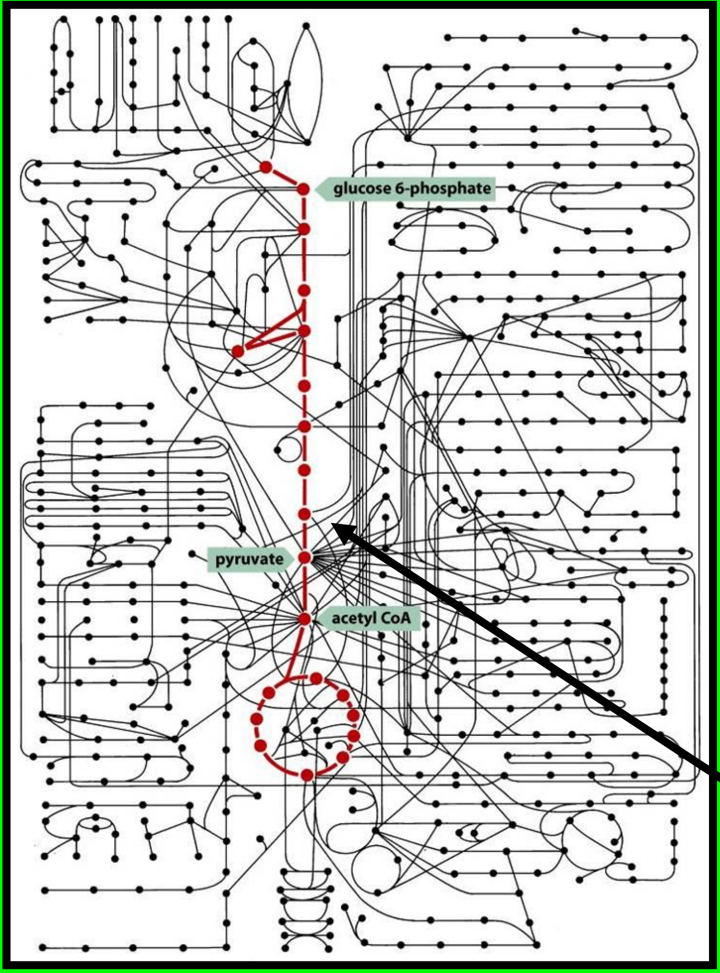
Metabolic pathway

Never-ending stream of chemical reactions



Created by enzyme-catalysed reactions

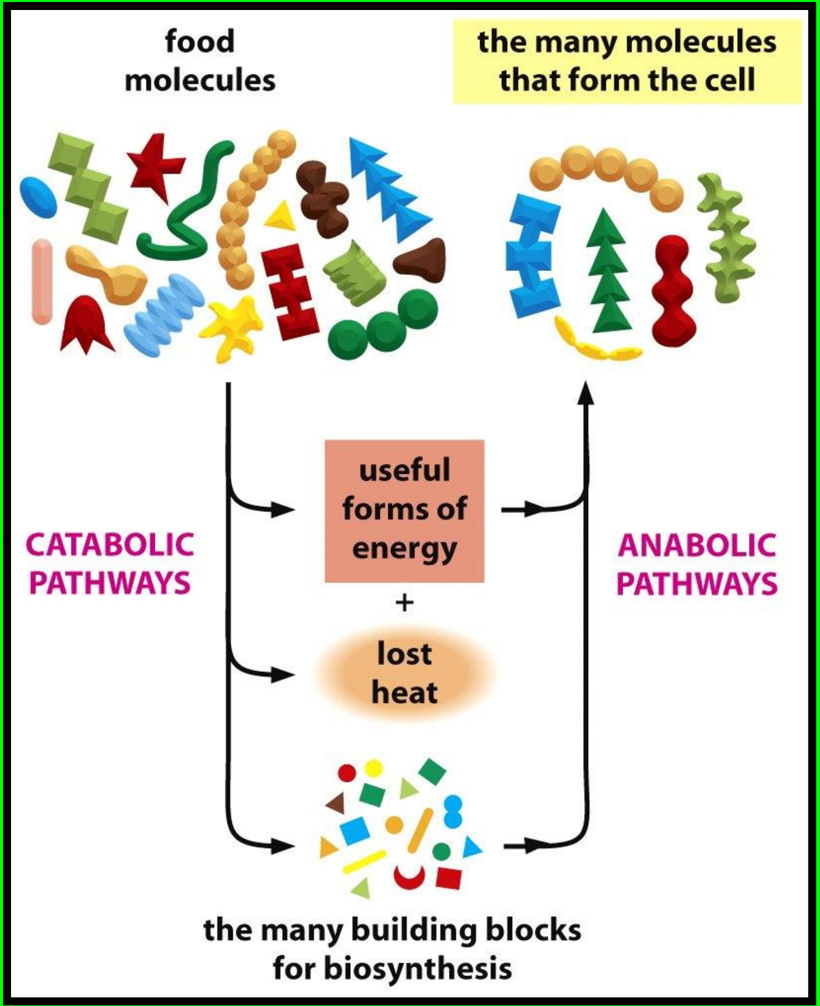
Interconnections of the pathways



Long linear reaction of metabolic pathways are in turn linked to one another forming a maze of interconnected reactions that enable the cell to survive, grow, and reproduce

The individual metabolic pathways

Two opposing streams



Catabolic pathways

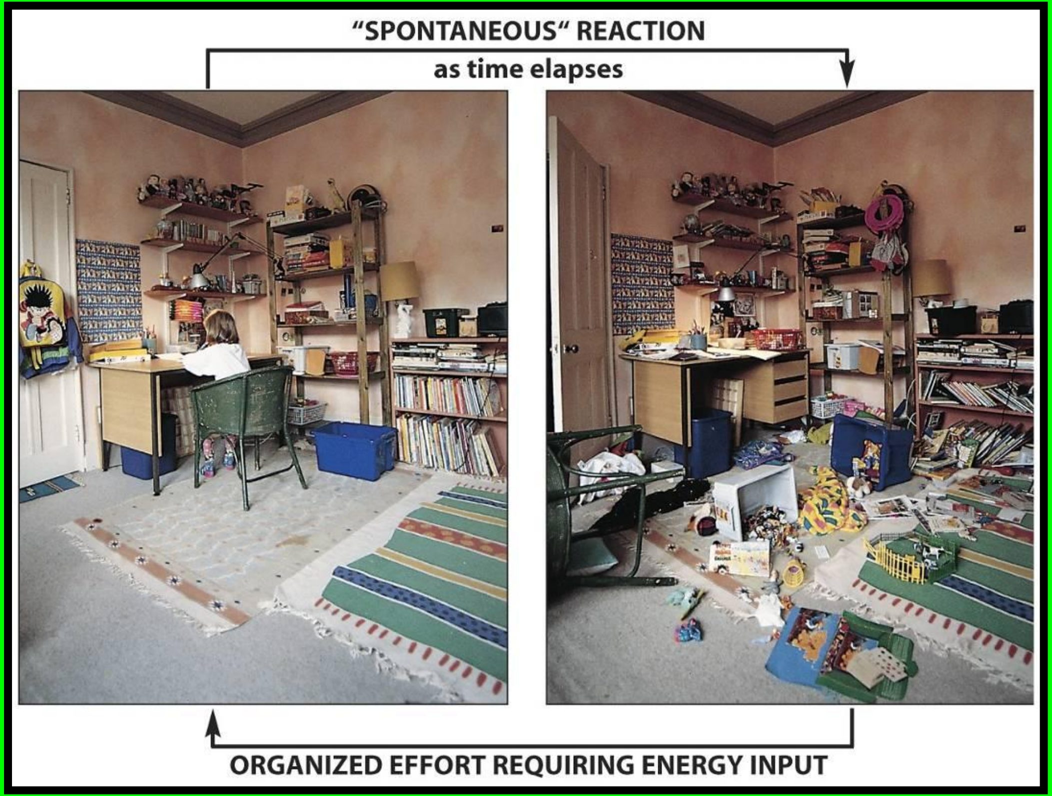
- **break down foodstuffs into smaller molecules**
- **produce energy and building blocks**

Anabolic pathways

- **drive the synthesis of many other molecules that form the cell**
- **biosynthetic**

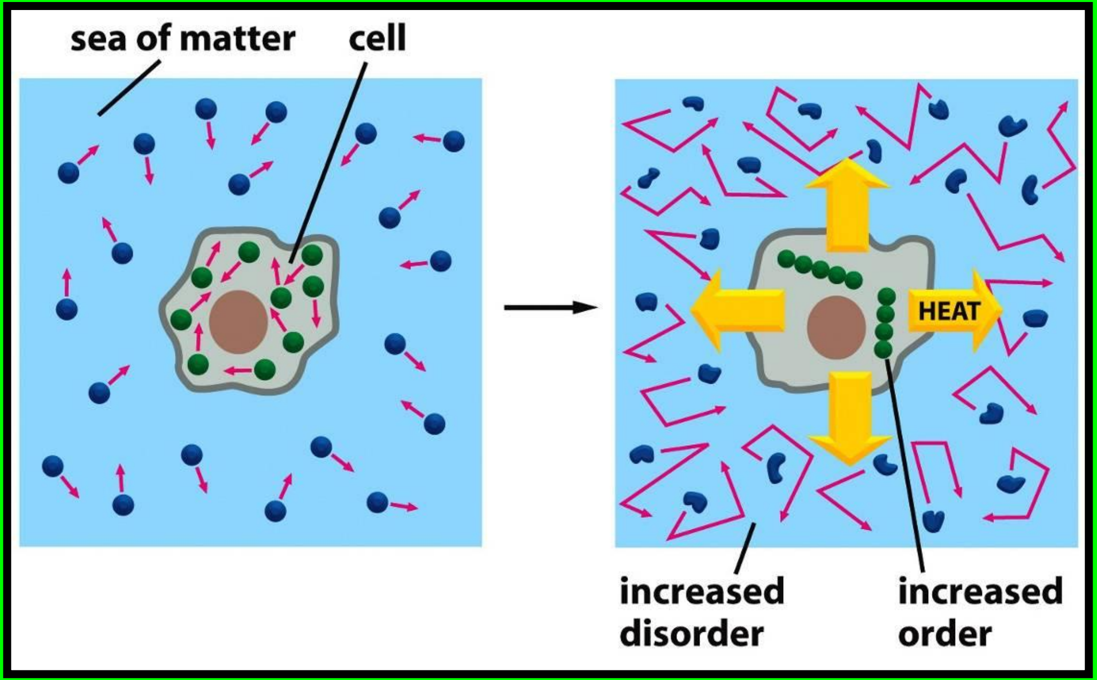
The second law of thermodynamics

The degree of disorder only decrease



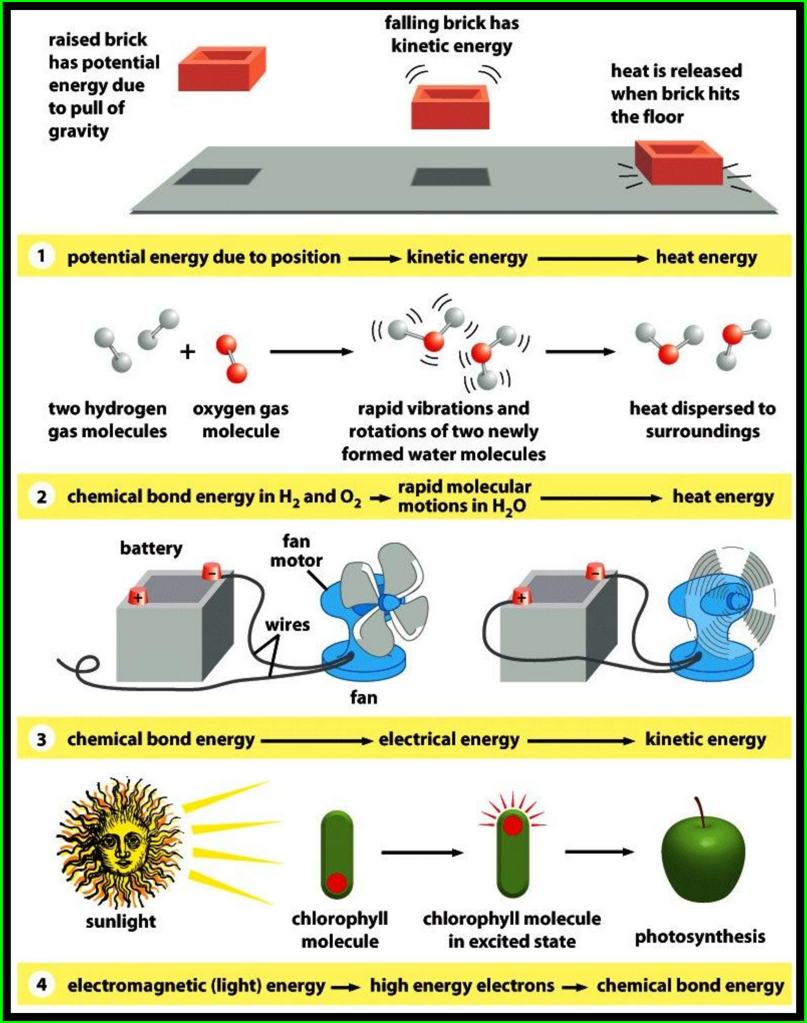
Only for any isolated system !

A simple thermodynamic in cell



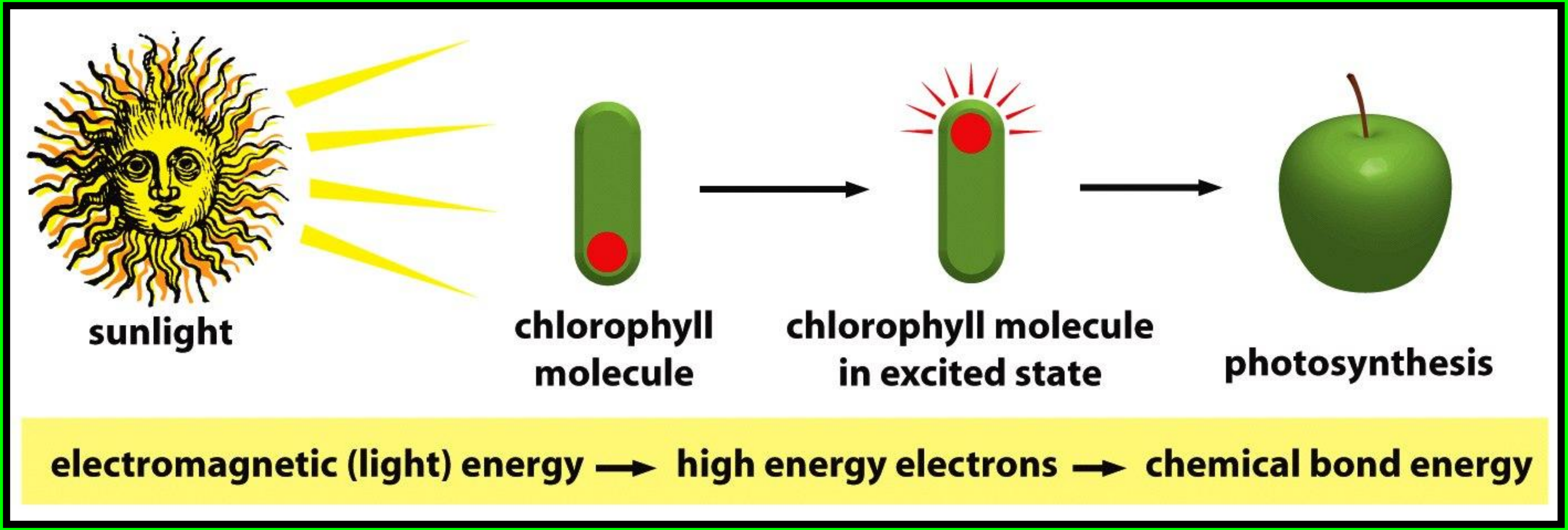
- **a cell surrounded by a sea (rest of the universe)**
- **as the cell lives and grows, it creates internal order**
- **it constantly release heat energy (most disordered form) = increasing the intensity of molecular motion**

Interconversions of energy



- **all energy forms are, in principle, convertible**
- **total amount of energy is conserved**

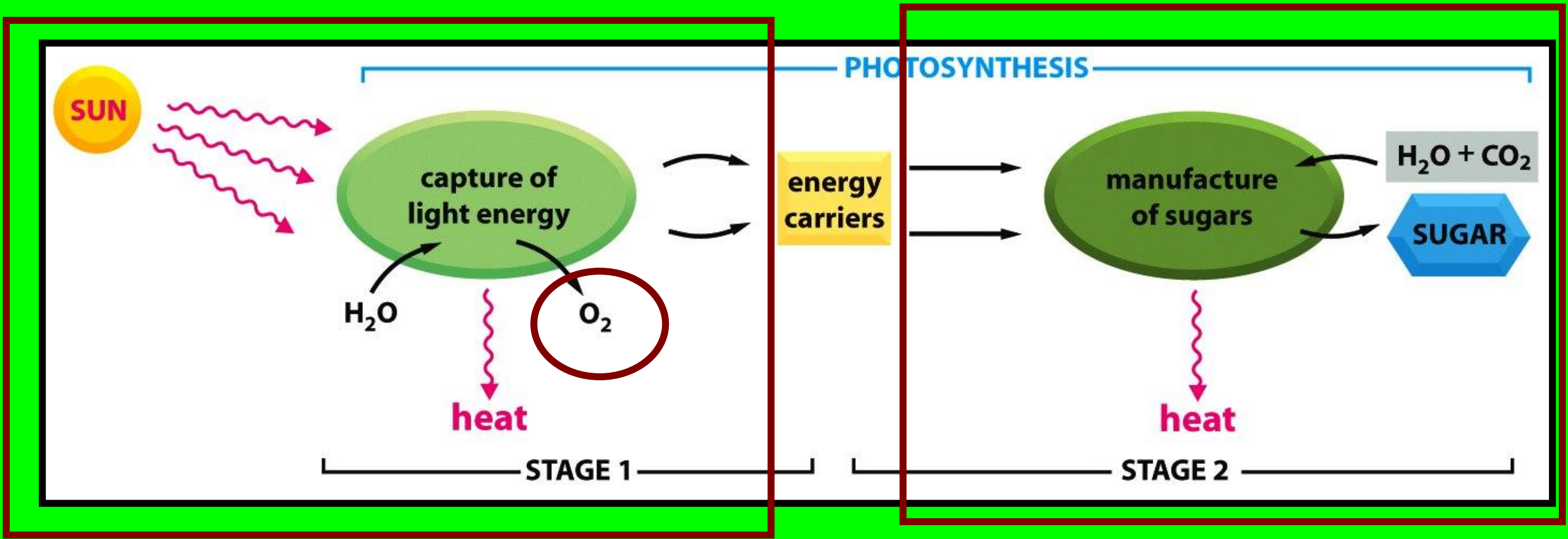
Photosynthetic organisms



They use sunlight to synthesize organic molecules = photosynthesis

Performed in plants, algae, and photosynthetic bacteria

Photosynthesis

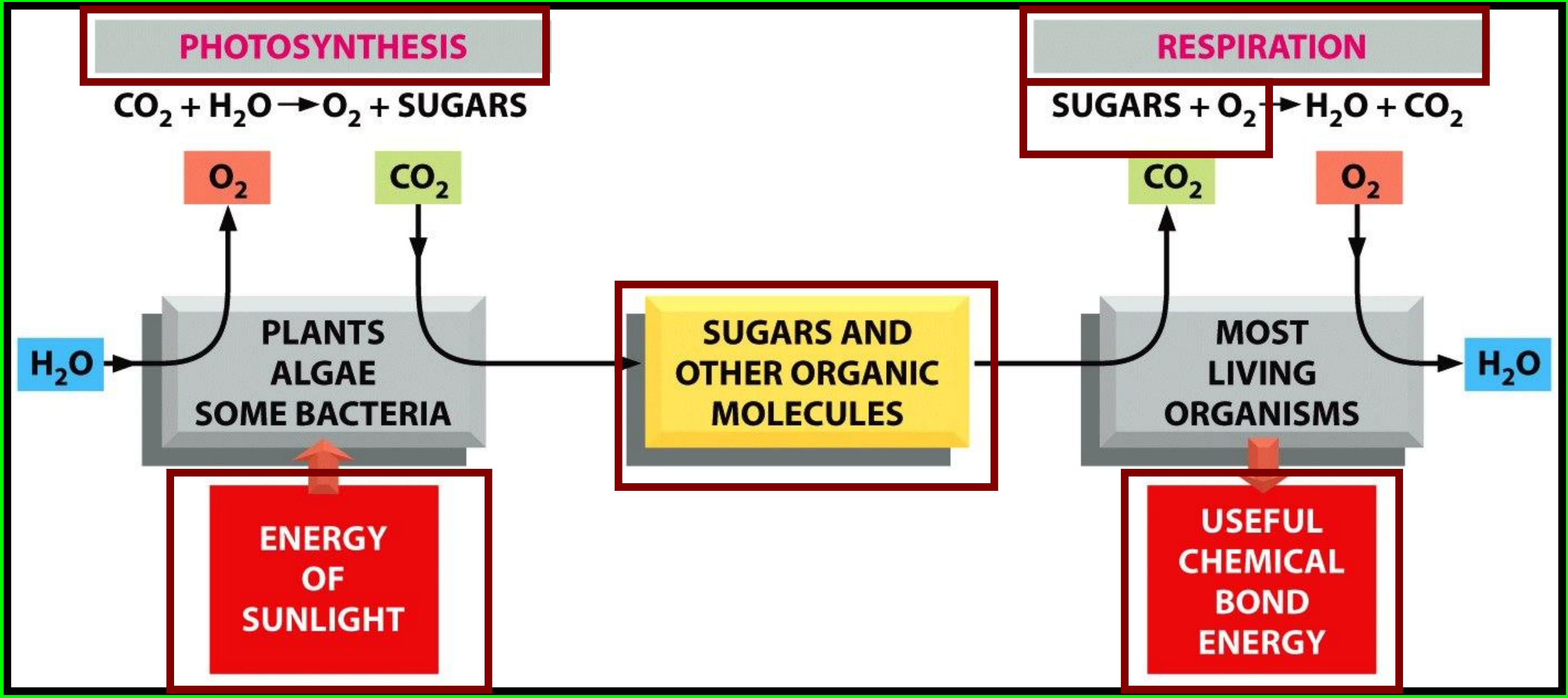


Two stages

- **<u>capturing energy</u> from sunlight and storing as chemical bond energy (<u>waste product</u> = oxygen)**
- **manufacturing of <u>sugar</u> from CO_2 + water**

Oxidation

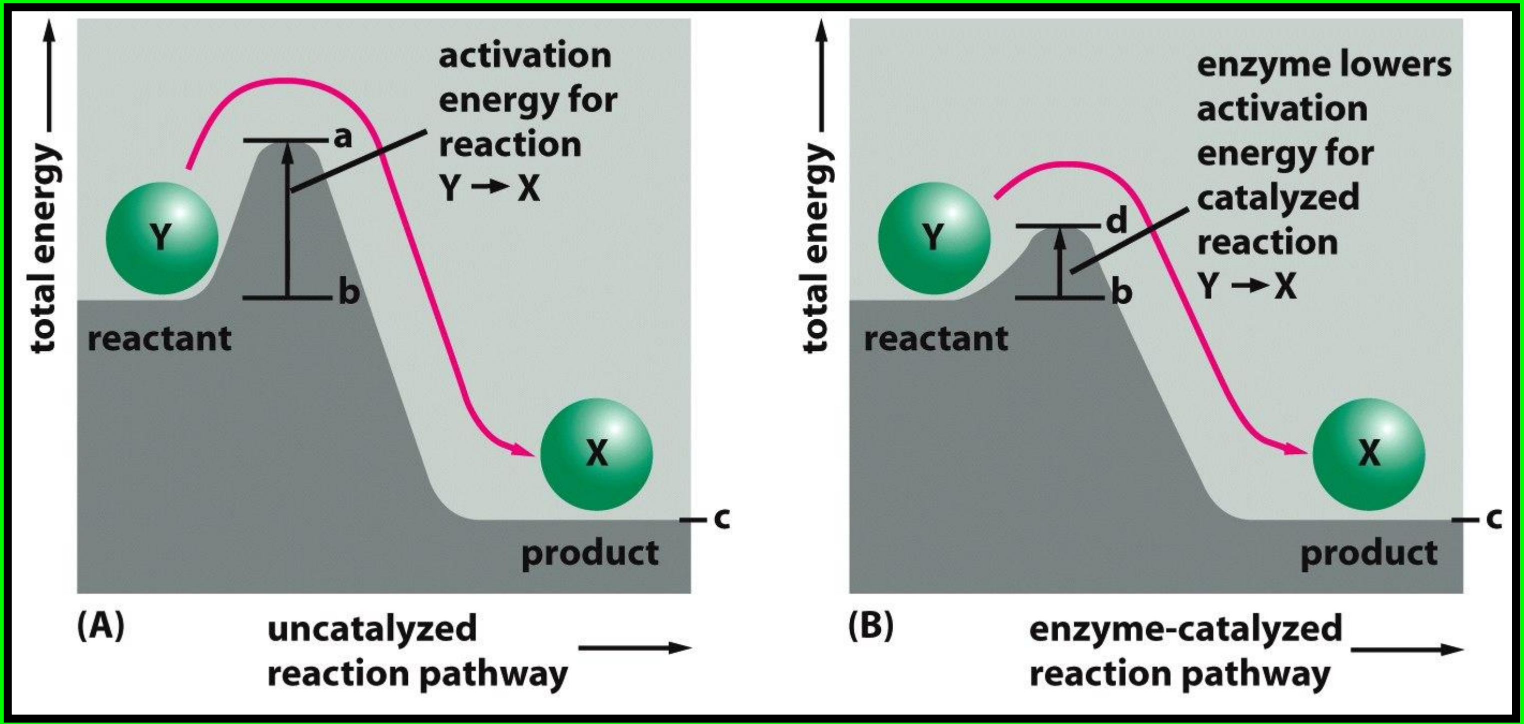
Cell obtain energy by oxidation of organic molecules



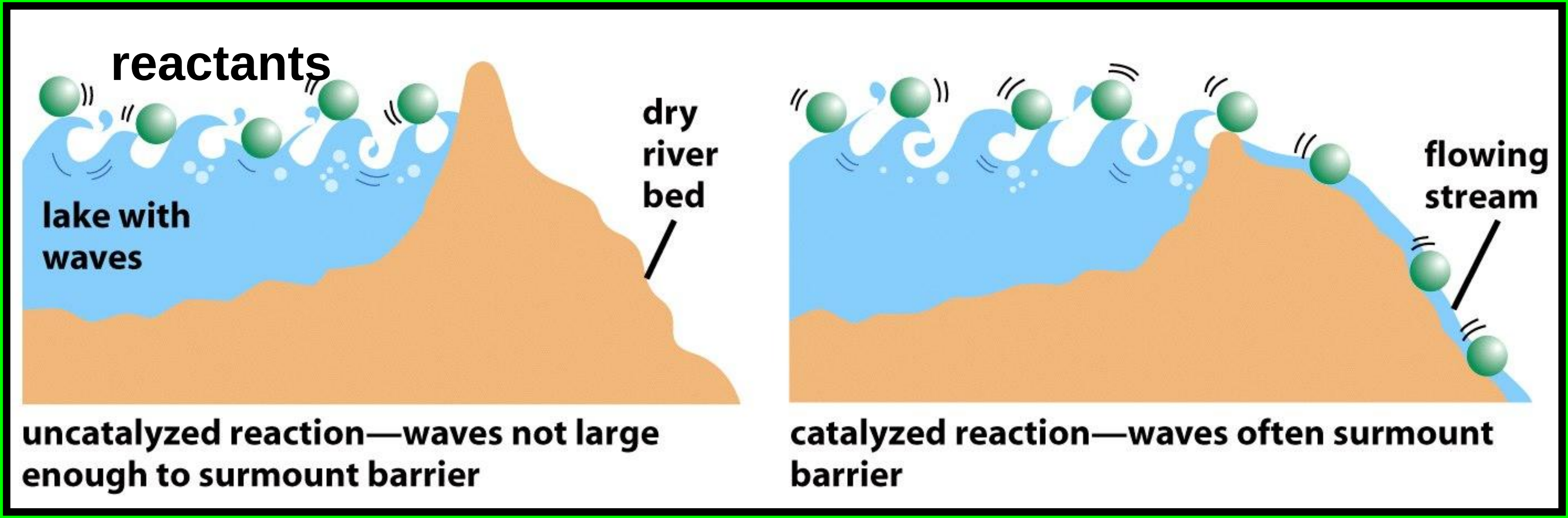
Enzymes

Enzymes lower barriers …

… the barriers that block chemical reactions

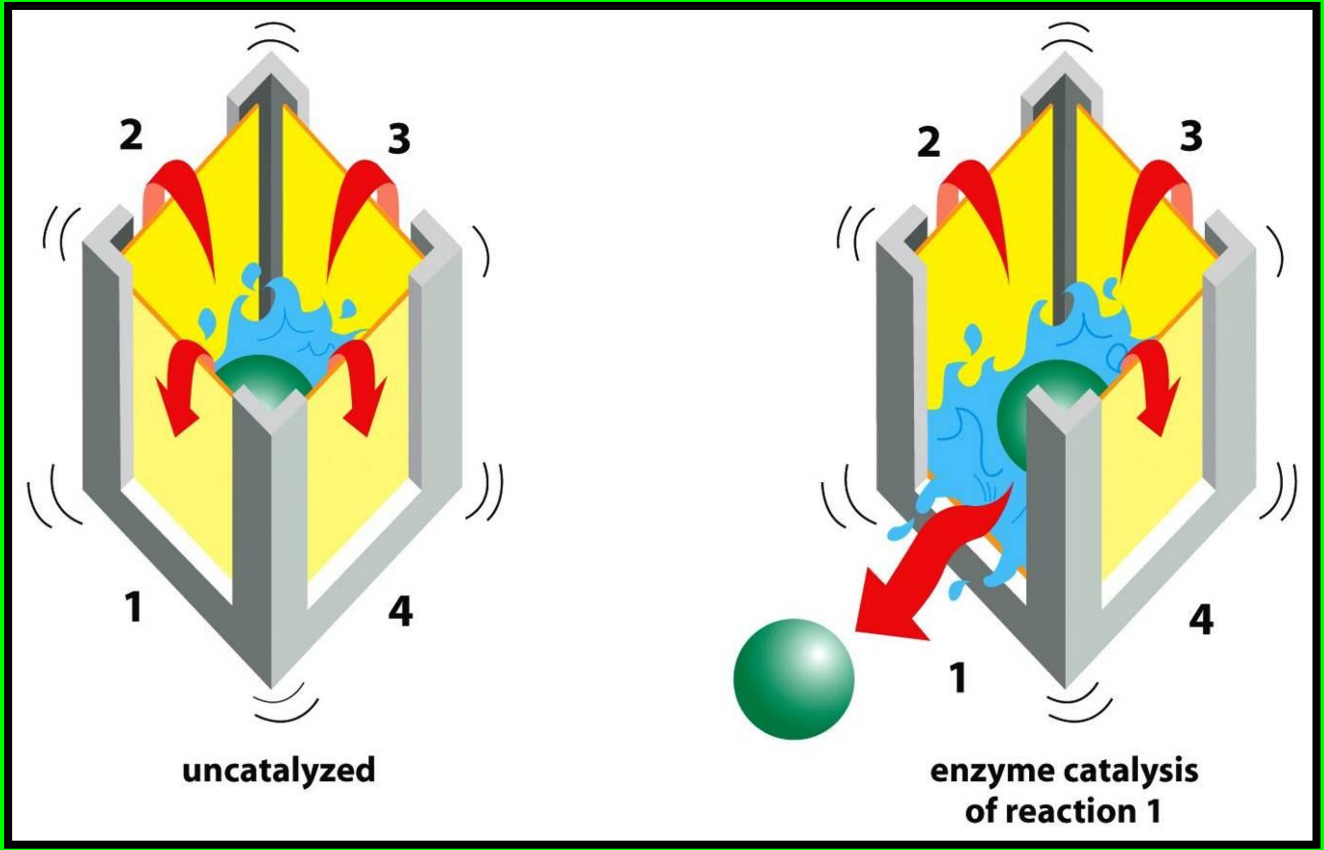


Floating ball analogy 1/3



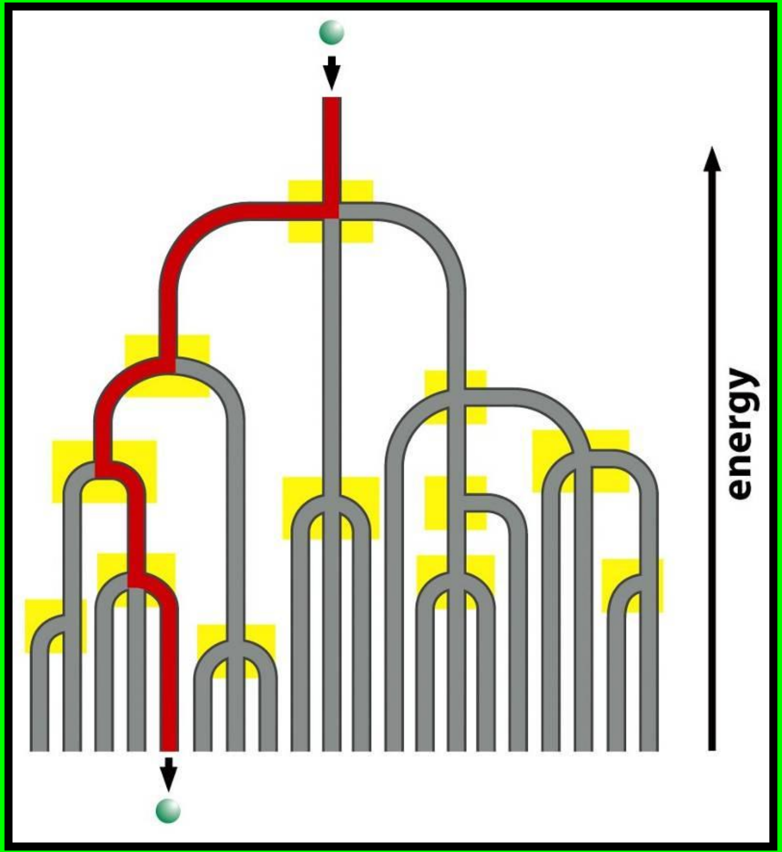
A barrier dam (activation energy) is lowered to represent enzyme catalysis

Floating ball analogy 2/3



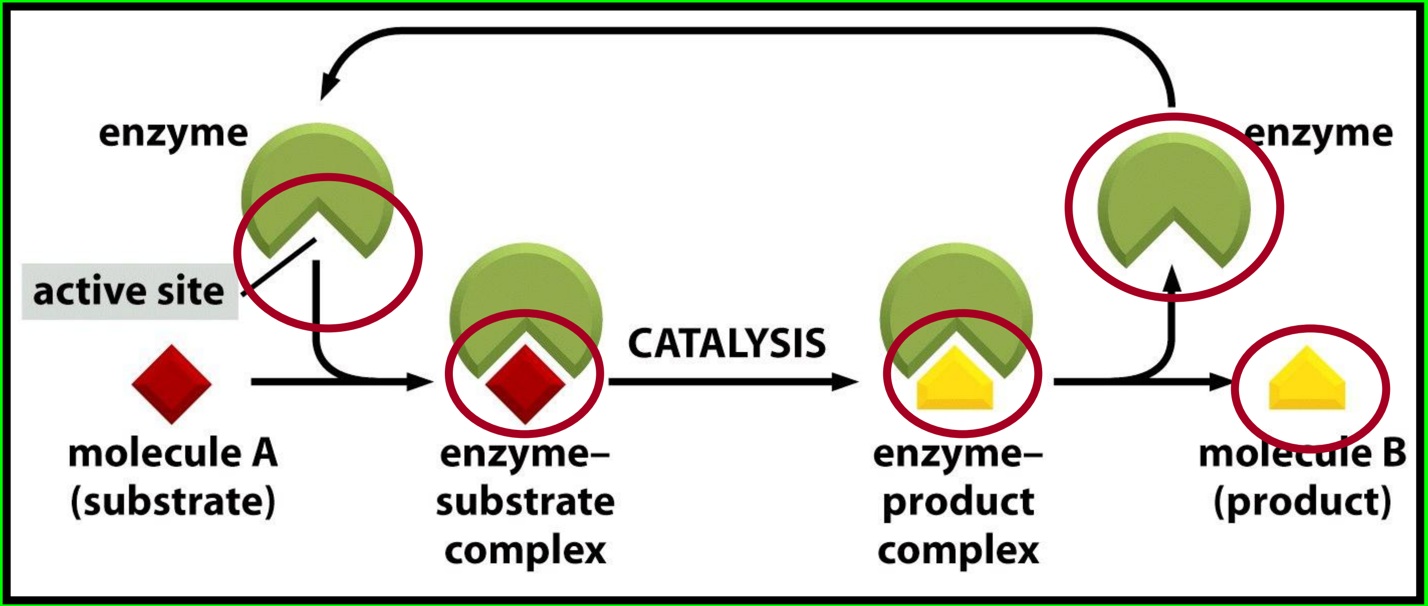
The four walls of the box represent the activation energy barriers

Floating ball analogy 3/3



A branching river with a set of barrier dams (yellow boxes) = series of enzyme-catalyzed reactions determines the exact reaction pathway

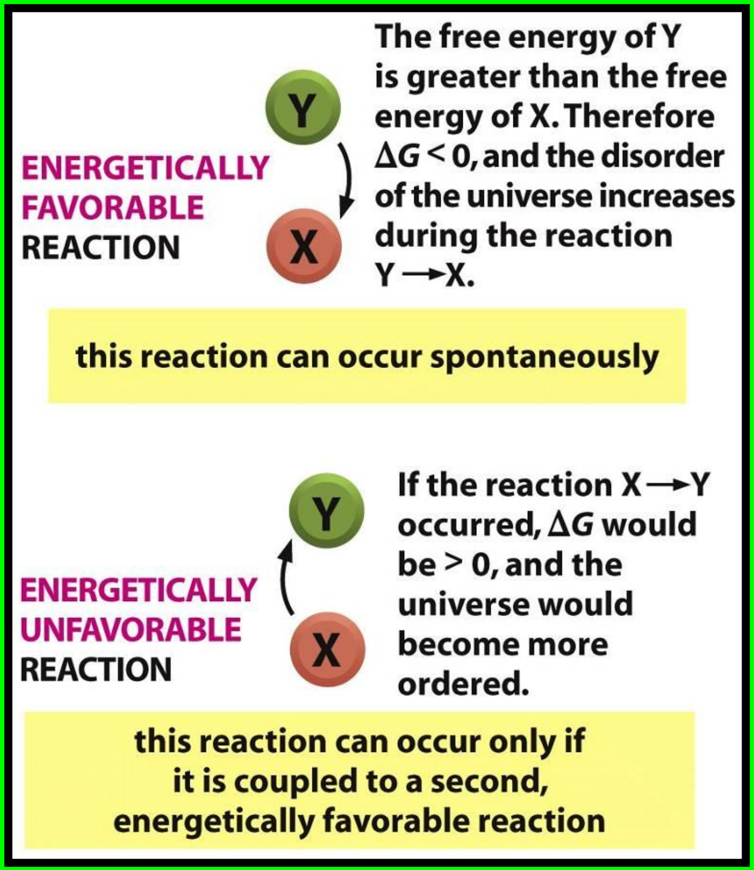
How enzymes work



- each enzyme has an active site to which substrate binds
- an enzyme-substrate complex is formed
- reaction in the active site producing enzyme-product complex
- the product is then released, allowing the enzyme to bind further substrate molecules

Free-energy change

The free-energy change for a reaction determines whether it can occur

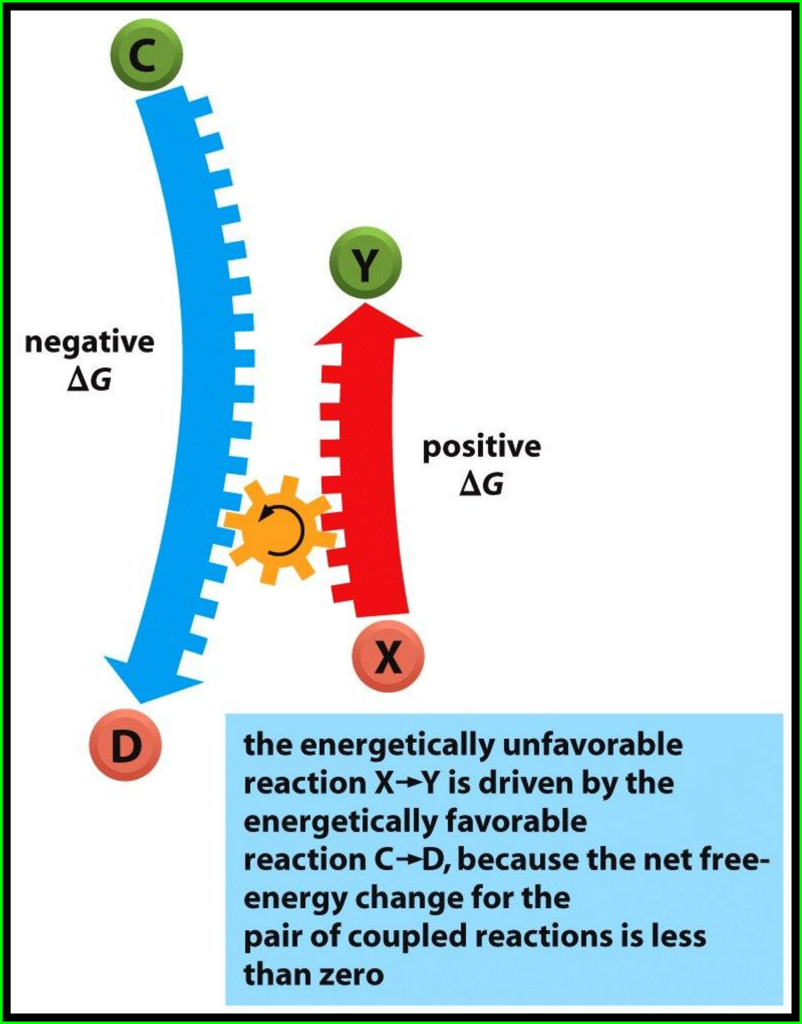


- **free energy is marked G**
- **change of G must be negative = negative ΔG**

Reaction with a positive ΔG are energetically unfavourable,

BUT !

Reaction coupling

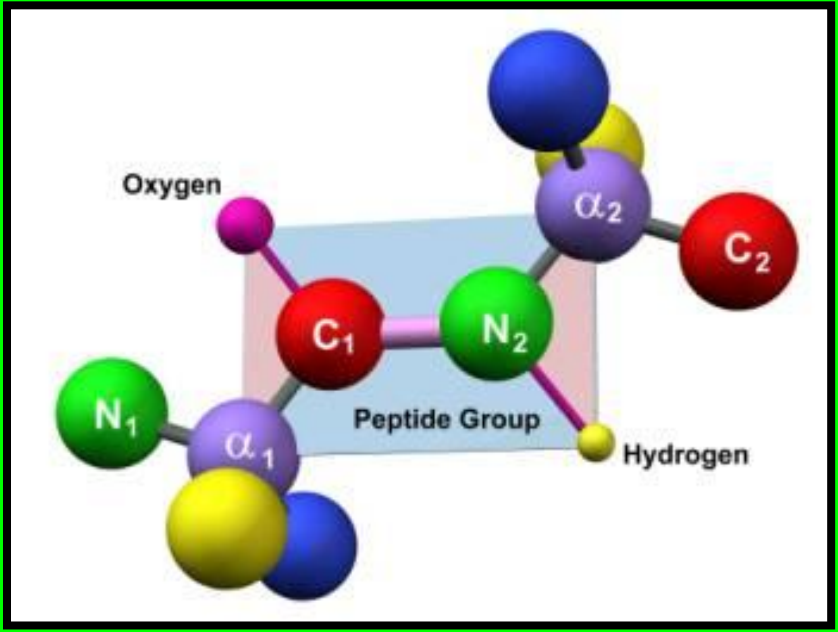


They are possible, if coupled with a second reaction with a negative ΔG

The entire process must be negative

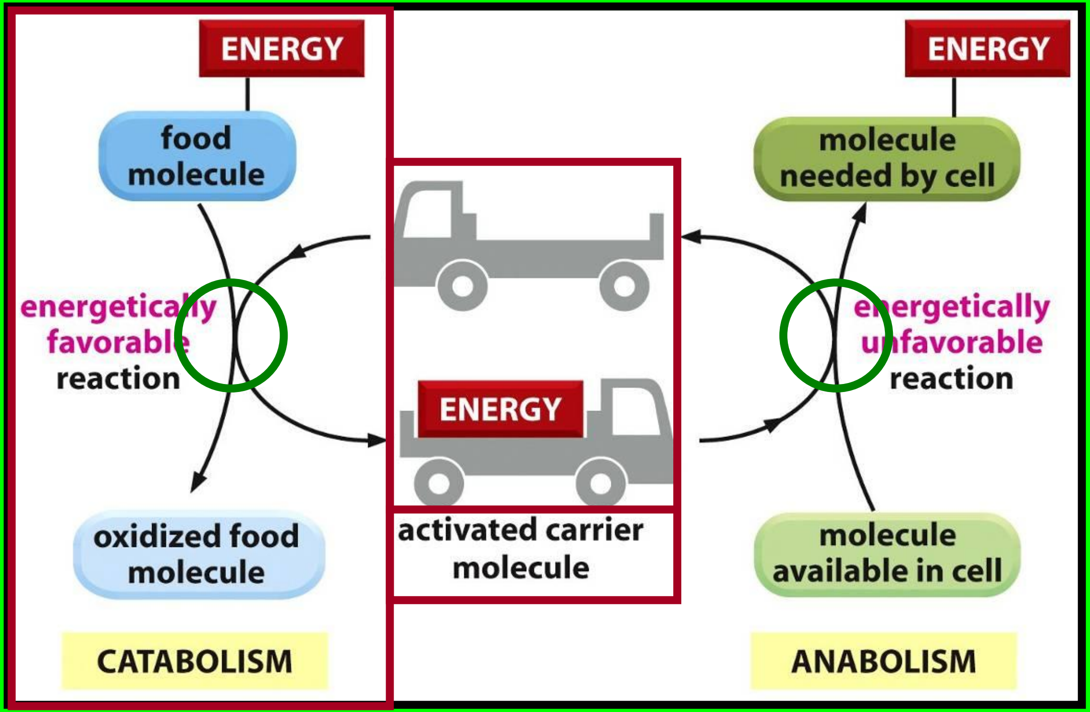
Example

Joining of two AAs create order in the universe



Enjoy „molecular biology“ lecture for explanation

Activated carrier molecules



- **energy released by oxidation of food must be stored – as a chemical bond energy in activated „carriers“**
- **the carriers difuse rapidly to the biosynthesis site**
- **energy in carriers is easily exchangeable**

Carrier molecules

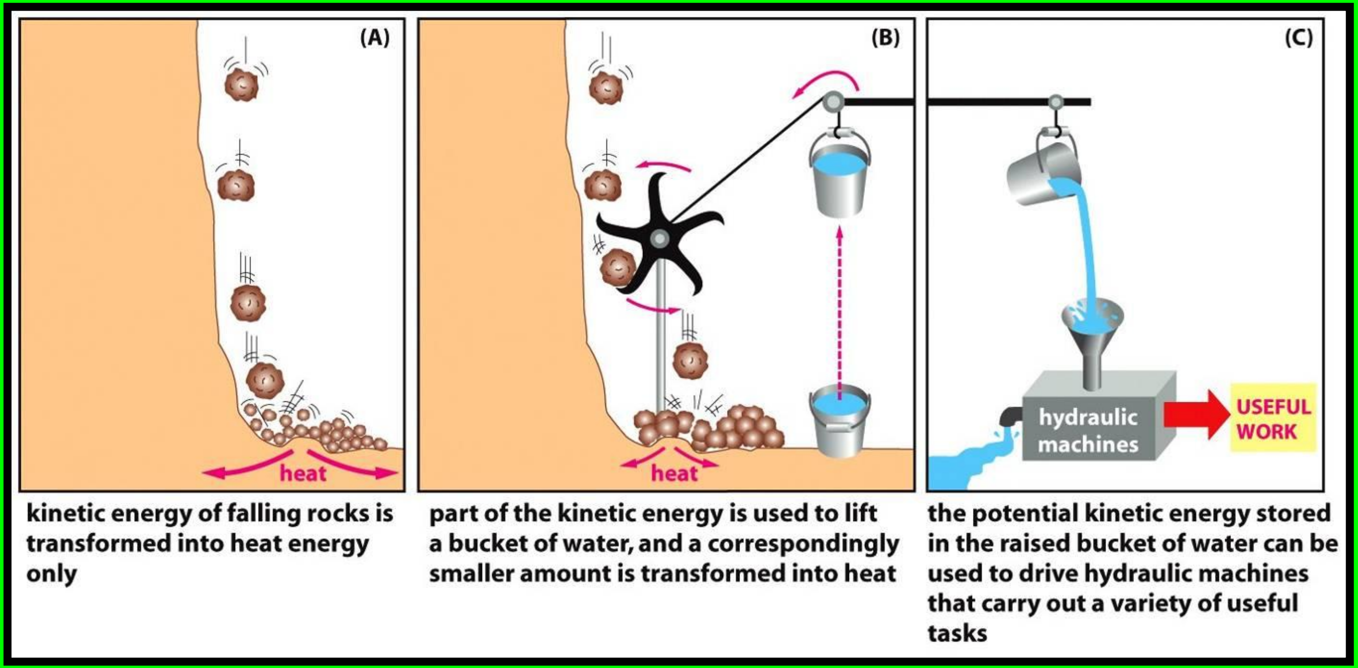
Activated carrier molecules are money to pay for reactions that otherwise could not take place

Adenosine triphosphate = ATP

Nicotinamide adenine dinucleotide (reduced) = NADH

Nicotinamide adenine dinucleotide phosphate (reduced) = NADPH

Principle of coupled chem. reaction

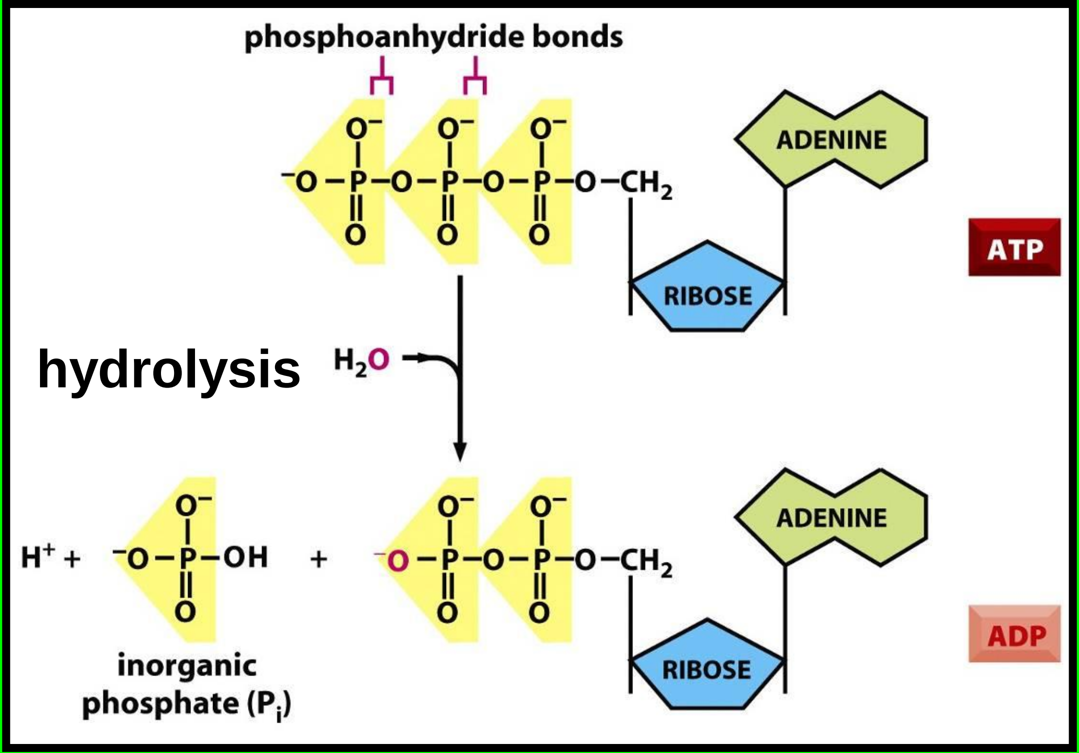


A = direct oxidation of glucose to CO_2 and water

B = coupled reaction is analogue of carrier molecule

C = carrier molecule is used in a variety of otherwise energetically unfavourable reactions

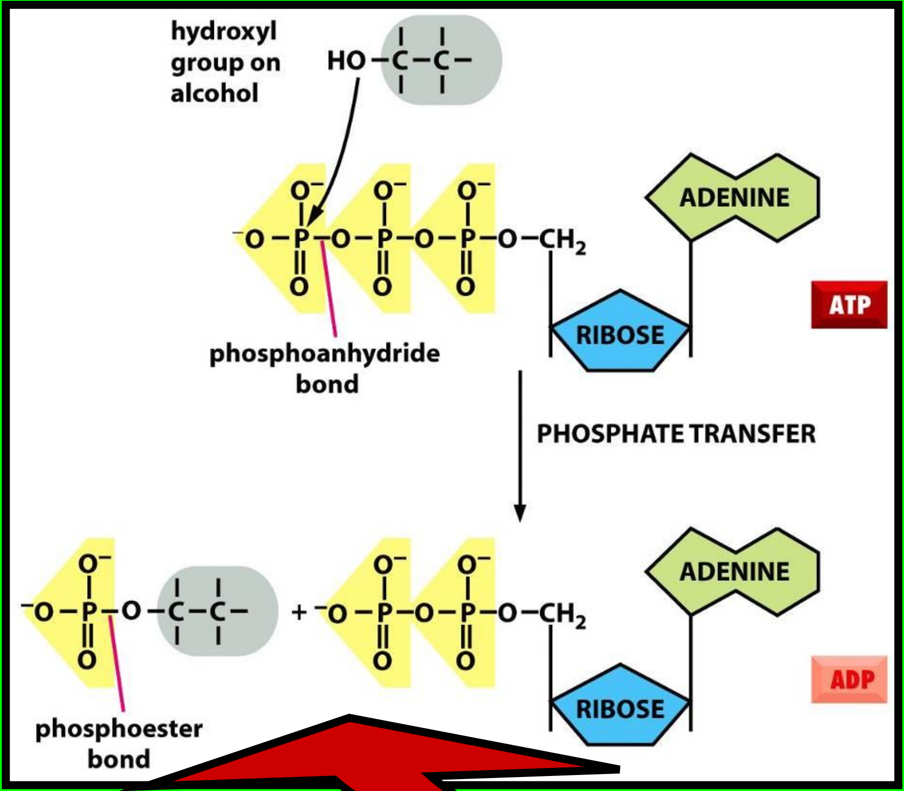
ATP is most widely used



The large negative ΔG

- **hydrolysis of the terminal phosphate of ATP yields 11 and 13 kcal/mole of usable energy**

Example of a phosphate transfer reaction



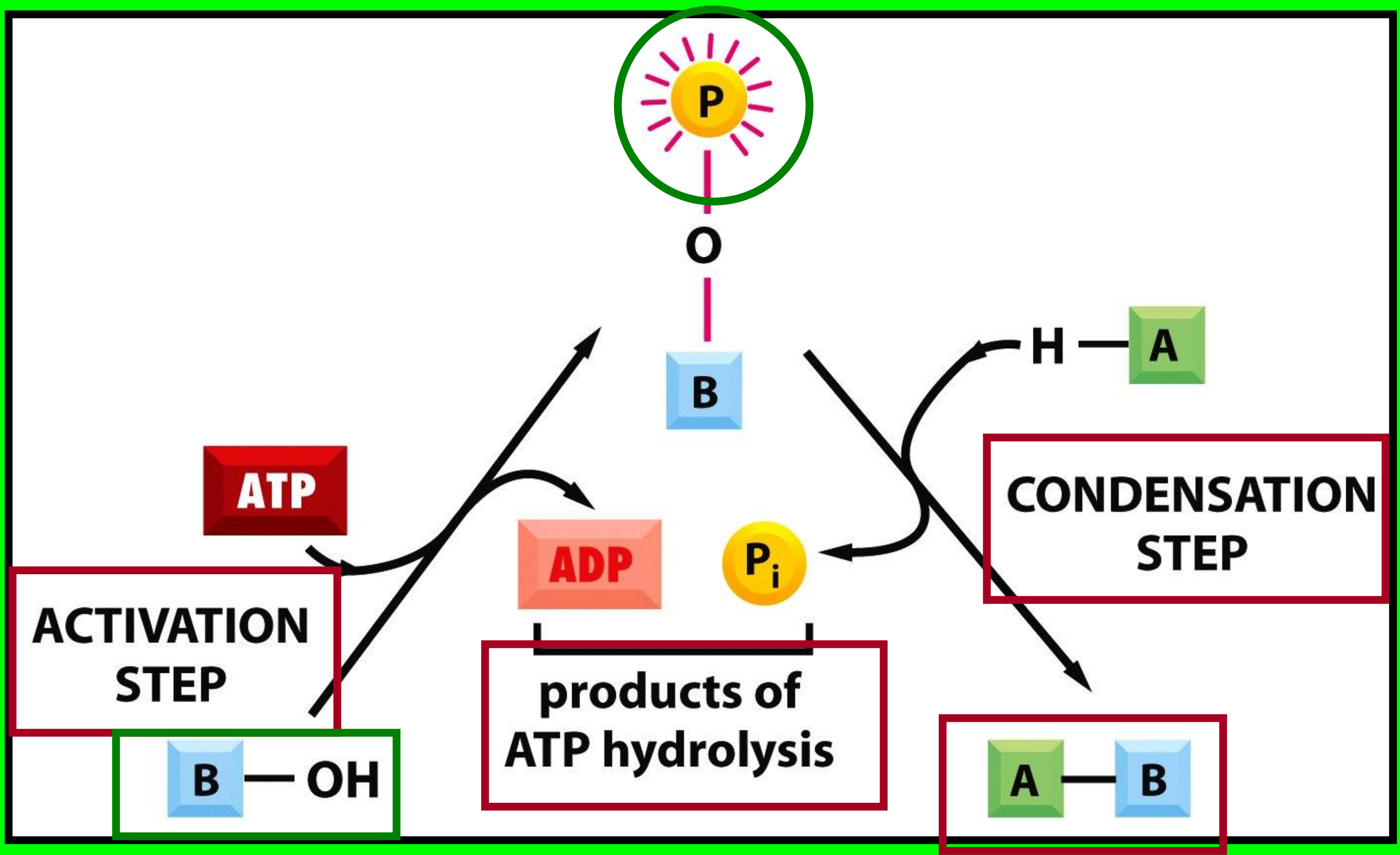
Transfer of the terminal phosphate in ATP to another molecule

↓

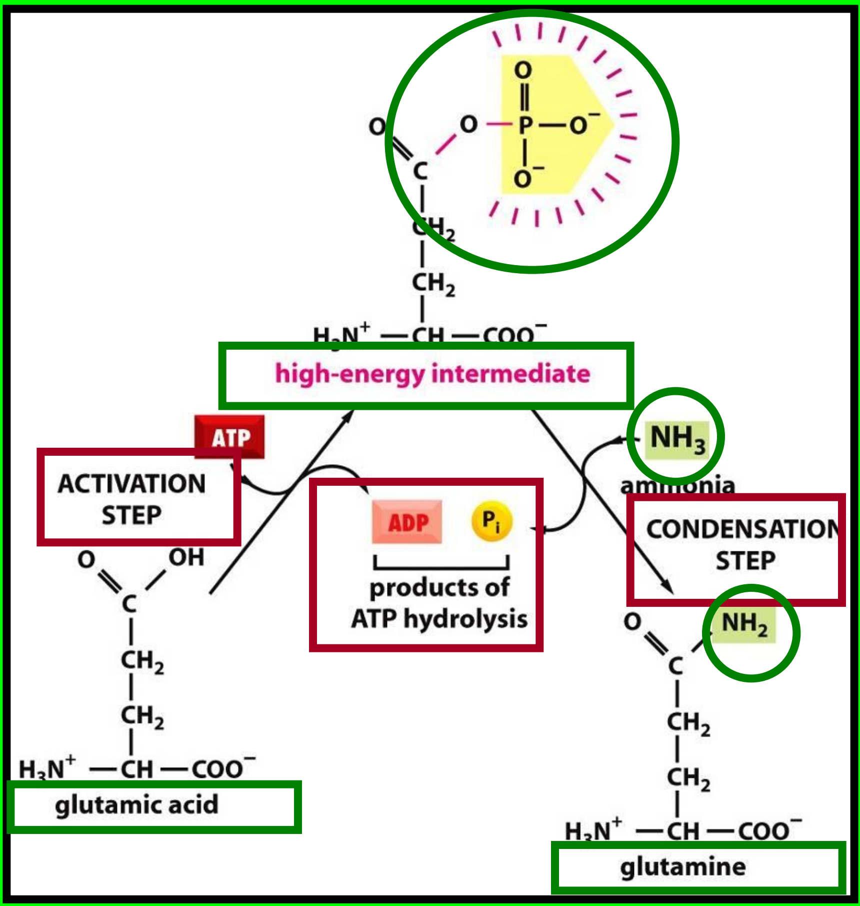
phosphorylation

Biosynthesis driven by ATP hydrolysis

Illustration of the formation of A-B in the condensation reaction

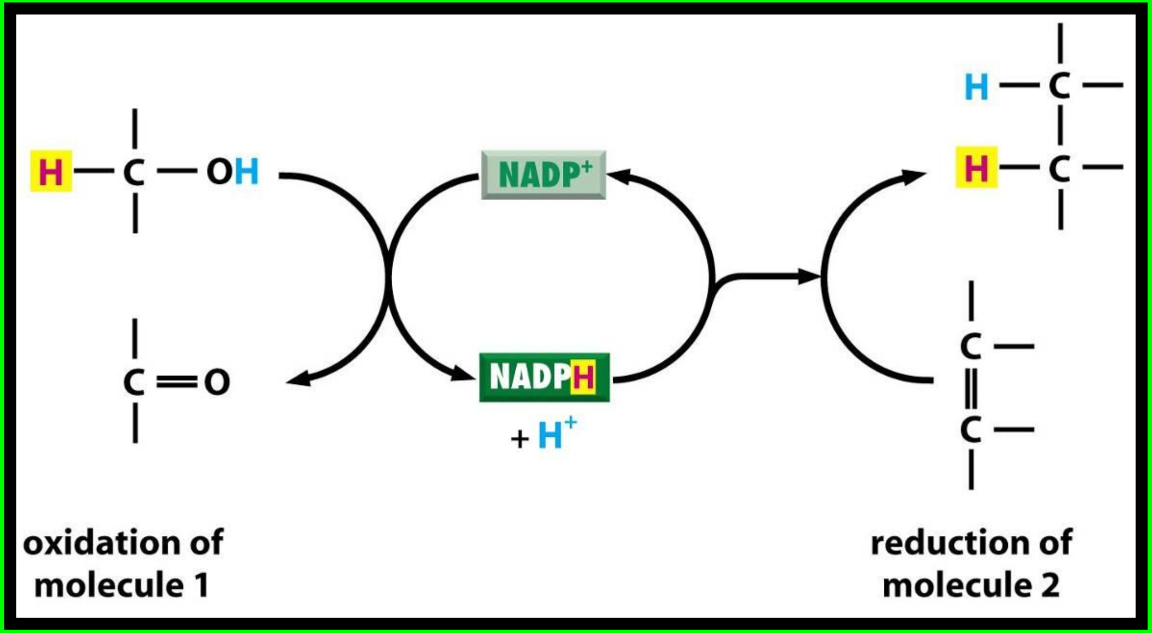


Glutamine biosynthesis



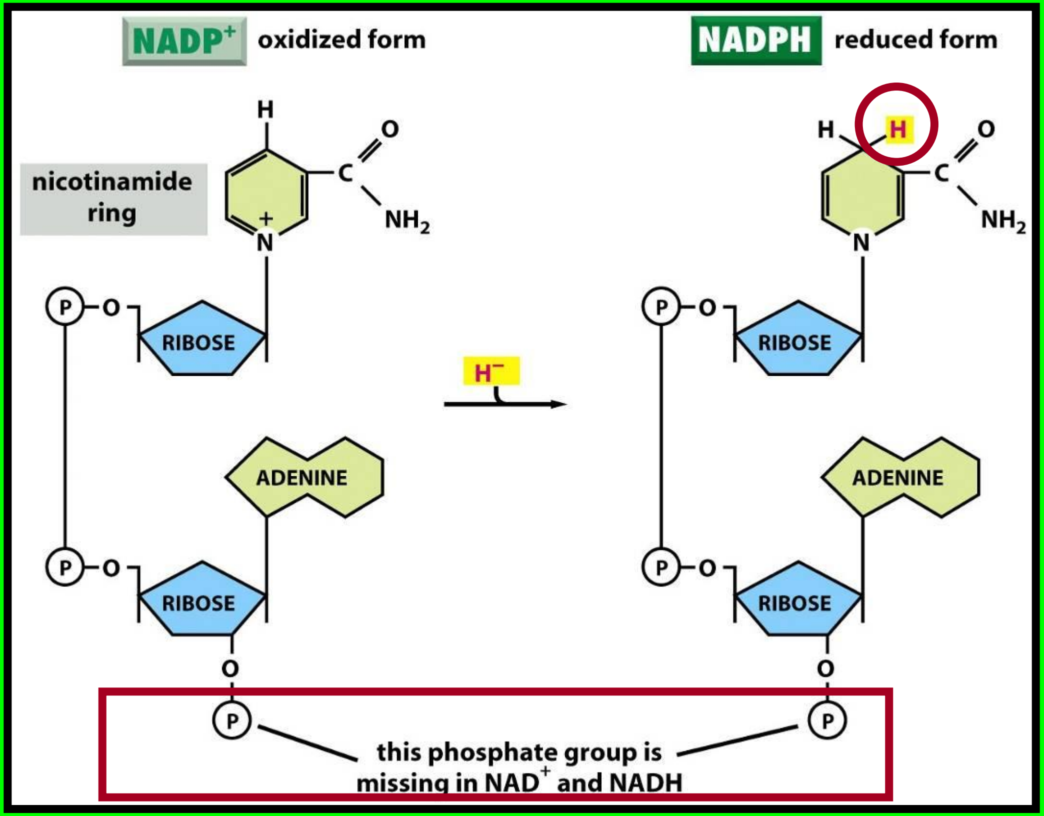
Catalysed by glutamine synthetase

NADPH, a carrier of electrons



- **produced in reactions of the general type (left) = two hydrogen atoms are removed from a substrate**
- **the oxidised form NADP+ receives one hydrogen plus one electron**
- **second proton is released into solution**
- **hydride ion has high energy, it can be easily transferred to other molecules (right)**

The structures of NADP+ and NADPH



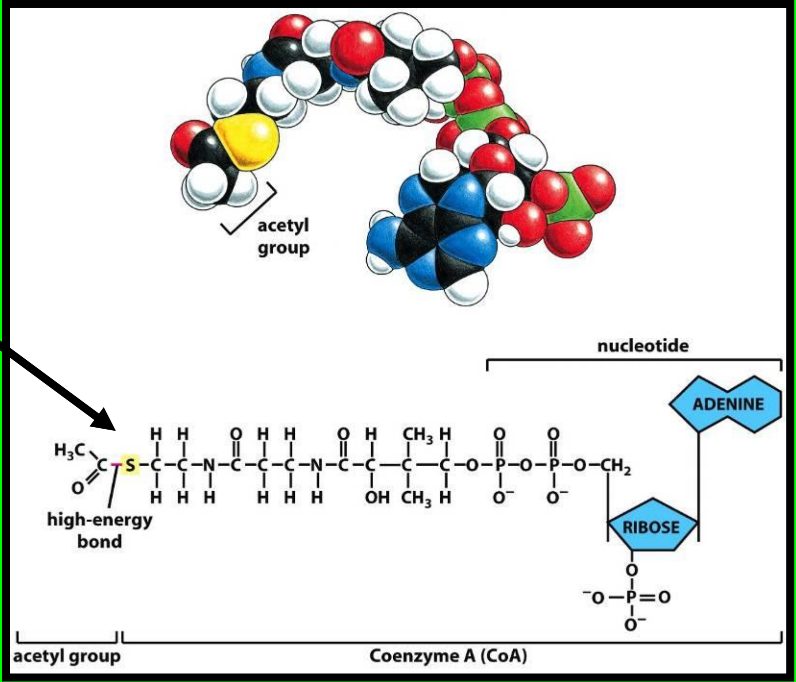
NAD+ and NADH are identical in structure to NADP+ and NADPH, respectively, except phosphate group

- **Nicotinamide ring accepts two electrons together with a proton forming NADPH**

Coenzyme A is also an carriers

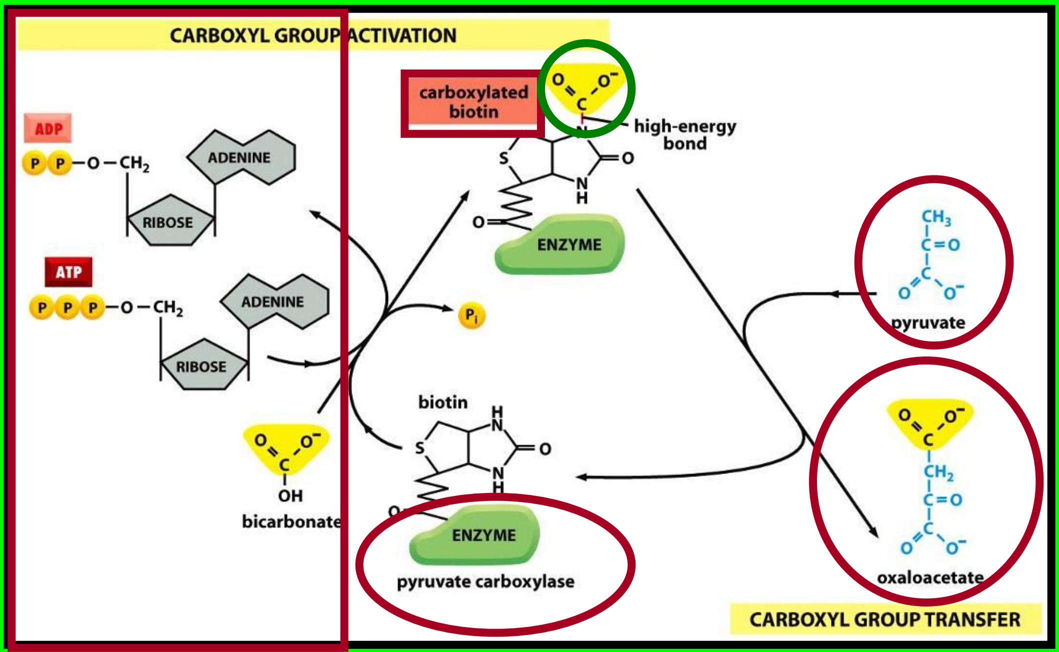
thioester bond to acetate

(macroergic)



- **carries an acetyl group**
- **in the activated form is known as „acetyl CoA“**
- **add two carbon units in the biosynthesis of larger molecules**

Carboxyl group transfer



Carboxylated biotin

Pyruvate carboxylase

- **transfer a carboxyl group in the production of oxaloacetate, a molecule needed for the citric acid cycle**
- **the acceptor molecule is pyruvate**
- **synthesis of carboxylated biotin requires ATP !**

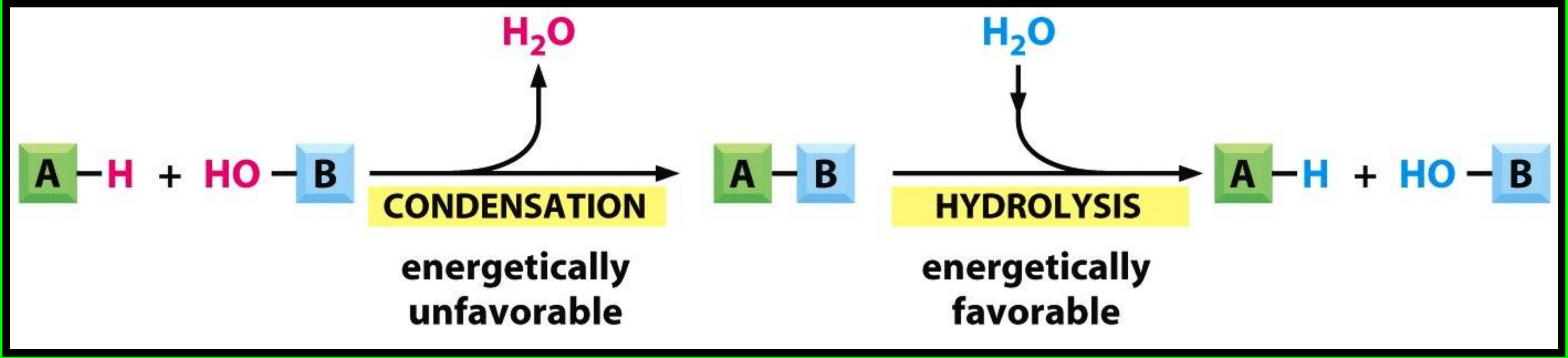
Other activated carriers

Activated carrier	Group carried in high-energy linkage
ATP	Phosphate
NADH, NADPH, $FADH_2$	Electrons and hydrogen
Acetyl CoA	Acetyl group
Carboxylated biotin	Carboxyl group
S-Adenosylmethionine	Methyl group
Uridin diphosphate glucose	Glucose

The synthesis of polymers is driven by ATP hydrolysis

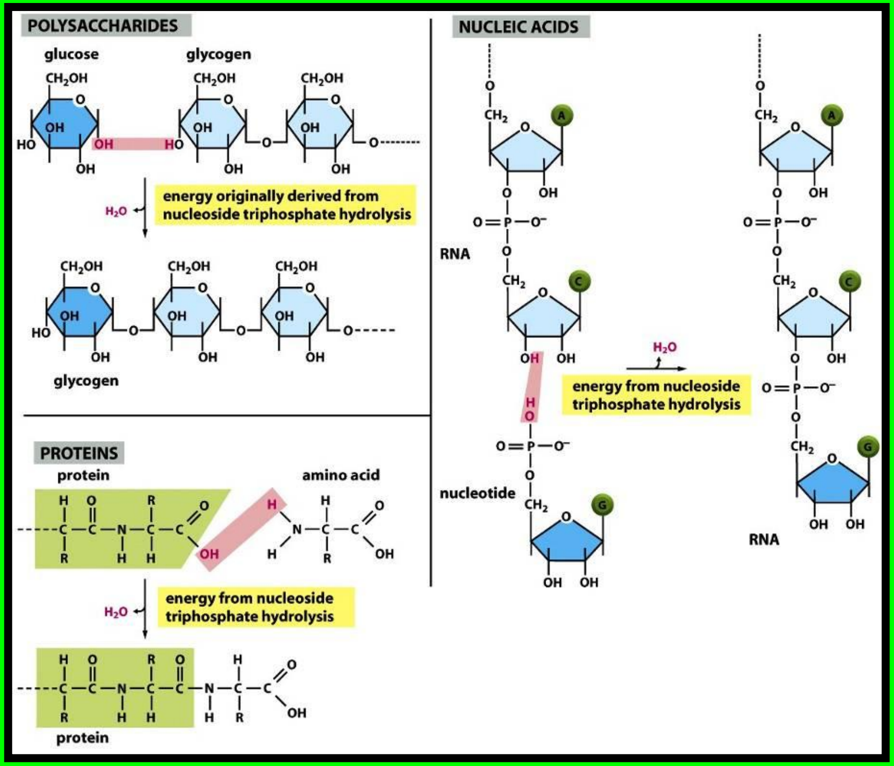
Condensation and hydrolysis

- **The macromolecules of the cell are polymers formed from monomers by a condensation**
- **The macromolecules are broken down by hydrolysis**



The condensation reactions are all energetically unfavourable

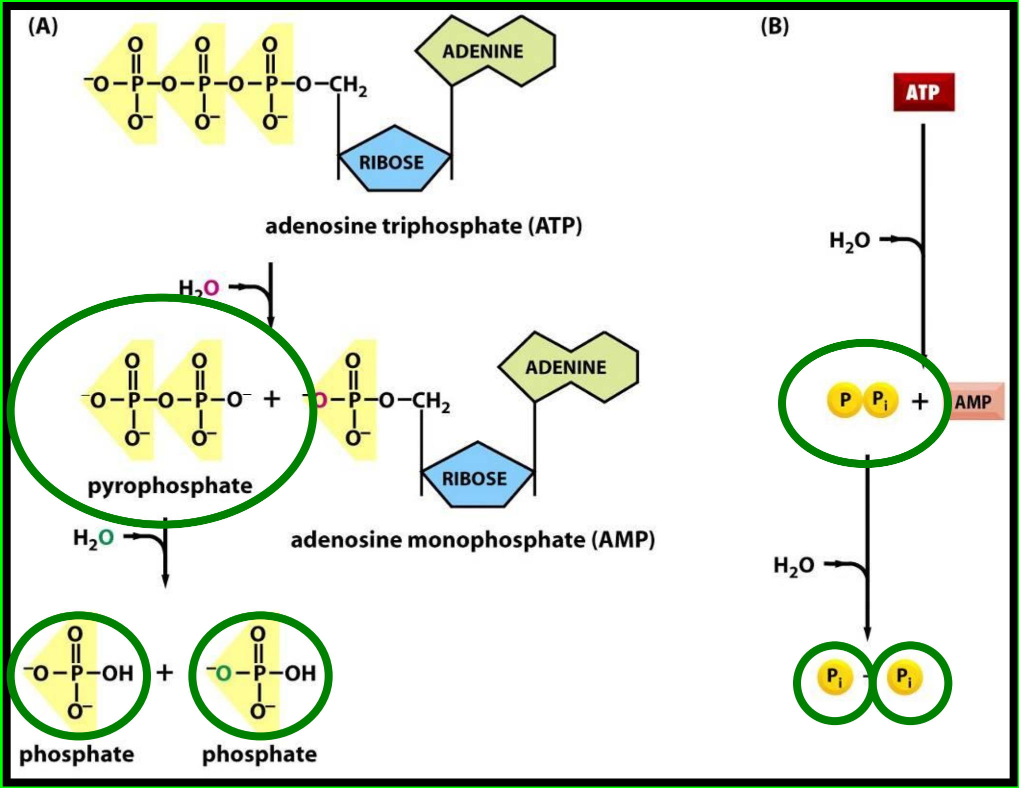
Synthesis of macromolecules



The condensation step depends on energy from NTP hydrolysis

The nucleic acids, proteins, and polysaccharides are produced by the repeated addition of a monomer onto one end of growing chain

Alternative pathway of ATP hydrolysis

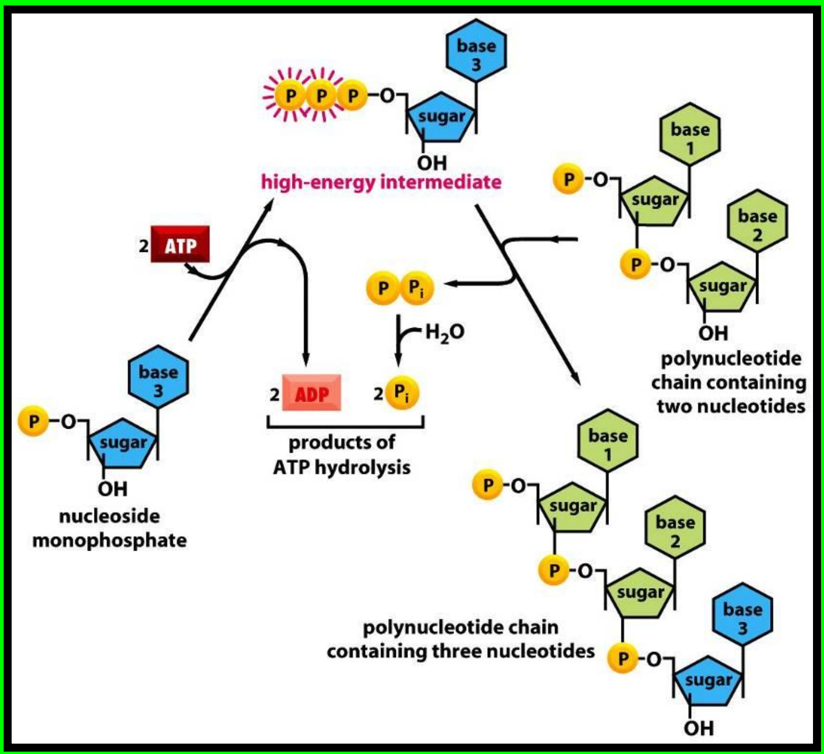


Pyrophosphate is first formed

and then hydrolysed

- **this route release about twice as much free energy**
- **it forms AMP instead of ADP**

Synthesis of RNA or DNA



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- **multistep process driven by ATP hydrolysis**

Control of metabolism

#***Types of control mechanisms***

Allosteric regulation

Feedback loop

Cooperation

Enzyme localisation

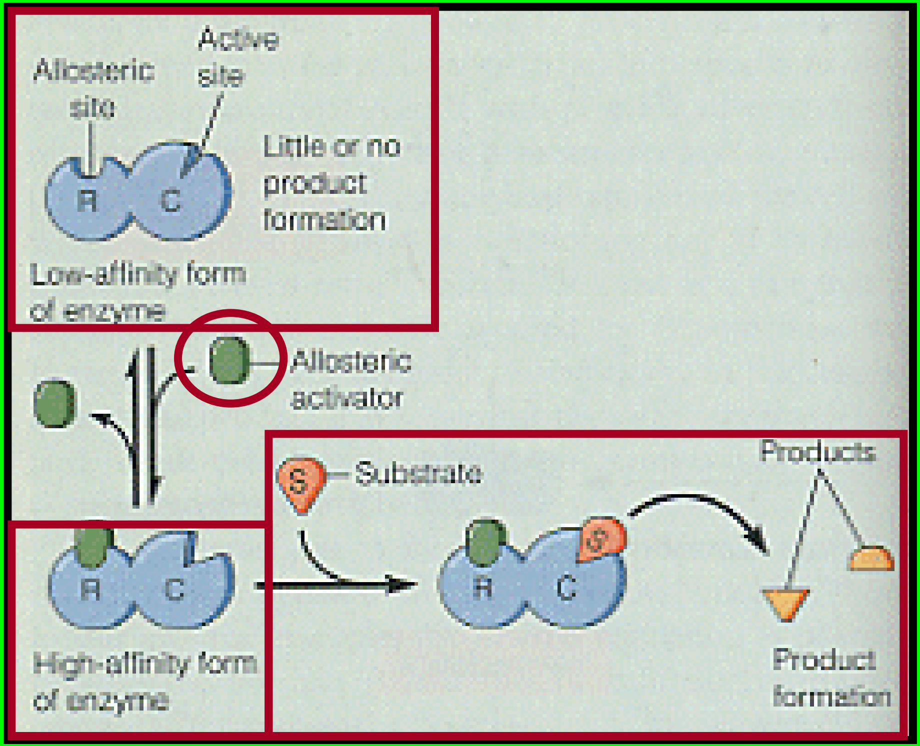
Allosteric regulation

1) allosteric activation

2) allosteric inhibition

http://www.mindcreators.com/DevelopmentalSim/ProteinRegulators.htm

Allosteric activation

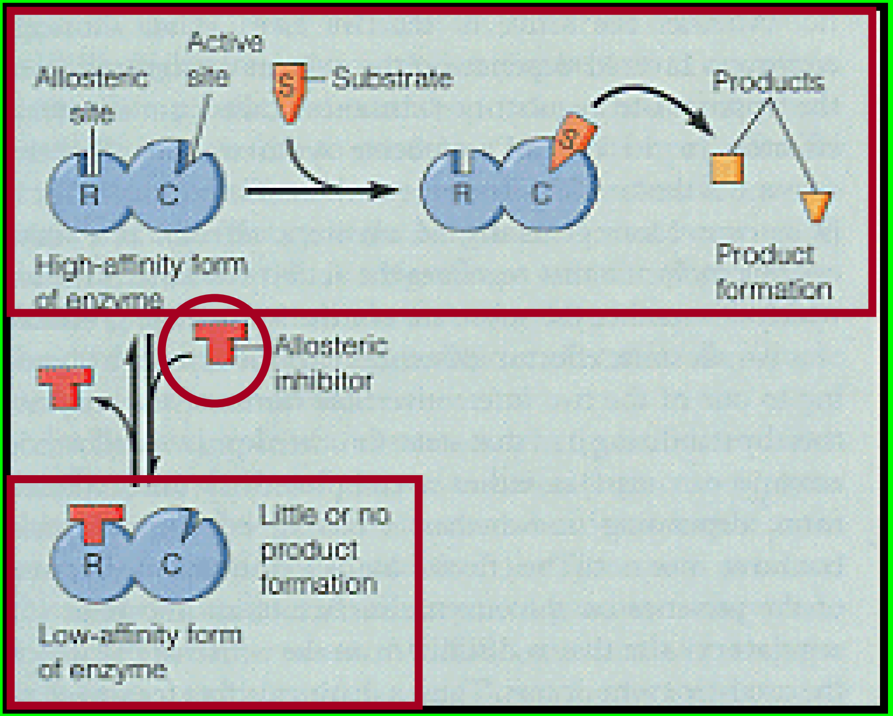


An enzyme subject to allosteric activation is inactive in its uncomplexed form, which has a low affinity to its substrate

Binding of an allosteric activator (green) stabilizes the enzyme in its high-affinity form,

resulting in enzyme activity

Allosteric inhibition



An enzyme subject to allosteric inhibition is active in its uncomplexed form, which has a high affinity to its substrate (S)

Binding of an allosteric inhibitor (red) stabilizes the enzyme in its low-affinity form, resulting in little or no activity

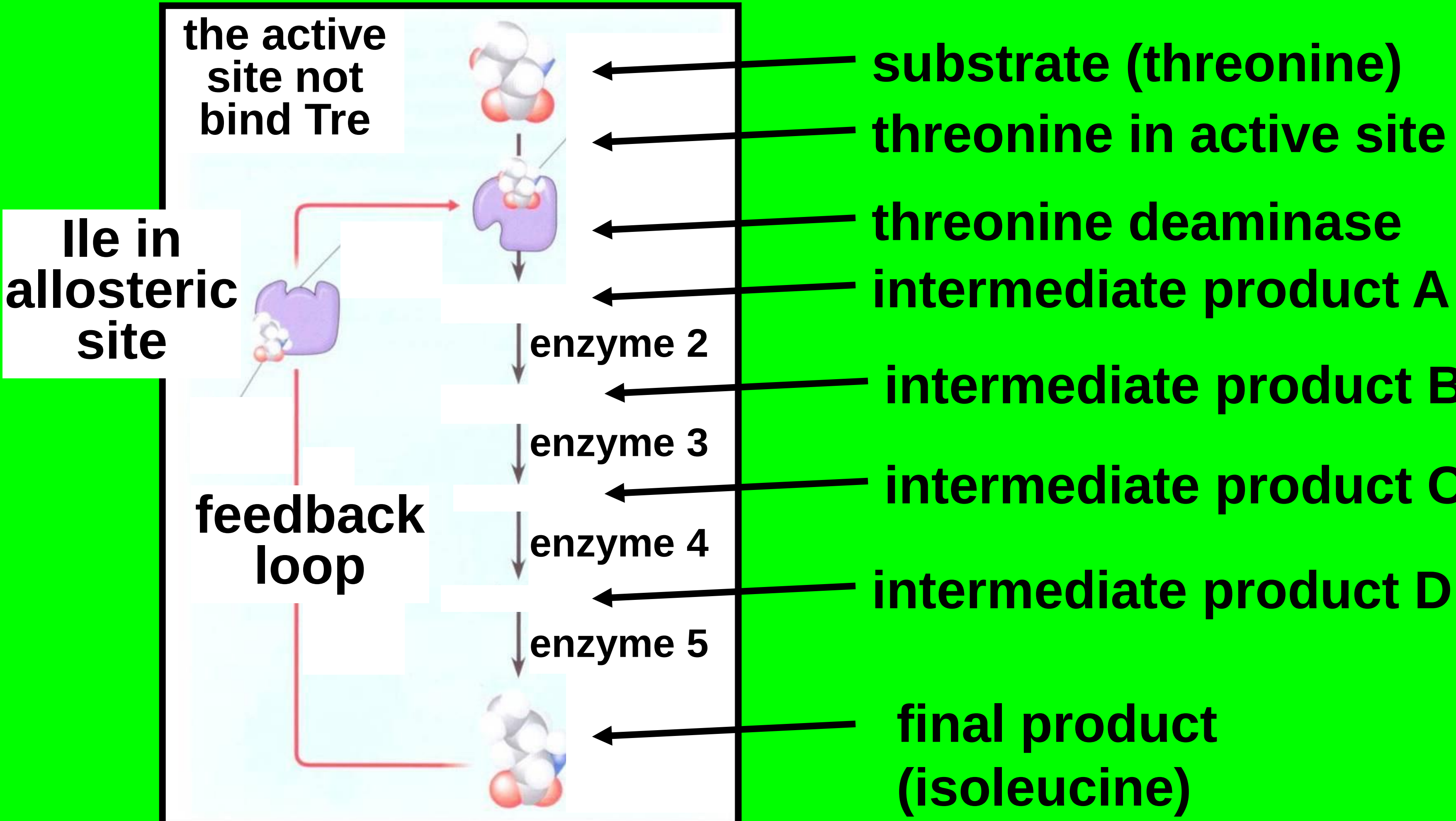
Feedback loop

The metabolic pathway is inhibited by its own product

ATP inhibition in katabolic metabolic pathways

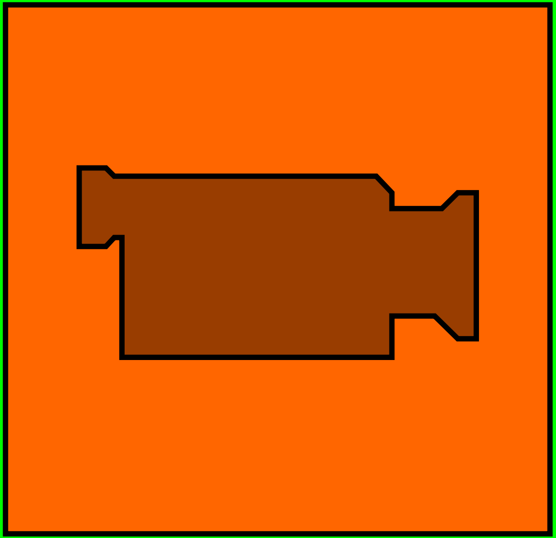
Anabolic metabolic pathways – aminoacids synthesis

Feedback loop



Feedback loop

Feedback Inhibition of Biological Pathways.wmv

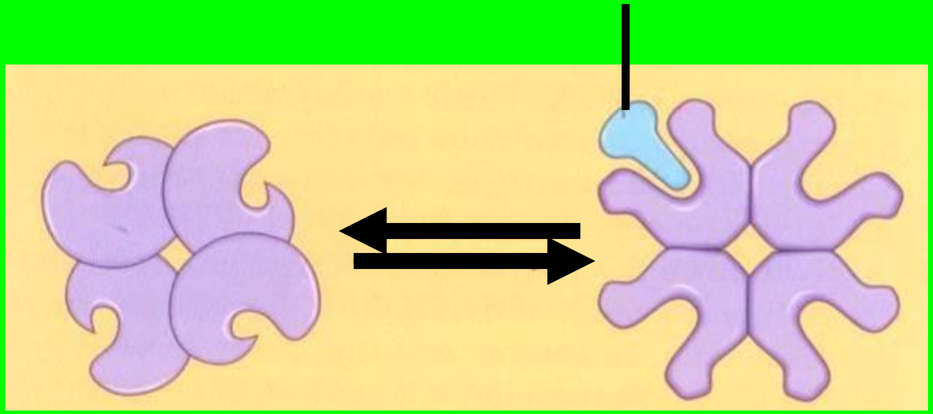


Cooperation

Similar to allosteric activation

Substrate molecules can stimulate enzyme

substrate



nonactive enzyme

active enzyme

Substrate activate conformational changes in all subunits of nonactive enzyme

Enzyme localisation

- **Internal cellular structure is responsible for metabolic pathways separation**
- **Multienzyme complexes guarantee the correct order of individual reactions**
- **Some enzymes and enzyme complexes are build in membranes**
- **Other are in solutions inside organelles**

The typical example – respiratory enzymes in mitochondria

Gene expression regulation

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Cell respiration

Cells need energy

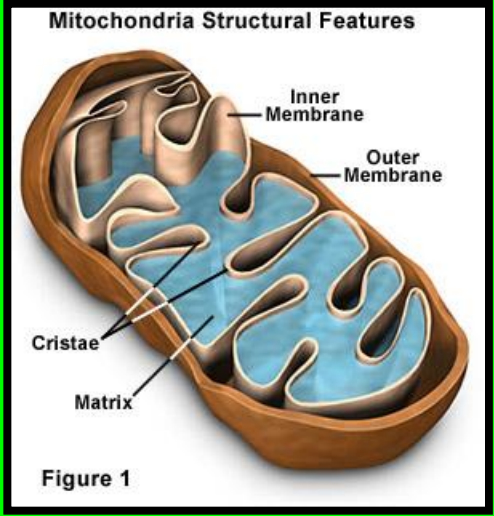
Prokaryotic cells produce energy (ATP) in their plasma membrane

So, what the eukaryotic plasma membrane does?

Plasma membrane in eukaryotic cells is reserved for the transport processes

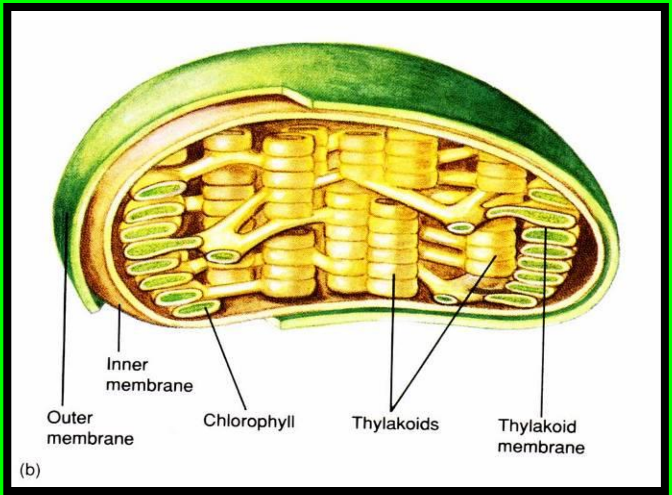
Eukaryotes instead use the specialized membranes inside *energy-converting organelles* to produce most of their ATP

Energy-converting organelles



mitochondria

- present in the cells of virtually all eukaryotic organisms

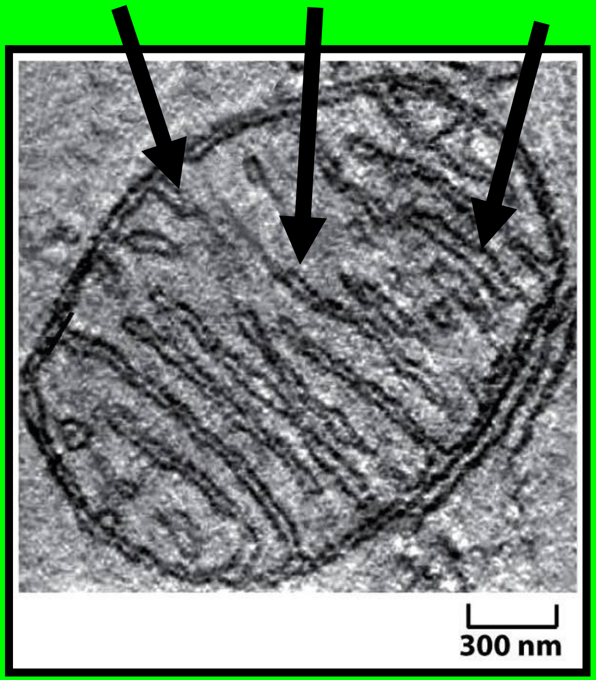


plastids

- most notably chloroplasts which occur only in plants and algae

Internal membranes for ATP

Mitochondria and chloroplasts contain large amount of internal membrane



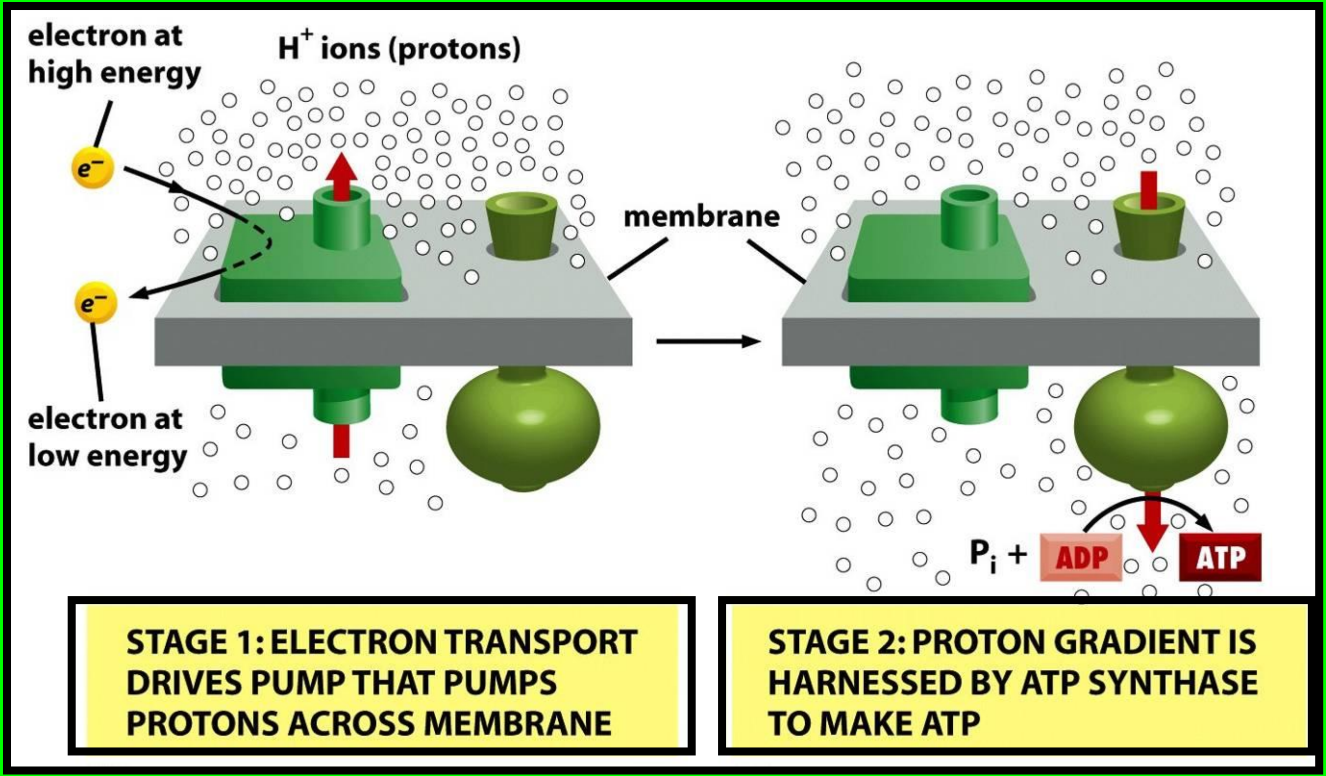
This internal membrane provides the framework for an elaborate set of <u>electron-transport processes</u> that produce most of the cell´s ATP

Chemiosmotic coupling

Common pathway used by mitochondria, chloroplast, and prokaryotes to harness energy for biological purposes

The term „chemiosmotic coupling“ reflect a link between the chemical bond-forming reaction that generate ATP („chemi“) and membrane-transport processes („osmotic“)

The coupling process

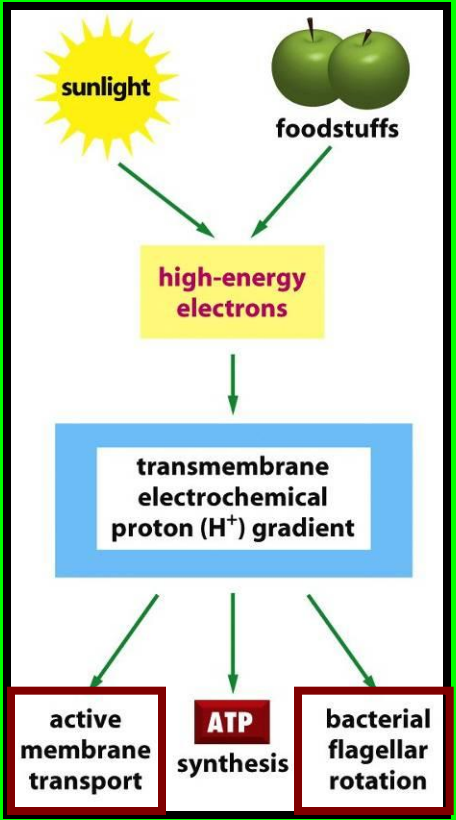


electrochemical proton gradient

ATP synthase

Other protein machine

The electrochemical proton gradient also drive other membrane-embedded protein machines



- **<u>in eukaryotes</u> special proteins couple H^+ flow t<u>o transport metabolites</u> in and out of the organelles**
- **<u>in bacteria</u> besides ATP synthesis and transport also drives rapid <u>rotation of the bacterial flagellum</u>**

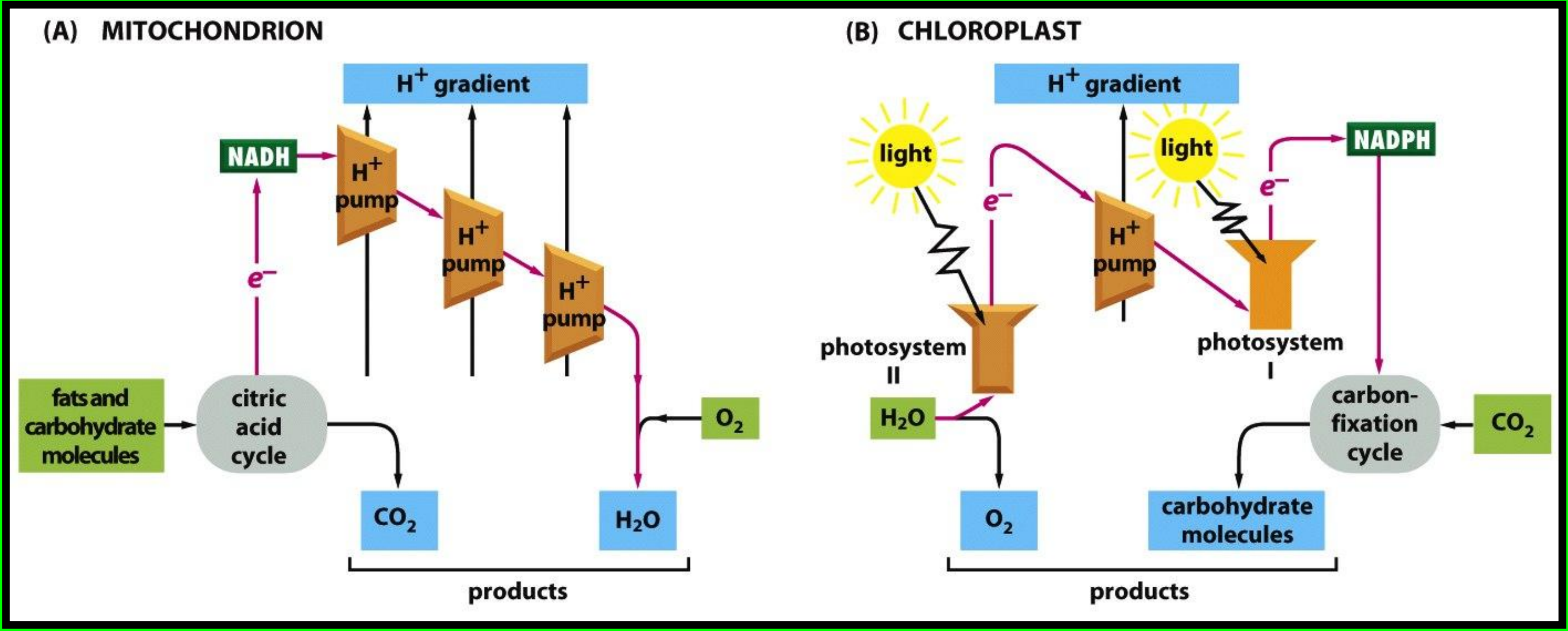
Electron transport chain

Is formed by the entire set of proteins in membrane, together with the small molecules involved in the orderly sequence of electron transfers

- **Electrons are transferred between one site and another by diffusible molecules that can pick up electrons at one location and deliver them to another**

- **For mitochondria, the first of these electron carriers is NAD^+**

Electron-transport process



Mitochondria convert energy from chemical fuels

Chloroplasts convert energy from sunlight

Mitochondria-chloroplast differences

Mitochondria

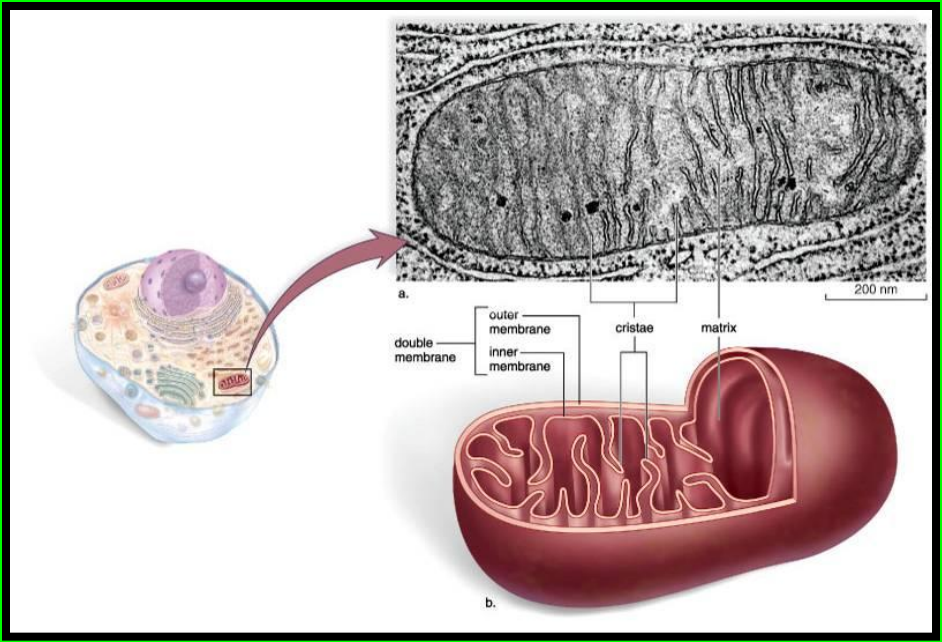
- convert energy from chemical fuels
- drive electron transfer from carbohydrate to CO_2 and water

Chloroplast

- convert energy from sunlight
- drive electron transfer from H_2O to carbohydrate

Inputs for mitochondrion are products of the chloroplasts

The mitochondrion



Bounded by double membrane

Cristae **– infoldings of inner membrane that encloses matrix**

Matrix **– inner semifluid containing respiratory enzymes**

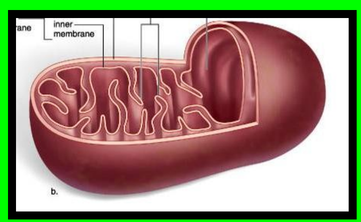
The mitochondrion function

Glucose

glycolysis ↓ → ATP

Pyruvate

↓



15x more ATP

↓ + O_2 → ATP ATP ATP ATP ATP

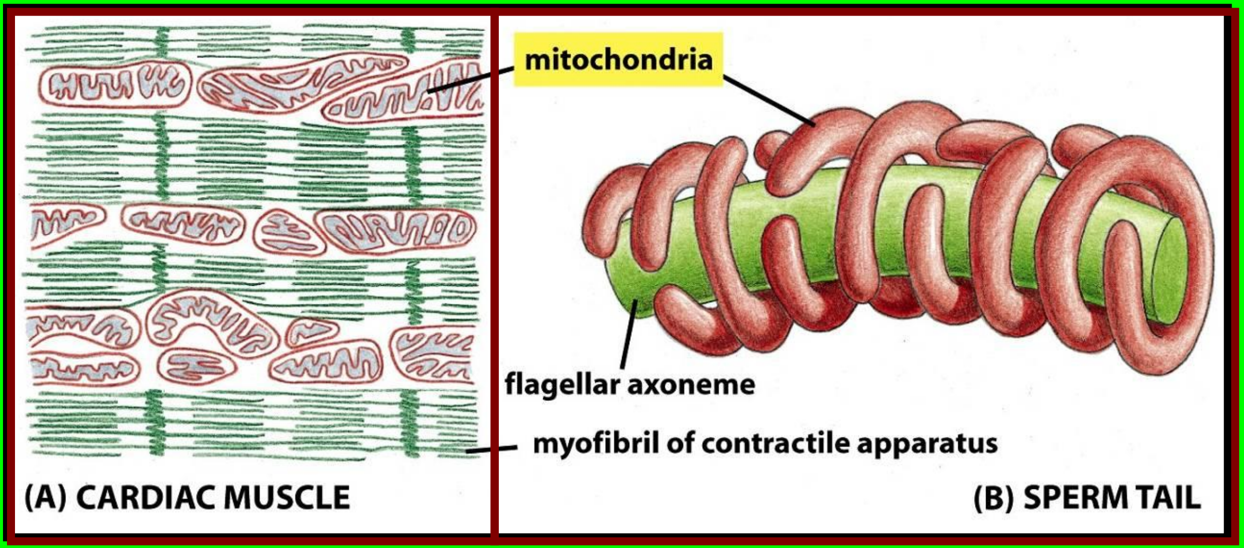
$CO_2 + H_2O$

Localization of mitochondria

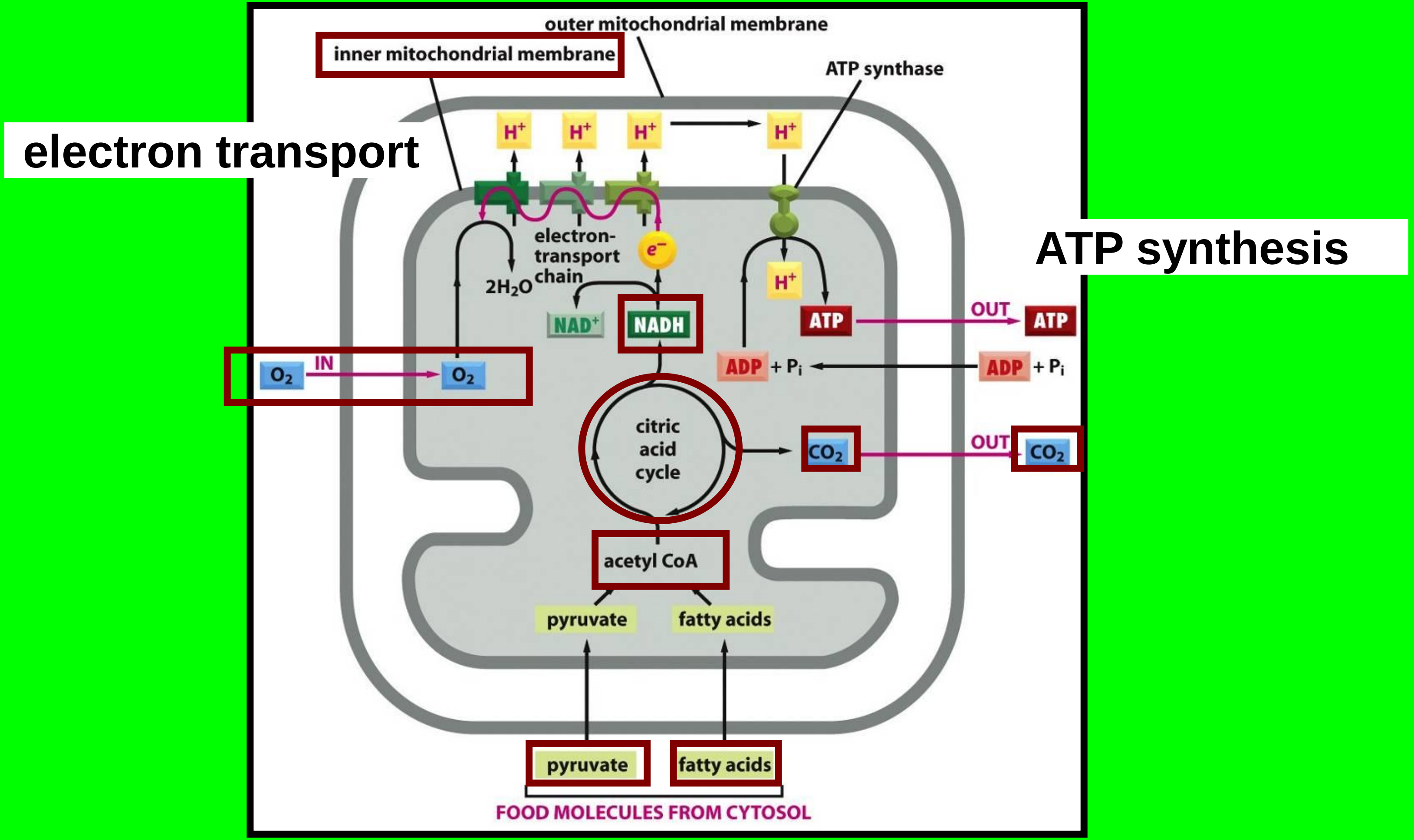
- in some cells form long moving filaments
- in others they remain fixed in one position

Near sites of high ATP utilization

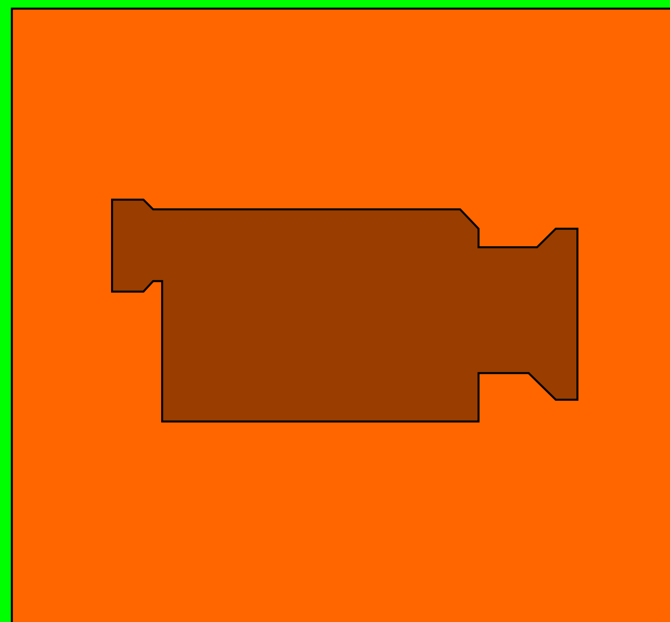
- packed between myofibrils in a cardiac muscle cell
- wrapped tightly around the flagellum in a sperm



Citric acid cycle



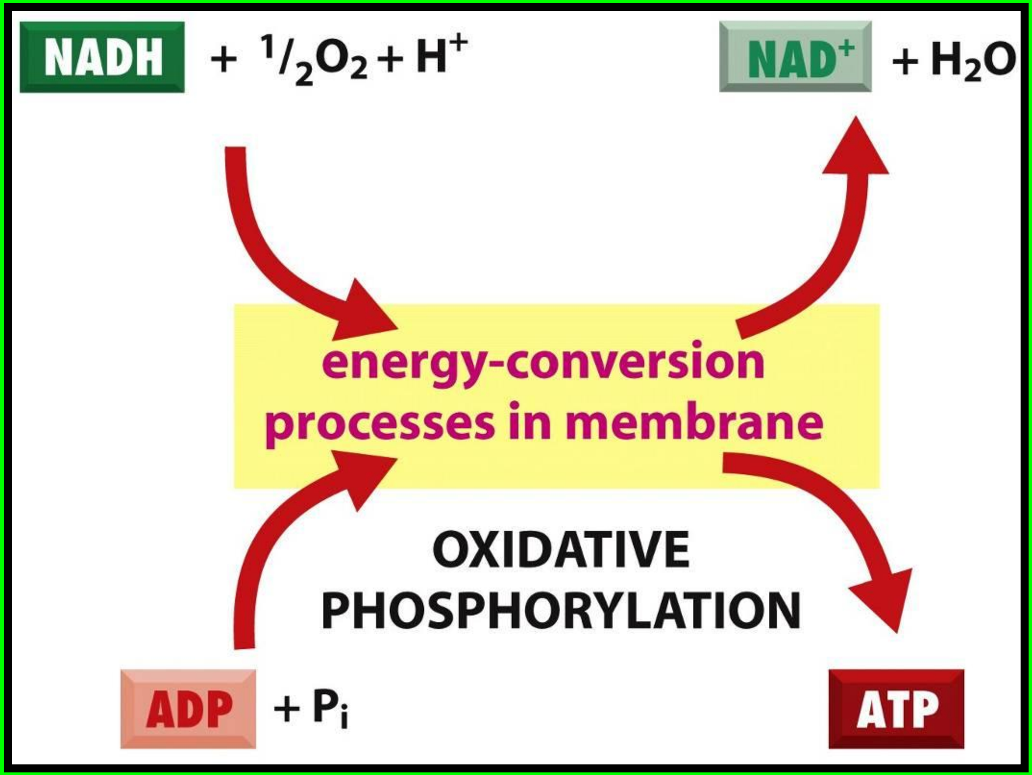
Citric acid cycle



Molecular Biology of the Cell/Media/Animation/2.5 Citric Acid Cycle

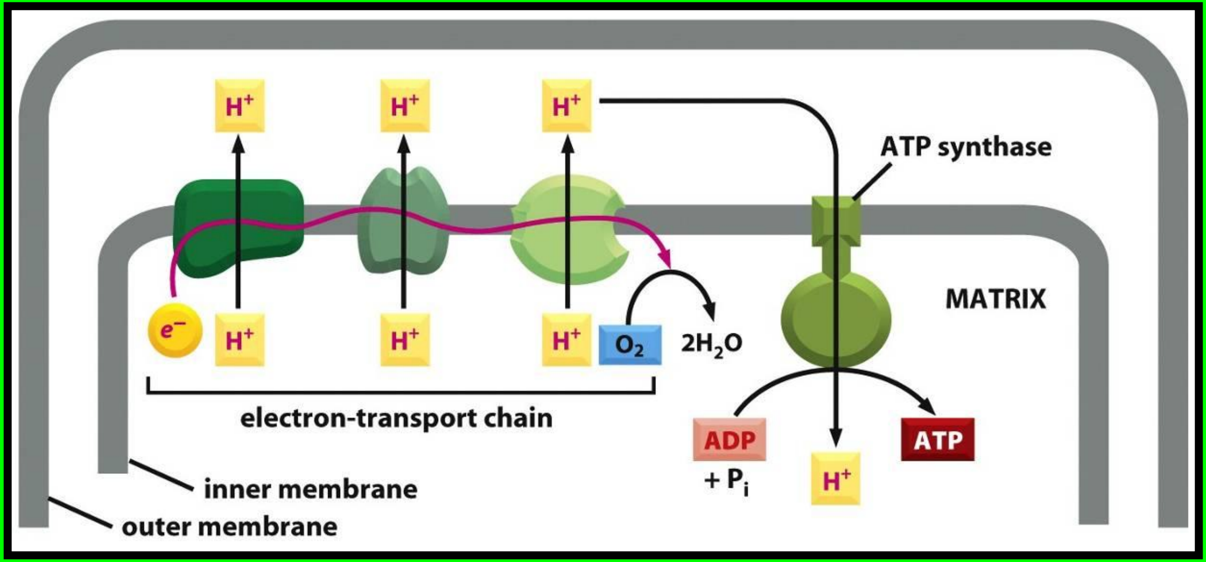
Oxidative phosphorylation

- **the process of ATP production from ADP + Pi**
- **it is performed on <u>inner</u> mitochondrial membrane**

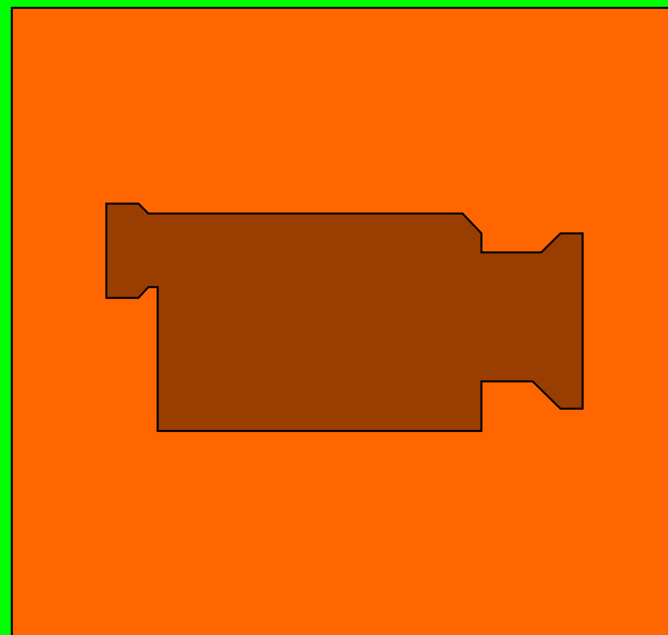


The general mechanism

- high energy electron pass along the electron-transport chain
- three respiration enzyme complexes pump H^+ out
- the resulting electrochemical proton gradient across the inner membrane drives H^+ back through ATP synthase
- the enzyme complex synthesize ATP in matrix



ATP synthase – a molecular turbine



Molecular Biology of the Cell/Media/animation/14.4 ATP Synthase

Photosynthesis

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

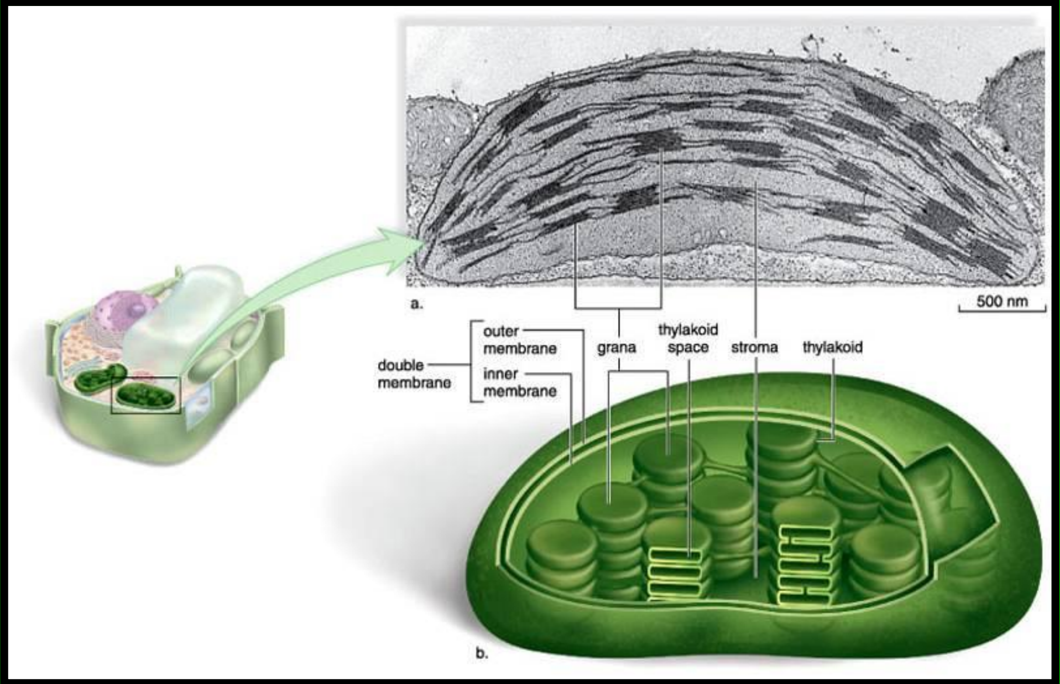
The chloroplast

Chloroplasts are organelles in which photosynthesis occur

- **They perform photosynthesis during the daylight hours**
- **The products of photosynthesis, NADPH and ATP are used to production of many organic molecules**

- **Based on biochemical and genetic evidence the chloroplasts are suggested as descendant of oxygen-producing photosynthetic bacteria that were endocytosed and lived in symbiosis with primitive eukaryotic cells**

The chloroplast structure



Green due to chlorophyll

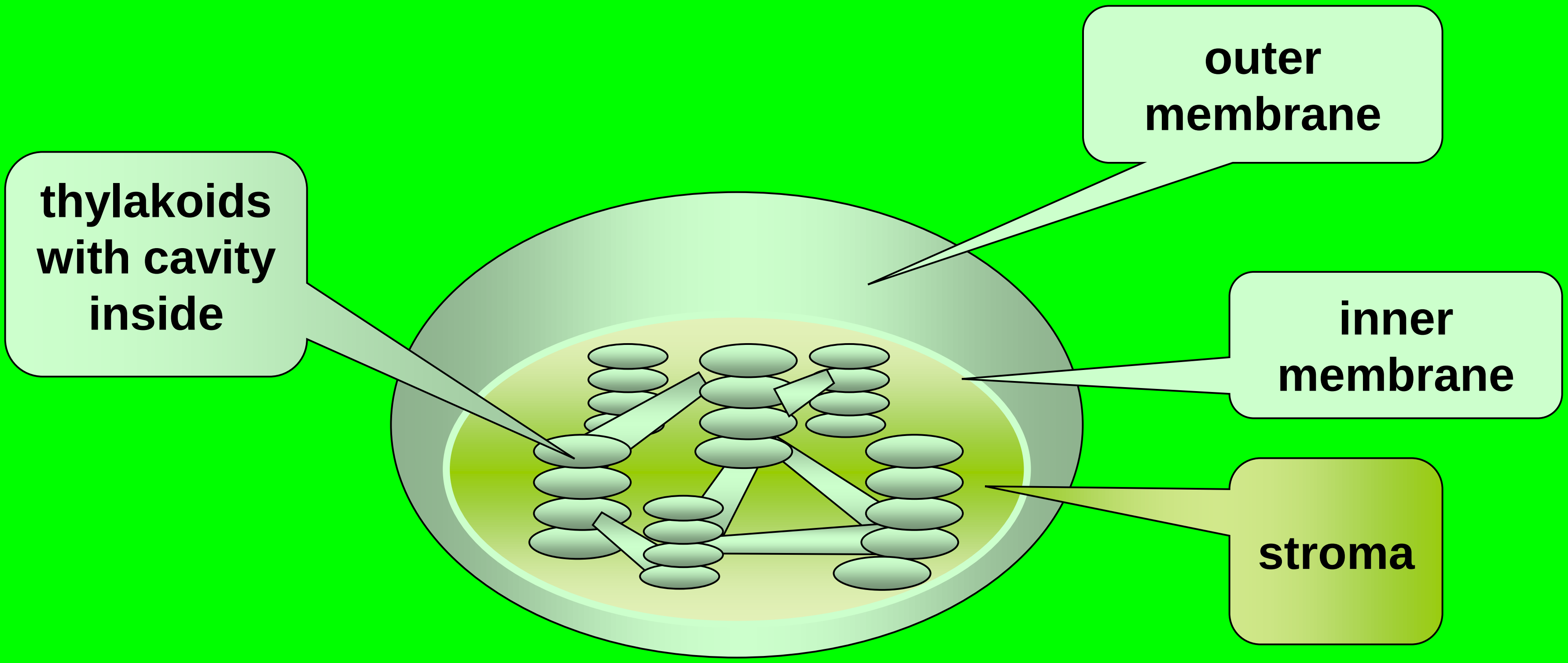
- **Green photosynthetic pigment**
- **Found ONLY in inner membranes of chloroplast**

Bounded by double membrane

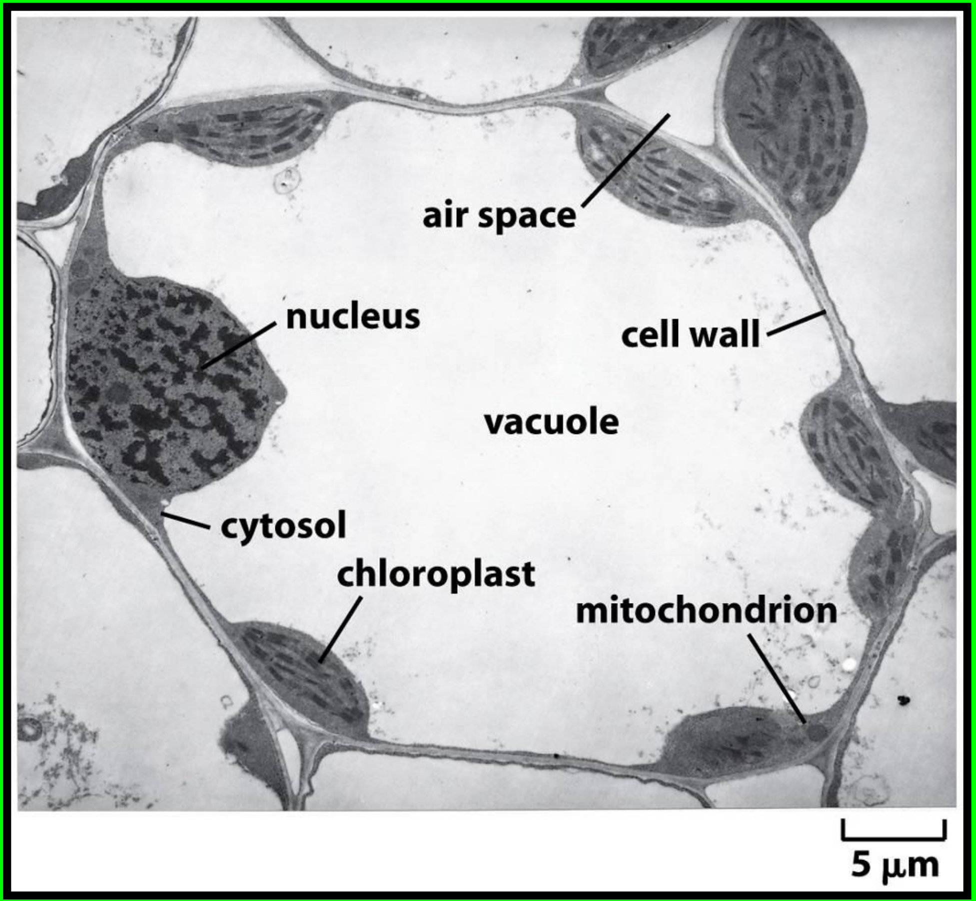
Inner membrane infolded

- **Forms disc-like thylakoids, which are stacked to form grana**
- **Suspended in semi-fluid stroma**

The chloroplast scheme



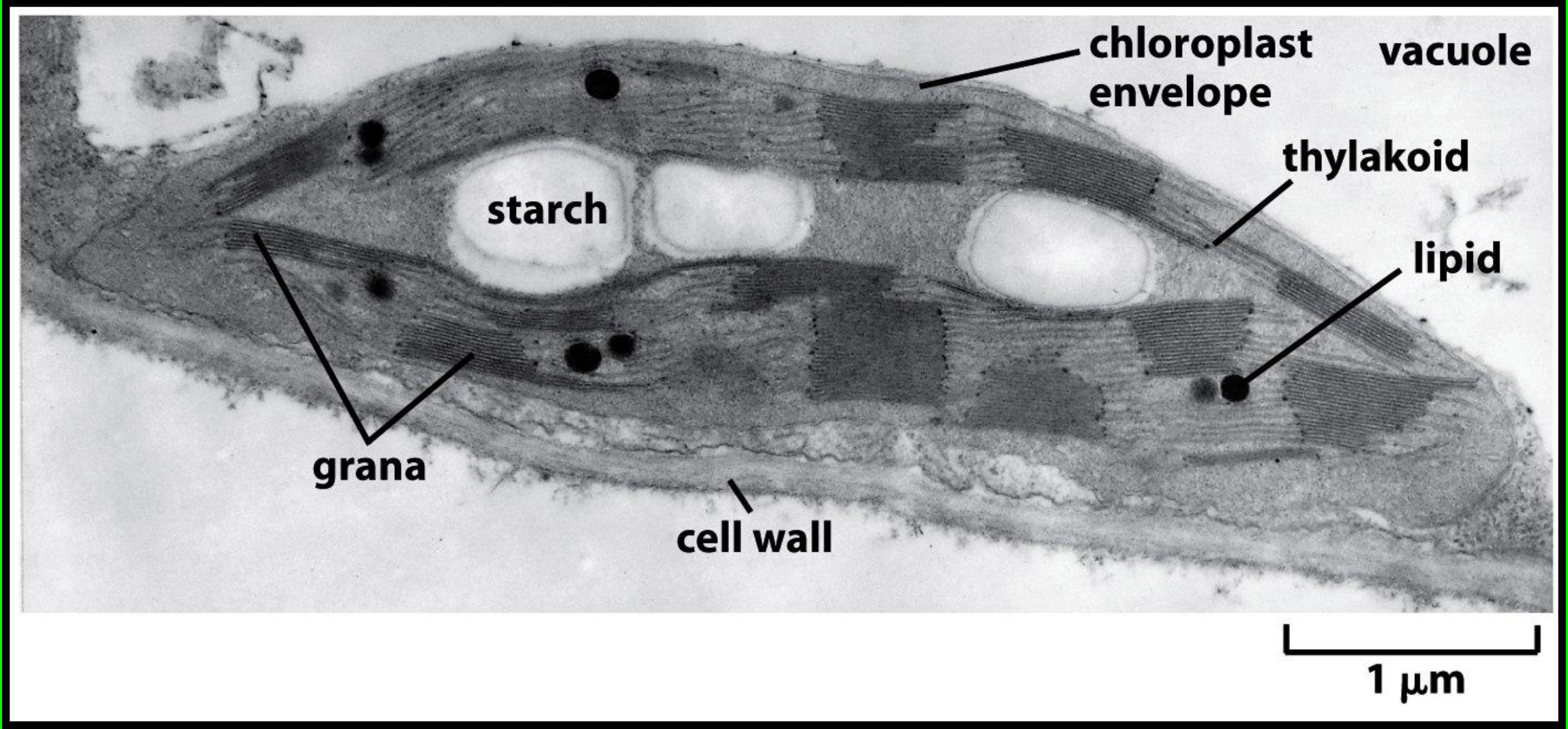
Electron micrographs 1/3



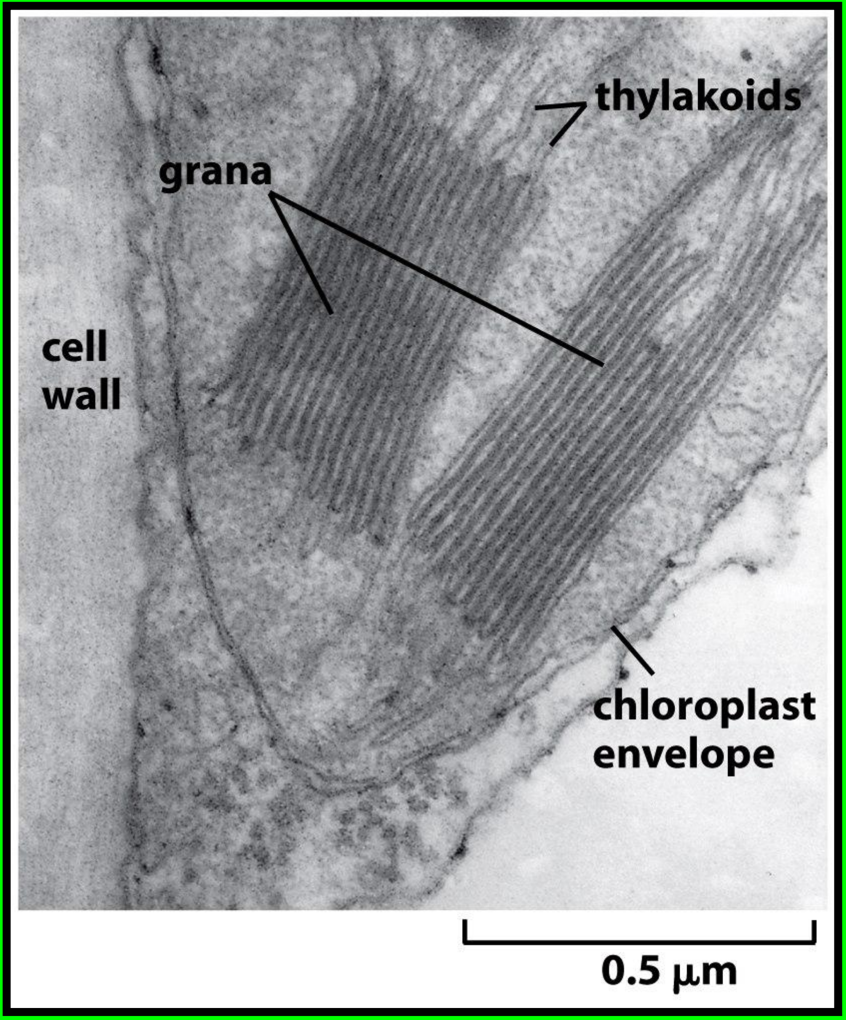
Wheat leaf cell containing chloroplasts, the nucleus, and mitochondria surrounded by a large vacuole

Electron micrographs 2/3

Single chloroplast



Electron micrographs 3/3



A high-magnification view of two grana (a stack of thylakoids)

Capturing energy in chloroplasts

Two categories of reactions in plant

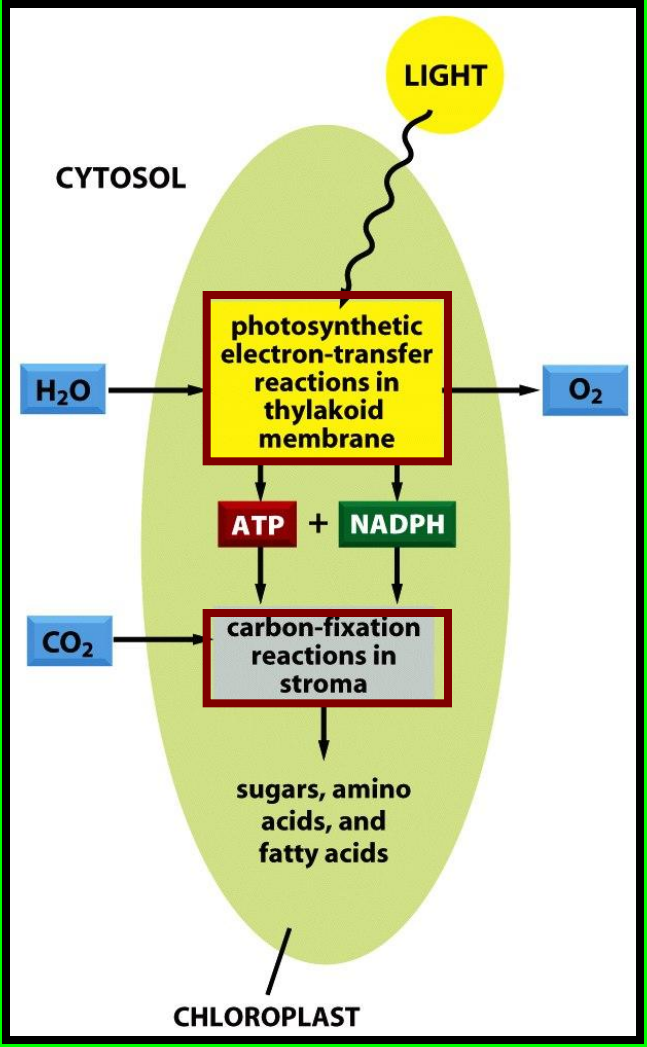
1) photosynthetic electron-transfer reactions (light)

- **energy from sunlight energizes an electron in chlorophyll**
- **electron is transported along respiratory chain**
- **producing H+, ATP, NADPH and as waste product O_2**

2) carbon-fixation reaction (dark)

- **ATP and NADPH serve as a source of energy and reducing power – to drive the conversion of CO_2 to carbohydrate**
- **begins in chloroplast stroma and continue in cytosol**

Photosynthesis in a chloroplast

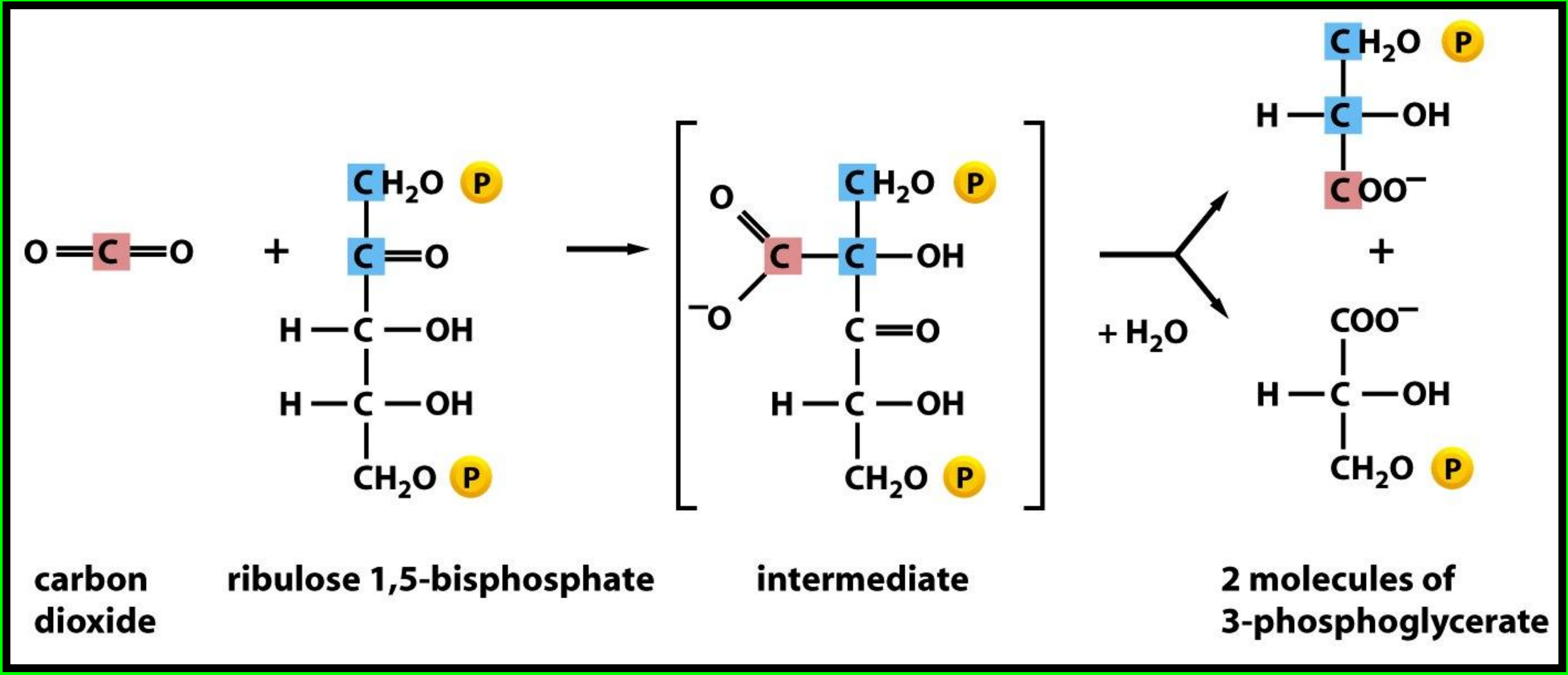


Formation of ATP, NADPH and O_2 and conversion of CO_2 to carbohydrates are <u>separate processes</u> although elaborate feedback mechanisms

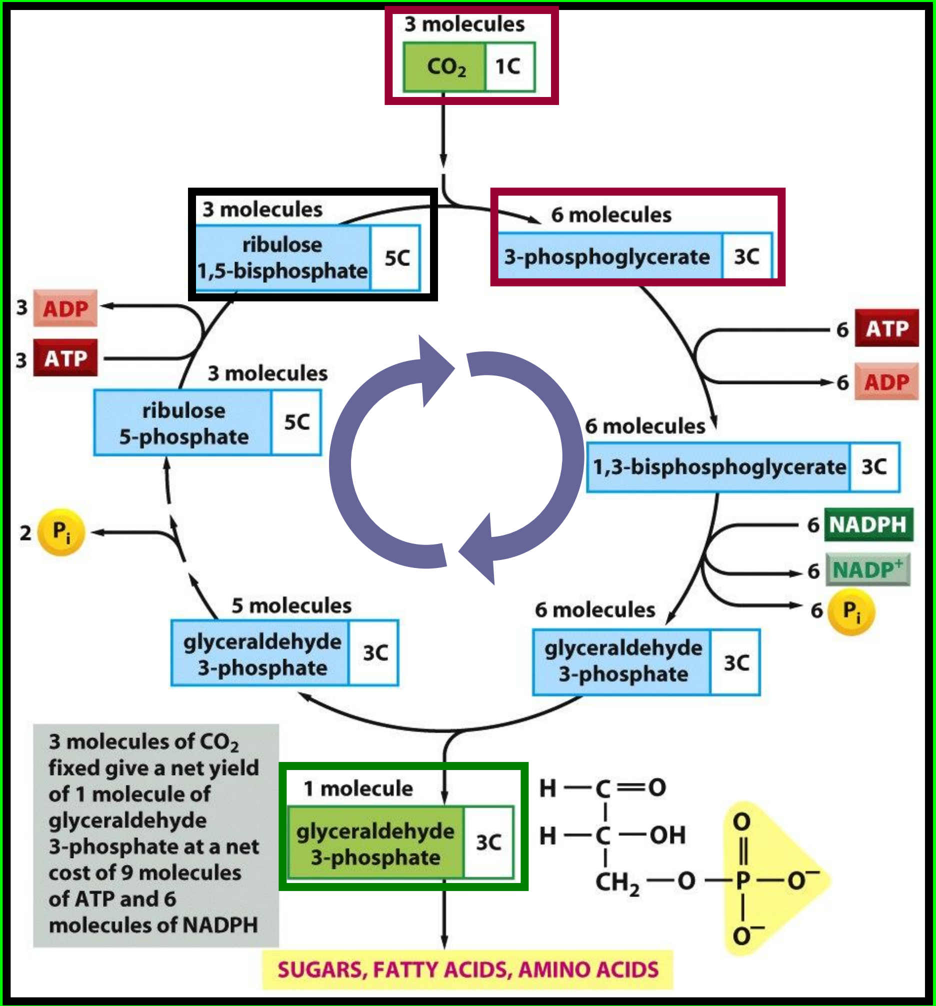
Several chloroplast <u>enzymes</u> required for carbon fixation <u>are inactivated in the dark</u> and <u>reactivated by light</u>-stimulated electron-transport processes

Carbon fixation

Is catalysed by ribulose bisphophate carboxylase (Rubisco)



Calvin cycle



- 3 molecules of CO_2 are fixed by Rubisco to 6 molecules of 3-P-glycerate
- cycle of reactions that regenerates the 3 molecules of ribulose-1,5-bis-P
- this leaves 1 molecule of glyceraldehyde 3-P

Calvin cycle - results

Each CO_2 molecule converted into carbohydrate consumes a total of 3 molecules of ATP and 2 molecules of NADPH

$$3CO_2 + 9ATP + 6NADPH + water$$

$$\downarrow$$

$$\text{glyceraldehyde-3-phosphate} + 8Pi + 9ADP + 6NADP^+$$

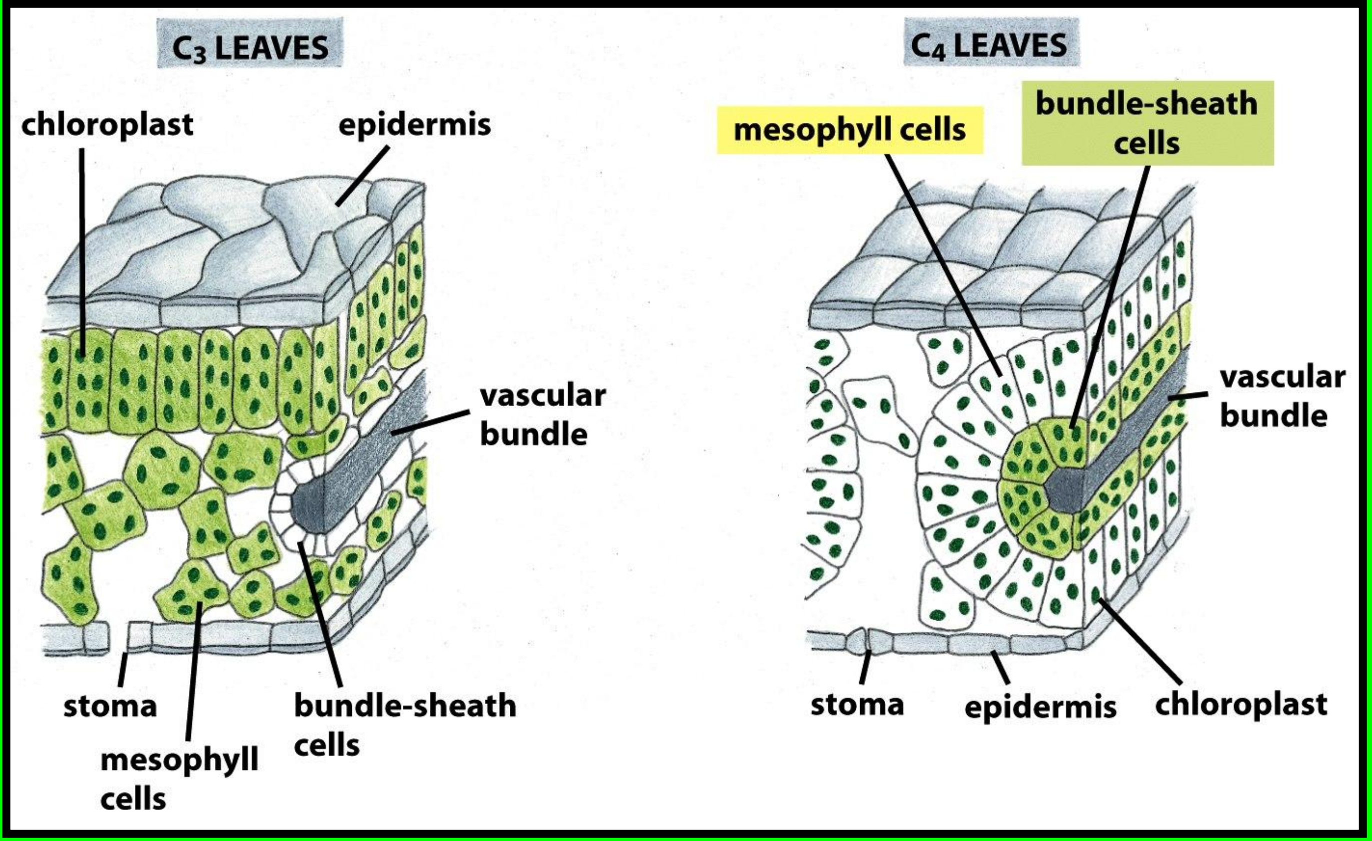
Central role of gly-3-P

Glyceraldehyde-3-phosphate serves as a central intermediate in glycolysis

- **It is exported to the <u>cytosol</u> where is converted into <u>fructose-6-P</u> or <u>glucose-1-P</u>**
- **these sugars are converted to another carbohydrates, especially to <u>sucrose</u>**
- **glyceraldehyde-3-phosphate that remains in the chloroplast is converted to <u>starch</u> <u>in the stroma</u>**

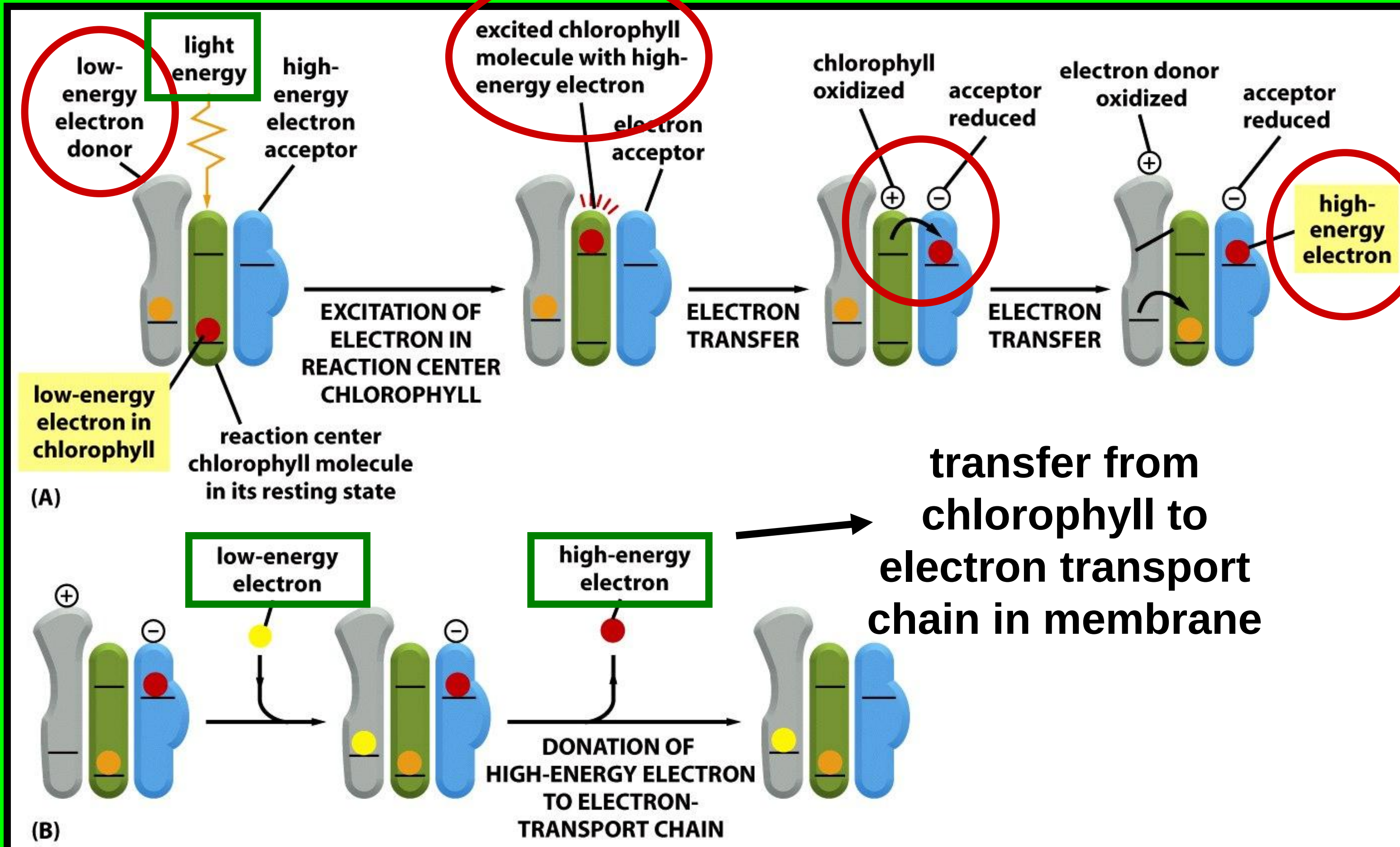
C3 and C4 plants

Compartmentalisation at low CO_2 concentrations



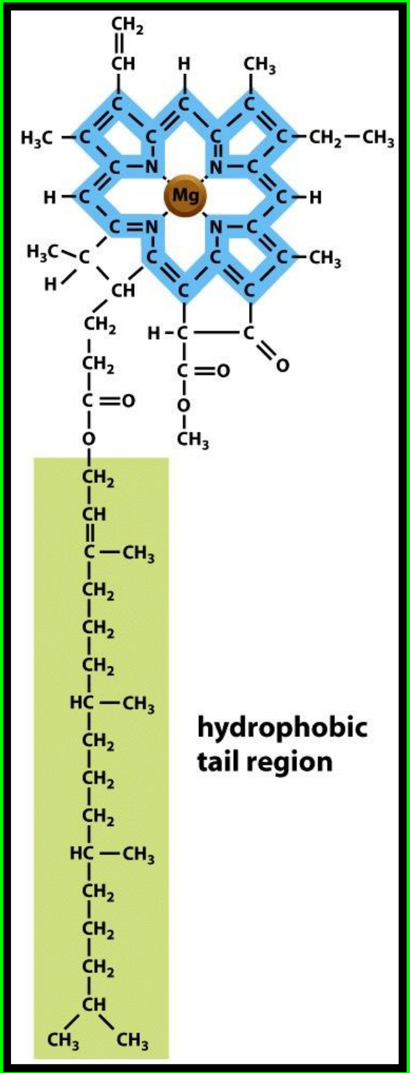
Electron transfer

Charge separation

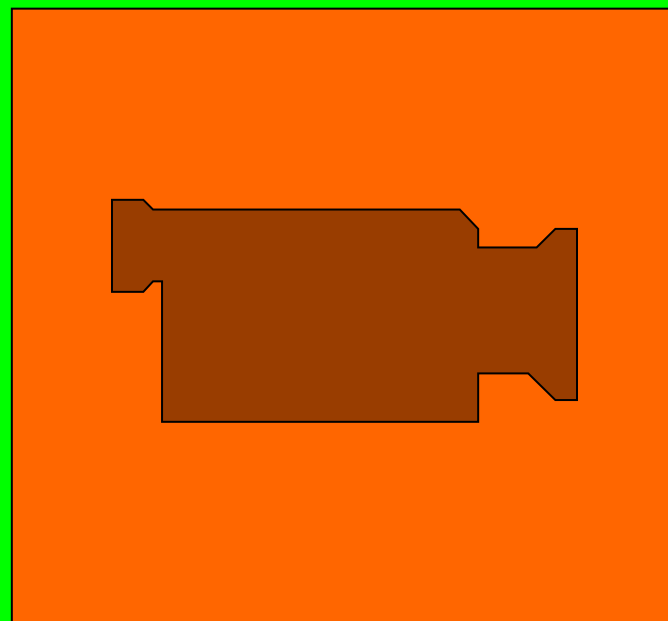


Restoration of the photosynthetic centre

The structure of chlorophyll



- **a <u>magnesium</u> atom is held in a <u>porphyrin ring</u>, which is related to the porphyrin ring that binds iron in heme**
- **process of energy conversion begins when a photon excites a chlorophyll molecule causing an electron in the chlorophyll to move from one orbital to another**
- **excited molecules return back by <u>photochemical reaction</u>**



Photosynthetic Electron Transport and ATP Synthesis.avi