MEDICAL UNIVERSITY – PLEVEN
FACULTY OF PHARMACY

DIVISION OF PHYSICS AND BIOPHYSICS, HIGHER MATHEMATICS AND INFORMATION TECHNOLOGIES

LECTURE No8

BIOENERGETICS
Energy Transfer in Living Systems

Energy. Metabolism. Oxidation as a source of metabolic energy. ATP and energy transduction. Oxidative phosphorylation reactions

Prof. M. Alexandrova, DSc

Bioenergetics

Bioenergetics is a term used to describe the science of energy formation, transfer and use within a biological system

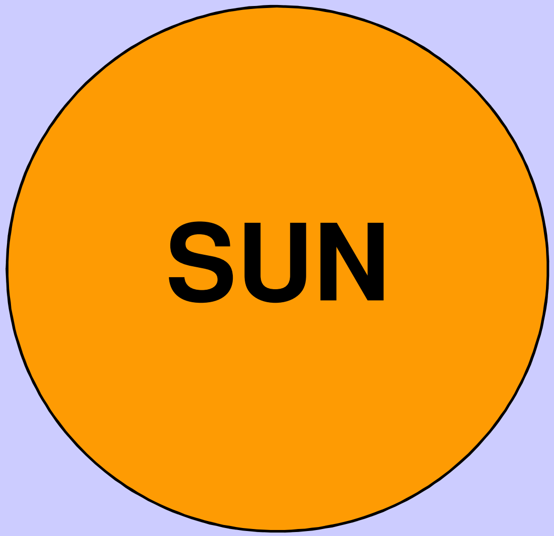
Energy

- Capacity to perform work.
- Two examples:

1. Kinetic energy
2. Potential energy

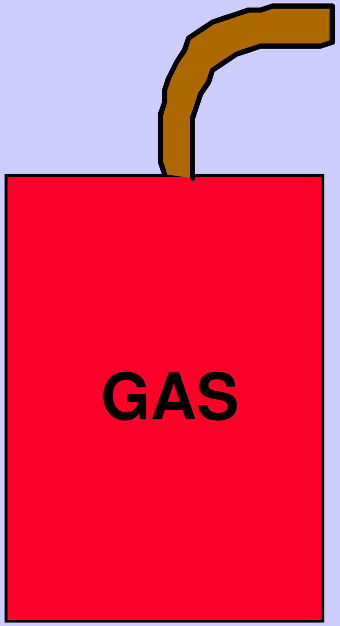
Kinetic Energy

- **Energy** in the process of doing work.
- **Energy** of **motion**.
- **Examples:**
  1. **Heat**
  2. **Light energy**



Potential Energy

- **Energy** that matter occupies because of it's location, arrangement, or position.
- **Energy** of position.
- **Examples:**
  1. **Water behind a dam**
  2. **Chemical energy (gas)**



Energy is used to:

1. Synthesize organic molecules;

2. Drive active transport across membranes;

3. Drive endocytosis;

4. Drive muscle contractions and other bodily functions (cell division, growth etc.).

Cellular Metabolism

- **The total sum of the chemical activities of all cells.**
- **Endergonic** and **Exergonic** reactions
- **2 Examples:**
  1. **Anabolic Pathways**
  2. **Catabolic Pathways**

Metabolism means:

- to obtain chemical energy from environment by degradation of energy rich nutrients (animals) or by capturing solar energy (plants)
- to convert nutrient molecules into building blocks
- to assemble building blocks into macromolecules (protein, nucleic acids, lipids, polysaccharides)
- to assemble macromolecules into cells

Stages to catabolism/anabolism

- nutrient molecules are hydrolyzed to building blocks;
- building blocks are converted to easily oxidized forms---acetyl-CoA being the most important end product of glycolysis;
- energy is captured by linking ATP synthesis to electron transport pathway;
- new molecules are resynthesized using energy derived from ATP;
- cells are constantly breaking down and resynthesizing molecules.

Catabolic Pathway

- **Metabolic reactions** which **release energy (exergonic)** by **breaking down** complex molecules in simpler compounds.

- **Example:**

  1. Cellular Respiration

energy

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{ATP}$$

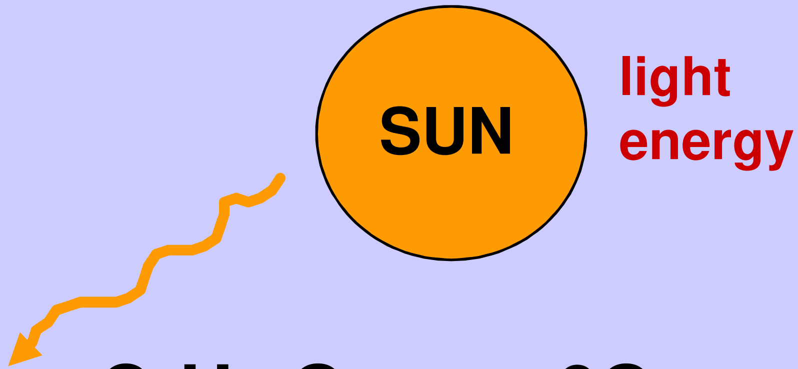
(glucose)

Anabolic Pathway

- **Metabolic reactions,** which **consume energy (endergonic),** to **build** complicated molecules from simpler compounds.

- **Example:**

  1. Photosynthesis



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

(glucose)

Exergonic Reactions

- **Chemical reactions** that **release energy**.

- **Example:**
  1. **Cellular Respiration**

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{ATP}$$

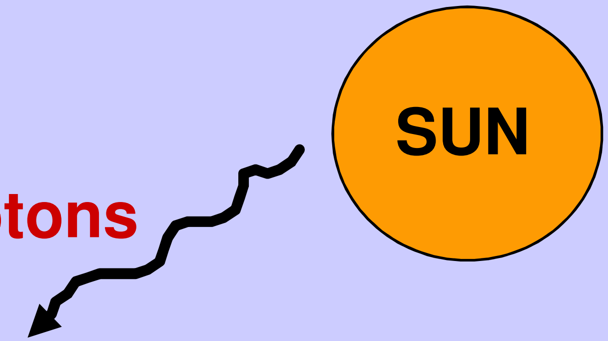
(glucose)

Energy

Endergonic Reactions

- **Chemical reaction** that **requires a net input** of **energy**.
- **Example:**

  1. Photosynthesis



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

(glucose)

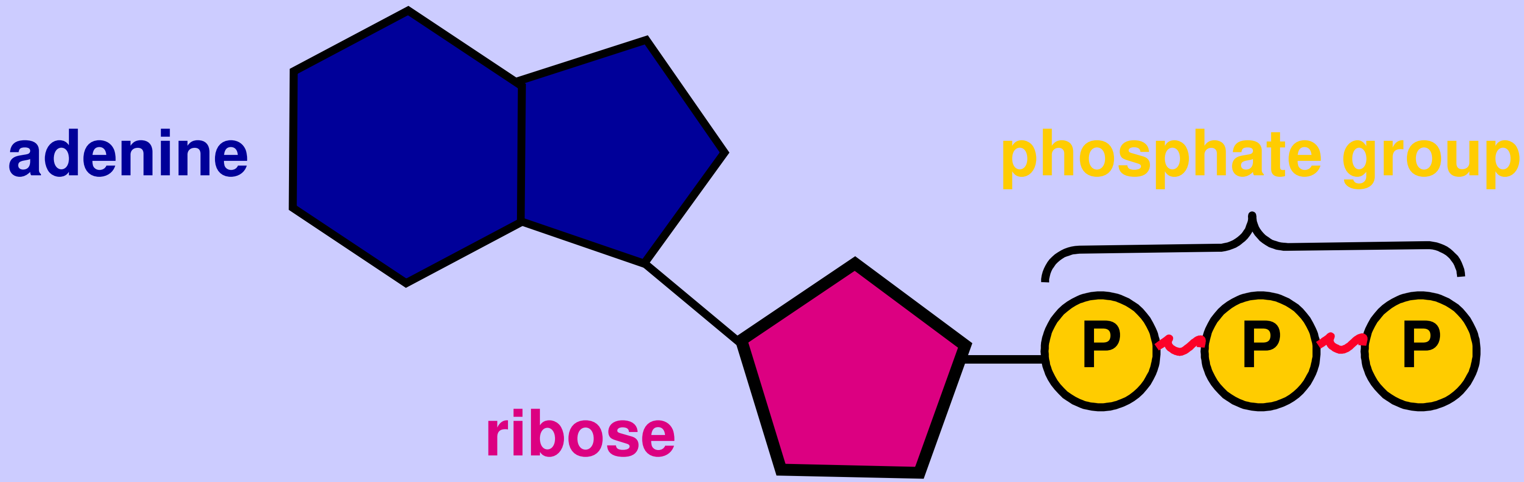
Question:

- What is **ATP?**

Answer:

- adenosine triphosphate (ATP)
- Components:

1. adenine: nitrogenous base
2. ribose: five carbon sugar
3. phosphate group



Question:

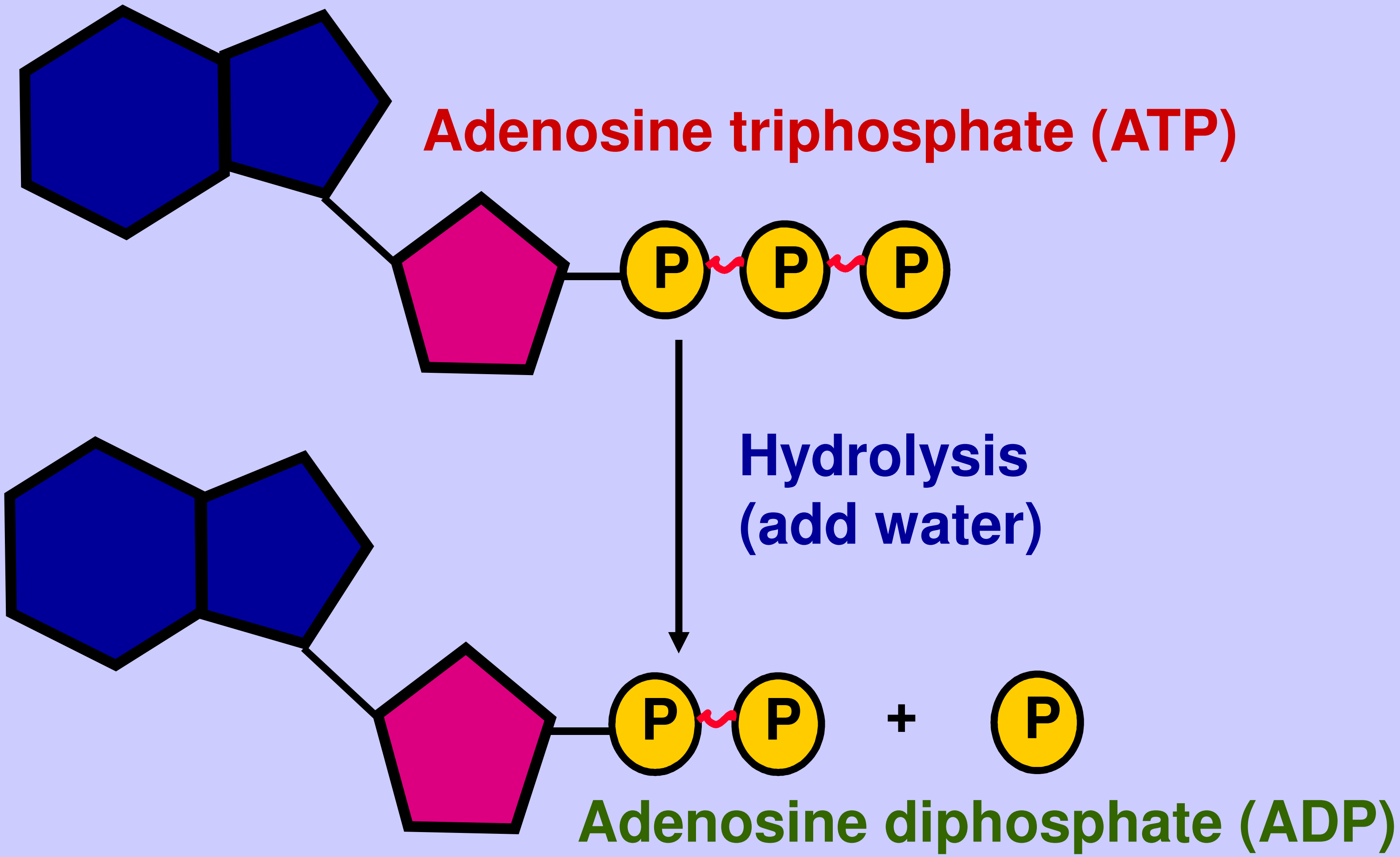
- **How does ATP work?**

Answer:

- Works by the **direct chemical transfer** of a **phosphate group**.
- This is called **"phosphorylation"**.
- The **exergonic hydrolysis** of **ATP** is coupled with the **endergonic processes** by **transferring** a **phosphate group** to another molecule.

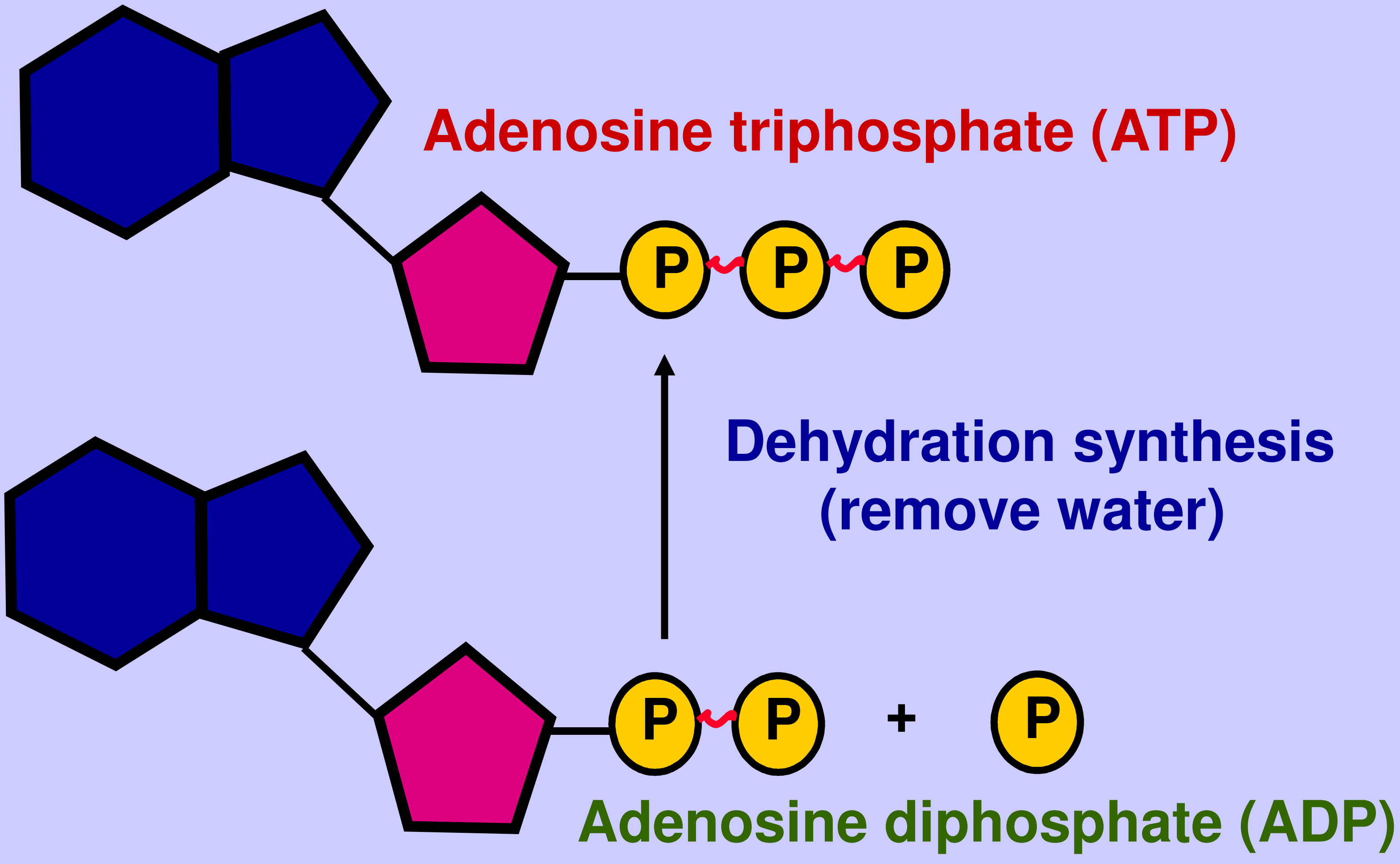
Hydrolysis of ATP

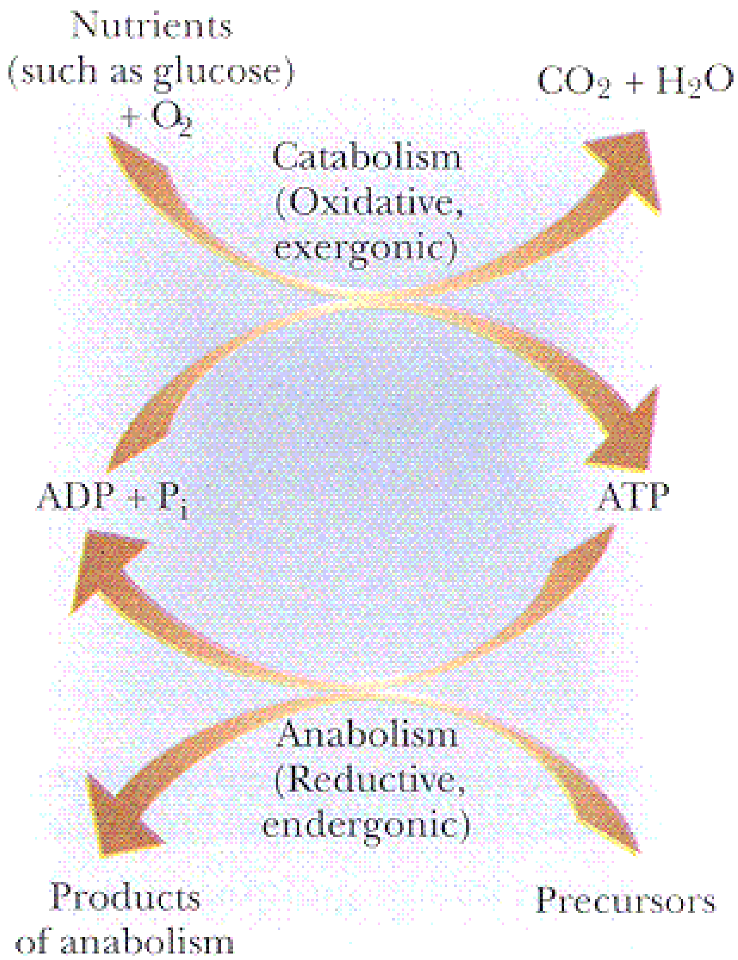
- ATP + H_2O → ADP + P (exergonic)



Dehydration of ATP

ADP + P → ATP + H_2O (endergonic)





The role of ATP as energy currency in processes that require energy and processes that use energy.

Coupled reactions

Glycerol + HPO_4^{2-} --> (Glycerol-3-Phosphate)$^{2-}$ + H_2O **dG°= +9.2 kJ** **(nonspontaneous)** **(1)**

\+ **(2)**

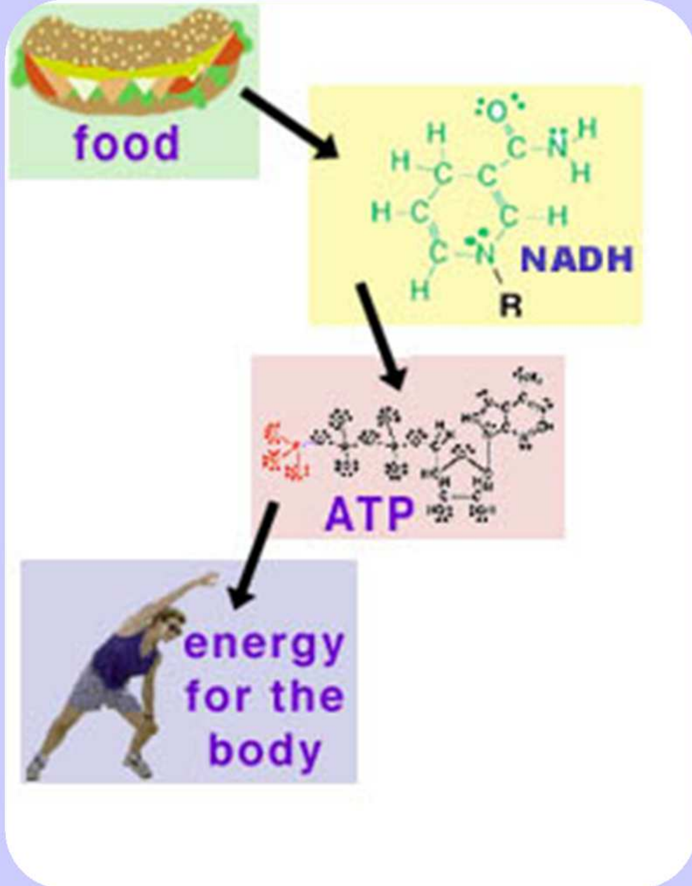
ATP^{4-} + H_2O -->ADP^{3-} + HPO_4^{2-} + H^+ **dG°= -30.5 kJ** **(spontaneous)**

Glycerol + ATP^{4-} --> (Glycerol-3-Phosphate)$^{2-}$ +ADP^{3-} + H^+ **dG°= -21.3 kJ** **(spontaneous)** **(3)**

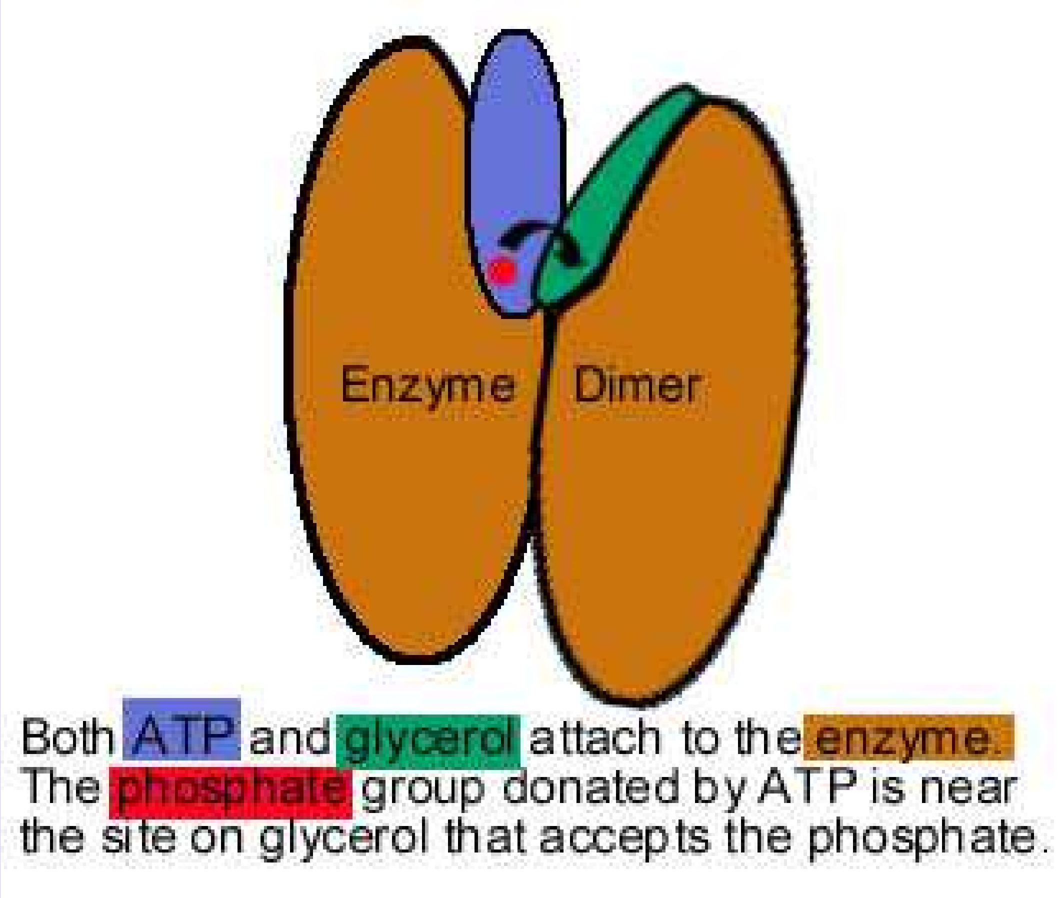
ATP is a useful free-energy currency because the dephosphorylation reaction is very spontaneous; i.e., it releases a large amount of free energy (30.5 kJ/mol).

Thus, the dephosphorylation reaction of ATP to ADP and inorganic phosphate (Equation 2) is often coupled with nonspontaneous reactions (e.g., Equation 1) to drive them forward.

The body's use of ATP as a free-energy currency is a very effective strategy to cause vital nonspontaneous reactions to occur.



The energy used by the body for its many activities ultimately comes from the chemical energy in our food. The chemical energy in our food is converted to reducing agents (NADH and $FADH_2$). These reducing agents are then used to make ATP. ATP stores chemical energy, so that it is available to the body in a readily accessible form.



A schematic representation of ATP and glycerol bound (attached) to glycerol kinase.

The enzyme glycerol kinase is a dimer (consists of 2 identical subuits).
There is a deep cleft between the subunits where ATP and glycerol bind.
Since ATP and glycerol are physically so close together when they are bound to the enzyme, the phosphate can be transferred directly from ATP to glycerol.

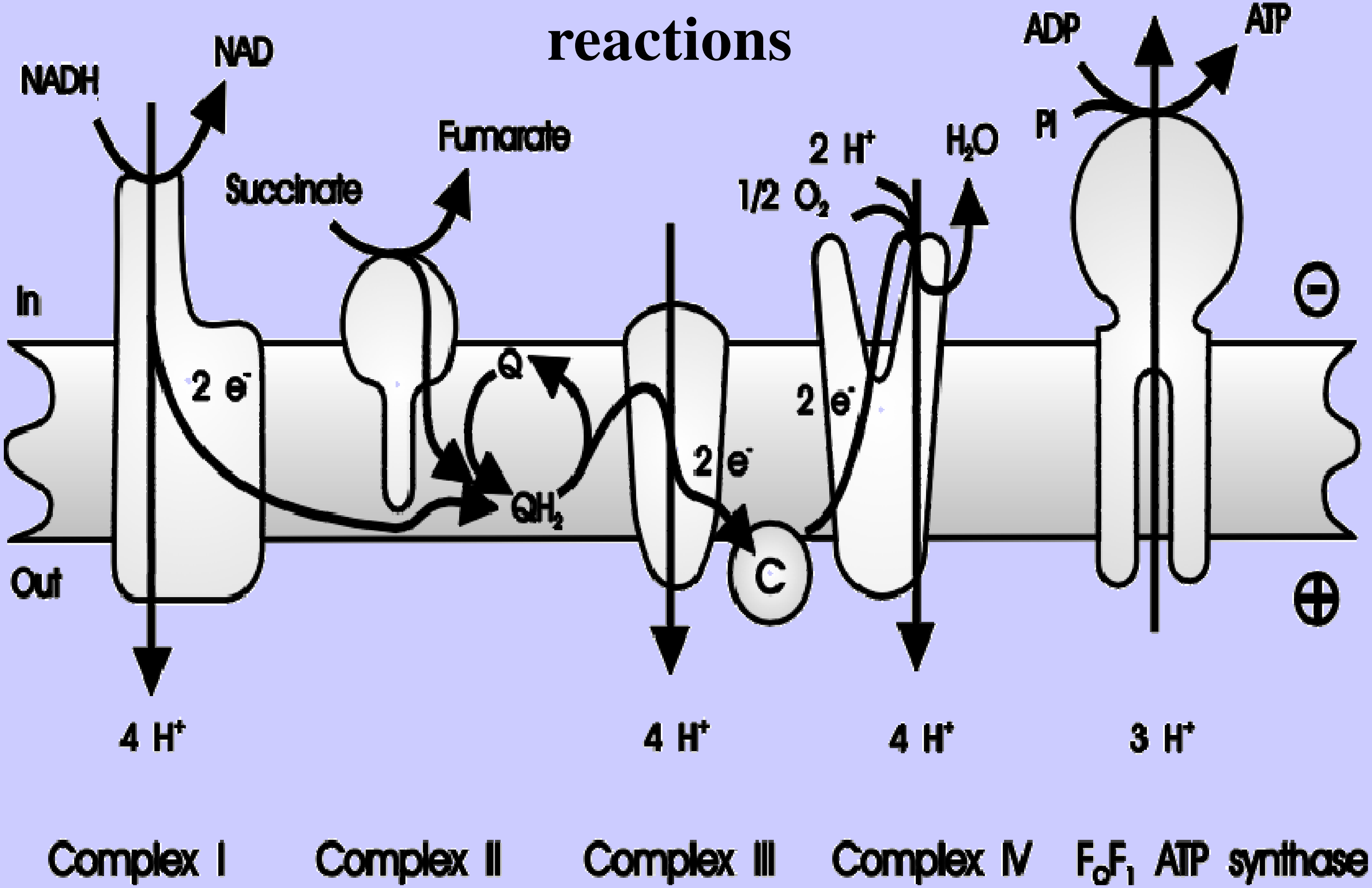
The processes of ATP losing a phosphate (spontaneous) and glycerol gaining a phosphate (nonspontaneous) are coupled together as one spontaneous process.

Mechanism of coupling the oxidative phosphorylation reactions

The individual reactions of interest for **oxidative phosphorylation** are:

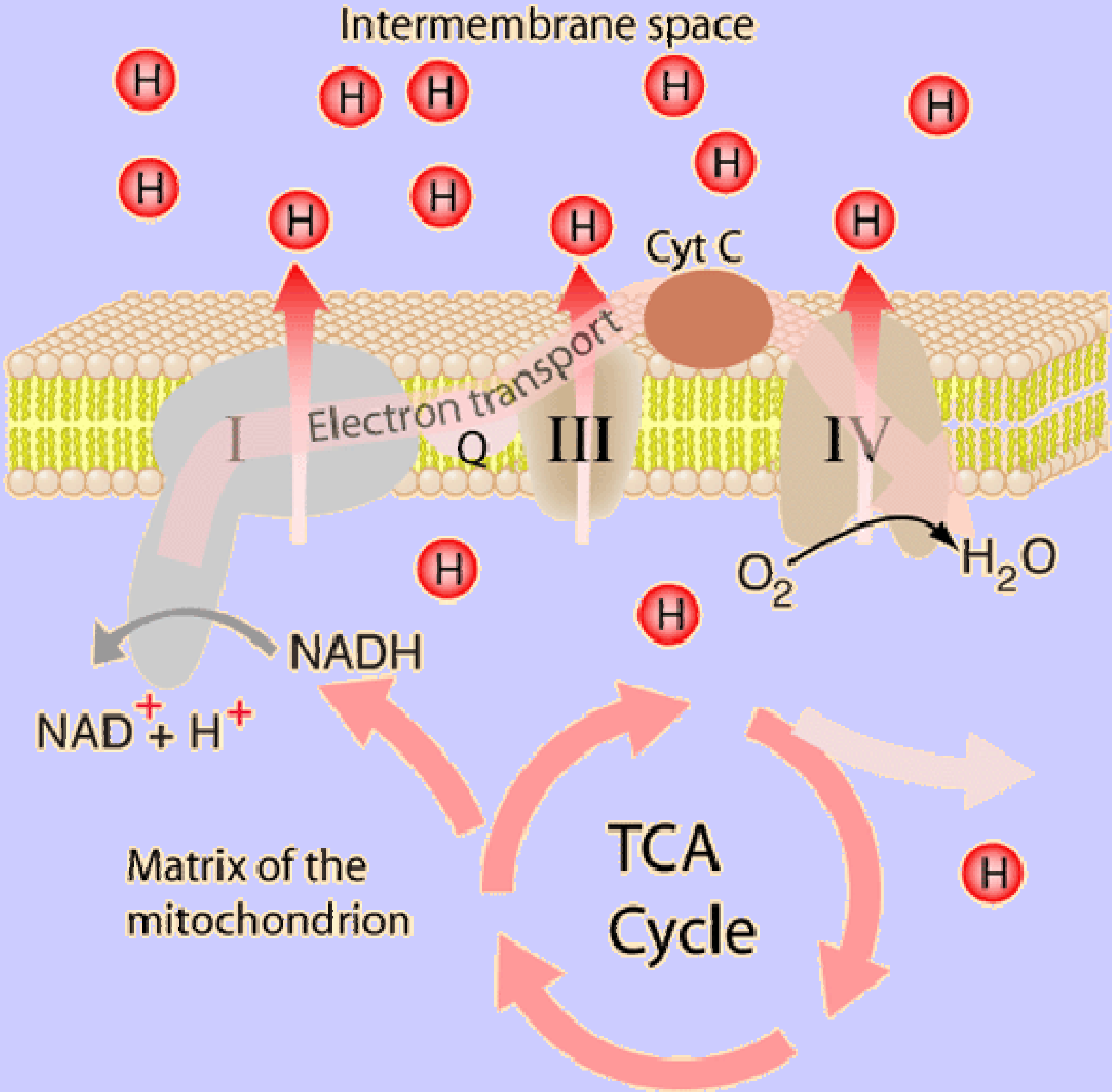
phosphorylation	$ADP^{3-} + HPO_4^{2-} + H^+ \text{-->} ATP^{4-} + H_2O$	**dGº= +30.5 kJ** **(nonspontaneous)**
oxidation	$NADH \text{-->} NAD^+ + H^+ + 2e^-$	**dGº= -158.2 kJ** **(spontaneous)**
reduction	$^1/_2\ O_2 + 2H^+ + 2e^- \text{-->} H_2O$	**dGº= -61.9 kJ** **(spontaneous)**

Mechanism of coupling the oxidative phosphorylation reactions



The electron transport chain components involved in oxidative phosphorylation are located within the mitochondrial inner membrane. C, cytochrome c; Q, ubiquinone.

Mechanism of coupling the oxidative phosphorylation reactions



TCA cycle in the context of what is happening in the inner mitochondrial membrane.

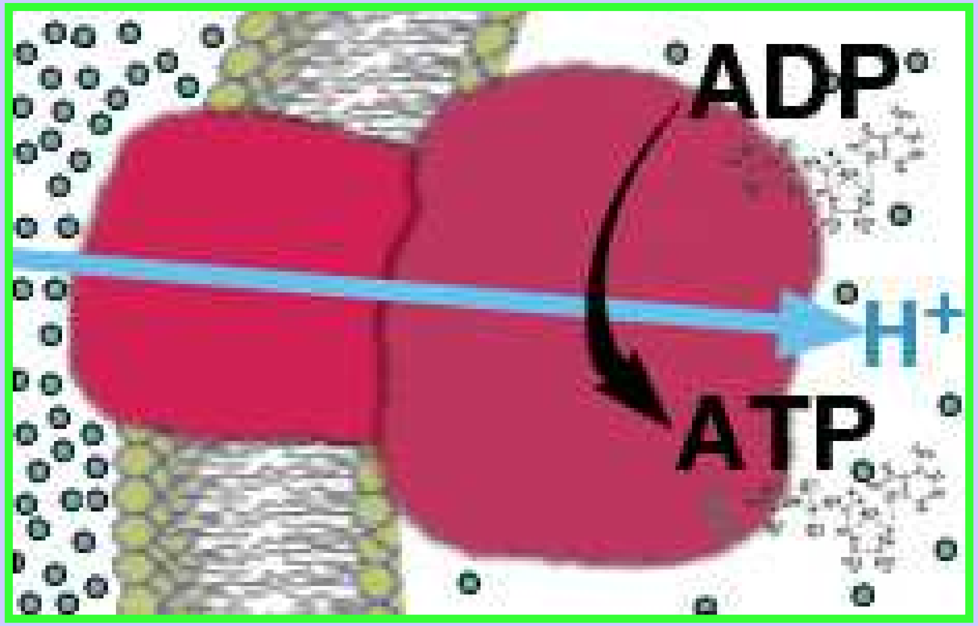
It's role can be seen as giving energy to the reduced coenzyme NADH which then powers the electron transport process in the membrane. The energy is used by the protein complexes to produce a proton gradient which in turn powers ATP synthase in its role of producing the needed ATP.

Basic steps

a. Electron transport (oxidation-reduction reactions) through a series of proteins in the inner membrane of mitochondria

b. Generation of H+ (proton) concentration gradient across the inner mitochondrial membrane during the electron-transport process (via a proton pump) (which occurs simultaneously with step a.

c. Synthesis of ATP using free energy released from spontaneous diffusion of H^+ back to the matrix inside the inner mitochondrial membrane



- Summary

In this lecture, we have learned that the ability of the body to perform daily activities is dependent on thermodynamic concepts. These activities, which are typically based on nonspontaneous chemical reactions, are performed by using free-energy currency. The common free-energy currency is ATP, which is a molecule that easily dephosphorylates (loses a phosphate group) and releases a large amount of free energy. In the body, the nonspontaneous reactions are coupled to this very spontaneous dephosphorylation reaction, thereby making the overall reaction spontaneous. As the coupled reactions occur (i.e., as the body performs daily activities), ATP is consumed and the body regenerates ATP by using energy from the food we eat.

The breakdown of glucose (glycolysis) obtained from the food we eat cannot by itself generate the large amount of ATP that is needed for metabolic energy by the body. However, glycolysis and the subsequent step, the citric-acid cycle, produce two easily oxidized molecules: NADH and $FADH_2$. These redox molecules are used in an oxidative-phosphorylation process to produce the majority of the ATP that the body uses. This oxidative-phosphorylation process consists of two steps: the oxidation of NADH (or $FADH_2$) and the phosphorylation reaction which regenerates ATP.

- Oxidative phosphorylation occurs in the mitochondria, and the two reactions (oxidation of NADH or $FADH_2$ and phosphorylation to generate ATP) are coupled by a proton gradient across the inner membrane of the mitochondria . The oxidation of NADH occurs by electron transport through a series of protein complexes located in the inner membrane of the mitochondria. This electron transport is very spontaneous and creates the proton gradient that is necessary to then drive the phosphorylation reaction that generates ATP.
- Hence, oxidative phosphorylation demonstrates that free energy can be easily transferred by proton gradients. Oxidative-phosphorylation is the primary means of generating free-energy currency for aerobic organisms, and as such is one of the most important subjects in the study of bioenergetics (the study of energy and its chemical changes in the biological world).