

**Course- Microbiology
Semester- II
MBIO CC 203. Biochemistry**

ENERGY RICH COMPOUNDS

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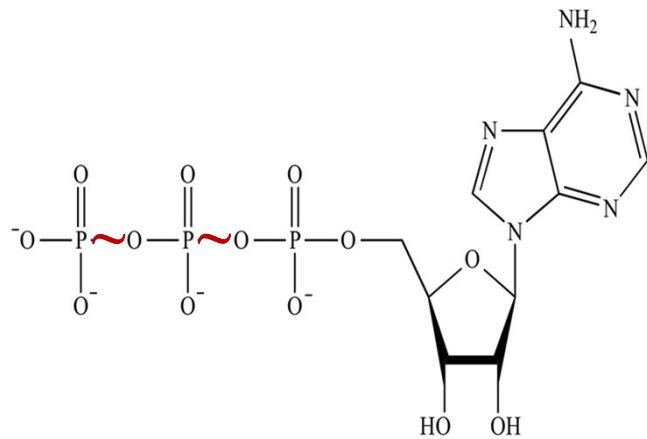
Energy Rich Compounds

- **Energy-rich compounds:** Such compounds in biological system whose ΔG^0 of hydrolysis yields free energy equal to or greater than -25 kJ/mol are called energy-rich compounds or high-energy compounds, while, those whose ΔG^0 of hydrolysis yields free less than -25 kJ/mol are called low-energy compounds.
- Most of the high-energy compounds contain phosphate group (viz., phosphoanhydride, enol phosphates, acyl phosphates and guanido phosphates) are also called **high-energy phosphates** having high phosphoryl transfer potential **except thiol esters** that have high acyl transfer potential.
- **High-energy bonds:** The bonds in the energy-rich compounds, which yields high energy upon hydrolysis are called high-energy bonds. A squiggle '~~~~' is used to indicate energy-rich bonds. In 1941 Fritz Lipmann introduced this convention.
- The term "high-energy bond," is however incorrect and misleading because it wrongly suggests that the bond itself contains the energy. The fact is that breaking of chemical bonds requires an input of energy. The free energy released by hydrolysis of high-energy compounds results from the products of the reaction having a smaller free-energy content than the reactants and that's not from breaking of any specific bond.
- ΔG^0 - It is the difference in free energies of the products and reactants.

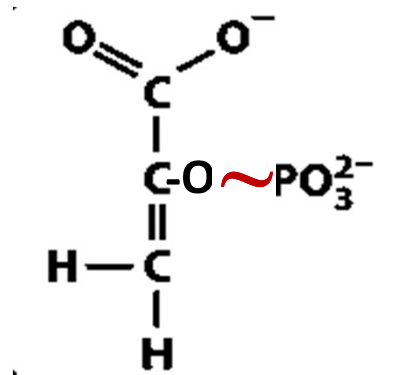
Classification of Energy-rich compounds: Based on type of bonds

S. No.	Energy-rich compounds	Energy-rich bond		Example	ΔG°	
					(kJ/mol)	(kcal/mol)
1	Pyrophosphates	Acid anhydride (formed by condensation of acid groups or its derivatives)	$-\text{C}-\text{P}\sim\text{P}$	ATP to ADP	-30.5	-7.3
2	Enol phosphates	Enol phosphate (It is formed when phosphate group attaches to a hydroxyl group which is bounded to a carbon atom having double bond.)	$-\text{CH}\overset{\parallel}{\text{C}}-\text{O}\sim\text{P}$	Phosphoenol pyruvate	-61.9	-14.8
3	Acyl phosphates	Bond between carboxy and phosphate (The high energy bond in this compound is formed by the reaction between carboxylic acid group and phosphate group)	$\text{O}\overset{\parallel}{\text{C}}-\text{O}\sim\text{P}$	1,3-bisphosphoglycerate	-49.4	-11.8
4	Thiol esters	Thioester (Thioester bond results from the reaction between thiol and carboxylic acid group)	$\text{O}\overset{\parallel}{\text{C}}-\text{S}-$	Acetyl CoA	-31.4	-7.5
5	Guanido phosphates (phosphagens)	Guanidine phosphate bond (It is formed by the attachment of phosphate group to guanidine group)	$ \text{N}\sim\text{P}$	Phosphocreatine	-43.1	-10.3

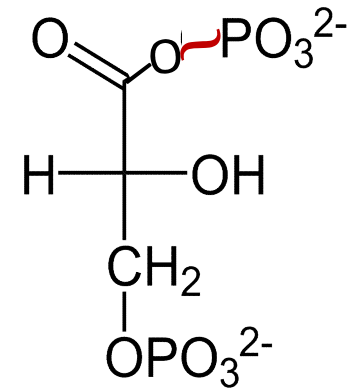
Structure of some energy-rich compounds



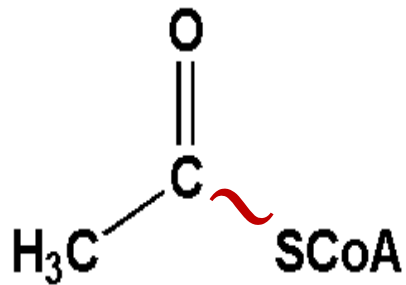
ATP



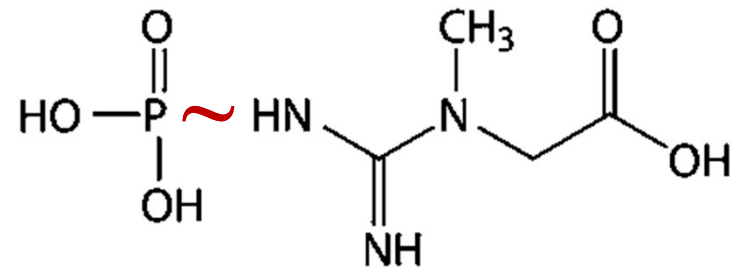
Phosphoenol phosphate



1,3-bisphosphoglycerate



Acetyl CoA



Phosphocreatine

What makes these compounds energy-rich?

Resonance stabilization, solvation and/or electrostatic repulsion

Let's have a look at the structure of individual energy-rich compound and their hydrolytic product...

Adenosine triphosphate (ATP)

- ATP is a nucleotide made up of adenine, ribose sugar and a triphosphate group (viz., α , β and γ designated from C5').
- Adenine is linked to C1' of sugar via N-glycosidic bond.
- α - phosphate is attached to C5' of sugar via phosphoester bond, while β - and γ - phosphate via phosphoanhydride bond.
- It is a energy rich compound because it contains 2 energy-rich phosphoanhydride bonds, one between α - and β -, while second between β - and γ - phosphoryl groups.

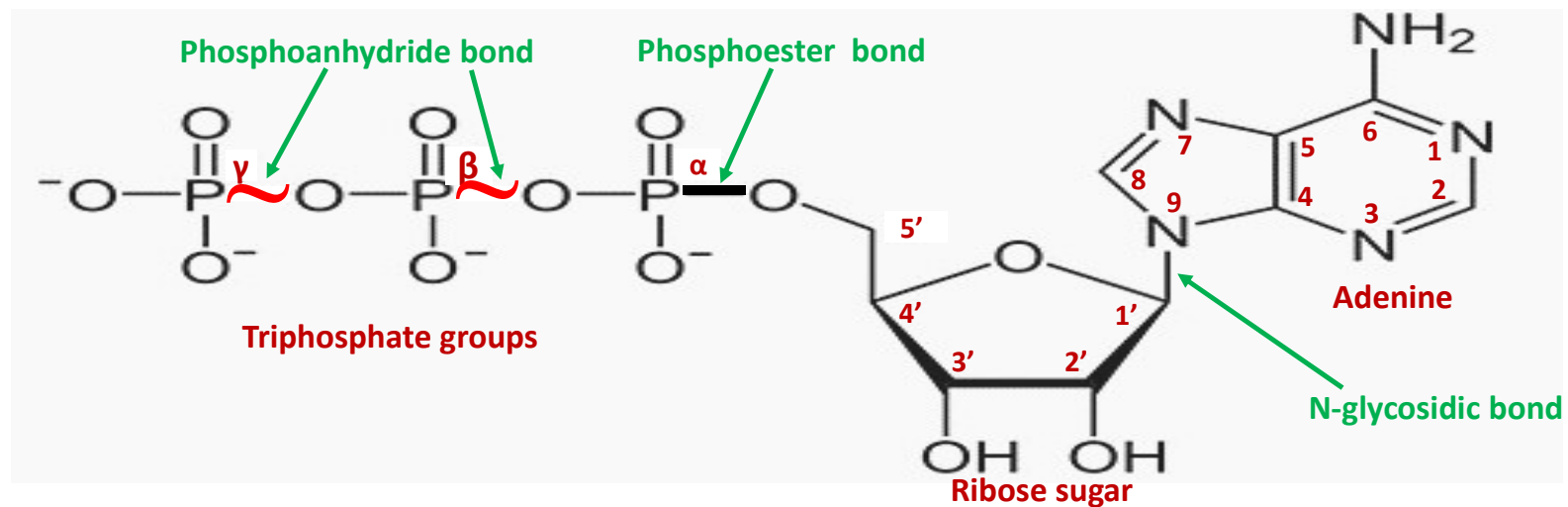
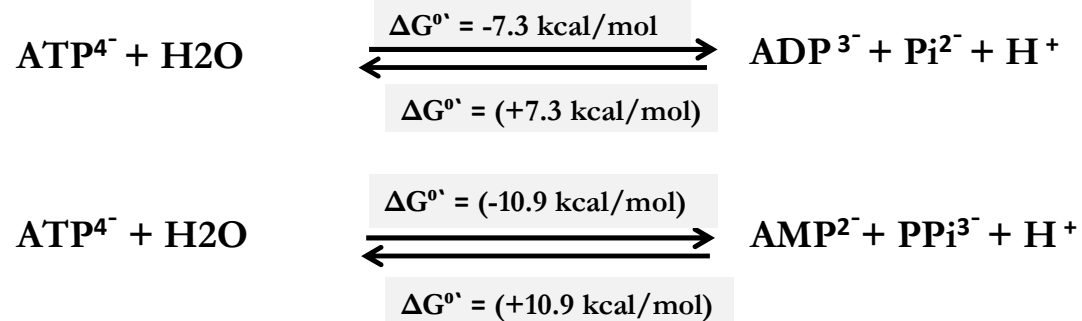


Fig.1. Structure of ATP

ATP hydrolysis is highly exergonic

- **ATP hydrolysis is highly exergonic i.e.,** a large amount of free energy is liberated when ATP is hydrolyzed to adenosine diphosphate (ADP) and orthophosphate (Pi) or when ATP is hydrolyzed to adenosine monophosphate (AMP) and pyrophosphate (PPi).
- While, the **synthesis of ATP** by phosphorylation of ADP is a **highly endergonic reaction**.



What makes ATP hydrolysis exergonic?

- Since $\Delta G^{0'}$ is the difference of free energy of reactant (ATP) and product (ADP & Pi), so structure of both need to be examined to understand this.
- 3 factors responsible for making ATP hydrolysis exergonic i.e. **high phosphoryl transfer potential** are: 1. Resonance stabilization 2. Electrostatic repulsion 3. Stabilization due to hydration

cont.

1. Resonance stabilization:

- Products (ADP and Pi) has greater resonance stabilization than that of reactant (ATP).
- Pi has a number of resonance forms of similar energy, whereas the γ - phosphoryl group of ATP has a smaller number.

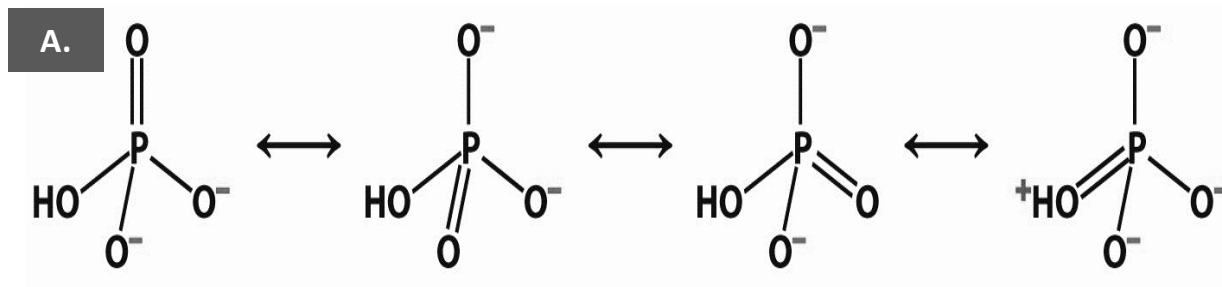


Fig.2A. Resonance structure of orthophosphate (Pi)

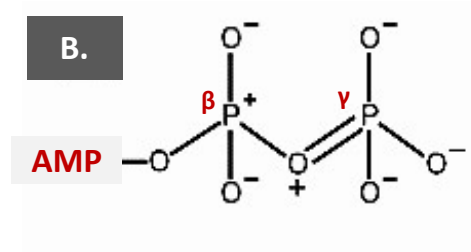


Fig.2B. Improbable resonance structure of terminal part of ATP

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2. Electrostatic repulsion:

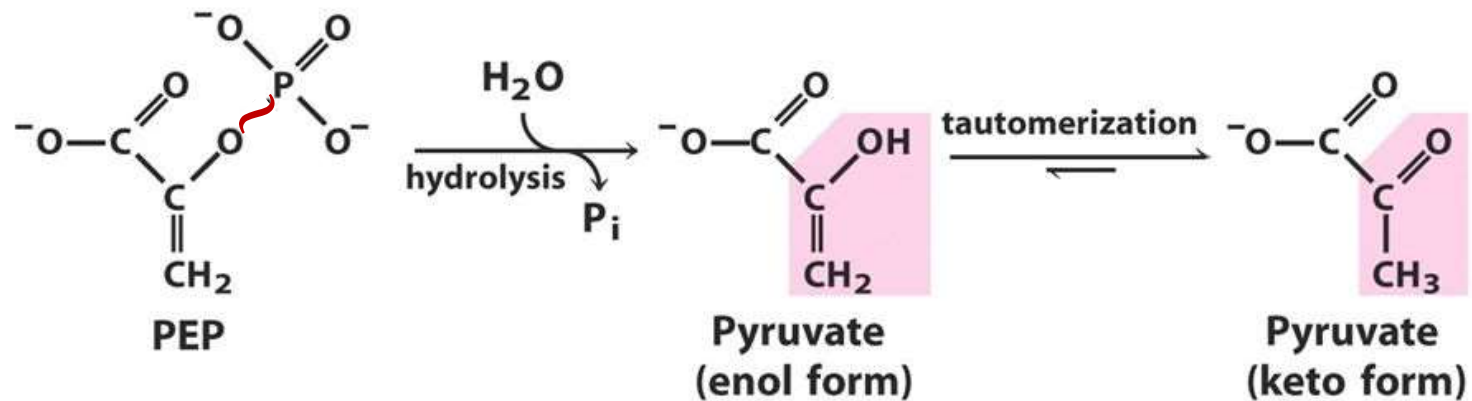
- Improbable resonance structure of terminal part of ATP (Fig. 2B) is unfavorable because a **+vely charged O-atom** is **adjacent to a +vely charged P-atom**, an electrostatically unfavorable juxtaposition.
- ATP carries **4 -ve charges** in close proximity (Fig 1.) at neutral pH leading to electrostatic charge repulsion. Release of the terminal phosphate group removes an unfavorable repulsion between adjacent negative charges. This repulsion is reduced by hydroxylation.

3. Stabilization due to hydration:

- Water can bind more effectively to ADP and Pi than it can to the phosphoanhydride part of ATP, stabilizing the ADP and Pi by hydration.
- In other words solvation of products (ADP and Pi) or (AMP and PPi) is better than solvation of ATP.

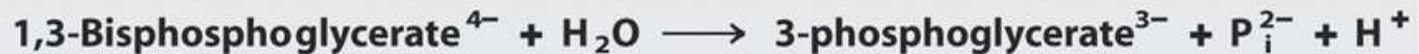
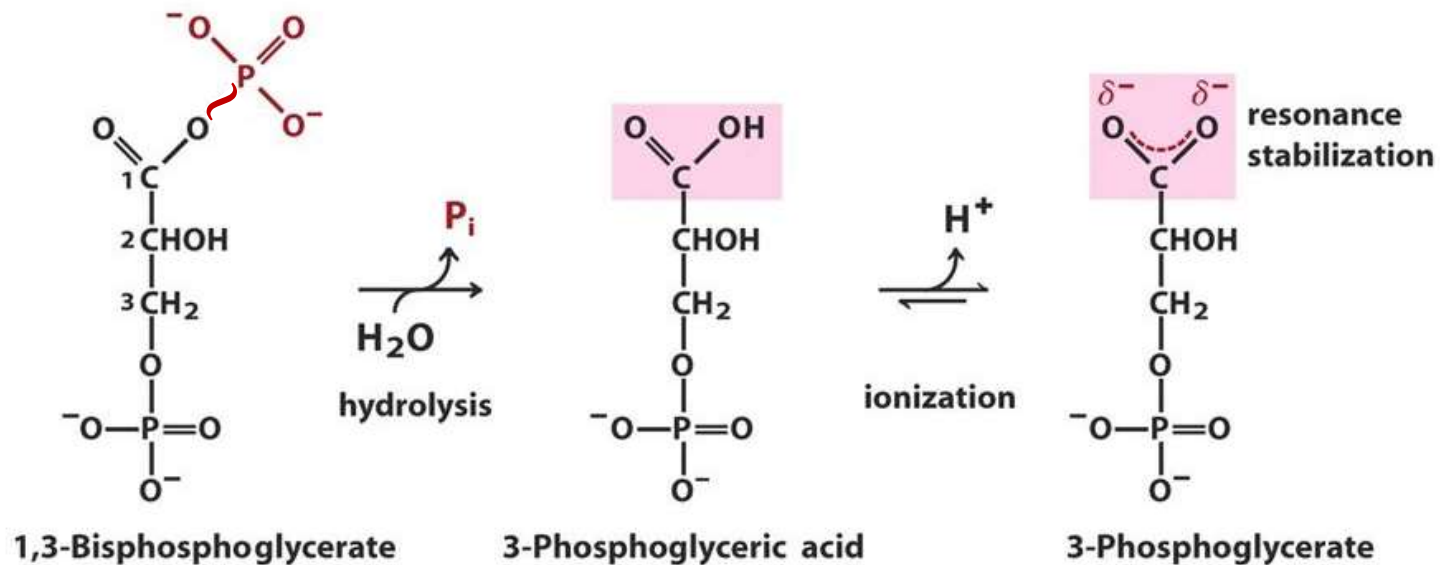
Phosphoenolpyruvate (PEP)

- Reasons that favors hydrolysis of PEP to pyruvate:
 - **Electrostatic charge repulsion** between negatively charged oxygen of phosphoryl group and carboxyl group favors removal of P_i .
 - **Resonance stabilization** of hydrolytic product P_i .
 - Isomerization (tautomerization) of hydrolytic product pyruvate into enol- keto form.



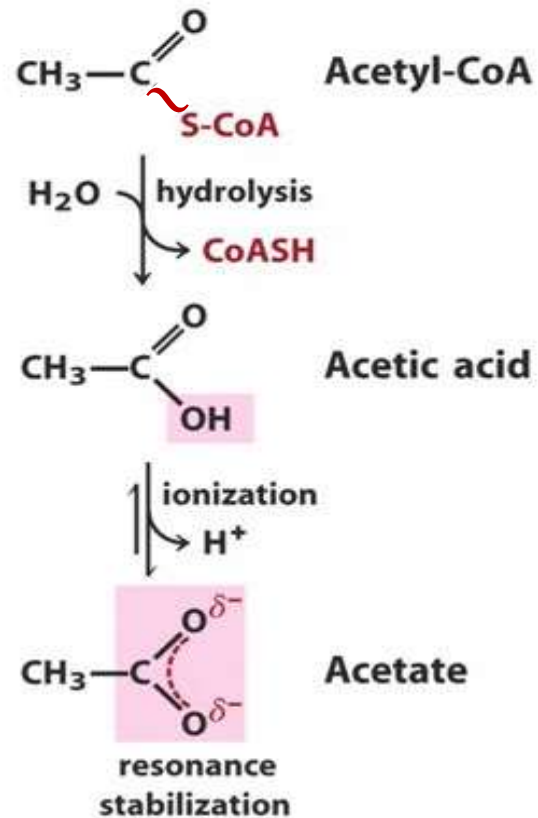
1,3-Bisphosphoglycerate (1,3-BPA)

- Reasons that favors hydrolysis of 1,3-BGA to 3-Phosphoglyceraldehyde:
 - **Resonance stabilization** of hydrolytic product P_i .
 - **Release of proton** from hydrolytic product 3-phosphoglyceric acid to maintain pH of cell.
 - **Resonance stabilization of carboxylic group** of 3-phosphoglycerate.



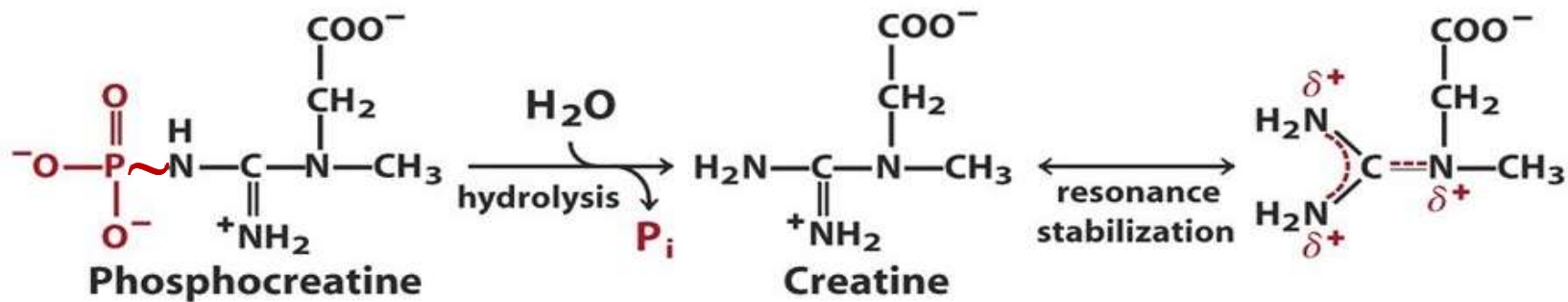
Acetyl CoA

- Reasons that favors hydrolysis of phosphocreatine to creatine: Hydrolytic removal of CoA from Acetyl CoA favors **ionization** and **resonance stabilization** of carboxylic group of the hydrolytic product.



Phosphocreatine

- Reasons that favors hydrolysis of phosphocreatine to creatine:
- **Resonance stabilization** of hydrolytic product P_i .
- **Resonance stabilization** of hydrolytic product creatine.



ATP : UNIVERSAL ENERGY COULER

Intermediate position in phosphate-rich compounds

Phosphoryl-transfer potential : Intermediate position of ATP

- **Phosphate transfer potential:** It is defined as the negative of the standard free energy change ($\Delta G^0'$) for the hydrolytic removal of phosphate from the phosphorylated compounds.
- Phosphates can be transferred from compounds with higher $\Delta G^0'$ to those with lower $\Delta G^0'$.
- ATP occupies an **intermediate position** in overall spectrum of energy-rich phosphorylated compounds (i.e., compounds with high phosphoryl transfer potential (Table 1).
- Compounds viz., **phosphoenolpyruvate (PEP)**, **1,3-bisphosphoglycerate (1,3-BPG)**, and **creatine phosphate** have a higher phosphoryl-transfer potential than that of ATP, while glucose-6-phosphate, glycerol-3-phosphate, etc. have low potential.

Table1. Standard free energy of some phosphorylated compound

	Phosphorylated Compound	$\Delta G^0'$ (kcal/mol)
High Energy Comps	Phosphoenolpyruvate	-14.8
	1,3-bisphosphoglycerate	-11.8
	Creatine phosphate	-10.3
	ATP (to ADP)	-7.3
Low Energy comps	Glucose-1-phosphate	-5.0
	Pyrophosphate	-4.6
	Glucose-6-phosphate	-3.3
	Glycerol-3-phosphate	-2.2

cont.

- This intermediate position ATP makes it an efficient carrier of phosphoryl groups, where **ATP can act as a phosphate donor** and **ADP, its dephosphorylated form can act as a phosphate acceptor** linking energy producing and energy requiring reactions.
- Compounds possessing high-phosphoryl-transfer-potential (1,3-BPG, PEP, and creatine phosphate) derived from the metabolism of fuel molecules can transfer their phosphoryl group to ADP to form ATP. This mechanism for making ATP is called **substrate-level phosphorylation**.
- During glycolysis PEP and 1,3-BPG transfer its phosphoryl group to ADP to form ATP.

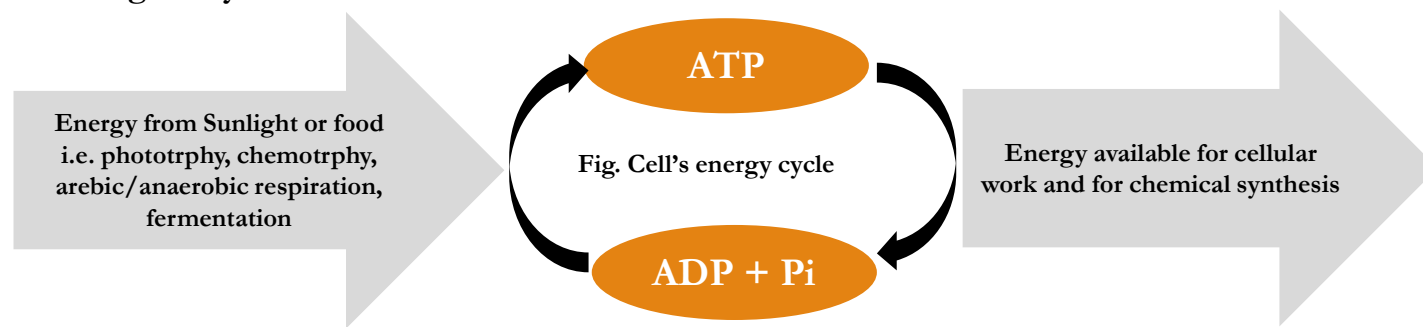


- Creatine phosphate serves as an energy reserve in vertebrate muscle. It is used to regenerate ATP from ADP every time we exercise strenuously. $\text{Phosphocreatine} + \text{ADP} + \text{H}^+ \xrightarrow{\text{Creatine kinase}} \text{Creatine} + \text{ATP}$
- In turn, ATP donates a phosphoryl group to form low energy compounds to facilitate their metabolism.



Role of ATP/ADP System: An intermediate in cellular energy metabolism

- The free energy liberated during hydrolysis of ATP is harnessed to drive reactions that require an input of free energy, such as muscle contraction. In turn, ATP is formed from ADP and Pi when fuel molecules are oxidized in chemotrophs or when light is trapped by phototrophs. This ATP–ADP cycle is the fundamental mode of energy exchange in biological systems.



- ATP is the major energy currency for cells, but it is not the only energy currency.
- Other nucleoside triphosphates (NTPs) have major roles in metabolism. Guanosine 5'-triphosphate (GTP) supplies some of the energy used during protein synthesis. Cytidine 5'-triphosphate (CTP) is used during lipid synthesis, and uridine 5'-triphosphate (UTP) is used for the synthesis of peptidoglycan and other polysaccharides.

THANK YOU