

BIOL 157: BIOLOGICAL CHEMISTRY

Lecture 5:
Laws of Thermodynamics

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LECTURE OBJECTIVES

- Flow of energy
- Transformation of energy
- Laws of thermodynamics
- Factors responsible for the spontaneity of reactions
 - enthalpy, entropy and free energy changes
 - free energy changes in biological systems
- Exergonic and endergonic reactions and Biologically coupled reactions
- High energy phosphate compounds

Explanation of some terms in thermodynamics

- **Energy** --- the capacity to do work
- **Heat** ---- energy transferred because of temperature difference between a system and its surrounding.
- **Temperature** --- this gives a measure of the degree of hotness
 - It is a measure of the average kinetic energy of the molecules that make up an object.
- **System** --- A collection of matter under study.
 - It could be a cell, a chemical reaction in a test tube, an entire organism or a class of students.

- **Surrounding** --- everything outside the system constitutes the surrounding.
 - It can be affected by changes in the system or vice versa.
- **Universe** --- the system and the surrounding put together
- **Open system** -- if a system can exchange matter and energy with its surrounding, it is said to be open.
 - An example of an open system is an exposed beaker with hot water.
 - Some water vapour (matter) can be lost to the surrounding, likewise, heat (energy)

- **Close system** --- energy can be exchanged with the surrounding but not matter.
- **Isolated system** --- A type of system in which neither matter nor energy is exchanged with the surrounding.
- **Adiabatic process** --- If a change occurs in a system in such a way that heat cannot be transferred across the interface or boundary between the system and surrounding.
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- **Isothermal change** --- such a change takes place at a constant temperature.

- **State functions** --- these are properties that depend on the state of a system but not on the process or path taken to reach a certain state.
- **Extensive property** --- this is a property which depends on the amount of material present.
 - Examples are volume, entropy, enthalpy, mass, internal energy etc.
- **Intensive property** --- this does not depend on the amount of material present.
 - It is an intrinsic property: e.g. temperature, pressure, refractive index, melting point, boiling point, emf, density, colour, odour etc.

Laws of thermodynamics

The first law of thermodynamics

- This is also the law of conservation of energy.
- It states that energy can neither be created nor destroyed; it can however be converted from one form to the other.
 - An electric motor can transform electric into mechanical energy.
 - A galvanic cell converts chemical energy to electrical energy.
 - Electrolytic cell converts electrical energy into chemical etc.
- Mathematically, the first law is stated as; $\Delta U = q - w$ or $q = \Delta U + w$
 - where ΔU is the change in internal energy,
 - **q** is the heat energy supplied to the system and
 - **w** is work done.

- The sign convention used is that heat absorbed by the system and work done by the system is given positive quantities.
- Let us look at a system made up of gas molecules confined to a cylinder by a piston.
- The gas molecules have several kinds of energy.
 - They have kinetic energy of translation and rotation.
 - They have energy of vibration due to the displacement of atoms within molecules.
- In translational motion, the entire molecule moves in one direction or the other in straight lines.
- In rotational motion, the molecules spin on their axes.

- Also contributing to the internal energy of molecules is the electronic energy of the molecules, including electron-electron interactions and electron-nucleus interactions.
 - The electronic energies make greatest contributions to the internal energy of a chemical reaction, even though many electronic energy terms do not change in the reaction.
- The most important electronic interactions are the electrostatic attractions that produce chemical bonds between atoms (intramolecular forces).
- The intermolecular forces (electrostatic attraction between molecules) are also important.

Heat (q)

- This is the energy transfer between a system and its surrounding, caused by a difference in temperature between them.
 - Heat is transferred spontaneously from the region of higher temperature to a region of lower temperature.
 - The heat transfer stops when the system and surrounding attain thermal equilibrium.
- When heat energy is added to a system (like the gas molecules confined to the cylinder by piston), the added energy, Δq may be used to increase U by an amount of ΔU .
 - The system under discussion can use the added heat energy in another way.
 - As the gas receives the heat energy, it can expand.

- If the piston were to be frictionless, the expanding gas could move the piston.
 - In so doing, the gas does work on the piston.
- The work done by the system is represented by w : it has positive value.
 - When work is done on the gas (like compression), w is negative.
- Thus the first law is saying that the heat energy q , added to a system can increase the internal energy by an amount ΔU , and it can also cause work to be done.
 - The heat energy added to a system should be equal to the sum of the system's change in internal energy and the work done by the system.

Enthalpy

- The enthalpy of a system is the internal energy of the system plus the changes in pressure and volume of the system.
 - $\Delta H = \Delta U + \Delta PV$
 - At a constant pressure, $\Delta PV = 0$
 - Thus enthalpy becomes equal to internal energy.
- Meanwhile, the internal energy could also be looked at as the heat change of a system at a constant volume.
 - For most biochemical reactions, what is of relevance is the enthalpy change at constant pressure.
 - However, for such biochemical reactions, there is little change in both pressure and volume, so the difference between ΔH and ΔU can be regarded as insignificant.

- Being a state function, it is the changes in enthalpy between the final and initial states which is of importance.
- $\Delta H = H_{\text{final}} - H_{\text{initial}}$
 - where H stands for enthalpy
- For a reaction of the form $A+B \rightarrow C + D$, the enthalpy change can be calculated as follows;
 - $\Delta H = (H_C + H_D) - (H_A + H_B)$
 - If the enthalpy of the final state is higher than the initial state, then ΔH is positive
 - Such a reaction is said to be endothermic as heat is absorbed from the surrounding.
- On the other hand, if the enthalpy of the final state is lower than the enthalpy of the initial state, then ΔH is negative:
 - The reaction is said to be exothermic as heat is released to the surrounding.

Enthalpy and spontaneity of reactions.

- A spontaneous change is the type which takes place on its own accord, without any external influence.
 - Many exothermic reactions are spontaneous.
 - Ice melts spontaneously at room temperature.
- However, there are some endothermic reactions which are also spontaneous.
 - Ammonium sulphate and ammonium chloride dissolve in water even though the dissolution process is endothermic.
 - The driving factor is the increased disorder of the system.
- So it can be said that the tendency towards decreased enthalpy favours reactions.

Entropy and the second law of thermodynamics

- The second law of thermodynamics states that the entropy of the universe increases during physical and chemical processes.
 - Entropy is another state function It is a measure of the disorder or randomness in a system.
- A reaction in which there is increase in entropy ($+\Delta S$) is more likely to occur than the one with lowered entropy ($-\Delta S$).
 - Entropy is associated mainly with translational and rotational motion like enthalpy in which electronic terms are important.

- Entropy per mole increases with molecular weight.
 - Entropy of hydrocarbons increases by 5.8 entropy units (eu) for each - CH₂ in the solid state, 7.7 eu in liquid state and 10.0 eu in the gas phase.
- Hexylbromide has the same number of atoms and bonds as hexane, but due to the higher molecular weight and correspondingly higher translational entropy, its entropy is higher than that of hexane.
- Structural features that make molecules more rigid reduce rotational and vibrational contributions to entropy
 - A double bond will reduce entropy by about 3.5 eu, triple bond by about 4.5 eu, a ring by about 14 eu, and a branch in a chain by about 3.0 eu.

- The reduction of entropy in forming a ring depends on the size of the ring.
- The physical state is also an important factor in determining the entropy of a compound.
 - The order of increasing magnitude of entropy for the physical states is solid<liquid<gas.
 - Not unexpectedly, gases have the highest entropy as they have most translational and rotational freedom.

Why systems move spontaneously to a state of maximum disorder

- A random state is more probable than an ordered state.
 - This is because a random state can be achieved in more ways.
- If ten coins, for example, are tossed, the probability of getting all heads is less than getting a combination of heads and tails.
- There is only one way of obtaining a very ordered arrangement of ten heads.
- But the random arrangement can be achieved in as many as 2^{10} ways.
- $S = k \ln W$
 - where **k** is the Boltzmann's constant and **W** is the number of ways to arrange the components of a system without changing the internal energy.

Standard molar entropy(S^0)

- This is the entropy of 1 mole of a pure substance at 298K and a pressure of 101 .325kPa.
 - The units are joules per Kmol.
- Absolute entropies are measured with respect to an absolute point - the entropy of the substances at 0K.
- The standard entropy change for a reaction is given as follows
 - $\Delta S^0 = \Delta S^0 \text{ products} - \Delta S^0 \text{ reactants}$
- Being an extensive property, if there are coefficients in the equation, we have to multiply the standard entropies by these coefficients

Problem

- Find the standard entropy change for the reaction $\text{N}_2\text{O}_{4(g)} = 2\text{NO}_{2(g)}$ given 1116 standard entropies of NO_2 and N_2O_4 to be 240 and 304.2 J/K-mol respectively.

Living organism and the second law of thermodynamics

- It may appear that living organisms violate the second law of thermodynamics as these organisms take in simple nutrients to form macromolecules for the elaboration of cells and tissues as the case may be.
 - These cellular or tissue structures thus become more ordered highly organized (reduced entropy).
- But if we consider the organism together with its surrounding (i.e. the universe), there is increased entropy, in line with the second law.
 - The organism returns to the surrounding heat energy, waste materials like CO₂, water vapour, etc which randomize the surrounding.

Living cells and free energy

- Heat is not a significant source of energy for living cells because heat can only be used to do work if it passes from a region of higher temperature to another region of lower temperature.
 - For heat engines which require heat for doing work, their efficiency depends on the temperature differential.
 - The greater the temperature drop, the higher the percentage of the input heat energy that can be realized as work output.
- Since living cells have essentially the same temperature throughout, they cannot make significant use of heat energy to do work
 - However, heat is useful to cells for the maintenance of an optimal working temperature.
- The form of energy that cells use is free energy or Gibbs energy (G).
 - This is the energy available to do work at constant temperature and pressure (isothermal and isobaric conditions).

Free energy change and spontaneity of reactions

- It has been mentioned that systems tend towards the state of lowest enthalpy and the highest entropy.
 - But neither of the two terms makes it possible to always predict whether a reaction would be spontaneous.
- The best criterion for predicting the spontaneity of a reaction is the free energy change (ΔG).
- It was an American mathematician, Gibbs who developed an equation relating ΔH and ΔS to ΔG as follows:
 - $\Delta G = \Delta H - T\Delta S$

- The sign on ΔG tells us in which direction a reaction in equilibrium would go.
- A negative ΔG means that the forward reaction as written is spontaneous
 - that reaction would have energy available to do work.
- A positive ΔG means that work must be done on the reaction for it to proceed as written; such a reaction is not spontaneous.
- If $\Delta G = 0$, then the reaction is in equilibrium, the rate of forward reaction is equal to the rate of backward reaction.

How the signs of enthalpy and entropy affect free energy changes

ΔH	ΔS	ΔG	Inference
-ve (favourable)	+ve (favourable)	-ve	Reaction spontaneous at all temperatures
-ve (favourable)	-ve (unfavourable)	+ve	Temperature determines spontaneity. Reaction will be spontaneous at low temperature.
+ve (unfavourable)	+ve (favourable)	+ve	Temperature determines spontaneity. Reaction will be spontaneous at high temperature
+ve (unfavourable)	-ve (unfavourable)	+ve	Reaction will be non spontaneous at all temperatures.

- From the table where enthalpy and entropy changes are favourable, then reaction will be spontaneous at all temperatures.
- On the other hand, where the enthalpy and entropy changes are not favourable, then ΔG is positive at all temperatures
 - indicating the reaction will be non-spontaneous at all temperatures.
- As an example, let us use the outlined thermodynamic principle to explain why the melting of ice is spontaneous at room temperature but not at temperatures below 0°C.



- The melting of ice is an endothermic process, so ΔH is positive.

- There is increased entropy as a more disordered liquid is formed from a solid.
 - Therefore, entropy change is positive.
- From the relation, $\Delta G = \Delta H - T\Delta S$, to make ΔG negative, the temperature should be higher than 0°C , so that the $T\Delta S$ term will be higher than the $+\Delta H$.

Problem

- Why is the freezing of ice spontaneous below 0°C ?

Solution

- Entropy decreases, so ΔS is negative. The freezing is an exothermic process (ΔH -ve).
- Using the relation $\Delta G = \Delta H - T\Delta S$.
- At low temperature below 0°C , the $T\Delta S$ term is low, and the high -ve ΔH will make ΔG negative.
- Reaction in which ΔG is negative means that the reaction is thermodynamically feasible.
- However, the free energy change does not determine how fast the reaction would be.

- A reaction could be thermodynamically feasible but not kinetically feasible because there is no pathway available.
- A catalyst may be added to provide an alternative pathway.
- Free energy change is the most useful of all the thermodynamic functions, but it is the least understood because it is a combined function of entropy and enthalpy.
- Free energy change cannot be directly measured
 - however, it can be calculated.

Various ways of calculating ΔG

From thermodynamic tables

- There are tables in which values of the free energy of formation at Compounds are given.
- To calculate the free energy change for a reaction, we can look up for the values of the free energy of formation of the compounds involved, then use the equation:
 - $\Delta G = \Delta G \text{ products} - \Delta G \text{ reactants}$
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From emf or chemical cell potential: $\Delta G = - nF\Delta E$

- Where ΔE is the emf of the cell.

From equilibrium constants or reaction quotients.

- For a reaction of the type $A + B = C + D$, the free energy change for the reaction can be written as
 - $\Delta G = -RT \ln K$
 - or $\Delta G = \Delta G^\circ + RT \ln K$
 - or $\Delta G = \Delta G^\circ + RT \ln Q$
- ΔG is the free energy change under non-standard conditions.
- ΔG° is the standard free energy change which is constant for each individual reaction in which the reactants and products are present at concentrations of 1.0M.
- At equilibrium, $\Delta G = 0$
- So the expression $\Delta G = \Delta G^\circ + RT \ln K$ becomes
 - $\Delta G^\circ = -RT \ln K$

Problem

- An enzyme hydrolyses fructose 1 - phosphate as follows:
Fructose-1-phosphate \rightarrow fructose + Pi
- At 25°C, the initial concentration of the fructose-1-phosphate was 0.2M, but at equilibrium, the concentration of fructose 1-phosphate was 0.012M. Calculate the equilibrium constant for the reaction as well as the standard free energy hydrolysis of fructose- 1-phosphate.

Solution

$$K = \frac{[\text{fructose}][\text{Pi}]}{[\text{fructose-1-Phosphate}]}$$

Since the initial concentration of fructose-1-phosphate was 0.2M, and its equilibrium concentration, 0.012M, the concentration of fructose produced at equilibrium would be

$$0.2 - 0.012 = 0.188\text{M}.$$

The concentration of inorganic phosphate (Pi) produced at equilibrium will be the same as that of fructose.

$$K = \frac{(0.2 - 0.012)(0.2 - 0.012)\text{M}^2}{0.012\text{ M}}$$

Standard free energy changes of chemical reactions are additive

- In metabolic pathways made up of a sequence of reactions in which the product of one reaction becomes the reactant for another step, the free energy changes of the individual reactions can be added.
- Consider the reaction sequence, $A \rightarrow B \rightarrow C \rightarrow D$.
- Each reaction in the pathway is catalysed by a different enzyme.
- It is possible for some of the enzyme-catalysed reactions to have a positive free energy change, making those steps non-spontaneous.
- However, as long as the sum of all the free energy change is negative, the pathway would proceed spontaneously.

- In glycolysis, for example, some of the steps have positive ΔG or have ΔG values close to zero.
- But there are other reactions with large negative
- ΔG values which tend to drive the entire pathway.
- This introduces us to the principle of coupled reactions in biological systems.

Biologically coupled reactions

- For reactions which are thermodynamically feasible, there is release of free energy ($-\Delta G$).
- Such reactions are said to be exergonic, and will have energy to do work.
- Those reactions with positive ΔG changes are not thermodynamically feasible, and are said to be Endergonic.
- For such reactions, work has to be done on them before they proceed.

- In biological systems, the arrangement of reactions is such that a reaction which is thermodynamically feasible is linked to another reaction which is not thermodynamically feasible, so that the free energy released in the exergonic reaction is used to drive the endergonic reaction.
- Interconnected endergonic and exergonic reactions are termed coupled reactions.
- Such coupled reactions show the flow of energy between reactions.
- Another feature shown by coupled reactions is the formation of common intermediates.

ATP as the major link between exergonic and endergonic reactions

- If ATP is hydrolysed in isolation, its free energy of hydrolysis would just be dissipated as heat.
- Such a process would be of little utility to a cell.
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- For the utmost utility of ATP, its hydrolysis should be linked to an energy-requiring reaction.
- When ATP undergoes hydrolysis to lose its terminal phosphate to form ADP, a lot of free energy is released



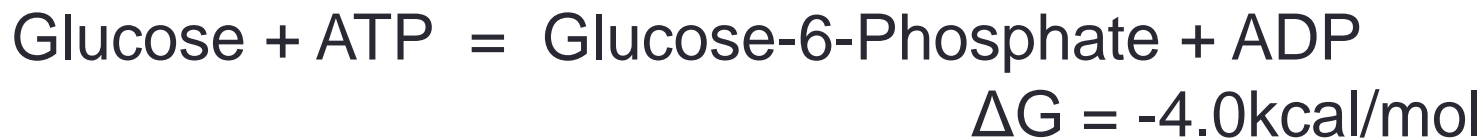
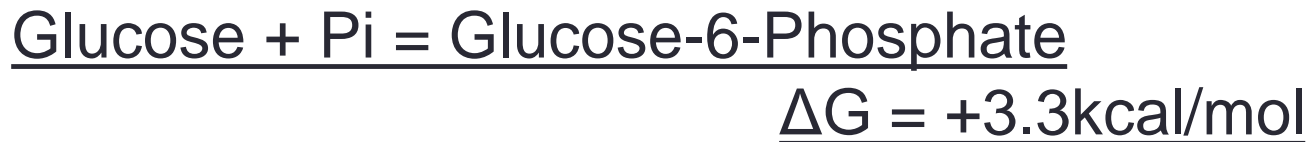
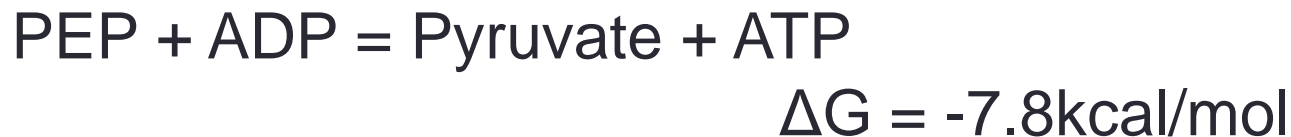
- Due to the high free energy released when ATP is hydrolysed, it is referred to as a high energy compound.
- It is also said to have a high phosphate group transfer potential.
- There are some other phosphorylated compounds whose phosphate group transfer potential could be higher or lower than that of ATP.
- Those with lower phosphate group transfer potential on hydrolysis yield less free energy than ATP.
- Eg. Glucose-6- phosphate \rightarrow Glucose + Pi
 $\Delta G = -3.3 \text{ kcal/mol}$

- For those with higher phosphate group transfer potential, when hydrolysed, the free energy of hydrolysis is higher.
 - Phosphoenolpyruvate \rightarrow Pyruvate + Pi $\Delta G = -14.8$ kcal/mol.
- Such compounds are called 'super high' energy compounds.
- Compounds with phosphate group transfer potentials could be arranged on a thermodynamic scale based on the magnitude of the free energy of hydrolysis.
- Those with very high phosphate group transfer potential would be placed above ATP, while those with lower transfer potential would be placed below ATP.

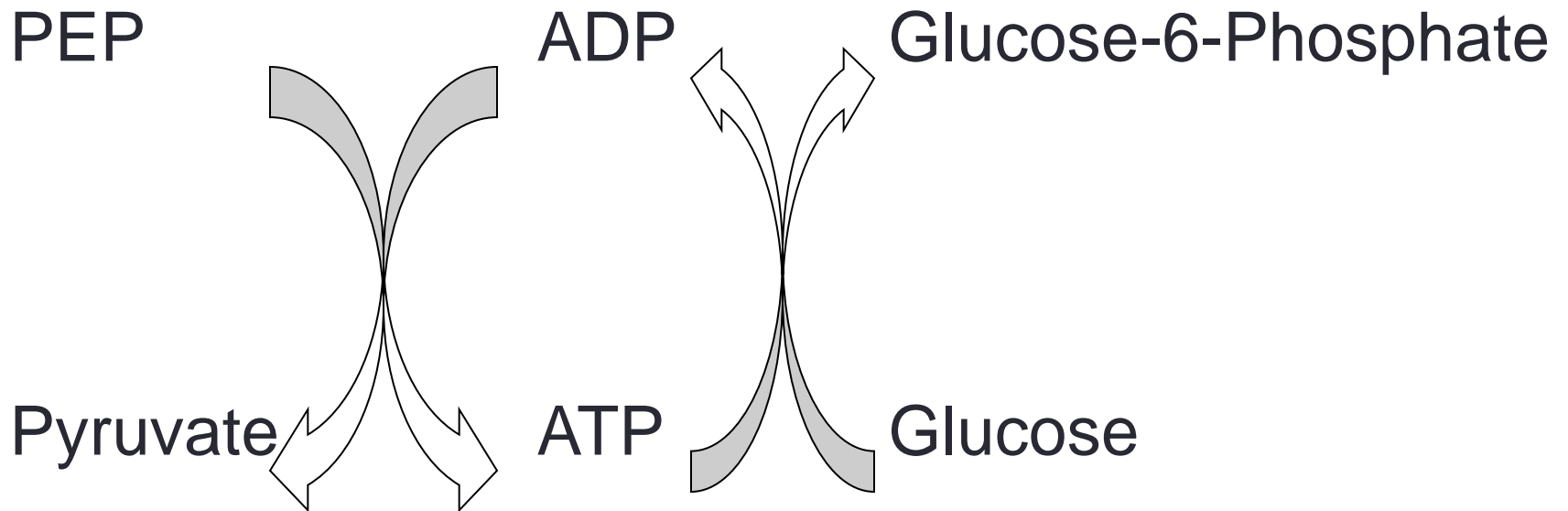
- Thus ATP occupies an intermediate position.
- In energy metabolism, a super high energy compound would transfer its phosphate to ADP to form ATP, which in turn, gives its terminal phosphate to another compound to form a low energy phosphate compound.
- Such low energy compounds cannot be formed directly from the 'super high' energy compounds without the intermediation of ATP:
 - this is because there is no enzyme available to catalyse this direct transfer.

	ΔG
PEP \rightarrow Pyruvate + Pi	-14.8
3-phosphoglyceroyl phosphate \rightarrow 3-phosphoglycerate + Pi	-11.8
Phosphocreatine + ADP \rightarrow ATP + Creatine	-10.3
ATP + H₂O \rightarrow ADP + Pi	-7.3
AMP \rightarrow Adenosine + Pi	-3.4
Glucose-1-Phosphate \rightarrow Glucose + Pi	-5.0
Fructose-1-Phosphate \rightarrow Fructose + Pi	-3.8

- We will now look at the energy changes involved in the transfer of phosphate group of PEP to glucose via ATP



- A biological notation for these coupled reactions is shown as:



Chemical nature of energy-rich compounds.

- The energy-rich compounds are of the following groups of compounds.
- Phosphoric acid anhydrides. Examples are ATP, ADP, GTP, UTP, CTP and pyrophosphate (PPi).
- Mixed anhydrides of phosphoric and carboxylic acids. These are the acyl phosphates. examples being acetyl phosphate and 1, 3-bisphosphoglycerate.
- Guanidinium phosphates: eg. creatine and arginine phosphates
- Enol phosphate: eg. Phosphoenolpyruvate

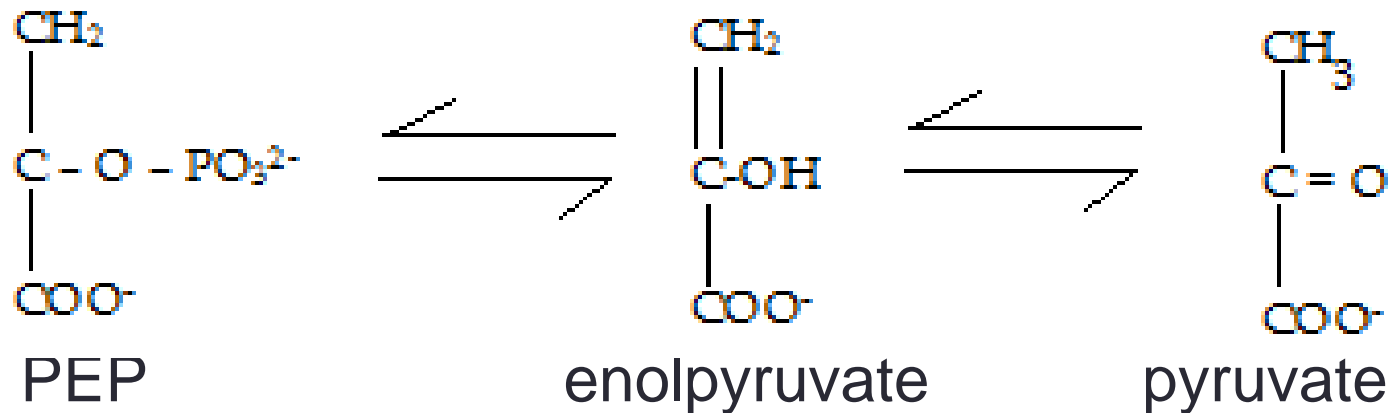
- Thiol esters which are acetyl-CoA derivatives such as acetyl-CoA and succinyl Co-A.
- Cyclic nucleotides, such as 3',5'-cyclic AMP.
- Amino acid esters: eg. aminoacyl-tRNA
- Pyridine nucleotides like NADH and NADPH
- Sugar nucleotides: eg. UDP-glucose
- Methyl group donor like S-adenosyl methionine

Why some compounds serve as high energy compounds

Reasons accounting for the large negative free energy of hydrolysis of high energy compounds

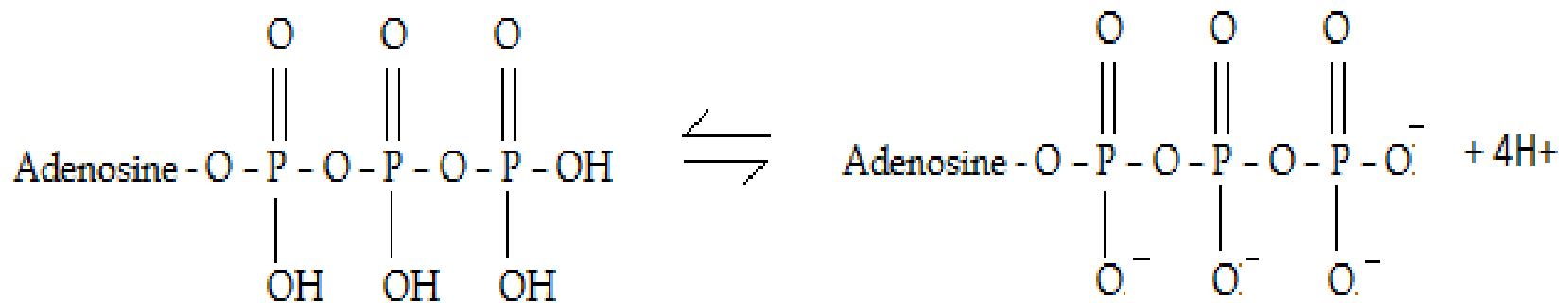
- Electrostatic repulsion on molecules causing bond strain which destabilizes the molecule.
- Stabilisation of products of hydrolysis by ionization
- Stabilisation of products of hydrolysis by resonance
- Hydrolysis of certain energy-rich compounds results in the formation of unstable compounds which may isomerise spontaneously to form a more stable compound.

- Phosphoenolpyruvate undergoes this process;
- PEP = enol pyruvate = Pyruvate



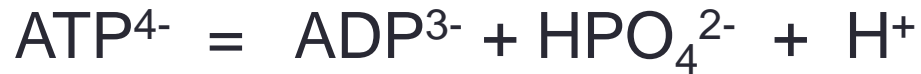
- With ATP being the universal energy currency, let us now focus on the structural features which make it the high energy compound it is.

- Factors like bond strain due to electrostatic repulsion, stabilization of products of hydrolysis by resonance and ionization are important.
- At the physiological pH, ATP dissociates as follows



- The dissociated ATP forms a tetraanion which has four closely—spaced negative charges which repel each other, creating a bond strain in the anion.

- To relieve itself of this strain, a phosphate is hydrolysed to form ADP^{3-} and HPO_4^{2-}

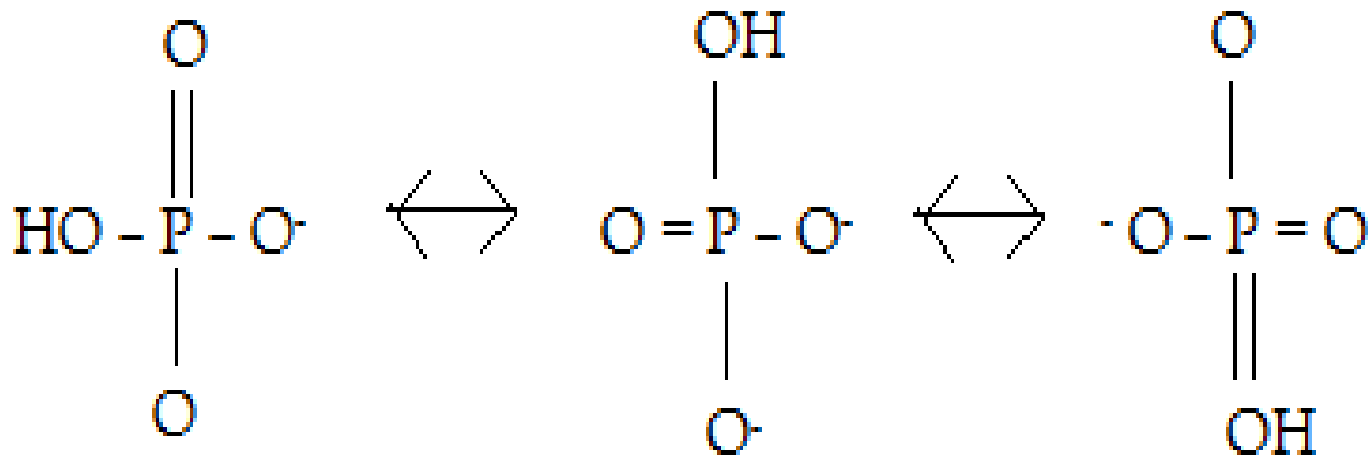


- The two anionic products formed have little tendency to approach each other to combine in reverse direction to form ATP^{4-} again.
- For a low energy compound like glucose-6-phosphate, it hydrolyses this way:



- An uncharged glucose molecule is formed, together with the anionic inorganic phosphate.
- The likelihood of the two products recombining to form Glucose-6-phosphate is high as there repulsion.

- The more the resonating structures, the higher the stability of the molecule.
- On the hydrolysis of ATP, the resonating structures of the products, particularly, the organic phosphate are more than the unhydrolysed ATP^{4-}



- Another factor is that after the hydrolysis of ATP, one of the products, inorganic phosphate, can further dissociate to give H ion,
 - and the subsequent buffering of this ion contributes to the overall free energy of hydrolysis.
- This last factor is supported by the observation that when ATP is hydrolysed in a medium of pH around 1, the free energy of hydrolysis is far lower than when it is carried out at physiological pH.

The effect of Mg^{2+} ion on the free energy of hydrolysis of ATP

- Cellular fluid contains high concentration of Mg^{2+} ions.
-
- These ions can form complexes with ATP^{4-} or ADP^{3-}
$$Mg^{2+} + ATP^{4-} \rightarrow [Mg\ ATP]^{2-}$$
- On forming such a complex, some of the negative charges on the ATP^{4-} anion are neutralized.
- As a result, the repulsive forces between the negative charges decrease.
- The tendency to cleave the terminal phosphate due to destabilisation gets less and the free energy of hydrolysis becomes lower.

The significance of ATP and related triphosphates

- The hydrolysis of ATP in a cell is coupled with any of the following processes.
 - Synthesis of macromolecules
 - Molecular contraction in animals
 - Active transport of substances across membranes
 - Transmission of nerve impulses.
- Other examples are
 - Guanosine triphosphate (GTP) is important in signal transduction and protein synthesis.
 - Uridine triphosphate (UTP) is used in polysaccharide biosynthesis
 - Cytidine triphosphate (CTP) is for phospholipid biosynthesis.
 - dATP, dTTP, dCTP and dGTP are for DNA synthesis.