
# 418 Chem.
# Bioinorganic Chemistry

## Part II. Transport and Storage of Metal Ions

### a. Sodium and Potassium

# Outline- Part II-a

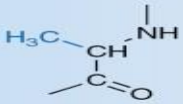
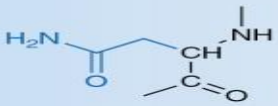
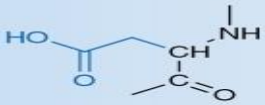
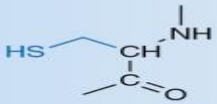
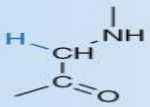
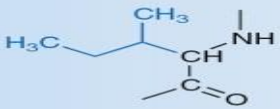
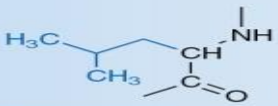
- Metal coordination sites
- Sodium and potassium transport

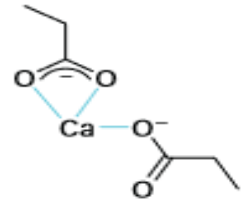
# Metal binding in Biological Systems

- The roles of metal ions reflect their fundamental properties; charge, size, electronic configuration and rates of ligand exchange.
- Major binding sites for metal ions are provided by the amino acids that make up protein molecules.
- Ligation sites range from backbone peptide carbonyls to the side chains that provide more specific complexation.

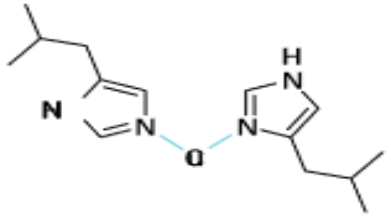
What is a peptide?

**Table 26.2** The amino acids and their codes

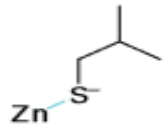
| Amino acid | Structure in peptide chain (side chain shown in blue) | Three-letter abbreviation | One-letter abbreviatio |
|---|---|---|---|
| Alanine |  | Ala | A |
| Arginine |  | Arg | R |
| Asparagine |  | Asn | N |
| Aspartic acid |  | Asp | D |
| Cysteine |  | Cys | C |
| Glutamic acid |  | Glu | E |
| Glutamine |  | Gln | Q |
| Glycine |  | Gly | G |
| Histidine |  | His | H |
| Isoleucine |  | Ile | I |
| Leucine |  | Leu | L |



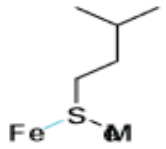
**3** $Ca^{2+}$ coordination



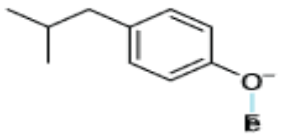
**4** Cu–imidazole coordination



**5** Zn–cysteine coordination



**6** Fe–methionine coordination



**7** Fe–tyrosine coordination

# How do:

- charge
- size
- electronic configuration
- and rates of ligand exchange

affect the roles of metals?

# Metal binding in Biological Systems

Defining metal binding classes:

- The s-block metals ($Na^+$, $K^+$, $Mg^{2+}$, $Ca^{2+}$) interact weakly with ligands due to their poor polarizing power and prefer to bind to oxygen donor ligands.

Are these hard or soft acids?

# Metal binding in Biological Systems

- The transition metals

with partially filled *d -orbitals* bind ligands more strongly than the *s-block* metals.

- 3*d* metals (V- Zn) are all essential elements, while Mo appears to be the only essential metal in the second row of transition metals)
- They adopt different coordination numbers and geometries, and therefore undergo changes in coordination numbers (have different oxidation states) during the redox process.

# Metal binding in Biological Systems

- One advantage of studying transition metals in biological systems is that their electronic properties help us characterize their binding sites
- Unlike main group elements like Na+ and K+, which offer limited information from NMR alone due to their simpler electronic structures

Why do transition metals bind ligands more strongly than the s-block metals?

# Metal binding in Biological Systems

- Toxic elements usually:

➢ $4d^{10}$, $5d^{10}$ (Cd, Hg)

➢ *p*-block metals (Th, Sn, Pb, and As)

They are all readily polarized (soft), bind strongly to many ligands, particularly soft ligands, and displace essential metals from their binding sites resulting in conformations .

Why are these metals toxic?

# Special ligands

Ligand groups available include:

- Negatively charged groups ( e.g. carboxylate, thiolate or phosphate)

- Groups such as amine, which coordinate to the metal center through lone pairs of electrons.

- Macrocyclic ligands ( e.g. porphyrins).

- Bridging sulphide or oxide ligands.

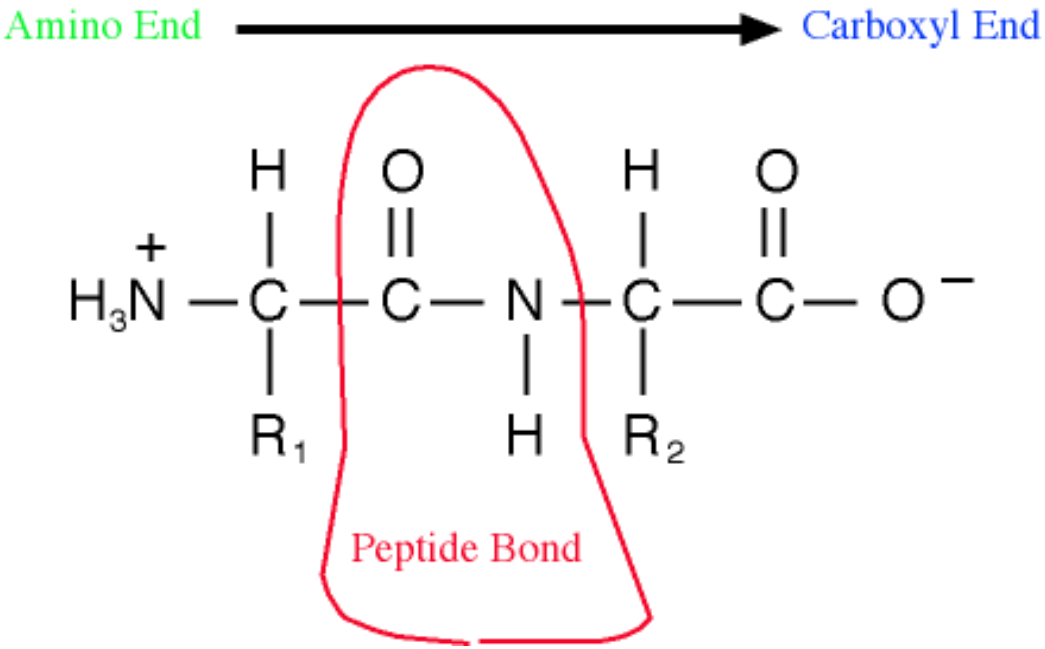
Write the chemical formulae for carboxylate, thiolate , amine, phosphate and sulphide.

# Special ligands

We can categorize ligands accordingly to:

1. Ligand groups on peptides and proteins

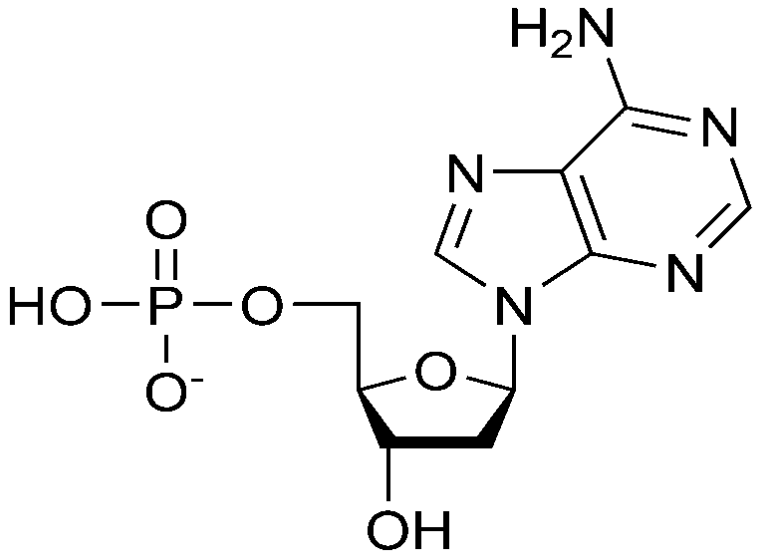
(present in cell walls) with amine and carboxylate termini, deprotonated peptide links, thiols…



# Special ligands

2. Ligand groups on nucleotides and nucleic acids. Here the metal binds to phosphates and nucleotide base moieties and only weakly to sugar groups.

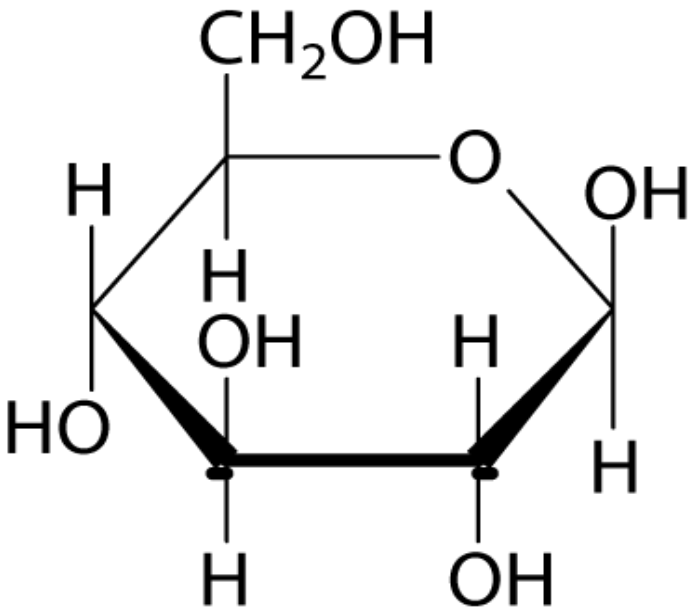
**Nucleotide= N base+ pentose + phosphate group**



# Special ligands

3. Ligand groups on polysaccharides, which are always extremely diverse in their metal binding sites.

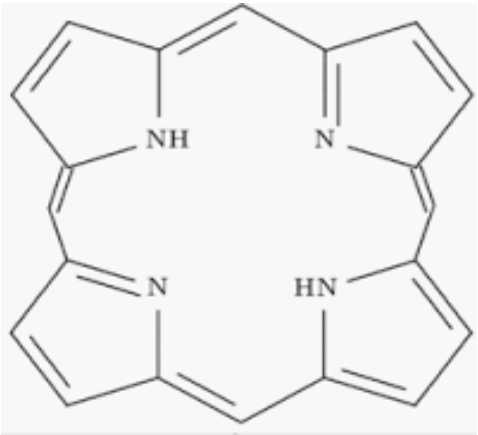
**Saccharide= made only from H, C, O**



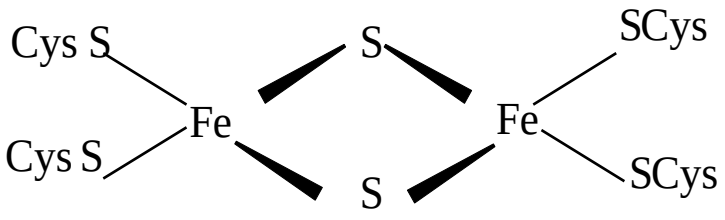

Can you guess where can a metal bind?

# Special ligands

4. Macrocyclic ligands: A range of tetrapyrole ligands are available to bind metals as Fe (e.g. porphyrin)




5. Metal clusters with bridging sulphide or oxide (such as Fe-S clusters) found in some proteins where they bind via cysteine thiolate groups



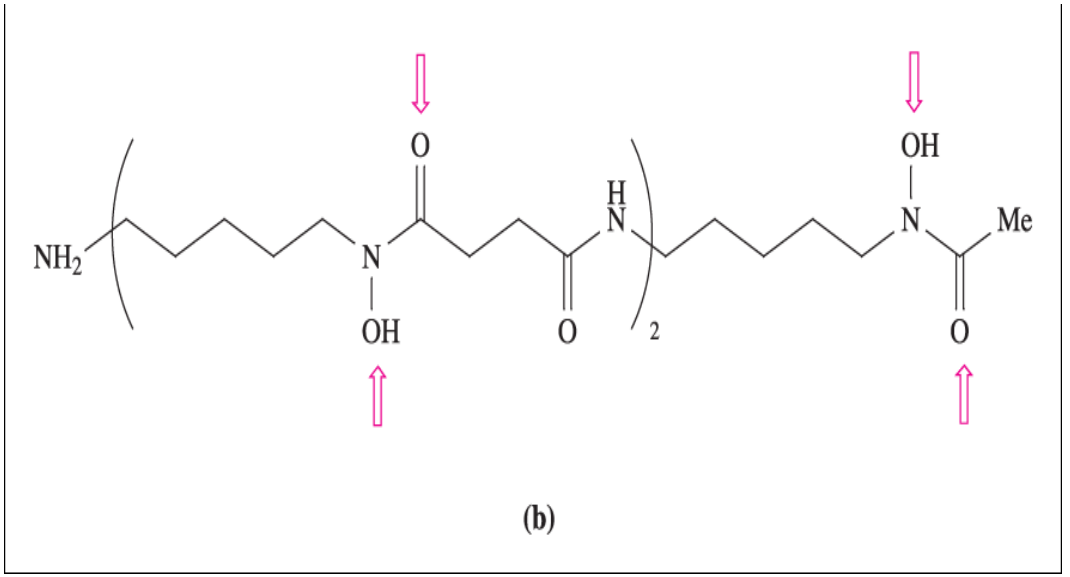
# Special ligands

6. Specialized ligands: such as Fe-carriers siderophores.

(*All siderophores form very stable chelate complexes with approximately octahedrally coordinated high spin Fe(III)*)

Example: Desferrioxamine

(OH groups are deprotonated before coordination to $Fe^{3+}$.)



Construct a table listing ligand groups in biological systems and the functional metal-binding group in each

# Metal-ligand interactions

Metal-ligand interaction is associated with all terms that relate to functions in biology;

- ✓ Selectivity
- ✓ Stabilization
- ✓ Cross-linking
- ✓ Orientation
- ✓ Reactivity
- ✓ Redox potential values

Define each of the above terms.

- **The strength of metal-ligand interaction**

  - Is characterized by a formation constant, which is usually measured at fixed temperatures and ionic strengths.
  - A higher formation constant indicates a stronger binding between the metal ion and the ligand.
  - formation constant can vary depending on the specific metal ion and ligand involved and the experimental conditions.
  - Metal ions compete with protons for ligands, so they bind less well at lower pH values. Competition for a metal from two ligands could well be determined by the $pK_a$ values of the protonated ligands.
  - at a certain pH, one ligand may be protonated and therefore less able to bind the metal ion, while the other may be deprotonated and more able to bind the metal ion.

# Metal-ligand interactions

- **Factors affecting metal-ligand interaction**

The complexing power of a metal ion depends upon its polarizing power (charge/radius ratio).

***1. Hard and soft acids and bases***

$M^{n+}$ of biological significance are hard or borderline acids;

- main cellular constituents (binding groups) are generally hard ligands (with N or O donor atoms).

# Metal-ligand interactions

- Some biological ligands are soft (S containing side chains), they moderate the overall hardness /softness of a metal binding site to control selectivity and stabilize the lower oxidation states.

Discuss the above.

# Metal-ligand interactions

## *2. Chelation and ion exchange*

Molecular models of metal binding are usually either :

-chelation, in homogenous reactions,

- ion exchange in heterogenous reactions.

## *3. Back -bonding*

Metal sites in biological systems are involved in binding and activation of small molecules such as gaseous $O_2$, $N_2$, CO ….

# Metal-ligand interactions

Complex formation here arises from the synergic effect resulting from:

- Sigma ($\sigma$) ligand-to-metal and

- back-bonding metal-to-ligand pi ($\pi$) bond

**Example:**

$O_2$ molecule is activated by binding to Fe(II). Electron transfer to dioxygen takes place via overlap of a metal *3d* and the antibonding $\pi$ molecular orbitals of dioxygen.

# Metal-ligand interactions

➢ ***Metals and selectivity for binding***

- $M^{n+}$ may be bound selectively by a ligand which possess the appropriate donor atoms and is able to accommodate the normal geometry of the metal ion.

-In biological systems, the nature of the groups at the binding sites discriminates immediately between metals.

How does this relate to HS acids and bases?

# Metal-ligand interactions

**Example**

If the binding site is made up of N or S ligands, the binding of the transition metal or zinc is favoured and the group I and II cations will be excluded.

*Note*

*Other factors are important, e.g metal ion concentration.*

# Outline- Part II-a

- Metal coordination sites
- Sodium and potassium transport

# Na and K

- Sodium and potassium have high natural abundances, occurring widely as salts such as chlorides

- Valence electron configuration $ns^1$.

- Chemical properties are those of the Group 1 elements which correlate with the trend in their atomic radii.

# Na and K

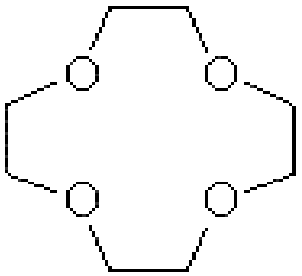
- The Group 1 element ions are hard Lewis acids and complexes are formed mainly with small, hard donors such as O or N atoms.

- Their hardness decreases down the group with increasing ionic radius (hence more covalent character)

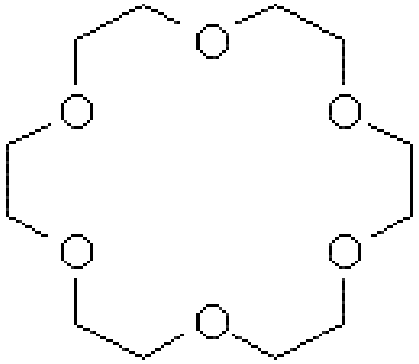
- $Na^+$ and $K^+$ are two ions that are very similar except for their radii

# Na and K

- Differentiating between these two ions is achieved through their selective complexation by special ligands, such as crown ethers, with dimensions appropriate for coordination to one particular kind of ion.



[12]-crown-4



[18]-crown-6

What is the basis of differentiation?

# $Na^+$ and $K^+$ transport

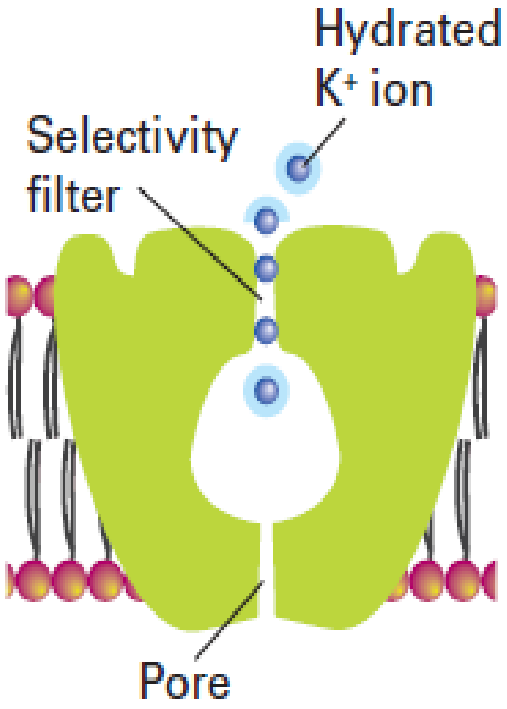
These ions are transported through the membranes by:

**1. Ion channels**; large membrane- spanning proteins that allow selective transport of $K^+$ and $Na^+$ (as well as $Ca^{2+}$ and $Cl^-$) and are responsible for electrical conduction in the nervous systems as well as in coupled transport of solutes. *Passive transport*.

# $Na^+$ and $K^+$ transport

**Mechanism**:

- Moving from the inside surface of the membrane, there is a pore leading into a central cavity about 1 nm diameter; $K^+$ ions can remain hydrated.

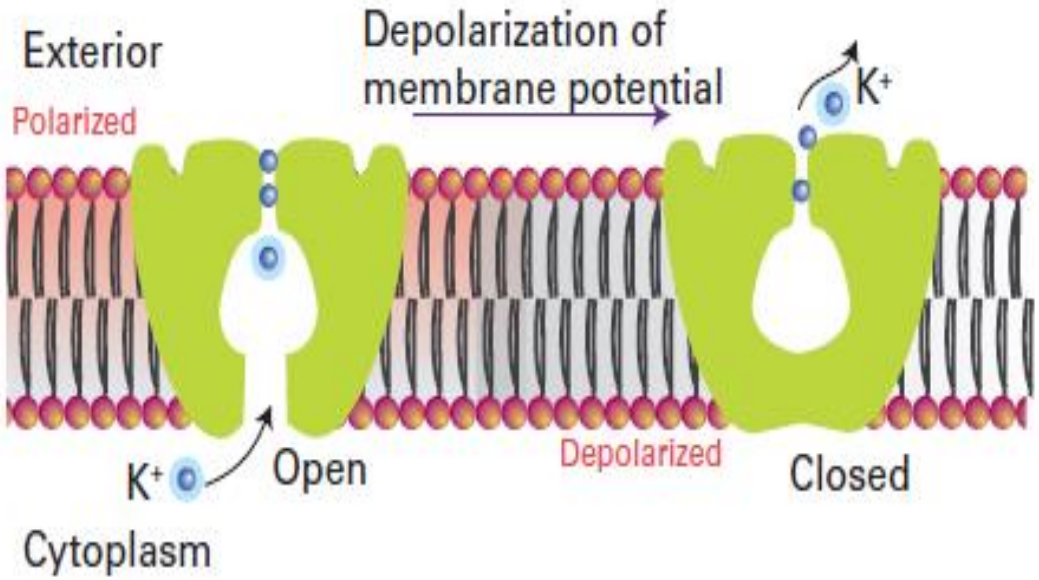



- The binding is weak and fast because it is important to convey but not to trap $K^+$.

# $Na^+$ and $K^+$ transport

Summary:

The potential difference across the membrane is sensed by the protein, causing the pore to open, allowing hydrated ions to enter the cavity. After shedding the hydration sphere, $K^+$ ions pass up the selectivity filter.



# $Na^+$ and $K^+$ transport

## 2. The Na/K pump;

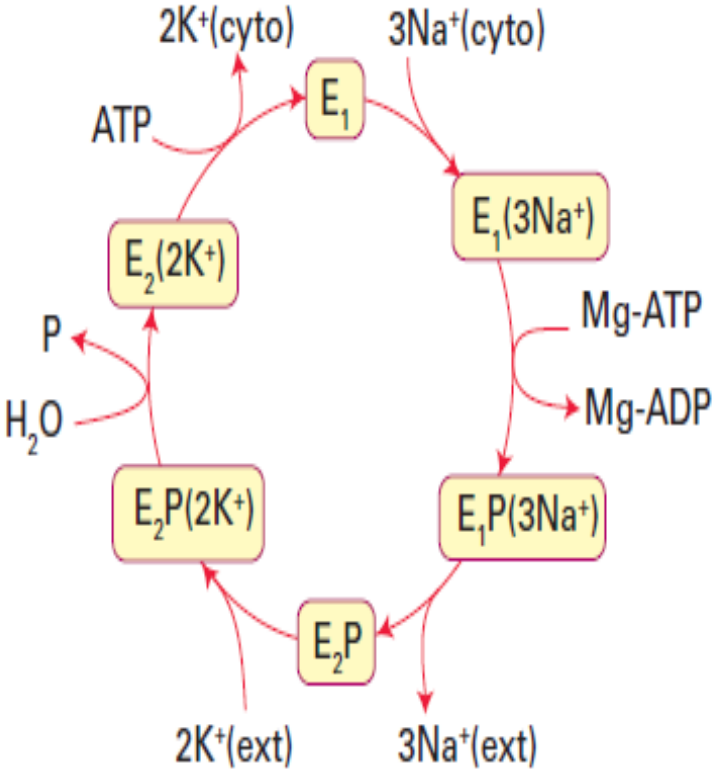
maintains the concentration differential of $Na^+$ and $K^+$ inside and outside a cell. The ions are pumped against their concentration gradients by coupling the process to ATP hydrolysis. *Active transport.*

General principle of the Na, K-ATPase (the Na pump) is shown in the next figure:

# $Na^+$ and $K^+$ transport

In the cytoplasm

- Release of two $K^+$ accompanies binding of ATP and conversion of the enzyme, which binds three $Na^+$.
- A phosphate group (P) is transferred to the enzyme, which opens to the external side, expels three $Na^+$ then binds two $K^+$.
- Release of (P) causes release of $K^+$ and the cycle begins again

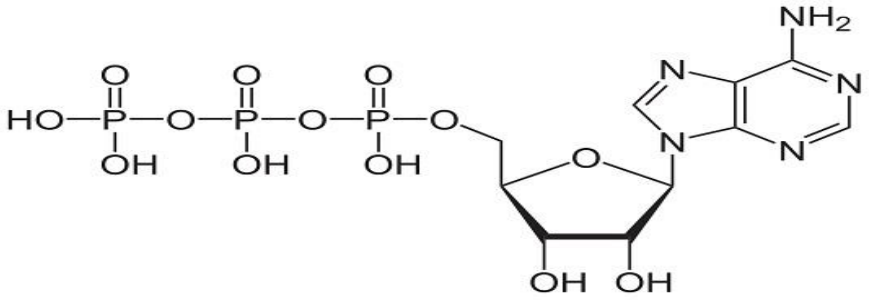


# What is ATP?

## *Adenosine triphosphate*

Is considered by biologists to be the energy currency of life.

- It is the high-energy molecule that stores the energy we need to do just about everything we do.
- It is present in the cytoplasm and nucleoplasm of every cell,
- All the physiological mechanisms that require energy for operation obtain it directly from the stored ATP.



https://youtu.be/DiOkwOEsVNk

Differentiate between ion channels and ion pumps (compare).