ATPases

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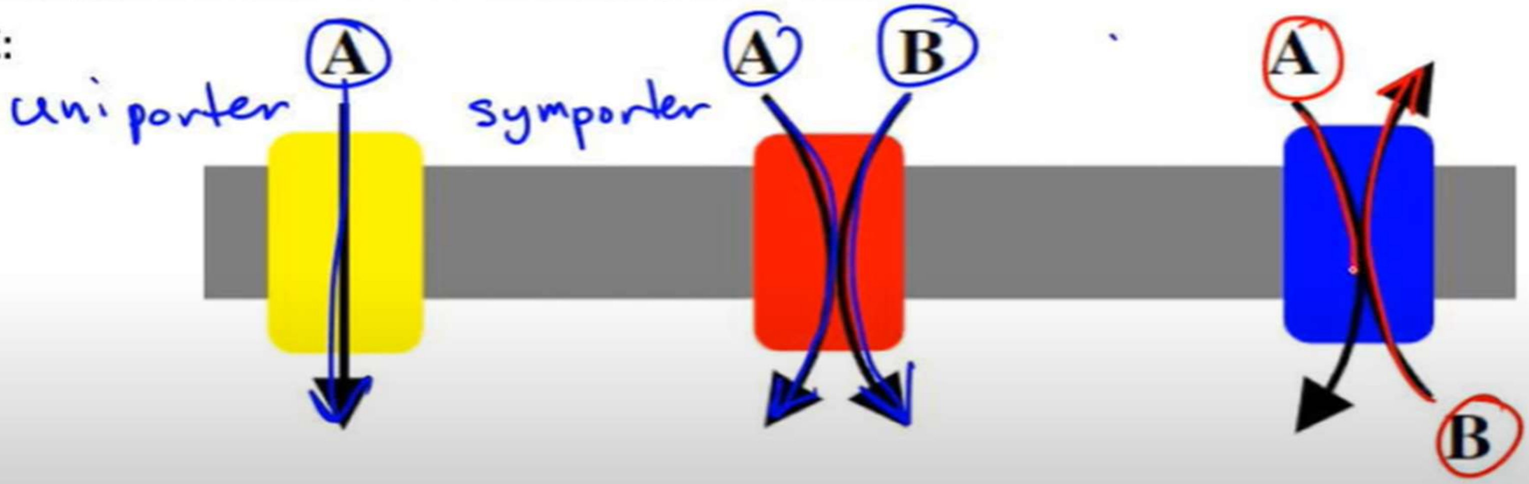
CONCEPT: ACTIVE TRANSPORT

Active transport uses energy to move molecules or ions across the membrane

- ***Primary active transport*** uses energy directly, usually by hydrolyzing ATP to power proteins.
  - □ ***Uniporters*** move one substance in one direction
  - □ ***Symporters*** move two substances in the same direction
  - □ ***Antiporters*** move two substances in opposite directions

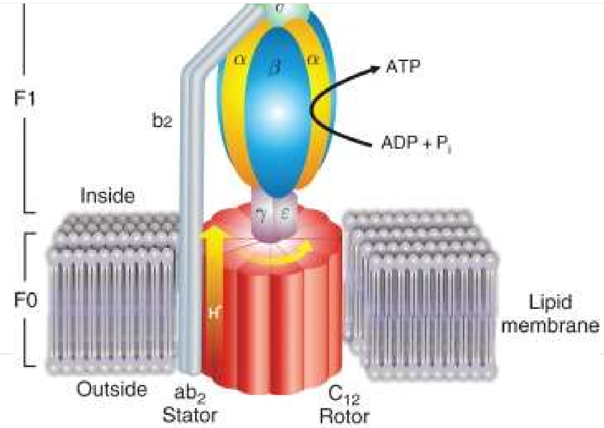
EXAMPLE:



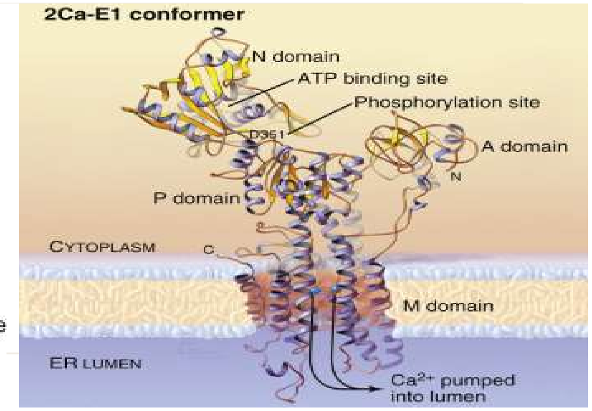
ATPases

- **ATPases** are a group of enzymes that catalyze the hydrolysis of a phosphate bond in adenosine triphosphate (ATP) to form adenosine diphosphate (ADP).
- They are associated the energy released from the breakdown of the phosphate bond and utilize it to perform other cellular reactions.
- ATPases are essential enzymes in all known forms of life and have fundamental roles in energy conservation, active transport and pH homeostasis.
- Some such enzymes are integral membrane proteins (anchored within biological membranes), and move solutes across the membrane, typically against their concentration gradient. These are called *transmembrane ATPases*.

Classification of ATPases



F-ATPases



P-ATPases

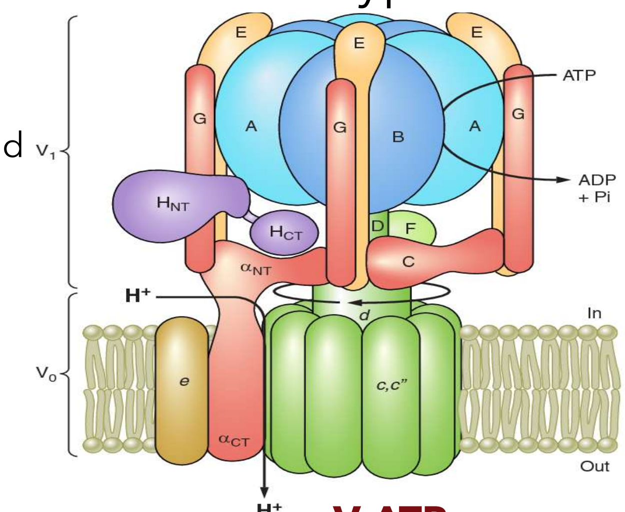
- There are three classes of ATPases, which differ in structure and the type of ion that they transport;

1. F-ATPases (e.g. mitochondrial H^+-ATPase, chloroplasts and bacterial plasma membranes ATPases)

2. P-ATPases (e.g. Ca^{2+}-ATPase, Na^+,K^+-ATPase)

Found in bacteria and also in eukaryotic plasma membranes and organelles

3. V-ATPases (e.g. lysosomal H^+-ATPase) eukaryotic vacuoles,

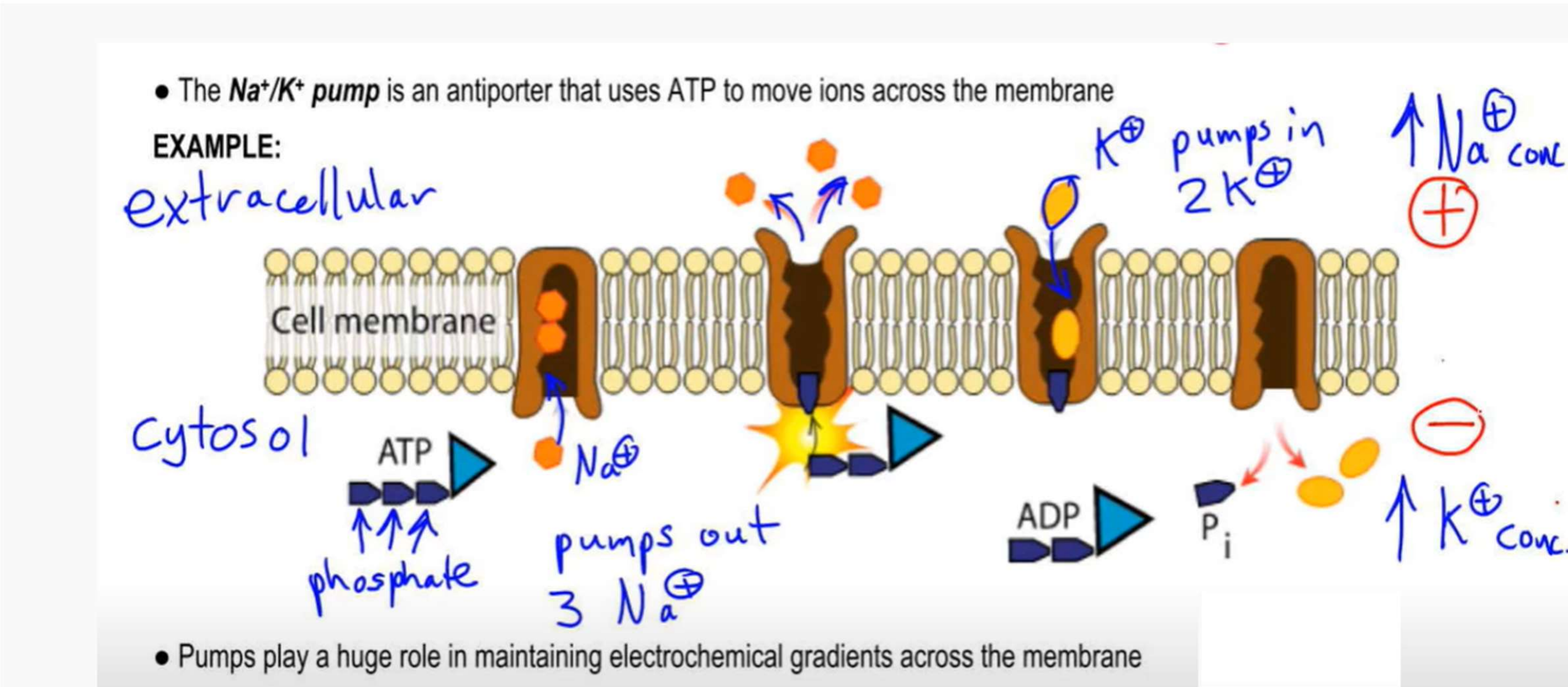


V-ATPases

P-type ATPase

- The first category is that of P-type ATPases. The key feature of these is reversible phosphorylation of an Asp residue and inhibition by a phosphate analog Vanadate.
- P-type ATPase have wide distribution. All animal tissues have Na^+-K^+ ATPase (an anti-porter), Ca^{++}. uniporter
- These help to maintain ionic gradient between cytosol and extracellular milieu.
- In higher plants, an ATPase creates a difference of 2 pH units across the plasma membrane that creates the electrochemical gradient,
- Bacteria also operate a P-type ATPase pump to get rid of the metal ions such as Ca2+, Hg2+ from their cells

Antiporter



• The Na^+/K^+ ***pump*** is an antiporter that uses ATP to move ions across the membrane
EXAMPLE:
extracellular
Cell membrane
cytosol
ATP
phosphate
$Na^{\oplus}$
pumps out
3 $Na^{\oplus}$
$K^{\oplus}$ pumps in
2 $K^{\oplus}$
↑ $Na^{\oplus}$ conc.
↑ $K^{\oplus}$ conc.
ADP
P_i
• Pumps play a huge role in maintaining electrochemical gradients across the membrane

Uniporter

Calcium Pump

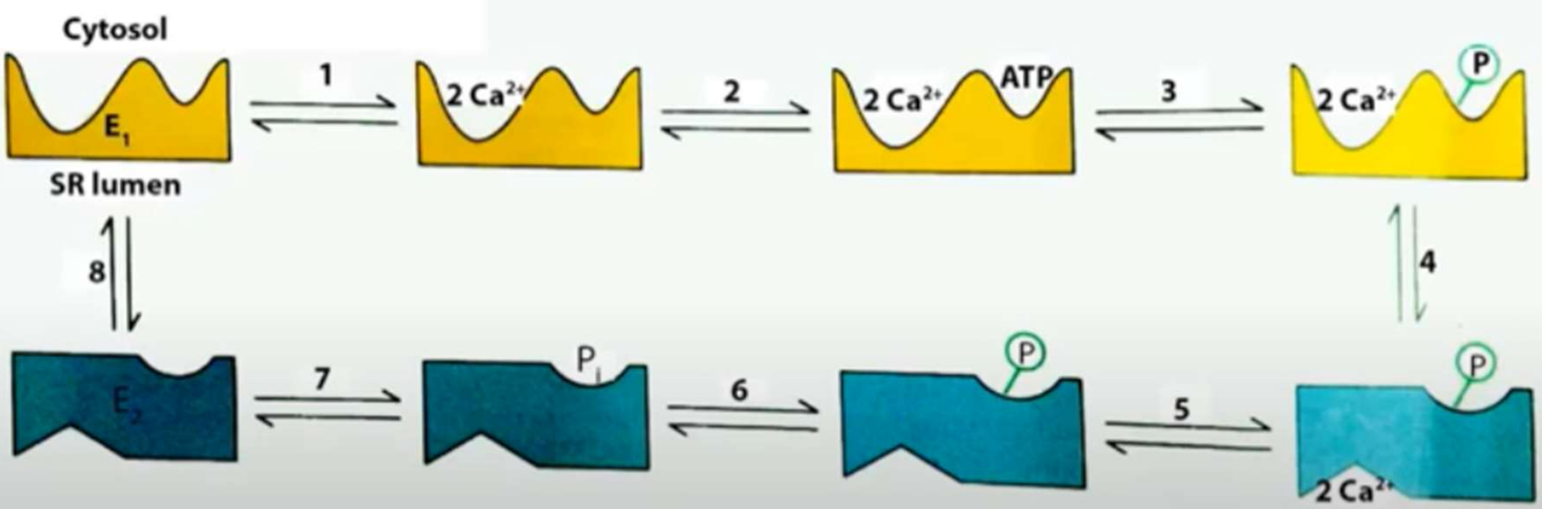
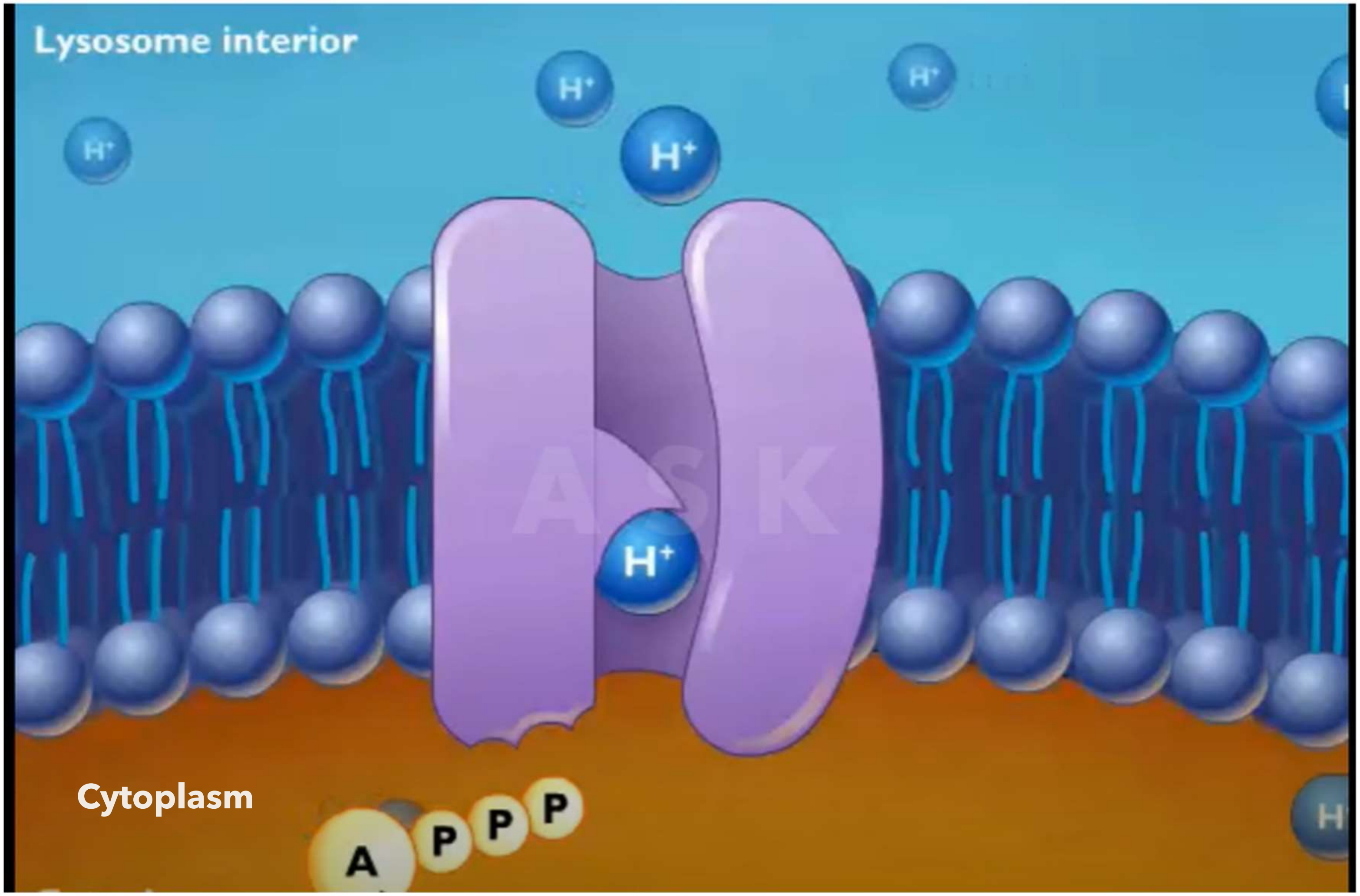


Figure 37-13
Conformation cycle of the calcium pump in the sarcoplasmic reticulum (SR) membrane

V-type ATPases

- V type ATPase are bigger in size (>400 KD). In these, different subunits are involved in steps like ATP hydrolysis and proton movement.
- While these were named V-type after vacuoles, these are not restricted to just yeast, fungi and plants.
- V-type ATPase also play an important role in clatherin coated vesicles and golgi apparatus.
- In fact, acidifying intracellular compartments is their general role.
- V-type ATPase do not undergo reversible phosphorylation cycles.
- The low pH in some of these compartments activates proteases and other hydrolytic enzymes.
- The V-type ATPases are closer to F-type ATPases.
- Hence F-type ATPase involves H+ gradient, however their physiological function is to form ATP rather than hydrolysing it.


Lysosome interior
H+
H+
H+
H+
H+
Cytoplasm
A
P
P
P

F-Type ATPase

- **F-ATPase**is an ATP synthase found in bacterial plasma membranes, in mitochondrial inner membranes (in oxidative phosphorylation, where it is known as Complex V), and in chloroplast thylakoid membranes.

- It uses a proton gradient to drive ATP synthesis by allowing the passive flux of protons across the membrane down their electrochemical gradient and using the energy released by the transport reaction to release newly formed ATP from the active site of F-ATPase.

- In some bacteria, sodium ions may be used instead of protons. Together with V-ATPases and P-ATPases, F-ATPases belong to superfamily of related ATPases.

Functions

- Transmembrane ATPases import many of the metabolites necessary for cell metabolism and export toxins, wastes, and solutes that can hinder cellular processes.
- An important example is the sodium-potassium exchanger (or Na^{+}/K^{+}ATPase) that maintains the cell membrane potential.
- And another example is the hydrogen potassium ATPase (H^{+}/K^{+}ATPase or gastric proton pump) that acidifies the contents of the stomach.
- Besides exchangers, other categories of transmembrane ATPase include co-transporters and pumps (however, some exchangers are also pumps). Some of these, like the Na^{+}/K^{+}ATPase, cause a net flow of charge, but others do not. These are called "electrogenic" and "nonelectrogenic" transporters, respectively.

Type	P	F	V
Substances Transported	**H^+, Na^+, K^+, Ca^{2+}**	**H^+ only**	**H^+ only**
Structural and Functional Features	Large catalytic α-subunits become phosphorylated during solute transport. β-subunits regulate transport	Multiple transmembrane and cytosolic subunits synthesize ATP on β-subunits, powered by movement of H^+ down an electrochemical gradient	Multiple transmembrane and cytosolic subunits use energy released from ATP hydrolysis to pump H^+ from cytosol to organelle lumen
Localization	H^+ pump: plasma membrane of plants, fungi, bacteria Na^+/K^+ pump: plasma membrane of higher eukaryotes H^+/K^+ pump: plasma membrane of gastric chief cells Ca^{2+} pump: plasma membrane of eukaryotic cells Ca^{2+} pump: sarcoplasmic reticulum membrane in muscle cells	Bacterial plasma membranes Inner mitochondrial membrane Thylakoid membrane of chloroplast	Vacuolar membranes in plants, yeast and other fungi Endosomal and lyosomal membranes in eukaryotic cells Plasma membrane of acid-secreting cells (e.g. osteoclasts)