Molecular Motors

- **Molecular motors** are amazing biological machines that are responsible for most forms of movement we encounter in the cellular world
- In general, a motor is a device that consumes energy in one form and converts it into motion or mechanical work

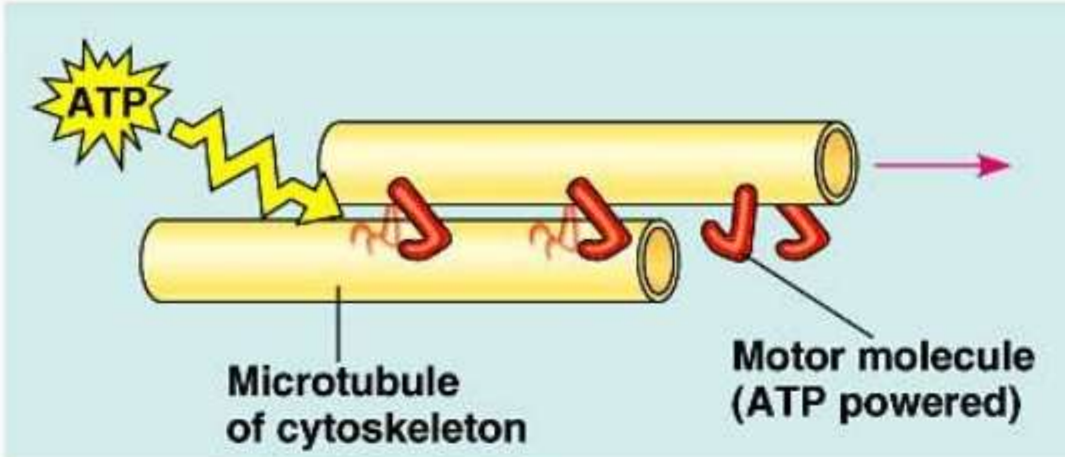
- For example, many protein-based molecular motors harness the chemical free energy released by the hydrolysis of ATP in order to perform mechanical work

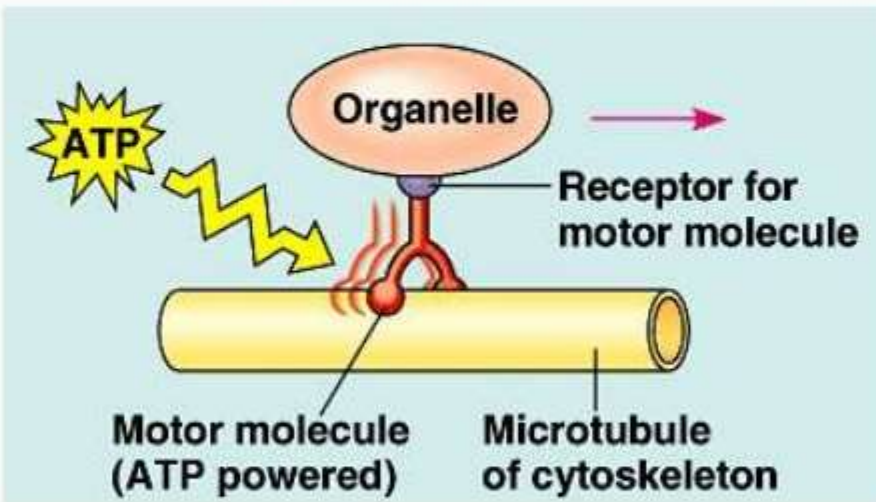
- Three types of cytoplasmic motors are known: myosins, which move on actin filaments, and dyneins and kinesins, which use microtubules as tracks
- Some other examples: Rotary motors: F_oF_1-ATP synthase family of proteins, Nucleic acid motors like topoisomerases and helicases

- The mechanism cytoplasmic motors use to convert chemical energy into mechanical work is both simple and ingenious

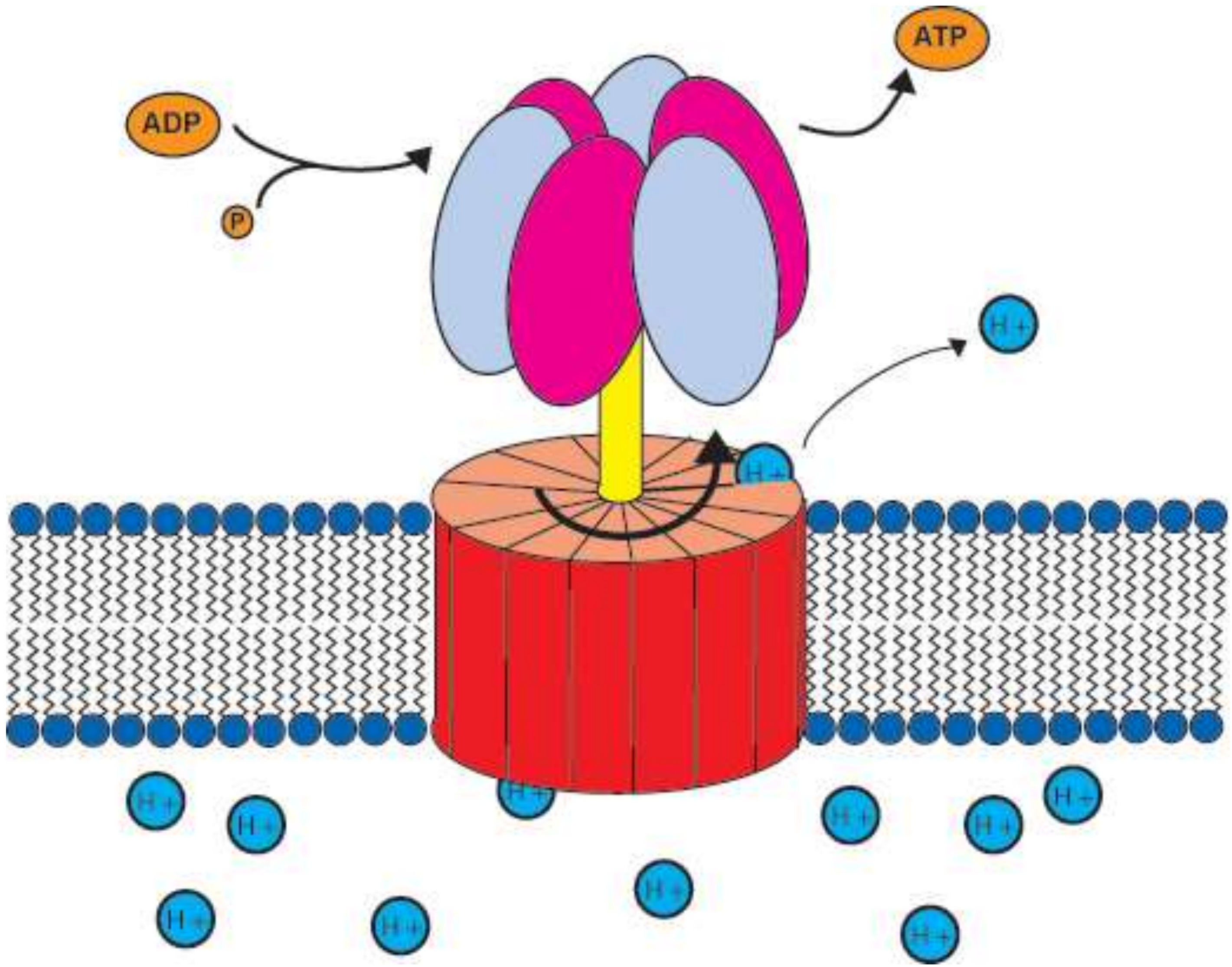
- In all three motor classes, ATP hydrolysis causes a small conformational change in a globular motor domain that is amplified and translated into movement with the aid of accessory structural motifs

Motor proteins pull components of the cyto-skeleton past each other.





Motor molecules also carry vesicles or organelles to various destinations along “monorails’ provided by the cytoskeleton.


ADP
P
ATP
H+

- Today, we can distinguish at least 18 different classes of myosins, 10 different families of kinesins, and 2 groups of dyneins, each with up to several dozen members

- The complement of motors varies widely between different organisms
- Yeast, for example, gets by with 6 kinesins, 5 myosins and 1 dynein, whereas mammals have genes for over 40 kinesins, 40 myosins and more than a dozen dyneins

- Differ in the type of filament they bind to (either actin or microtubules), the direction in which they move along the filament, and the “cargo” they carry

- Cytoskeletal motor proteins that move unidirectionally along an oriented track have the ability to use chemical energy
- All of them generate motion by coupling nucleoside triphosphate hydrolysis to a large-scale conformational change in a protein

Rotational motor mechanism in ATP synthesis

- **ATP synthase** is an enzyme that creates the energy storage molecule adenosine triphosphate (ATP)
- The overall reaction catalyzed by ATP synthase is:
- $ADP + P_i + H^+_{out} \rightleftharpoons ATP + H_2O + H^+_{in}$
- The formation of ATP from ADP and P_i is energetically unfavorable and would normally proceed in the reverse direction

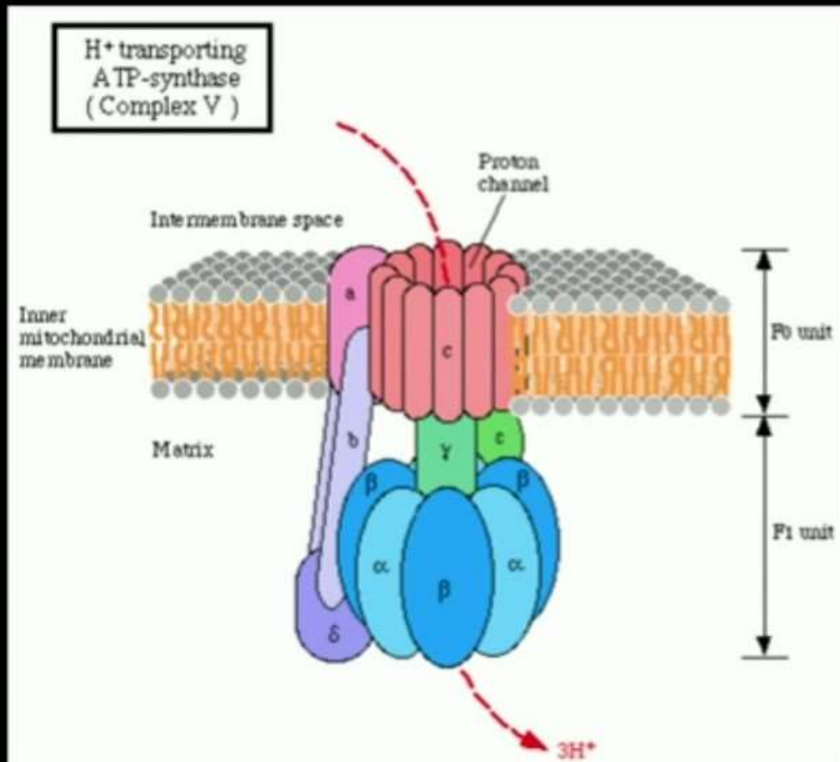
- In order to drive this reaction forward, ATP synthase couples ATP synthesis during cellular respiration to an electrochemical gradient created by the difference in proton (H^+) concentration across the mitochondrial membrane in eukaryotes or the plasma membrane in bacteria

- **ATP synthase**, a major ATP supplier in the cell, is a rotary machine in the biological world
- This enzyme is composed of two motors, F_0 and F_1

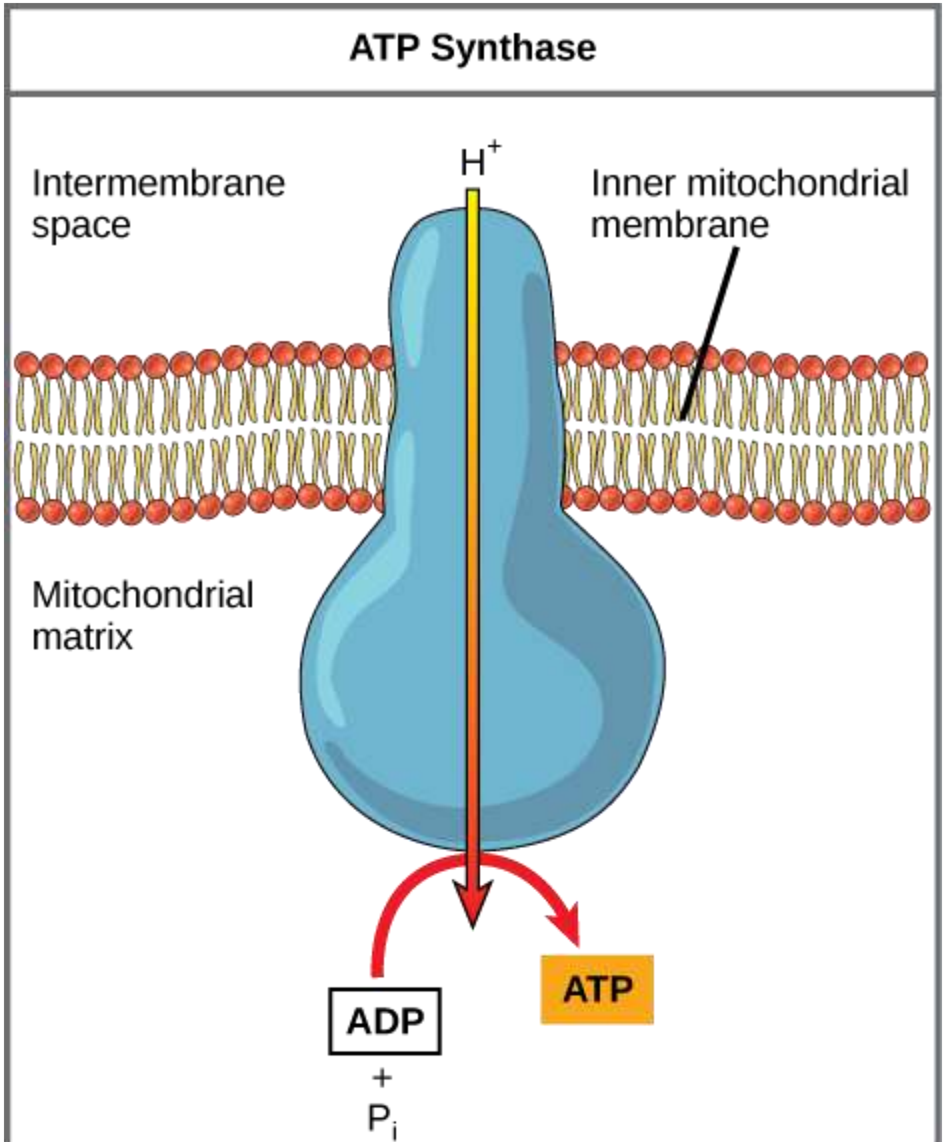
- They are connected by a common rotor shaft to exchange the energy of proton translocation and ATP synthesis/hydrolysis through mechanical rotation

- During photosynthesis in plants, ATP is synthesized by ATP synthase using a proton gradient created in the thylakoid lumen through the thylakoid membrane and into the chloroplast stroma

ATP Synthase Structure



- Critical Subunits:
  - beta: ADP/P_i-binding
  - alpha: link beta subunits; can bind ATP
  - gamma: rotates to change alpha/beta conformations
  - c: contains proton half-channels
  - a: site of proton entry into c subunits


ATP Synthase
H^+
Intermembrane space
Inner mitochondrial membrane
Mitochondrial matrix
ADP
+
P_i
ATP

ATP Synthase

- ATP synthase is a ubiquitous enzyme that is located in the inner membranes of mitochondria, thylakoid membranes of chloroplasts, or the plasma membranes of bacteria

- ATP synthase employs mechanical rotation to convert the electrochemical potential energy of protons across the membranes
- Built up by respiration or a photoreaction, to the chemical energy of ATP synthesis

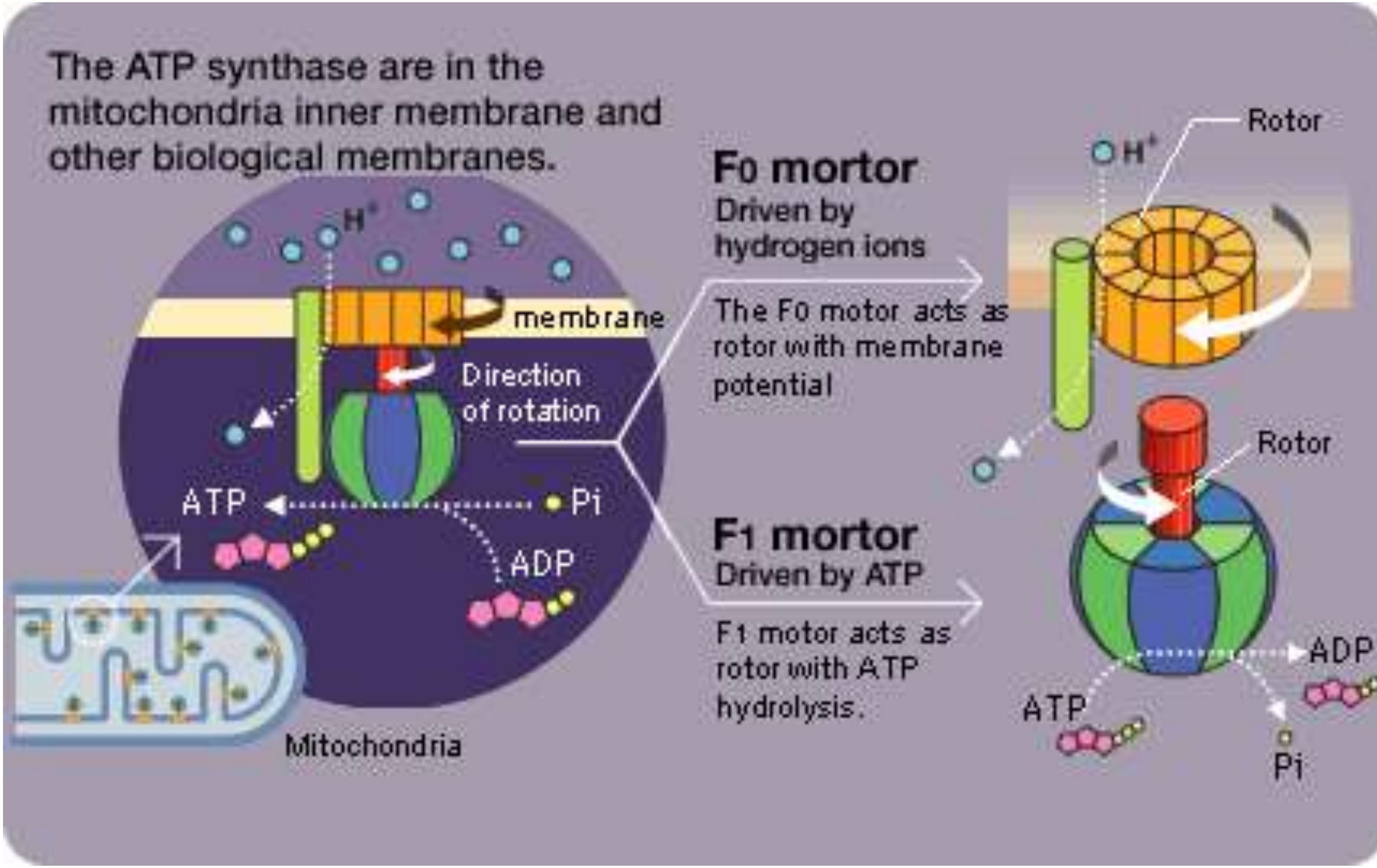
- This enzyme is comprised of two motors sharing a common rotor shaft
- The F_1 motor, a subcomplex of the ATP synthase corresponding to the protruding portion from the membrane, can generate rotary torque using the energy of ATP hydrolysis

- The F_0 motor, a membrane-embedded subcomplex, generates torque coupled with proton movement
- Bacterial F_0 has the simplest subunit structure
- The eukaryotic F_0 contains several kinds of subunits

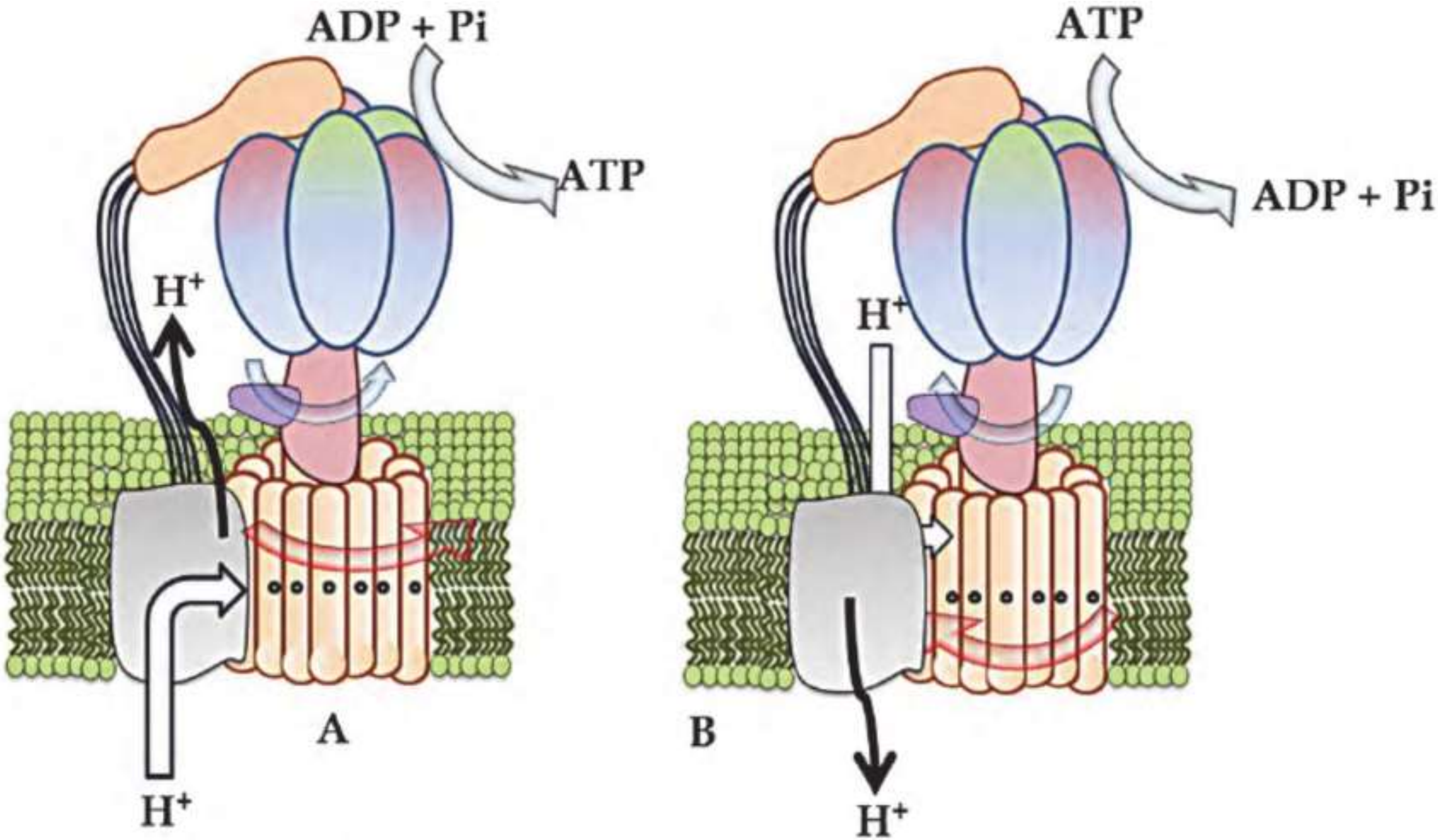
- ATP synthase is composed of the F_1 and F_0 motor sharing a common rotary shaft
- A stator stalk connects two motors that do not slip
- The F_0 motor generates a rotary torque powered by the proton flow-enforcing F_1 motor to synthesize ATP

- The rotational direction is clockwise viewed from the membrane side
- The $\alpha_3\beta_3$ cylinder hydrolyzing ATP makes an anti-clockwise rotation of the rotor part composed of the γ and ε subunits

- Proton flow accompanies a clockwise rotation of the ring structure made of 10–14 copies of the c subunit



The ATP synthase are in the mitochondria inner membrane and other biological membranes.
H+
membrane
Direction of rotation
ATP
Pi
ADP
Mitochondria
F0 mortor
Driven by hydrogen ions
The F0 motor acts as rotor with membrane potential
F1 mortor
Driven by ATP
F1 motor acts as rotor with ATP hydrolysis.
Rotor
H+
Rotor
ADP
ATP
Pi


ADP + Pi
ATP
H+
H+
A
ATP
ADP + Pi
H+
B
H+