December 2005: ATP Synthase

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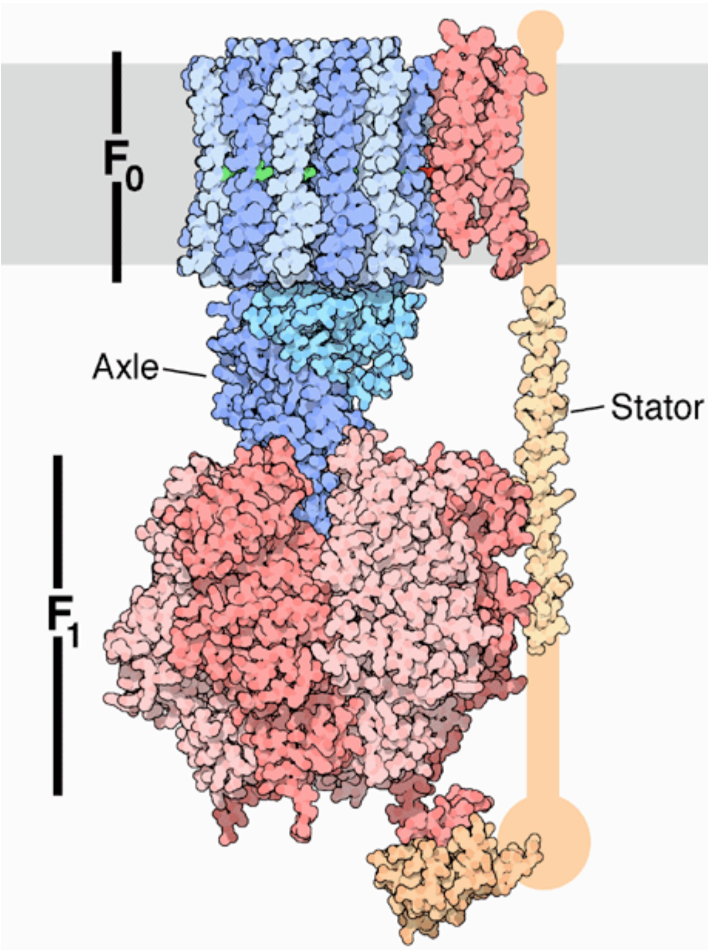
ATP synthase is one of the wonders of the molecular world. ATP synthase is an enzyme, a molecular motor, an ion pump, and another molecular motor all wrapped together in one amazing nanoscale machine. It plays an indispensable role in our cells, building most of the ATP that powers our cellular processes. The mechanism by which it performs this task is a real surprise.



Rotary Motors

ATP synthesis is composed of two rotary motors, each powered by a different fuel. The motor at the top, termed F0, an electric motor. It is embedded in the cell membrane (shown schematically as a gray stripe here), and is powered by the flow of hydrogen ions across the membrane. As the protons flow through the motor, they turn a circular rotor (shown in blue). This rotor is connected to the second motor, termed F1. The F1 motor is a chemical motor, powered by ATP. The two motors are connected together by a stator, shown on the right, so that when F0 turns, F1 turns too.

Motor to Generator

So why have two motors connected together? The trick is that one motor can force the other motor to turn, and in this way, change the motor into a generator. This is what happens in our cells: the F0 motor uses the power from a proton gradient to force the F1 motor to generate ATP. In our cells, food is broken down and used to create a large excess of hydrogen ions outside the cell. The F0 portion of ATP synthase allows these ions to reenter the cell, turning the rotor in the process. As the rotor turns, it turns the axle and the F1 motor becomes a generator, creating ATP as it turns.

Parts List

Large, complex molecular machines like ATP synthase pose difficult problems for structural scientists, so the structures of these machines are often determined in parts. The picture shown here is a composite of four different structures, combining structures determined by X-ray crystallography and NMR spectroscopy. The F0 motor is included in PDB file 1c17. The F1 motor and the axle that connects the two are included in PDB file 1e79. The stator has proven to be the most elusive part--the two pieces shown here are from PDB files 2a7u and 1l2p.

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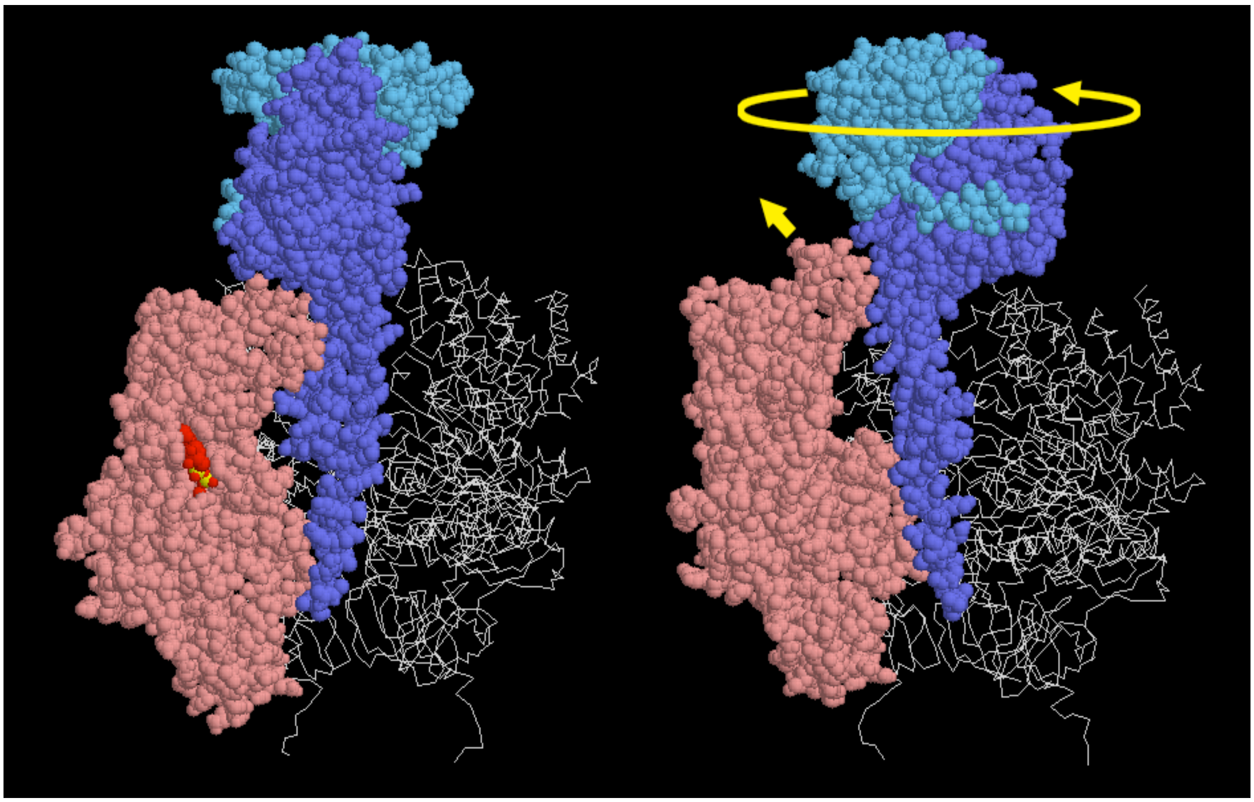
Exploring the F1 Structure

PDB entry 1e79 includes the F1 motor of ATP synthase. When operating as a generator, it uses the power of rotational motion to build ATP, or when operating as a motor, it breaks down ATP to spin the axle the opposite direction. The two difficult steps in the synthesis of ATP are the binding of ADP and the release of ATP--the formation of the phosphate-phosphate bond is not the major problem. As the axle turns, it forces the motor into three different conformations that assist these difficult steps. Two states are shown here. The one on the left shows a conformation that assists the binding of ADP, and the one on the right shows a conformation that has been forced open to release ATP. Notice how the oddly-shaped axle forces the change in conformation.



You can look at this structure yourself by clicking on the accession code and picking one of the options under View Structure. The central axle is composed of chains G, H, and I in this file. Three of the subunits, chains D, E, and F in the file, are the ATP-generating parts--subunit E is shown in red in the left picture and subunit D is shown in the right picture. Subunits A, B, and C are similar, but play a structural role, holding everything in place. In these pictures, I have removed the two nearest two subunits to make the interaction clearer.

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Exploring the F0 Structure

PDB entry 1c17 includes the F0 electric motor. In this picture, we are looking down the axis of rotation, as if we where looking down at the top of the picture on the first page. The rotor is composed of 12 identical protein chains, colored blue here, and the ion pump is a single chain, colored red. The pump has an arginine amino acid that hands off a hydrogen ion to aspartates on the rotor. Aspartate amino acids typically have a negative charge, but since the rotor is surrounded by membrane lipids, this would be very unfavorable. So, the rotor only turns when the aspartates have a hydrogen attached, neutralizing their charge. Hydrogen ions take a convoluted path through the F0 motor, turning the rotor in the process. They are gathered from outside the cell by a chain of amino acids in the pump, and transferred to the arginine. The arginine passes the hydrogen to the rotor, which turns all the way around. Then the hydrogen is offloaded by other amino acids on the pump, and finally passed inside the cell. The exact path of the hydrogen ions through the pump is still a matter of intense study.