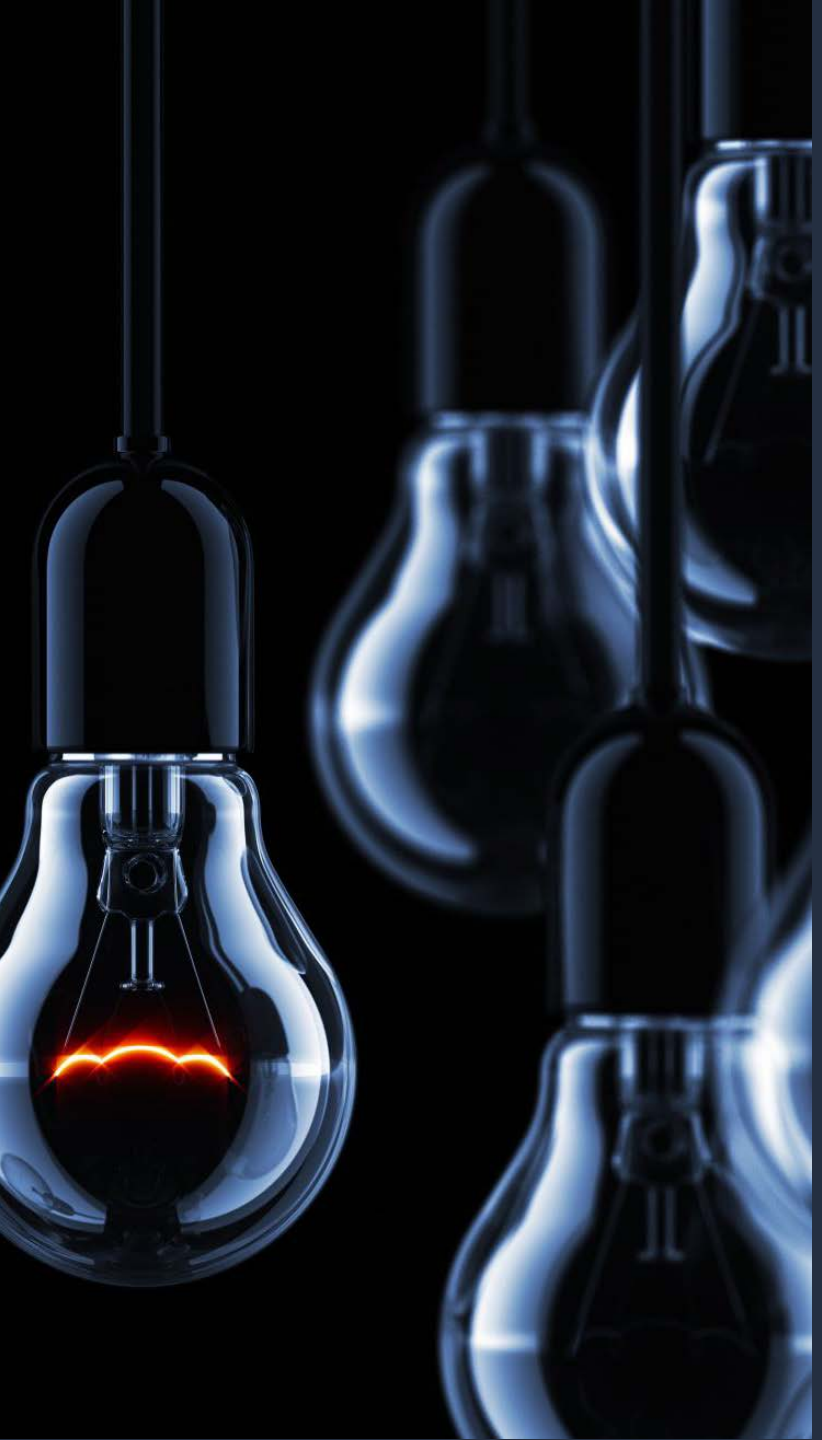


MITOCHONDRIA

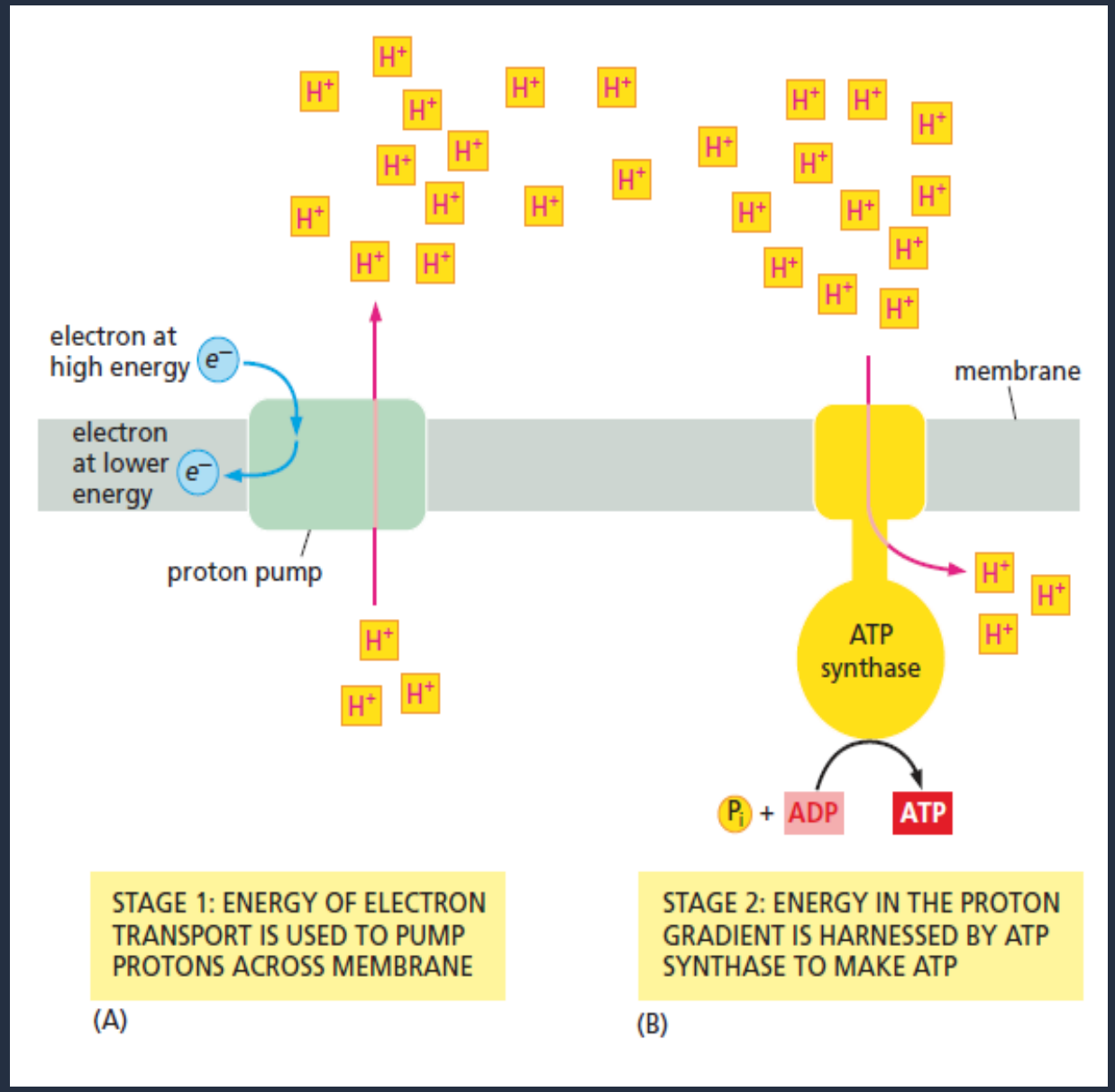
The cellular “Energy Storehouse”

MEMBRANE-BASED SYSTEMS USE THE ENERGY STORED IN AN ELECTROCHEMICAL PROTON GRADIENT TO SYNTHESIZE ATP

- The process occurs in two stages.

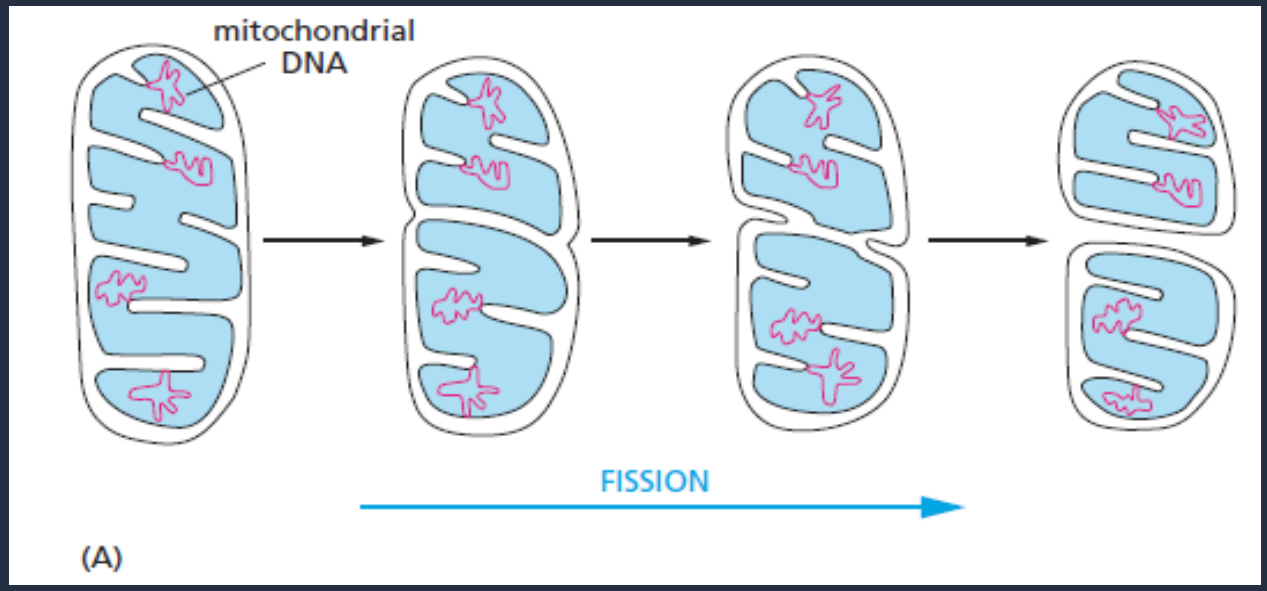
- (A) In the first stage, a proton pump harnesses the energy of electron transfer (details not shown here) to pump protons (H+) derived from water, creating a proton gradient across the membrane. The *blue arrow* shows the direction of electron movement. These high-energy electrons can come from organic or inorganic molecules, or they can be produced by the action of light on special molecules such as chlorophyll.

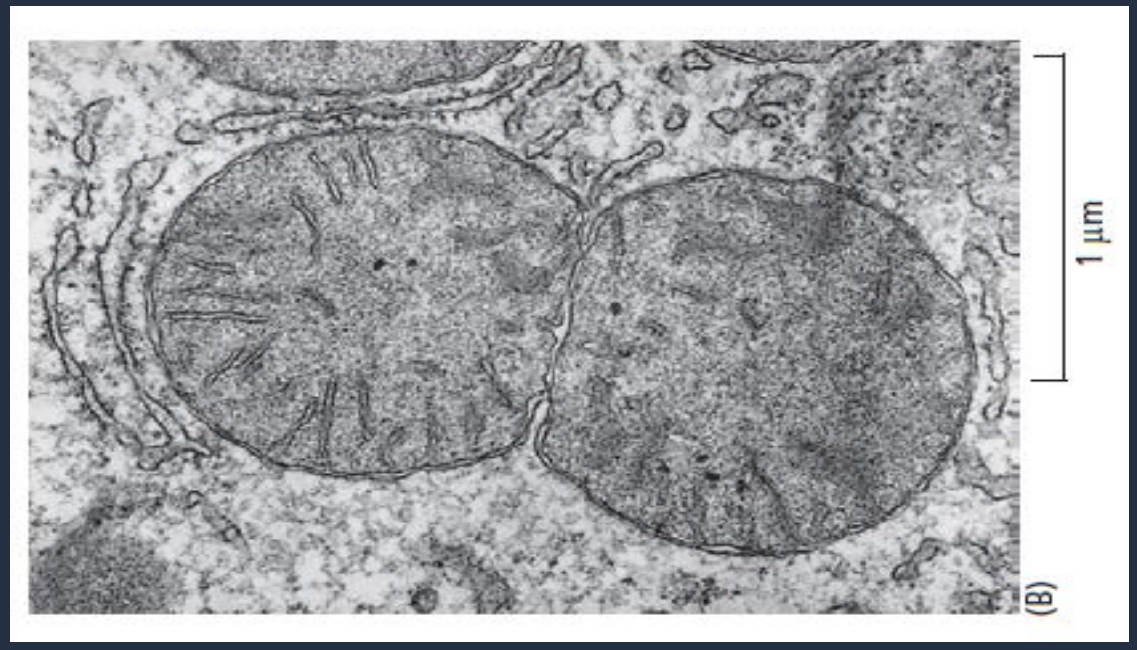
- (B) The proton gradient produced in (A) serves as a versatile energy store. It is used to drive a variety of energy-requiring reactions in mitochondria, chloroplasts, and prokaryotes–including the synthesis of ATP by an ATP synthase.



A MITOCHONDRION CAN DIVIDE LIKE A BACTERIUM

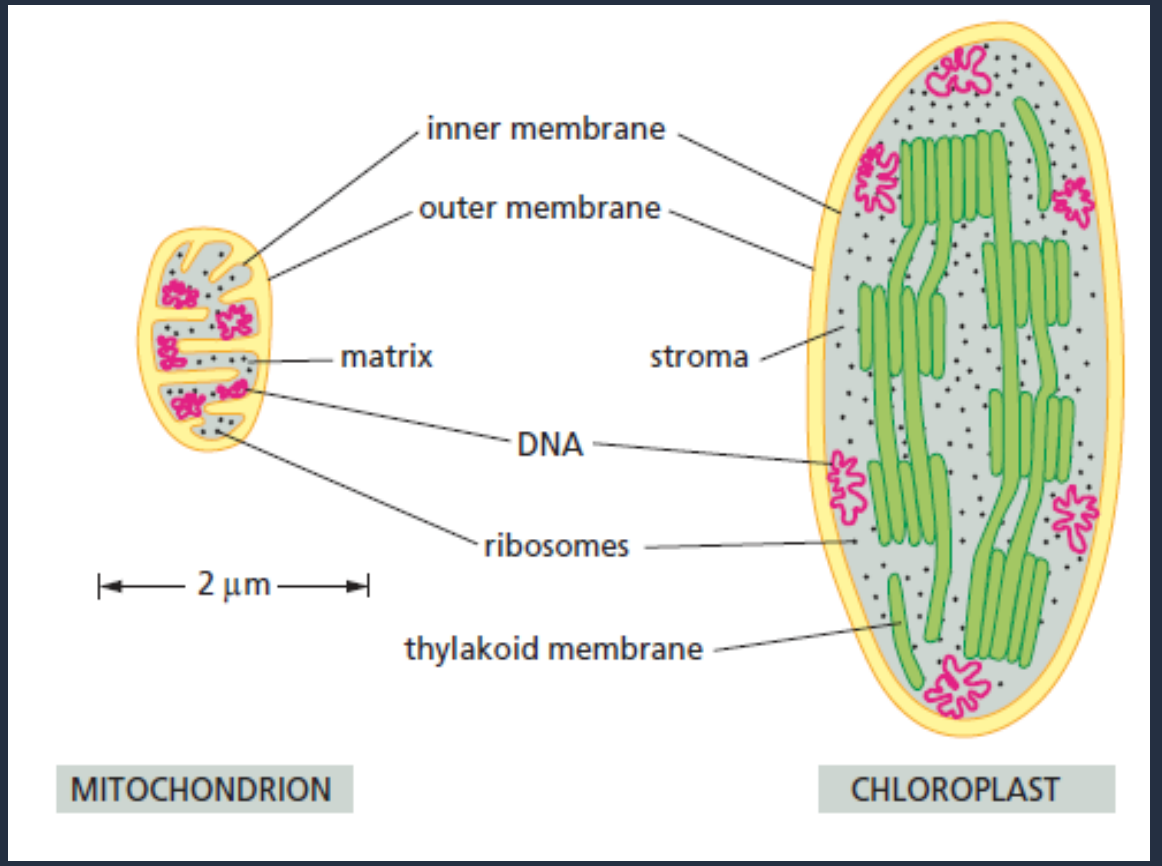
- (A) It undergoes a fission process that is conceptually similar to bacterial division.
- (B) An electron micrograph of a dividing mitochondrion in a liver cell.





THE ENDOSYMBIOTIC THEORY

- The organelles that produce ATP in eukaryotic cells–the chloroplasts and mitochondria–evolved from bacteria that were engulfed by ancestral cells more than a billion years ago.
- As evidence of their bacterial ancestry, both chloroplasts and mitochondria reproduce in a manner similar to that of most prokaryotes.
- They also harbor bacterial-like biosynthetic machinery for making RNA and proteins, and they retain their own genomes.
- Many chloroplast genes are strikingly similar to those of cyanobacteria–the photosynthetic bacteria from which chloroplasts are thought to have been derived.
- Although mitochondria and chloroplasts still contain DNA, the bacteria that gave rise to these organelles gave up many of the genes required for independent living as they developed the symbiotic relationships that led to the evolution of eukaryotic animal and plant cells.
- These genes were not lost, however; many moved to the cell nucleus, where they continue to direct the production of proteins that mitochondria and chloroplasts import to carry out their specialized functions–including the generation of ATP.



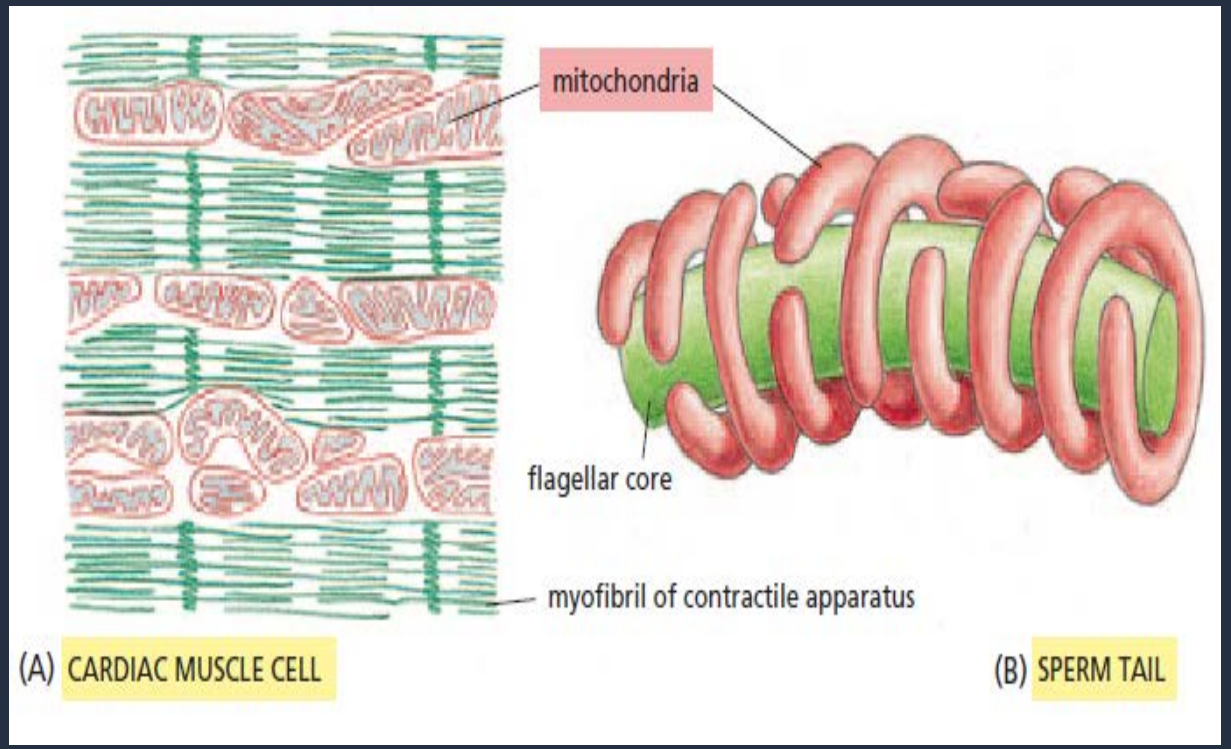
Mitochondria and chloroplasts share many of the features of their bacterial ancestors. Both organelles contain their own DNA-based genome and the machinery to copy this DNA and to make RNA and protein. The inner compartments of these organelles–the mitochondrial matrix and the chloroplast stroma–contain the DNA (*red*) and a special set of ribosomes. Membranes in both organelles–the mitochondrial inner membrane and the chloroplast thylakoid membrane–contain the protein complexes involved in ATP production.

MITOCHONDRIA & OXIDATIVE PHOSPHORYLATION

Mitochondria are present in nearly all eukaryotic cells, where they produce the bulk of the cell's ATP. Without mitochondria, eukaryotes would have to rely on the relatively inefficient process of glycolysis for all of their ATP production. When glucose is converted to pyruvate by glycolysis in the cytosol, the net result is that only two molecules of ATP are produced per glucose molecule, which is less than 10% of the total free energy potentially available from oxidizing the sugar. By contrast, about 30 molecules of ATP are produced when mitochondria are recruited to complete the oxidation of glucose that begins in glycolysis. Had ancestral cells not established the relationship with the bacteria that gave rise to modern mitochondria, it seems unlikely that complex multicellular organisms could have evolved.

The importance of mitochondria is further highlighted by the dire consequences of mitochondrial dysfunction. For example, patients with an inherited disorder called *myoclonic epilepsy and ragged red fiber disease* (*MERRF*) are deficient in multiple proteins required for electron transport. As a result, they typically experience muscle weakness, heart problems, epilepsy, and often dementia. Muscle and nerve cells are especially sensitive to mitochondrial defects, because they need so much ATP to function normally.

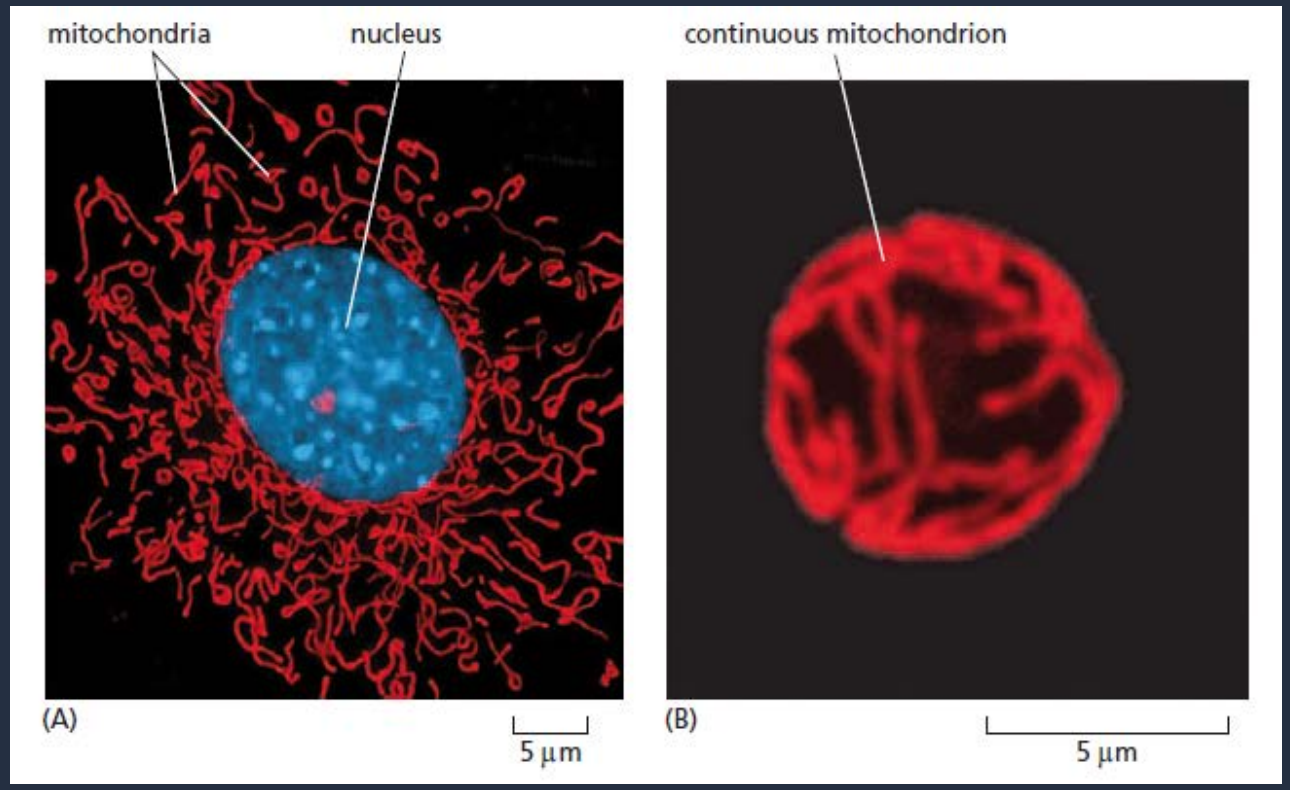
SOME MITOCHONDRIA ARE LOCATED NEAR SITES OF HIGH ATP UTILIZATION



(A) In a cardiac muscle cell, mitochondria are located close to the contractile apparatus, in which ATP hydrolysis provides the energy for contraction.

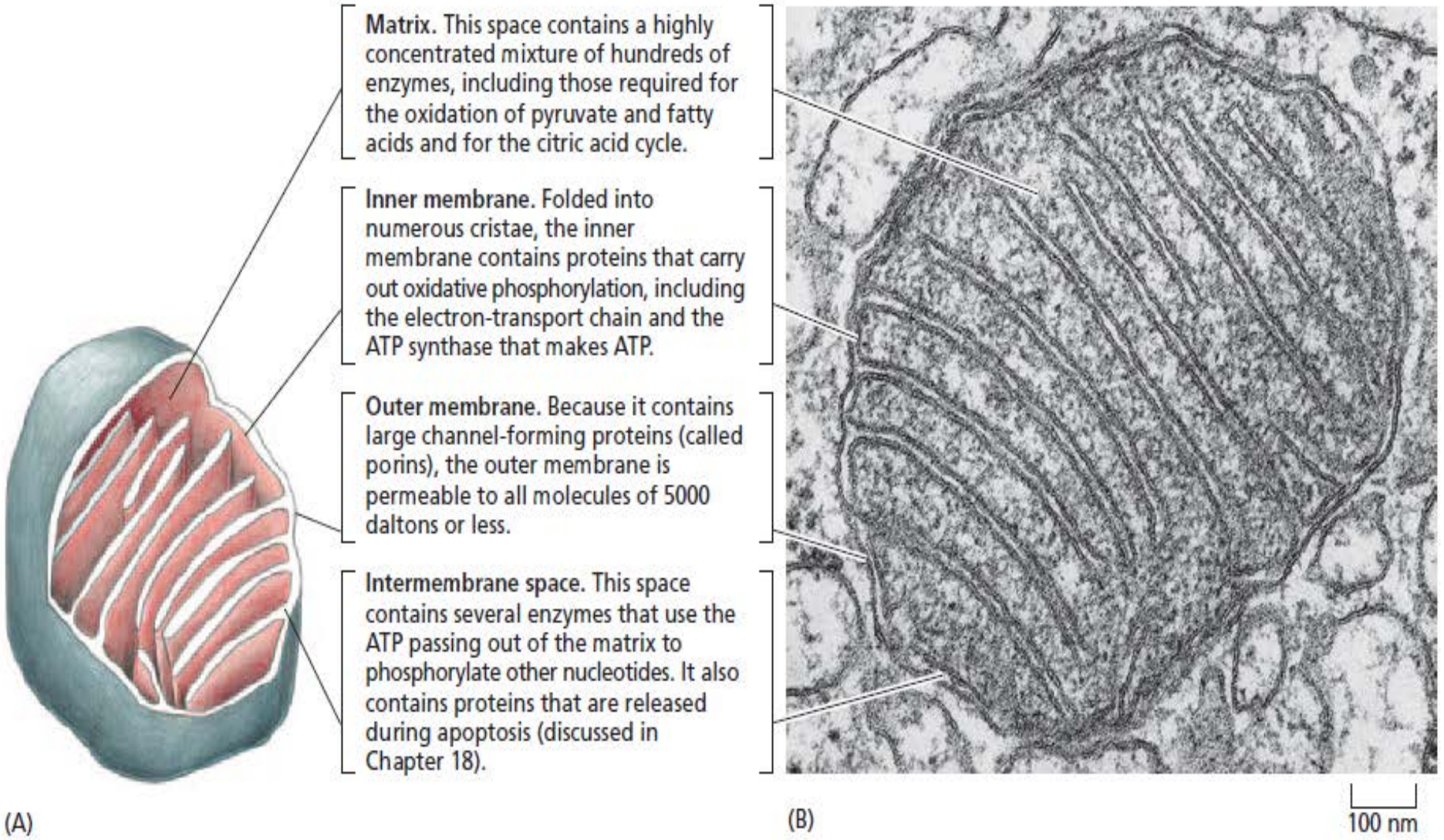
(B) In a sperm, mitochondria are located in the tail, wrapped around a portion of the motile flagellum that requires ATP for its movement.

MITOCHONDRIA OFTEN FUSE TO FORM ELONGATED TUBULAR NETWORKS, WHICH CAN EXTEND THROUGHOUT THE CYTOPLASM



(A) Mitochondria (*red*) are fluorescently labeled in this cultured mouse fibroblast.
(B) In a yeast cell, the mitochondria (*red*) form a continuous network, tucked against the plasma membrane.
(A, courtesy of Michael W. Davidson, Carl Zeiss Microscopy Online Campus;
B, from J. Nunnari et al., Mol. Biol. Cell. 8:1233–1242, 1997. With permission by The American Society for Cell Biology.)

A MITOCHONDRION CONTAINS AN OUTER MEMBRANE, AN INNER MEMBRANE, AND TWO INTERNAL COMPARTMENTS

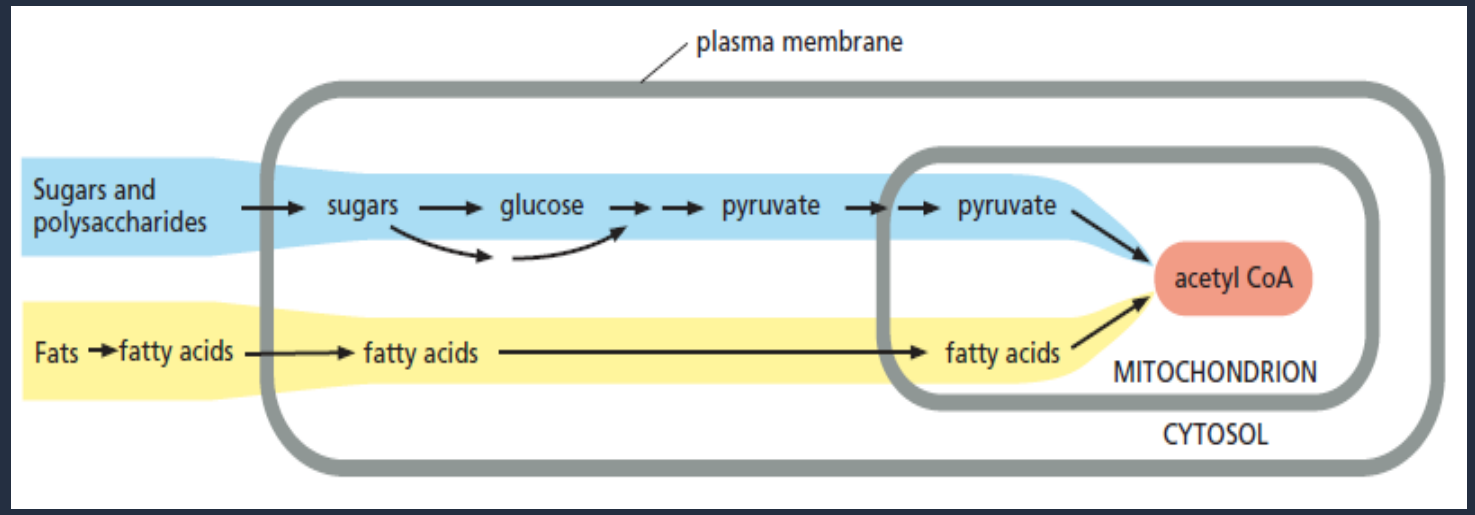


(A) A schematic drawing and

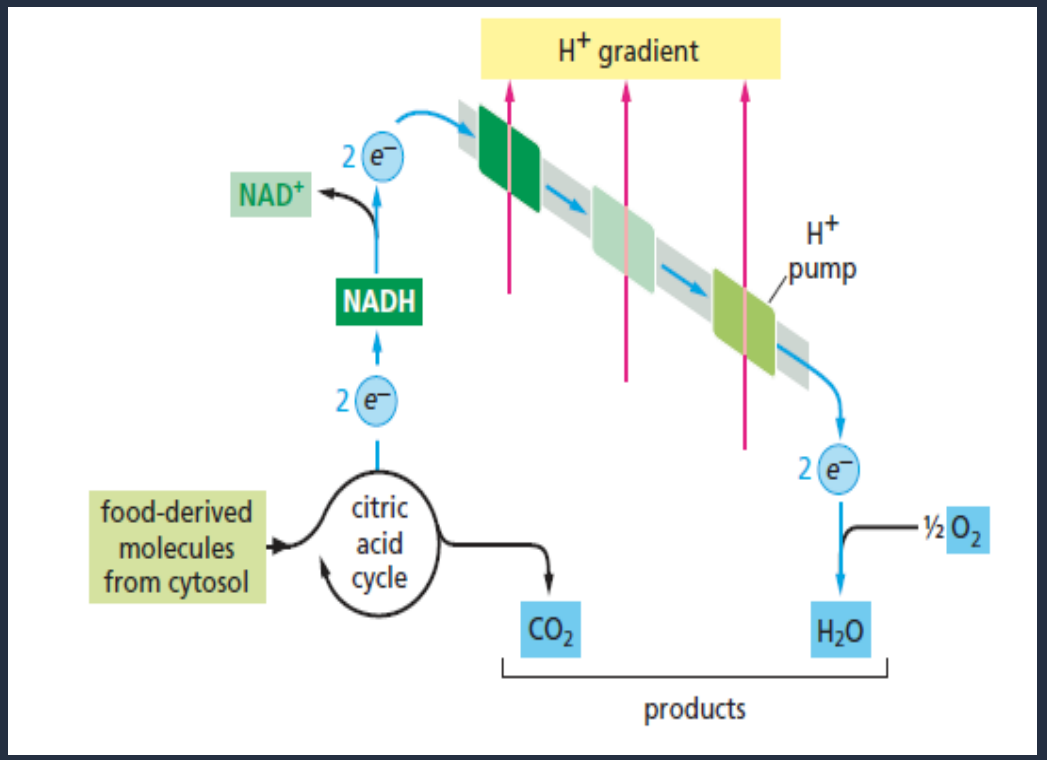
(B) An electron micrograph of a mitochondrion.

- Each compartment contains a unique set of proteins, enabling it to perform its distinct functions. In liver mitochondria, an estimated 67% of the total mitochondrial protein is located in the matrix, 21% in the inner membrane, 6% in the outer membrane, and 6% in the intermembrane space.

MITOCHONRIA & ENERGY METABOLISM

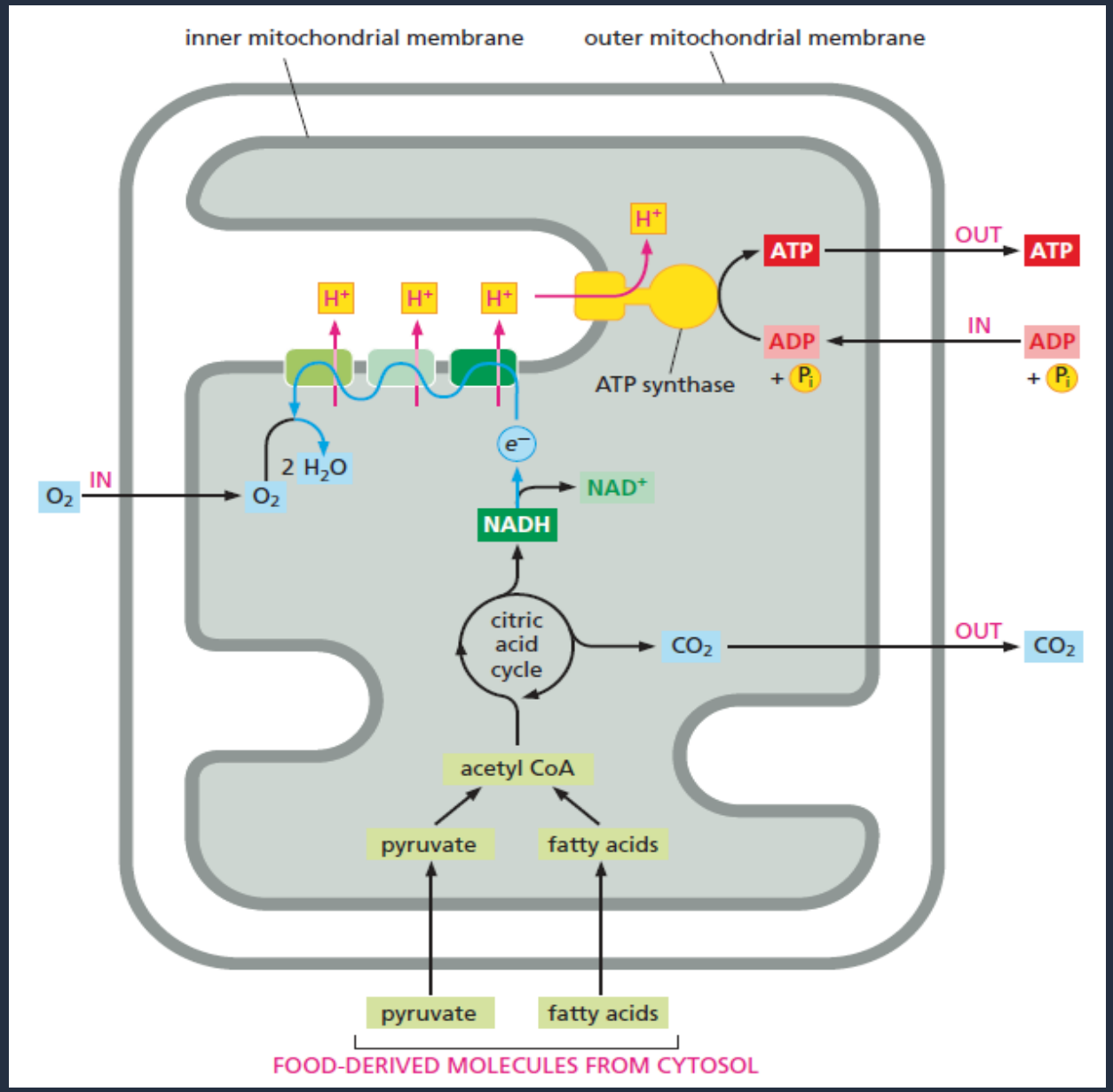


In eukaryotic cells, acetyl CoA is produced in the mitochondria from molecules derived from sugars and fats. Most of the cell's oxidation reactions occur in these organelles, and most of its ATP is made here.



As electrons are transferred from activated carriers to oxygen, protons are pumped across the inner mitochondrial membrane. This is stage 1 of chemiosmotic coupling. The path of electron flow is indicated by *blue arrows.*

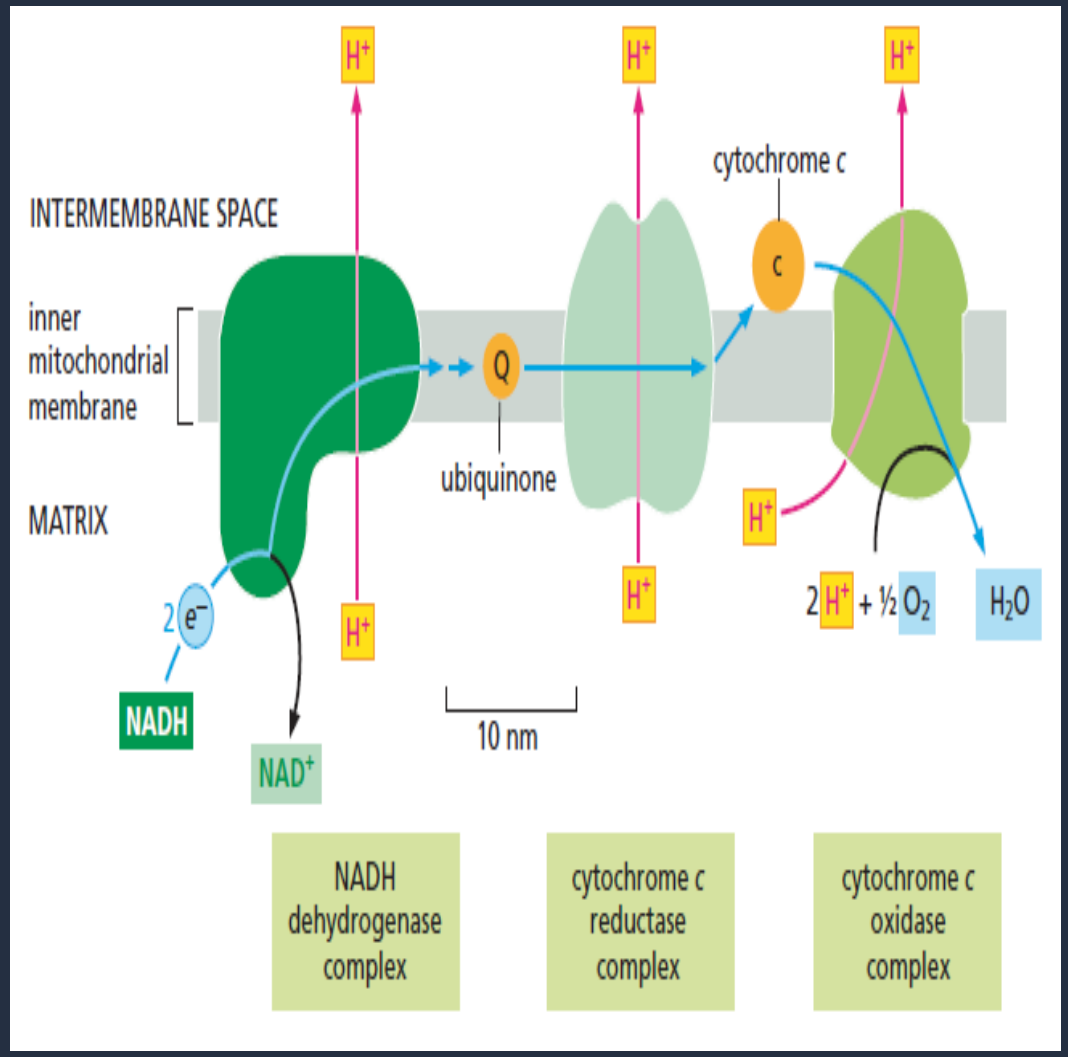
ACTIVATED CARRIERS GENERATED DURING THE CITRIC ACID CYCLE POWER THE PRODUCTION OF ATP



- Pyruvate and fatty acids enter the mitochondrial matrix (*bottom*), where they are converted to acetyl CoA.
- The acetyl CoA is then metabolized by the citric acid cycle, which produces NADH (and $FADH_2$, not shown).
- During oxidative phosphorylation, high energy electrons donated by NADH (and $FADH_2$) are then passed along the electron transport chain in the inner membrane to oxygen (O_2).
- This electron transport generates a proton gradient across the inner membrane, which is used to drive the production of ATP by ATP synthase.
- *The exact ratios of "reactants" and "products" are not indicated in this diagram: for example, it requires four electrons from four NADH molecules to convert O2 to two H2O molecules.*

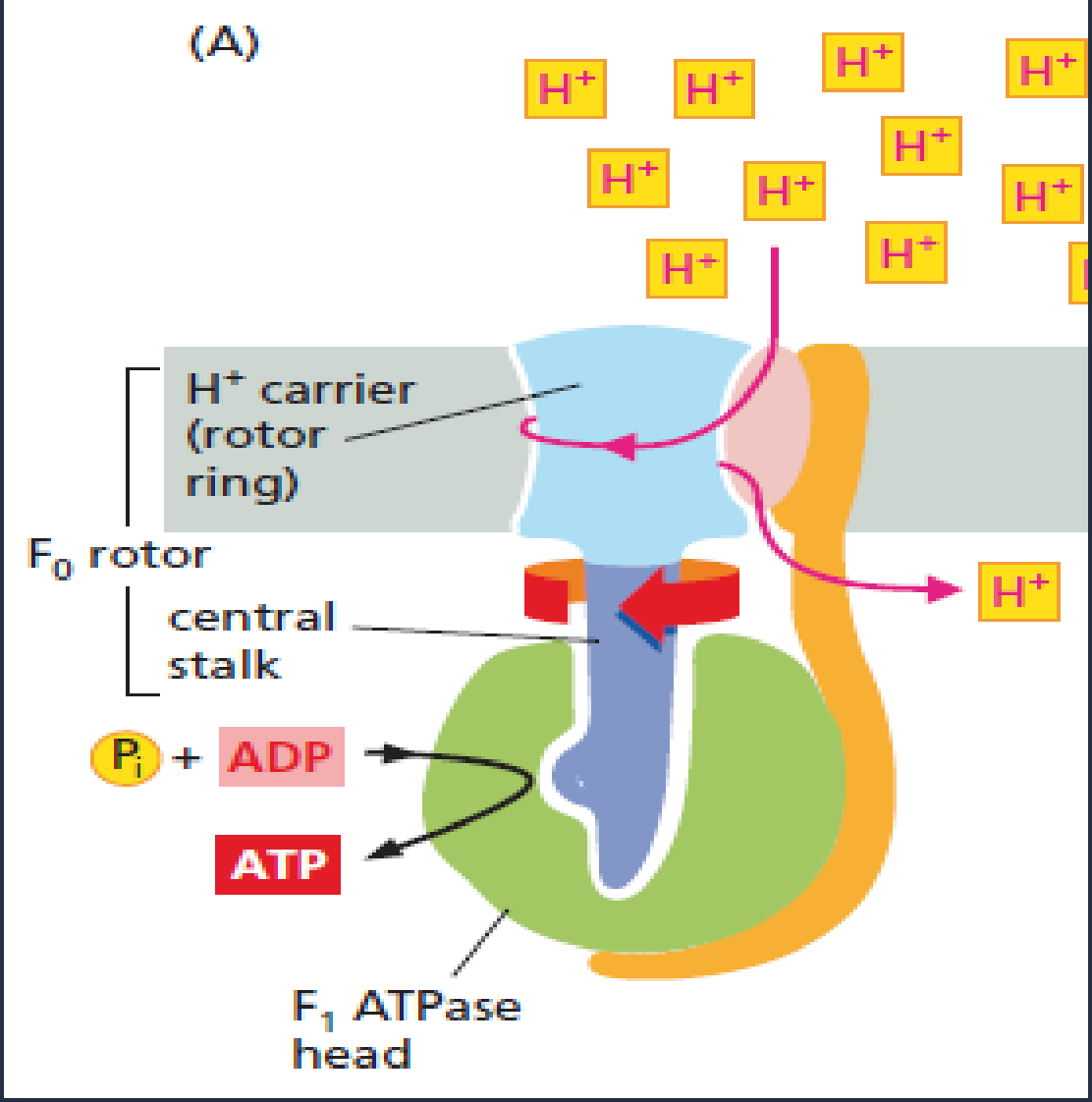
THE ELECTRON TRANSPORT CHAIN

- The electron-transport chain—or *respiratory chain*—that carries out oxidative phosphorylation is present in many copies in the inner mitochondrial membrane.
- Each chain contains over 40 proteins, grouped into three large respiratory enzyme complexes. These complexes each contain multiple individual proteins, including transmembrane proteins that anchor the complex firmly in the inner mitochondrial membrane.
- The three respiratory enzyme complexes, in the order in which they receive electrons, are:
- (1) *NADH dehydrogenase complex*,
- (2) *cytochrome* c *reductase complex*, and
- (3) *cytochrome* c *oxidase complex*.
- Each complex contains metal ions and other chemical groups that act as stepping stones to facilitate the passage of electrons.
- The movement of electrons through these respiratory complexes is accompanied by the pumping of protons from the mitochondrial matrix to the intermembrane space. Thus each complex can be thought of as a proton pump.



❑ During the transfer of high-energy electrons from NADH to oxygen (*blue lines*), protons derived from water are pumped across the membrane from the matrix into the intermembrane space by each of the complexes. Ubiquinone (Q) and cytochrome *c* (c) serve as mobile carriers that ferry electrons from one complex to the next.

ATP SYNTHASE



- ATP synthase acts like a motor to convert the energy of protons flowing down their electrochemical gradient to chemical-bond energy in ATP.
- The multi-subunit protein is composed of a stationary head, called the F_1 ATPase, and a rotating portion called F_0. Both F_1 and F_0 are formed from multiple subunits.
- Driven by the electrochemical proton gradient, the F_0 part of the protein—which consists of the transmembrane H^+ carrier (*blue*) plus a central stalk (*purple*)—spins rapidly within the stationary head of the F_1 ATPase (*green*), causing it to generate ATP from ADP and P_i.
- The stationary head is secured to the inner membrane by an elongated protein "arm" called the peripheral stalk (*orange*).
- The F_1 ATPase is so named because it can carry out the reverse reaction—the hydrolysis of ATP to ADP and P_i—when detached from the F_0 portion of the complex.