An outline of glycolysis.

Each of the 10 steps shown is catalyzed by a different enzyme. Note that step 4 cleaves a six-carbon sugar into two three-carbon sugars, so that the number of molecules at every stage after this doubles. As indicated, step 6 begins the energy generation phase of glycolysis, which causes the net synthesis of ATP and NADH molecules.

Fermentations Allow ATP to Be Produced in the Absence of Oxygen

For most animal and plant cells, glycolysis is only a prelude to the third and final stage of the breakdown of food molecules. In these cells, pyruvate formed at the end of glycolysis is rapidly transported into the mitochondria, completely oxidized to CO₂ and H₂O. But for many anaerobic organisms, which do not use molecular oxygen and can grow and divide in its absence, glycolysis is the principal source of the cell’s ATP. The same is true in certain animal tissues, such as skeletal muscle, that can continue to function at low levels of molecular oxygen.

Sugars and Fats Are Both Degraded to Acetyl CoA in Mitochondria

In aerobic metabolism, pyruvate produced by glycolysis is rapidly decarboxylated by a giant complex of three enzymes called pyruvate dehydrogenase complex. The products of pyruvate decarboxylation are a molecule of CO₂ (waste product), a molecule of NADH, and acetyl CoA. The three-enzyme complex is located in the mitochondria of the eukaryotic cells.
Pyruvate is oxidized to acetyl CoA and CO2 by pyruvate dehydrogenase. The enzymes that degrade fatty acids derived from fats likewise produce acetyl CoA in mitochondria. Each molecule of fatty acid is broken down completely by a cycle of reactions that trims two carbons at a time from its carboxylated end, generating one molecule of acetyl CoA.

In eukaryotic cells, acetyl CoA is produced in the mitochondria from molecules derived from sugars and fats.

The citric acid cycle (TCA or Krebs cycle) accounts for about two-thirds of the total oxidation of carbon compounds in most cells, and its major end products are CO2 and high-energy electrons in the form of NADH. The CO2 is released as waste product, while the high-energy electrons are passed to a membrane-bound electron transport chain, eventually combining with O2 to produce H2O. Although the citric acid cycle itself does not use O2, it requires O2 to proceed because there is no efficient way for the NADH to get rid of its electron and thus regenerate the NAD+ that is needed to keep the cycle going.

The citric acid cycle takes place in mitochondria in eukaryotic cell. It catalyzes complete oxidation of the carbon atoms of acetyl groups in acetyl CoA, converting them into CO2.
Step 1: When the enzyme removes a proton from the C4 group of acetyl-CoA, the negatively charged C4− forms a bond to a carbon/nitrogen of oxaloacetate. The subsequent loss by hydrolysis of the coenzyme A (CoA) drives the reaction strongly forward.

Step 2: An isomerase reaction, in which water is first removed and then added back, moves the hydroxyl group from one carbon atom to its neighbor.

Step 3: In the first of four oxidation steps in the cycle, the oxaloacetate is oxidized to oxalosuccinate. The immediate product is unstable, losing CO₂, which is then bound to the enzyme.

Step 4: The isocitrate dehydrogenase complex catalyzes the conversion of isocitrate to α-ketoglutarate. This enzyme catalyzes an oxidation that produces NADH, CO₂, and a high-energy thiolate bond to coenzyme A (CoA).

Step 5: A phosphate molecule from solution displaces the CoA, forming a high-energy phosphate bond to succinate. This phosphate is then passed to GDP to form GTP, on bacteria and plants, ATP is formed instead.

Step 6: In the third oxidation step in the cycle, FAD removes two hydrogen atoms from succinate.
Electron Transport Drives the Synthesis of the Majority of the ATP in Most Cells

It is in the last step in the oxidation of a food molecule that the major portion of its chemical energy is released. In this final process, the electron carriers NADH and FADH_2 transfer the electrons that they have gained when oxidizing other molecules to the electron-transport chain, which is embedded in the inner membrane of the mitochondrion.

Many Biosynthetic Pathways Begin with Glycolysis or Citric Acid Cycle

Catabolism produces both energy for the cell and building blocks from which many other molecules are made. Many of the intermediates formed in glycolysis and in citric acid cycle are siphoned off by other biosynthetic pathways, where enzymes use them to produce the amino acids, nucleotides, lipids, and other small organic molecules that the cell needs.
Cells Obtain Most of Their Energy by a Membrane-based Mechanism

The main chemical energy currency in cells is ATP. In eukaryotic cells, small amounts of ATP are generated during glycolysis in the cytosol, but most ATP is produced by membrane-based processes in mitochondria. Very similar processes also occur in the cell membranes of many bacteria. The process consists of two-linked stages, both of which are carried out by protein complexes embedded in a membrane.

Stage 1: Electrons (from oxidation of food molecules) are transferred along a series of electron carriers called the electron-transport chain embedded in the membrane. These electron transfers release energy that is used to pump protons across the membrane and thus generate an electrochemical proton gradient.

Stage 2: H+ flows back down its electrochemical gradient through a protein complex called ATP synthase, which catalyzes the energy-requiring synthesis of ATP from ADP and Pi. The linkage of electron transport, proton pumping, and ATP synthesis was called the chemiosmotic hypothesis (now known as chemiosmotic coupling).

Mitochondria and Oxidative Phosphorylation

Mitochondria are present in nearly all eukaryotic cells and it is in these organelles that most of a cell’s ATP is generated. When glucose is converted to pyruvate by glycolysis, less than 10% of total free energy potentially available from the glucose is released. In mitochondria, the metabolism of sugars is completed, the energy is harnessed so efficiently that about 30 molecules of ATP produced from each glucose molecule. The same metabolic reactions that occur in mitochondria also take place in aerobic bacteria, which do not possess these organelles. In these organisms, the plasma membrane carries out the chemiosmotic process.
Mitochondria are located near sites of high ATP utilization
A) 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, around the core of the motile flagellum, which requires ATP for its movement.

Each mitochondrion is bounded by two highly specialized membranes that play a crucial role in its activity. The outer and inner mitochondrial membranes create two mitochondrial compartments: a large internal space called the matrix and a much narrower intermembrane space.

High Energy Electrons Are Generated via the Citric Acid Cycle
In the mitochondria, the metabolism of food molecules is completed. Mitochondria can use both pyruvate and fatty acid as fuel. The cycle converts the carbon atom in acetyl CoA to CO2, which is released from the cells as a waste product. In addition, the cycle generates high-energy electrons carried by activated carrier molecules NADH and FADH2.

Matris. This large internal space contains a highly concentrated mixture of hundreds of enzymes, including those required for the oxidation of pyruvate and fatty acids and for the citric acid cycle. The matrix also contains several identical copies of the mitochondrial DNA-genome, special mitochondrial ribosomes, tRNAs, and various enzymes required for expression of the mitochondrial genes.

Inner membrane. The inner membrane (red) is folded into numerous creases, which greatly increases its total surface area. It contains proteins with three types of functions: (1) those that carry out the oxidation reactions of the electron transport chain, (2) the ATP synthase that makes ATP in the matrix, and (3) transport proteins that allow the passage of metabolites into and out of the matrix. An electrochemical gradient is established across this membrane, and so it must be impermeable to ions and most small charged molecules.

Outer membrane. Because it contains a large channel-forming protein (called porin), the outer membrane is permeable to all molecules of 5000 daltons or less. Other proteins in this membrane include enzymes involved in mitochondrial lipid synthesis and enzymes that convert lipid substrates into forms that are subsequently metabolized in the matrix.

Intermembrane space. This space (white) contains several enzymes that use the ATP-pumping out of the matrix to phosphorylate other nucleotides.
The high-energy electrons are then transferred to the inner mitochondrial membrane, where they enter the electron transport chain; the loss of electrons regenerates NAD+ and FAD that are needed for continuation of oxidative metabolism.

Mitochondria can use pyruvate or fatty acids to generate energy. They enter the mitochondrion, are converted to acetyl coA and then metabolized by the citric acid cycle which reduces NAD+ to NADH. In the process of oxidative phosphorylation, high energy electrons from NADH are then passed along the electron transport chain in the inner membrane to oxygen. This electron transport generated a proton gradient across the inner membrane which is used to drive the production of ATP by ATP synthase.

Electrons Are Transferred Along a Chain of Proteins in the Inner Mitochondrial Membrane

The electron transport chain that carries out oxidative phosphorylation is present in many copies in the inner mitochondrial membrane. Also known as the respiratory chain, it contains over 40 proteins, of which about are directly involved in electron transport. Mitochondrial electron transport chains are grouped into three:

- the NADH dehydrogenase complex: accept electron from NADH and pass along the chain to each other of other enzyme complex.
- the cytochrome b-c1 complex
- the cytochrome oxidase complex: involve in water molecule formation using oxygen.

Electrons are transferred through three respiratory enzyme complexes in the inner mitochondrial membrane.