Introduction to cellular respiration and redox

Intro to redox in cellular respiration. Substrate-level vs. oxidative phosphorylation. Electron carriers.

Introduction

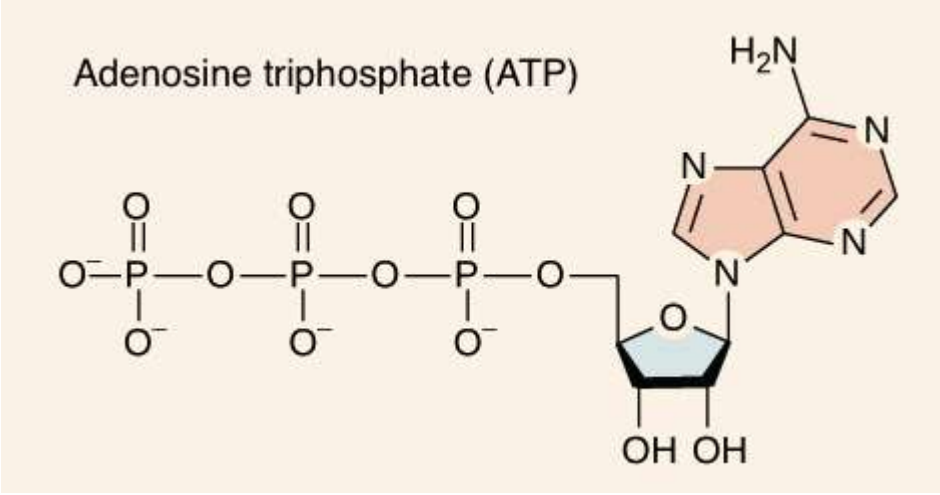
Let's imagine that you are a cell. You've just been given a big, juicy glucose molecule, and you'd like to convert some of the energy in this glucose molecule into a more usable form, one that you can use to power your metabolic reactions. How can you go about this? What's the best way for you to squeeze as much energy as possible out of that glucose molecule, and to capture this energy in a handy form?

Fortunately for us, our cells – and those of other living organisms – are excellent at harvesting energy from glucose and other organic molecules, such as fats and amino acids. Here, we'll get a high-level overview of how cells break down fuels. Then, we'll take a closer look at some of the electron transfer reactions (redox reactions) that are key to this process.

Overview of fuel breakdown pathways

The reactions that extract energy from molecules like glucose are called **catabolic reactions**. That means they involve breaking a larger molecule into smaller pieces. For example, when glucose is broken down in the presence of oxygen, it's converted into six carbon dioxide molecules and six water molecules. The overall reaction for this process can be written as:
$C_6H_{12}O_6 + 6O_{26} \rightarrow 6CO_{26} + 6H_2O_6$ O $\Delta G = -686 kcal/mol$ G = -686 kcal/mol

In a cell, this overall reaction is broken down into many smaller steps. Energy contained in the bonds of glucose is released in small bursts, and some of it is captured in the form of **adenosine triphosphate** (**ATP**), a small molecule that powers reactions in the cell. Much of the energy from glucose is dissipated as heat, but enough is captured to keep the metabolism of the cell running.

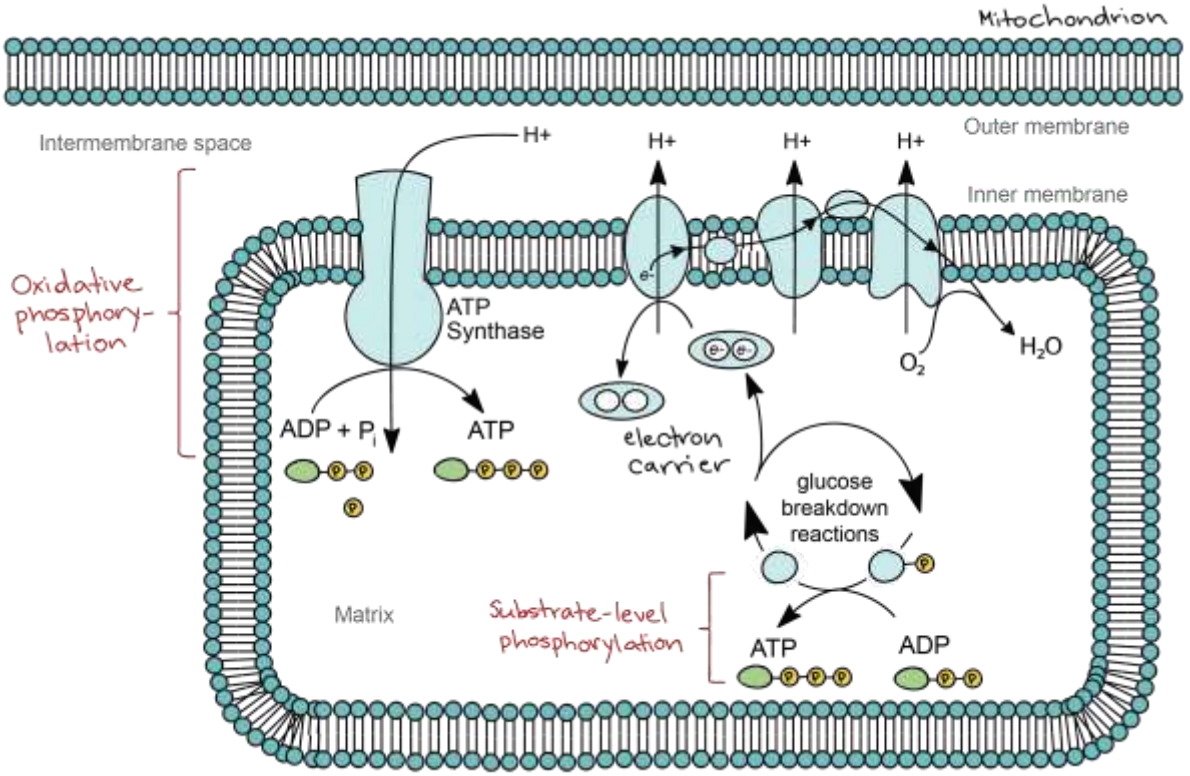


Structure of ATP.[

Image modified from "ATP: Adenosine triphosphate: Figure 1," by OpenStax College, Biology, CC BY 4.0.

As a glucose molecule is gradually broken down, some of the breakdowns steps release energy that is captured directly as ATP. In these steps, a phosphate group is transferred from a pathway intermediate straight to ADP, a process known as **substrate-level phosphorylation**.

Many more steps, however, produce ATP in an indirect way. In these steps, electrons from glucose are transferred to small molecules known as electron carriers. The electron carriers take the electrons to a group of proteins in the inner membrane of the mitochondrion, called the electron transport chain. As electrons move through the electron transport chain, they go from a higher to a lower energy level and are ultimately passed to oxygen (forming water).
As an electron passes through the electron transport chain, the energy it releases is used to pump protons (H^+) out of the matrix of the mitochondrion, forming an electrochemical gradient. When the H^+ superscript flow back down their gradient, they pass through an enzyme called ATP synthase, driving synthesis of ATP. This process is known as **oxidative phosphorylation**. The diagram below shows examples of oxidative and substrate-level phosphorylation.



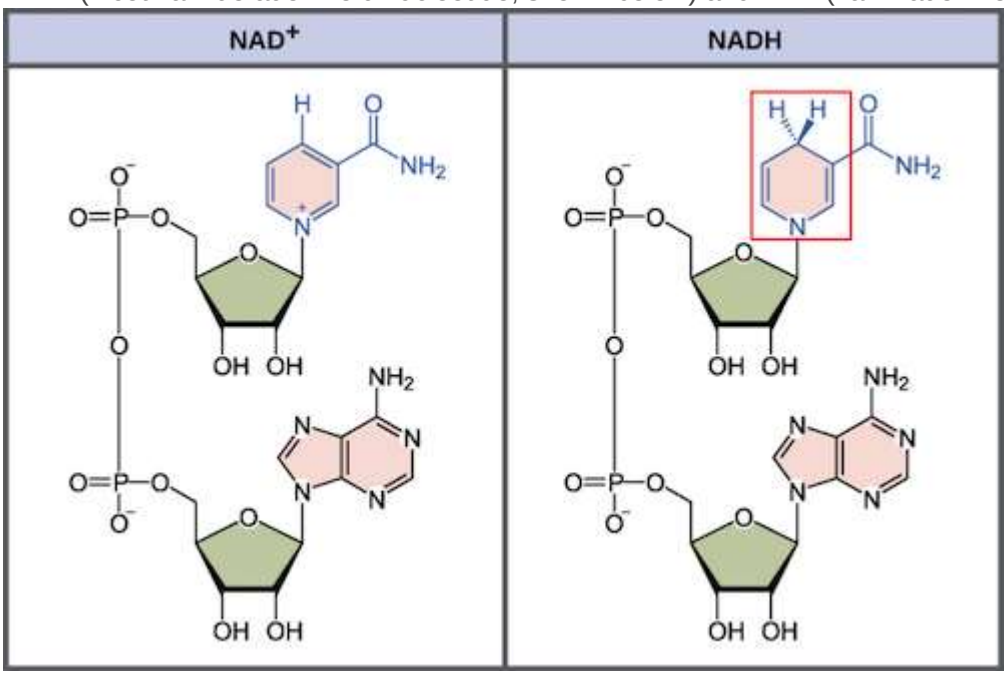
Simplified diagram showing oxidative phosphorylation and substrate-level phosphorylation during glucose breakdown reactions. Inside the matrix of the mitochondrion, substrate-level phosphorylation takes place when a phosphate group from an intermediate of the glucose breakdown reactions is transferred to ADP, forming ATP. At the same time, electrons are transported from intermediates of the glucose breakdown reactions to the electron transport chain by electron carriers. The electrons move through the electron transport chain, pumping protons into the inter-membrane space. When these protons flow back down their concentration gradient, they pass through ATP synthase, which uses the electron flow to synthesize ATP from ADP and inorganic phosphate (Pi). This process of electron transport, proton pumping, and capture of energy from the proton gradient to make ATP is called oxidative phosphorylation.

Not exactly! This is a simplified diagram that is designed to help us get a feel for how oxidative phosphorylation works. In a real mitochondrion, the matrix would be much a much larger space than it appears here, and the inner mitochondrial membrane surrounding it would contain lots of folds and tunnels. These folds and tunnels increase its surface area, so that it can hold many, many copies of the enzymes (such as ATP synthase and the electron transport chain proteins) that are involved in energy harvesting.

When organic fuels like glucose are broken down using an electron transport chain, the breakdown process is known as **cellular respiration**.

Electron carriers

Electron carriers, also called electron shuttles, are small organic molecules that play key roles in cellular respiration. Their name is a good description of their job: they pick up electrons from one molecule and drop them off with another. You can see an electron carrier shuttling electrons from the glucose breakdown reactions to the electron transport chain in the diagram above. There are two types of electron carriers that are particularly important in cellular respiration: **NAD^+** (nicotinamide adenine dinucleotide, shown below) and **FAD** (flavin adenine dinucleotide).



Chemical structures of NAD+ and NADH. NADH has a hydrogen attached to one nitrogen-containing ring, whereas in NAD+ this same ring lacks a hydrogen and has a positive charge. *Image modified from"Energy in living systems: Figure 1," by OpenStax College, Biology (CC BY 3.0).*

When NAD^+ and FAD pick up electrons, they also gain one or more hydrogen atoms, switching to a slightly different form:

$$NAD + 2e^{-2} + 2H + 2 \rightarrow NAD + H + FAD + 2e^{-2} + 2\,H^{+2} \rightarrow 2FADH2$$

And when they drop electrons off, they go neatly back to their original form:

$$NADH \rightarrow + NAD + 2e^{-2+} H + 2FADH2 \rightarrow FAD + 2e^{-2} + 2\,H + 2$$

The reactions in which NAD+ and FAD gain or lose electrons are examples of a class of reactions called redox reactions. Let's take a closer look at what these reactions are and why they're so important in cellular respiration.

Redox reactions: What are they?

Cellular respiration involves many reactions in which electrons are passed from one molecule to another. Reactions involving electron transfers are known as **oxidation-reduction reactions** (or **redox reactions**).

You may have learned in chemistry that a redox reaction is when one molecule loses electrons and is **oxidized**, while another molecule gains electrons (the ones lost by the first molecule) and is **reduced**. Handy mnemonic: “LEO goes GER”: *L*ose *E*lectrons, *O*xidized; *G*ain *E*lectrons, *R*educed.

The formation of magnesium chloride is one example of a redox reaction that nicely matches our definition above:

$$Mg+Cl_2 \rightarrow Mg_2+2Cl\text{-}Mg+Cl_2 \rightarrow Mg_2+2Cl$$

In this reaction, the magnesium atom loses two electrons, so it is oxidized. These two electrons are accepted by chlorine, which is reduced.

However, as Sal points out in his video on oxidation and reduction in biology, we should really put quotes around "gains electrons" and "loses electrons" in our description of what happens to molecules in a redox reaction. That's because we can also have a reaction in which one molecule *hogs* electrons rather than fully gaining them or is *hogged from* rather than fully losing them.

What do we mean by that? To illustrate, let's use the example from Sal's video:

$$2H_2+ O_2 \rightarrow 2H_2O+\{heat\}$$

This reaction does not involve an obvious electron transfer, but it's still an example of a redox reaction. That's because the amount of electron density on the H and O atoms is different in the products than in the reactants.

Why that's true is not obvious, so let's break it down using the properties of atoms. When H atoms are bonded to each other in H_2 they share electrons equally: neither can win the tug-of-war for the electrons. The same is true for O atoms bonded to each other in O_2. However, the situation is different in the product, H_2O. Oxygen is much more electronegative, or electron-hungry, than hydrogen, so in an $O-H$ bond in a water molecule, the electrons will be hogged by the O atom and spend more time close to it than to the H.

So, even though no electrons were fully gained or lost in the above reaction:

- O has more electron density after the reaction than before (was reduced)
- H has less electron density than it did before (was oxidized)

For you chemistry buffs out there, this change in electron hogging during the reaction can be more precisely described as a change in oxidation states of the O atoms.

What about gaining and losing H and O atoms?

Oxidation and reduction reactions are fundamentally about the transfer and/or hogging of electrons. However, in the context of biology, there is a little trick we can often use to figure out where the electrons are going. This trick lets us use the gain or loss of H and O atoms as a proxy for the transfer of electrons.

In general:

- If a carbon-containing molecule gains H atoms or loses O\ atoms during a reaction, it's likely been reduced (gained electrons or electron density)

- On the other hand, if a carbon-containing molecule loses H atoms or gains O atoms, it's probably been oxidized (lost electrons or electron density)

For example, let's go back to the reaction for glucose breakdown:

$C_6H_{12}O_6 + 6O_{26} \rightarrow\ 6CO_{26} + 6H_2O_6$

In glucose, carbon is associated with H atoms, while in carbon dioxide, it is not associated with any H's. So, we would predict that glucose is oxidized in this reaction. Similarly, the O atoms in O_2 end up being associated with more H's after the reaction than before, so we would predict that oxygen is reduced.

- The atoms that H is usually bound to in organic molecules, such as C, O, N and P are more electronegative than H itself. So, if a H atom and its electron join a molecule, odds are that whatever's bonded to the new H is going to hog the electron and become reduced.

- O is more electronegative than any of the other major atoms found commonly in biological molecules. If it joins a molecule, it's likely going to pull away electron density from whatever it's attached to, oxidizing it.

What's the point of all this redox?

Now that we have a better sense of *what* a redox reaction is, let's spend a moment thinking about the *why*. Why does a cell go to the trouble of ripping electrons off of glucose, transferring them to electron carriers, and passing them through an electron transport chain in a long series of redox reactions?

The basic answer is: to get energy out of that glucose molecule! Here is the glucose breakdown reaction we saw at the beginning of the article:

$C_6H_{12}O_6 + 6O_{26} \rightarrow 6CO_{26} + 6H_2O_6\ \Delta G = -686 \text{kcal/mol}$

Which we can rewrite a bit more clearly as:

$C_6H_{12}O_6 + 6O_{26} \rightarrow + 6H_2O_6 \text{ energy!}$

Electrons are at a higher energy level when they are associated with less electronegative atoms (such as C or H) and at a lower energy level when they are associated with a more electronegative atom (such as O). So, in a reaction like the breakdown of glucose above, energy

is released because the electrons are moving to a lower-energy, more "comfortable" state as they travel from glucose to oxygen.

The energy that's released as electrons move to a lower-energy state can be captured and used to do work. In cellular respiration, electrons from glucose move gradually through the electron transport chain towards oxygen, passing to lower and lower energy states and releasing energy at each step. The goal of cellular respiration is to capture this energy in the form of ATP.

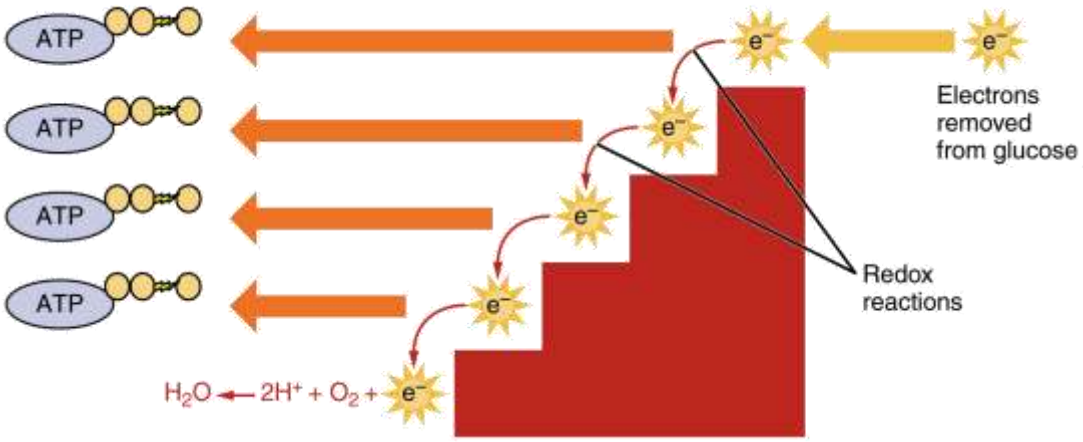


Image modified from *Carbohydrate metabolism: Figure 1* by OpenStax College, Anatomy & Physiology, CC BY 3.0

Great question! No, the process is not quite that direct. This diagram is just illustrating the concept, not the mechanism.

What actually happens? The energy released in electron transfers in the electron transport chain is captured as a proton gradient (discussed at the beginning of the article), and the proton gradient provides energy for the conversion of ADP to ATP by an enzyme called ATP synthase. In other words, energy doesn't turn into ATP. (It's pretty hard to make energy into matter, outside of special relativity!) Instead, some of the released energy is used to stick ADP and inorganic phosphate together to make ATP. Energy is stored in the newly formed bond that is present in ATP but not ADP.

In the next articles and videos, we'll walk through cellular respiration step by step, seeing how the energy released in redox transfers is captured as ATP.