Enzymes and the active site

Enzymes as biological catalysts, activation energy, the active site, and environmental effects on enzyme activity.

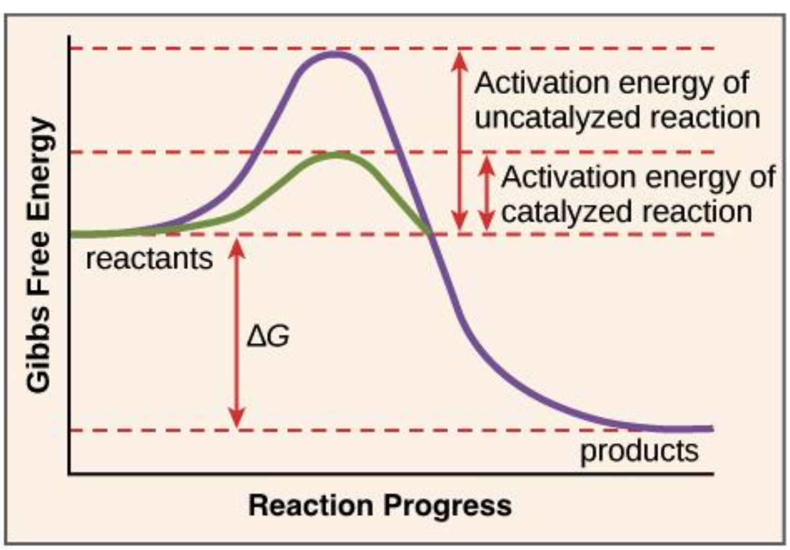
Introduction

As a kid, I wore glasses and desperately wanted a pair of contact lenses. When I was finally allowed to get contacts, part of the deal was that I had to take very, very good care of them, which meant washing them with cleaner every day, storing them in a sterile solution, and, once a week, adding a few drops of something called “enzymatic cleaner.” I didn’t know exactly what “enzymatic cleaner” meant, but I did learn that if you forgot you’d added it and accidentally put your contacts in your eyes without washing them, you were going to have burning eyes for a good fifteen minutes.

As I would later learn, all that “enzymatic” meant was that the cleaner contained one or more **enzymes**, proteins that catalyzed particular chemical reactions – in this case, reactions that broke down the film of eye goo that accumulated on my contacts after a week of use. (Presumably, the reason it stung when I got it in my eyes was that the enzymes would also happily break down eye goo in an intact eye.) In this article, we’ll look in greater depth at what an enzyme is and how it catalyzes a particular chemical reaction.

Enzymes and activation energy

A substance that speeds up a chemical reaction, but is not consumed by that reaction, is called a **catalyst**. The biological molecules that catalyze reactions in living organisms and cells are more specifically called **enzymes**. The great majority of enzymes are proteins, although some RNAs are also catalytic. Enzymes perform the critical task of lowering a reaction's activation energy, the amount of energy that must be put into the reaction before it can begin. Enzymes lower activation energy by binding to the reactant molecules and positioning or bending them in a way that makes the breaking of existing bonds, and the formation of new ones, take place more readily.



Reaction coordinate diagram showing the course of a reaction with and without a catalyst. With the catalyst, the activation energy is lower than without. However, the catalyst does not change the ∆G for the reaction.

Image modified from OpenStax Biology.

Although enzymes are very good at lowering activation energy for a reaction, it's important to realize that they don't change a reaction's ∆*G* value (don't change whether a reaction is energy-releasing or energy-absorbing overall). This is because they don't affect the free energy of the reactants or products. They just reduce the activation energy by making it easier for molecules to reach the transition state (the unstable intermediate state at the top of the energy "hill" of the reaction), as shown above. In other words, enzymes speed up the reaction rate without altering the reaction equilibrium.

Enzyme active sites and substrate specificity

To catalyze a reaction, an enzyme will bind to one or more reactant molecules, known as its **substrates**. In some reactions, a single substrate is broken down into multiple products. In others, two substrates may come together to create one larger molecule. Two reactants might also enter a reaction, swap pieces or change shape, and leave the reaction as two separate products. For any biological reaction you can think of, there's probably an enzyme whose job is to catalyze that reaction!

The part of the enzyme where the substrate binds is called the **active site** (since that's where the catalytic "action" happens). Usually, the active site will be a pocket or cleft in the enzyme's surface, and it's often just a small part of the overall molecule. In a protein enzyme, the active site gets its properties, including its shape and ability to bind substrates, from the amino acids that make it up. These amino acids may have side chains that are large or small, acidic or basic, hydrophilic or hydrophobic. The set of amino acids present in the active site, along with how these amino acids are organized in 3D, creates a specialized environment in the active site, one that can bind to – and exert catalytic effects on – just one or a few substrates. In other words, the active site is just the right size, and has just the right pattern of charges, for the correct substrate to fit inside.

The matching between enzyme and substrate isn't just like two puzzle pieces fitting together (though scientists once thought it was, in an old model called the "lock-and-key" model). Instead, an enzyme actually changes shape slightly when it binds its substrate, which results in an even tighter fit and primes the enzyme to catalyze conversion of the substrate into product. This adjustment of the enzyme to snugly fit the entering substrate is known as **induced fit**, and it happens because of interactions (such as hydrogen and ionic bonding) between the substrate and the amino acid side chains of the active site.

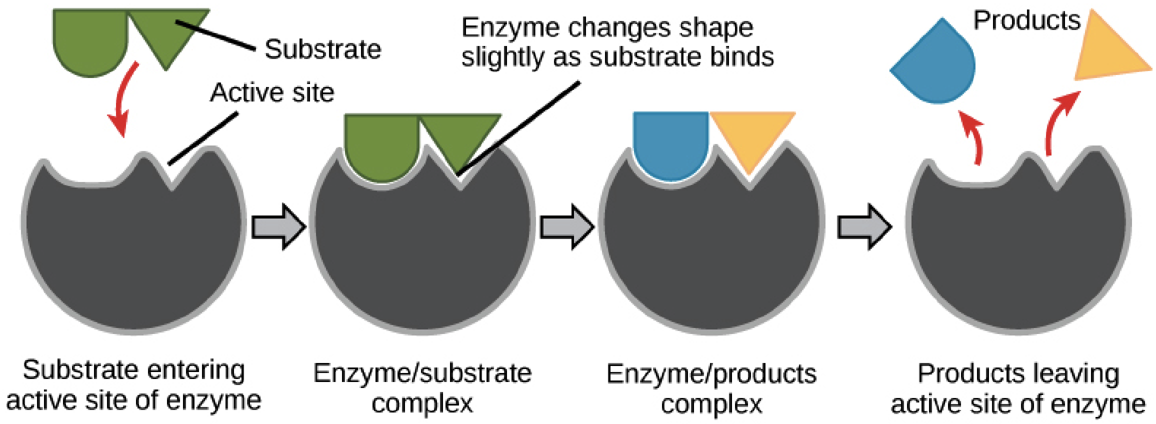


Illustration of the induced fit model of enzyme catalysis. As a substrate binds to the active site, the active site changes shape a little, grasping the substrate more tightly and preparing to catalyze the reaction. After the reaction takes place, the products are released from the active site and diffuse away.

Image credit: OpenStax Biology.

Once substrates have entered the active site, how does an enzyme make it easier for them to turn into products? The exact answer varies from reaction to reaction. Some major strategies include:

- In reactions with multiple substrates, the enzyme may hold the substrates in the correct position and orientation for formation of a new bond.
- An enzyme may bend the substrate or strain its bonds, bringing it closer to the transition state and thus reducing the amount of energy needed to reach that state (the activation energy).
- Enzymes may provide a chemical micro-environment that makes it easier for a reaction to proceed. This can involve making an acidic or basic "pocket" that favors a reaction, donating or receiving electrons (often, through metal ions bound in the active site), or even forming a temporary covalent bond with the substrate. All of these interactions depend on specific amino acid side chains found in the active site.

In all of these cases, the enzyme will release its product or products at the end of the reaction. It will then be back in its original form, able to bind new substrate molecules and catalyze more reactions. Indeed, one of the hallmark properties of enzymes (and catalysts in general) is that they remain unchanged by the reactions they catalyze. A typical enzyme will process many molecules of substrate in its lifetime, continuously cycling between empty, substrate-bound, and product-bound forms.

Environmental effects on enzyme function

Because active sites are so finely tuned to provide an ideal environment for a chemical reaction, they are also sensitive to changes in the enzyme's surrounding environment. Important factors include:

- **Temperature.** Each enzyme has a temperature at which it works best, as well as a range of temperatures at which it works decently. Increasing or decreasing temperature beyond this range can affect the shape or chemical state of the active site, making it less able to bind substrates. Very high temperatures (for animal enzymes, above 40 degrees C or 104 degrees F may cause an enzyme to denature, losing its three-dimensional shape and activity. This is part of why a high fever can be dangerous to humans.
- **pH**. The pH of the environment can also affect enzyme function. Active site amino acids often have acidic or basic side chains that play important roles in catalysis. If the enzyme is in an environment of the wrong pH, the side chains may be inappropriately protonated (or deprotonated) and unable to bind the substrate or catalyze the reaction. As for temperature, enzymes work best in a certain pH range, and extreme pHs can cause denaturation.
- **Inhibitors, activators, and cofactors.** A variety of regulatory molecules may bind to an enzyme and change its activity. These include **inhibitors**, which block catalysis; **activators**, which enhance catalysis; and **cofactors**, small molecules required for enzyme activity. You can learn more about inhibitors, activators, and cofactors in the section on enzyme regulation.