**Why do reactions occur?** - As we spoke about previously, ionic and covalent bonds form to give the atoms octets. The noble gas electron configurations are said to be more "stable". The term stability refers to the amount of potential energy the system has. The two atoms involved in the bond, for example, have a higher total potential energy than the bonded atoms. The tendency to lower the potential energy (i.e. to make a more stable system) is the **driving force** behind bond formation AND chemical reactions.

We can imagine a chemical reaction between two molecules as first breaking the bonds of the reactant molecules to make atoms, then reforming bonds between these atoms to make the product molecules. Therefore, if the product bonds have an overall lower potential energy than the reactant bonds, the net effect in going from products to reactants is the LOWERING of the overall potential energy.

**Where does this energy go?** - As we lose potential energy, the overall energy must remain constant. The classical picture is of a ball on the top of a slanted board. When the ball is not moving, all of its energy is potential. Once it starts rolling, it has kinetic energy.

The potential energy of the bonds "transforms" into a different kind of energy. Generally, the energy associated with bonds forming/breaking is manifested as **heat**. In strict terms, heat is defined as the "energy that, when transferred from one place to another, causes a rise in the temperature". So, if a reaction proceeds, and heat is given off, the reaction vessel will get hot. This type of reaction is said to be **exothermic**. The amount of heat associated with a reaction is called the **enthalpy change**, and is given in units of Joules, calories, or some other convenient unit. The symbol for enthalpy change is **ΔH**. For exothermic reactions, the enthalpy is always negative (i.e. $\Delta H < 0$).

**Are all reactions exothermic?** - If we examine all reactions to see whether heat is always released, we would find that the answer is NO. There are reactions which are said to be **endothermic**, with $\Delta H > 0$. These reactions require heat, so they absorb heat from the surroundings, thus the reaction vessel gets cold!
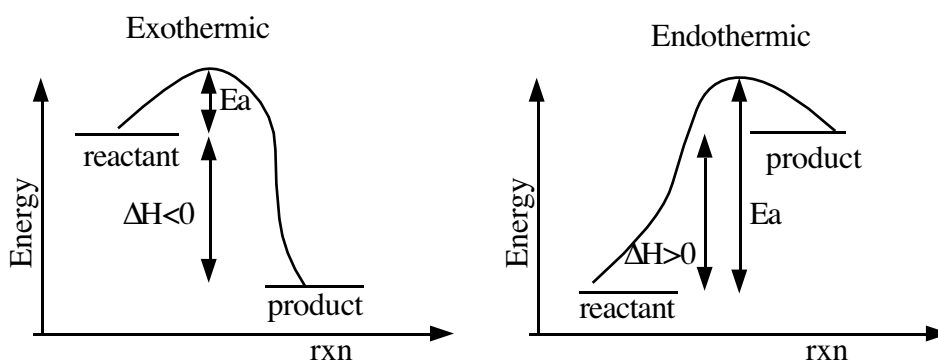


The ball analogy holds true here as well. To get the ball from the bottom of the inclined board to the top, enrgy must be exerted on the ball (i.e. "absorbed" from you).

**First Law of Thermodynamics** - This is the law of conservation of energy. There are literally hundreds of ways of stating this law.

**Entropy** - $\Delta S$, the tendency toward disorder. The more disorderly the system, the more favorable it is. Thus, the second law of thermodynamics can be stated: $\Delta S_{universe} > 0$.

**Gibbs Free Energy** - $\Delta G = \Delta H - T\Delta S$. This is a function that maximizes (i..e makes very positive) $\Delta S$ while simultaneously minimizes (i.e. making very negative) $\Delta H$. The ultimate criteria for spontaneity is to have $\Delta G < 0$.

It should be noted that $\Delta H$ and $\Delta S$ both vary with temperature. However, over fairly large ranges of temperature, the amount by which they change is negligible. Thus, we often treat them as constants.

**Kinetics** - We have, so far, talked about what drives a reaction. We have not yet talked about how fast reactions occur, or what happens during a reaction. These two subjects fall into the category of chemical kinetics. By many people's estimate, this is the single most difficult and interesting field of chemistry. We will not be treating it in the greatest depth, but you should walk away with an appreciation for this subject.

**Activation Energy** - As we mentioned above, even exothermic reactions need a little push to go. The size of the "push" is called the activation energy. It is a little hurdle that the reactants must overcome in order to proceed to products. Without this push, the reaction can never proceed.

How do the reactants get this much-needed push? Generally speaking, the easiest way to do this is by adding heat to the system. In practical terms, this amounts to raising the temperature of the reaction mixture. The temperature to which the mixture must be raised for optimal speed is proportional to the $E_a$ by a constant, $R = 1.987$ cal/mol K. This is not to say that ONLY when the temperature reaches this value will the reaction occur, Quite the contrary. Even the reactions with very high $E_a$s can take place at low temperatures. However, the extent of the reaction (i.e. the % yield) will be very, very small. This is because some of the reactant molecules can, by sheer luck, have the right energy. The chances are better that at higher temperatures, more molecules will have the "right" energy. So, the rate of a reaction can be thought of an average over all the molecules present.

**Other Factors that Influence the extent of Reaction** - Since we have just stated that the number of molecules with the correct energy are the ones that react, AND that the rate is an average of the speed of these reactions relative to all the molecules present, then we can imagine, strictly from a probability point of view, that the more molecules we have, overall there will be more reactant molecules with the correct energy. Thus, we can state that the rate of a reaction not only depends of temperature, but it also depends on the **concentration** (number of particles per unit volume) of reactant molecules.

In the next section we will talk a little about how reactions occur. But, first we will mention something called the **collision model** of reactions. Basically, the idea is that in order for a reaction to occur, the reactant molecules must come into contact (i.e. collide)

with another reactant. So, besides having a higher chance of having high $E_a$s, having a large concentration also increases the net number of collisions. The more collisions, the better the chance of reaction occurring.

**Rate Laws and Mechanisms**: The rate of a chemical reaction is often a difficult thing to measure. But, once it is measured, the question arises "what can you do with it?" And, since it depends on concentrations and temperatures, what is a good way of describing the rate that unambiguously tells you all there is to know?

The description of a rate that fits this criterion is called the **rate law**. It gives the rate for a reaction in terms of a temperature dependent **rate constant** and the concentrations of the reactants. The way in which these are determined is by doing many experiments where the reaction is repeated several times while changing one **variable** (either the changing the concentration of one of the reactants while temperature is help constant, or changing the temperature several times, keeping the concentrations constant). The overall mathematical description of the rate has the appearance: rate = k $n_{reactants}^{power}$ (n=moles). Note, the powers ARE not related to the coefficients in the balanced equation.

Oddly, when this is done, one often finds that the comparison between two of the experiments shows a non-linear increase between the concentration and the rate. How and why this is governed by the **mechanism** of the reaction.

Thermodynamics tells us whether a reaction is "spontaneous", that is favored in the direction written, and Kinetics tells us how the reaction takes place, and how fast it goes. The **reaction mechanism** is the step-wise, atomic level description of how molecules internal during a reaction. The rate of a reaction, therefore, is limited by the rate of the individual steps. Thus, the slowest step, is known as the **rate determining step**, because the overall reaction can not be any faster than its slowest step.

Finally, a **catalyst** is a substance that lowers the activation energy, thereby speeding up the reaction. The catalyst is an active member in the chemical reaction, but, overall, it is not altered by the reaction.

**Enzymes, Coenzymes, and Vitamins** – In the last section, we looked at amino acids and polypeptides. An important group of polypeptides, known as proteins, is subdivided into several subgroups. One very important group is called the **enzymes**. These proteins are **biological catalysts** that catalyze very specific reactions. It is useful, therefore, to remember what a catalyst is, and see how enzymes act as catalysts.

**Catalysis** – Chemical reactions do not always occur by themselves. More often than not, an amount of energy (**activation energy**) must be supplied in order for the reaction to start. Once started, the thermodynamics of the process drives the reaction forward. The general diagram we use to represent this is:
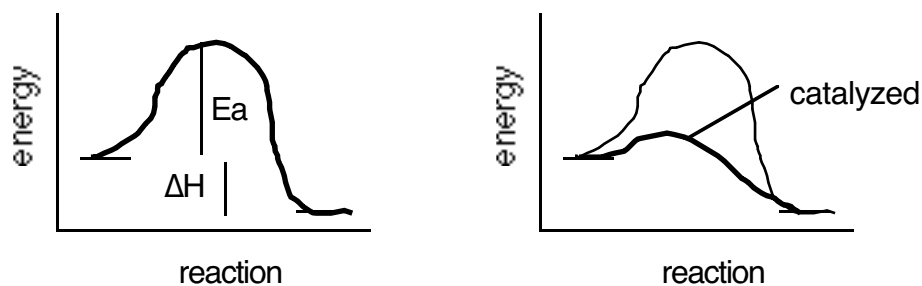
What a catalyst does is it lowers the activation energy of the reaction (by providing an alternate pathway) so that the amount of energy needed to start the reaction is greatly reduced. An important property of catalysts is that they catalyze the forward reaction as well as the reverse reaction. Also, even though they play an active role in the reaction, they are not "consumed" by the reaction. In other words, after the reaction is over, the catalyst can be recovered from the reaction mixture, unchanged from its original form.

Some catalysts act by bringing the reacting molecules closer together. Others "activate" the covalent bonds within the molecules to make them more reactive. Enzymes do both. The reactants (known in biochemistry as **substrates**) are attracted to the enzyme protein and form ionic bonds and/or H-bonds to the protein. The reaction between the substrates then takes place (rapidly), and the products are released. There are several different types of mechanisms of enzyme catalysis. However, all of them share certain basic features, namely "binding" the substrate. Therefore, we will discuss the mechanics and chemistry of this binding.

**Active Site** – The polypeptides that comprise enzymes tend to be very large. The average molar masses of enzymes are in the 10 – 100 kg/mol range. The overall size of these molecules is considerable larger than the average substrate molecule. The enzyme, therefore, has enough flexibility in its peptide chain to form a pocket where the substrate can fit. This pocket is called the **active site** of the enzyme, since it is here that the reactions take place.

Since the substrate must fit into the enzyme, and since the shape of the substrate is non-standard (i.e. not all reactants are the same), there are hundreds of enzymes, each of which catalyzes a specific (type) of reaction for specific (types of) substrates. There are some general classes of enzymes, which we will mention later.

**Cofactors** – Besides the reactants, many enzymes require other molecules to help the reactions proceed. For example, if the reaction to be catalyzed produces a by-product that is undesirable, the enzyme might need a molecule that can remove this stuff. Nature, in its infinite wisdom, is very much in favor of self-preservation. In the example above, requiring the **co-factor** to be present in order for the enzyme to be operational is one way of ensuring this.

Some cofactors are metal ions, generally referred to as **trace minerals** by nutritionists. These ions (e.g. $Zn^{2+}$, $Mg^{2+}$, $Fe^{2+}$, $Cu^{2+}$) serve many varied functions. Other cofactors are medium sized organic molecules (with and without metal ions) that are collectively called **co-enzymes**. Enzymes that require the coenzymes to be tightly bound to the

protein are called apoenzymes when the cofactor is not present, and holoenzymes when they are. These serve many different functions, ranging from redox agents to functional group transfers. As we learn more about the reactions, we will mention the various cofactors and their role in the catalysis.

Most of the **precursors** of the coenzymes must be eaten in order for the body's enzymes to have them available. The precursors that are obtained through diet are known as the water-soluble **vitamins**. These include the B-vitamins and vitamin C. Vitamins A, D, E, and K are all fat soluble, and serve other functions.

The list below gives some of the coenzymes formed from the common B vitamins.

| | |
|---|---|
| Thiamine (B1) | Thiamine pyrophosphate |
| Riboflavin (B2) | Flavin adenine dinucleotide (FAD) |
| Niacin | Nicitinamide adenine dincleotide (NAD) |
| Pantothenic acid | Coenzyme A |
| Pyridoxine (B6) | Pyridoxal phosphate |
| Biotin | Biotin |
| Folic acid | Tetrahydrofolate |
| B12 | Deoxyadenosyl cobalamin |

**Classes of Enzymes** – There are many enzymes that perform similar tasks, but due to the specificity of the active site, they are not interchangeable. On the other hand, some are quite versatile, and can catalyze many similar reactions. Generally speaking, the more specific the enzyme is, the more efficient it is. However, the need for more enzymes somewhat outweighs this efficiency.

At any rate, the six main classifications of enzymes are as follows:

| | |
|---|---|
| Oxidoreductases | Catalysis of redox reactions |
| Transferases (kinase) | Catalyze the transfer of a functionality from one molecule to another |
| Hydrolases | Catalysis of bond hydrolysis |
| Lyases | Catalysis of the cleavage of bonds by means other than hydrolysis, and addition to double bonds by means other than redox |
| Isomerases | Catalysis of rearrangement of moieties within a molecule |
| Ligases (synthetases) | Catalyze bond formation (other than the addition above) |

**Inhibition and Allosteric Effects** – When the substrate approaches an enzyme, several things can occur. For instance, the enzyme might already have a molecule bound in the active site, so the substrate cannot bind to it. Or, the enzyme might not "look" right, i.e. the active site is not the correct shape for the substrate. In the first case, if the bound molecule is another substrate molecule, then, once the reaction is complete, the next

substrate can bind and do its thing. However, there might be some other kind of molecule bound. This molecule might not take part in any reaction, but it fits exactly into the active site the same way as the substrate would. This type of molecule is called a **competitive inhibitor**, since it competes for the active site.

There are other inhibitors, called **non-competitive inhibitors**, which have their own binding site away from the active site, but none-the-less render the enzyme inactive. This type of situation falls into the category of an **allosteric** effect. In an allosteric system, the actual shape of the enzyme changes when the allosteric factor is bound. Often, coenzymes play an allosteric role, usually in a positive, non-inhibitory, manner.

Sometimes the allosteric effector does its thing after the substrate binds. For instance, the bound enzyme-substrate **complex** can undergo a major shape change once the effector binds. In certain cases, this involves a motion that is reminiscent of a door shutting over the active site. In other cases, the reaction does not occur until the effector binds. We will talk more about these cases when we get to them.

**Metabolism** - We have thus far discussed the general ideas of enzymatic reactions. We looked at binding in active sites, and the overall energetics of catalysis by enzymes. We will look at several specific enzymatic reactions that fall into the classification of **metabolism**. Simply put, metabolism is the sum of all chemical reactions that occur in a living organism.

There are two main subcategories of metabolism: **Anabolism** and **Catabolism**. In anabolism, large molecules are made by combining smaller molecules. This, for example, includes polypeptide formation from amino acids. The other category (catabolism) is just the opposite - breaking down large molecules into smaller ones. We will first look at catabolism, using the carbohydrates as our first example. Then, we will study anabolism of carbohydrates. Unfortunately, this involves a little jumping around in the textbook, but we will try to keep it simple.

Before we delve into carbohydrate metabolism, we first need to discuss bio-energetics. This involves a quick rehashing of thermodynamics and the introduction of the "gasoline of metabolism" - ATP.