AN INTRODUCTION TO METABOLISM
ENERGY AND ENZYMES

Metabolism

This chapter is really about enzymes. However, before you can understand enzymes, you need to understand some physical parameters associated with energy. To understand energy, we need to begin with metabolism. Metabolism is from the Greek *metabole* which means change. For biological purposes, metabolism is the sum of the building and breakdown processes, whether it is in a cell, an organism, or whatever system you define. There are two parts to metabolism: anabolic and catabolic reactions.

Anabolic and Catabolic Reactions

Anabolic reactions are building processes. For example, when you convert excess glucose in your system into starch, that is anabolic. Catabolic reactions are breakdown processes. The hydrolysis of starch is an example. Mathematically, they may be related as follows:

Metabolism = anabolic processes + catabolic processes

Energy

To understand enzymes and metabolism, you must understand energy. For our definition, energy is the ability to do work. That sounds somewhat non-technical, but work has a specific definition: when you exert a force on some object and move that object over a distance, you have accomplished work or,

W = force x distance.

Types of Energy

Most of you know there are many types of energy. Some examples are

- electrical
- chemical
- mechanical (two types)
  - potential (energy of position)
  - kinetic (energy of motion)
- nuclear
- thermal
- solar, etc.

What many people often don't understand is the amount of energy available is constant. It follows the first law of thermodynamics.

1st Law of Thermodynamics

You have heard of this idea even though you may not recognize its name.
The first law of thermodynamics states "Energy is neither created nor destroyed, but may be transformed from one form to another." What scientists are saying is that the amount of energy in a system is constant. We are neither making more nor destroying or using up any. A system may be defined as a cell, a human, an automobile, or even the universe. As an example, take mechanical energy. Mechanical energy is subdivided into two categories: kinetic and potential. Kinetic energy is energy of motion. Potential

energy is energy by virtue of its position. In any system, the mechanical energy of a system is equal to the amount of potential energy + the amount of kinetic energy. In other words, $E_{\text{total of system}}$ = P.E. + K.E.

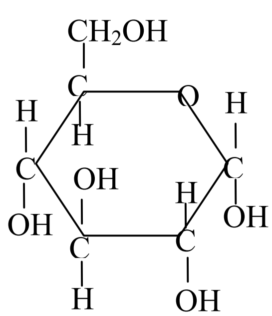
Assume a system (in our case, defined as a rock on a cliff) has an E_{total} of 100 joules (unit of energy). Since the rock is not moving, the kinetic energy (KE) is zero. That means the potential energy must be

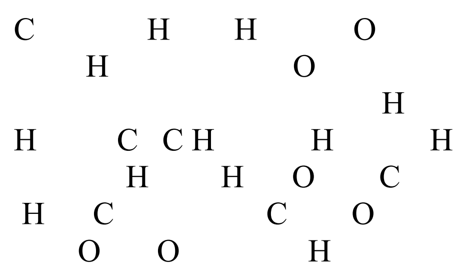
E_{total} (100joules) = PE + 0 or PE must be 100 joules.

The minute someone pushes the rock off the cliff, the rock begins to accelerate due to gravity at 9.8 m/s^2. At some point the rock will have 20 units of KE and 80 units of PE (for an E_{total} of 100). At another point of fall, the rock will have 50 joules KE and 50 joules PE. At the moment before impact, the rock will have 100 joules KE and 0 joules PE.

Have we created any energy? No. Have we destroyed energy? No. All we have done is convert it from one form to another – the first law of thermodynamics.

2nd Law of Thermodynamics
The bad news is if there is a first law of thermodynamics, there is a second law. The second law of thermodynamics states “Everything in the universe tends toward entropy.” Entropy is the amount of disorder in a system. Everything in the universe would prefer to move as far apart from each other as possible. That’s why scientists say the universe is expanding. As a means of understanding this concept and how it relates to energy and the ability to do work, consider glucose. Remember, it has the formula $C_6H_{12}O_6$. Below are two molecules of glucose. What’s the difference?





The glucose on the left, the one you probably recognize, is glucose with low entropy (disorder). The glucose on the right, which you probably don't recognize, is glucose with high entropy (disorder). However, if I take a carbon from the glucose on the right, exert a force on it and move it over some distance (work), then it may covalently bond with another carbon. If I do this often enough, I may, by work, form the molecule on the left. The ability to do work is energy. As a consequence, the molecule on the left has low entropy, but high energy (the ability to do work). The molecule on the right has high entropy but low energy. When the molecule on the left is broken apart, the stored chemical energy is released to do work.

Chemical Reactions and Chemical Equations
If you can cook, you can do chemistry. Cooking is often following a recipe.

Two cups of flour
One cup of sugar
1 tablespoon salt
1 teaspoon pepper, etc.

An equation is a chemical recipe. When you trade recipes, you don't write out in longhand tablespoon; instead, you abbreviate it, *i.e.* tblspn. For cup, you write c.; for teaspoon, you write tsp. The symbols on the periodic table are like the abbreviations in recipes.

Reactants and Products
One way to represent the "recipe" in chemistry is by the chemical equation
A + B <==> C + D
Everything to the left of the arrows are called <u>reactants</u>.
Everything to the right of the arrows are called <u>products</u>.
The arrows mean "yields" or "produces".

AN INTRODUCTION TO METABOLISM
ENERGY AND ENZYMES

Reactions That Release Energy
Some reactions, when they occur, release energy in the form of heat, light, flames, smoke, etc.

A + B <====> C + D + energy
This type of reaction is called an exergonic reaction.

Reactions That Require Energy
Other chemical reactions need energy added to them in order to get them to take place, such as your air conditioning system.

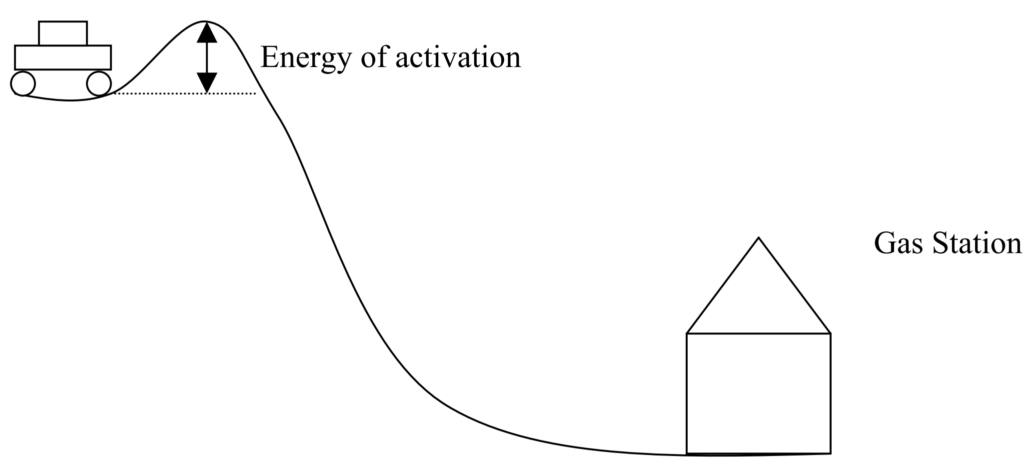
A + B + energy <===> C + D
This type of reaction is called endergonic.

A Favorite Exergonic Reaction
Take equal amounts of powdered zinc (gray metal) and powered sulfur (yellow nonmetal) and mix together. Strike a match and stand back! Flames shoot up, sparks fly into the room, and a huge cloud of smoke is produced. (This is the same type of reaction used at rock concerts for special effects.)

The way you could write the "recipe" is:
Zn + S =====> ZnS + energy
(zinc) (sulfur) (zinc sulfide - a white powder)

What about the match? Isn't that adding energy? Why isn't this an endergonic reaction? Yes, it's true, some energy was added to get it to go. However, compare the energy added to the energy output. Overall, more energy was produced than required. It is an exergonic reaction.

It is very similar to the idea of you being out on a date and your car really does run out of gas.



AN INTRODUCTION TO METABOLISM
ENERGY AND ENZYMES

The problem is your car is on a hill, just below the crest of that hill. Your cell phone is out, so you cannot call for gas. What to do? You could get out of the car and walk to the bottom of the hill to get the gas, and then walk back up the hill with it (or better yet, get your date to do it)! Or, you could push the car to the crest and let it coast down to the gas station. The amount of energy you have to provide to move the car to the crest is more than offset by the amount of energy released as you coast down the hill. It's the same with the reaction of Zn and Sulfur. The match is the amount of energy you add to get it started. Once started, it releases a lot more energy.

The amount of energy you must add is called the energy of activation. Human nature, being what it is, often causes us to look for methods of reducing the amount of energy we must add to get it to start. Is there a way? Yes.

Methods to Lower the Energy of Activation
There are several ways to lower the energy of activation. They include:
1. Increase the proximity (nearness) of the reactants
2. Increase the concentration of the reactants
3. Increase the surface area of the reactants
4. Increase the temperature of the reactants
5. Use a catalyst
6. Use an enzyme

Increase the Proximity of the Reactants
Refer again to the Zn and S reaction. What if you have one zinc atom and one sulfur atom in a room? What is the likelihood that through <u>random</u> molecular motion, these two atoms will find one another and react to form zinc sulfide? Little to none. However, bring the two atoms together and there is a better chance for them to react.

Increase the Concentration of the Reactants
Why not fill the room with zinc and sulfur atoms? What is the likelihood that at least a pair will find each other by <u>random</u> molecular motion and form zinc sulfide? Much better than if there were only one atom each in the room!

Increase the Surface Area of the Reactants
Notice the original recipe called for "powdered" zinc and "powdered" sulfur. Why not lumps of zinc and sulfur? By grinding the lumps into powder, you increased the surface areas of the two for them to react with each other. Compare what happens to a lump of coal to powdered coal. A lump of coal will burn. Powder that same lump of coal and ignite it, it will undergo rapid combustion. Rapid combustion is called an <u>explosion.</u> That's why coal mines are constantly wetting the coal seams down as they mine it; to keep down the danger of explosions.

Increase the Temperature of the Reactants

How can I get atoms of zinc and sulfur to have more frequent collisions? Increase the temperature, you increase the heat energy, you increase the thermal energy, you increase the kinetic energy, and thus increase the energy of motion. This causes the molecules to undergo more collisions, increasing the chance they will react.

Rule of Thumb

For every 10^oC you increase the temperature, you double the rate of the reaction. In other words, the reaction will occur twice as fast.

If a reaction normally takes 30 minutes to take place at 26^oC, how long will it take to occur at 36^oC? 15 minutes (You halve the reaction time.)

Conversely, if a reaction normally takes 30 minutes to react at 26^oC, how long will it take if I drop the temperature by 10^o to 16^oC? 1 hour (The reaction takes twice as long.) That's why munitions workers work in cold rooms, to keep down the danger of explosions.

Use A Catalyst

A catalyst is defined as a substance that speeds up a chemical reaction, but is not used up. An important chemical reaction on earth and in the space program is the following:

$2H_2O \Longleftrightarrow 2H_2 + O_2$

Have you ever wondered how astronauts on the shuttle missions can stay in space for so long and have enough drinking water? Do you think astronauts take enough water to last them two weeks? Not likely. Water is extremely heavy. One gallon of water weighs around 8.3 lbs. So how do astronauts get enough water to drink? They don't load the shuttle water. They load compressed gas cylinders of oxygen and hydrogen. In a controlled reaction, they mix the two gases and ignite. There is a small explosion and a water vapor is formed. Condense that water vapor and you have drinking water.

$2H_2 + O_2 \longrightarrow 2H_2O + \text{energy}$

What if they run out of oxygen but have plenty of water? Reverse the reaction!

$\text{energy} + 2H_2O \longrightarrow 2H_2 + O_2$

They can then breathe the oxygen.

$2H_2O \Longleftrightarrow 2H_2 + O_2$

This is an interesting reaction for more than one reason. Oxygen, of course, is inspired (breathed) by animals and plants to burn glucose in a cellular process called respiration. However, for every molecule of oxygen produced by this reaction, you produce two molecules of hydrogen. What can you do with the hydrogen generated?

Hydrogen As A Fuel Source
Why not use it as a fuel source for automobiles? Look at the reaction of burning hydrogen gas in oxygen gas.

$$2H_2 + O_2 \Longleftrightarrow 2H_2O$$

When you burn hydrogen as a fuel, you produce water as a by product. That water is pure and unpolluted. As a comparison, what do you get when you burn gasoline in an automobile? Carbon dioxide and carbon monoxide and pollution! So why not drive hydrogen powered cars?

Some people are scared of hydrogen due to the *Hindenburg* disaster.
The *Hindenburg* was a 245 m, lighter than air ship (filled with hydrogen gas). After 10 transatlantic crossings, it crashed at Lakehurst, NJ in 1937 with 35 passenger deaths and 1 ground crew death.

They died because they either jumped too soon, or they jumped too late. Many people think those that died on the *Hindenburg* died because of hydrogen gas. Indeed, afterwards, there was a move to remove hydrogen gas as a lifting mechanism in dirigibles. They now use helium gas. Those that did die (and many passenger lived) either died because they jumped too soon and fell too far to the tarmac or, they didn't jump soon enough and the superstructure of the air ship crashed down on them. The superstructure was aluminum, canvas (on fire) and diesel fuel to run the engines. They didn't burn to death because of hydrogen gas. Remember gases go up into the atmosphere when released.

Hydrogen Gas
Strangely, hydrogen burns with an invisible flame. You can't see it burn in its pure form. Hydrogen gas is relatively safe. Gasoline, as in your car, however, is exceptionally dangerous. Shoot a cylinder of compressed hydrogen gas with an incendiary bullet, and the gas will NOT explode, just leak out gas and ignite. Try that with gasoline. Explosion city! To ease people's fear of hydrogen gas, there is a hydrogen powered community in Arizona. Electricity is powered by hydrogen, stoves and water heaters are hydrogen gas, etc. There's even a street called Hindenburg Lane!

So Why Don't We Use Hydrogen As A Fuel Source?
How many "hydrogen" stations did you pass on the way to school today (tonight)? Can autos run on hydrogen? Yes. They are very easily converted to burn hydrogen gas.

So why not use it? The way to make hydrogen gas is to run an electric current through water to form hydrogen and oxygen gas.

$$\text{energy} + 2H_2O \Longrightarrow 2H_2 + O_2$$

The cost of the electricity means you would pay more in electric bills than in gasoline bills… …UNLESS you performed the reaction in the presence of the metal platinum. The reaction then becomes very economical and you could run you auto MORE CHEAPLY on hydrogen gas than gasoline.

Platinum

One problem, platinum is the world's most precious metal … more expensive than gold. However, platinum serves as a catalyst in this reaction. Catalysts speed up a chemical reaction, *but are not used up*. You would have one initial cost outlay for platinum, but it could be used over and over again. So again, why not use hydrogen gas? Perhaps oil companies are not real fond of a fuel that would replace gasoline and be nonpolluting and renewable (remember, burning hydrogen and oxygen makes water, which you can break apart to form hydrogen gas and oxygen gas).

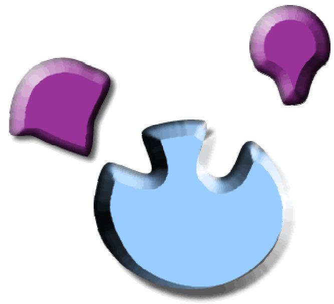
Use an Enzyme

Enzymes are organic catalysts. All enzymes are proteins (remember the tertiary structure proteins). An enzyme is an organic catalyst, usually in the form of a tertiary structure protein.

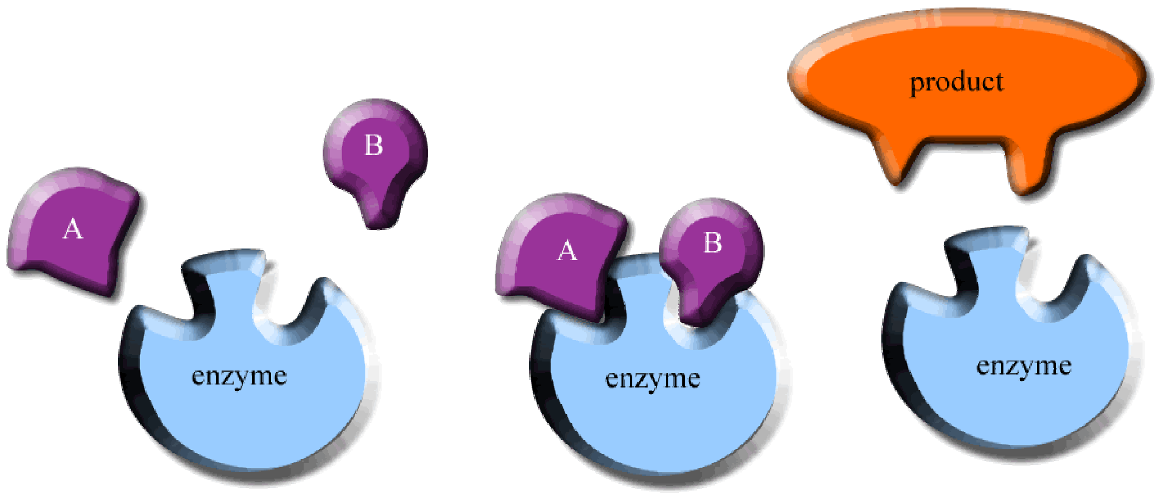
Enzymes

Enzymes, as tertiary proteins, tend to have a globular structure. An example of a tertiary structure protein is below.

Notice all the nooks and crannies in the tertiary structure. These nooks and crannies serve a purpose. They are called active sites. The active sites serve as locations for the reactants (called substrates in enzyme terminology) to lock into place.



You should be able to determine that what an enzyme does is to bring the substrates into close proximity for them to react. This can be shown as follows:



E + S ←→ ES Complex ←→ E + P

The problem becomes stopping the action of an enzyme. Once an enzyme is “turned on”, how do you turn it off?

How Do You Stop an Enzyme?

The answer is through feedback inhibition. Most biochemical reactions that occur are as series of reactions. For example, the digestion of amylose begins in the mouth of humans when salivary amylase is added. Salivary amylase breaks amylose down into maltose (hydrolysis). Maltose is broken down into glucose by the enzyme maltase. From there, glucose is broken down into a series of smaller and smaller molecules, until it forms a three carbon compound called pyruvate.

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  E    E     E    E    E   E  E  E
A → B → C → D →  →  → → → Z
```

What often happens is a product (many times the final product in a series of reactions) interferes with some beginning enzymatic reaction.

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  E̸    E     E    E    E   E  E  E
A → B → C → D →  →  → → → Z
  ↑                                       ↓
  └──────────────────────┘
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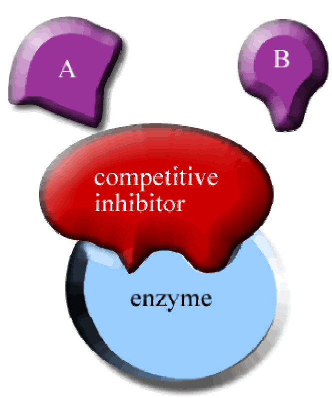
Inhibition of Enzymes

There are three ways to inhibit enzymes:

1. competitive inhibition
2. uncompetitive inhibition
3. noncompetitive inhibition.

Competitive Inhibition

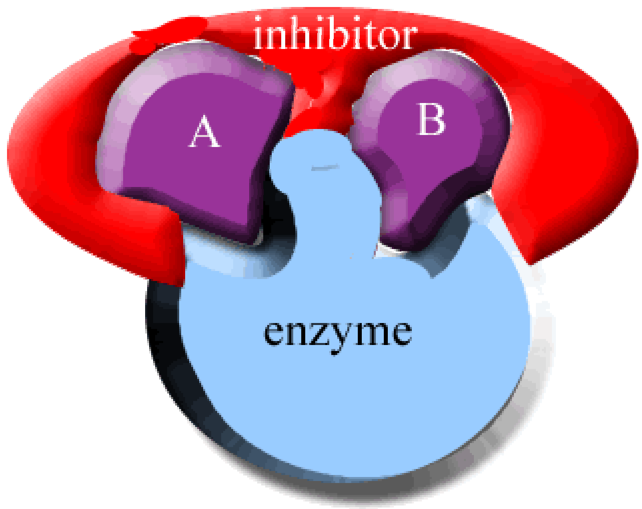
Competitive Inhibition occurs when an inhibitor competes for the active site with the substrate. The result is the inhibitor attaches before the substrate can. This may be represented by a chemical equation: E + I ↔ EI Complex.



Uncompetitive Inhibition

Uncompetitive Inhibition occurs when the substrates do react with the active site but before the product can be released, an inhibitor blocks that release. The chemical equation for this is:

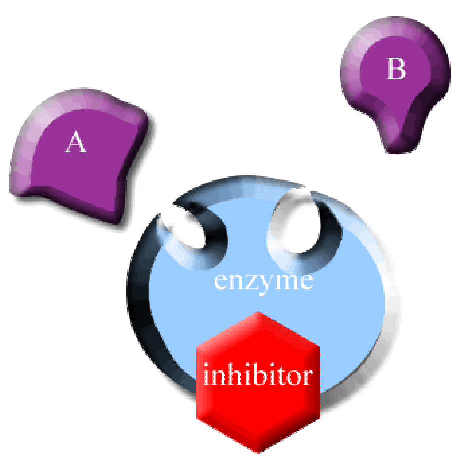
ES + I ←→ ESI Complex



Non-Competitive Inhibition Allosteric Modification

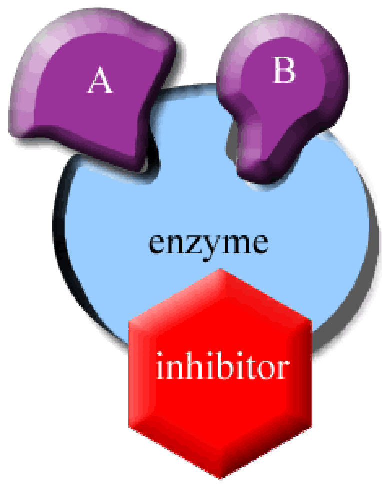
When the enzyme's shape is modified, it is called allosteric modification. Allosteric modification may take place *before* substrates react with active site or *after* the substrate reacts with the active site. . Either way, allosteric modification occurs as noncompetitive inhibition. The reaction for allosteric modification *before* the substrates react is:

E + I ←→ EI Complex.



Note this is the same equation for competitive inhibition, yet it is not the same reaction. Allosteric modification *after* the substrates react may be represented by the equation:

ES + I ←→ ESI Complex.



Again, note this is the same reaction as uncompetitive inhibition, but this occurs because of a modification to the enzyme.

Coenzymes
Coenzymes are non-protein, organic compounds that help enzymes do their job. An example is vitamin B-12. B-12 is responsible for the maturation of healthy red blood cells.

Cofactors
Cofactors are metal ions found in molecules that make the molecules active. Cobalt in B 12 is an example. Without cobalt, B-12 does not function. Other examples of cofactors are

1. Mg in chlorophyll
2. Fe in hemoglobin

Oxidation – Reduction (Redox) Reactions
Reactions that occur in biological systems are regulated by enzymes. These enzymatic reactions are often of a specific type. They are called oxidation-reduction reactions – or redox for short. There are 3 methods to have a redox reactions:

1. addition of oxygen = oxidation; removal of oxygen = reduction
2. loss of electrons = oxidation; gain of electrons = reduction
3. loss of hydrogen = oxidation; gain of hydrogen = reduction

Some Compounds That Easily Undergo Redox

Nicotinamide Adenine Dinucleotide (NAD)

$NAD^+ + 2H^+ + 2e^- \Longleftrightarrow NADH + H^+$

(oxidized) (reduced)

Nicotinamide Adenine Dinucleotide Phosphate (NADP)
Flavin Adenine Dinucleotide (FAD)
Flavin Mononucleotide (FMN)
Quinone
Cytochromes
Plastocyanin
Plastoquinone
Oxygen (forms water)

All of the above, except oxygen, are coenzymes.