3. Machinery of a factory: The cell

3.1 ATP provides energy

In the last chapter we introduced the chemical units of molecules that are the basis of our food. Molecules of food are used to make energy. The molecule that provides energy is ATP. The chemical structure of ATP is given later in this chapter. Tissues of the body are composed of cells and ATP is found within every cell.

Let us make a mechanical analogy. Consider a factory making a car. Raw material goes into the factory, and a car comes out. Work is done on the raw material, most of the work being done using electricity. Intelligence is needed to properly assemble the parts, and humans supply this intelligence. To make the car, more than one factory is used. Parts may be made in Kentucky, Japan, Germany, China or other places. Each of these factories requires electricity to power them. And the production in one factory must be correlated with the production in other factories. If hubcaps made at one-factory lags in production, the production of the whole car will be slowed down.

ATP is like the electricity that runs each factory. Electricity must be constantly supplied at a certain level in each factory. When the electricity stops, the production in that factory stops. The overall assembly of cars in another factory will be affected. Like electricity, the amount of ATP in a cell is low, but it must be constantly supplied. If ATP levels drop, the tissue is no longer able to function and it will die.

Unlike a factory, where electricity can be supplied from the outside, every one of the trillion or so cells in the body must make its own ATP. For all the cells to work harmoniously so the whole body functions properly, there must be a way for the production of energy to be regulated in every cell.

Enzymes are proteins that make reactions go faster. Enzymes control the rate that fuel is being used for energy within each cell. Some enzymes are inhibited when metabolites get high. The product of one enzyme is transformed by another enzyme and so on, so that fuel is broken down. In this way enzymes work together to form a pathway, changing one metabolite into another.
But, the rate that food is used, also needs to be controlled by means outside of the cell.

There are several ways that cells communicate with each other. One way is by hormones. Hormones are chemicals that are produced in one part of the body that regulate the cells in other tissues. Hormones control the reactions of most enzymatic pathways. Hormones are the means that the actions of cells in one tissue are correlated with the function of another tissue.

Some pathways are regulated by innervation. The brain sends an electrical signal via the nerves to trigger the action of a certain pathway.

### 3.2 Cells

All of our tissues are composed of cells, and as we mentioned we have about a trillion cells. (A large person has more cells than a small person). A simplified cell is shown in Figure 3.1:

![Figure 3.1](image_url)

To supply a factory, raw materials must go in, and the product of the factory must come out. The same is true of the cell. Surrounding the cell is the cell membrane; it is like the wall around factory with gates to control access to the factory. Nutrients go into the cell across this membrane and by-products of metabolism go out in a controlled manner. Only some things have a “tracking number” enabling it to go in or out of the cell. The “gates” for cell membranes are specialized transporter molecules. The cell must communicate with other cells. Receptor molecules in the cell membrane recognize hormones that signal from the outside for changes to occur in the inside.

Within the cell certain things occur only at defined locations. DNA resides in the nucleus. Information in DNA determines the sequence of all of the proteins that are made in our body. It is what makes each of us unique.

The endoplasmic reticulum is an organelle composed of membranes within the cell. Proteins and other molecules are made and modified on these membranes. You can think of the endoplasmic reticulum as making the enzymes, which are the “machinery” for metabolism.
Within another membrane structure, the lyzosome, many molecules are degraded. The lyzosome is analogous to the garbage-recycling center.

In the next chapters, metabolism that occurs in the cytoplasm and mitochondria will be described. In the cytoplasm sugars are metabolized to three carbon units. In the mitochondria three carbon molecules (mostly from sugar) and two carbon molecules (mostly from fat) are transformed to CO$_2$ and water by reacting with O$_2$. In the reactions occurring in the cytoplasm and mitochondria all of the cell’s ATP is produced. Most of the ATP is made by mitochondria -- the power generators of the cell.

**3.3. Membranes separate compartments of cells**

Cells are beautiful things. They do many things – all at once. For instance they may be consuming ATP to make proteins at the same time they are using fat to make ATP. In order to do many things at once reactions must be separated from each other. Membranes accomplish this separation. Substances inside of the must not leak out. Again membranes keep what should be inside from leaking out. What are biological membranes?

One of the major components of membranes is lecithin. Lecithin is very similar to fat. You remember that fat is composed of three fatty acids bound to the three OH’s of glycerol. Lecithin has two fatty acids bound to glycerol. On the third OH of glycerol is a substance called choline.

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**Figure 3.2.A**
The chemical name for fat is triglyceride. It has three fatty acids attached to glycerol.

**Figure 3.2.B**
Lecithin (also called phosphatidyl choline). It has two fatty acids attached to glycerol. A choline group is attached to the third OH of glycerol. The choline group is circled by blue.

Choline has a positive charge on the N, and a negative charge on the phosphate. This group is hydrophilic, meaning that it likes water. The fatty acid part is hydrophobic, meaning it does not like water.

Lecithin molecules associate with each other so that the fatty acids are oriented away from the water, and the choline is in the water. By so doing, the lecithin makes a membrane. There are
two sides: an inside and an outside, both exposed to water. The choline group is called the head group, and the fatty acids are called the tails. This is shown in Figure 3.3

Biological membranes are composed of lecithin plus many other compounds similar to lecithin. Instead of the “choline” part, there may be a compound resembling an amino acid or sugar. When the head group is sugar, the compound is called a glycolipid. Glycolipids are found in high amounts in nerve cells. There are a large number of different types of lipids in membranes. Membranes have different lipids within them. Unsaturated lipids are fluid, and they keep the center, hydrophobic part, flexible. We cannot make lipids that have many unsaturated double bonds, and we must get them from our diet.

Embedded into the bilayer of lipids are proteins. The blobs in Figure 3.4 represent proteins. Some proteins go across the membranes. Ion pumps and receptor molecules have one part of them on the outside. Other proteins are attached to one side of the membrane or the other.

Many enzymes are located on or in membranes, and therefore many reactions in cells occur at membrane surfaces.

### 3.4 ATP is the energy unit of the cell

We introduced a new term – ATP. ATP is a molecule that gives the energy used to power everything the cell does. But then we have the question: what is the energy? This may seem
like a deep philosophical question – and indeed it is! (Who am I? What is matter? What is energy?) However, the answer is simple for living systems. Most energy that is used for all cells comes from the molecule ATP. The full name of ATP is adenosine triphosphate.

ATP is composed of N, H, C’s. (Remember that wherever there is a bend in the structure, there is a C with its attached H’s.) It also contains a new element phosphorous, P. In fact, it has three P’s, and hence it is called triphosphate. This is ATP:

![ATP diagram]

ATP is made of three parts: adenine, ribose (a sugar) and phosphate groups. The thing that you should know is that the business end of ATP deals with the element phosphorous, denoted as P. P is bonded to oxygen, O, as shown in the figure, and oxygen and phosphorous together is called phosphate. The bond indicated by the blue arrow is especially unstable. This bond produces energy when it is broken. When the cell needs energy, the phosphate (P and O) comes off, and energy is produced. The amount of energy is described in calories. One mole of phosphate coming off of ATP gives about 10 calories of energy. (A mole tells the number of molecules. One mole is 602,000,000,000,000,000,000 molecules. Since it takes too much time to write this big number, the term mole is used.)

ATP that loses one phosphate becomes ADP (adenosine diphosphate). ADP is shown below. It is identical to ATP but has two phosphate groups rather than three.

![ADP diagram]

During metabolism of food, ATP is formed from ADP. When the cell needs energy ATP breaks down to ADP. An adult person has about 0.1 mole of ATP in the body. But an adult uses about 200 moles of ATP every day. ADP must be constantly be made back into ATP. This is what food does. It makes ATP from ADP, constantly supplying the body with energy.

### 3.5 Every cell must make its own ATP

A factory in France does not share its electricity with a factory in Dubai. Each factory must have its own energy source. Likewise, cells do not share ATP molecules. ATP is inside cells, not in

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1 In scientific notation this number is $6.02 \times 10^{23}$. 

blood or other fluids surrounding cells. The membrane surrounding the cell does not allow ATP to leak out into blood.

It then follows: each and every cell uses energy from its own ATP and uses its own metabolism to remake ATP from ADP.

There are a few reactions in the cell that derive their energy from compounds other than ATP, but for species on earth the overwhelming source of energy is ATP. ATP is so universally found in life species, that the presence of ATP was used as a biomarker to search for life on Mars. The thinking is that if life forms on Mars and on Earth have common origins, then Martian life will also use ATP for energy.

3.6 Why does every cell need ATP (energy)?

Cells use ATP to “buy” various actions that occur in the cell. What are the uses of ATP in the cell?

3.6.1 Energy is required to keep the ions (aka “electrolytes”) in the proper concentration

Table salt is sodium chloride (NaCl) and when it dissolves into water it becomes the ions Na⁺ (sodium) and Cl⁻ (chloride), where Na⁺ and the Cl⁻ are separate from each other. Blood plasma has Na⁺ and Cl⁻ in it; in fact blood plasma is about as salty as ocean water. Whereas blood plasma and the fluids around cells are high in Na⁺, inside of the cell there is another ion, potassium (K⁺). Nerve cells especially need the proper salt concentration. Your brain will not function if too much Na comes into the cells and too much K⁺ comes out. The heart will not beat if K⁺ levels in the blood get too high.

At all times some of the K⁺ leaks out of the cell and Na⁺ leaks in through the cell membrane. To keep Na⁺ out and K⁺ in requires energy.

Figure 3.5 shows a little guy pumping Na⁺ out and K⁺ in. Of course, there is no “little guy” in your cell membranes. The pumps really are proteins in the cell membrane. The inset shows a magnification of the cell membrane. Na and K ions cannot go through the fatty acid part of lecithin very well. The red cylinder, representing a pump or transporter
molecule, is a protein. Pumps take Na that is inside the cell and moves it to the outside to the blood plasma. Other pumps take K that is outside and move it inside. Just like the little man needs to exert energy to work his pump, the pumps that transport ions need to accomplish their tasks. That energy is comes from ATP; it releases energy when the phosphate detaches, the ion is transported and ATP becomes ADP.

Because the K that is inside of the cell gradually leaks out and Na gradually leaks in, the pumps have to be working all the time. So metabolism occurs all the time to transform ADP back into ATP. A large percentage of basal metabolism – the amount of food used when you are not exercising – is used to maintain ion levels in cells.

Blood plasma is high in calcium (Ca\(^{++}\)) and phosphate. Ca\(^{++}\) and phosphate are found in bone, but all cells require them. Ca and P have separate pumps, i.e. proteins in the membrane that are transporters. Basically, all substances that the cell needs have transporters or pumps to bring the substance into the cell, and transporters also take substances that are products of metabolism from inside the cell and deposit these chemicals into the blood.

3.6.2 ATP is needed for cell division. DNA is in the nucleus. During growth, each of our chromosomes containing DNA gets replicated and the cell divides to make a new cell. Many cells and proteins are as old as we are. The proteins that are in the center of your eye lens are as old as you are. Some cells, such as nerves and muscles, do not often form new cells in an adult. Although the proteins within these cells are constantly being degraded and reformed, the cell itself does not often multiply to make new cells to replace old cells. Other cells are being formed and removed from our body constantly. An example is red blood cells. Red blood cells last around 120 days in the blood; then they are removed from the blood by the spleen. The body is constantly making new red blood cells. Cells in the intestinal wall are also constantly regenerating, and skin cells are constantly being shed, and remade. The constant formation of new cells requires cell division and, hence, energy.

There are conditions when the body needs to make many new cells. During a child’s growth spurt, the parents are aware that suddenly the child is eating them out of house and home. Milk, bread, everything suddenly disappear from the refrigerator. The calorie intake is very large. Burn victims also need to synthesize new tissue. A high protein, high calorie diet is often recommended for these patients. When you get a little paper cut on your finger, cells die and the body repairs the cut by making more cells. Energy is needed! After major surgery or severe infection, more mending is needed. More cells are destroyed and more need to be remade. Making new cells requires much energy.

3.6.3 ATP is needed to synthesize molecules. Not only are whole cells dying and being regenerated, but also protein, fat and glycogen molecules within cells are being degraded and remade. The old adage is, “You are what you eat” is not true! In fact, that carrot that you are eating contains its own DNA, proteins and membranes. Carrot DNA and protein molecules do not become your DNA and proteins. Your cells make complicated molecules and structures like DNA and proteins, fat and glucose from simple molecules. The synthesis of complicated molecules takes energy.

3.6.4 ATP is needed for motion; muscles use ATP during exercise. Running, jumping, walking and all exercise activities require many calories, supplied by many ATP molecules. A training athlete may use 4000 Kcal (kilocalories) and about 3000 of these
calories are used for motion. Most diet regimens suggest exercise along with reduced calories to lose weight.

### 3.7 Cells and organs are specialized

The metabolism of cells and tissues is specialized and one tissue may need more ATP than another tissue at a given time. The brain always needs ATP, since it constantly needs to maintain ions such as Na and K at the right levels. The brain is somewhat unique as a tissue because it does not use fat as a fuel. It uses carbohydrates, although there is an exception – during long term starvation a product of fat is used, which we will discuss later.

In chapter 1, we considered what happens in a brain after eating sugar and during fasting. In contrast to the brain, muscles do not need much ATP when they are resting. But they suddenly need energy during exercise. The diagram explains what occurs in muscle.

![Diagram](https://via.placeholder.com/150)

**Figure 3.6** After GB eats carbohydrates, sugar circulates in the blood. Muscles take up some of the sugar and transform the sugar into glycogen. This glycogen is stored in muscle.

During strenuous exercise muscle glycogen is broken down to 6 C sugar (glucose-phosphate) and then to 3 C. In this process ATP is formed to provide energy for the muscle. The final 3 C compound that is formed in muscle is lactate.

During less strenuous exercise, muscle uses fat and O$_2$ to form ATP.

Exercise illustrates how various organs interact. When glucose is high in blood, muscle uses glucose from blood for energy. Muscle also stores glycogen and it breaks down to form glucose that gets broken down to 3 C compounds, namely pyruvate and lactate. Metabolism of glucose and glycogen to form pyruvate and lactate produces ATP, and does not require O$_2$.

Fat is also used by muscle to form ATP, but the use of fat requires O$_2$. So glycogen and glucose are used when exercise is so rigorous that O$_2$ supplied to the muscle does not keep up with the demand for ATP.

The muscle will use up the produced lactate during anerobic (fast) exercise, if after a vigorous work-out, exercise is continued slowly so that O$_2$ is delivered to the muscle and the muscle continues to work. This is the rationale for the “cool down” phase on exercise machines. If you suddenly stop exercising, the lactate stays in the muscle, but it gradually leaks out, and the liver ultimately metabolizes it to CO$_2$. In the meantime, however, your muscles may be feeling a bit sore.

### 3.8 Metabolism is regulated: how cells and organs communicate with each other
You may be getting a feeling of the marvelous engine that is the human body. Instead of one motor, every cell makes its own ATP. But, if you are hungry, it does not mean that all your tissues and cells need nourishment. The metabolism of every single cell in every tissue is regulated so that the right thing is happening at the right time.

The human body is complicated and there are many levels of regulation of metabolism.

**3.8.1 One level of regulation occurs within cells.** Enzymes are specialized protein molecules found in all cells. (All enzymes are proteins, but not all proteins are enzymes). Enzymes catalyze all reactions in the body and we have thousands of enzymes. Enzymes determine the speed that a reaction will go. For life to be maintained there must always a flux of metabolites. Some are going into the cell, ATP is being generated and the waste products are going out.

How enzymes work is that they bind a metabolite, and then the reaction occurs at a cleft on the enzyme surface. Since the regulation of glucose levels is such an important part of metabolism we use glucokinase as an illustration for an enzyme. Glucokinase catalyzes (i.e. makes go faster) the reaction in which a phosphate from ATP gets attached to glucose:

$$\text{ATP} + \text{glucose} \rightarrow \text{glucose-6-phosphate} + \text{ADP}$$

After glucose enters the cell, glucokinase is the first enzyme that reacts with the metabolite glucose. Glucose binds to glucokinase and then ATP binds. The adenine and ribose part of the molecule (see the structure given above) serve to anchor ATP to the enzyme, glucokinase. Within milliseconds after glucose and ATP binds, a phosphate gets transferred to glucose. ATP becomes ADP. Glucose becomes glucose-6-phosphate. Then both ADP and glucose-6-phosphate are released from the enzyme.

Enzymes make reactions go much faster than the reaction would go without the enzyme. Without the enzyme the reaction may take several years, with it, the reaction is completed in less than a second. Glucose-6-phosphate can not cross the cell membrane; it is trapped in the cell, and other enzymes ultimately act to break it down to give energy to the cell.

If glucose-6-6phosphate concentrations get high, it will stay bound to the enzyme and the enzyme will no longer be able to bind glucose, and the enzyme will no longer be able to put phosphate on. When the enzyme is no longer able to work, we say that the enzyme is inhibited. Glucose-6--phosphate is an inhibitor of the enzyme glucokinase. This prevents too much glucose from entering the cell.
Some enzymes bind other substances too. These substances can activate enzymes or inhibit. Products of the reactions often inhibit. Then when too much product builds up, the enzyme will not work as well; this prevents more product being formed. This kind of inhibition is called feedback inhibition.

3.8.2 Hormones regulate metabolism. Superimposed upon the regulation of metabolism at the cellular level by enzymes, there are there is a more general regulation by hormones. Hormones are chemical compounds that are made in one organ, but affect the metabolism within cells of other organs.

Many hormones do not go into the cell, but they regulate what is going on inside by binding to the outside of the cell membrane. Insulin is one such hormone.

When glucose in the blood is high, the pancreas secretes insulin into the blood. Therefore, in normal conditions when blood glucose is high, the blood insulin level is also high. Insulin binds to a receptor in the cell membrane. Receptor is like a traffic light; it tells some reactions in the cell to “go” and others to slow down or stop. This shown in the scheme showed on Figure 3.8. The receptors acts indirectly by activating an enzyme that takes ATP to put a phosphate on a specific amino acid of important enzymes. This enzyme then changes other enzymes. One such protein that is changed is the transporter of the sugar glucose. In this case, the binding of insulin to the insulin receptor triggers the removal of glucose from blood, and transport into the cell.

Insulin is a major hormone that regulates overall metabolism. It serves to remove glucose, fat and amino acids from the blood. Insulin is a protein; it is made of amino acids. It is one of several hormones made in the pancreas. All cells have insulin receptors. In Figure 3.10, arrows show how insulin is affecting various organs.
Figure 3.9.

The effects of insulin are wide-ranging. It stimulates muscle and other tissues to take in glucose from the blood plasma. Insulin stimulates protein synthesis of muscle. It stimulates glycogen and fat synthesis in the liver. Fat transport from the liver to adipose (fat) tissue is stimulated by insulin.

High insulin stimulates glycogen synthesis and fat synthesis in the liver, and the transport of fat to adipose (fat) tissue. It also stimulates protein synthesis in muscle and other tissues. All cells in the body have receptors for insulin. The over-arching effect of insulin is to stimulate enzymes that act to store fuel, and inhibit enzymes that release fuel from glycogen and fat stores.

3.8.3 Nervous system also regulates metabolism

Many additional hormones are involved in the regulation of metabolism. Cortisol, adrenaline (also called epinephrine) and glucagon are hormones that serve to mobilize stored fats, carbohydrates and proteins and thereby restore glucose levels. The production of adrenaline is controlled by the nervous system.

Our patient GB is walking on a path through the woods. Suddenly a great big ugly brown bear jumps out in front of GB. What happens to GB? His brain signals the adrenal gland to make adrenaline. The adrenal gland is found on top of the kidneys. Adrenaline goes into the blood circulation and then signals the break down of glucagon in muscle and liver. The muscles have a sudden source of energy from glucose. GB has energy to run away and fortunately GB survives!
Figure 3.10.

The hypothalamus sends an electrical signal to the adrenal gland under emergency conditions. The adrenal gland is stimulated to secrete adrenaline. Adrenaline stimulates the break-down of glycogen from muscle and liver. The break-down product of glycogen is glucose, an energy source for muscle.

The direct link between a pathway and the nervous system is illustrated above for the production of adrenaline.

There is also much anecdotal evidence for the role of the brain in controlling metabolism. When people are sick we try to do something to “cheer them up”, thinking that this will help the patient. People who develop new medicines notice that giving a patient a sugar pill instead of the drug often causes improvement. This is called the “placebo effect”, and, and since interactions with other people is so important to us humans, the placebo effect is thought to be due to positive effects by the attention of the researcher on the patient.

Long-term stress, such as what someone may experience with an unsatisfactory personal or work situation (or students having too many exams!), causes the production of cortisol, which has major effects on metabolism. We will discuss cortisol in Chapter 6.