BIOL213: Genetics
What is a Cell & How Does it Work?

Welcome to Genetics! For the great majority of you this is going to be a tough course. We hope very much that it is tough like working out hard is tough, where after a few weeks you realize you have stronger muscles you didn't even know you had. This will happen only if you understand that education does not take place in the classroom, but in the quiet of your own head. We can only show you how to do the exercises and point out flaws in your technique. We can't move your brain cells for you.

Reading Assignment: Nothing in the book is really pertinent.

Outline:

- A. Genes and organisms
- B. Components of a cell
  - 1. Membranes: proteins within a lipid bilayer
  - 2. Organelles within cells
- C. Metabolism: monomers, polymers, central metabolism
- D. Control points of metabolism
- E. Summary

A. Genes and organisms

Two major goals in this course are to understand how genes determine the structure and physiology of an organism and how genetic information is passed from one generation to the next. The answers to both of these questions lie in the nature of DNA. Genes, composed of DNA, contain the information required to specify a functional organism, and it is DNA that is carried over to succeeding generations.

We will grapple early on with the question of what a gene is and what exactly it can and cannot do. You should walk away from this course realizing that when people talk about the gene for intelligence, they are speaking nonsense. Genes don't specify intelligence or beauty or truth or even eye color. In fact genes don't DO anything at all, at least not directly.

Isn't this a contradiction? Genes contain the information that determines practically everything about the cell, but they cannot act? Let's look more closely at this (Table 1). What a cell can do (e.g., how a skin cell differs from an amoeba) and what a cell is doing (e.g., how a firing nerve cell is different from one at rest) depends on the chemical reactions taking place within it. These reactions are controlled by enzymes. Without enzymes to catalyze the reactions, they would not take place to an appreciable extent.

Table 1: Deterministic view of how genes determine organismal function
Function of organism is determined by **function of its cells**
Function of cells determined by **chemical reactions** that take place within them
Chemical reactions occur or not according to presence and **activity of enzymes**
- Enzymes restricted to certain species
(e.g. mammals make lactase to consume milk sugar)
- Enzymes restricted to certain tissues
(e.g. enzymes to make neurotransmitters confined to nerves)
- Enzymes restricted to certain developmental states
(e.g. enzymes required to make yeast spores found only during sporulation)
- Enzymes restricted to certain environmental states
(e.g. heat induces production of enzymes to repair damage due to heat)
Enzymes are **proteins**
Proteins are determined by **genes**
Therefore, **genes** determine **organismal function**

It follows, then, that the enzymes that are present and active in a cell will determine the cell's type and state. If you tell me what enzymes are in a cell, how many, and how active they are, I could, in principle, tell you that the cell is from the liver of a mouse and not from the spleen of a codfish. I could tell you that the cell is embryonic and not terminally differentiated. I could tell you whether the cell is responding to heat stress. (Interestingly, I could not tell you the race of the individual who donated the cell). In principle, I could tell you everything there is to be told about the capabilities of a cell, just by knowing what enzymes are present.

Whatever controls enzymes controls the cell. The function of the gene is to provide the information required to synthesize enzymes. Even though genes play no direct role in the functioning of a cell, they determine what proteins are present and, in the end, what the cell can do.

SQ1. What at root do enzymes control?
SQ2. How do genes exert control over a cell?

B. Components of a cell

Those of us who find it difficult to assemble a swing set appreciate the enormity of the task of assembling an entire cell. How can genes, lacking insight or example, direct the construction of the complex structures found within cells? Fortunately, cellular structures for the most part assemble themselves. While this course will focus on how genes provide the necessary information for proteins to assemble themselves, it will be instructive to start with the self-assembly of a cell.

A cell and many of its internal components are defined by their membranes. Membranes serve many functions. One basic function is to keep the innards of a cell or organelle inside, and in this view one might think of cells as soap bubbles in water. But biological membranes are much more than mere walls. Much of what the cell does takes place on or in membranes. For example, most of the ATP used to power the cell is made through structures on membranes.

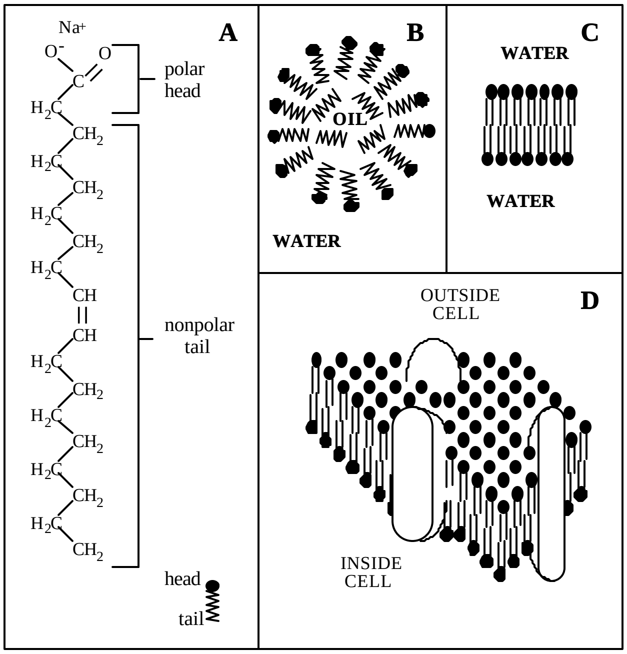


Figure 1. Amphipathic lipids.
(A) Chemical representation and cartoon of sodium oleate, a fatty acid.
(B) Oil droplet composed of fatty acids surrounding oil.
(C) Phospholipid membrane composed of two layers of phospholipids, hydrophobic tail to hydrophobic tail, with the hydrophilic head groups exposed to water.
(D) Biological membrane, composed of proteins swimming in a matrix of phospholipids.

1. Membranes Just as life to a great extent is the play of membranes, so are membranes largely the play of lipids. Lipids (literally, fats) are oily substances that can't dissolve in water. There are a wide variety of them in cells -- fat and cholesterol are two -- but the ones that form the structure of membranes are of a special class: *amphipathic* lipids. These are lipids that are *hydrophobic* (water hating) on one end of the molecule and *hydrophilic* (water loving) on the other. Pure hydrophobic molecules, like oil, separate from water, while purely hydrophilic molecules, like salt, freely dissolve. A class of amphipathic lipids that we see every day (or should!) is soap, one of which is oleic acid (Figure 1a). This fatty acid has a long, 18 carbon hydrophobic chain and an acidic, hydrophilic head group. Oleic acid is also a common component of phospholipids, the primary material of biological membranes. Note that fatty acids and derived amphipathic lipids are often portrayed in cartoon fashion as hydrophilic balloons over a hydrophobic string.

Soaps work precisely because they are amphipathic. The hydrophobic tails surround oily dirt, permitting the dirt to be dispersed in water (Figure 1b). When you rinse off the soap, the dirt goes with it. No one has to teach soap how to form oil droplets or bubbles: because of the interaction between water molecules, bubbles form themselves. The geometry of tiny bubbles is determined by the geometry of the soap. The size of the hydrophilic headgroup (the balloon) of soap determines how curved the bubble can be.

The amphipathic lipids of membranes differ from soaps in part because of their geometry. Fatty acids like oleic acid have bulky head groups relative to their thin tails, so if you put them side by side, you get a curved surface, just as assembling wedged-shaped pieces would form a circular pie. However, most of the lipids of membranes are *phospholipids*, containing two hydrophobic chains along with the polar headgroup (Figure 1c). These lipids are more or less cylindrical, that is, the headgroup has about the same area as the chains, so when you put them side-by-side you get not a curved surface but a plane. To prevent exposure of the hydrophobic chains to water, the plane is of two layers, a bilayer. The bilayer forms because of the amphipathic properties and geometry of its components. There is no need for some molecular machine to insert each component in place.

A cell membrane, then, is a vast bilayer composed in large part of amphipathic lipids (Figure 1d). The bilayer serves to exclude hydrophilic molecules from passing the membrane -- they can't get past the hydrophobic zone. It is thus possible to maintain a concentrated salt solution on one side of the membrane and a very dilute solution on the other, and this is precisely what the cell does.

The membrane is not pure lipid, however. If it were, the cell would be in virtual isolation from the outside world and would starve to death. It contains also protein that sit on the surface or span the membrane. These proteins serve a multitude of purposes. Many are involved in facilitating transport of hydrophilic molecules that the cell wants to be able to traverse the membrane (food, for example). Some proteins are involved in anchoring cell components to the membrane. As we shall see later, proteins find their way to the membranes in large part due to the same hydrophobic properties that govern the structure of the lipid bilayer.

SQ3. What are membranes? What are their functions?
SQ4. What is an example of a household item that is hydrophobic? Amphipathic?
SQ5. Identify the protein in Figure 1D.

2. Organelles and functions Eukaryotic cells contain organelles within the confines of the cell membrane. I'll just mention three organelles: the nucleus, which contains the chromosomes of the cell, the mitochondria, responsible for respiratory energy generation and metabolism, and in plant cells, the chloroplasts, the sites of photosynthesis. Each of these three organelles is themselves bounded by membranes and contains its own genetic material. They are in many respects like cells within cells. In fact, chloroplasts and mitochondria and possibly nuclei appear to have arisen by the engulfment of one cell by another. The eukaryotic cell thus has the problem both of communicating across the cell membrane to the outside world and communicating to itself across intracellular membranes.

Since the functions of these organelles and of the cytoplasm (the interorganellar space) are quite different, it is not surprising that they differ as well in what proteins they contain. The cell thus has the further problem of making sure that different proteins are directed to the proper cellular compartment.

Eating: The basics

Wheat, cow, tomatoes -----------------> Spaghetti + Marinara Sauce
(carbohydrate) (protein + lipid)

(mysterious metabolic conversions)

Glycogen + Actin / Mysin + Fat ---------------- **Human**
-->
(carbohydrate) (muscle protein) (better cut down)

Figure 2. Polymers from food are broken down and reused as the polymers particular to our own bodies.

SQ6. Modify Fig. 1D by drawing a mitochondrion and a molecule of glucose in the blood.

C. Metabolism: monomers, polymers, central metabolism

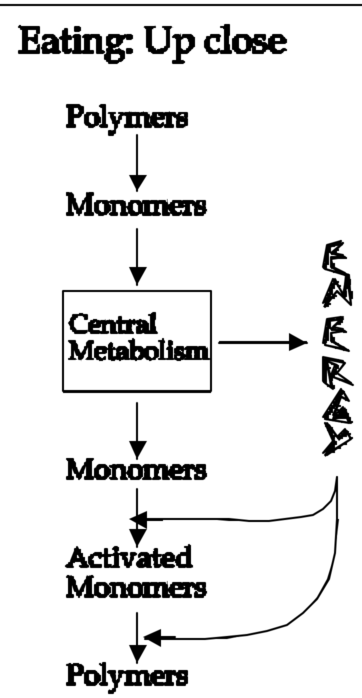


Figure 3. The strategy of metabolism. Polymers are broken down to small molecules, which are interconverted through central metabolism. From these small molecules, the polymers required by the organism are synthesized.

Complex soap bubbles within even more complex soap bubbles -- that is a simple view of what a cell looks like frozen in time. In real life, however, a cell is a high-powered organic chemistry factory, busily converting materials from its environment to its own uses. Take us, for example. We eat a meal -- the government now tells us it should be high carbohydrate, some protein, and not much fat -- chew well, and in the end we've converted it into our own protein, our own carbohydrate, etc (Figure 2). We eat thousands of different kinds of protein -- it really doesn't matter too much which they are -- but in the end they're turned into our own. How do we do it? The trick is to take the *polymers* we eat -- carbohydrate, protein, lipid, and nucleic acids and break them down into their component *monomers*. While the polymers are different from organism to organism, we all use the same monomers -- simple sugars to make carbohydrate, amino acids to make protein, and so forth (Table 2). So, a better representation of how we eat is seen in Figure 3. We eat a huge variety of proteins and other polymers, break them down to amino acids and other monomers, interconvert them through central metabolic pathways (although humans are partially defective in this regard) to create the proportion of monomers suitable to our needs, then synthesize a huge variety of polymers. It is like cars converging from hundreds of surface streets to a few entrance points to the turnpike, leaving at a few exit points to go to hundreds of other surface streets in another city. Very logical, but something needs to control the flow of traffic.

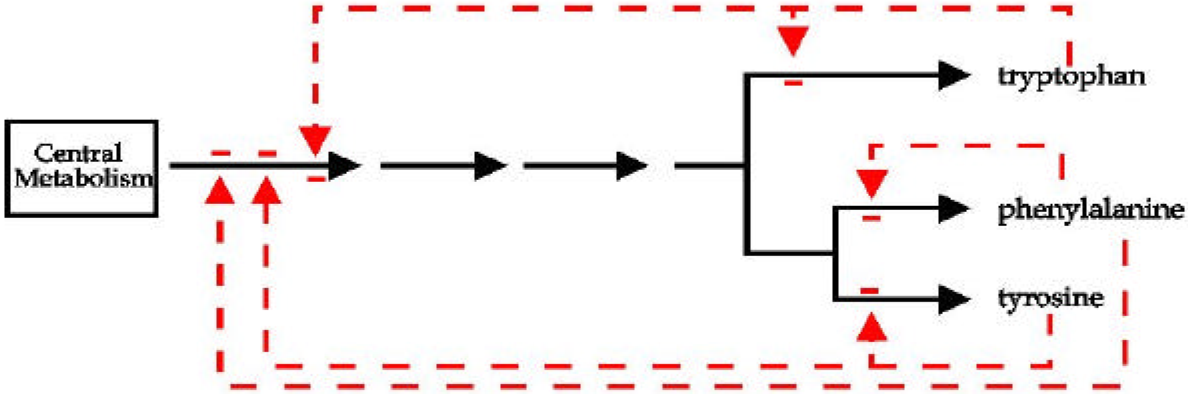
SQ7 (=PS1.3). Pick out from the list below those compounds that are polymers. Which are identical whether isolated from snails or whales?

A. phenylalanine
B. protein
C. starch
D. sugar
E. acetyl CoA
F. actin / myosin
G. nucleoside triphosphates
H. hydrophilic compounds

D. Control points of metabolism

What controls traffic is enzymes, proteins that act as catalysts in biochemical reactions. There is a limitless number of chemical reactions a compound can undergo, but at low temperatures, most biochemical reactions occur very slowly unless enzymes facilitate them. Enzymes provide the roads. At high temperature, a compound can jump the curb, plow through a few houses, and go wherever it likes, but with little control. At high temperatures we burn up. If you make the roads, if you control the enzymes, then you control the traffic. You can determine what compounds are made or not. And that means that you control the cell.

How are enzymes controlled? Let's take a look at one set of related pathways, concerning the metabolism of the amino acid phenylalanine (Figure 4). Phenylalanine is related in structure to two other amino acids: tyrosine and tryptophan. The first several steps leading to their synthesis from compounds in the central pathway are the same, which is reasonable enough. Each step is catalyzed, hence made possible, by a different enzyme. The pathway branches off to each of the three amino acids. If the cell doesn't need any phenylalanine, because it is already overabundant, then the presence of excess phenylalanine shuts off the first enzyme in the pathway specific for the synthesis of the amino acid. Similarly, if there's too much tyrosine or tryptophan, then they shut of the first enzyme in their particular pathway. If all three aren't needed, then the first step of the common pathway is turned off. Regulation of enzyme activity by feedback control is a quick means to fine tune the metabolic output, to make sure you have the right proportion of monomers.



Let's look at the other side of phenylalanine metabolism (Figure 5): it's conversion into other compounds and degradation products. In animals, phenylalanine is the source of neurotransmitters and hormones, while in plants, it is the source of a bewildering collection of compounds, including wood lignin, poison ivy toxin, and flower pigment. It makes no sense to control by feedback inhibition the level of neurotransmitter in plants that don't have nerves or the level of wood in the brain. A more reasonable means of control in these cases is simply to lack the enzymes catalyzing those pathways. However, a woody plant needs wood in its bark but never in its leaves -- here too, feedback inhibition is ridiculous. There needs to be some means of making sure that the proper enzymes are present in the proper tissue at the proper time.

Control of gene expression provides the answer. In tissues that don't need neurotransmitters, the gene encoding the enzyme that produces them is turned off. Plants that don't make wood don't have the genes that encode the enzymes that catalyze the synthesis of lignin.

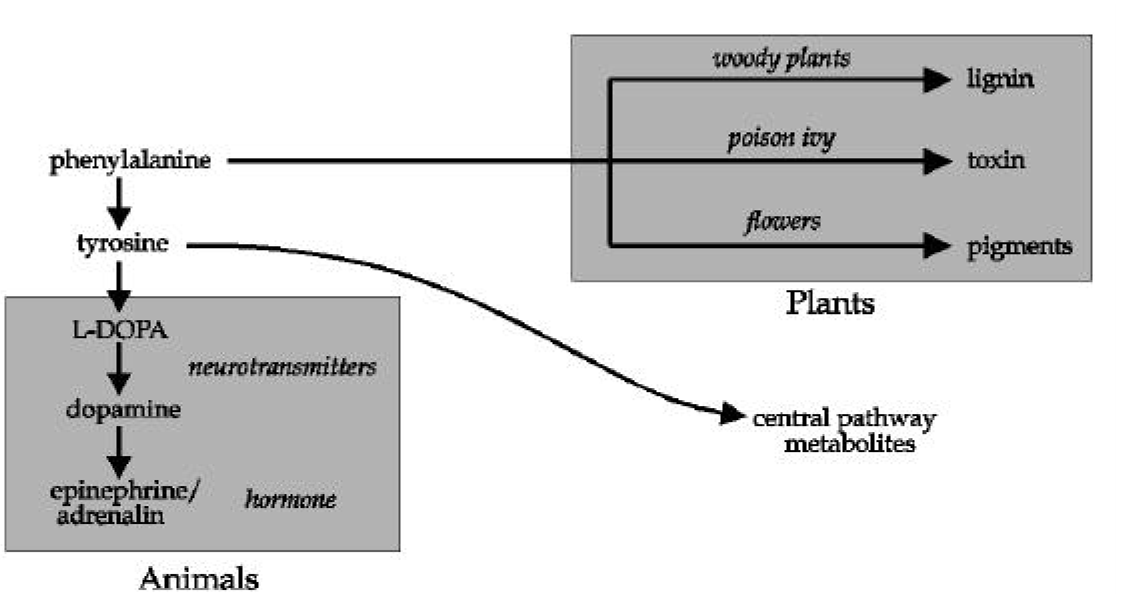


Figure 5. Conversion of the amino acid phenylalanine to different metabolites. Some conversions occur only in certain organisms. Some occur only in certain cell types.

SQ8 (=PS1.6). Which of the following responses would be best controlled by (a) regulation of enzyme activity, or (b) synthesis of specific enzymes.

A. Response of nerves to touch

B. Response to hormones that mark puberty

C. Diversion of glucose from a meal to production of fat instead of production of energy

SQ9. In not too long, just a few years, the entire sequence of DNA from a human will be known. What information will we be able to extract from a complete DNA sequence?

A. The adult size of the person

B. The proteins the person was capable of making

C. The number of legs the person had

D. The color of the person's hair

E. Summary

1. Genes and organisms
   - DNA controls cell function through determining its protein
2. Components of a cell
   - Cells are delimited by membranes, each made up of a self-assembling lipid bilayer with protein floating within it.
   - There are intercellular compartments, organelles, some of which are also delimited by membranes.
3. Metabolism: monomers, polymers, central metabolism
   - Polymers from the outside are broken down to monomers.
   - Monomers are built up into the organism's own polymers.
   - Monomers can be interconverted.
4. Control points of metabolism
   - Reactions are made possible through the catalysis by enzymes
   - Control at the level of enzyme activity is useful in effecting rapid responses to changes in the environment.
   - Control at the level of enzyme synthesis is useful for long term control.