

Introduction to Bioinformatics (Fall 2003)

Strategies of Life

Outline:

- A. Genes and organisms
- B. Self-assembly of cell membranes
- C. Metabolism: monomers, polymers, central metabolism
- D. Summary

A. Genes and organisms

Almost all of bioinformatics, as it is presently practiced, focuses on genes and their products. Even as the focus shifts from the small to the large – how metabolism is integrated, how a cell works, how an organism is formed – the task is informed by the wealth of genomic information becoming available to us, for in the end, DNA contains the information to answer the larger questions.

However, DNA does not contain a blueprint for an organism. There isn't any. And when you hear someone talk about the gene for intelligence, that person is 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 provide no vision for the end product nor do they play an active role in even the meanest cellular function. Let's look more closely at the relationship between genes and organisms. Figure 1 illustrates that what a cell is (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. Certain neurons express enzymes that convert the amino acid tyrosine to the neurotransmitter dopamine, while skin cells in the same organism convert tyrosine instead to melanin because of the different set of enzymes present. Finally, enzymes are proteins, encoded by genes.

It follows, then, that the enzymes that are present and active in a cell will determine the cell's type and state (Table 1). 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. (Ironically, in view of the history of genetics, 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.

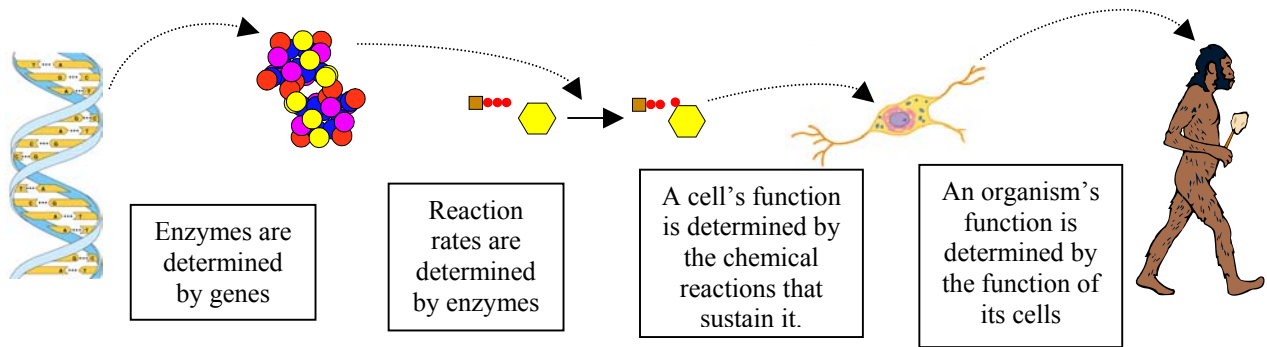


Figure 1: Reductionist view of how genes determine organismal function

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. Self assembly of cell membranes

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.

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.

Table 1: Differential expression of enzymes

Enzymes restricted to:	Example
Certain organisms	Mammals but not fish make lactase to consume milk sugar
Certain tissues	Skin but not neurons make enzymes to synthesize melanin from tyrosine
Certain developmental states	Fetal hemoglobin disappears as the organism matures
Certain environmental conditions	Heat induces production of enzymes to repair damage caused by heat

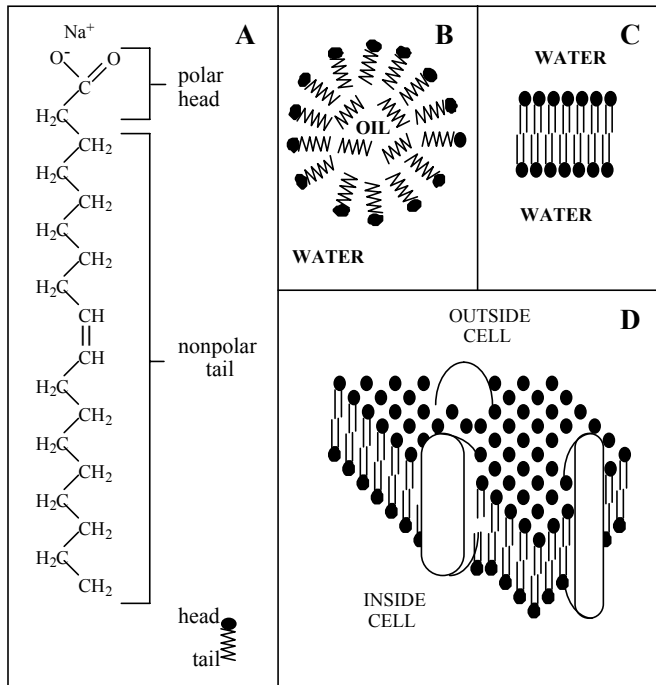


Figure 2. Amphipathic lipids

- (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.

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 2a](#)). This fatty acid has a long, 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 amphipathic lipids are often portrayed in cartoon fashion as hydrophilic balloons over a hydrophobic lines or squiggles.

Oil or water... what's an amphipathic lipid to do? Soaps illustrate the solution. The hydrophobic tails aggregate together and surround oily dirt, permitting the dirt to be dispersed in water ([Figure 2b](#)). 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 2c](#)). 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 2d). 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?


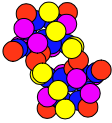






SQ5. Identify the protein in Figure 2D.

C. Metabolism: monomers, polymers, central metabolism

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 (Figure 3), in so doing consuming the various components that make up the plants and animals on the table. 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). We eat a huge variety of

Table 2: Biological polymers and their monomeric subunits

Polymer	 Nucleic acid (DNA, RNA)	 Proteins (e.g. myosin, ...)	 Complex carbohydrates (e.g. glycogen, cellulose)	 Fatty acid (e.g. stearic, oleic)
Monomer	 Nucleotides AMP, CMP, GMP, TMP	 Amino acids (e.g. tyr, phe, glu)	 Simple sugars (e.g. glucose, fructose)	 Acetyl CoA

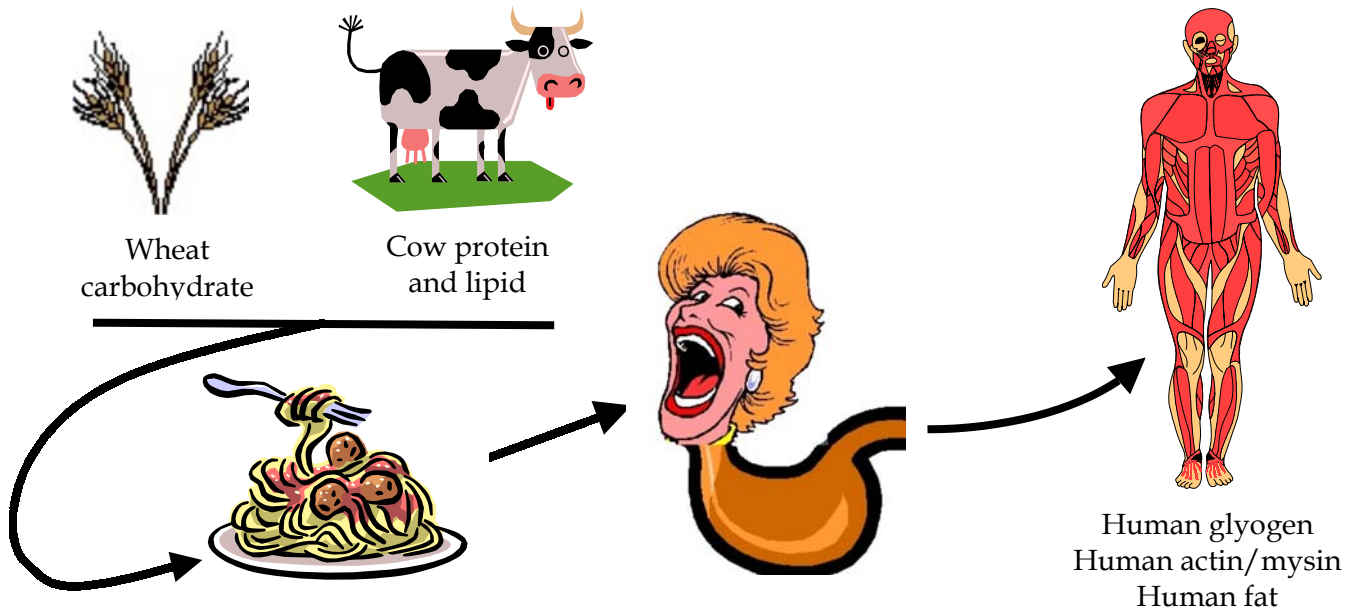


Figure 3. Polymers from food are broken down and reused as the polymers particular to our own needs.

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 our own 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.

SQ6. Pick out from the list below those compounds that are polymers. Which are identical whether isolated from snails or whales?

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

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.

Enzymes are protein. Ultimately, the identity of a cell and of an organism depends on what proteins are present and active. Notice I haven't mentioned DNA or genes. They *don't* control the nature of the cell, except indirectly. To understand that indirect control, we need to look more closely at what proteins are and then how genes determine them.

D. Summary

- DNA controls cell function by determining protein
- Cell membranes self-assemble, just as soap bubbles do (cells self-assemble in much the same way)
- Polymers from the outside are broken down to monomers.
- Monomers are built up into the organism's own polymers.
- Monomers can be interconverted.