Chapter 2
The Cell

Introduction
You and I began as a single cell. Now, both of us are composed of well over a trillion cells. One of these trillion cells, either a sperm or an egg, will join with one of the trillion cells, again a sperm or an egg, of our partner. This cell, now a fertilized egg, will divide into two cells, these two into four, and so on, until another trillion-celled organism develops. This organism, our offspring, will contribute a single cell to a union with his/her partner’s single cell. This fertilized egg divides, and the next trillion-celled organism is our grandchild.

Cells beget cells beget cells. And cells have always begotten cells, ever since the first viable cells capable of begetting cells developed on our planet. Looking backwards, you and I began as a single fertilized egg that was the union of two single cells, each coming from the trillion-celled organisms that are our parents. Each of our parents began as a single cell formed from the sperm and eggs of our grandparents. And so on, and so on. The trillion cells that are you and the trillion that are me are the result of a chain of cellular transmission unbroken over billions of years. You and I share great-great-great-to-a-very-high-power grandparents in some long lost primordial soup. We have also shared grandparents continuously on the way. Sixty million years ago, we had a grandfather who was one of the first mammals and shortly thereafter, a grandmother who led to the first primates. Possibly as recently as 200,000 years ago, our grandfather and grandmother gazed at a sunset on the African Savannah and spoke about their love for each other.

Because cells beget cells, not only are you and I related, but we are also cousins to chimpanzees, orangutans, cows, snakes, frogs, mosquitoes, and oak trees. Why? Because we all share DNA, because DNA instructs a cell on how to make another cell, and because cells beget cells. To understand genetics, we must first understand the cell.

Cell Structure
Although cells can have quite complicated structures, there are certain features common to all cells that are important for understanding genetics. A schematic of such a cell is given in Figure 2.1.¹

---
¹ This figure depicts what biologists call a eukaryotic cell (a cell that has a nucleus). Some organisms like bacteria are prokaryotic and do not contain a nucleus.
The first—and very important—structure in the cell is the cell wall, referred to in “biologistese” as the plasma membrane. It is very incorrect to think of the cell wall as only a physical structure to keep the insides from spilling out, much as a sealed plastic bag contains a cup of clam chowder. The cell wall has dynamic properties in addition to its structural properties. Embedded in the cell wall is a wide range of molecules called receptors. Receptors on the cell surface act as sentinels, permitting some substances to enter the cell, refusing entry to others, and signaling to the inside of the cell that something is knocking at the gate. Likewise, receptors regulate which substances inside the cell can exit the cell.

The nucleus is much like a cell within a cell, having its own “wall.” The most important structures within the nucleus are the chromosomes. These are packages of DNA and other molecules. They are the physical structures for genetic information and for the transmission of that genetic information when the cell divides.

The material outside the nucleus is termed the cytoplasm. Of the various structures in the cytoplasm, three are important here. The first of these is the endoplasmic reticulum. This is a series of convoluted, wall-like structures connected like a large network snaking throughout the cytoplasm. The endoplasmic reticulum is less noteworthy in its own right than it is for being the location of the second important cytoplasmic structure, the ribosome.

A ribosome is a protein factory. Think of the ribosome as a building that contains all the tools and some of the raw materials for making proteins but does not have a blueprint. Without instructions, such a structure is incapable of manufacturing a protein. It is the DNA that provides the blueprint to a ribosome. After the blueprint is provided, the ribosome can manufacture a protein. There are thousands of ribosomes in the cytoplasm, so there are literally thousands of protein factories in each cell.

The third cytoplasmic structure is the mitochondrion (plural = mitochondria). Mitochondria are little energy packets that help the cell to convert chemicals efficiently. Of equal importance, is the fact that mitochondria contain DNA. This mitochondrial DNA is abbreviated as mtDNA and is minuscule compared to the amount of DNA in the nucleus. Mitochondrial DNA is maternally transmitted in the egg; apparently sperm have no mitochondria. Consequently, all siblings in a family receive their mitochondrial DNA from their mother. The fact of maternal transmission for mtDNA makes it an excellent system with which to study evolutionary trees.

---

2 Technically, mitochondria are responsible for oxidative metabolism, the process of using oxygen as an energy source to break down or synthesize chemical compounds within a cell. Anaerobic metabolism, i.e., metabolism without oxygen, is a much slower and less efficient process.
Before leaving cell structure, we note an interesting hypothesis about the origin of mitochondria. It is speculated that billions of years ago, the ancestors of mitochondria were their own individual life forms that had a leg up on most other single-celled organisms because of their efficient metabolism. The other, much larger organisms would tend to engulf and then feed on the smaller mitochondria. During evolution, these large unicellular organisms began to devour the ancient mitochondria. Instead of digesting the primitive grandparents of mitochondria, the cells evolved to enslave them. The mitochondria then provided their host with efficient metabolism while the host saved the mitochondria from being eaten to extinction. If this hypothesis is true, then all of us modern life forms owe our existence to an ancient form of slavery!\(^3\)

\(^3\) Of course, a different scenario is entirely possible. The mitochondria might have developed a mechanism to prevent them from being digested but found that being engulfed by some species provided a safe refuge from their other predators. Like much evolutionary speculation, the true answer is lost in history.
Life in the big cell: Intracellular processes

Metabolism

Life inside a cell can be hell. It is a continual and never ending process of chemical reactions, termed metabolism. Few molecules within the cell have the luxury of sitting back and relaxing. There is always some chemical ready to chop the molecule up, grab it and attach it to some other molecule, or kidnap it by moving it to some other section of the cell or, sometimes, entirely out of the cell. A very important class of molecules in this turbulent scene is the enzyme. An enzyme is a particular type of protein that is responsible for a chemical reaction. The suffix “ase” is conventionally used to denote an enzyme, e.g., hydroxylase, decarboxylase, tyrosinase.

There are both a language and a model for the action of enzymes, depicted here in Figure 2.2. A molecule termed the substrate physically binds with a specific enzyme forming a substrate-enzyme complex. The analogy of a lock and key is used to describe this process. Not every substrate can bind to a particular enzyme and not every enzyme can bind to a specific substrate. The substrate and enzyme must physically fit together as a particular key opens a specific lock. Thus, one encounters such lingo as “binding site” to refer to that portion of the enzyme that the substrate recognizes and binds to.

Once a substrate-enzyme complex is formed, a chemical reaction occurs. For example, a hydrogen atom might get lopped off of the substrate, or a hydroxyl group (a combination of hydrogen and oxygen atoms) may be added. The altered substrate is now called a product. The product and the enzyme dissociate. The enzyme goes its merry way hoping to encounter another substrate molecule to mutilate, while the product usually becomes the substrate for a different enzyme. In this way, a chain of chemical reactions occurs until something of importance is made. This chain of reactions is called a metabolic pathway.

---

4 Strictly defined, metabolism is a generic term for either the breakdown of a molecule into more basic units or the synthesis of a new substance from basic units. The more specific term catabolism refers to only the breakdown of a substance into its constituent compounds.

5 Enzymes, by the way, have little immunity from intracellular warfare. There are often other enzymes ready to chew them up.
Figure 2.3 illustrates the metabolic pathway in the synthesis of norepinephrine, an important neurotransmitter in the nervous system. The process begins with a molecule called tyrosine that acts as a substrate for the enzyme tyrosine hydroxylase. Tyrosine binds to tyrosine hydroxylase that converts it into the product dihydroxyphenylalanine, better known as DOPA. DOPA is then converted into dopamine (DA) by the action of the enzyme DOPA decarboxylase. At this point, one of two things can happen to dopamine, depending on the type of cell in which the metabolic path is operating. In some nerve cells, no further chemical conversions will take place, and the DA will be used as a neurotransmitter. In other cells, the enzyme dopamine β hydroxylase converts dopamine into norepinephrine (NE) which will be used as the neurotransmitter.

We can now begin to glimpse the important role of genes in this process. DNA contains the blueprint for proteins. Enzymes are a particular class of proteins. Consequently, DNA has the instructions for the enzymes that are responsible for the chemical reactions in hundreds of metabolic pathways occurring in each one of our cells.

**Transportation**

DNA contains the blueprint for making a protein or an enzyme. The actual manufacture of the protein, however, takes place at a ribosome that could be on the endoplasmic reticulum almost anywhere in the cell. Many proteins, however, have to be at a specific place in the cell in order to perform their appropriate cellular duties. It is very inefficient, although it actually occurs at times, for the protein to be left alone to bang into this molecule and collide with that substance until, by dumb luck, it gets to where it belongs. More often, there are mechanisms and structures within the cell that transport the protein to its appropriate location.

Transportation is not limited to just proteins and enzymes. Many other substances, especially the end products of a metabolic path, are actively transported.

**Storage**

Much as you and I might have a special location in the refrigerator for the butter dish, many cells have storage units for certain molecules. These storage units are called vesicles and they usually serve two purposes. First, vesicles can store large amounts of a molecule in a strategic location so that they can be released en masse at a critical time. Second, storage in vesicles can prevent the molecules from being degraded—a fancy term for maiming and mutilation by roving gangs of psychopathic enzymes.

For example, consider the molecule CRH (corticotropin releasing hormone). This is manufactured in the cells of a particular area of the hypothalamus (a structure in our brains) called the paraventricular nucleus. Newly made CRH is transported to a vesicle in these cells until the

---

6 A neurotransmitter, of which we will learn more later, is a chemical in a nerve that communicates with adjacent nerves.
number of vesicles and amount of CRH is large enough to inhibit the manufacture of new CRF. Within the vesicle, a molecule of CRH has a happy and placid existence relaxing with its neighboring CRH molecules. That is, until something dreadful occurs. If a person encounters something that provokes anxiety, stress, or fear, the nerves in the brain that lie next to the CRH storage cells fire, the CRH containing cells fire in response, and the CRH is released to enter the bloodstream that carries it to other cells. There, CRH initiates a cascade of physiological responses.\footnote{A thorough overview of the stress response initiated by CRH is given in Chapter 4.}

**Cell Talk: How cells communicate**

Cells must communicate—and not merely to their immediate neighbors. When my bladder is full, the appropriate cells in my lower gut must get the message to my eyeballs to look around for a restroom. By far the most frequently used mechanism for cell talk is chemical communication.

The mechanism for chemical communication is very analogous to the binding lock and key model of enzyme action. One cell sends out a chemical message. Another cell contains a molecule called a receptor. Just as the physical conformation of an enzyme is specific for its substrate, so is the physical conformation of the receptor specific to the chemical messenger. The messenger and receptor bind together in the same way that a substrate binds to an enzyme. Just what happens after the messenger-receptor binding depends on the particular system—there are a wide array of mechanisms. The result, however, is always the same. Some chemical reaction or binding with yet other molecules occurs, informing the cell what has happened and how to respond.

Receptors can reside on the cell wall, in which case they are called cell *surface* or *membrane receptors*, or within the cytoplasm and the nucleus of the cell (intracellular receptors). Most receptors are proteins or have a protein somewhere within their structure.

Cell talk can happen between very different types of cells quite far away from each other. For example, certain cells in the pituitary gland, located just underneath the brain, send a messenger called ACTH to cells in the adrenal gland, located on the top of the kidney. The mode for this type of distance communication is to send the message through the blood. We will explore cell talk more in the next section.

**Cell Division**

Cell division is important and must be carried on with a high degree of fidelity to assure that all the genetic material is present in both daughter cells. The intricacies of the cell cycle and cell division need not concern us here, but two terms are important. *Mitosis* is the ordinary form of cell division that occurs for all of our cells save sperm and egg. It is depicted in Figure 2.4. The chromosomes duplicate, each one making a carbon copy of itself, and the two copies\footnote{The two copies are called *sister chromatids*.} are joined together in a region called the *centromere*. During this stage, the chromosomes coil and condense, giving a characteristic X-like shape that is visible under the microscope, and the wall separating the nucleus from the cytoplasm begins to degrade. In a complicated series of steps, two sets of spindles are constructed, one on the right and the other on the left hand side of the cell. The spindles then attach themselves to the chromosomes and pull apart the joined...
chromosomes so that one is pulled in one direction while its carbon copy is pulled in the opposite direction. This eventually gives two complete sets of chromosomes, one on the right and the other on the left of the cell. Nuclear membranes form around the two sets of chromosomes and a cell wall is constructed down the middle of the cytoplasm. When this process is completed, there are now two cells.

The second major type of cell division is meiosis (the adjectival form is meiotic) and it refers to the specialized cell division that produces sperm and eggs (see Figure 2.5). Obviously, ordinary mitosis cannot be used for these important cells. Otherwise, the number of chromosomes would double each generation. Meiosis begins with the replication and condensing of the chromosomes that takes place in ordinary cell division. But then an important difference occurs--there is a physical pairing of the chromosome that you received from your father with its counterpart that you received from your mother. At this point a very important phenomenon, termed recombination or crossing over, occurs. In recombination, the maternal and the paternal chromosome exchange DNA with each other. We will talk more about recombination in a later chapter. For now, it is important to recognize that there are four strands of DNA physically connected to one another--the "maternal" chromosome and its "carbon copy" and the "paternal" chromosome and its "carbon copy." (Quotes are used here to signify that the terms "maternal" and "paternal" are used loosely because the two will have already exchanged DNA. Hence, the "maternal" chromosome contains one or more sections of the original paternal chromosome and the "paternal" chromosome contains maternal DNA. The same applies to the "carbon copies" because they too will have exchanged genetic material.)

Spindles appear and separate the "maternal" chromosome and its "carbon copy" from the "paternal" chromosome and its "carbon copy." Ordinary cell division then takes place, generating two cells each with the complete chromosome complement. That is, each of us humans have 23 pairs of chromosomes, so the two cells will also have 23 pairs of chromosomes.

The next stage of cell division is called reduction division, and it is essentially mitosis in the two pre-germ cells. Here, spindles appear just as they do in mitosis and attach themselves to the chromosomes and their "carbon copies." The spindles then pull the chromosomes into the two poles of the cell and the cell divides. Now each cell will contain 23 chromosomes instead of 23 pairs of chromosomes. Hence, the necessary reduction in the number of chromosomes is accomplished.

---

9 These complementary chromosomes are called homologous chromosomes.
Figure 2.4 Mitosis: Division of somatic cells.

(a) Chromosomes are elongated and invisible under the light microscope. With appropriate staining, they can now be seen under the microscope.

(b) Chromosomes replicate and condense. Spindles pull the chromosomes and chromosomes align themselves along the opposite poles of the cell. Spindles are synthesized.

(c) Nuclear membrane disappears; chromosomes align themselves along the center of the cell; spindles synthesized.

(d) Spindles pull the chromosomes and their replicates apart, drawing them to opposite poles of the cell.

(e) Nuclear membrane and nucleus starts to form; cell wall membrane is synthesized.

(f) Nucleus and cell membrane synthesis is complete; chromosomes elongate.
Figure 2.5. Meiosis: cell division for gametes.

(a) As in mitosis, the chromosomes replicate and condense.

(b) Unlike mitosis, the maternal (solid) and paternal (dotted) chromosomes pair up and exchange genetic material.

(c) Spindles form and separate the homologous chromosomes. Note how genetic material has been exchanged between the maternal and paternal chromosomes.

(d) The cell divides. Note how the chromosomes and their original replicates are still attached.

(e) In both daughter cells, spindles form and pull the chromosomes and their original replicates apart.

(f) Each daughter cell divides, giving a total of four gametes from the original cell in panel (a).
The Nerve Cell

One of the most important types of cells for behavior is the nerve cell or neuron. Popular similes and metaphors for the nervous system often invoke electricity and electrical engineering. A psychotic person may be described as having a short circuit in the brain, but who ever refers to an incontinent person as having a short circuited kidney? It is indeed true that nerve cells generate electrical impulses, but it is equally true that they, just like all other cells, are an organized bundle of chemical reactions. Furthermore, genes play just as important a role in the chemical reactions of the nerve cell as they do in the kidney cell.10

Nerve cells have the same logical structure as other cells. Neurons have a cell wall, and there are a host of chemical sentinels embedded in the cell wall that perform the same function as the receptors on other cells. They announce to the neuron that some messenger is knocking at the gate, let other messengers in, keep certain ones out, and see to it that the appropriate molecules inside the neuron either stay inside or exit the neuron as needed. Neurons have mitochondria, an endoplasmic reticulum, and thousands of ribosomes busily making proteins and enzymes from the DNA blueprint. And, just like other cells, neurons have a nucleus with chromosomes. Like your bone marrow, muscles, skin, and lungs, the DNA in the nerves of your brain is actively telling your neurons which proteins and enzymes to make and which proteins and enzymes not to make.

What then, besides the ability to depolarize11, distinguishes a nerve cell from other cells? The answer is nothing, really. It is just that nerve cells look funny.

The neuron

A typical neuron, depicted in Figure 2.6, resembles a regular elliptoid cell extruded from a pasta machine that was having a bad day. Suppose that you intend to make vermicelli.12 Instead of a long, very thin cylinder, the pasta dough starts coming out as a frizzled mess, followed by the desired structure for a strand of spaghetti, but finished off a big irregular blob. That is a neuron. It looks like an octopus with a neck the size of a giraffe.

There is a very good reason for this structure and for the electrical nature of the impulse in neurons. Imagine that you mistakenly sat on an anthill, and the little critters, resenting the intrusion, declare war on your bottom. How long would it take your body to react if those assaulted cells in your gluteus maximus had to chemically communicate this fact to their neighboring cells, those cells to their own neighbors and so on, until the message finally got to your brain? Then the brain cells would have to chemically communicate the message “Ouch! Get off this stupid anthill!” back down the millions of cells, one cell at a time, until it would prompt movement of the appropriate muscles.

---

10 Although no one knows, it is theoretically possible that genes play a more important role in the nervous system than in many other systems. Tens of thousands of genes are estimated to be working in the central nervous system, far more than any other organ in the human body.
11 Depolarization is the biologist’s way of saying that a nerve fires and generates an electrical impulse. Unlike other cells, neurons do not divide and replenish themselves.
12 Vermicelli is the biologist’s way of saying spaghetti.
The speed of electrical transmission is on the order of turning on a switch and watching the bulb light up. That is why nerves use electricity. But why the funny structure? The answer is that one nerve uses chemistry, not electricity, to communicate with the next nerve. If nerves were just like other cells, there could be a million very tiny neurons between your butt and your brain. The chemical transmission between neurons would be painfully slow, even if each individual neuron fired an electrical burst. But with that very long, thin, spaghetti-like structure in Figure 2.4, only a few neurons are needed to connect your seat to your central processing unit. The chain of chemical transmission to electrical impulse to chemical transmission to electrical impulse becomes a very efficient way to send rapid messages. In the case of the anthill, electric impulses along very elongated cells permit a speedy retreat and allow you to live to sit another day.

Naturally, scientists must come up with fancier names than “spaghetti-like structure” to refer to the anatomy of the neuron. The large blob that contains the nucleus is called the cell body; the long vermicelli portion, along which the electrical impulse is carried, is termed the axon; and the frizzled ends are dendrites. Finally, the series of railways and superhighways that transport molecules from the cell body along the axon to the dendrites are referred to as neurofilaments and neurotubules.

Do not imagine any of these structures, especially the dendrites, as being like a copper wire. They are parts of cells and thus have cytoplasm, cell walls, vesicles, proteins, enzymes, and a host of other chemical molecules. This is highlighted in the bottom portion of Figure 2.6, which shows an exploded view of the end of one dendrite. An important structure in the dendrites of most neurons is the vesicle that contains many molecules of neurotransmitter—the chemical that transmits a message to the next nerve.

**Cell talk between nerve cells: Neural Transmission**

It is important to place the chemical transmission of neurons under a microscope to examine the process in more detail. Not only will it give us a better appreciation for cell talk, but it will also help us to understand an important focus of today’s genetic research on behavior, especially for psychiatric disorders.
The process of neural cell talk is outlined in Figure 2.7. Pictured here are portions of two neurons—the one that fires (the presynaptic neuron) and the one that responds to the firing of the first one (the postsynaptic neuron). Note that the two neurons do not physically touch each other. This is apparently true for all neurons. There is a physical gap between neurons called the synapse (aka synaptic cleft or synaptic junction). The adjectival form of this word—synaptic—is used as a suffix for a number of biological terms (e.g., presynaptic receptor—a receptor on the presynaptic neuron; postsynaptic receptor—a receptor on the postsynaptic neuron).

When the first neuron fires, vesicles containing the chemical messenger (aka neurotransmitter) move to the cell wall and release the messenger into the synapse. This process occurs very rapidly. And with a large number of vesicles and thousands of neurotransmitter molecules, release resembles a flash flood more than a trickling stream.

The force of release pushes the neurotransmitter across the synapse. Sitting on the plasma membrane of the postsynaptic neuron are a host of receptors. The neurotransmitter and receptor bind together in the same lock-and-key way that substrate and enzyme bind. The binding between neurotransmitter and receptor sparks a chemical reaction in the postsynaptic neuron that, in turn, initiates a whole cascade of chemical events that alters the whole chemical state of the neuron. In some cases, this change of state is excitatory and makes the postsynaptic neuron more likely to fire. In other cases, the change is inhibitory and decreases the probability of firing.

The final step in the process is really an exercise in tidy housekeeping. It is important not to let the large mass of neurotransmitter stay in the synapse. Otherwise, the constant binding, unbinding, and rebinding of the neurotransmitter with the postsynaptic receptor would keep the postsynaptic neuron in a state of perpetual change. Two major mechanisms take care of the excess neurotransmitter. The first is called reuptake. Here, the neurotransmitter binds to a specific receptor on the presynaptic neuron and gets “reabsorbed” back into the cell. The second mechanism is enzymatic degradation. One set of enzymes is lurking around the synapse, just ready to pounce on any wayward neurotransmitter. Another set lies low in the presynaptic neuron, waiting to ambush any neurotransmitter that went through the reuptake process but has not made it back to the safety of a vesicle.
Neurotransmitters, receptors, and genes

How do genes fit into neuronal transmission? There are several different ways. In the previous discussion of metabolic pathways, we have already seen how DNA contains the blueprint for the enzymes that synthesize neurotransmitters (review Figure 2.2). DNA also has the blueprint for a number of proteins and enzymes that transport neurotransmitters to the end of the dendrites and store them in vesicles. The receptors for neurotransmitters, both on the firing neuron and its recipient, do not appear from nowhere. DNA contains the code for these receptor proteins and/or the enzymes that synthesize them. Finally, DNA has the information on making the enzymes that metabolize the extra neurotransmitter that gets released.

Not only does DNA have the blueprint for these important proteins and enzymes, but it may also play a role in the numbers of protein or enzyme molecules that are synthesized and their distribution in the neuron. Scientific knowledge on this is skimpy, but it is likely that genes may influence such factors as the number and size of vesicles containing neurotransmitters, the number of receptor molecules, and perhaps even the density at which these receptors cluster at various places on the neuronal wall. Much research is needed to clarify the role of DNA in the human nervous system, but there is no doubt that without DNA in each and every neuron, we humans would have no nervous system at all.

Three disclaimers about the nervous system

1. If it has not already been done, I hope that one day an historian of the English language will trace the evolution of the word “nervous.” The Latin word “nervus,” from which the English word derives, means a sinew, and the word was apparently taken up by anatomists to refer to the tendon-like structure of the axons of some nerves. Somehow along the way, the word developed connotations of worry and apprehension on the one hand and jitteriness and agitation on the other. This is very curious because our nervous system plays just as important a role when we are calm and relaxed as it does when we are tense and anxious.

2. Although the nervous system plays a crucial role in behavior, one should not conclude that genes influencing behavior must do so by acting directly in the nervous system. All of us large, multicellular life forms are conglomerations of many different systems that talk to one another and can influence behavior. Later on we will see how a gene for an enzyme in the liver can reduce the risk of alcoholism.

3. Finally, a disclaimer is needed for the simplicity with which the nervous system has been described. From a scientific view, almost every statement made above requires qualifications because the nervous system is a very, very, very complicated place where virtually every rule has its exception. For example, a few neurons do communicate electrically and not chemically, and not every neurotransmitter is synthesized from enzymes. We will soon see that with genes and their physiological effects, complexity and perplexity are the rule instead of the exception.