Timberlane High School Science Summer Reading Assignment:

Course: Biology Accelerated

Instructions

- Please read the following selection(s) from the book A Short History of Nearly Everything by Bill Bryson.
- Please provide written answers (short essay style) to the questions at the end.
- The written assignment is to be turned into your teacher by **Thursday, September 5th and Friday, September 6th,** for potential full credit. Accepted until Sept 12th with 10% deduction in grade per day. Not accepted after Sept 12th.
- This is a graded assignment worth up to 3% of your quarter 1 grade.

Grading Rubric:

The writing will be assessed on the following 0 to 3 scales

- Each answer should be in a short essay style (minimum one paragraph).
  - 1: most answers are short one word answers.
  - 3: complete thoughts and sentences that fully convey the answers.
- Each answer should demonstrate evidence of reading to comprehension.
  - 1: answers indicate that the reading was not completed o 3: answers show clear comprehension of the reading
- Each answer should be correct, relevant to the topic, should strive for detail and completeness.
  - 1: answers are not relative to question or reading o 3: Answers demonstrate clear relevancy to passage and get to the heart of the rationale for question in relation to subject area.
- Each answer should refer to a specific statement or include a quote from the reading.
  - 1: the writing is vague, incomplete and contains little detail
  - 3: writing is detailed, complete and references specific statements or quotes from the reading passage.
- Each answer should be original (no plagiarism)

Tips on how to read science text for comprehension:

Break the reading into more than one session (2 to 4 pages per day). This should take about 15 minutes each time. Read slowly! Understand each sentence before reading the next. Be sure to examine unfamiliar words and concepts; try to determine meaning from the reading (or look them up). Make notes on each paragraph! It is OK to reread as you go or even reread the entire text. Read to understand, think about the ideas as you read and relate to what you already know, and what you may want to find out.

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Chapter 24 CELLS

IT STARTS WITH a single cell. The first cell splits to become two and the two become four and so on. After just forty-seven doublings, you have ten thousand trillion (10,000,000,000,000,000) cells in your body and are ready to spring forth as a human being.[1] And every one of those cells knows exactly what to do to preserve and nurture you from the moment of conception to your last breath.

You have no secrets from your cells. They know far more about you than you do. Each one carries a copy of the complete genetic code—the instruction manual for your body—so it knows not only how to do its job but every other job in the body. Never in your life will you have to remind a cell to keep an eye on its adenosine triphosphate levels or to find a place for the extra squirt of folic acid that's just unexpectedly turned up. It will do that for you, and millions more things besides.

Every cell in nature is a thing of wonder. Even the simplest are far beyond the limits of human ingenuity. To build the most basic yeast cell, for example, you would have to miniaturize about the same number of components as are found in a Boeing 777 jetliner and fit them into a sphere just five microns across; then somehow you would have to persuade that sphere to reproduce.

But yeast cells are as nothing compared with human cells, which are not just more varied and complicated, but vastly more fascinating because of their complex interactions.

Your cells are a country of ten thousand trillion citizens, each devoted in some intensively specific way to your overall well-being. There isn't a thing they don't do for you. They let you feel pleasure and form thoughts. They enable you to stand and stretch and caper. When you eat, they extract the nutrients, distribute the energy, and carry off the wastes—all those things you learned about in junior high school biology—but they also remember to make you hungry in the first place and reward you with a feeling of well-being afterward so that you won't forget to eat again. They keep your hair growing, your ears waxed, your brain quietly purring. They manage every corner of your being. They will jump to your defense the instant you are threatened. They will unhesitatingly die for you—billions of them do so daily. And not once in all your years have you thanked even one of them. So let us take a moment now to regard them with the wonder and appreciation they deserve.

We understand a little of how cells do the things they do—how they lay down fat or manufacture insulin or engage in many of the other acts necessary to maintain a complicated entity like yourself—but only a little. You have at least 200,000 different types of protein

[1] Actually, quite a lot of cells are lost in the process of development, so the number you emerge with is really just a guess. Depending on which source you consult the number can vary by several orders of magnitude. The figure of ten thousand trillion (or quadrillion) is from Margulis and Sagan, 1986.

laboring away inside you, and so far we understand what no more than about 2 percent of them do. (Others put the figure at more like 50 percent; it depends, apparently, on what you mean by "understand.")

Surprises at the cellular level turn up all the time. In nature, nitric oxide is a formidable toxin and a common component of air pollution. So scientists were naturally a little surprised when, in the mid-1980s, they found it being produced in a curiously devoted manner in human cells. Its purpose was at first a mystery, but then scientists began to find it all over the place—controlling the flow of blood and the energy levels of cells, attacking cancers and other pathogens, regulating the sense of smell, even assisting in penile erections. It also explained why nitroglycerine, the well-known explosive, soothes the heart pain known as angina. (It is converted into nitric oxide in the bloodstream, relaxing the muscle linings of vessels, allowing blood to flow more freely.) In barely the space of a decade this one gassy substance went from extraneous toxin to ubiquitous elixir.

You possess "some few hundred" different types of cell, according to the Belgian biochemist Christian de Duve, and they vary enormously in size and shape, from nerve cells whose filaments can stretch to several feet to tiny, disc-shaped red blood cells to the rod-shaped photocells that help to give us vision. They also come in a sumptuously wide range of sizes—nowhere more strikingly than at the moment of conception, when a single beating sperm confronts an egg eighty-five thousand times bigger than it (which rather puts the notion of male conquest into perspective). On average, however, a human cell is about twenty microns wide—that is about two hundredths of a millimeter—which is too small to be seen but roomy enough to hold thousands of complicated structures like mitochondria, and millions upon millions of molecules. In the most literal way, cells also vary in liveliness. Your skin cells are all dead. It's a somewhat galling notion to reflect that every inch of your surface is deceased. If you are an average-sized adult you are lugging around about five pounds of dead skin, of which several billion tiny fragments are sloughed off each day. Run a finger along a dusty shelf and you are drawing a pattern very largely in old skin.

Most living cells seldom last more than a month or so, but there are some notable exceptions. Liver cells can survive for years, though the components within them may be renewed every few days. Brain cells last as long as you do. You are issued a hundred billion or so at birth, and that is all you are ever going to get. It has been estimated that you lose five hundred of them an hour, so if you have any serious thinking to do there really isn't a moment to waste. The good news is that the individual components of your brain cells are constantly renewed so that, as with the liver cells, no part of them is actually likely to be more than about a month old. Indeed, it has been suggested that there isn't a single bit of any of us—not so much as a stray molecule—that was part of us nine years ago. It may not feel like it, but at the cellular level we are all youngsters.

The first person to describe a cell was Robert Hooke, whom we last encountered squabbling with Isaac Newton over credit for the invention of the inverse square law. Hooke achieved many things in his sixty-eight years—he was both an accomplished theoretician and a dab hand at making ingenious and useful instruments—but nothing he did brought him greater admiration than his popular book Microphagia: or Some Physiological Descriptions of Miniature Bodies Made by Magnifying Glasses, produced in 1665. It revealed to an enchanted public a universe of the very small that was far more diverse, crowded, and finely structured than anyone had ever come close to imagining.

Among the microscopic features first identified by Hooke were little chambers in plants that he called "cells" because they reminded him of monks' cells. Hooke calculated that a one-inch square of cork would contain 1,259,712,000 of these tiny chambers—the first appearance of such a very large number anywhere in science. Microscopes by this time had been around for a generation or so, but what set Hooke's apart were their technical supremacy. They achieved magnifications of thirty times, making them the last word in seventeenth-century optical technology.

So it came as something of a shock when just a decade later Hooke and the other members of London's Royal Society began to receive drawings and reports from an unlettered linen draper in Holland employing magnifications of up to 275 times. The draper's name was Antoni van Leeuwenhoek. Though he had little formal education and no background in science, he was a perceptive and dedicated observer and a technical genius.

To this day it is not known how he got such magnificent magnifications from simple handheld devices, which were little more than modest wooden dowels with a tiny bubble of glass embedded in them, far more like magnifying glasses than what most of us think of as microscopes, but really not much like either. Leeuwenhoek made a new instrument for every experiment he performed and was extremely secretive about his techniques, though he did sometimes offer tips to the British on how they might improve their resolutions.[2]

Over a period of fifty years—beginning, remarkably enough, when he was already past forty—he made almost two hundred reports to the Royal Society, all written in Low Dutch, the only tongue of which he was master. Leeuwenhoek offered no interpretations, but simply the facts of what he had found, accompanied by exquisite drawings. He sent reports on almost everything that could be usefully examined—bread mold, a bee's stinger, blood cells, teeth, hair, his own saliva, excrement, and semen (these last with fretful apologies for their unsavory nature)—nearly all of which had never been seen microscopically before.

After he reported finding "animalcules" in a sample of pepper water in 1676, the members of the Royal Society spent a year with the best devices English technology could produce searching for the "little animals" before finally getting the magnification right. What Leeuwenhoek had found were protozoa. He calculated that there were 8,280,000 of these tiny beings in a single drop of water—more than the number of people in Holland. The world teemed with life in ways and numbers that no one had previously suspected.

Inspired by Leeuwenhoek's fantastic findings, others began to peer into microscopes with such keenness that they sometimes found things that weren't in fact there. One respected Dutch observer, Nicolaus Hartsoecker, was convinced he saw "tiny preformed men" in sperm cells. He called the little beings "homunculi" and for some time many people believed that all humans—indeed, all creatures—were simply vastly inflated versions of tiny but complete precursor beings. Leeuwenhoek himself occasionally got carried away with his enthusiasms. In one of his least successful experiments he tried to study the explosive properties of gunpowder by observing a small blast at close range; he nearly blinded himself in the process.

[2] Leeuwenhoek was close friends with another Delft notable, the artist Jan Vermeer. In the mid-1660s, Vermeer, who previously had been a competent but not outstanding artist, suddenly developed the mastery of light and perspective for which he has been celebrated ever since. Though it has never been proved, it has long been suspected that he used a camera obscura, a device for projecting images onto a flat surface through a lens. No such device was listed among Vermeer's personal effects after his death, but it happens that the executor of Vermeer's estate was none other than Antoni van Leeuwenhoek, the most secretive lens-maker of his day.

In 1683 Leeuwenhoek discovered bacteria, but that was about as far as progress could get for the next century and a half because of the limitations of microscope technology. Not until 1831 would anyone first see the nucleus of a cell—it was found by the Scottish botanist Robert Brown, that frequent but always shadowy visitor to the history of science. Brown, who lived from 1773 to 1858, called it nucleus from the Latin nucula, meaning little nut or kernel. Not until 1839, however, did anyone realize that all living matter is cellular. It was Theodor Schwann, a German, who had this insight, and it was not only comparatively late, as scientific insights go, but not widely embraced at first. It wasn't until the 1860s, and some landmark work by Louis Pasteur in France, that it was shown conclusively that life cannot arise spontaneously but must come from preexisting cells. The belief became known as the "cell theory," and it is the basis of all modern biology.

The cell has been compared to many things, from "a complex chemical refinery" (by the physicist James Trefil) to "a vast, teeming metropolis" (the biochemist Guy Brown). A cell is both of those things and neither. It is like a refinery in that it is devoted to chemical activity on a grand scale, and like a metropolis in that it is crowded and busy and filled with interactions that seem confused and random but clearly have some system to them. But it is a much more nightmarish place than any city or factory that you have ever seen. To begin with there is no up or down inside the cell (gravity doesn't meaningfully apply at the cellular scale), and not an atom's width of space is unused. There is activity every where and a ceaseless thrum of electrical energy. You may not feel terribly electrical, but you are. The food we eat and the oxygen we breathe are combined in the cells into electricity. The reason we don't give each other massive shocks or scorch the sofa when we sit is that it is all happening on a tiny scale: a mere 0.1 volts traveling distances measured in nanometers. However, scale that up and it would translate as a jolt of twenty million volts per meter, about the same as the charge carried by the main body of a thunderstorm.

Whatever their size or shape, nearly all your cells are built to fundamentally the same plan: they have an outer casing or membrane, a nucleus wherein resides the necessary genetic information to keep you going, and a busy space between the two called the cytoplasm. The membrane is not, as most of us imagine it, a durable, rubbery casing, something that you would need a sharp pin to prick. Rather, it is made up of a type of fatty material known as a lipid, which has the approximate consistency "of a light grade of machine oil," to quote Sherwin B. Nuland. If that seems surprisingly insubstantial, bear in mind that at the microscopic level things behave differently. To anything on a molecular scale water becomes a kind of heavy-duty gel, and a lipid is like iron.

If you could visit a cell, you wouldn't like it. Blown up to a scale at which atoms were about the size of peas, a cell itself would be a sphere roughly half a mile across, and supported by a complex framework of girders called the cytoskeleton. Within it, millions upon millions of objects—some the size of basketballs, others the size of cars—would whiz about like bullets. There wouldn't be a place you could stand without being pummeled and ripped thousands of times every second from every direction. Even for its full-time occupants the inside of a cell is a hazardous place. Each strand of DNA is on average attacked or damaged once every 8.4 seconds—ten thousand times in a day—by chemicals and other agents that whack into or carelessly slice through it, and each of these wounds must be swiftly stitched up if the cell is not to perish.

The proteins are especially lively, spinning, pulsating, and flying into each other up to a billion times a second. Enzymes, themselves a type of protein, dash everywhere, performing up to a thousand tasks a second. Like greatly speeded up worker ants, they busily build and rebuild molecules, hauling a piece off this one, adding a piece to that one. Some monitor passing proteins and mark with a chemical those that are irreparably damaged or flawed. Once so selected, the doomed proteins proceed to a structure called a proteasome, where they are stripped down and their components used to build new proteins. Some types of protein exist for less than half an hour; others survive for weeks. But all lead existences that are inconceivably frenzied. As de Duve notes, "The molecular world must necessarily remain entirely beyond the powers of our imagination owing to the incredible speed with which things happen in it."

But slow things down, to a speed at which the interactions can be observed, and things don't seem quite so unnerving. You can see that a cell is just millions of objects—lysosomes, endosomes, ribosomes, ligands, peroxisomes, proteins of every size and shape—bumping into millions of other objects and performing mundane tasks: extracting energy from nutrients, assembling structures, getting rid of waste, warding off intruders, sending and receiving messages, making repairs. Typically a cell will contain some 20,000 different types of protein, and of these about 2,000 types will each be represented by at least 50,000 molecules. "This means," says Nuland, "that even if we count only those molecules present in amounts of more than 50,000 each, the total is still a very minimum of 100 million protein molecules in each cell. Such a staggering figure gives some idea of the swarming immensity of biochemical activity within us."

It is all an immensely demanding process. Your heart must pump 75 gallons of blood an hour, 1,800 gallons every day, 657,000 gallons in a year—that's enough to fill four Olympic-sized swimming pools—to keep all those cells freshly oxygenated. (And that's at rest. During exercise the rate can increase as much as sixfold.) The oxygen is taken up by the mitochondria. These are the cells' power stations, and there are about a thousand of them in a typical cell, though the number varies considerably depending on what a cell does and how much energy it requires.

You may recall from an earlier chapter that the mitochondria are thought to have originated as captive bacteria and that they now live essentially as lodgers in our cells, preserving their own genetic instructions, dividing to their own timetable, speaking their own language. You may also recall that we are at the mercy of their goodwill. Here's why. Virtually all the food and oxygen you take into your body are delivered, after processing, to the mitochondria, where they are converted into a molecule called adenosine triphosphate, or ATP.

You may not have heard of ATP, but it is what keeps you going. ATP molecules are essentially little battery packs that move through the cell providing energy for all the cell's processes, and you get through a lot of it. At any given moment, a typical cell in your body will have about one billion ATP molecules in it, and in two minutes every one of them will have been drained dry and another billion will have taken their place. Every day you produce and use up a volume of ATP equivalent to about half your body weight. Feel the warmth of your skin. That's your ATP at work.

When cells are no longer needed, they die with what can only be called great dignity. They take down all the struts and buttresses that hold them together and quietly devour their component parts. The process is known as apoptosis or programmed cell death. Every day billions of your cells die for your benefit and billions of others clean up the mess. Cells can also die violently—for instance, when infected—but mostly they die because they are told to. Indeed, if not told to live—if not given some kind of active instruction from another cell—cells automatically kill themselves. Cells need a lot of reassurance.

When, as occasionally happens, a cell fails to expire in the prescribed manner, but rather begins to divide and proliferate wildly, we call the result cancer. Cancer cells are really just confused cells. Cells make this mistake fairly regularly, but the body has elaborate mechanisms for dealing with it. It is only very rarely that the process spirals out of control. On average, humans suffer one fatal malignancy for each 100 million billion cell divisions. Cancer is bad luck in every possible sense of the term.

The wonder of cells is not that things occasionally go wrong, but that they manage everything so smoothly for decades at a stretch. They do so by constantly sending and monitoring streams of messages—a cacophony of messages—from all around the body: instructions, queries, corrections, requests for assistance, updates, notices to divide or expire. Most of these signals arrive by means of couriers called hormones, chemical entities such as insulin, adrenaline, estrogen, and testosterone that convey information from remote outposts like the thyroid and endocrine glands. Still other messages arrive by telegraph from the brain or from regional centers in a process called paracrine signaling. Finally, cells communicate directly with their neighbors to make sure their actions are coordinated.

What is perhaps most remarkable is that it is all just random frantic action, a sequence of endless encounters directed by nothing more than elemental rules of attraction and repulsion. There is clearly no thinking presence behind any of the actions of the cells. It all just happens, smoothly and repeatedly and so reliably that seldom are we even conscious of it, yet somehow all this produces not just order within the cell but a perfect harmony right across the organism. In ways that we have barely begun to understand, trillions upon trillions of reflexive chemical reactions add up to a mobile, thinking, decision-making you—or, come to that, a rather less reflective but still incredibly organized dung beetle. Every living thing, never forget, is a wonder of atomic engineering.

Indeed, some organisms that we think of as primitive enjoy a level of cellular organization that makes our own look carelessly pedestrian. Disassemble the cells of a sponge (by passing them through a sieve, for instance), then dump them into a solution, and they will find their way back together and build themselves into a sponge again. You can do this to them over and over, and they will doggedly reassemble because, like you and me and every other living thing, they have one overwhelming impulse: to continue to be.

And that's because of a curious, determined, barely understood molecule that is itself not alive and for the most part doesn't do anything at all. We call it DNA, and to begin to understand its supreme importance to science and to us we need to go back 160 years or so to Victorian England and to the moment when the naturalist Charles Darwin had what has been called "the single best idea that anyone has ever had"—and then, for reasons that take a little explaining, locked it away in a drawer for the next fifteen years.

Chapter 24: Cells

1. Bryson emphasizes the smallness of cells and the amazingly large numbers required to make up individual organisms. Why do you think cells are so small, or put another way, why are there no really big cells?

2. One large cell you are familiar with is the yolk of a chicken egg. That cell is large because of the tremendous amount of nutrients stored in it for use by a developing chick. Why do you think the human egg cell is so much larger than the human sperm cell (p. 373)?

3. Who first described and named a cell? Why did he use the term "cell"?

4. The Cell Theory is simply the idea that all living organisms are made up of cells. Although this seems so obvious today, it was not widely accepted by biologists until the mid 1800's, relatively recently in term of human history. Why did it take us so long to figure out this simple fact?

5. Bryson refers to a cell as "a complex chemical refinery". Not a bad analogy, but another way to look at a cell is as a center for energy conversion. Organisms take in energy stored in certain forms such as carbohydrates or lipids and convert these forms to chemical energy that can be used by the cell. What is the form of this chemical energy? What do cells use this energy for?

6. Cells are capable of reproducing themselves by cell division. For single celled organisms, cell division is essentially reproduction. For multicelled organisms, division is necessary for growth and renewal. Even though cell division is natural and necessary, what happens when the rate of cell division becomes too rapid and out of control? How can we get rid of such rapidly dividing cells in the human body?

26 THE STUFF OF LIFE

IF YOUR TWO parents hadn't bonded just when they did—possibly to the second, possibly to the nanosecond—you wouldn't be here. And if their parents hadn't bonded in a precisely timely manner, you wouldn't be here either. And if their parents hadn't done likewise, and their parents before them, and so on, obviously and indefinitely, you wouldn't be here.

Push backwards through time and these ancestral debts begin to add up. Go back just eight generations to about the time that Charles Darwin and Abraham Lincoln were born, and already there are over 250 people on whose timely couplings your existence depends. Continue further, to the time of Shakespeare and the Mayflower Pilgrims, and you have no fewer than 16,384 ancestors earnestly exchanging genetic material in a way that would, eventually and miraculously, result in you.

At twenty generations ago, the number of people procreating on your behalf has risen to 1,048,576. Five generations before that, and there are no fewer than 33,554,432 men and women on whose devoted couplings your existence depends. By thirty generations ago, your total number of forebears—remember, these aren't cousins and aunts and other incidental relatives, but only parents and parents of parents in a line leading ineluctably to you—is over one billion (1,073,741,824, to be precise). If you go back sixty-four generations, to the time of the Romans, the number of people on whose cooperative efforts your eventual existence depends has risen to approximately 1,000,000,000,000,000,000, which is several thousand times the total number of people who have ever lived.

Clearly something has gone wrong with our math here. The answer, it may interest you to learn, is that your line is not pure. You couldn't be here without a little incest—actually quite a lot of incest—albeit at a genetically discreet remove. With so many millions of ancestors in your background, there will have been many occasions when a relative from your mother's side of the family procreated with some distant cousin from your father's side of the ledger. In fact, if you are in a partnership now with someone from your own race and country, the chances are excellent that you are at some level related. Indeed, if you look around you on a bus or in a park or café or any crowded place, most of the people you see are very probably relatives. When someone boasts to you that he is descended from William the Conqueror or the Mayflower Pilgrims, you should answer at once: "Me, too!" In the most literal and fundamental sense we are all family.

We are also uncannily alike. Compare your genes with any other human being's and on average they will be about 99.9 percent the same. That is what makes us a species. The tiny differences in that remaining 0.1 percent—"roughly one nucleotide base in every thousand," to quote the British geneticist and recent Nobel laureate John Sulston—are what endow us with our individuality. Much has been made in recent years of the unraveling of the human genome. In fact, there is no such thing as "the" human genome. Every human genome is different. Otherwise we would all be identical. It is the endless recombinations of our genomes—each nearly identical, but not quite—that make us what we are, both as individuals and as a species.

But what exactly is this thing we call the genome? And what, come to that, are genes? Well, start with a cell again. Inside the cell is a nucleus, and inside each nucleus are the chromosomes—forty-six little bundles of complexity, of which twenty-three come from your mother and twenty-three from your father. With a very few exceptions, every cell in your body—99.999 percent of them, say—carries the same complement of chromosomes. (The exceptions are red blood cells, some immune system cells, and egg and sperm cells, which for various organizational reasons don't carry the full genetic package.) Chromosomes constitute the complete set of instructions necessary to make and maintain you and are made of long strands of the little wonder chemical called deoxyribonucleic acid or DNA—"the most extraordinary molecule on Earth," as it has been called.

DNA exists for just one reason—to create more DNA—and you have a lot of it inside you: about six feet of it squeezed into almost every cell. Each length of DNA comprises some 3.2 billion letters of coding, enough to provide $10^{3,480,000,000}$ possible combinations, "guaranteed to be unique against all conceivable odds," in the words of Christian de Duve. That's a lot of possibility—a one followed by more than three billion zeroes. "It would take more than five thousand average-size books just to print that figure," notes de Duve. Look at yourself in the mirror and reflect upon the fact that you are beholding ten thousand trillion cells, and that almost every one of them holds two yards of densely compacted DNA, and you begin to appreciate just how much of this stuff you carry around with you. If all your DNA were woven into a single fine strand, there would be enough of it to stretch from the Earth to the Moon and back not once or twice but again and again. Altogether, according to one calculation, you may have as much as twenty million kilometers of DNA bundled up inside you.

Your body, in short, loves to make DNA and without it you couldn't live. Yet DNA is not itself alive. No molecule is, but DNA is, as it were, especially unalive. It is "among the most nonreactive, chemically inert molecules in the living world," in the words of the geneticist Richard Lewontin. That is why it can be recovered from patches of long-dried blood or semen in murder investigations and coaxed from the bones of ancient Neandertals. It also explains why it took scientists so long to work out how a substance so mystifyingly low key—so, in a word, lifeless—could be at the very heart of life itself.

As a known entity, DNA has been around longer than you might think. It was discovered as far back as 1869 by Johann Friedrich Miescher, a Swiss scientist working at the University of Tübingen in Germany. While delving microscopically through the pus in surgical bandages, Miescher found a substance he didn't recognize and called it nuclein (because it resided in the nuclei of cells). At the time, Miescher did little more than note its existence, but nuclein clearly remained on his mind, for twenty-three years later in a letter to his uncle he raised the possibility that such molecules could be the agents behind heredity. This was an extraordinary insight, but one so far in advance of the day's scientific requirements that it attracted no attention at all.

For most of the next half century the common assumption was that the material—now called deoxyribonucleic acid, or DNA—had at most a subsidiary role in matters of heredity. It was too simple. It had just four basic components, called nucleotides, which was like having an alphabet of just four letters. How could you possibly write the story of life with such a rudimentary alphabet? (The answer is that you do it in much the way that you create complex messages with the simple dots and dashes of Morse code—by combining them.) DNA didn't do anything at all, as far as anyone could tell. It just sat there in the nucleus, possibly binding the chromosome in some way or adding a splash of acidity on command or fulfilling some other trivial task that no one had yet thought of. The necessary complexity, it was thought, had to exist in proteins in the nucleus.

There were, however, two problems with dismissing DNA. First, there was so much of it: two yards in nearly every nucleus, so clearly the cells esteemed it in some important way. On top of this, it kept turning up, like the suspect in a murder mystery, in experiments. In two studies in particular, one involving the Pneumonococcus bacterium and another involving bacteriophages (viruses that infect bacteria), DNA betrayed an importance that could only be explained if its role were more central than prevailing thought allowed. The evidence suggested that DNA was somehow involved in the making of proteins, a process vital to life, yet it was also clear that proteins were being made outside the nucleus, well away from the DNA that was supposedly directing their assembly.

No one could understand how DNA could possibly be getting messages to the proteins. The answer, we now know, was RNA, or ribonucleic acid, which acts as an interpreter between the two. It is a notable oddity of biology that DNA and proteins don't speak the same language. For almost four billion years they have been the living world's great double act, and yet they answer to mutually incompatible codes, as if one spoke Spanish and the other Hindi. To communicate they need a mediator in the form of RNA. Working with a kind of chemical clerk called a ribosome, RNA translates information from a cell's DNA into terms proteins can understand and act upon.

However, by the early 1900s, where we resume our story, we were still a very long way from understanding that, or indeed almost anything else to do with the confused business of heredity.

Clearly there was a need for some inspired and clever experimentation, and happily the age produced a young person with the diligence and aptitude to undertake it. His name was Thomas Hunt Morgan, and in 1904, just four years after the timely rediscovery of Mendel's experiments with pea plants and still almost a decade before gene would even become a word, he began to do remarkably dedicated things with chromosomes.

Chromosomes had been discovered by chance in 1888 and were so called because they readily absorbed dye and thus were easy to see under the microscope. By the turn of the twentieth century it was strongly suspected that they were involved in the passing on of traits, but no one knew how, or even really whether, they did this.

Morgan chose as his subject of study a tiny, delicate fly formally called Drosophila melanogaster, but more commonly known as the fruit fly (or vinegar fly, banana fly, or garbage fly). Drosophila is familiar to most of us as that frail, colorless insect that seems to have a compulsive urge to drown in our drinks. As laboratory specimens fruit flies had certain very attractive advantages: they cost almost nothing to house and feed, could be bred by the millions in milk bottles, went from egg to productive parenthood in ten days or less, and had just four chromosomes, which kept things conveniently simple.

Working out of a small lab (which became known inevitably as the Fly Room) in Schermerhorn Hall at Columbia University in New York, Morgan and his team embarked on a program of meticulous breeding and crossbreeding involving millions of flies (one biographer says billions, though that is probably an exaggeration), each of which had to be captured with tweezers and examined under a jeweler's glass for any tiny variations in inheritance. For six years they tried to produce mutations by any means they could think of—zapping the flies with radiation and X-rays, rearing them in bright light and darkness, baking them gently in ovens, spinning them crazily in centrifuges—but nothing worked. Morgan was on the brink of giving up when there occurred a sudden and repeatable mutation—a fly that had white eyes rather than the usual red ones. With this breakthrough, Morgan and his assistants were able to generate useful deformities, allowing them to track a trait through successive generations. By such means they could work out the correlations between particular characteristics and individual chromosomes, eventually proving to more or less everyone's satisfaction that chromosomes were at the heart of inheritance.

The problem, however, remained the next level of biological intricacy: the enigmatic genes and the DNA that composed them. These were much trickier to isolate and understand. As late as 1933, when Morgan was awarded a Nobel Prize for his work, many researchers still weren't convinced that genes even existed. As Morgan noted at the time, there was no consensus "as to what the genes are—whether they are real or purely fictitious." It may seem surprising that scientists could struggle to accept the physical reality of something so fundamental to cellular activity, but as Wallace, King, and Sanders point out in Biology: The Science of Life (that rarest thing: a readable college text), we are in much the same position today with mental processes such as thought and memory. We know that we have them, of course, but we don't know what, if any, physical form they take. So it was for the longest time with genes. The idea that you could pluck one from your body and take it away for study was as absurd to many of Morgan's peers as the idea that scientists today might capture a stray thought and examine it under a microscope.

What was certainly true was that something associated with chromosomes was directing cell replication. Finally, in 1944, after fifteen years of effort, a team at the Rockefeller Institute in Manhattan, led by a brilliant but diffident Canadian named Oswald Avery, succeeded with an exceedingly tricky experiment in which an innocuous strain of bacteria was made permanently infectious by crossing it with alien DNA, proving that DNA was far more than a passive molecule and almost certainly was the active agent in heredity. The Austrian-born biochemist Erwin Chargaff later suggested quite seriously that Avery's discovery was worth two Nobel Prizes.

Unfortunately, Avery was opposed by one of his own colleagues at the institute, a strong-willed and disagreeable protein enthusiast named Alfred Mirsky, who did everything in his power to discredit Avery's work—including, it has been said, lobbying the authorities at the Karolinska Institute in Stockholm not to give Avery a Nobel Prize. Avery by this time was sixty-six years old and tired. Unable to deal with the stress and controversy, he resigned his position and never went near a lab again. But other experiments elsewhere overwhelmingly supported his conclusions, and soon the race was on to find the structure of DNA.

Had you been a betting person in the early 1950s, your money would almost certainly have been on Linus Pauling of Caltech, America's leading chemist, to crack the structure of DNA. Pauling was unrivaled in determining the architecture of molecules and had been a pioneer in the field of X-ray crystallography, a technique that would prove crucial to peering into the heart of DNA. In an exceedingly distinguished career, he would win two Nobel Prizes (for chemistry in 1954 and peace in 1962), but with DNA he became convinced that the structure was a triple helix, not a double one, and never quite got on the right track. Instead, victory fell to an unlikely quartet of scientists in England who didn't work as a team, often weren't on speaking terms, and were for the most part novices in the field.

Of the four, the nearest to a conventional boffin was Maurice Wilkins, who had spent much of the Second World War helping to design the atomic bomb. Two of the others, Rosalind Franklin and Francis Crick, had passed their war years working on mines for the British government—Crick of the type that blow up, Franklin of the type that produce coal.

The most unconventional of the foursome was James Watson, an American prodigy who had distinguished himself as a boy as a member of a highly popular radio program called The Quiz Kids (and thus could claim to be at least part of the inspiration for some of the members of the Glass family in Franny and Zooey and other works by J. D. Salinger) and who had entered the University of Chicago aged just fifteen. He had earned his Ph.D. by the age of twenty-two and was now attached to the famous Cavendish Laboratory in Cambridge. In 1951, he was a gawky twenty-three-year-old with a strikingly lively head of hair that appears in photographs to be straining to attach itself to some powerful magnet just out of frame.

Crick, twelve years older and still without a doctorate, was less memorably hirsute and slightly more tweedy. In Watson's account he is presented as blustery, nosy, cheerfully argumentative, impatient with anyone slow to share a notion, and constantly in danger of being asked to go elsewhere. Neither was formally trained in biochemistry.

Their assumption was that if you could determine the shape of a DNA molecule you would be able to see—correctly, as it turned out—how it did what it did. They hoped to achieve this, it would appear, by doing as little work as possible beyond thinking, and no more of that than was absolutely necessary. As Watson cheerfully (if a touch disingenuously) remarked in his autobiographical book The Double Helix, "It was my hope that the gene might be solved without my learning any chemistry." They weren't actually assigned to work on DNA, and at one point were ordered to stop it. Watson was ostensibly mastering the art of crystallography; Crick was supposed to be completing a thesis on the X-ray diffraction of large molecules.

Although Crick and Watson enjoy nearly all the credit in popular accounts for solving the mystery of DNA, their breakthrough was crucially dependent on experimental work done by their competitors, the results of which were obtained "fortuitously," in the tactful words of the historian Lisa Jardine. Far ahead of them, at least at the beginning, were two academics at King's College in London, Wilkins and Franklin.

The New Zealand–born Wilkins was a retiring figure, almost to the point of invisibility. A 1998 PBS documentary on the discovery of the structure of DNA—a feat for which he shared the 1962 Nobel Prize with Crick and Watson—managed to overlook him entirely.

The most enigmatic character of all was Franklin. In a severely unflattering portrait, Watson in The Double Helix depicted Franklin as a woman who was unreasonable, secretive, chronically uncooperative, and—this seemed especially to irritate him—almost willfully unsexy. He allowed that she "was not unattractive and might have been quite stunning had she taken even a mild interest in clothes," but in this she disappointed all expectations. She didn't even use lipstick, he noted in wonder, while her dress sense "showed all the imagination of English blue-stocking adolescents."[1]

However, she did have the best images in existence of the possible structure of DNA, achieved by means of X-ray crystallography, the technique perfected by Linus Pauling. Crystallography had been used successfully to map atoms in crystals (hence "crystallography"), but DNA molecules were a much more finicky proposition. Only Franklin was managing to get good results from the process, but to Wilkins's perennial exasperation she refused to share her findings.

If Franklin was not warmly forthcoming with her findings, she cannot be altogether blamed. Female academics at King's in the 1950s were treated with a formalized disdain that dazzles modern sensibilities (actually any sensibilities). However senior or accomplished, they were not allowed into the college's senior common room but instead had to take their meals in a more utilitarian chamber that even Watson conceded was "dingily pokey." On top of this she was being constantly pressed—at times actively harassed—to share her results with a trio of men whose desperation to get a peek at them was seldom matched by more engaging qualities, like respect. "I'm afraid we always used to adopt—let's say a patronizing attitude toward her," Crick later recalled. Two of these men were from a competing institution and the third was more or less openly siding with them. It should hardly come as a surprise that she kept her results locked away.

That Wilkins and Franklin did not get along was a fact that Watson and Crick seem to have exploited to their benefit. Although Crick and Watson were trespassing rather unashamedly on Wilkins's territory, it was with them that he increasingly sided—not altogether surprisingly since Franklin herself was beginning to act in a decidedly queer way. Although her results showed that DNA definitely was helical in shape, she insisted to all that it was not. To Wilkins's presumed dismay and embarrassment, in the summer of 1952 she posted a mock notice around the King's physics department that said: "It is with great regret that we have to announce the death, on Friday 18th July 1952 of D.N.A. helix. . . . It is hoped that Dr. M.H.F. Wilkins will speak in memory of the late helix."

The outcome of all this was that in January 1953, Wilkins showed Watson Franklin's images, "apparently without her knowledge or consent." It would be an understatement to call it a significant help. Years later Watson conceded that it "was the key event . . . it mobilized us." Armed with the knowledge of the DNA molecule's basic shape and some important elements of its dimensions, Watson and Crick redoubled their efforts. Everything now seemed to go their way. At one point Pauling was en route to a conference in England at which he would in all likelihood have met with Wilkins and learned enough to correct the misconceptions that had put him on the wrong line of inquiry, but this was the McCarthy era and Pauling found himself detained at Idlewild Airport in New York, his passport confiscated, on the grounds that he was too liberal of temperament to be allowed to travel abroad. Crick and Watson also had the no less convenient good fortune that Pauling's son was working at the Cavendish and innocently kept them abreast of any news of developments and setbacks at home.

Still facing the possibility of being trumped at any moment, Watson and Crick applied themselves feverishly to the problem. It was known that DNA had four chemical

[1] In 1968, Harvard University Press canceled publication of The Double Helix after Crick and Wilkins complained about its characterizations, which the science historian Lisa Jardine has described as "gratuitously hurtful." The descriptions quoted above are after Watson softened his comments.

components—called adenine, guanine, cytosine, and thiamine—and that these paired up in particular ways. By playing with pieces of cardboard cut into the shapes of molecules, Watson and Crick were able to work out how the pieces fit together. From this they made a Meccano-like model—perhaps the most famous in modern science—consisting of metal plates bolted together in a spiral, and invited Wilkins, Franklin, and the rest of the world to have a look. Any informed person could see at once that they had solved the problem. It was without question a brilliant piece of detective work, with or without the boost of Franklin's picture.

The April 25, 1953, edition of Nature carried a 900-word article by Watson and Crick titled "A Structure for Deoxyribose Nucleic Acid." Accompanying it were separate articles by Wilkins and Franklin. It was an eventful time in the world—Edmund Hillary was just about to clamber to the top of Everest while Elizabeth II was imminently to be crowned queen of England—so the discovery of the secret of life was mostly overlooked. It received a small mention in the News Chronicle and was ignored elsewhere.

Rosalind Franklin did not share in the Nobel Prize. She died of ovarian cancer at the age of just thirty-seven in 1958, four years before the award was granted. Nobel Prizes are not awarded posthumously. The cancer almost certainly arose as a result of chronic overexposure to X-rays through her work and needn't have happened. In her much-praised 2002 biography of Franklin, Brenda Maddox noted that Franklin rarely wore a lead apron and often stepped carelessly in front of a beam. Oswald Avery never won a Nobel Prize either and was also largely overlooked by posterity, though he did at least have the satisfaction of living just long enough to see his findings vindicated. He died in 1955.

Watson and Crick's discovery wasn't actually confirmed until the 1980s. As Crick said in one of his books: "It took over twenty-five years for our model of DNA to go from being only rather plausible, to being very plausible . . . and from there to being virtually certainly correct."

Even so, with the structure of DNA understood progress in genetics was swift, and by 1968 the journal Science could run an article titled "That Was the Molecular Biology That Was," suggesting—it hardly seems possible, but it is so—that the work of genetics was nearly at an end.

In fact, of course, it was only just beginning. Even now there is a great deal about DNA that we scarcely understand, not least why so much of it doesn't actually seem to do anything. Ninety-seven percent of your DNA consists of nothing but long stretches of meaningless garble—"junk," or "non-coding DNA," as biochemists prefer to put it. Only here and there along each strand do you find sections that control and organize vital functions. These are the curious and long-elusive genes.

Genes are nothing more (nor less) than instructions to make proteins. This they do with a certain dull fidelity. In this sense, they are rather like the keys of a piano, each playing a single note and nothing else, which is obviously a trifle monotonous. But combine the genes, as you would combine piano keys, and you can create chords and melodies of infinite variety. Put all these genes together, and you have (to continue the metaphor) the great symphony of existence known as the human genome.

An alternative and more common way to regard the genome is as a kind of instruction manual for the body. Viewed this way, the chromosomes can be imagined as the book's chapters and the genes as individual instructions for making proteins. The words in which the instructions are written are called codons, and the letters are known as bases. The bases—the letters of the genetic alphabet—consist of the four nucleotides mentioned a page or two back: adenine, thiamine, guanine, and cytosine. Despite the importance of what they do, these substances are not made of anything exotic. Guanine, for instance, is the same stuff that abounds in, and gives its name to, guano.

The shape of a DNA molecule, as everyone knows, is rather like a spiral staircase or twisted rope ladder: the famous double helix. The uprights of this structure are made of a type of sugar called deoxyribose, and the whole of the helix is a nucleic acid—hence the name "deoxyribonucleic acid." The rungs (or steps) are formed by two bases joining across the space between, and they can combine in only two ways: guanine is always paired with cytosine and thiamine always with adenine. The order in which these letters appear as you move up or down the ladder constitutes the DNA code; logging it has been the job of the Human Genome Project.

Now the particular brilliance of DNA lies in its manner of replication. When it is time to produce a new DNA molecule, the two strands part down the middle, like the zipper on a jacket, and each half goes off to form a new partnership. Because each nucleotide along a strand pairs up with a specific other nucleotide, each strand serves as a template for the creation of a new matching strand. If you possessed just one strand of your own DNA, you could easily enough reconstruct the matching side by working out the necessary partnerships: if the topmost rung on one strand was made of guanine, then you would know that the topmost rung on the matching strand must be cytosine. Work your way down the ladder through all the nucleotide pairings, and eventually you would have the code for a new molecule. That is just what happens in nature, except that nature does it really quickly—in only a matter of seconds, which is quite a feat.

Most of the time our DNA replicates with dutiful accuracy, but just occasionally—about one time in a million—a letter gets into the wrong place. This is known as a single nucleotide polymorphism, or SNP, familiarly known to biochemists as a "Snip." Generally these Snips are buried in stretches of noncoding DNA and have no detectable consequence for the body. But occasionally they make a difference. They might leave you predisposed to some disease, but equally they might confer some slight advantage—more protective pigmentation, for instance, or increased production of red blood cells for someone living at altitude. Over time, these slight modifications accumulate in both individuals and in populations, contributing to the distinctiveness of both.

The balance between accuracy and errors in replication is a fine one. Too many errors and the organism can't function, but too few and it sacrifices adaptability. A similar balance must exist between stability in an organism and innovation. An increase in red blood cells can help a person or group living at high elevations to move and breathe more easily because more red cells can carry more oxygen. But additional red cells also thicken the blood. Add too many, and "it's like pumping oil," in the words of Temple University anthropologist Charles Weitz. That's hard on the heart. Thus those designed to live at high altitude get increased breathing efficiency, but pay for it with higher-risk hearts. By such means does Darwinian natural selection look after us. It also helps to explain why we are all so similar. Evolution simply won't let you become too different—not without becoming a new species anyway.

The 0.1 percent difference between your genes and mine is accounted for by our Snips. Now if you compared your DNA with a third person's, there would also be 99.9 percent correspondence, but the Snips would, for the most part, be in different places. Add more people to the comparison and you will get yet more Snips in yet more places. For every one of your 3.2 billion bases, somewhere on the planet there will be a person, or group of persons, with different coding in that position. So not only is it wrong to refer to "the" human genome, but in a sense we don't even have "a" human genome. We have six billion of them. We are all 99.9 percent the same, but equally, in the words of the biochemist David Cox, "you could say all humans share nothing, and that would be correct, too."

But we have still to explain why so little of that DNA has any discernible purpose. It starts to get a little unnerving, but it does really seem that the purpose of life is to perpetuate DNA. The 97 percent of our DNA commonly called junk is largely made up of clumps of letters that, in Ridley's words, "exist for the pure and simple reason that they are good at getting themselves duplicated."[2] Most of your DNA, in other words, is not devoted to you but to itself: you are a machine for reproducing it, not it for you. Life, you will recall, just wants to be, and DNA is what makes it so.

Even when DNA includes instructions for making genes—when it codes for them, as scientists put it—it is not necessarily with the smooth functioning of the organism in mind. One of the commonest genes we have is for a protein called reverse transcriptase, which has no known beneficial function in human beings at all. The one thing itdoes do is make it possible for retroviruses, such as the AIDS virus, to slip unnoticed into the human system.

In other words, our bodies devote considerable energies to producing a protein that does nothing that is beneficial and sometimes clobbers us. Our bodies have no choice but to do so because the genes order it. We are vessels for their whims. Altogether, almost half of human genes—the largest proportion yet found in any organism—don't do anything at all, as far as we can tell, except reproduce themselves.

All organisms are in some sense slaves to their genes. That's why salmon and spiders and other types of creatures more or less beyond counting are prepared to die in the process of mating. The desire to breed, to disperse one's genes, is the most powerful impulse in nature. As Sherwin B. Nuland has put it: "Empires fall, ids explode, great symphonies are written, and behind all of it is a single instinct that demands satisfaction." From an evolutionary point of view, sex is really just a reward mechanism to encourage us to pass on our genetic material.

Scientists had only barely absorbed the surprising news that most of our DNA doesn't do anything when even more unexpected findings began to turn up. First in Germany and then in Switzerland researchers performed some rather bizarre experiments that produced curiously unbizarre outcomes. In one they took the gene that controlled the development of a mouse's eye and inserted it into the larva of a fruit fly. The thought was that it might produce something interestingly grotesque. In fact, the mouse-eye gene not only made a viable eye in the fruit fly, it made a fly's eye. Here were two creatures that hadn't shared a common ancestor for 500 million years, yet could swap genetic material as if they were sisters.

The story was the same wherever researchers looked. They found that they could insert human DNA into certain cells of flies, and the flies would accept it as if it were their own.

2 Junk DNA does have a use. It is the portion employed in DNA fingerprinting. Its practicality for this purpose was discovered accidentally by Alec Jeffreys, a scientist at the University of Leicester in England. In 1986 Jeffreys was studying DNA sequences for genetic markers associated with heritable diseases when he was approached by the police and asked if he could help connect a suspect to two murders. He realized his technique ought to work perfectly for solving criminal cases-and so it proved. A young baker with the improbable name of Colin Pitchfork was sentenced to two life terms in prison for the murders.

Over 60 percent of human genes, it turns out, are fundamentally the same as those found in fruit flies. At least 90 percent correlate at some level to those found in mice. (We even have the same genes for making a tail, if only they would switch on.) In field after field, researchers found that whatever organism they were working on—whether nematode worms or human beings—they were often studying essentially the same genes. Life, it appeared, was drawn up from a single set of blueprints.

Further probings revealed the existence of a clutch of master control genes, each directing the development of a section of the body, which were dubbed homeotic (from a Greek word meaning "similar") or hox genes. Hox genes answered the long-bewildering question of how billions of embryonic cells, all arising from a single fertilized egg and carrying identical DNA, know where to go and what to do—that this one should become a liver cell, this one a stretchy neuron, this one a bubble of blood, this one part of the shimmer on a beating wing. It is the hox genes that instruct them, and they do it for all organisms in much the same way.

Interestingly, the amount of genetic material and how it is organized doesn't necessarily, or even generally, reflect the level of sophistication of the creature that contains it. We have forty-six chromosomes, but some ferns have more than six hundred. The lungfish, one of the least evolved of all complex animals, has forty times as much DNA as we have. Even the common newt is more genetically splendorous than we are, by a factor of five.

Clearly it is not the number of genes you have, but what you do with them. This is a very good thing because the number of genes in humans has taken a big hit lately. Until recently it was thought that humans had at least 100,000 genes, possibly a good many more, but that number was drastically reduced by the first results of the Human Genome Project, which suggested a figure more like 35,000 or 40,000 genes—about the same number as are found in grass. That came as both a surprise and a disappointment.

It won't have escaped your attention that genes have been commonly implicated in any number of human frailties. Exultant scientists have at various times declared themselves to have found the genes responsible for obesity, schizophrenia, homosexuality, criminality, violence, alcoholism, even shoplifting and homelessness. Perhaps the apogee (or nadir) of this faith in biodeterminism was a study published in the journal Science in 1980 contending that women are genetically inferior at mathematics. In fact, we now know, almost nothing about you is so accommodatingly simple.

This is clearly a pity in one important sense, for if you had individual genes that determined height or propensity to diabetes or to baldness or any other distinguishing trait, then it would be easy—comparatively easy anyway—to isolate and tinker with them. Unfortunately, thirty-five thousand genes functioning independently is not nearly enough to produce the kind of physical complexity that makes a satisfactory human being. Genes clearly therefore must cooperate. A few disorders—hemophilia, Parkinson's disease, Huntington's disease, and cystic fibrosis, for example—are caused by lone dysfunctional genes, but as a rule disruptive genes are weeded out by natural selection long before they can become permanently troublesome to a species or population. For the most part our fate and comfort—and even our eye color—are determined not by individual genes but by complexes of genes working in alliance. That's why it is so hard to work out how it all fits together and why we won't be producing designer babies anytime soon.

In fact, the more we have learned in recent years the more complicated matters have tended to become. Even thinking, it turns out, affects the ways genes work. How fast a man's beard grows, for instance, is partly a function of how much he thinks about sex (because thinking about sex produces a testosterone surge). In the early 1990s, scientists made an even more profound discovery when they found they could knock out supposedly vital genes from embryonic mice, and the mice were not only often born healthy, but sometimes were actually fitter than their brothers and sisters who had not been tampered with. When certain important genes were destroyed, it turned out, others were stepping in to fill the breach. This was excellent news for us as organisms, but not so good for our understanding of how cells work since it introduced an extra layer of complexity to something that we had barely begun to understand anyway.

It is largely because of these complicating factors that cracking the human genome became seen almost at once as only a beginning. The genome, as Eric Lander of MIT has put it, is like a parts list for the human body: it tells us what we are made of, but says nothing about how we work. What's needed now is the operating manual—instructions for how to make it go. We are not close to that point yet.

So now the quest is to crack the human proteome—a concept so novel that the term proteome didn't even exist a decade ago. The proteome is the library of information that creates proteins. "Unfortunately," observed Scientific American in the spring of 2002, "the proteome is much more complicated than the genome."

That's putting it mildly. Proteins, you will remember, are the workhorses of all living systems; as many as a hundred million of them may be busy in any cell at any moment. That's a lot of activity to try to figure out. Worse, proteins' behavior and functions are based not simply on their chemistry, as with genes, but also on their shapes. To function, a protein must not only have the necessary chemical components, properly assembled, but then must also be folded into an extremely specific shape. "Folding" is the term that's used, but it's a misleading one as it suggests a geometrical tidiness that doesn't in fact apply. Proteins loop and coil and crinkle into shapes that are at once extravagant and complex. They are more like furiously mangled coat hangers than folded towels.

Moreover, proteins are (if I may be permitted to use a handy archaism) the swingers of the biological world. Depending on mood and metabolic circumstance, they will allow themselves to be phosphorylated, glycosylated, acetylated, ubiquitinated, farneysylated, sulfated, and linked to glycophosphatidylinositol anchors, among rather a lot else. Often it takes relatively little to get them going, it appears. Drink a glass of wine, as Scientific American notes, and you materially alter the number and types of proteins at large in your system. This is a pleasant feature for drinkers, but not nearly so helpful for geneticists who are trying to understand what is going on.

It can all begin to seem impossibly complicated, and in some ways itis impossibly complicated. But there is an underlying simplicity in all this, too, owing to an equally elemental underlying unity in the way life works. All the tiny, deft chemical processes that animate cells—the cooperative efforts of nucleotides, the transcription of DNA into RNA—evolved just once and have stayed pretty well fixed ever since across the whole of nature. As the late French geneticist Jacques Monod put it, only half in jest: "Anything that is true of E. coli must be true of elephants, except more so."

Every living thing is an elaboration on a single original plan. As humans we are mere increments—each of us a musty archive of adjustments, adaptations, modifications, and providential tinkerings stretching back 3.8 billion years. Remarkably, we are even quite closely related to fruit and vegetables. About half the chemical functions that take place in a banana are fundamentally the same as the chemical functions that take place in you.

It cannot be said too often: all life is one. That is, and I suspect will forever prove to be, the most profound true statement there is.

Chapter 26: The Stuff of Life

1. What do the letters DNA stand for?

2. Because of Mendel, scientists knew that some sort of "packets" of hereditary information was passed from one generation to the next. What do we call these packets today? Where are they located in your body? What are they made of?

3. Why has the fruit fly (*Drosophila melanogaster*) proved to be so important for much or our understanding of genetics?

4. The quest to discover and define the molecule responsible for inheritance is filled with much of what scientific progress is really like – building on previous discoveries, experimental evidence, theoretical hypotheses, as well as competition, desire for recognition and fame, conflicting egos and personalities. Science as a "pure" process is carried out by people, and people are emotional beings. This combination of a logical process practiced by emotional beings both helps and hinders the progression of knowledge. Identify the various logical and emotional events leading to the discovery of DNA (pp. 403-407).

5. One characteristic of DNA is its ability to replicate itself. Why is this important? Sometimes, mistakes are made during DNA replication. Why are such mistakes potentially harmful? Why are such mistakes necessary for evolution?

6. Why is potentially 97% of human DNA referred to as "junk DNA"? What does this imply about how much DNA actually instructs the formation of organisms? What might it imply about our knowledge of DNA?

7. On average, Bryson reports that individual human genomes are 99.9% similar. When comparing human and chimp DNA, scientists estimate that anywhere from 95-98.8% similarity. Even humans and fruit flies share approximately 60% DNA similarity. What does this imply about DNA? About evolutionary relatedness?

8. What was the Human Genome Project? How many genes do humans have? How does this compare to other organisms?