

Author Bill Bryson set out to answer the question “how we went from there being nothing at all to there being something and how a little of that something turned into us and also some of what happened in between and since.” This chapter entitled “Cells” is a wonderful description of the basic units of life.
Bryson, Bill. A Short History of Nearly Everything. New York: Broadway Books, 2003.

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

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.*

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 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 hand held 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

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.*

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.

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 *everywhere* 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.