# THE STUFF CALLED LIFE

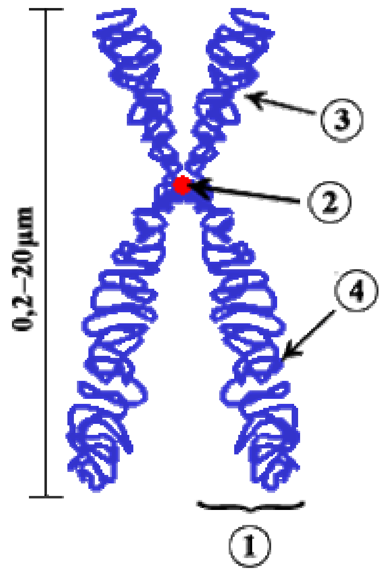
## CHROMOSOMES(A package for carrying DNA in the cells)

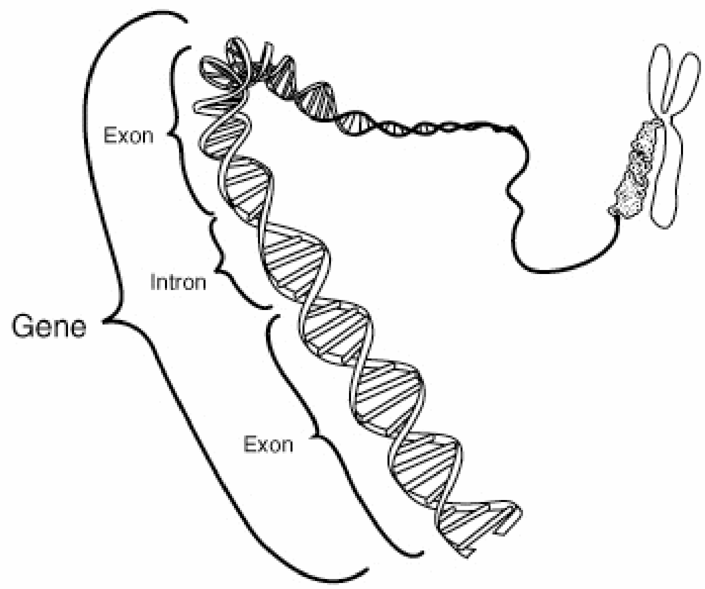
In the nucleus of each cell, the DNA molecule is packaged into thread-like structures called chromosomes. Each chromosome is made up of DNA tightly coiled many times around proteins called histones that support its structure.

Chromosomes are not visible in the cell's nucleus—not even under a microscope—when the cell is not dividing. However, the DNA that makes up chromosomes becomes more tightly packed during cell division and is then visible under a microscope. Most of what researchers know about chromosomes was learned by observing chromosomes during cell division.

Different species of plants and animals have different numbers and sizes of chromosomes.

## CHROMOSOME




## GENE(A segment of DNA)

The function of genes is to provide the information needed to make molecules called proteins in cells

. Genes are like sentences made of the "letters" of the nucleotide alphabet, between them genes direct the physical development and behavior of an organism. Genes are like a recipe or instruction book, providing information that an organism needs so it can build or do something - like making an eye or a leg, or repairing a wound.

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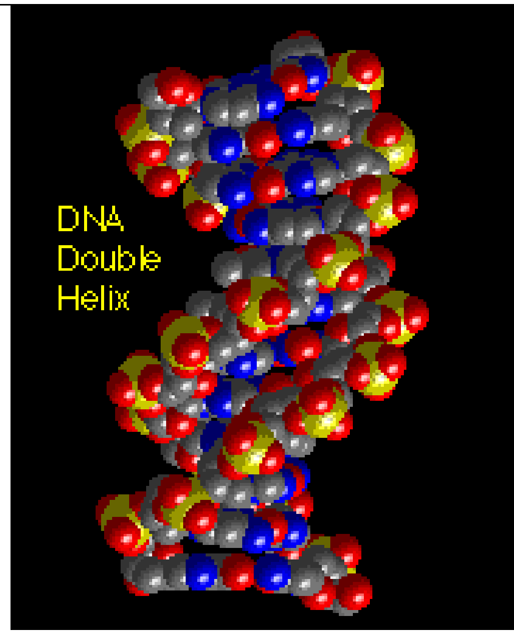
| DNA(A long molecule that looks like a twisted ladder carrying genetic information)<br><br>It is made of four types of simple units and the sequence of these units carries information, just as the sequence of letters carries information on a page.<br><br>DNA is copied and inherited across generations. Traits are carried in DNA as instructions for constructing and operating an organism. These instructions are contained in segments of DNA called genes. DNA is made of a sequence of simple units, with the order of these units spelling out instructions in the genetic code. This is similar to the orders of letters spelling out words. The organism "reads" the sequence of these units and decodes the instruction. |  |

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.

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

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.

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."

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. 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.

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.

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.

Excerpts from A Brief History Of Nearly Everything
By Bill Bryson
Courtesy : A.K.Otta