

WHAT A WONDERFUL WORLD

*One Man's Attempt to Explain  
the Big Stuff*

MARCUS CHOWN



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## PART ONE: How we work

I:

I AM A GALAXY

*Cells*

A good case can be made for our non-existence as  
entities.

LEWIS THOMAS

There's someone in my head and it's not me.

PINK FLOYD

I think I am me. But I am not. I am a galaxy. In fact, I am a thousand galaxies. There are more cells in my body than there are stars in a thousand Milky Ways. And, of all those myriad cells, not a single one knows who I am or cares. *I* am not even writing this. The thought was actually a bunch of brain cells – neurons – sending electrical signals down my spinal cord to another bunch of cells in the muscles of my hand.<sup>1</sup>

Everything I do is the result of the coordinated action of untold trillions upon trillions of cells. ‘I like to think my cells work in *my* interest, that each breath they draw for *me*, but perhaps it is *they* who walk through a park in the early morning, sensing my senses, listening to my music, thinking my thoughts,’ wrote American biologist Lewis Thomas.<sup>2</sup>

The first step on the road to discovering that each and every one of us is a super-colony of cells was the discovery of the cell itself. Credit for this goes to Dutch linen merchant Antonie van Leeuwenhoek. Aided by a tiny magnifying glass he had adapted from one used to check the fibre density of fabrics, he became the first person in history to *see* a living cell. In a letter published in April 1673 in the *Philosophical Transactions* of the Royal Society of London, van Leeuwenhoek wrote, ‘I have observ’d taking some blood out of my hand that it consists of small round globuls.’

The term ‘cell’ had actually been coined two decades earlier by the English scientist Robert Hooke. In 1655, he had examined

plant tissue and noticed dead compartments stacked together. However, neither he nor van Leeuwenhoek realised that cells are the Lego bricks of life. But that is what they are. A cell is the ‘biological atom’. There is no life – as far as we know – *except cellular life*.

*Prokaryotes: a protected micro-universe*

The first evidence of cells comes from fossils about 3.5 billion years old. But there is more tentative evidence, from about 3.8 billion years ago, in the shape of telltale chemical imbalances in rocks that are characteristic of living things. The first cells, known as prokaryotes, were essentially just tiny transparent bags of gloop less than a thousandth of a millimetre across. The bag, by concentrating stuff inside, speeded up key chemical reactions such as those that generate energy. It also protected proteins and other fragile products of those reactions from toxic substances such as acids and salt in the environment. The bag of gloop was an island haven in an ocean of disorder and chaos, a protected micro-universe where order and complexity might safely grow.

The complexity of such cells was in large part due to the proteins – megamolecules assembled from amino-acid building blocks and made of millions of atoms. Depending on their shape and chemical properties, these Swiss-army-knife molecules can carry out a myriad tasks, from speeding up chemical reactions to acting as cellular scaffolding to flexing like coiled springs to power the movement of cells. Even a simple bacterium possesses about four thousand different proteins, though some proteins, such as those needed for reproduction, are assembled, or expressed, only intermittently. The structure of these proteins is encoded by

deoxyribonucleic acid, or DNA, a double-helical molecule floating freely as a loop in the chemical soup, or cytoplasm, inside a cell.

Cellular structure is beautifully intricate. First, there is the bag, or membrane. This is made of fatty acids, molecules that are characterised by having a water-loving end and a water-hating end. When such lipids come together in large numbers – typically a billion – they spontaneously self-assemble into two layers, with their water-hating ends on the interior and their water-loving ends on the outside.

The lipid layers that enclose a cell are not a passive barrier. Far from it. This double skin regulates the molecules coming in and going out of the cell. Imagine the cell as an ancient city surrounded by a wall. In the same way that small creatures such as mice can pass easily back and forth through the city wall, small molecules can pass unhindered in and out of the cell membrane. And, just as bigger creatures such as people are admitted only through gates in a city wall, the passage of big molecules is regulated by ‘gates’ in the cell membrane. For instance, there are proteins shaped like hollow tubes spanning the width of the membrane through which bigger molecules can tunnel into and tunnel out of the cell. And there are transporter proteins whose job is to shuttle bigger molecules physically from one side of the membrane to the other.

The molecules that come in to the cell are those needed for energy and to make proteins and to provide information about the outside world. For instance, an abundance in the surrounding environment of molecules necessary for building new cells might trigger a cell to reproduce.<sup>3</sup> On the other hand, a shortage of water molecules coming across the membrane might warn a cell

that it is in danger of drying out. This might trigger a cascade of chemical reactions inside the cell, ultimately causing a stretch of DNA to be copied repeatedly into molecules called ribonucleic acid, or RNA. These find their way to ribosomes, nanomachines that use the RNA templates to make proteins that might be components of a mucus that will protect the cell from dehydration.<sup>4</sup> Too big to pass through the cell membrane, the proteins flooding out through the cytoplasm in their millions are packaged into membrane sacs, or vesicles, which fuse with the cell membrane. The membrane can then open up, without rupturing and losing its structural integrity, and cast them into the outside world.

But cells, in addition responding to molecules in their environment, also respond to molecules from *other cells*. Even the simplest and most ancient prokaryotes cooperated with each other, which is revealed by fossils of large microbial communities known as stromatolites. Living stromatolites can still be found today – for instance, in shallow tropical waters off the western coast of Australia – but the oldest of these fossil communities is about 3.5 billion years old.

At the same time that a cell makes proteins to protect itself from environmental changes, it might produce proteins that warn others of its kind to do the same. Such chemical signalling is crucial to the survival of simple prokaryotes, which often live in huge colonies known as biofilms, quite possibly the first organised structures to appear on Earth. The cells on the inside of such a biofilm might secrete a sugary protein that sticks their membranes to the membrane of other cells, whereas those on the outside of the film might produce proteins that help protect them from environmental toxins. Some cells will even kill themselves in order to yield up precious nitrogen for the good of their com-

panions. This kind of cooperation, with cells within a group differentiating to carry out different tasks, is reminiscent of the cells in our bodies. It hints at how such cellular super-cooperation might have got started billions of years ago.

There are limits on the size and complexity of prokaryotes. For one thing, the proteins assembled, or expressed, by their DNA can travel only by drifting slowly, or diffusing, across a cell. Beyond a certain size, a prokaryote is therefore suicidally slow in reacting to environmental dangers. This problem has been solved by rare prokaryotes such as *Thiomargarita namibiensis*, discovered only in 1997. The giant sulphur bacterium, which is about 0.75 millimetres across and easily visible to the naked eye, possesses not one loop of DNA but *thousands*, spread evenly throughout its cytoplasm. This means that proteins expressed by local strands of DNA, even if they diffuse slowly, can still get to all parts of the cell rapidly.

But there is another serious problem that keeps prokaryotes small. The bigger one of them grows the more energy it needs. If it were to use the strategy of *T. namibiensis*, however, an increasing proportion of that energy would be needed for manipulating large quantities of DNA. Since this would be at the expense of any other cellular processes, the road to increased complexity is well and truly blocked.

But there is another way to grow big: take up cannibalism.

### *Eukaryotes: cities in bags*

About 1.8 billion years ago, a prokaryote swallowed another prokaryote. Prokaryotes actually include bacteria and more exotic archaea bacteria, microorganisms that survive in extreme

environments such as boiling sulphur springs and so were probably among the first life forms on Earth.<sup>5</sup> What actually happened 1.8 billion years ago was that an *archaeobacterium* swallowed a *bacterium*.

Such an event must have occurred innumerable times before. But, in all cases, the bacterium was either devoured or spat out. This time, for some unknown reason, the bacterium survived. More than that. *It thrived*. There was some mutual benefit for the swallower and swallowee. The latter found a protective environment, safe from the hostile outside world, and the former a new power source.

The evidence that something like this did indeed happen was gathered by the American biologist Lynn Margulis (the first wife of TV astronomer Carl Sagan). And the evidence is still around us today. The energy-generating mitochondria inside the eukaryotic cells of all animals are not only the same size as free-living bacteria but they *look like them too*.<sup>6</sup> Even more striking, they have their own DNA, which is separate and distinct from the DNA of the whole cell, and fashioned into a loop exactly as in prokaryotes.

In fact eukaryotes may have hundreds, or even thousands, of such mitochondria. These are self-contained power stations, furiously reacting hydrogen from food with oxygen to make life's mobile power packs, adenosine triphosphate, or ATP.<sup>7</sup> 'My mitochondria comprise a very large proportion of me,' wrote American biologist Lewis Thomas. 'I suppose there is almost as much of them in sheer dry weight as there is of the rest of me. Looked at this way, I could be taken for a very large, motile colony of respiring bacteria.'<sup>8</sup>

With a cell's mitochondria working semi-autonomously in this way, it is no longer necessary for it to devote so much of its DNA

to the task of generating energy. The DNA is free to encode other things, other protein nanomachinery. Consequently, when cells gained mitochondria 1.8 billion years ago, they were suddenly free to grow a whole lot bigger and more complex.

A large eukaryote compared with a typical prokaryote is like a cat beside a flea. Such a mega-cell might contain hundreds, even thousands, of membrane-enshrouded bags. These organelles divvy up the chores of the cell, functioning as the equivalent of factories, post-office sorting offices and other specialist buildings in a modern-day city.

Lysosomes, for instance, are the garbage-disposal units of the cell. They break down molecules such as proteins into their building blocks so they can be used again. The reason the lettuce in your burger wilts is that heat from the beef breaks down the lysosome membranes of the lettuce cells. This unleashes enzymes, which devour the lettuce. Other organelles include the rough endoplasmic reticulum, which acts like a cellular DHL office. Dotted with ribosomes, it translates RNA arriving from the nucleus into proteins destined for foreign parts beyond the cell. Yet another organelle is the Golgi apparatus, which acts like a packaging centre. It can modify proteins, wrapping them, for instance, in a sugar coating that absorbs water. Such proteins can be used to make the surfaces of blood cells slimy so they can move about more easily.<sup>9</sup>

In fact, a eukaryotic cell is less like a single organism than a colony of organisms, each of which long ago lost its ability to survive alone. 'For the first half of geological time our ancestors were bacteria,' says Richard Dawkins. 'Most creatures still are bacteria, and each one of our trillions of cells is a colony of bacteria.' And all of this has come about by chance. 'The mitochondrion that

first entered another cell was not thinking about the future benefits of cooperation and integration,' says Stephen Jay Gould. 'It was merely trying to make its own living in a tough Darwinian world.'<sup>10</sup>

The organelles are subservient to the cell's nucleus, which contains its DNA and orchestrates pretty much all cellular activity. The English botanist Robert Brown recognised the nucleus as a common feature of complex cells in 1833.<sup>11</sup> Enclosed in a double membrane, the nucleus is reminiscent of a walled castle inside the walled city of the cell. The membrane controls the passage of molecules into the nucleus and the passage of proteins expressed by the DNA out of the nucleus.

The presence of a nucleus is one of the defining features of a eukaryote, along with the presence of a plethora of organelles. A prokaryote has neither a nucleus nor organelles. In fact, the very word *prokaryote* means 'before kernel, or nucleus', while *eukaryote* means 'true nucleus'. Very probably, a nucleus is a necessity in a cell as complex as a eukaryote because of the need to protect the precious DNA from the frenzied activity going on in every corner.<sup>12</sup>

In addition to having a nucleus and a large number of organelles, a eukaryote contrasts with a prokaryote in having a cytoskeleton. Proteins such as tubulin form long scaffolding poles that criss-cross the cell. Such microtubules stiffen the soft bag of the cell, giving it a shape. They also anchor organelles to the membrane. This ensures that they are arranged in a similar way in all eukaryotes much as internal organs are arranged in a similar way in all humans. But, in addition to providing internal scaffolding, microtubules act as an internal rail network that can rapidly transport material about the cell. They do this by growing

at one end and disintegrating at the other, so, bizarrely, *it is the track rather than the train that provides the motive power*. Newly made proteins, enclosed in bags, or vesicles, simply hop on a convenient microtubule and are instantly speeded off to a far-away destination within the cell.

The cellular rail network enables a eukaryote to overcome one of the biggest obstacles preventing a prokaryote becoming big: getting stuff around the cell. A eukaryote, rather than having to wait for proteins to diffuse slowly through the cytoplasm, speeds them around on its rapid transit network.

But eukaryotes, despite being an enormous advance over prokaryotes, also have their limits. Orchestrating organelles is a complex activity. If a cell contained more than a few thousand of them, such orchestration would be beyond the capability of a nucleus. Eukaryotes, like prokaryotes, are a biological dead end. The way to increasing complexity lies in another direction – in cooperation on an unprecedented scale.

### *Multicellular organisms*

From the moment they arose, eukaryotes almost certainly cooperated with each other in increasingly sophisticated ways. But, about 800 million years ago, they crossed a critical threshold. Nature had put together colonies of symbiotic prokaryotes to make eukaryotes. Now it repeated the trick. It put together colonies of symbiotic eukaryotes to make multicellular organisms.

The fact that life on Earth spent about 3 billion years at the single-cell stage before it took the step to the multicellular stage is probably telling us that the step is a difficult one. This has implications for the prospects of finding extraterrestrial life.

Despite fifty years of searching, astronomers have seen no sign of intelligence elsewhere in our Galaxy. One possibility is that life is common in the Milky Way but only in the form of single-celled microorganisms.

Humans – as well as animals, plants and fungi – are all multi-cellular organisms. Each of us is a colony of about 100 million million cells. They come in about 230 different types, ranging from brain cells and blood cells to muscle cells and sex cells, and all are enclosed in a bag made of skin cells, no less a container than the membrane of a single cell.

Each cell has its own copy of the same DNA (apart from blood cells in their mature form, which are so utilitarian they lack even a nucleus). But whether a cell becomes a kidney cell or a pancreatic cell or a skin cell depends on the particular section of the DNA that is read, or expressed. This, in turn, depends on regulatory genes – themselves stretches of DNA – which can turn off and turn on the reading of DNA, depending on things such as the concentration of a particular chemical in the locality.

Each of the 100 million million cells that makes up a human being is a micro-world as complex as a major city, buzzing with the ceaseless activity of billions of nanomachines. It has storehouses, workshops, administrative centres and streets heaving with traffic. ‘Power plants generate the cell’s energy,’ says American journalist Peter Gwynne. ‘Factories produce proteins, vital units of chemical commerce. Complex transportation systems guide specific chemicals from point to point within the cell and beyond. Sentries at the barricades control the export and import markets, and monitor the outside world for signs of danger. Disciplined biological armies stand ready to grapple with invaders. A centralised genetic government maintains order.’<sup>13</sup>

And all of this is going on every moment of every day of our lives while we remain utterly oblivious to it. In the words of biologist and writer Adam Rutherford, ‘Each movement, every heartbeat, thought, and emotion you’ve ever had, every feeling of love or hatred, boredom, excitement, pain, frustration or joy, every time you’ve ever been drunk and then hungover, every bruise, sneeze, itch or snotty nose, every single thing you’ve ever heard, seen, smelt or tasted *is your cells communicating with each other and the rest of the Universe.*’<sup>14</sup>

We all start our lives as a single cell when a sperm, the smallest cell in the body, fuses with an ovum, the biggest cell in the body and one actually visible to the naked eye. Every human in fact spends about half an hour as a single cell before it splits into two. This is a phenomenal process in itself. In a mere thirty minutes, not only must a cell make a copy of its DNA – a process that, for speed, occurs simultaneously at multiple sites on the DNA – but it must construct something like 10 billion complex proteins. This is more than *100,000 a second*.

Within sixty minutes, the two cells split into four, then later eight, and so on. After several divisions, chemical differences across the developing embryo cause the cells to differentiate. It is a process that culminates in cells ‘knowing’ they have to be kidney cells or brain cells or skin cells. Over years, a single cell becomes a galaxy of cells – or, rather, a *thousand galaxies of cells*.

Hardly any of the cells in your body – apart from brain cells – are permanent. The cells lining the wall of the stomach are bathed in hydrochloric acid strong enough to dissolve a razor blade, so must be remade constantly. You get a new stomach lining every three or four days. Blood cells last longer but even they self-destruct after about four months. It is fair to say

that you are pretty much a new person every seven years, something that maybe explains the seven-year itch. You look at your partner and suddenly think, ‘That’s not the person I got together with!’

The cells of your body die in such prodigious numbers that, simply to replace them, you must build about 300 billion new cells every day. That is more cells than there are stars in our Galaxy. No wonder it can be tiring doing nothing.

### *Aliens*

There may be an astronomical number of cells in your body. But they are not able to carry out all the functions necessary for your survival. Not without assistance from legions of alien cells such as prokaryotes, fungi and single-celled animals called protozoans.<sup>15</sup> In your stomach, for instance, hundreds of species of bacteria work constantly to extract nutrients from your food. If some of these ‘good’ bacteria are inadvertently killed by antibiotics, the result can be an affliction such as diarrhoea.

The alien bacteria protect you from illness by filling niches in your body that otherwise might be filled by disease-causing pathogens. The Human Microbiome Project, a five-year study funded by the US government, presented its findings in 2012. It found that the nasal passages of about 29 per cent of people contain *Staphylococcus aureus* – better known as the MRSA superbug. Since such people suffer no ill effects, the implication is that in healthy people the bugs act as good bacteria, keeping harmful pathogens at bay.

Remarkably, the Human Microbiome Project found that there are more than 10,000 species of alien cells in your body – 40 times

the number of cell types that actually belong to you. You are only 2.5 per cent human. In fact, about 5 million bacteria call every square centimetre of your skin home. The most densely populated regions are your ears, the back of the neck, the sides of the nose and your belly button. What all these alien bacteria are doing is a mystery. The Human Microbiome Project found that 77 per cent of the species in your nose, for instance, have completely unknown functions.

The sheer number of alien bacteria in your body might actually underrate their importance. The Human Microbiome Project found that microorganisms that inhabit your body have a total of at least 8 million genes, each of which codes for a protein with a specific purpose. By contrast, the human genome contains a mere 23,000 genes.<sup>16</sup> Consequently, there are about 400 times as many microbial genes exerting their effect on your body as human genes. In a sense, you are not even as much as 2.5 per cent human – you are merely 0.25 per cent human.

Since the alien cells in your body are largely prokaryotes, which are much smaller than eukaryotes, they add up to a few kilograms or a mere 1–3 per cent of your mass. They are not encoded by your DNA but infected you after birth, via your mother's milk or directly from the environment. They were pretty much all in place by the time you were three years old. It is fair to say that we are born 100 per cent human but die 97.5 per cent alien.

### *The biological event horizon*

Every cell is born from another cell. '*Omnis cellula e cellula*', as François-Vincent Raspall first recognised in 1825. Consequently,

every cell in our body – every cell on the Earth – can trace its ancestry in an unbroken line back to the very first cell, which appeared about 4 billion years ago. The first cell is generally referred to as the last universal common ancestor, or LUCA. Nobody knows how exactly it came about. Undoubtedly, there was a vast amount of experimentation – a huge amount of pre-evolution – before nature hit on the design.

Mistakes, or mutations, in genes accumulate at a steady rate over time. So, if one species has twice as many mutations of a particular gene as a second species, we can say it split from a common ancestor twice as far back. This is how the tree of life, first envisaged by Charles Darwin, is constructed. However, bacteria have an inconvenient habit of swapping DNA as well as passing DNA to their descendants. This means that, in the vicinity of LUCA, the tree of life is less a tree and more like an impenetrable thicket.

In physics, scientists talk of the ‘event horizon’ of a black hole – the point of no return for infalling matter. It cloaks the black hole so that nothing can be seen of its interior. Similarly, biologists talk of the biological event horizon beyond which nothing can be known. There, unfortunately, lies LUCA.

Since the time of LUCA, the Earth, despite dabbling in multicellularity, has been a bacterial world. There are believed to be something like 10,000 billion billion billion bacteria on our planet. That is a billion times more bacteria than there are stars in the observable Universe. But this might not give a true picture of terrestrial biology. Consider viruses. ‘We live in a dancing matrix of viruses,’ wrote Lewis Thomas. ‘They dart, rather like bees, from organism to organism, from plant to insect to mammal to me and back again, and into the sea, tugging along pieces of this

genome, strings of genes from that, translating grafts of DNA, passing around heredity as though at a great party.<sup>17</sup> Incapable of reproducing without hijacking the machinery of cells, viruses are generally not considered to be precursors of cellular life. But who knows?