THE SECRET LIFE OF CELLS
The history of everything that lives and what we are made of

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Introduction

When I first saw my own cells, I was so excited that I accidentally smashed my nose on the microscope. I was in a brightly-lit laboratory at the University of Oslo, and had just carefully scraped the inside of my cheek with a q-tip. This can't possibly work, I'd thought pessimistically, before pressing the cotton swab onto the little glass slide. Cells don't come off *that* easily do they? I placed the sample under the microscope lens while cursing my eyelashes which always got in the way as I adjusted the focus. But then, finally, I could see them: thin, knobbly flakes with a tiny round core. They reminded me of the birch-tree seeds that fall to the ground in the summer. So here they were, the tiny, mythical units I had read so much about. A tiny cluster of my trillions of cells was there in front of me.

I was totally captivated.

' I can see them, I can see my cells! 'I yelled behind me, before quickly turning back to the lens, *too quickly*, smashing my face into the eyepiece. It left me with a large, red bruise that lasted the rest of the day – and an entirely new plan for the next few years. Since then I've completed a PhD in cell biology and spent many long workdays behind a microscope. Although I've lost count of the hours I have sat peering down a lens, I am still discovering new things. I have given cells the DNA from luminous jellyfish and watched as they light up under the microscope. I have filmed immune cells stretching curiously towards each other, and cancer cells as they multiply. When a cell divides, I think it looks like a firework.

Most of what happens in our bodies goes unseen by the naked eye. In this book I'll give you a glimpse of the invisible world within us: what's hiding in our bones and creeping through our skin. I will show you the tiny, strange-looking building blocks that work so hard at keeping us alive, every second of every day.

I don't hope you will smash your nose against this book. But I do hope you will be equally captivated.

1
The hidden universe

In 1665, a new bestseller was published in London. It was neither a love story nor a gripping crime novel. Instead, the book everyone was talking about became best known for its gigantic and detailed fold-out portrait of a flea. *Micrographia* was the world's first fully-illustrated, popular science book on microscopy.

The work was commissioned by the King of England himself. King Charles II had been sent a few drawings of insects which had been enlarged to monstrous dimensions, and was thrilled. He wanted more and asked The Royal Society of London to produce a book that showed and explained microscopic observations. The assignment went to the physicist and mathematician Robert Hooke, who was already fascinated in microscopy and had previously shown several of his observations to the Royal Academy of Sciences. Hooke's microscope consisted of a wooden tube attached to a brass stand. The tube was covered in leather, beautifully decorated with swirling gold patterns, and had three lenses inside for magnifying the sample. Hooke peered through the top of the tube and turned a screw to focus. For better illumination he concentrated light onto the sample using an oil lamp and a round, water-filled glass flask.[1]

The first illustrations in *Micrographia* were of a needle point, a razor blade, and a full stop taken from a printed book. Totally ordinary things – but when viewed through a microscope, they totally change. The needle is no longer sharp, the smooth razor-blade is actually jagged, and the round full stop at the end of a sentence just like this, looks like a scraggly hairball. All these man-made things, Hooke stressed, are full of imperfections.[2] Nature, on the other hand, was shown to be more complex and beautiful than anyone could have imagined. Even a simple insect became almost majestic once it was under the microscope. When Hooke describes a flea, he is isn't looking at an irritating pest, but a beautiful creature dressed in polished armour, with bright, black eyes.[3] And after looking at a louse under the microscope, he describes it as 'so proud and aspiring with all, that it fears not to trample on the best'[4] – before showing a monster with six hairy legs clinging to a human hair. In the name of science, he even let the louse suck blood from his own finger, then observed how the blood flowed from the little creature's mouth and into its stomach. He also studied ants, but they were trickier to handle because they tended to move around too much. The solution, it turned out, was to dip them in brandy which made them relaxed and somewhat inebriated, like partygoers at the end of a boozy night.[5]

Hooke showed the world that there is more to life than our senses can perceive. His microscope revealed not only new details, but also entirely new creatures that no one had ever imagined. The hairy moulds growing on one of his more worn-out books resembled an extraterrestrial garden. He depicted elegant little shoots with transparent stems, some topped with white balls, others which looked like flowers. It was probably the world's first description of a microorganism: the mould *Mucor*.[6] The white balls, in any case, contained the spores this fungus makes to reproduce. And when they burst open, they take on the specific flower-like shape Hooke observed.

Micrographia quickly became a success, largely thanks to Hooke's striking illustrations and simple language. Instead of devising new and advanced concepts, he compared what he saw with everyday things. One of his most enthusiastic fans was Samuel Pepys who in the 1600s was the closest you can get to an influencer.

Pepys is best known for his diary, which over the course of nine years depicts everything from political events to everyday life in London. The diary features comments on key events such as the Great Fire of London and the Coronation of Charles II. It is also full of everyday details: We learn what time he got up in the morning and what he saw at the theatre. When describing the Great Fire, he writes about digging a hole in his garden to save important possessions from the flames. This included papers from the office and, not least, his much-loved wine and Parmesan cheese.[7] Pepys also writes of his many romantic affairs, but is careful to use his own 'coded language' (based on a combination of Spanish and French among other things) in the raciest passages.[8] It was probably best his wife didn't find out what happened in the bedroom between him and the chambermaid.

One January day in 1665, the 32-year-old Pepys wrote that he stayed up until 2.00 a.m., engrossed in *Micrographia* – calling it the most ingenious book he had ever read.[9] But not everyone was quite as enthusiastic. Because what did these rich men really want to achieve with these microscopes? What good would it do for humanity? To Hooke's great annoyance, a play, which quickly became a hit, was staged in London and its protagonist was clearly a parody of him: A man who had spent thousands of pounds on microscopes, only to study eels in vinegar and mites in cheese.[10]' Damned doggs, 'he wrote in *his* diary after coming home from the performance.[11]

Hooke was a polymath who engaged with far more than the microscopic world. His name is given to a physical law of elasticity, and he also researched the properties of light, gravity, and the movements of the planets. He unfortunately developed a particularly bad relationship with his colleague Isaac Newton, and the two men quarrelled bitterly until Hooke's death in 1703.[12] That same year, Newton was appointed president of The Royal Society, and many speculate whether it was Newton who ensured that there are today no surviving portraits of Hooke. All that remains are descriptions of a thin and pale man, somewhat hunched, with a pointed chin, bulging eyes and long, brown curls.[13]

Although he never achieved Newton's level of fame, Hooke did secure a place in the history books with his microscopic observations of a thin slice of cork. This may have been less impressive to readers of the day compared with his striking drawings of monstrous insects. Here he merely described a series of tiny cavities that were separated by thin walls. They reminded him slightly of the little rooms in a monastery – so he called them *cells*. Without realising it himself, Hooke had introduced one of the most important concepts in biology.

2
The smallest living things

What exactly is a cell? At school I was taught that cells are the building blocks that we – and everything else living – are made of. That might explain why for years I imagined that cells were square, like bricks, and sat neatly and tidily in rows. The cork cells Hooke saw in the microscope in the 1600s were of course similarly arranged. When I started my own cell research, however, I didn't see anything that resembled bricks. The immune cells I studied under the microscope were always changing shape and moving about like amoebas. Sometimes they would turn sharply and vanish from the area I was filming – to my great annoyance. But it was then I realised that every cell in my body is alive.

But what do we really mean by alive? It is actually a surprisingly difficult question to answer. Although we don't have a clear definition of life, we can list criteria that must be met for something to be described as living. What this list should contain varies depending on who you ask, but three particular criteria are stated repeatedly: First, everything that lives has a metabolism. This means that the organism can break down molecules into simpler compounds and reassemble them into new, complex molecules. For example, our cells can make proteins by connecting amino acids, or they can make DNA by combining nucleic acids. Our metabolism also provides the energy that cells use for all of their processes.

The second criterion for defining life is reproduction.

Life multiplies: Single cells divide into two, sunflowers produce seeds, and humans have babies. Whenever this happens, the organism copies DNA molecules containing recipies for how it will look and function. This is closely linked to the third criterion, which concerns evolution. The recipes are not constant: DNA molecules change from generation to generation. All living organisms evolve and change over time.

This is how the enormously diverse lifeforms found on earth today have arisen – from tiny ocean-dwelling plankton, to pine trees, elephants and albatrosses.

Then we have viruses, which always get biologists quarrelling. Are they alive or not? Viruses are small, typically 300 times smaller than a skin cell and 3,000 times smaller than a grain of salt.[1] Too small to be seen with a normal microscope, it took a long time before anyone understood what viruses really are. When discovered in the late 1800s, they were thought to be a fluid, poisonous substance, and that's how they came to be named: Virus comes from Latin and means slime or poison. In the 1930s, powerful electron microscopes finally made it possible to study viruses in detail. Researchers then discovered that viruses come in many different forms. *Norovirus*, known for causing gastric flu, looks like tiny, uneven balls. *Ebola* viruses are thread-like and resemble tiny worms, while the infamous coronavirus appears to be covered in spikes. And it's not just humans that are affected – not even bacteria escape. Viruses that attack bacteria are called *bacteriophages*. One of the best known of these, bacteriophage T4, eerily resembles a kind of robot spider with an elongated neck.

Viruses borrow the machinery of the host – a cell in the lining of your nose, for example – in order to make copies of themselves. Many believe therefore that viruses cannot be considered alive. Essentially, viruses are a form of bundled genetic material.

Most are smaller and simpler than bacteria, but there are exceptions. In the early 2000s, a giant virus was discovered in amoebae – a virus that was both larger and contained more genes than the tiniest bacteria.[2] Since then biologists have discovered more unusually large viruses, some with genes similar to those only previously found in cells.[3] Genes linked to the production of proteins and DNA repair, for example. The complex viruses made it clearer that viruses exist in a grey area between the living and the dead, although one thing is still clear: They are dependent on having a host in order to copy themselves, and thus lack one of the fundamental properties that bacteria, amoeba, plant cells and animal cells have.

This is one reason why the cell is often defined as the smallest unit of life. It means we cannot divide a cell into a smaller unit and describe it as living. If we remove what's inside a cell and sort it into different piles, these parts are no longer alive.

But if we remove cells from a body and grow them in a dish, they will carry on living; in the plastic dish, absorbing nutrients, growing and dividing. In the laboratory, I grow cells that haven't been in their original body for more than fifty years. Provided I keep them warm and well fed, they continue to divide as though everything is fine. Their food, a pink liquid similar to raspberry juice, contains the sugar, vitamins, amino acids and salts that cells need in order to grow and thrive. Some cells are so hungry they need to be fed every day, others just a couple of times week. When the plastic dish starts getting crowded, I split the cells into two new dishes, or discard the ones I don't need. It's actually quite similar to having a sourdough starter. If I'm going on vacation, I just collect some of the cells in a sterile plastic tube, add a substance that prevents ice crystals from forming, and freeze them. We use freezers that keep them at -80°C, or for long-term storage put them in liquid nitrogen that keeps them at -196°C. At this temperature they can lie dormant for years – then brought back to life when needed.

Immortal Henrietta

When thawing the small plastic tube marked‘ HeLa ’at the cell lab, I often think about the woman whose cells it contains. Unlike the other cells I grow, I know where these came from, the person's name, where she lived, and how she died. Henrietta Lacks was a mother of five living in the state of

Maryland, USA. In January 1951, Lacks went to Johns Hopkins Hospital, one of the few hospitals at the time which treated poor African Americans, for a gynaecological check-up.[4] There the doctor discovered a large, malignant tumour in her cervix. She began treatment and a sample from the tumour was sent to the laboratory of cancer researcher George Gey. For years Gey had been collecting samples from patients with cervical cancer while he researched the disease. At the same time, however, Gey had another goal: He wanted to grow human cells in the laboratory and get them to keep dividing outside the body. Whenever new samples were received, he tried to grow them in sterilised glass tubes filled with nutrient-rich liquid. Cells normally died after a short time, but Lacks ’cells would be different. After one day, the number of cells in the glass tube had doubled. One day later, they had doubled again. Gey’s lab assistant transferred the cells to new tubes, fed them new food, and put them back in the 37°C cabinet. The next day, she fetched more tubes and repeated the process. Day after day the cells continued to divide, and before long the lab was full of tubes of cancer cells, which they named ‘HeLa ’after Henrietta Lacks.

In the 1950s, getting consent to use samples in research wasn’t standard practice. When Lacks died in October 1951, she had no idea that her cancer cells were still alive in a warm, humid cabinet at the hospital.

Gey had also started distributing tubes of HeLa cells to colleagues, since they were exactly what they needed to accelerate their research. Having perpetual access to human cells at the laboratory enabled them to map disease mechanisms and test drugs. Soon – and entirely unbeknownst to her family – Henrietta Lacks ’cells were in laboratories all over the world.

When the Lacks family was finally contacted by researchers at Johns Hopkins in 1973, they were shocked. How could cells taken from their mother’s body be living in laboratories all around the world? Shortly afterwards, a journalist managed to trace her identity, and the donor of the extraordinary HeLa cells was no longer anonymous. In 2010, Rebecca Skloot’s book *The Immortal Life of Henrietta Lacks* was published, and with that, Henrietta Lacks became truly world-famous.

The case illustrated the importance of getting informed consent and protecting the privacy of those who contribute to research. Fortunately the legislation has evolved since the 1950s. Today, I have many different types of immortal cells which can be grown in the laboratory, but I only know the donor-name of the HeLa cells.

HeLa cells were crucial for the development of the polio vaccine and later the vaccine for Covid-19. Thanks to Henrietta Lacks, we have discovered new treatments for diseases and have a growing understanding of how our cells work.

Different and the same

A cell can be many different shapes: hairy or smooth, long or short, round or rectangular. It can float around on its own or latch on to others. A thousand cells can link up and become a roundworm crawling in the soil. About thirty trillion cells, as in, *thirty thousand billion*, can join forces and become you or me.[5] But whether they come from a roundworm, a tiny bacterium, or one of us, all cells are constructed in the same fundamental way. Every one is surrounded by a thin membrane, *the cell membrane*, which separates it from the outside world. The cell membrane contains fatty substances, and determines what gets in and out. Some cell types, such as bacteria and plant cells, have an additional more solid wall around the membrane which offers support and protection. It had actually been the walls of the cork cells that Hooke observed, when coining the word, not the cells themselves.

What cells also have in common is that they contain water. H_2O is the most common molecule in all living organisms. Inside a cell, salts, proteins, carbohydrates and other substances are dissolved in a fluid with a jelly-like consistency. We call this fluid *cytosol*.

All living things also have DNA, the genetic material containing the recipes that cells need in order to do their jobs and make copies of themselves. The DNA molecule consists of two coiled strands that form a long, spiral-shaped ladder. The ladder's rungs are made up of the bases *adenine, thymine, cytosine* and *guanine* – A, T, C and G. This is the alphabet of life: Everything you are made of is coded using these letters. When we sequence DNA, we read the order of the letters to determine which genes the organism has. We can think of the DNA molecule as a cookbook in which genes are recipes for various proteins. Some proteins are ball shaped, while others resemble long fibres, spirals or rings.

They can do anything, from breaking down nutrients to transporting substances or conveying signals in the cell.

Unlike a regular cookbook, however, our DNA contains masses of text that we don't understand. When researchers mapped all three billion letters that make up human DNA, they expected to find about 100,000 genes. Instead, they found approximately 20,000 – roughly the same amount as the one-millimetre-long roundworm C. *elegans*. It actually turned out that protein-coding genes account for less than 2 percent of our DNA. So what do the remaining 98 percent do? At first, many believed it to be mainly leftovers from millions of years of evolution, and it was nicknamed 'junk DNA'. But in recent years it has been shown that the parts outside of genes are important as well. This includes codes that determine when different genes are switched on and off. An organism's final shape is not solely about the recipes it contains, but also about how and when they are used. For example, all our different cell types contain copies of the same DNA molecules, but have switched on different genes as they developed. This means that a skin cell makes different proteins than a nerve cell or an intestinal cell. By regulating the activity of genes, cells can adapt to environmental changes. Many diseases have been shown to be caused by mutations in DNA outside the genes.[6] Still, there are large parts of our DNA that we don't understand, and we are likely to discover many new things about it in the coming years.

Endnotes

1: The hidden universe

1 Mol. Expr. Microsc. Primer Mus. Microsc., 'Hooke's Microscope'.
2 Hooke, 'Observ. V. Of watered Silks, or Stuffs'.
3 Hooke, 'Observ. LIII. Of a Flea'.
4 'So proud and aspiring with all, that it fears not to trample on the best'
Hooke, 'Observ. LIV. Of a Louse'.
5 Hooke, 'Observ. XLIX. Of an Ant or Pismire'.
6 Gest, 'The Remarkable Vision of Robert Hooke (1635–1703)'.

7 Pepys, ‘Tuesday 4 September 1666’.
8 Loveman, ‘Shorthand and Secrecy’.
9 Pepys, ‘Saturday 21 January 1664/65’.
10 Shadwell, *The Virtuoso. A Comedy, as It Is Acted by Their Majesties Servants*.
11 Lawson, ‘Bears in Eden, or, This Is Not the Garden You’re Looking For’.
12 Stone, ‘Championing a 17th Century Underdog’.
13 Andrade, ‘Wilkins Lecture – Robert Hooke’.

2: The smallest living things

1 Louten, ‘Virus Structure and Classification’; ‘How Big Is Grain of Salt?’
2 Wessner, ‘Discovery of the Giant Mimivirus’; Brown og Bhella, ‘Are viruses alive?’
3 Moreira and López-García, ‘Evolution of Viruses and Cells’.
4 ‘The Legacy of Henrietta Lacks’.
5 Hatton *et al*., ‘The Human Cell Count and Size Distribution’.
6 Cox, ‘The Mystery of the Human Genome’s Dark Matter’.