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Life's big bang

Simple explanations of how life got started don't add up, which leaves a surprising alternative, finds **Michael Marshall**

WHEN Earth formed 4.5 billion years ago, it was a sterile ball of rock, slammed by meteorites and carpeted with erupting volcanoes. Within a billion years, it had become inhabited by microorganisms. Today, life covers every centimetre of the planet, from the highest mountains to the deepest sea. Yet, every other planet in the solar system seems lifeless. What happened on our young planet? How did its barren rocks, sands and chemicals give rise to life?

Many ideas have been proposed to explain how it began. Most are based on the assumption that cells are too complex to have formed all at once, so life must have started with just one component that survived and somehow created the others around it. When put into practice in the lab, however, these ideas don't produce anything particularly lifelike. It is, some researchers are starting to realise, like trying to build a car by making a chassis and hoping wheels and an engine will spontaneously appear.

The alternative – that life emerged fully formed – seems even more unlikely. Yet perhaps astoundingly, two lines of evidence are converging to suggest that this is exactly what happened. It turns out that all the key molecules of life can form from the same simple carbon-based chemistry. What's more, they easily combine to make startlingly lifelike "protocells". As well as explaining how life began, this "everything-first" idea of life's origins also has implications for where it got started – and the most likely locations for extraterrestrial life, too.

The problem with understanding the origin of life is that we don't know what the first life was like. The oldest accepted fossils are 3.5 billion years old, but they don't help much. They are found in ancient rock formations in Western Australia known as stromatolites and are single-celled microorganisms like modern bacteria. These are relatively complex: even the simplest modern bacteria have more than 100 genes. The first organisms must have been simpler. Viruses have fewer genes, but can reproduce only by infecting cells and taking them over, so can't have come first.

The bare necessities

With physical evidence lacking, origin-of-life researchers begin by asking two questions. What are the fundamental processes underpinning life? And what chemicals do these processes use? Here, there are answers.

Life can be boiled down to three core systems. First, it has structural integrity: that means each cell has an outer membrane holding it together. Second, life has metabolism, a set of chemical reactions that obtain energy from its surroundings. Finally, life can reproduce using genes, which contain instructions for building cells and are passed on to offspring.

Biochemists know the chemicals underpinning these processes too. Cell membranes are made of lipids, molecules containing long chains of carbon atoms. Metabolism is run by proteins – chains of amino acids, twisted into pretzel shapes – especially enzymes, which help catalyse chemical reactions, speeding them up. And genes are encoded in molecules called nucleic acids, such as deoxyribonucleic acid, better known as DNA.

Beyond this, things start to become more complicated. Life's three core processes are intertwined. Genes carry instructions for making proteins, which means proteins only exist because of genes. But proteins are also essential for maintaining and copying genes, so genes only exist because of proteins. And proteins – made by genes – are crucial for constructing the lipids for membranes. Any hypothesis explaining life's origin must take account of this. Yet, if we suppose that genes, metabolism and membranes were unlikely to have arisen simultaneously, that means one of them must have come first and "invented" the others.

An early idea put proteins in the driving seat. In the 1950s, biochemist Sidney Fox discovered that heating amino acids made them link up into chains. In other words, they formed proteins, albeit with a random sequence of amino acids rather than one determined by a genetic code. Fox called them "proteinoids" and found that they could form spheres, which resembled cells, and catalyse chemical reactions. However, the proteinoids never got much further. Some researchers still hunt for lifelike behaviour in simple proteins, but the idea that proteins started life on their own has now been largely rejected.

More recently, much research has focused on an idea called the RNA world. Like DNA, ›

OLLIE HIRST

Death to panspermia

A handful of scientists argue that life didn't begin on Earth, but elsewhere in the universe, and that it was carried here on meteoroids and other space bodies. The origin could be somewhere nearby, like Mars, or light years away. The idea is called "panspermia".

Aside from the fact that this simply relocates the problem of how life got going, we also haven't found evidence of life elsewhere. If panspermia were true, bacteria would be raining down on Earth from space, and neighbouring worlds like the moon would be scattered with their remains. But there is no evidence of incoming bacteria, and moon rocks are sterile.

Furthermore, space is hostile to life. In experiments where bacteria were placed outside the International Space Station, even exposures of a year took a heavy toll. This leaves a window for life to travel within the solar system, but it is a narrow one: the trip from Mars to Earth would take many months at least. Travel from other stars would take millennia, so looks impossible.

Panspermia advocates may also be disappointed to learn that scientists are finally cracking the mystery of how life began on Earth (see main story). Like the planet itself, its raw materials came from space – but it seems more than likely it was Earth that brought them to life.

NASA

A billion years after Earth formed, life emerged. Did it happen elsewhere too?

RNA (ribonucleic acid) carries genes. The discovery that some kinds of RNA can also catalyse chemical reactions hinted that the first RNA molecules could have been enzymes that made copies of themselves and so got life started. However, biochemists have spent decades struggling to get RNA to self-assemble or copy itself in the lab, and now concede that it needs a lot of help to do either.

Perhaps, then, membranes came first. David Deamer at the University of California, Santa Cruz, has championed this option. In the 1970s, his team discovered that lipids found in cell membranes could be made when two simple chemicals, cyanamide and glycerol, were mixed with water and heated to 65°C. If these lipids were subsequently added to salt water and shaken, they formed spherical blobs with two outer layers of lipids, just like cells. "The simplest function is the self-assembly of membranes. It's spontaneous," says Deamer. Nevertheless, he now accepts that this isn't enough, because lipids can't carry genes or form enzymes.

The shortcomings of these simple models of life's origin have led Deamer and others to explore the seemingly less plausible alternative that all three systems emerged together in a highly simplified form.

This isn't a new idea. In 1971, Hungarian biochemist Tibor Gánti wrote a book in which he imagined the simplest object that biologists would consider alive. His "chemoton" consisted of a crude metabolism, based on enzymes, which made genes and a membrane. When the genes copied themselves, they released by-products that ended up in the membrane, causing the chemoton to grow and ultimately divide. Gánti's ideas failed to get recognition until the early 2000s, however, by which time others had independently hit on something similar. Now, the everything-first hypothesis is gaining momentum.

The first line of support for it comes from the biochemistry of life's three key systems. Nucleic acids such as RNA are chemically very different from proteins, which differ again from lipids. So, until recently, biochemists had assumed that these three components of life were unlikely to form in the same place from the same starter chemicals. That assumption seems to be wrong.

An early clue came from meteorites, many of which are as old as Earth, and therefore tell us what the planet was like when it was new. One of the most studied is the Murchison meteorite, which hit Australia in 1969. In 1985, Deamer found lipid-like molecules in it, which could form membranes. Others have found amino acids and, in 2008, Zita Martins, then at Imperial College London, identified a component of RNA in the Murchison meteorite. None of these chemicals was plentiful, but their presence indicated they could form together.

Simple ingredients

Meanwhile, Ernesto Di Mauro at Sapienza University of Rome in Italy has spent two decades exploring how this might happen on Earth. He focuses on formamide, a chemical related to cyanide, with just six atoms in each molecule. It is found throughout the universe and was probably common on the newly formed planet. In 2001, his team found that formamide could give rise to several components of RNA if it was heated to 160°C in the presence of minerals like limestone. The researchers later discovered that a common type of clay called montmorillonite helps. Formamide can also generate amino acids, the building blocks of proteins. "It produces complex mixtures," says Di Mauro.

And formamide isn't the only chemical capable of such feats. By combining a similar organic compound called cyanamide with other simple chemicals, John Sutherland at the MRC Laboratory of Molecular Biology in Cambridge, UK, has created nucleotides, the building blocks of RNA. The reaction requires

"Life's key molecules can form together thanks to 'Goldilocks' chemistry"

PHILIPPE PLAILLY/SCIENCE PHOTO LIBRARY

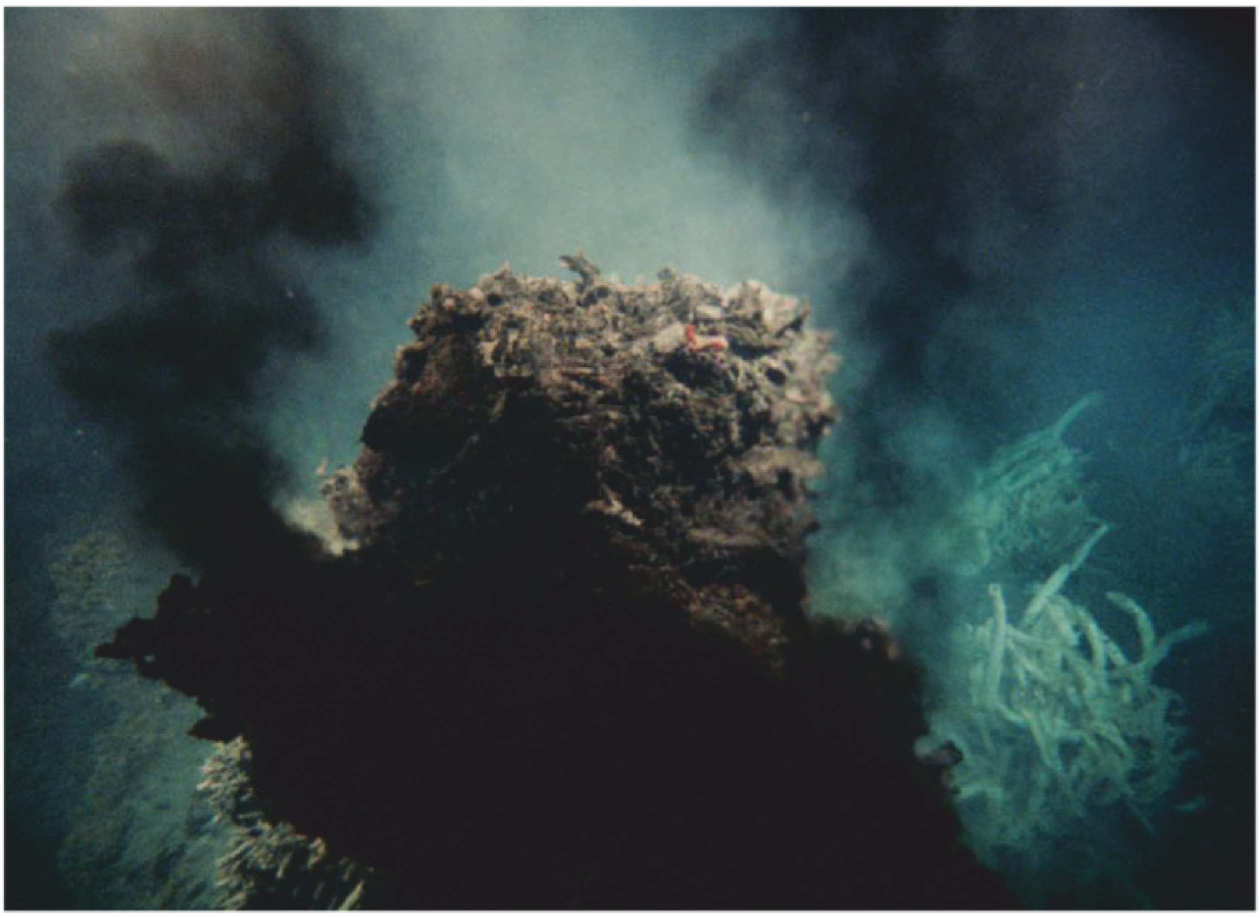
Stromatolite fossils are the oldest evidence of life here

ultraviolet light, heating and drying, and wetting with water. Sutherland's team found that the same starting chemicals can also make the precursors of amino acids and lipids. "All the cellular subsystems could have arisen simultaneously through common chemistry," he concluded. The key is what Sutherland calls "Goldilocks chemistry": a mixture with enough variety for complex reactions to occur, but not so much that it becomes a jumbled mess.

So there are ways in which the key molecules of life might all have been created together. But how did they then combine into a crude cell? Deamer still argues that the first lipids spontaneously formed membrane-based protocells, but he now thinks the three groups of molecules work together closely. Lipid containers help RNA and proteins to form and RNA to replicate, and RNA stabilises the lipid membranes. If all are present, the system works better, he says.

Jack Szostak at Harvard Medical School has taken remarkable strides toward revealing how this might have happened. Beginning in 2003, his team built model cells with outer layers of fatty acids surrounding an internal space that could host RNA. These protocells formed particularly quickly in the presence of tiny particles of montmorillonite, which often became trapped inside them, carrying RNA inside too. The more RNA a protocell obtained, the more it grew: they were competing. What's more, they could divide to form daughter cells, much like modern cells do. "Growth and division can result from simple physico-chemical forces, without any complex biochemical machinery," the team wrote. Szostak's group has even persuaded RNA to copy itself within protocells.

The one system still missing from these protocells is metabolism. This is particularly challenging because it means creating entire sequences of chemical reactions. In modern organisms, these are controlled by battalions of protein enzymes, which can't have existed when life began. However, other researchers have begun finding ways to get metabolic chemical reactions going without proteins. It turns out that many of the key reactions ›



RALPH WHITE/GETTY IMAGES

New research suggests life didn't emerge in deep sea vents after all

can be driven by metals like iron, often paired with sulphur, which have always been abundant on Earth. Szostak and others have recently shown that clusters of iron and sulphur atoms can form within protocells, driven by ultraviolet light. It remains to be seen whether metabolic reactions can work in the protocells.

A crude prototype

Nevertheless, Szostak's protocells are our best model yet for what the first living organisms might have looked like. Despite containing just a handful of chemicals, they grow and reproduce and carry RNA "genes" that can copy themselves. It is too early to say whether they arose from the sorts of chemistry advocated by Di Mauro or whether Sutherland is closer to the mark. That depends on the setting in which life emerged, which we can never know for certain. Intriguingly, though, the chemistry itself helps us narrow down the options.

If the everything-first idea of life's origins is correct, then genesis occurred under specific conditions. Most of Sutherland's and Di Mauro's chemical reactions depend on ultraviolet light and some key steps require drying. This implies that, to get started, life needed a solid mineral surface ideally including a clay such as montmorillonite, sunlight with a fair bit of ultraviolet radiation, and enough warmth to periodically evaporate water. That seems to rule out the popular idea that it originated on chemical-rich hydrothermal vents in the deep sea. Instead, the everything-first researchers believe life began in chemical-rich pools on land. Sutherland has developed a scenario involving streams of water running down a meteorite impact crater. Deamer favours geothermal ponds in volcanic settings and is focusing research on these. For instance, he has shown that lipids can form protocells in the water of these ponds, but not in seawater.

As well as helping to locate where on Earth life originated, the everything-first idea also suggests where to look for it elsewhere in the solar system. The biochemical requirements rule out two current front runners: Jupiter's moon Europa and Saturn's moon Enceladus. Both are thought to have deep oceans beneath a layer of ice. Those oceans might sustain life if it were introduced, but aren't a promising site for it to form. Instead, the most likely place to find life – or at least fossil evidence of it – is Mars. Today, it is cold and lacks liquid water on the surface, but billions of years ago it probably had rivers running over its rocks. It was also volcanically active, so may have had geothermal ponds like those Deamer is exploring.

"The most likely place to find other life, or at least fossil evidence of it, is Mars"

Of course, all this depends on the everything-first idea proving correct. Szostak's protocells and the new biochemical insights have won over many researchers, but some pieces of the puzzle are still missing. Perhaps the most persuasive argument is that the simpler ideas don't work. As is the case with many things in life, the beginning was probably more complicated than we had thought. ■

Michael Marshall is a writer based in Devon, UK. His book *The Genesis Quest* is out in the UK on 20 August and in the US on 22 October