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Life: Inevitable or fluke?

If life arises wherever conditions are right, where are all the aliens? Biochemist **Nick Lane** thinks he might have an answer

UNDER the intense stare of the Kepler space telescope, more and more planets similar to our own are revealing themselves to us. We haven't found one exactly like Earth yet, but so many are being discovered that it appears the galaxy must be teeming with habitable planets.

These discoveries are bringing an old paradox back into focus. As physicist Enrico Fermi asked in 1950, if there are many suitable homes for life out there and alien life forms are common, where are they all? More than half a century of searching for extraterrestrial intelligence has so far come up empty-handed.

Of course, the universe is a very big place. Even Frank Drake's famously optimistic "equation" for life's probability suggests that we will be lucky to stumble across intelligent aliens: they may be out there, but we'll never know it. That answer satisfies no one, however.

There are deeper explanations. Perhaps alien civilisations appear and disappear in a galactic blink of an eye, destroying themselves long before they become capable of colonising new planets. Or maybe life very rarely gets started even when conditions are perfect.

If we cannot answer these kinds of questions by looking out, might it be possible to get some clues by looking in? Life arose only once on Earth, and if a sample of one were all we had to go on, no grand conclusions could be drawn. But there is more than that. Looking at a vital ingredient for life – energy – suggests that simple life is common throughout the universe, but it does not inevitably evolve into more complex forms such as animals. I might be wrong, but if I'm right, the immense delay between life first appearing on Earth and the emergence of complex life points to another, very different explanation for why we have yet to discover aliens.

Living things consume an extraordinary amount of energy, just to go on living. The food we eat gets turned into the fuel that powers all living cells, called ATP. This fuel is continually recycled: over the course of a day, humans each churn through 70 to 100 kilograms of the stuff. This huge quantity of fuel is made by enzymes, biological catalysts fine-tuned over aeons to extract every last joule of usable energy from reactions.

The enzymes that powered the first life cannot have been as efficient, and the first cells must have needed a lot more energy to grow and divide – probably thousands or millions of times as much energy as modern cells. The same must be true throughout the universe. ›

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This phenomenal energy requirement is often left out of considerations of life's origin. What could the primordial energy source have been here on Earth? Old ideas of lightning or ultraviolet radiation just don't pass muster. Aside from the fact that no living cells obtain their energy this way, there is nothing to focus the energy in one place. The first life could not go looking for energy, so it must have arisen where energy was plentiful.

Today, most life ultimately gets its energy from the sun, but photosynthesis is complex and probably didn't power the first life. So what did? Reconstructing the history of life by comparing the genomes of simple cells is fraught with problems. Nevertheless, such studies all point in the same direction. The earliest cells seem to have gained their energy and carbon from the gases hydrogen and carbon dioxide. The reaction of H_2 with CO_2 produces organic molecules directly, and releases energy. That is important, because it is not enough to form simple molecules: it takes buckets of energy to join them up into the long chains that are the building blocks of life.

A second clue to how the first life got its energy comes from the energy-harvesting mechanism found in all known life forms. This mechanism was so unexpected that there were two decades of heated altercations after it was proposed by British biochemist Peter Mitchell in 1961.

Universal force field

Mitchell suggested that cells are powered not by chemical reactions, but by a kind of electricity, specifically by a difference in the concentration of protons (the charged nuclei of hydrogen atoms) across a membrane. Because protons have a positive charge, the concentration difference produces an electrical potential difference between the two sides of the membrane of about 150 millivolts. It might not sound like much, but because it operates over only 5 millionths of a millimetre, the field strength over that tiny distance is enormous, around 30 million volts per metre. That's equivalent to a bolt of lightning.

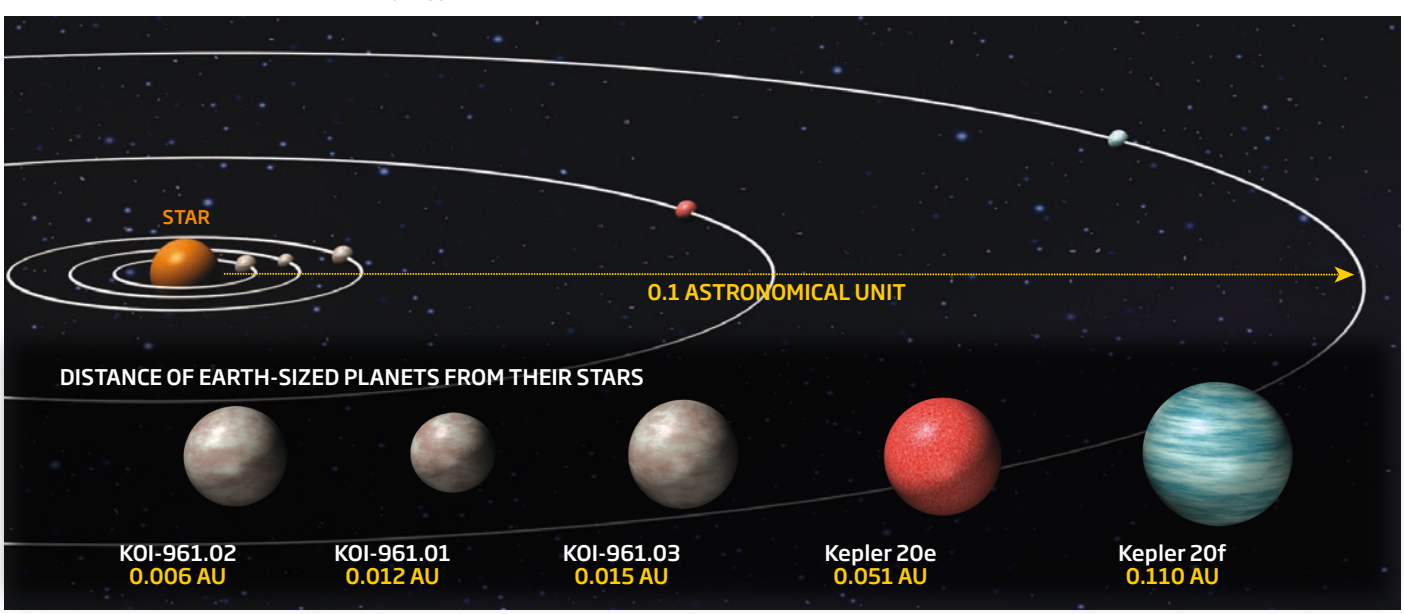
Mitchell called this electrical driving force the proton-motive force. It sounds like a term from *Star Wars*, and that's not inappropriate. Essentially, all cells are powered by a force field as universal to life on Earth as the genetic code. This tremendous electrical potential can be tapped directly, to drive the motion of flagella, for instance, or harnessed to make the energy-rich fuel ATP.

However, the way in which this force field is generated and tapped is extremely complex. The enzyme that makes ATP is a rotating motor powered by the inward flow of protons. Another protein that helps to generate the membrane potential, NADH dehydrogenase, is like a steam engine, with a moving piston for pumping out protons. These amazing nanoscopic machines must be the product of prolonged natural selection. They could not have powered life from the beginning, which leaves us with a paradox.

Life guzzles energy, and inefficient primordial cells must have required much more energy, not less. These vast amounts of energy are most likely to have derived from a proton gradient, because the universality of this mechanism means it evolved early on. But how did early life manage something that today requires very sophisticated machinery?

Other worlds

The search for distant planets has only just begun, but we have already found several Earth-sized planets around other stars. All orbit too close to their stars to be habitable, but their discovery suggests that habitable planets are common. So where are all the aliens?



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Alkaline thermal vents may have incubated the first life

There is a simple way to get huge amounts of energy this way. What's more, the context makes me think that it really wasn't that difficult for life to arise in the first place.

The answer I favour was proposed 20 years ago by the geologist Michael Russell, now at NASA's Jet Propulsion Laboratory in Pasadena, California, who had been studying deep-sea hydrothermal vents. Say "deep-sea vent" and many people think of dramatic black smokers surrounded by giant tube worms. Russell had something much more modest in mind: alkaline hydrothermal vents. These are not volcanic at all, and don't smoke. They are formed as seawater percolates down into the electron-dense rocks found in the Earth's mantle, such as the iron-magnesium mineral olivine.

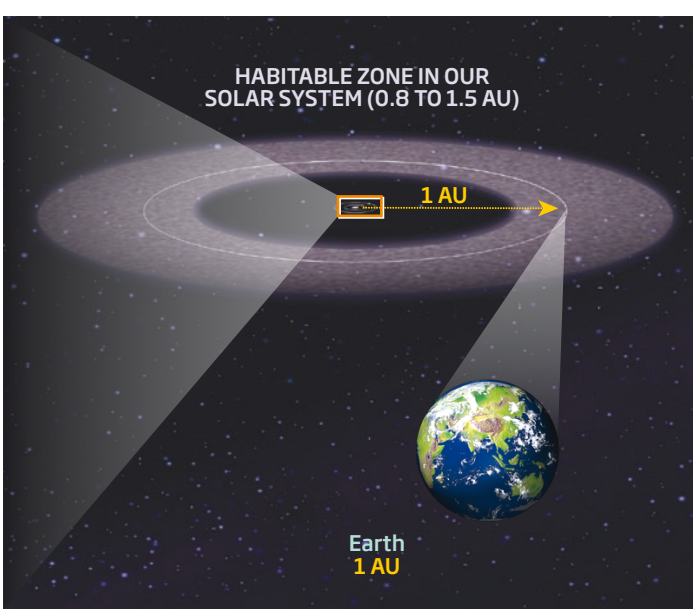
Olivine and water react to form serpentinite in a process that expands and cracks the rock, allowing in more water and perpetuating the reaction. Serpentinisation produces alkaline – proton poor – fluids rich in hydrogen gas, and the heat it releases drives these fluids back up to the ocean floor. When they come into contact with cooler ocean waters, the minerals precipitate out, forming towering vents up to 60 metres tall. Such vents, Russell realised, provide everything needed to incubate life. Or rather they did, four billion years ago.

Back then, there was very little, if any, oxygen, so the oceans were rich in dissolved iron. There was probably a lot more CO_2 than there is today, which meant that the oceans were mildly acidic – that is, they had an excess of protons.

Just think what happens in a situation like this. Inside the porous vents, there are tiny, interconnected cell-like spaces enclosed by flimsy mineral walls. These walls contain the same catalysts – notably various iron, nickel and molybdenum sulphides – used by cells today (albeit embedded in proteins) to catalyse the conversion of CO_2 into organic molecules.

Fluids rich in hydrogen percolate through this labyrinth of catalytic micropores. Normally, it is hard to get CO_2 and H_2 to react: efforts to capture CO_2 to reduce global warming face exactly this problem. Catalysts alone may not be enough. But living cells don't capture carbon using catalysts alone – they use proton gradients to drive the reaction. And between a vent's alkaline fluids and acidic water there is a natural proton gradient.

Could this natural proton-motive force have driven the formation of organic molecules? It is too early to say for sure. I'm working on exactly that question, and there are exciting times ahead. But let's speculate for a moment that the answer is yes. What does that solve? A great deal. Once the barrier to the reaction between CO_2 and H_2 is down, the reaction can proceed apace. Remarkably, under conditions typical of alkaline hydrothermal vents, the combining of H_2 and CO_2 to produce the molecules found in living cells – amino ›



acids, lipids, sugars and nucleobases – actually releases energy.

That means that far from being some mysterious exception to the second law of thermodynamics, from this point of view, life is in fact driven by it. It is an inevitable consequence of a planetary imbalance, in which electron-rich rocks are separated from electron-poor, acidic oceans by a thin crust, perforated by vent systems that focus this electrochemical driving force into cell-like systems. The planet can be seen as a giant battery; the cell is a tiny battery built on basically the same principles.

I'm the first to admit that there are many gaps to fill in, many steps between an electrochemical reactor that produces organic molecules and a living, breathing cell. But consider the bigger picture for a moment. The origin of life needs a very short shopping list: rock, water and CO_2.

Water and olivine are among the most abundant substances in the universe. Many planetary atmospheres in the solar system are rich in CO_2, suggesting that it is common too. Serpentinisation is a spontaneous reaction, and should happen on a large scale on any wet, rocky planet. From this perspective, the universe should be teeming with simple cells – life may indeed be inevitable whenever the conditions are right. It's hardly surprising that life on Earth seems to have begun almost as soon as it could.

Then what happens? It is generally assumed that once simple life has emerged, it gradually evolves into more complex forms, given the right conditions. But that's not what happened on Earth. After simple cells first appeared, there was an extraordinarily long delay – nearly half the lifetime of the planet – before complex ones evolved. What's more, simple cells gave rise to complex ones just once in four billion years of evolution: a shockingly rare anomaly, suggestive of a freak accident.

If simple cells had slowly evolved into more complex ones over billions of years, all kinds of intermediate cells would have existed and some still should. But there are none. Instead, there is a great gulf. On the one hand, there are the bacteria, tiny in both their cell volume and genome size: they are streamlined by selection, pared down to a minimum: fighter jets among cells. On the other, there are the vast and unwieldy eukaryotic cells, more like aircraft carriers than fighter jets. A typical single-celled eukaryote is about 15,000 times larger than a bacterium, with a genome to match.

The great divide

All the complex life on Earth – animals, plants, fungi and so on – are eukaryotes, and they all evolved from the same ancestor. So without the one-off event that produced the ancestor of eukaryotic cells, there would have been no plants and fish, no dinosaurs and apes. Simple cells just don't have the right cellular architecture to evolve into more complex forms.

Why not? I recently explored this issue with the pioneering cell biologist Bill Martin of the University of Düsseldorf in Germany. Drawing on data about the metabolic rates and genome sizes of various cells, we calculated how much energy would be available to simple cells as they grew bigger (*Nature*, vol 467, p 929).

What we discovered is that there is an extraordinary energetic penalty for growing larger. If you were to expand a bacterium up to eukaryotic proportions, it would have tens of thousands of times less energy available per gene than an equivalent eukaryote. And cells need lots of energy per gene, because making a protein from a gene is an energy-intensive process. Most of a cell's energy goes into making proteins.

At first sight, the idea that bacteria have nothing to gain by growing larger would seem to be undermined by the fact that there are some giant bacteria bigger than many complex cells, notably *Epulopiscium*, which thrives in the gut of the surgeonfish. Yet *Epulopiscium* has up to 200,000 copies of its complete genome. Taking all these multiple genomes into consideration, the energy available for each copy of any gene is almost exactly the same as for normal bacteria, despite the vast total amount of DNA. They are perhaps best seen as consortia of cells that have fused together into one, rather than as giant cells.

So why do giant bacteria need so many copies of their genome? Recall that cells harvest energy from the force field across their membranes, and that this membrane potential equates to a bolt of lightning. Cells get it wrong at their peril. If they lose control of the membrane potential, they die. Nearly 20 years ago, biochemist John Allen, now at Queen Mary, University of London, suggested that genomes are essential for controlling the membrane potential, by controlling protein production. These genomes need to be near the membrane they control so they can respond swiftly to local changes in conditions. Allen and others have amassed a good deal of evidence that this is true for eukaryotes, and there are good reasons to think it applies to simple cells, too.

So the problem that simple cells face is this. To grow larger and more complex, they have to generate more energy. The only way they can do this is to expand the area of the

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membrane they use to harvest energy. To maintain control of the membrane potential as the area of the membrane expands, though, they have to make extra copies of their entire genome – which means they don't actually gain any energy per gene copy.

Put another way, the more genes that simple cells acquire, the less they can do with them. And a genome full of genes that can't be used is no advantage. This is a tremendous barrier to growing more complex, because making a fish or a tree requires thousands more genes than bacteria possess.

So how did eukaryotes get around this problem? By acquiring mitochondria.

About 2 billion years ago, one simple cell somehow ended up inside another. The identity of the host cell isn't clear, but we know it acquired a bacterium, which began to divide within it. These cells within cells competed for succession; those that replicated fastest, without losing their capacity to generate energy, were likely to be better represented in the next generation.

And so on, generation after generation, these endosymbiotic bacteria evolved into tiny power generators, containing both the membrane needed to make ATP and the genome needed to control membrane potential. Crucially, though, along the way they were stripped down to a bare minimum. Anything unnecessary has gone, in true bacterial style. Mitochondria originally had a genome of perhaps 3000 genes; nowadays they have just 40 or so genes left.

For the host cell, it was a different matter. As the mitochondrial genome shrank, the amount of energy available per host-gene copy increased and its genome could expand. Awash in ATP, served by squadrons of mitochondria, it was free to accumulate DNA and grow larger. You can think of mitochondria as a fleet of helicopters that "carry" the DNA in the nucleus of the cell. As mitochondrial genomes were stripped of their own unnecessary DNA, they became lighter and could each lift a heavier load, allowing the nuclear genome to grow ever larger.

These huge genomes provided the genetic raw material that led to the evolution of complex life. Mitochondria did not prescribe complexity, but they permitted it. It's hard to imagine any other way of getting around the energy problem – and we know it happened just once on Earth because all eukaryotes descend from a common ancestor.

Freak of nature

The emergence of complex life, then, seems to hinge on a single fluke event – the acquisition of one simple cell by another. Such associations may be common among complex cells, but they are extremely rare in simple ones. And the outcome was by no means certain: the two intimate partners went through a lot of difficult co-adaptation before their descendents could flourish.

This does not bode well for the prospects of finding intelligent aliens. It means there is no inevitable evolutionary trajectory from simple to complex life. Never-ending natural selection, operating on infinite populations of bacteria over billions of years, may never give rise to complexity. Bacteria simply do not have the right architecture. They are not energetically limited as they are – the problem only becomes visible when we look at what it would take for their volume and genome size to expand. Only then can we see that bacteria occupy a deep canyon in an energy landscape, from which they are unable to escape.

So what chance life? It would be surprising if simple life were not common throughout the universe. Simple cells are built from the most ubiquitous of materials – water, rock and CO_2 – and they are thermodynamically close to inevitable. Their early appearance on Earth, far from being a statistical quirk, is exactly what we would expect.

The optimistic assumption of the Drake equation was that on planets where life emerged, 1 per cent gave rise to intelligent life. But if I'm right, complex life is not at all inevitable. It arose here just once in four billion years thanks to a rare, random event. There's every reason to think that a similar freak accident would be needed anywhere else in the universe too. Nothing else could break through the energetic barrier to complexity.

This line of reasoning suggests that while Earth-like planets may teem with life, very few ever give rise to complex cells. That means there are very few opportunities for plants and animals to evolve, let alone intelligent life. So even if we discover that simple cells evolved on Mars, too, it won't tell us much about how common animal life is elsewhere in the universe.

All this might help to explain why we've never found any sign of aliens. Of course, some of the other explanations that have been proposed, such as life on other planets usually being wiped out by catastrophic events such as gamma-ray bursts long before smart aliens get a chance evolve, could well be true too. If so, there may be very few other intelligent aliens in the galaxy.

Then, again, perhaps some just happen to live in our neighbourhood. If we do ever meet them, there's one thing I would bet on: they will have mitochondria too. ■

Nick Lane is the first Provost's Venture Research Fellow at University College London. His research on the origin of life is funded by the Leverhulme Trust