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Energy & Matter at the Origin of Life

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For more than half a century, the origin of life has been a question in chemistry. That makes good sense. It could hardly be a question in biology, because there wasn't any biology yet. Cells are made from organic molecules, and before there were cells, there presumably must have been organic molecules that didn't yet form cells; just plain chemistry. If so, the origin of life can be reframed as two separate questions. What chemical reactions could bring the molecules of life into existence? And how did these molecules assemble themselves into the first primitive cells? Only at that stage, and perhaps a little grudgingly, does biology come into it. How do these primitive cells grow and reproduce themselves? That's usually seen as a question of genetic information: genes specify metabolism, growth and replication, hence 'life as we know it' begins with genes. Chemistry must therefore take us right up to the emergence of genes, when natural selection can finally take over and create the living world as we know it.

I dislike almost every step in my first paragraph. I can't say for certain that it is totally wrong, but as a biologist there is something… lifeless about it. Chemistry does its thing, and then a miracle happens. Stuff comes alive and grows. Oh, the power of information! Life is a sticky computer. But what could biology have to say about the time before biology?

I'd like to think quite a lot. Of all the sciences there are fewer strict laws in biology, and more rules of thumb. Exceptions to everything. If we were to compare the sciences with languages, I suppose that Physics is closest to Latin, with its strict laws of grammar, whereas Biology is closer to English, a living growing language that 'cocks a snook' at the rules. Chemistry is more like French, with a certain *je ne sais quoi* that emerges mysteriously from the rules of grammar or quantum mechanics. That means it is hard to predict anything in biology, least of all the stuff that happened before biology began. But it might be possible to *smell* it, to have some feeling for where the rules of thumb might lead us. And biology being a science, it is also possible to test those hunches quite rigorously in the lab, to see if they make any kind of sense. That's fun, but one thing is certain: it will give us very different insights to the world according to chemistry.

I've come to associate one word in particular with biology – growth. In its broadest sense, growth is fundamental to life. A cell can get bigger – accumulate more stuff – or it can become two cells. The bigger a cell gets the more likely it is to simply fall apart, to divide in a haphazard way into two cells, or three or more. It's still growth. So is strict replication – the genetic material, DNA, copies itself so one copy becomes two. Growth. Seen from that point of view, heredity is a sub-discipline of growth, a more exact partitioning of the copies. To make all the extra building blocks needed to copy DNA requires growth. It seems to me that as a rule of thumb, growth must come first, heredity later. But what does growth really mean?

You might think that my title is a little pompous, dragging the laws of physics into the origin of life. I prefer to see it as strictly accurate. Growth is about the accumulation of matter, and organic matter costs some energy to make. Or at least it would seem to. In fact, that's not strictly true either. Here's a fact that I still find hard to swallow. If you were to mix hydrogen gas and carbon dioxide in water, inside a warm test tube, let's say the temperature of a hot bath, and then shake it up, cells should spontaneously appear. Believe it or not, that's what the laws of physics decree. The second law of thermodynamics states that in a closed system such as the universe, entropy must increase – stuff gets more disordered. But disorder is a funny thing. It is really about the degrees of freedom: how many places could a molecule possibly be? And that depends in part on temperature. A chemical reaction usually only happens spontaneously if it releases heat. Heat is released if the products of a reaction have less energy than the reactants did, which is to say, if the products are more stable than the reactants (being in an energetically favourable state). The heat released from the reaction warms everything up, making all the surrounding molecules jiggle around a little faster. That gives them more degrees of freedom, which means entropy increases. Far from escaping the second law of thermodynamics, through some semblance of order, life increases the entropy of the universe by speeding up reactions that release energy as heat, in our own case burning food in oxygen. It might not surprise you much, but we hasten the heat death of the universe.

That brings us back to the strange case of hydrogen and carbon dioxide. Don't think that they are comparable with sodium in water, which fizzes and bangs, but they do 'want' to react together, and the products of the reaction – organic molecules – are more stable than the reactants. They have a lower energy state and release the left-over energy as heat, increasing the entropy of the universe. That's important because (with the usual exceptions) there is a good rule of thumb in biology. Life hydrogenates carbon dioxide. That's to say, life cobbles hydrogen onto carbon dioxide to generate organic matter. So, it's convenient that hydrogen and carbon dioxide spontaneously react to form organic matter – in theory, cells – because that doesn't break any rules of chemistry or physics. On the contrary, physics and chemistry should conjure life into existence. Gases turn into cells and the reactions release enough energy to power growth.

But I'm pulling a cheap trick on you here and using a nice English word in a tricky way. Spontaneous. That has a technical meaning in chemistry too – it means it will happen just as soon as it can, so long as there is a way for it to happen. In the case of hydrogen and carbon dioxide, it's not so easy to find that way. To all intents and purposes, they are inert. Life helps them react all the time, of course, but life uses clever catalysts called enzymes, which are encoded by genes; life uses information. Enzymes break down the so-called kinetic barriers to reaction – they enable a reaction that should take place 'spontaneously' to actually happen quickly, and in so doing life increases entropy. That fuels growth. Cells convert some carbon dioxide and hydrogen into organic molecules – into more of themselves – and so long as there is a continuous replenishment of these gases in the environment, they'll go on converting them into more of themselves. Growth.

Here's where a few biological hunches come into play. Can we somehow see past the details coded in the genes to the principles beneath it all? That's tricky. We could build a tree of life, and attempt to probe its deepest roots, but bacteria have a frustrating trick of swapping genes around like loose change, meaning that the genes in any one cell need not reflect what it inherited from its parents, but could have been picked up from some random bacterial passer-by. Alternatively, we could try to see how the simplest and arguably most ancient cells work. Let's keep it simple and stick with cells that live from hydrogen bubbling out of the ground, cells like methanogens. You could call me out here and say you don't believe that they are genuinely ancient, that their simplicity merely reflects their adaptation to a meagre environment, and you'd have a point. Your biological intuition would be different to mine. In the end, experiments will tell us who is right, but in the meantime, we just have to disagree. Politely, I hope. I'm writing this, so we'll take my hunch.

Here's what methanogens do. They use a form of electricity, combined with its evil manipulative sister, proticity. Electricity is a flow of negatively charged electrons. Proticity is a flow of positively charged protons. Together an electron and a proton make up a hydrogen atom, which means that if you have one, you'll often have the other. They're linked in an intimate way. If you want to convert carbon dioxide into an organic molecule by adding on hydrogen, you don't transfer hydrogen atoms but the component bits – electrons and protons. Transfer an electron and you transfer a negative charge. That tends to stop you transferring another electron, because the negative charges repel each other. But throw in a positively charged proton and you'll offset the negative charge. Now you can add another electron, another proton, and so on. Softly, softly, catchee monkey. It's easier to convert carbon dioxide into an organic molecule under mildly acidic conditions, which is to say, when protons are abundant.

But there's a problem with that. Hydrogen is resistant to these easy charms. To transfer electrons and protons onto carbon dioxide, you first need to extract them from hydrogen gas, H_2, which is composed of two electrons and two protons. Hydrogen is stable, and it doesn't like being broken into its component parts. But it breaks down more easily when protons are scarce – in an alkaline solution, which by definition has a low concentration of protons and a high concentration of the hydroxide ions, OH^-. Now hydrogen can thrust its electrons onto carbon dioxide, because the left-over protons will react vigorously with hydroxide ions to form water, releasing heat and increasing the entropy of the universe. Hooray! A recap: hydrogen should react with carbon dioxide so long as the hydrogen is in alkaline solution and the carbon dioxide is in acidic solution. But how could you bring these drastically different conditions together? Acids and alkalis react immediately. Remember titrating them in your mouth in school Chemistry lessons? That titration should obliterate the very conditions necessary for hydrogen and carbon dioxide to react.

Here's the beauty of what methanogens do. Like all (all!) other cells, they pump out protons from the inside to the outside. That's a complicated process, so let's put it aside for now and focus on what happens next. They allow the protons to flow back into the cell through tiny protein pores in the membrane. Deep inside this protein there is a channel, a continuous stream of protons flowing in, before mixing into the ocean that is the inside of the cell. Shrink yourself down to the size of a molecule. If you are close to this channel you would want to pick up electrons because you could balance the charge with a nearby proton. If you are across on the other side of the protein, in the alkaline interior of the cell, you would want to push your electrons onto something else. Now you simply connect the two locations with something that will transfer electrons – a conductor. In the protein, that is achieved by tiny clusters of iron and sulphur atoms, with structures that look a lot like pocket-sized minerals. In other words, the combination of this spatial structure with a mineral conductor can theoretically break down the barrier to the reaction between hydrogen and carbon dioxide, to make organic molecules. Bingo! You have lowered the barrier to a thermodynamically favoured reaction, so the formation of organic molecules will now happen quickly, and technically costs no energy whatsoever. On the contrary, it releases enough energy for methanogens to grow.

That might sound like magic to you, but it is not. It is simply that hydrogen and carbon dioxide are out of equilibrium: in the places where methanogens can grow, there is a free supply of both from the environment, and the two gases 'want' to react, to form organic molecules, release heat and increase entropy. The methanogens just help them to do so. The methanogens are the *product* of them doing so.

So the real question is: why is the environment continuously out of equilibrium like this? The answer is that the Earth itself is like a methanogen, the inside replete with electrons, the outside more acidic, with fewer electrons. The core of the Earth is composed mostly of iron, which is heavy, and was therefore dragged down to the centre by gravity when the Earth was forming. Iron has plenty of electrons, which it would pass straight onto carbon dioxide if it ever got the chance. But it rarely does, because the iron is separated from the carbon dioxide in the atmosphere by the Earth's crust. Why is the carbon dioxide in the atmosphere? That's related to the temperature of magma. When carbonate rocks such as limestone get drawn down (subducted) into the upper mantle, the higher temperatures in effect vaporise the rock, which now erupts from volcanos as carbon dioxide. That dissolves in the oceans, making them acidic, before precipitating out as more carbonate rocks, being subducted, and entering another round of the cycle. There's no strict need for the sun. Gravity, heat, convection (planetary processes) separate the electron-rich interior from the electron-poor exterior. The Earth is a giant battery, almost literally a fuel cell. It is recharged continuously over millions of years by plate tectonics. And plate tectonic is driven by heat, which derives in part from the descent of iron into the core.

The Earth's mantle and oceans are not completely insulated. Water can percolate down in the crust beneath the oceans, kilometres down towards the mantle. There it can react with iron-rich minerals such as olivine, rusting them, and transferring the electrons from the iron onto fragments of reacting water molecules to form hydrogen gas, bubbling in warm alkaline solutions. These hydrothermal fluids bubble back up through the crust and then react with minerals in the cold oceans above. The minerals precipitate as vent structures on the ocean floor, riddled with pores. The vents bubble with hydrogen gas in warm alkaline solution, while acidic ocean waters rich in carbon dioxide percolate inwards from the outside. I say riddled with pores: alkaline vents don't have a central chimney like the famous black smokers, but form a labyrinth of interconnected pores, a mineralised sponge. Four billion years ago, before there was any oxygen in the atmosphere, the oceans had a very different chemistry, and that should have favoured the precipitation of iron-sulphur minerals in the walls of the pores. All that means these vents were electrochemical flow reactors, in which heated, reactive fluids percolated through interconnected pores with catalytic walls. Like a methanogen, these pores should have had protons outside and been alkaline inside, with the two phases separated by a thin semiconducting barrier. The topology is uncannily similar to a cell.

You might think all this is very imaginative, I'd hate to say speculative. But it is also science, because it suggests experiments. We have built a miniature flow reactor, called a microfluidic chip, to try and simulate the conditions inside one of these vents. Slow progress, I have to say. But the idea is simple: we juxtapose hydrogen, primed to react in alkaline solution, with carbon dioxide, primed to react in acidic solution, separated by the thin semiconducting barrier containing iron-sulphide minerals. We have had some success in making organics, as predicted, but have been frustrated by the problem of getting hydrogen gas to dissolve at atmospheric pressure, while flowing through a miniature reactor. It will take a little longer to pressurize everything. We hope it doesn't explode. There is a health and safety aspect to placing giant hydrothermal reactors at the bottom of the ocean. And of course, the high pressure, hundreds of Bars, dissolves hydrogen just beautifully.

What if it works? I don't anticipate cells crawling out of the reactor, but I do hope we will be able to drive the formation of organic molecules from hydrogen and carbon dioxide by using the structure of the pores and steep differences in proton concentration across barriers. If you use more forceful methods to push electrons and protons onto carbon dioxide – direct current or raw iron, neither of which is very comparable to how cells work – then the organic molecules formed are exactly those at the very heart of biochemistry – carboxylic acids, amino acids and fatty acids, which make up cell membranes.

Why is that so very different to the chemistry that I was criticising at the beginning? Aren't we still just making organic molecules? Well yes, but here their formation should be continuous and coupled with growth from the beginning. The flow of hydrogen keeps on giving, picosecond by picosecond, minute by minute, year by year, millennium by millennium, perhaps over tens of millions of years. If a small fraction of this continuous flux reacts with carbon dioxide to form organic molecules, these will build up, accumulate – grow. And we get structure for free. Fatty acids should form in alkaline hydrothermal conditions, and we've just shown that, once formed, they will spontaneously form into cell-like structures (protocells!) with a bilayer structure just like modern cells, even under the harsh conditions in alkaline vents. These protocells just love the mineral surfaces in the vents and stick on rather than being washed out. They form spontaneously – not a trick of the language this time – because the oily tails of fatty acids like to snuggle up together and exclude water, while the charged end of the molecule prefers to dissolve in water. A bilayer is the best of both worlds. Being an energetically favourable state, heat is released when a bilayer forms, and yeah, you got it – even though this is an ordered state, entropy increases as the surrounding water molecules jiggle about a little more excitedly in the heat of the moment.

Here, then, is this biologist's hunch. Growth is the key. The continuous flow of hydrogen and carbon dioxide, stubbornly resistant to reacting, is massaged into forming organics through a topological structure that foreshadows, nay it predetermines, the structure of cells. This structure forces the reaction, drives growth. Even if only a tiny fraction reacts at any moment, a vent is a never-ending stack of moments. The organics grow, how could they do anything else? And growth spontaneously yields cell-like structures with thinner membranes that get even better at breaking down the kinetic barriers to the reaction between hydrogen and carbon dioxide. Growth dissipates the chemical need to react, the yearning tension implicit in unreacted hydrogen and carbon dioxide, and each reaction is rewarded by a little kick of entropy. Positive feedbacks drive faster growth. Now, I imagine, there are whole populations of protocells colonising the vents and competing among themselves for more hydrogen, more nitrogen and phosphorus, even if they still lack genes. But genes are just a form of growth, and where better could they arise than in a setting where they do what they must from the very beginning. Promote growth.