

## My astrobiologist view of life

## by Natalie Grefenstette

I've been fascinated with life in the universe since I was a kid. Who hasn't spent hours thinking of what else is out there, or if we're alone, or where we come from? In my case, I also spent a lot of time wondering how different life could be, on the most basic level, and the circumstances that lead to life emerging in the first place. I decided that since we only have one example of life, here on Earth, I should get to know that one first. So, I decided to first study biochemistry and then went on to research the origin of life on Earth through a Ph.D. in prebiotic chemistry.

I went into my Ph.D. thinking that the molecules that our biology is built on, and the chemistry that our life uses in general, were born of complete chance, and that life could have easily chosen a very different path. I came out of it with a slightly different point of view. To be clear, I still think that when we find life elsewhere, it will be based on completely different biochemistry; there is no reason to think that the biomolecules we use are the only ones that can fulfill that role. However, perhaps there weren't as many potential chemical avenues for biology to take on the early Earth. Let me explain how my research changed my opinion on this.

I did my Ph.D. at University College London with Matthew Powner, and in our lab, one of the main interests was in understanding how the building blocks of ribonucleic acid (RNA) could be assembled from simple molecules that were (most likely) around on the early Earth. In particular, we wanted to understand under what reaction conditions the products we were interested in formed selectively, without too much of all the other very similar molecules that could form. One of the reactions I was performing involved producing potential precursors to ribonucleotides that already contain the sugar ring structure of the final nucleotide. This sugar moiety could be one of four orientations (diastereomers): xylose, arabinose, lyxose, and ribose (as you'll recognize, the R in RNA).

Early on, I was struck by how consistently, in the reactions I was performing, the precursor containing the ribose orientation was preferred. Under a slew of reaction conditions, such as changing pH, starting material, temperature, etc, the ribose-containing molecule was the main product. Turns out, there is a reason that our life uses ribonucleic acids, and not lyxonucleic acids or others: chemistry. For example, and without going into too much (chemistry) detail, ribose-containing molecules in this case are more stable and less strained than other conformations, making it the preferred outcome of the reaction.

This made me wonder about what other features of our biochemistry were not due to just chance. After my PhD, I had the chance to work with Jim Cleaves at the Earth Life Science Institute in Tokyo, doing a short computational biology project there with a large international team. The project sought



to understand why we use the 20 amino acids (canonical amino acids) that we do in biology, when there are loads of different ones possible. We looked at how well our 20 amino acids covered the chemical space (here defined as charge, hydrophobicity and mass ranges) compared to 20 other amino acids (selected at random from a large pool of possible amino acids). As it turns out, the set of canonical amino acids covers the space better: more evenly and more broadly (most of the time). The same thing happens when we look at subsets of those 20 amino acids vs smaller sets of random amino acids. This could explain why our life uses these 20 amino acids specifically, they're better at what they do than other sets of amino acids.

Ok, so perhaps the biochemistry we use here on Earth isn't completely random, and perhaps there is a (chemical) reason why we use the biomolecules that we do, to some extent. But what about life elsewhere? What if we started with completely different conditions, different molecules - what patterns would be the same? What would change? Are there any things that are universal in all possible biologies? And more importantly, how can we find those fundamental laws of biology when we only have one example to work with?

These are the questions that the astrobiological community are asking, and questions that I am trying to chip away at. I've now let go of lab work, and am using another powerful tool to try and work on these problems: modelling. Computational and theoretical modelling allow us to open up new spaces and, for example, "wind back the clock" again and again, and see how things can happen differently, or similarly, throughout the experiments. Are some things path-dependent and just due to chance? Or are some things conserved throughout repeated experiments or even through different experiments? Of course, we don't have any way of knowing exactly what to input at the beginning of our models to replicate the conditions of the origin of life (here or elsewhere). But we can simplify, propose hypotheses for certain phenomena and test them out.

Right now, I am using these tools to try to understand if we can tell the difference between polymers that are made 'abiotically' (randomly, with no selection) versus some that are made through biology. The polymers I'm working with aren't sophisticated computational chemical models resembling DNA or proteins, but rather strings of zeros and ones. Despite the extreme simplicity of the model, we can still get some very interesting insights into how different ways of making the polymers, and different dynamics of the environment, influence the final population in a distinct and detectable way.

The answers we gain from these kinds of models help us understand better what we are looking for when we look for life elsewhere, because ultimately, we don't know. We don't know how different life could be in different environments and we don't really know what to look for. But by trying to understand the universal patterns in our life, hopefully we can understand a bit more about life in general, and ultimately help guide the search for life in the universe.



Natalie is an astrobiologist based at the Santa Fe Institute where she works with Chris Kempes on the Agnostic Biosignatures project, a multi-institution NASA-funded project. She is interested in using her multidisciplinary background (biochemistry and chemistry) to help develop a deeper understanding of the organizing principles of biology and its very nature, and gain a better understanding of life's emergence on Earth and elsewhere. You can visit her website <u>here</u>.

