Alien Biochemistry: Embracing the Carbon Chauvinist

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I think I might be a carbon chauvinist.

Don't get me wrong; I *like* the idea of really out-there alien life—silicon based Hortas, nucleonic neutron star inhabitants, photino birds, and all that. But it occurs to me that in my own fiction I've strayed from carbon chemistry only once. Why? Because carbon biochemistry works. It has a track record.

I know; a sample of one life-bearing planet is a terrible basis for extrapolating. But carbon's unique versatility is hard to overlook. It can form single, double, and triple bonds that are stable (so that it can form long chains) but not too stable (so that they can't be broken when needed). In contrast, silicon chains become increasingly unstable the longer they get, and good luck getting Si=Si double bonds to last very long. More, carbon's ability to form four bonds gives it a huge advantage over elements like boron and nitrogen in terms of building the wide range of diverse molecules needed to make life.

Okay, so carbon it is. And from carbon we can build the major biomolecules—proteins,

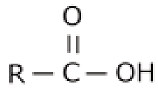
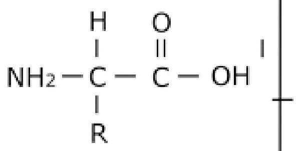
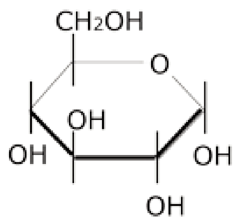
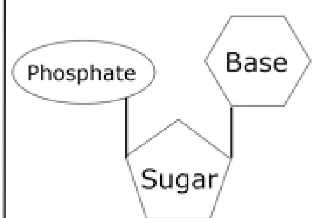
Biomolecule	Structure	Produces	Examples
Fatty Acid		Lipids	Triglycerides Phospholipids
Amino Acid		Protiens	Collagen Myosin Insulin
Sugar		Carbohydrates	Starch Cellulose Glycogen
Nucleotide		Nucleic Acids	DNA RNA

Figure 1: Biomolecules

carbohydrates, lipids, and nucleic acids. **Figure 1** shows the four major types of building block molecules and the typical biochemical polymers they make.[1] The R in the structures is shorthand for “generic organic group.” It can be something simple like a methyl (CH_3) group, a complex branching chain, a ring system, or anything else organic chemists can come up with. A hallmark of biochemistry is that simple molecules like amino acids chain together to form large polymers like proteins. These polymers are the stuff of life.

But is Earth’s way the only way of doing things? Does alien life have to use the same building blocks in the same way? That would make the Universe rather boring, at least for science fiction writers and fans. Fortunately, there’s plenty of room for variations on the theme, from minor tweaks to wholesale revision.

From a science fiction perspective, the big question is compatibility. Will human visitors to an alien world be able to safely interact with the native life? Can colonists “live off the land,” using local food sources? Entire stories can hinge on a biochemical quirk that makes alien life incompatible with Earth life. Maybe I'm strange, but that's the kind of thing that sparks my sense of wonder.

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Trying on Some New Genes

The genetic code is a good place to start. Most people learned about the GTCA (and sometimes U) thing in high school. The four nucleotide bases present in DNA are guanine (G), thymine (T), cytosine (C), and adenine (A). In RNA, uracil (U) replaces thymine. A string of three nucleotides forms a codon, the basic unit of the genetic code. Each codon corresponds to a specific amino acid used to make a protein; for example, AUG codes for the amino acid methionine. There are 64 possible combinations, but they only code for twenty amino acids, so there is plenty of room for redundancy in the genetic code. [2]

Life that evolved on an alien world, even if it used the same nucleotides, could use a different code. This is just about as compatible with Earth life as you can get. Using the same building blocks means that humans would be able to gain nutrition by eating alien life (and vice versa). What if something like an alien virus injected its DNA code into Earth life? Transcription proteins would still be able to read it, but the code would be nonsense. We won't get any *Andromeda Strain* viruses out of this type of alien life!

A step further away from Earth life is to expand the genetic alphabet. Our DNA uses two pairs of nucleotides—G pairs with C, and A pairs with T. Size and shape constraints prevent incorrect pairings. Biochemists have been experimenting with additional base pairs that don't occur in nature . . . at least on Earth. Several teams have managed to build DNA using a six-nucleotide alphabet (i.e., three pairs rather than two) that functions and replicates like natural DNA.[3]

Alien life could use the full six-member alphabet or it could replace one pair (say G and C) with a new pair, or replace both pairs with new ones. Again, this would be less troublesome to human settlers than you might think. Just about all living things can synthesize their own nucleotides, so the absence of G and C in the native food would not be a problem.

* * *

Do You Allow Substitutions?

Genes code for proteins, so that's our next stop. Proteins are built by chaining amino acids together. In principe, any amino acids will do, but with some few exceptions, life on Earth uses a template of only twenty.[4] Whether Earth's original amino acids were formed through chemical reactions in space (and seeded by meteorites) or reactions in the organic soup, hundreds of them would have been present. Why life chose to use only those twenty is a bit of a mystery.[5]

Life on an alien world might use a different set of amino acids. As long as the alien biology sticks with alpha amino acids, ones whose amine group and acid group are attached to the same carbon, that won't cause much difficulty for human visitors who want to try the local cuisine. Our bodies can synthesize some amino acids on their own, so if they're missing from the alien template, we've got it covered. There are a few, called essential amino acids, that we can't produce. If any of them are missing from the local life, colonists will have to synthesize them in a lab and take supplements. In Michael Flynn's *Eifelheim,* aliens stranded on Earth lacked the facilities to synthesize an essential (for them) amino acid. Humans in a similar situation wouldn't fare any better.

I limited the discussion above to alpha amino acids because they are by far the most commonly formed in primordial soup. Beta amino acids, those with the acid and amine group on adjacent carbons, are much rarer. Worse, it takes real effort to make them bond together, and with a more wobbly carbon backbone, they don't form the pleated sheet structures that our proteins use. We can assume that naturally occurring beta proteins are very unlikely, even on alien worlds. On the off chance that some alien life does manage to base itself on beta proteins, human colonists wouldn't be able to use any of the amino acids for protein synthesis.

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No, Your Other Left

Sugars and amino acids exhibit a property called chirality. In an amino acid, for example, there is a carbon atom with four different side groups attached—an acid, an amine, a hydrogen, and an organic chain. Because they're arranged in a 3D tetrahedral shape, if you switch the positions of two of the groups you get a new molecule, one that is the mirror image of the first (see **figure 2).** These are called enantiomers and are referred to as right-handed (using the prefix D for dextro) and left-handed (L for levo) because of the way they rotate polarized light.[6] Thus, you can have right-handed glucose (D-glucose, often called dextrose) or left-handed glucose.

All this matters because your enzymes are very picky about the shapes of the molecules they act on. D-glucose fits perfectly into the active sites of your metabolic enzymes but L-glucose, with its atoms shifted, does not. So you have a choice—pick either left- or right-handed sugars for your metabolism, or produce a redundant set of enzymes so you can metabolize both. Earth life picks D-sugars and L-amino acids.

Could life on other worlds choose differently? That depends on why we use the particular orientation we do. And, well, we don't really know for sure. We do know that if you have D-sugars you're going to end up with L-amino acids, and vice versa,[7] so alien life is likely to be limited to left/right or right/left configurations. But is one pair preferred over the other, or is it just a coin flip? A few mechanisms have been suggested that would make the L-amino acid/D-sugar orientation used on Earth the preferred way, but they are far from proven.

If there are planets with flipped chirality, the biomolecules would work the same way they do on Earth. You wouldn't be able to tell the difference without doing some analytical chemistry, but it would all be biologically incompatible with our form of life. Your metabolic enzymes can't recognize left-handed sugars, and so they pass right through your digestive system without providing any nutritional value.[8]

Worse, right-handed amino acids suppress your body's biosynthesis of the proper amino acids. Using alien life as a food source will cause you to sicken and eventually die. If you want to colonize such a world, you're going to have to find a way to get Earth crops to grow. With alien life already entrenched right down to the wrong-handed soil bacteria (or alien equivalent), that might not be easy. Colonists in Larry Niven's *Destiny's Road* used fusion flame to scour alien life from a peninsula before seeding it with Earth life. That may well be what it takes.

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It's Sort of Like DNA

Scientists think that life on Earth started with RNA, acting both as genetic code and its own enzymes.[9] Later, DNA evolved to replace RNA as the keeper of the genetic code. Why? Because

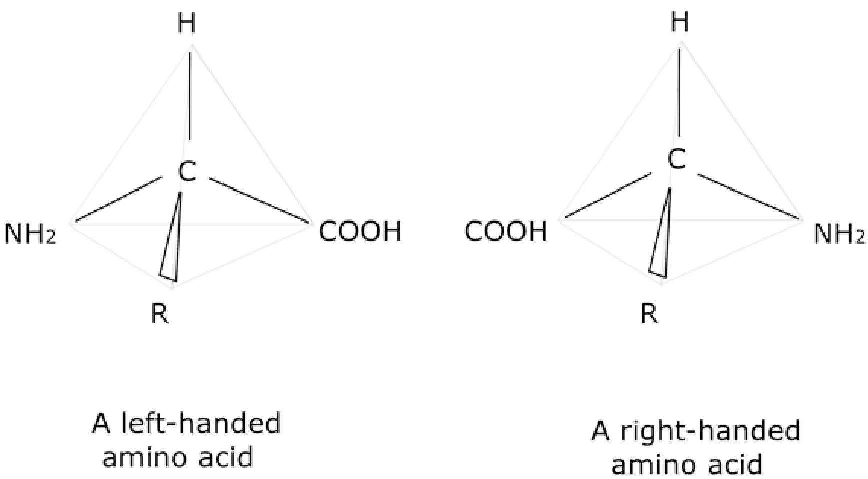

Figure 2: Chirality in Amino Acids

it's a more stable molecule and readily forms the double helix structure that allows for easy replication and error correction. It's difficult to imagine higher forms of life using only RNA.

Difficult . . . but not impossible. RNA life would be limited to multiple short segments of genetic material, which isn't conducive to centralization. Thus, alien RNA-based life would probably never develop the cell nucleus. Cells might swap RNA fragments as a way of supplementing their genetic code and adapting to new environments. Consuming other cells would provide a jackpot of new genes to use. Certainly, predation and reproduction would work in very different ways than they do on Earth. Could complex multicellular life evolve? It's questionable at best, but it sure would be different.

The R in RNA comes from the five-carbon sugar ribose; in DNA it's deoxyribose.[10] Ribose forms a five-member ring with four carbons and an oxygen atom. The fifth carbon hangs off the ring and is connected to a phosphate group, which then attaches to the next sugar in the chain. A few years ago, a bacterium was discovered that looked like it used arsenate in place of phosphate in its DNA backbone.[11] It was later shown that the bacterium actually prefers phosphorus, but it's still a possibility for alien worlds. Edward Lerner used this idea in his novel *Dark Secret* [*Analog,* April 2013–July/August 2013]. Alien life packed full of arsenic would, oddly enough, be rather poisonous to most Earth life.

But let's get back to the sugar at the heart of the nucleotide. There's no law saying that ribose *has* to form five-member rings. Remember that extra carbon hanging off the ring? You can incorporate it into the ring, creating what is called pyranosyl RNA.[12] The DNA equivalent is called homo-DNA. There is speculation that life on Earth got started with pyranosyl RNA and then switched to the furanosyl form used today. In some ways, pyranosyl RNA outperforms normal RNA, so it's unclear why life would have switched over early in its history. We can imagine an alien world where life didn't make the change and now uses homo-DNA for its genetic material. This alien world would almost definitely use different nucleotide base pairings than we do, but otherwise the genetic material could function much like ours. As when we changed the genetic alphabet, such life wouldn't be toxic (at least not on the basis of its DNA), but it would be incompatible in terms of genetic interaction. Other than my own *Kepler's Law* [*Analog,* May/June 2017], I'm not aware of any fictional worlds using pyranosyl RNA.

Going further afield, we can replace ribose with a different sugar. Chemists have synthesized nucleic acids using the four-carbon sugar threose, creating TNA. Threose forms more readily than ribose in organic soup, and some scientists think that TNA, not pRNA, was the precursor basis to life on Earth. TNA works very much like RNA, but it is a simpler molecule, and it's questionable whether life based on it could progress very far. Another contender to the precursor title is peptide nucleic acid, PNA, which uses proteins in place of sugars in its backbone. PNA can form double helices and can even intertwine with DNA, making it useful in genetic research. It's not as good as RNA at catalytic activity because its backbone is more rigid, so PNA life would probably need help from protein-based enzymes right from the start. On a world with an overabundance of nitrogen in its ecosystem, where proteins are plentiful in the organic soup, PNA could be a reasonable choice for life's genetic material.

Can I Have Some H_2O, Too?

Perhaps I can learn to live with carbon chauvinism, but I will not be a water chauvinist.[13] It's time we take all those carbon-based proteins, sugars, and nucleic acids and dissolve them in something else. Odor aside, ammonia has some intriguingly water-like properties, and so it is often considered as an alternative solvent for alien life. There are drawbacks to ammonia, though, not least of which is its tendency to burn in oxygen. Also, it vaporizes more readily than water, so we'd need a world with high atmospheric pressure or very cold temperature. Needless to say, such environments would not be hospitable to Earth life and so the question of biochemical compatibility is largely moot.

An ammonia solvent would change biomolecules in two major ways.[14] First, changes in acid-base chemistry would force some substitutions. In water, H_3O^+ ions define acids and OH^- ions define bases. In ammonia solution, we have NH_4^+ and NH_2^- ions respectively. The upshot of this is that, if you look back at figure 1, you'll have to replace every hydroxyl (OH) group that you see with an amide (NH_2) group. The second structural change we'd have to make happens because the carbonyl (C=O) group is unstable in ammonia solution. So while you've got your Wite-Out handy, change all those C=O groups to imine (C=NH) groups. You now have ammonia-based biomolecules. It's unclear whether such modified amino acids, sugars, and lipids would function as they do in Earth life, but it's certainly plausible that they would. It's also possible that entirely new types of biomolecules would emerge, either replacing or supplementing the types we know and love.

You can avoid a lot of ammonia's drawbacks by mixing it with water. An ammonia water solution can stay liquid over a broad range of temperatures and pressures, and we've already established that both would make good solvents for biomolecules. Both molecules are readily available throughout the Universe, so it's not a stretch to imagine a world with ammonia water oceans. Again, this wouldn't be a very pleasant place for human colonists.

Other solvents become increasingly speculative. Hydrogen fluoride (HF) shares some important properties with water and ammonia, but it is fairly rare in the Universe and so less likely to become the basis of an alien biology. Worse, HF is rather well-known for its ability to destroy biological tissues, so life using it as a solvent would need an entirely different suite of biomolecules. Methane is common in the Universe and, in cold places like Titan, is a liquid. The problem here is that things like sugars and amino acids are not soluble in methane. Once again, life is going to need a different set of molecules if it's going to evolve in a methane solvent. In his well-known article, "Not as We Know It," Isaac Asimov speculated that lipids would be the primary biomolecules in liquid methane. He also noted that lipids would work well in a liquid hydrogen solvent at extremely low temperatures.

But now we have strayed rather far from life as we know it. Not that there's anything wrong with that, but the further we go, the more speculative the chemistry becomes. We *know* DNA and proteins in water solution works. The further we go from there, the less certain we become.

* * *

Stirring the Biochemical Soup

To summarize, we have the following potential living systems:

- DNA coding for proteins in water solution (us!)
- Alternative nucleotides beyond G, T, C, and A used in the DNA
- Proteins made using an alternative list of amino acids
- Amino acids and sugars of reversed chirality
- Alternative nucleic acid (RNA, pyranosyl RNA, homo-DNA, TNA, or PNA) coding for proteins
- Replacing phosphate with arsenate in nucleic acids
- Ammonia (or other) solvent replacing water

* * *

Some of these are similar enough to be biologically compatible with Earth life in the sense that it wouldn't be inherently toxic based solely on the molecules present. Life on Earth has managed to come up with an impressive array of poisonous substances, so biochemical compatibility is no guarantee. But short of a planet full of nerve-gas-secreting alien plants, a planet with compatible life would allow human colonists to prosper. They might even be able to safely eat some of the local life-forms, although if they want to live primarily off local food sources they may well need supplements to make up for critical molecules missing from the local biology. Some alternatives, like switched chirality, are less forgiving. Human travelers to these worlds will have a harder time of it. They will need to cultivate Earth life for food and hope that the local biology isn't actively hostile to Earth crops.

There's no rule saying you can only change one thing. You could imagine alien life using PNA with six nucleotides coding for reversed chirality proteins. What if two different biochemical systems somehow manage to evolve independently on the same planet? Where they meet, evolution might make for some very unusual intermediate species adapted to both ecosystems. Things could get interesting for our intrepid human colonists.

Even for the carbon chauvinist, there's plenty of room for a variety of alien biochemistries. Next time you land on an alien world, you might want to take a close look at the biomolecules that make up the local life before you start sampling the alien cuisine. You might find wrong-handed proteins, amino acid deficiencies, arsenic and, who knows, maybe even silicon.

Perhaps I'm not as much a carbon chauvinist as I thought I was.

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Footnotes:

[1] Lipids are a rather diverse lot. Figure 1 simplifies matters quite a bit, leaving out entire classes of lipids like steroids.

[2] Three of the codons are stop signals, leaving only 61 codons for amino acids. Still plenty to go around. Methionine's AUG doubles as the start codon.

[3] In 2012, a team incorporated two new nucleotides with the ungainly designations d5SICS and dNaM. In 2015, another team used nucleotides Z and P. That's scientific progress, making alien genetics easier to map.

[4] Often, those exceptions are modified forms of the original twenty. For example, the thyroid gland adds iodine to tyrosine and uses that modified amino acid to make its hormones.

[5] Some amino acids that were likely plentiful in the ancient oceans aren't used, while others that did make the cut were probably rare, so it's not as simple as just picking the most abundant twenty.

[6] Organic chemists prefer to use R for rectus (right) and S for sinister (left). Bah. I'm sticking with the D and L notation used by biochemists.

[7] This is because like forms of sugars and amino acids react more rapidly with each other than unlike forms, so if you have excess L-amino acids in solution, they'll end up scavenging a lot of the L-sugars, leaving an excess of the D kind.

[8] So why don't we use L-sugars as calorie-free sweeteners? Because it's extremely difficult (and thus expensive) to artificially synthesize sugars. It's much more practical to get them from biological sources, and they're all right handed. If you find an inexpensive way to import L-sugars from an alien world in bulk, you'll be very rich.

[9] RNA segments that act as enzymes are called ribozymes. A prominent example in Earth life is the ribosome, whose specialized RNA assumes enzymatic functions.

[10] Each of a sugar's carbon atoms has an -OH group attached to it. In deoxyribose, the oxygen atom attached to carbon 2 is removed.

[11] Phosphate is a PO_4^{3-} group. Arsenate replaces the phosphorus atom with arsenic, AsO_4^{3-}.

[12] A five-member ring made of four carbons and an oxygen atom is called a furan, and a sugar built on that skeleton is a furanose. Add an extra carbon to make it a six-member ring and you have a pyranose. Glucose commonly forms pyranose rings.

[13] Credit where it's due—Carl Sagan said something along these lines years before I was old enough to know what carbon chauvinism was.

[14] Okay, probably more than that, but we'll focus our attention on the two big ones.

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(I've included a variety of sources, ranging from pop science through hardcore science journals. Let your level of interest in biochemistry guide you in deciding which, if any, of these you'd like to explore.)

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