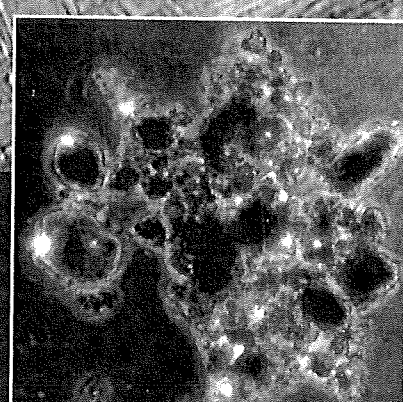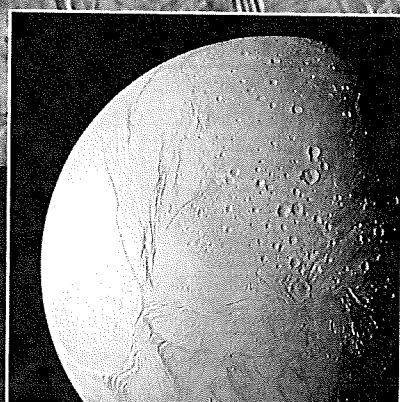# PLANETS AND LIFE

The Emerging Science of Astrobiology

Edited by **Woodruff T. Sullivan III**
and **John A. Baross**

CAMBRIDGE

27 Alien biochemistries

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27.1 Introduction

Common among the many definitions of life (Chapter 5) is mention of sets of chemical reactions that allow metabolism, replication, and evolution. The specifics of those reactions are generally not part of these definitions, although a century of study of the metabolisms that support life on Earth has given us a rich repertoire of illustrative biochemical examples. Unfortunately, because all known life on Earth is descended from a single common ancestor, our study of *terran*[1] biochemistry, no matter how extensive, cannot provide a comprehensive view of the full range of possible reactions that might generally support life.

This leaves open an important question. If life exists elsewhere in the Cosmos, will its chemistry be similar to the chemistry of life on Earth? Recent articles addressing this issue are by Irwin and Schulze-Makuch (2001), Crawford (2001), Bains (2004), and Benner *et al.* (2004), and several popular books are listed under "Further reading" at chapter's end. As in many areas in contemporary astrobiology, no clear methodology exists to address the question of "weird life." Chemistry, however, including the skills outlined in Chapter 7, provides one set of tools for constructing hypotheses about possible alternative biological chemistries.

The emerging field of *synthetic biology* (Benner and Sismour, 2005) provides another set of tools. Here, chemists attempt to give substance to concepts about alternative life forms by synthesizing molecules that might support alternative genetic systems or alternative metabolisms. These can be examined in the laboratory, thus learning about biochemical possibilities in ways inaccessible to those who simply analyze terran life.

Despite difficulties in generating hypotheses on which to base experimental research, these two strategies

have led to a consensus, of a sort, about a hierarchy of "weirdness": (1) alternative biochemistries that are clearly possible, (2) those that are well within the range of possibility, (3) those that are conceivable but (at least for now) confined to the *Star Trek* scripting room, and (4) those that are excluded as being inconsistent with fundamental physical law, or nearly excluded as being difficult to conceptualize within any realizable chemical model.

In some sense, consideration of how alien life might be constructed is the future of astrobiology. It certainly has important ramifications in the practical question of how one searches for extraterrestrial life, and where it might arise. This chapter briefly outlines current thoughts on some relevant biochemical issues; for the basics of terran biochemistry, see Section 6.3 and Chapter 7.

27.2 Life with different biopolymers

27.2.1 Different amino acids

One of the most compelling observations supporting the notion that all life on Earth is descended from a common ancestor is the planet-wide use of the same 20 amino acids (Fig. 7.5) as the standard components of encoded proteins. This biochemical uniformity is not obviously demanded by prebiotic chemistry. Nor is it required by terran metabolism, or constraints imposed by the machinery that terran life uses to biosynthesize encoded proteins.

For example, the famous Miller experiment generated a wide range of amino acids via nonbiological chemical processes (Section 6.2.2). A variety of amino acids is also found in meteorites, almost certainly generated without biology (Sections 3.8.2 and 7.4). No correlation exists, however, between the likelihood that an amino acid will be generated nonbiologically

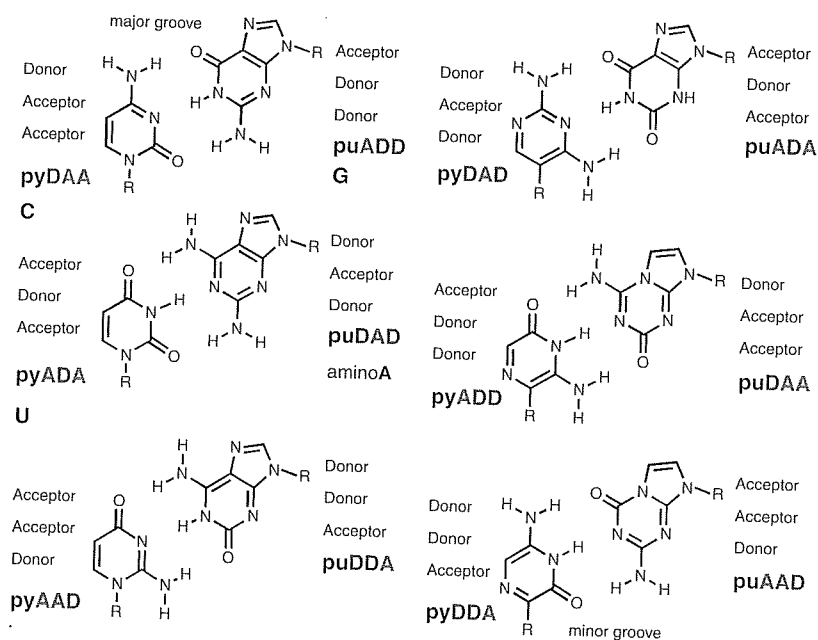[1] *Terran* means "associated with Earth or Earth's form of life."

FIGURE 27.1 An expanded genetic alphabet of artificial DNA. The standard Watson–Crick nucleobases pair small nucleobases (left partner) with large nucleobases (right partner), via three hydrogen-bond donor groups pairing with three hydrogen-bond acceptor groups. The specificity of the pairing is determined by the choice of the donor (D) and acceptor (A) groups, which are listed in order from the DNA's major groove (top) to its minor groove (bottom). The standard nucleobase pairs are the top two in the left column. Note that in the standard nucleobase adenine, the third hydrogen bond donor group is missing; what is shown is therefore aminoadenine. Adapted from Benner et al. (2004).

and its presence in the standard set of amino acids in terran proteins. For example, the non-standard amino acid norvaline, not found in encoded proteins on Earth, is more abundant in meteorites than many of the amino acids found in the standard set.

Likewise, terran metabolism generates many amino acids that do not end up as encoded parts of terran proteins. Ornithine and citrulline, for example, are amino acids biosynthesized in many forms of life on Earth, where they are metabolic precursors for the encoded amino acid arginine and serve as intermediates in pathways that metabolize nitrogen. Because of their abundance and prevalence, they are quite available to be part of encoded proteins; they just are not.

Experiments have shown that many more than the standard 20 amino acids are compatible with the machinery that life on Earth uses to synthesize encoded proteins (Hecht et al., 1978; Bain et al., 1989, 1992; Noren et al., 1989; Chin et al., 2003). Given the appropriate charged tRNA and an appropriate message, a ribosome is fully capable of incorporating virtually any amino acid into a protein via encoded translation. This includes the alpha methyl amino acids that are abundant in meteorites.

This makes inescapable the possibility that the amino acid inventory in terran proteins could have been quite different. A fortiori, this implies that non-terran life, if it exists, could use quite different amino acids, even if its catalytic molecules have the same backbone as proteins on Earth (Bain et al., 1992; Hohsaka and Masahiko, 2002). It is thus possible that DNA-based life might exist in the Cosmos, similar in all other respects to terran life, except for the use of different amino acids.

27.2.2 Chemically different "DNA"

An analogous conclusion for terran genetic matter is now possible based on many recent experiments in synthetic biology. On Earth, the Watson–Crick nucleobase pairing between the two strands of DNA follows two rules of complementarity. *Size complementarity* requires that large purines pair with small pyrimidines, while *hydrogen-bonding complementarity* requires that hydrogen bond donors from one nucleobase pair with hydrogen bond acceptors on the other. Thus, cytosine is a small pyrimidine that presents a donor–acceptor–acceptor pattern for its hydrogen bonds, which is complementary to guanine, a large purine that presents an acceptor–donor–donor hydrogen bonding pattern (Fig. 27.1). Uracil is a small pyrimidine that presents an acceptor–donor–acceptor pattern (major to minor groove) that is complementary to adenine, a large purine that presents a donor–acceptor pattern (adenine is missing the third hydrogen bond donor group).

These rules can be generalized (Geyer et al., 2003; Benner, 2004), where the large and the small components are always joined by three hydrogen bonds.

In this general structure, instead of the two hydrogen bonding patterns used by terran life, $2^3 = 8$ hydrogen bonding patterns are conceivable, of which six are readily accessible (Fig. 27.1). Synthetic biologists have not only made all of these in the laboratory, but further shown that they are all competent to support genetic recognition (Geyer et al., 2003; Benner, 2004; Sismour and Benner, 2005).

As with alternative amino acids, we cannot exclude these alternative nucleobases based on their incompatibility with the DNA polymerases (the enzymes that drive assembly of the DNA polymer chain). Given only modest modification of terran polymerases, DNA molecules built from expanded genetic alphabets can be copied, and then copied again (Benner, 2004; Sismour et al., 2004). This artificial genetic system has sustained up to 20 generations of replication (Sismour and Benner, 2005). They can even be copied with mutations, where the mutations themselves are replicated. Thus, these synthetic genetic molecules, together with standard terran polymerases, are artificial Darwinian chemical systems.

As with alternative sets of amino acids, these experiments suggest the possibility that the components of terran DNA could have been different. The case is not as strong for DNA as for proteins, however, since the alternative nucleotides, with few exceptions, are not as prominent in terran metabolism as are alternative amino acids. Further, we have no arguments based on possible routes to prebiotically synthesize nucleic acids (few good prebiotic routes are known even for the standard A, T, G, and C). Nevertheless, experiments in the laboratory make it quite conceivable that non-terran life, if it exists, could use quite different nucleobases in its genetic molecules, even if those molecules have the same backbone as DNA on Earth.

Several groups have now connected alternative genetic alphabets with alternative protein alphabets. For example, the Benner group encoded a non-standard amino acid, iodotyrosine, using a nucleobase pair that had its hydrogen bonding groups shuffled (Bain et al., 1992).

Other changes might be made in the way DNA and proteins interact. For example, the number of "letters" that encode an amino acid "word" might be increased or decreased. In making this change, the four traditional nucleobases of DNA (adenine, thymine, cytosine, and guanine) might still be used, but instead of a triplet being used to specify an amino acid, four or perhaps two nucleotides might encode an amino acid, allowing for, respectively, $4^2 = 16$ or $4^4 = 256$ possible amino acids.

What features of DNA might be universal in genetics throughout the Cosmos? Again, synthetic biology has provided some clues (Benner and Hutter, 2002). The backbone structure of DNA almost certainly reflects its need to function in water. The DNA double helix is built from two long strands of nucleosides joined by phosphates that at neutral pH each carry a negative charge. This repeating negative charge allows the DNA to be soluble in water. Further, the repeating charge on DNA dominates the physical properties of the molecule, meaning that replacement of the nucleobases in the DNA strand changes very little the overall physical properties of the DNA molecule. This allows mutation to occur without changes in biophysics, something that is very important for Darwinian evolution. Synthetic biological results (Huang et al., 1993) therefore suggest that a repeating charge will be a universal structure of genetic molecules in water (Benner and Hutter, 2002).

The other component of the backbone is the sugar, ribose in RNA and $2'$-deoxyribose in DNA. Many efforts have been made to change this part of the genetic molecule, in part because of perceived difficulties in forming ribose and $2'$-deoxyribose under prebiotic conditions (Section 7.6). As just one recent example, the glycerol backbone has been synthesized and studied (Zhang et al., 2005).

These experiments suggest that genetic matter could come in many varieties of languages. It would be interesting to know if, early in Earth's history, many separate kinds of DNA competed against each other. Is a twelve-nucleotide DNA more or less efficient than our familiar four-nucleotide DNA? Was there competition among a whole series of slightly different DNAs, with our current version proving competitively superior? Or was ours simply the first to achieve a tolerable ability to support life, suppressing a variety of equally, or even more, effective competitors through the advantage of incumbency?

27.3 Life with a different solvent

As synthetic biologists attempt to take steps away from standard terran biopolymers, they have become increasingly constrained by water, the solvent that surrounds terran life (Saenger, 1987). General experience in chemistry suggests that metabolism can efficiently operate only when metabolites are dissolved. Water is an excellent solvent by many measures, yet many compounds are not soluble in it. As one inspects terran biochemistry, one observes how terran life exploits *differential* solubility: (1) to manage

compartmentalization (using insoluble membrane components), (2) to build macroscopic structure (as in cellulose, for example, where the insolubility of a very polar compound arises from the high stability of a semi-crystalline phase), and (3) to achieve genetic regulation (for example, the solubility properties of steroids are key to their use in higher organisms).

Much has been made about the virtues of water as a biosolvent, at least at temperatures and pressures on the surface of Earth. It is an excellent solvent for salts. Water has a great ability to store heat. Bodies of water thus tend to stabilize their surroundings against rapid swings in temperature, in the same fashion that a coastal region is buffered against rapid temperature swings that are experienced in a desert. Water also floats when it freezes, insulating liquid water below.

Water has, however, many disadvantages as a bio-solvent. Water ice has a higher albedo than water liquid, for example. Thus, when water ice floats, it reflects more light from the sun, which leads to more cooling, more ice on the surface, a higher albedo, and still more cooling. The fact that water ice floats thus causes water to amplify, not damp, perturbations in the flux of energy coming to a planet – e.g., runaway glaciation of this sort may have occurred on Earth in the past, including within the past few million years.

The chemical reactivity of water, especially when considering RNA and DNA, also creates problems with its use as a biosolvent. Cytidine reacts with water to give uridine, losing ammonia in the process, with a half-life of ~70 years in water at 300 K. Adenosine likewise loses ammonia by reaction with water to give inosine, and guanosine loses ammonia to give xanthosine. As a consequence, terran DNA in water must be continually repaired.

Further, *liquid* water is not the usual form in the Cosmos. Water molecules are abundant, but generally in the form of ice on planets and moons (Chapter 15) and ice coatings on interstellar dust grains (Section 3.8), or alternatively water vapor in cool star atmospheres, in interstellar space, and in some planets' atmospheres (Chapter 4). Water can exist as a liquid on planetary surfaces only in a narrow range of distances from a particular star, and then only if the pressure/temperature of the planet's atmosphere is such that liquid water is stable. On Mars, for example, liquid water is not possible on the surface at any temperature, simply because the atmospheric pressure is too small. Note, however, that liquid water *can* more readily occur *beneath* the surface of planets and moons, as discussed in Chapter 18 for Mars and Chapter 19 for Europa.
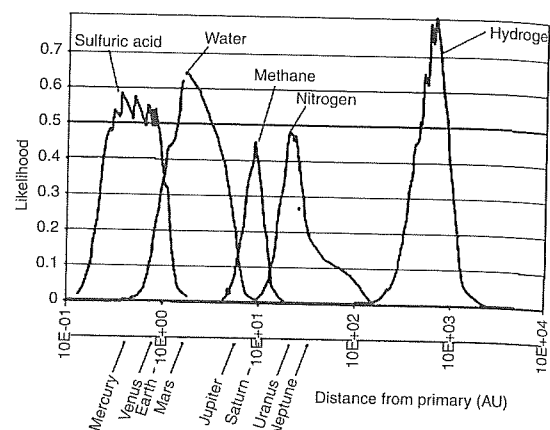

FIGURE 27.2 Potential liquids on the surface or subsurface of a planet or moon as a function of (the logarithm of) distance from a Sun-like star. Positions of the solar system's planets are indicated for comparison. Possible solvents for a form of life are discussed in the text. Adaped from Bains (2004).

Furthermore, at yet deeper levels (where pressures are very high and temperatures warmer), the crusts and mantles of rocky bodies also contain a great deal of water, some of which must be liquid, in accord with the phase diagram of water (Section 15.2).

These considerations have led many to consider alternative biosolvents that could work on a planetary body's surface with un-Earth-like conditions. Some of these, such as concentrated sulfuric acid, have very high boiling points and might support life at very high temperatures (Schulze-Mackuch *et al.*, 2004). Others, such as ammonia, dinitrogen (N_2), and supercritical dihydrogen-helium mixtures have very low freezing points, and thus might work at the other extreme (Bains, 2004; Benner *et al.*, 2004).

Bains (2004) has outlined the potential abundance of different liquids as one moves farther from a Sun-like star within a planetary system (Fig. 27.2). Less abundant solvents that have been considered include methyl alcohol, hydrogen sulfide, hydrogen fluoride, hydrogen cyanide, and hydrogen chloride.

Basic chemical principles suggest that life could easily be sustained in these solvents, given different core chemical structures and different cellular morphologies. The chemistry supporting this life would necessarily be, from a terran perspective, exotic and difficult to recognize for those familiar only with terran life. Furthermore, we lack much of the needed basic chemical data to evaluate such substances as potential biosolvents. Consider, for example, liquid dinitrogen, likely to be abundant in the outer planets and their larger moons. We do not know the solubilities of
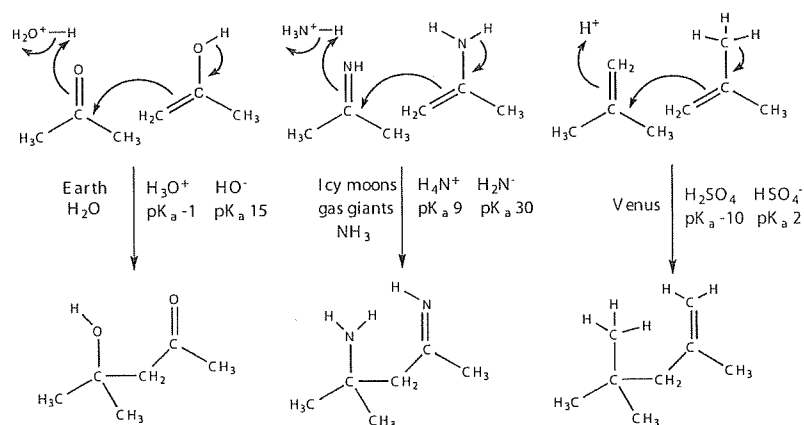
FIGURE 27.3 Different solvents would favor different, although analogous, chemical reactions to support metabolisms in life residing in different temperature regimes. Here are shown three analogous mechanisms for forming carbon–carbon bonds. The desired reactivity is conferred upon the reacting species by (left) a C=O unit (favored in water), (center) a C=N unit (favored in ammonia, such as in outer Solar System bodies), or (right) a C=C unit (favored in strongly acidic solvents such as sulfuric acid, as in Venus's atmosphere). Adapted from Benner *et al.* (2004).

most interesting organic species in this solvent at terran atmospheric pressure, let alone at the temperatures and pressures found on Triton, a moon of Neptune. Nor is much known about the chemical reactivity or self-assembly of key organic species in liquid dinitrogen. Thus, while it is clear that terran biochemistry could not function in liquid dinitrogen, it is not clear what chemistry might take its place.

Ammonia (NH_3) is more like water as a solvent, and is a useful solvent in the organic chemistry laboratory. The solubility of organic species and their reactivity have been better studied in ammonia than in most exotic solvents, and ammonia has long been discussed as an alternative solvent for life (see Bains, 2004). This discussion has intensified given recent evidence from the Cassini–Huygens mission on Titan (Sections 20.7 and 20.9).

Life in a water–ammonia mixture would need a different compartmentalization strategy, since liposomes, a major structural part of Earth-life cell walls (Sections 9.6 and 9.7), dissolve in ammonia. Benner *et al.* (2004) have suggested features of an alternative metabolism in ammonia, following the chemical principles outlined in Chapter 7. Whereas terran life in water exploits compounds containing oxygen doubly bonded to carbon (the carbonyl unit), life in ammonia would instead exploit compounds containing nitrogen doubly bonded to carbon (Fig. 27.3).

27.4 Life using different elements

Alternative solvents bring us in the hierarchy to the point where life becomes truly "weird." The next step considers alternative biochemistries that exploit different chemical elements.

Terran life is commonly called "carbon-based," or better, CHON-based (carbon, hydrogen, oxygen, nitrogen). But this ignores the vital contributions made by phosphorus and sulfur atoms to the physical properties and chemical reactivity of carbon. Terran life would be better described as CHONPS life.

There is little doubt that alternative forms of life could use these elements in different ratios, or introduce elements that are largely absent in terran biochemistry. Boron and silicon, which play only minor roles in the life that we know, could be used more, even perhaps in another form of terran life. Nevertheless, many investigators have persuasively argued that carbon is essential as a major component of life anywhere in the Universe (Pace, 2001).

This may indeed be so in water as a biosolvent. A change in solvent might, however, change the preferred elements. As mentioned above, life in ammonia would almost certainly switch the relative contributions of nitrogen and oxygen – CHNOPS life would be preferred over CHONPS life. A different environmental redox potential could also change the preferred elements.

These would be, however, only small changes. For much more profound changes, we now explore two other concepts.

27.4.1 Silicon life

As described above, cold is a challenge for carbon-based biochemistry. The bond energies intrinsic to functionalized organic species, and mechanisms for forming and breaking bonds to carbon, make common reactions slow at temperatures below 270 K. Likewise, the low temperatures that dominate the Cosmos create low solubilities, even in solvents that are liquid at those temperatures (such as dinitrogen, ethane, and methane).

Silicon-based compounds have been discussed for their potential for solving both problems (Bains, 2004). The silicon–oxygen single bond in compounds known as silanols is considerably more reactive than the analogous carbon–oxygen single bond. Further, silanes and silanols are soluble in a variety of solutes over a wide range of temperatures, including the very cold temperatures where dinitrogen is a liquid.

Furthermore, silicon–silicon bonds are well known, even in chains as long as 30 atoms. These are analogous, at least in size, to the carbon-based polymers necessary for terran life (Brook, 2000; West, 2002). The bonds are weaker and easier to transform at low temperature than the analogous bonds to carbon.

Bains (2004) has recently discussed these advantages for life in liquid dinitrogen. But again, little is known about the fundamental chemistry of silicon compounds in such a solvent. Much further work is needed.

27.4.2 Silicon/carbon clay life

A still more speculative type of life would allow minerals to play a larger role. These include silicon, but in its oxidized state as silicate (SO_3). Such ideas were suggested by Cairns-Smith (1982), who discussed a possible early form of life that exploited mineral-like crystals as structural elements. His model envisioned a form of life based on crystals of clay that would actively grow, and evolve as they did so.

27.5 Life with a different architecture

A variety of architectural features of terran biochemistry can be adjusted to create still more exotic life. For example, modern terran life uses three encoded biopolymers to manage its affairs: (1) *DNA* is used for genetics, (2) *proteins* are used to solve most of its structural and catalytic problems, and (3) *RNA* is used as an encoded biopolymer to act as an intermediate between the two, as well as to perform certain structural and catalytic roles. This combination almost certainly reflects contingencies in the history of life on Earth, as well as certain functional and vestigial features of these biopolymers.

An alternative architecture, however, might employ just one encoded biopolymer. Such a lifeform in fact is proposed in the "RNA World" models for the origin of life on Earth (Sections 6.5 and 8.2.1). Therefore, it does not stretch current theory to propose that life based on a single biopolymer might be more abundant in the Cosmos than life based on multiple biopolymers (Benner *et al.*, 2004).

There are, however, competing demands placed on a biopolymer by catalysis and genetics. A biopolymer specifically adapted to be used as a catalyst will be optimally built of many elemental and molecular building blocks, allowing a wider spectrum of chemical reactions. On the other hand, a biopolymer specifically adapted for genetics will perform better with the smallest possible number of separate components to ensure more accurate replication. Further, a molecule adapted to be a catalyst must be able to easily fold into multiple shapes; an information-carrying molecule cannot afford to fold easily if it is to serve as template (Benner & Hutter, 2002; Baross & Deming, 1995). A molecule adapted to be a catalyst should also change its physical properties easily through a small number of building-block substitutions; this allows it to explore "behavior space" most efficiently. In contrast, a genetic molecule should not change its physical behavior at all as a consequence of building-block substitutions – this allows Darwinian evolution to proceed unconstrained by the details of chemistry.

This illustrates why a lifeform might in general create two classes of biopolymers that are radically different from one another. The building blocks of each are adapted to the specific roles that the biopolymer is asked to perform. This dual-polymer strategy affords a far broader range of possibilities in both the nature of information stored, and the diversity of chemical reactions that can be undertaken. Thus, on Earth the amino acids found in proteins may be chosen to give an optimal framework for structure and catalysis, without concern for genetic demands. Conversely, it appears that, for a genetic molecule, the choice of deoxyribose as the sugar in terran DNA is superior to the ribose of RNA. Any single-biopolymer life will be far more limited in both respects.

Yet there may be environments where a form of life exploiting a single biopolymer has advantages. Such forms of life might be smaller, offering advantages where space is an important constraint (Benner, 1999). Single-biopolymer forms of life may require fewer resources, providing advantages where certain elements are scarce.

27.6 Summary

In this brief chapter, some potential kinds of "alien" biochemistries have been proposed. These are summarized in Table 27.1. While these kinds of "life as we do

TABLE 27.1 Possible biochemistries

Name	Scaffold element	Genetic material	Solvent	Scaffold element source	Energy source	Possible Solar System habitats
Terran life	Carbon	DNA	Water	CO_2, other organisms	Many	Earth, Mars, Europa, Titan
RNA life	Carbon	RNA	Water	Organic molecules	?	Titan, Mars, Europa, early Earth?
Protein life	Carbon	Proteins	Water	Organic molecules	?	Titan, Mars, Europa, Earth?
Silicon life	Silicon	?	cryosolvents?	?	?	Titan, Triton

not know it" may be theoretically plausible, they may not be present in the Cosmos simply because no pathway existed by which they could evolve. Nevertheless, continued research into how life different from our own might be built will provide valuable insights into how our own kind of life works, and help guide the design of missions that search for life in our Solar System in environments that differ significantly from Earth.

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