ARE ALIENS AMONG US?

In pursuit of evidence that life arose on Earth more than once, scientists are searching for microbes that are radically different from all known organisms

ALIEN MICROBES may be hiding in plain sight. Although they might look like ordinary bacteria, their biochemistry could involve exotic amino acids or different elemental building blocks.

The origin of life is one of the great unsolved problems of science. Nobody knows how, where or when life originated. About all that is known for certain is that microbial life had established itself on Earth by about three and a half billion years ago. In the absence of hard evidence of what came before, there is plenty of scope for disagreement.

Thirty years ago the prevailing view among biologists was that life resulted from a chemical fluke so improbable it would be unlikely to have happened twice in the observable universe. That conservative position was exemplified by Nobel Prize–winning French biologist Jacques Monod, who wrote in 1970: "Man at last knows that he is alone in the unfeeling immensity of the universe, out of which he emerged only by chance." In recent years, however, the mood has shifted dramatically. In 1995 renowned Belgian biochemist Christian de Duve called life "a cosmic imperative" and declared "it is almost bound to arise" on any Earth-like planet. De Duve's statement reinforced the belief among astrobiologists that the universe is teeming with life. Dubbed biological determinism by Robert Shapiro of New York University, this theory is sometimes expressed by saying that "life is written into the laws of nature."

How can scientists determine which view is correct? The most direct way is to seek evidence for life on another planet, such as Mars. If life originated from scratch on two planets in a single solar system, it would decisively confirm the hypothesis of biological determinism. Unfortunately, it may be a long time before missions to the Red Planet are sophisticated enough to hunt for Martian life-forms and, if they indeed exist, to study such extraterrestrial biota in detail.

An easier test of biological determinism may be possible, however. No planet is more Earth-like than Earth itself, so if life does emerge readily under terrestrial conditions, then perhaps it formed many times on our home planet. To pursue this tantalizing possibility, scientists have begun searching deserts, lakes and caverns for evidence of "alien" life-forms—organisms that would differ fundamentally from all known living creatures because they arose independently. Most likely, such organisms would be microscopic, so researchers are devising tests to identify exotic microbes that could be living among us.

Scientists have yet to reach a consensus on a strict definition of life, but most would agree that two of its hallmarks are an ability to metabolize (to draw nutrients from the environment, convert those nutrients into energy and excrete waste products) and an ability to reproduce. The orthodox view of biogenesis holds that if life on Earth originated more than once, one form would have swiftly predominated and eliminated all the others. This extermination might have happened, for example, if one form quickly appropriated all the available resources or "ganged up" on a weaker form of life by swapping successful genes exclusively with its own kind. But this argument is weak. Bacteria and archaea, two very different types of microorganisms that descended from a common ancestor more than three billion years ago, have peacefully coexisted ever since, without one eliminating the other. Moreover, alternative forms of life might not have directly competed with known organisms, either because the aliens occupied extreme environments where familiar microbes could not survive or because the two forms of life required different resources.

The Argument for Aliens

Even if alternative life does not exist now, it might have flourished in the distant past before dying out for some reason. In that case, scientists might still be able to find markers of their extinct biology in the geologic record. If alternative life had a distinctively different metabolism, say, it might have altered rocks or created mineral deposits in a way that cannot be explained by the activities of known organisms. Biomarkers in the form of distinctive organic molecules that could not have been created by familiar life might even be hiding in ancient microfossils, such as those found in rocks dating from the Archean era (more than 2.5 billion years ago).

A more exciting but also more speculative possibility is that alternative life-forms have survived and are still present in the environment, constituting a kind of shadow biosphere, a term coined by Carol Cleland and Shelley Copley of the University of Colorado at Boulder. At first this idea might seem preposterous; if alien organisms thrived right under our noses (or even in our noses), would not scientists have discovered them already? It turns out that the answer is no. The vast majority of organisms are microbes, and it is almost impossible to tell what they are simply by looking at them through a microscope. Microbiologists must analyze the genetic sequences of an organism to determine its location on the tree of life—the phylogenetic grouping of all known creatures—and researchers have classified only a tiny fraction of all observed microbes.

To be sure, all the organisms that have so far been studied in detail almost certainly descended from a common origin. Known organisms share a similar biochemistry and use an almost identical genetic code, which is why biologists can sequence their genes and position them on a single tree. But the procedures that researchers use to analyze newly discovered organisms are deliberately customized to detect life as we know it. These techniques would fail to respond correctly to a different biochemistry. If shadow life is confined to the microbial realm, it is entirely possible that scientists have overlooked it.

Ecologically Isolated Aliens

Where might investigators look for alien organisms on Earth today? Some scientists have focused on searching for organisms occupying a niche that is ecologically isolated, lying beyond the reach of ordinary known life. One of the surprising discoveries in recent years is the ability of known life to endure extraordinarily harsh conditions. Microbes have been found inhabiting extreme environments ranging from scalding volcanic vents to the dry valleys of Antarctica. Other so-called extremophiles can survive in salt-saturated lakes, highly acidic mine tailings contaminated with metals, and the waste pools of nuclear reactors.

Nevertheless, even the hardiest microorganisms have their limits. Life as we know it depends crucially on the availability of liquid water. In the Atacama Desert in northern Chile is a region that is so dry that all traces of familiar life are absent. Furthermore, although certain microbes can thrive in temperatures above the normal boiling point of water, scientists have not yet found anything living above about 130 degrees Celsius (266 degrees Fahrenheit). It is conceivable, though, that an exotic alternative form of life could exist under more extreme conditions of dryness or temperature.

Thus, scientists might find evidence for alternative life by discovering signs of biological activity, such as the cycling of carbon between the ground and the atmosphere, in an ecologically isolated region. The obvious places to look for such disconnected ecosystems are in the deep subsurface of Earth's crust, in the upper atmosphere, in Antarctica, in salt mines, and in sites contaminated by metals and other pollutants. Alternatively, researchers could vary parameters such as temperature and moisture in a laboratory experiment until all known forms of life are extinguished; if some biological activity persists, it could be a sign of shadow life at work. Scientists used this technique to discover the radiation-resistant bacterium Deinococcus radiodurans, which can withstand gamma-ray doses that are 1,000 times as great as what would be lethal for humans. It turns out that D. radiodurans and all the other so-called radiophiles that researchers have identified are genetically linked to known life, so they are not candidate aliens, but that finding does not rule out the possibility of discovering alternative life-forms in this way.

Investigators have already pinpointed a handful of ecosystems that appear to be almost completely isolated from the rest of the biosphere. Located far underground, these microbial communities are cut off from light, oxygen and the organic products of other organisms. They are sustained by the ability of some microbes to use carbon dioxide and hydrogen released by chemical reactions or radioactivity to metabolize, grow and replicate. Although all the organisms found to date in these ecosystems are closely related to surface-dwelling microbes, the biological exploration of Earth's deep subsurface is still in its infancy, and many surprises may lie in store. The Integrated Ocean Drilling Program has been sampling rocks from the seabed to a depth approaching one kilometer, in part to explore their microbial content. Boreholes on land have revealed signs of biological activity from even deeper locations. So far, however, the research community has not conducted a systematic, large-scale program to probe the deep subsurface of Earth's crust for life.

Ecologically Integrated Aliens

One might suppose it would be easier to find alternative life-forms if they were not isolated but integrated into the known biosphere existing all around us. But if shadow life is restricted to alien microbes that are intermingled with familiar kinds, the exotic creatures would be very hard to spot on casual inspection. Microbial morphology is limited—most microorganisms are just little spheres or rods. Aliens might stand out biochemically, though. One way to search for them is to make a guess as to what alternative chemistry might be involved and then look for its distinctive signature.

A simple example involves chirality. Large biological molecules possess a definite handedness: although the atoms in a molecule can be configured into two mirror-image orientations — left-handed or right-handed — molecules must possess compatible chirality to assemble into more complex structures. In known life-forms, the amino acids — the building blocks of proteins — are left-handed, whereas the sugars are right-handed and DNA is a right-handed double helix. The laws of chemistry, however, are blind to left and right, so if life started again from scratch, there would be a 50–50 chance that its building blocks would be molecules of the opposite handedness. Shadow life could in principle be biochemically almost identical to known life but made of mirror-image molecules. Such mirror life would not compete directly with known life, nor could the two forms swap genes, because the relevant molecules would not be interchangeable.

Fortunately, researchers could identify mirror life using a very simple procedure. They could prepare a nutrient broth consisting entirely of the mirror images of the molecules usually included in a standard culture medium; a mirror organism might be able to consume the concoction with gusto, whereas a known life-form would find it unpalatable. Richard Hoover and Elena Pikuta of the NASA Marshall Space Flight Center recently performed a pilot experiment of this kind, putting a variety of newly discovered extremophiles into a mirror broth and then looking for biological activity. They found one microbe that grew in the broth, an organism dubbed Anaerovirgula multivorans that had been isolated from the sediments of an alkaline lake in California. Disappointingly, this organism did not turn out to be an example of mirror life; rather it was a bacterium with the surprising ability to chemically alter the amino acids and sugars of the wrong handedness so as to make them digestible. The study, however, looked at just a small fraction of the microbial realm.

Another possibility is that shadow life might share the same general biochemistry with familiar life but employ a different suite of amino acids or nucleotides (the building blocks of DNA). All known organisms use the same set of nucleotides — designated A, C, G and T for their distinguishing bases (adenine, cytosine, guanine and thymine) — to store information and, with rare exceptions, the same 20 amino acids to construct proteins, the workhorses of cells. The genetic code is based on triplets of nucleotides, with different triplets spelling out the names of different amino acids. The sequence of triplets in a gene dictates the sequence of amino acids that must be strung together to build a particular protein. But chemists can synthesize many other amino acids that are not present in known organisms. The Murchison meteorite, a cometary remnant that fell in Australia in 1969, contained many common amino acids but also some unusual ones, such as isovaline and pseudoleucine. (Scientists are not sure how the amino acids formed in the meteorite, but most researchers believe that the chemicals were not produced by biological activity.) Some of these unfamiliar amino acids might make suitable building blocks for alternative forms of life. To hunt for such aliens, investigators would need to identify an amino acid that is not used by any known organisms nor generated as a by-product of an organism's metabolism or decay, and to look for its presence in the environment, either among living microbes or in the organic detritus that might be generated by a shadow biosphere.

To help focus the search, scientists can glean clues from the burgeoning field of synthetic, or artificial, life. Biochemists are currently attempting to engineer completely novel organisms by inserting additional amino acids into proteins. A pioneer of this research, Steve Benner of the Foundation for Applied Molecular Evolution in Gainesville, Fla., has pointed out that a class of molecules known as alpha-methyl amino acids look promising for artificial life because they can fold properly. These molecules, however, have not been found in any natural organism studied to date. As investigators identify new microbes, it would be a relatively simple matter to use standard tools for analyzing the composition of proteins, such as mass spectrometry, to learn which amino acids the organisms contain. Any glaring oddities in the inventory would signal that the microbe could be a candidate for shadow life.

If such a strategy were successful, researchers would face the difficulty of determining whether they were dealing with a genuine alternative form of life descended from a separate origin or with merely a new domain of known life, such as archaea, which were not identified until the late 1970s. In other words, how can scientists be sure that what seems like a new tree of life is not in fact an undiscovered branch of the known tree that split away a very long time ago and has so far escaped our attention? In all likelihood, the earliest life-forms were radically different from those that followed. For example, the sophisticated triplet DNA code for specifying particular amino acids shows evidence of being optimized in its efficiency by evolutionary selection. This observation suggests the existence of a more rudimentary precursor, such as a doublet code employing only 10, rather than 20, amino acids. It is conceivable that some primitive organisms are still using the old precursor code today. Such microbes would not be truly alien but more like living fossils. Nevertheless, their discovery would still be of immense scientific interest. Another possible holdover from an earlier biological epoch would be microbes that use RNA in place of DNA.

The chance of confusing a separate tree of life with an undiscovered branch of our own tree is diminished if one considers more radical alternatives to known biochemistry. Astrobiologists have speculated about forms of life in which some other solvent (such as ethane or methane) replaces water, although it is hard to identify environments on Earth that would support any of the suggested substances. (Ethane and methane are liquid only in very cold places such as the surface of Titan, Saturn's largest moon.) Another popular conjecture concerns the basic chemical elements that make up the vital parts of known organisms: carbon, hydrogen, oxygen, nitrogen and phosphorus. Would life be possible if a different element were substituted for one of these five?

Phosphorus is problematic for life in some ways. It is relatively rare and would not have existed in abundance in readily accessible, soluble form under the conditions that prevailed during the early history of Earth. Felisa Wolfe-Simon, formerly at Arizona State University and now at Harvard University, has hypothesized that arsenic can successfully fill the role of phosphorus for living organisms and would have offered distinct chemical advantages in ancient environments. For example, in addition to doing all the things that phosphorus can do in the way of structural bonding and energy storage, arsenic could provide a source of energy to drive metabolism. (Arsenic is a poison for regular life precisely because it mimics phosphorus so well. Similarly, phosphorus would be poisonous to an arsenic-based organism.) Could it be that arseno-life still lingers in phosphorus-poor and arsenic-rich pockets, such as ocean vents and hot springs?

Another important variable is size. All known organisms manufacture proteins from amino acids using large molecular machines called ribosomes, which link the amino acids together. The need to accommodate ribosomes requires that all autonomous organisms on our tree of life must be at least a few hundred nanometers (billionths of a meter) across. Viruses are much smaller—as tiny as 20 nanometers wide—but these agents are not autonomous organisms because they cannot reproduce without the help of the cells they infect. Because of this dependence, viruses cannot be considered an alternative form of life, nor is there any evidence that they stem from an independent origin. But over the years several scientists have claimed that the biosphere is teeming with cells that are too small to accommodate ribosomes. In 1990 Robert Folk of the University of Texas at Austin drew attention to tiny spheroidal and ovoid objects in sedimentary rocks found in hot springs in Viterbo, Italy. Folk proposed that the objects were fossilized "nannobacteria" (a spelling he preferred), the calcified remains of organisms as small as 30 nanometers across. More recently, Philippa Uwins of the University of Queensland has discovered similar structures in rock samples from a deep-ocean borehole off the coast of Western Australia. If these structures indeed arise from biological processes—and many scientists hotly dispute this contention—they may be evidence of alternative life-forms that do not use ribosomes to assemble their proteins and that thus evade the lower size limit that applies to known life.

Perhaps the most intriguing possibility of all is that alien life-forms inhabit our own bodies. While observing mammalian cells with an electron microscope in 1988, Olavi

Kajander and his colleagues at the University of Kuopio in Finland observed ultrasmall particles inside many of the cells. With dimensions as small as 50 nanometers, these particles were about one-tenth the size of conventional small bacteria. Ten years later Kajander and his co-workers proposed that the particles were living organisms that thrive in urine and induce the formation of kidney stones by precipitating calcium and other minerals around themselves. Although such claims remain controversial, it is conceivable that at least some of these Lilliputian forms are alien organisms employing a radically alternative biochemistry.

What Is Life, Anyway?

If a biochemically weird microorganism should be discovered, its status as evidence for a second genesis, as opposed to a new branch on our own tree of life, will depend on how fundamentally it differs from known life. In the absence of an understanding of how life began, however, there are no hard-and-fast criteria for this distinction. For instance, some astrobiologists have speculated about the possibility of life arising from silicon compounds instead of carbon compounds. Because carbon is so central to our biochemistry, it is hard to imagine that silicon- and carbon-based organisms could have emerged from a common origin. On the other hand, an organism that employed the same suite of nucleotides and amino acids as known life-forms but merely used a different genetic code for specifying amino acids would not provide strong evidence for an independent origin, because the differences could probably be explained by evolutionary drift.

A converse problem also exists: dissimilar organisms subjected to similar environmental challenges will often gradually converge in their properties, which will become optimized for thriving under existing conditions. If this evolutionary convergence were strong enough, it could mask the evidence for independent biogenesis events. For example, the choice of amino acids may have been optimized by evolution. Alien life that began using a different set of amino acids might then have evolved over time to adopt the same set that familiar life-forms use.

The difficulty of determining whether a creature is alien is exacerbated by the fact that there are two competing theories of biogenesis. The first is that life begins with an abrupt and distinctive transformation, akin to a phase transition in physics, perhaps triggered when a system reaches a certain threshold of chemical complexity. The system need not be a single cell. Biologists have proposed that primitive life emerged from a community of cells that traded material and information and that cellular autonomy and species individuation came later. The alternative view is that there is a smooth, extended continuum from chemistry to biology, with no clear line of demarcation that can be identified as the genesis of life.

If life, so famously problematic to define, is said to be a system having a property—such as the ability to store and process certain kinds of information—that marks a well-defined transition from the nonliving to the living realm, it would be meaningful to talk about one or more origin-of-life events. If, however, life is weakly defined as something like organized complexity, the roots of life may meld seamlessly into the realm of general complex chemistry. It would then be a formidable task to demonstrate independent origins for different forms of life unless the two types of organisms were so widely separated that they could not have come into contact (for instance, if they were located on planets in different star systems).

It is clear that we have sampled only a tiny fraction of Earth's microbial population. Each discovery has brought surprises and forced us to expand our notion of what is biologically possible. As more terrestrial environments are explored, it seems very likely that new and ever more exotic forms of life will be discovered. If this search were to uncover evidence for a second genesis, it would strongly support the theory that life is a cosmic phenomenon and lend credence to the belief that we are not alone in the universe.

In pursuit of evidence that life arose on Earth more than once, scientists are searching for microbes that are radically different from all known organisms