Comment

The life aquatic

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I don't normally find myself agreeing with George W. Bush on virtually anything, but I have to admit he might have a point about going to Mars. On 14 January 2004, in a speech at the headquarters of the US National Aeronautics and Space Administration (NASA), he outlined a number of goals for the future of that agency. Here's what he said about one of them: "With the experience and knowledge gained on the moon, we will then be ready to take the next steps of space exploration: human missions to Mars and to worlds beyond. Robotic missions will serve as trailblazers - the advanced guard to the unknown. Probes, landers and other vehicles of this kind continue to prove their worth, sending spectacular images and vast amounts of data back to Earth. Yet the human thirst for knowledge ultimately cannot be satisfied by even the most vivid pictures, or the most detailed measurements. We need to see and examine and touch for ourselves. And only human beings are capable of adapting to the inevitable uncertainties posed by space travel."

Not that I agree with him completely. I think he said the right thing, but not necessarily for the right reasons. I don't know if, given the enormous costs and risks associated with manned space flight, especially over interplanetary distances, satisfying some nebulous thirst to see and touch for ourselves is enough justification for huge expenditures of public money when we have so many unmet social needs on earth. I do think it might be a reason for spending private money, but that's another matter. And I think he has it completely backwards about humans being capable of adapting to the inevitable uncertainties posed by space travel: experience suggests that, when it comes to manned space flight, uncertainties are frequently fatal. Robots are expendable, people are not (unless, of course, the President had in mind sending liberals - the way his administration treats them suggests he may believe they are expendable). But I think there is a justification that does make sense, on both societal and scientific grounds (President Bush, who doesn't seem to know or care much about science, didn't mention it). I think if we want to know for sure whether there was, or still is, life on Mars, we have to send people there.

We've been sending robots, without much luck. Of course, the amount and type of terrain that a robot can explore is limited. So are its preprogrammed options for finding evidence for the presence of life. Although the experiments built into the early Mars landers were clever, they were based on a restricted, conventional view of what chemical activities a living organism ought to perform. Two Viking landers that reached Mars in 1976 carried out four basic experiments to search for evidence of life. First, gas metabolism: look for changes in the atmosphere inside a test chamber induced by metabolism in the Martian soil. Second, labeled release: Look for release of radioactive carbon dioxide by metabolism from organic material labeled by radioactive carbon. Third, pyrolytic release: search for radioactive compounds in soil by heating soil exposed to radioactive carbon dioxide. And fourth, mass spectrometry: search directly in Martian soil for organic compounds known to be essential to Earth life.

All these experiments were designed around the hypothesis that if there were life on Mars it would have a similar metabolism to life on Earth, and that it would have a similar biochemistry that was based on the same sort of organic compounds essential for life on Earth. The results of these experiments were ambiguous. The first three gave positive results, but the complete absence of any organic compounds in the Martian soil according to the mass spectrometry experiment suggested that the positive results for the first three were not evidence for life, but rather evidence for some sort of complex inorganic chemistry in the Martian soil. At a press conference to discuss these results, a NASA spokesperson proclaimed, "Viking not only found no life on Mars, it showed why there is no life there.... the extreme dryness, the pervasive short-wavelength ultraviolet radiation... Viking found that Mars is even dryer than had previously been thought... The dryness alone would suffice to guarantee a lifeless Mars; combined with the planet's radiation flux, Mars becomes almost moon-like in its hostility to life." True? Perhaps, but even if true, true only for the thinnest surface layer of the planet, in only two locations, which was all the robots could explore. And true only for the kind of life we could easily imagine.

My argument is that life as we know it now, thirty years later (in large part as a result of microbial genomics), has turned out to be so diverse in its survival strategies, so unpredictable in its morphologies, so subtle in its manifestations, that only a human observer, on the spot, has a realistic chance of recognizing it when he or she stumbles across it. I'm saying, if you'll pardon the analogy, that life is like US Supreme Court Justice Potter Stewart's famous remark about pornography: it's hard to define but we probably will know it when we see it. I'm further arguing that actual life, not the traces of life long dead, is what we should be looking for. Not just because that would be so much more exciting to find, but because it's what we're likely to find.

If there ever was life on Mars, then I think the probability is quite high that there still is. The ability of life to adapt to supposedly hostile conditions, given enough time, is astounding. This is true to some extent of eukaryotes, even metazoans, but it is overwhelmingly true for microorganisms. The complete genome sequence of the bacterium *Deinococcus radiodurans* provides a dramatic illustration. This little microbe, which was first discovered as a contaminant of irradiated canned meat, has been isolated worldwide from soil, animal feces, and processed meats, as well as from dry, nutrient-poor environments, including weathered granite in a dry Antarctic valley, room dust, and irradiated medical instruments. It can survive radiation doses 1,000 times greater than those that were thought to be lethal to all forms of life. After acute exposures to ionizing radiation, early stationary phase *D. radiodurans* cells can reassemble their entire 3.285 megabase-pair genome, which consists of four haploid genomic copies per cell, from the hundreds of radiation-induced DNA double-strand broken fragments, without lethality or mutagenesis. And this is despite the fact that the number of genes in this bacterium devoted to DNA repair is actually smaller than that found in *Escherichia coli*. Microbiologists believe that the extraordinary resistance of *D. radiodurans* to DNA damage arose not as an adaptation to high levels of radiation, but rather as a response to desiccation. In an arid environment, dormant *D. radiodurans* cells would gradually accumulate DNA lesions of all kinds, including strand breaks, leading to the requirement for a full complement of repair capabilities.

Thus, if life similar in generation time and genetic plasticity to our earthly bacteria once existed on a Mars that was warmer and wetter than it is now, unless that particular environment disappeared literally overnight it is reasonable to suspect that such microbial life had enough time to adapt to the changing conditions. So far, our robotics missions haven't seemed to make much use of this reasoning in their attempts to find evidence for life there. We've either looked for indirect evidence that life existed once, or we've looked for existing life that has certain metabolic or other characteristics similar to mesophilic and, especially, thermophilic organisms on earth. The former is just too dicey - our own fossil record is woefully incomplete, plus it's not easy to be sure that what looks like a fossilized microorganism really is one - and the latter seems to me to be a classic example of the drunkard looking for his lost car keys under the lamppost, not because he dropped them there but because that's where the light is.

In this case, the lamppost is genomics. Ever since the US National Science Foundation launched its program for the study of 'extremophiles', microorganisms that live in extreme conditions of temperature and pressure, genome sequences of these extraordinary creatures have been piling up faster than they can be analyzed. Unfortunately, nearly all of them are sequences of thermophiles - bacteria and archaea that grow at temperatures above about 50°C. There are several reasons for this, including the utility of such organisms or their thermostable proteins in industrial processes, not to mention our curiosity as to just how that thermal stability is achieved.

At first glance, extreme thermophiles would seem to be ideal model organisms for life on other planets. They tend to have stripped-down genomes, perhaps because they don't need so many enzyme catalysts - a number of chemical reactions proceed pretty well on their own at high temperatures. Many of them are anaerobic and can survive nicely in the absence of an oxygen atmosphere; some even grow on methane, which is found in abundance in some planetary atmospheres. Thermophilic archaea, in particular, are thought to be the best examples we have of some of the earliest single-celled organisms in the evolution of life on earth. And if we were looking for evidence of ancient life on Mars, they would also be the best examples we have for what that might look like, assuming of course that it looked anything like something we know. But if we're looking for life that's still there today, they're probably not such good examples at all.

Mars might have had a hot surface once, but it certainly doesn't have one now. Early life on Mars may well have been - probably was - adapted to high temperatures, but any life there today must of needs be adapted to extreme cold; to an absence of molecular oxygen in the atmosphere; to scarcity, if not outright absence, of liquid water in the immediate environment; and to dangerously high levels of certain types of radiation. *D. radiodurans* proves that adapting to radiation is no problem. Neither is living without oxygen, the ultimate electron acceptor in eukaryotic metabolism. But the enormous range of solutions to the problem of deriving energy found among anaerobic bacteria - some of which utilize metal ions, others sulfur, still others nitrates or arsenates and so on in place of O_2 - suggests that it would be difficult, if not impossible, to program a robot to anticipate even the strategies we know about. (My favorite example of this sort of thing is the bacterium *Sulfolobus acidocaldarius*, which inhabits hot (+85°C) and sulfurous thermal springs: it lives in boiling sulphuric acid. *S. acidocaldarius* is a chemoautotroph, utilizing CO_2 as a source of carbon and hydrogen sulfide as a source of energy (electrons), in a process similar to anoxygenic photosynthesis.)

Then there's the problem of adaptation to low, as opposed to high, temperatures. Most evolutionary microbiologists believe that the earliest organisms were thermophiles: the early earth was hot, and primitive enzymes wouldn't need to have been very efficient in a thermophile because elevated temperatures would help push reactions along. The early history of life on earth therefore was probably largely governed by the need to adapt to reduced temperatures as the planet cooled, which required the evolution of better catalysts. Some organisms never had to do this, of course, because they remained in a hot environment, like the thermophilic bacteria and archaea found in hot springs or the volcanic ocean vents - and indeed, most of their enzymes, when assayed at room temperature, have relatively low catalytic activity compared with their homologs from mesophiles (organisms that grow best at 20-50°C, like *E. coli* or us). And a few organisms, such as those on the Antarctic continent or those existing far underground, would have had to adapt not just to reduced temperatures but to temperatures close to or below 0°C.

There is genome sequence information for a few psychrophiles, bacteria whose optimum growth temperature is below 20°C, but in general adaptation to sub-zero conditions has received little attention. Such adaptation might have consisted of biosynthesizing anti-freeze compounds that depress the freezing point of water (some Arctic fish make anti-freeze proteins for this purpose; some insect larvae biosynthesize glycerol in the winter to keep their body fluids liquid). Some psychrophiles are adapted for life in very cold environments, close to the freezing point of water; an example is *Polaromonas vacuolata*, which lives in antarctic sea ice. This organism reproduces best at temperatures of 4°C; above 13°C, it cannot reproduce at all. Not all psychrophiles are bacteria; there are some eukaryotes, and even some multicellular organisms. In 1997, colonies of tubeworms were discovered living in methane hydrate deposits (a combination of natural gas and ice), 1,800 feet down on the bottom of the Gulf of Mexico. These ice worms are believed to get their food via symbiosis with colonies of chemoautotrophic bacteria living within them.

More work is urgently needed, both to discover and to characterize such organisms, because the nighttime temperatures on the surface of Mars are low enough to freeze the liquid that is inside any of the organisms we have characterized thus far. Obvious places to look for extreme psychrophiles are the two polar regions, Siberia (which has a town called Oymyakon that is the coldest permanently inhabited place on earth, where the temperature can fall as low as -96°F (-71°C)), and of course Boston in mid-winter, San Francisco in mid-summer, or the interior of any English home any time.

Equally interesting is the problem of adaptation to low-water environments. Life as we know it can exist without molecular oxygen, without elevated temperatures, without sunlight. It can probably even, if our speculations about the primordial RNA world are correct, exist without DNA or proteins. But it can't exist without liquid water. There's nothing else like H_2O in the universe as far as we know. Very few simple substances are liquid at temperatures likely to support life. Most of them are either too reactive, like acetic acid, or too nonpolar, like liquid methane, to serve as the basis of an intracellular medium in which polar substances can be dissolved without decomposing. Only water, the 'universal solvent' of alchemical lore, has just the right amount of chemical reactivity plus suitable physical properties. Einstein, in a famous remark, said that when he retired he wanted to devote the rest of his life to thinking about light. I think that when I retire I'd like to think about water, and I suspect many biochemists would feel the same way. No computer model successfully predicts all of its remarkable properties - in other words, we still don't really know the details of the structure of arguably the most important chemical substance of them all. What we do know is that life without it seems to be impossible. A human being can go without food for two months and live. He can't last a week without water. Microbial life is equally dependent on liquid water, with one amazing exception: some bacteria and fungi, when dessicated, form spores and in that state they can exist for many years without external water, even when frozen solid.

Sporulation is my candidate for the model system to look at if we want to understand what we may find on Mars. No one knows exactly how long spores can survive dessication and still be able to germinate, but fungal spores found inside Egyptian tombs were still able to grow when rehydrated, after presumably several thousand years of drought. Extreme cold is also no problem for at least some bacterial spores, which can be cooled close to absolute zero without impairing their ability to germinate when warmed back up. Thus, spores are known to survive precisely those conditions that exist on Mars today. Spores are probably the closest thing we know of to true suspended animation - if indeed they are suspended. For the remarkable thing is that, with the exception of some pioneering work by Shelly Chu, Pat Brown, and the late Ira Herskowitz on genome-wide changes in gene expression during sporulation induced by nitrogen starvation in yeast, we know very little about what goes on, or does not go on, inside a spore. Bacterium-like creatures on a warm, wet Mars millions of years ago may, as the climate slowly changed into one of cold and dryness, not have been able to adapt fast enough still to be able to proliferate. But if they could sporulate, there's a chance that those spores are still there, waiting for a little liquid water - with, probably, the right nutrients in it - to wake them up. What those nutrients are I don't know. Where the spores are I don't know either. But I do know that if I'm right, NASA and other government science agencies should be funding a lot more microbiology and genomics on spore-forming, arid-surviving and extreme psychrophilic bacteria. And also, of course, bacteria that exist considerably below the surface of the earth, because it is deep in the Martian soil that we are most likely to find organisms, or their spores, that learned how to deal with the hostility of the planet's surface. I can't imagine a robot finding, or recognizing, such spores or such microbes, much less figuring out what to do with them. But I think a trained microbiologist walking around on the surface of the planet, and digging into it in the right places, might.

So, until we have a better idea just what the universal hallmarks of life really are - if, of course, there are any - I don't see any alternative to human exploration of other planets and their moons (at least those where conditions that might conceivably support life either seem to exist or are likely to have existed in the past). Answering the question, "Is there life on other worlds?" requires the flexibility and imagination of the human mind, with input from the human eye, guiding the human hand. That's assuming we think the question is so important that it's worth the risk to human life to be certain of the answer. But are there many, if any, scientific questions that are more important? Life elsewhere in our own solar system would virtually guarantee life - and probably intelligent life - elsewhere in the universe. Certainty of that would change so many things: our view of our place in the cosmos, our philosophies, perhaps some of our religious beliefs, our very sense of what is possible. And right now, of all the places in the solar system that we just might be able to send a human being to, there is only one that has a realistic chance of giving a "Yes" answer. If Mars ever had life, then the odds are it still does. I'd love to know if that's true before my own life is over. Wouldn't you?