WE HAVE NOT DETECTED EXTRATERRESTRIAL LIFE, OR HAVE WE?

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Dorothy (to Glinda the good witch of the North): "*I think that it...that it wasn't enough just to want to see Uncle Henry and Auntie Em...and it's that if I ever go looking for my heart's desire again, I won't look any further than my own backyard; because if it isn't there, I never really lost it to begin with."*

In the movie "The Wizard of Oz" Dorothy mounts an extensive, but unsuccessful observational program to find her heart's desire. Finally, she realizes she has been misinterpreting data from her own backyard. Similarly, we have looked for extraterrestrial life and haven't found any. Maybe we haven't looked long enough or hard enough and we will eventually succeed -- or maybe we need to take a lesson from Dorothy. Maybe we don't have to look any further than our own backyard. To find extraterrestrial life maybe all we need to do is redefine life by shifting our paradigm of what life is (Kuhn 1962).

In this article I challenge the assumption that we have not yet found extraterrestrial life. I argue that by redefining life in a more general way, we can legitimately conclude that we have already detected extraterrestrial life. I will also argue that this is not a semantic game -- that the thermodynamic justifications for a broader definition of life are compelling and more universal than the traditional definitions of life based on DNA, "self-reproduction" and the chemical complexity of the terrestrial life most familiar to us.

1. No Evidence for Extraterrestrial Life

The canals and faces on Mars have disappeared. In 1976, results from the Viking landers were initially ambiguous, but it was concluded that life on Mars had not been observed (e.g. McKay 1997, Klein 1999). SETI searches have not found any signal. No obelisks have been found on the Moon, no Dyson Spheres have betrayed themselves in the infrared and no eyewitnesses from Roswell are talking. With all this negative evidence piling up, every reasonable scientist I know is of the opinion that no evidence for life has been found beyond Earth: "...there is no evidence from the reconnaissance of the solar system that life exists on any planet other than Earth." (McKay and Stoker 1998).

However, if I were parochial enough to define language as anything that resembles English, and then traveled to China, I would conclude that "No evidence for language has been found in China." The meaningfulness of this statement depends entirely on how meaningful my definition of language is. Similarly, the meaningfulness of the statement "No evidence for life has been found beyond earth" depends entirely on how meaningful our definition of life is. Without knowing the cosmic range of life forms, how can we determine if our terrestrial-life-based definitions are meaningful in a cosmic context?

Many hours of human thought have been dedicated to constructing definitions of life suitable for application elsewhere in the universe (Sagan 1970, Lehninger 1970, Chyba and McDonald 1995, Nealson and Conrad 1999, Cleland and Chyba 2002). Biology textbooks are full of definitions of life. These definitions have been sculpted around the flora, fauna and fungi we know on earth. They usually mention growth, self-regulation, self-reproduction and chemical complexity. Some definitions are blatantly tautological: "Life is what is common to all living beings". I am not convinced that these standard definitions of life based on terrestrial examples are broad enough to have reasonable expectations of universality. Neither was Einstein:

"Whether there are some general characteristics which would apply not only to life on this planet with its very special set of physical conditions, but to life of any kind, is an interesting but so far purely theoretical question. I once discussed it with Einstein, and he concluded that any generalized description of life would have to include many things that we only call life in a somewhat poetical fashion." (Bernal 1949).

How then do we construct a definition of life general enough to give us some confidence in its universality? If our intuitive ideas about what is or is not alive are too parochial, where can we hunt down some generality? Physicists and chemists are qualified to practice their trade on the planets around Alpha Centauri or anywhere in the universe, but biologists will probably have to retool. So maybe we can rely on physicists to come up with a usefully broad definition of life. Inspired by the work of Schrödinger (1944), Prigogine (1947, 1980), Bernal (1949) and Schneider and Kay (1995), I think a definition of life based on general thermodynamic principles will prove more useful in an extraterrestrial context than our current terrestrial-life based definitions.

2. Are Viruses Alive?

Viruses outnumber bacteria and all other life forms by an order of magnitude (Bamford *et. al.* 2002). They are by far the most numerous inhabitants of our own backyard. There are 10 million viruses per milliliter in aquatic environments (Bergh *et. al.* 1989). Their variety is staggering: circular viroids, non-pathogenic plasmids, bacteriophages, viruses infecting other viruses, satellite viruses, satellite nucleic acids, jumping genes and a whole menagerie of virus-like entities.

Despite their number, their diversity and their possibly fundamental role in the origin of traditional life, when you ask your favorite thoughtful biologist if viruses are alive, you will hear hemming and having. Standard biologists deny viruses the status of living beings because, it is said, viruses cannot reproduce themselves. They need help. Who doesn't? Take any standard life form, a man for example, or a woman, or both -- put them into a hermetically sealed chamber in outer space and they will not self-reproduce. They will die and decay.

As far as I can tell, a single life form can do nothing by itself. Life forms are open systems deeply and obligatorily imbedded in the ecosystems in which they evolved. Because of this fundamental dependence of life forms on their environments and on the other life forms in their environments, defining life in terms of "self-reproduction" makes little sense to me. Definitions of life often use the word "self-reproduction", as if it meant something -- as if life came in little isolated bags called cells that could survive by themselves. They can't. The mutual dependence of life forms runs deep into the tree of life when the earliest life forms were probably tightly knit communities of bacterial mats (some of whom produced stromatilites), not individual cells (Paerl *et. al.* 2000).

We use the words "to reproduce" and think it different from "to be reproduced". This active/passive distinction comes intuitively to us but it is not obvious to me that nature cares about such subtleties--maybe we shouldn't use them with such confidence. For example, we say that humans 'reproduce' but laptops 'are reproduced'. However, humans can be conceived in vitro or in surrogate mothers and eventually we may mature in artificial wombs in factories, while laptops will soon control the assembly lines that manufacture laptops. With these almost inevitable developments, the distinction between "to reproduce" and "to be reproduced" will first become blurred and then become useless.

The main point I am trying to make is that our traditional definitions of life are lacking in generality. They include superficial distinctions between "to reproduce" and "to be reproduced" and they do not include viruses, possibly the most fundamental part of the biosphere (Fig. 1).

How can we measure whether our concept of life is general enough to be useful in a cosmic context? Estimates of the generality of a given property of life can be based on how fundamental or how ancient or how widespread that property is. If a property is fundamental, ancient and widespread among the life forms on Earth, it is almost certainly a property of the last common ancestor and it is a good candidate for being general enough to be present outside the Earth. Water, organic molecules, sugars, alcohols and amino acids are all over the universe -- they fall from the sky in carbonaceous chondrites. These chemical building blocks are ancient, widespread and fundamental to the biochemistry of all life on Earth. Therefore, it is probably from these same standard building blocks that chemical life emerges all over the universe (if it emerges at all).

As traditional life emerged and evolved from a rather deterministic form of molecular evolution, the most important part of a life form's environment became other life forms. Selection pressures became self-referential. This type of close feedback amplified the idiosyncrasies of random mutations. Diverging life forms got quirkier with time. According to this view, we might expect bacteria or archaea on other planets because these are the earliest and simplest forms of life we know of. And we should not expect sulfur-crested cockatoos, homo sapiens or naked mole-rats on other planets. These are later, more complicated and quirkier forms of life.



Viral-RNA world

Figure 1 Tree of life emerging from roots in an RNA/Viral World. Every branch is adorned (or infected) with viruses. Viruses may well be remnants from an earlier epoch in which they were the dominant life form and no stable gene lines had yet emerged. From the viral point of view our vertically transferred genomes are frozen, hardly-evolving non-participants in the lively cut and thrust of lateral gene transfer.

The tree of life that traces the evolution of DNA-life on this planet (e.g. Pace 1997, Xue et. al. 2003) tells us that there was an early divergence (3 or 4 billion years ago) that led to two separate branches: bacteria and archaea. However, the divergence between plants and animals was comparatively recent, ~ 1.5 billion years ago (Hedges et. al. 2004). Thus, if we want to ask reasonable questions about life on other planets, it probably makes more sense to ask: Are there bacteria and archaea on the planet? (this split is labeled "A" in Fig. 1) rather than the quirkier downstream question: Are there plants and animals on the planet? (split labeled "B" in Fig. 1). I mention this chronology-of-the-tree-of-life-based criterion for reasonable questions because it is

possible that viruses represent a very early form of life and thus a form of life that may be general enough to represent our best candidate for the type of life we should expect on other planets.

Viruses are an immensely important part of the present biosphere and may have played a vital role in the origin of life. In an influential article Woese (1998) describes an RNA world of proto-organisms in which horizontal gene transfer played the dominant role. Reproductive fidelity was low but as fidelity gradually increased, "annealing" took place and organisms with gene lines emerged from a genetic chaos. Viruses still belong to such a genetic chaos and are therefore good candidates for being representative survivors from this epoch. In other words, viruses may have diverged so early from the forms of life that led to us that we have difficulty recognizing them as our ancestors. If this scenario is correct, then the most reasonable questions that one can ask about life on another planet is: Are there viruses and cellular life on the planet? Did cellular life emerge from viral life when fixed gene lines started to emerge and vertical gene transfer started to compete meaningfully with the more ancient viral horizontal gene transfer? If this scenario is even approximately correct, then one of the most important players in the origin and evolution of life on earth and one of our best guesses about the form of life elsewhere, is excluded from our traditional definition of life simply because it diverged too long ago for us to recognize it as our ancestor. This seems analogous to being able to recognize our relationship to chimpanzees but not our more distant relationship to fish. In our xenophobia, we only want ancestors who were like we are now -- that is, ancestors who were preoccupied with making protein and having sex -- as if the ability to outsource protein production were a bad thing!

The origin of life from non-life involves a series of transitions, and viruses may represent a stage in this series. In an evolutionary sequence, it makes little sense to break the chain at a specific link and pontificate: links before this break are not alive while links after this break are alive. Thus, to dismiss viruses as non-living because they are survivors from a very early epoch reminds me of sending everyone born before Jesus into limbo. Even if the scenario for the viral origins of life is incorrect, we need to deconstruct traditional definitions of life to make sense of the continuum between life and non-life.

3. Are Japanese Alone in the Universe?

Another way to access the generality of a particular grouping such as "life", is to consider more specific and more general groups. A fundamental question of astrobiology is: Are We Alone? The "we" is vague. Who is "we"? To remove this ambiguity a japanese website is more specific and asks: "Are humans alone in the universe?" (<u>http://jvsc.jst.go.jp/universe/et_e/index_e.htm</u>). But why stop at that level of specificity? We could, for example ask: "Are Japanese alone in the Universe?" There is a hierarchy of generality to these types of questions, starting from the specific and becoming more general:

IS "WHO" ALONE? FROM THE SPECIFIC TO THE GENERAL

Question

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"Are Japanese alone in the Universe?"	yes
"Are Humans alone in the Universe?"	yes
"Are Mammals alone in the Universe?"	yes
"Are Vertebrates alone in the Universe?"	yes
"Are Eukaryotes alone in the Universe?"	yes
"Are DNA-based Terrestrial Life forms alone in the Universe?"	maybe
"Are Far From Equilibrium Dissipative Systems alone in the Universe"	no
"Are Terrestrial Atoms alone in the Universe"	no

On the right I have given what I believe are defensible answers. The most specific questions at the top and the most general questions at the bottom have easy answers. I think good arguments can be made that the Japanese people are alone in the universe – that is, on another planet, we will not find another Japan with Japanese people walking around speaking Japanese and playing baseball. Simpson (1964) in "The non-prevalence of humanoids" articulated the case that humans (or any given species) were a quirky product of terrestrial evolution that we should not expect to find elsewhere in any form that we could call "humanoid" (see Conway Morris 2003 for a dissenting opinion). Any given species that has evolved on the Earth will have its closest relatives here on Earth. Thus, if we consider humans to be alone on Earth, then humans are a fortiori alone in the universe.

Mammals and Vertebrates seem more generic, but these groups are monophyletic---they evolved from a single species that diverged into the range we see today. So although they are now more generic than a single species, they were a quirky single species a few hundred million years ago. We may be able to apply the same reasoning to even larger current groups, such as Eukaryotes, but we will need to go back a couple of billion years before the quirkiness of their humble and very specific beginnings are recognized (e.g. Bell 2001, Kostianovsky 2000). The next in this hierarchy of generality is DNA-based terrestrial life. Could it be that terrestrial life is as quirky as a species and therefore we should not expect it elsewhere. Opinions span the range from "our type of life is unique to Earth" to "our type of life is everywhere". Both seem reasonable to me, hence the answer "maybe" to this question.

The last two groups, Far From Equilibrium Dissipative Systems (FFEDS) and Atoms, are sufficiently general that we are sure that the answer is no; they are not alone. Detailed spectra of stars tell us that terrestrial atoms are all over the universe. Also far from equilibrium dissipative systems like stars, convection cells, atmospheric whirlpools like Jupiter's red spot and dust devils on Mars are all over the universe.

With this hierarchy in mind, I propose that we redefine "life" by shifting it one step more general and equate life with Far from Equilibrium Dissipative Systems (Figure 2). A similar shift was necessary when we generalized our notions of life to include newly discovered microscopic life. Such a generalizing shift should already have taken place with respect to viruses.

Answer

The book Scientists on Gaia (Schneider and Boston, 1998) was dedicated to the question of whether the biosphere as a whole is alive. It is an interesting issue that doesn't have an easy answer. Besides viruses, ant colonies, ecosystems and Gaia, there are other entities whose status as "life" forms is reluctantly bestowed. What about prions, and the artificial life we create in a computer. Is Google alive yet? Our definitions of life seem to lose their meaning for big things like ecosystems, Gaia, stars or the galaxy. They also fall apart for small things like viruses, viroids, and prions. Our traditional definition of life seems to be too narrow to classify even the range of structures we see on Earth. To divide up all the diversity found on Earth into two boxes, one called life and one called non-life may be a senseless task that we should forget about (Fig. 2, top panel). However, I believe that meaningful attempts based on more general features can be made (Fig. 2, bottom panel).

4. Thermodynamics as a Basis for a More Universal Definition of Life.

Where can we hunt down some generality to improve our definition of life? I would suggest chemistry and physics and specifically thermodynamics. When a chemical system is in equilibrium, no reactions take place. The temperature is constant. There is no heat flow and no chemical gradient. Equilibrium is another name for death. When thermal gradients, chemical concentration gradients or electric potential gradients are large enough, Gibbs free energy becomes available and organized structures emerge spontaneously that act to reduce the gradient and dissipate the free energy. In a fundamental sense, these spontaneous and ubiquitous structures are nature's way of reducing gradients and obeying the second law of thermodynamics (Schneider and Kay 1994).

Convection cells in the solar photosphere are organized structures maintained by the temperature gradient between the hot subsurface and cooler surface of the Sun. Bernard cells are an example of the same phenomena in the lab. Whirlpools exploit gravitational potential energy to maintain their structure while hurricanes and dust devils run on temperature and pressure gradients. Where there is a gradient or a far from equilibrium situation, dissipative structures emerge to remove the gradient and exploit the available free energy to maintain the structure that is doing the dissipation. These gradients are all over the universe and thus, so too are the structures associated with them.

At the equator there is more carbon-based life and there are more hurricanes. This is no accident. The trees of a rain forest and hurricanes are the same sort of structure. They are far from equilibrium dissipative structures that dissipate the radiative, thermal, pressure and chemical gradients set up by the flux of the Sun. In the open ocean there is abundant sunlight but not much chemical disequilibrium and therefore not much life. Similarly, chemical equilibrium at the bottom of the ocean precludes much life there. However, on the mid-oceanic ridges, where a strong thermal gradient produces black smokers, a strong chemical gradient provides the environment for dissipative structures called life forms.

As heterotrophes we maintain our structure by dissipating the chemical gradients between our low entropy food and our high entropy waste. Traditional carbon-based





Figure 2 Redefining Life. Here are two schemes for dividing up the Universe and defining life. At the top is the traditional dichotomy based on the presence or absence of DNA. The lower panel is a scheme based on the thermodynamic concept of equilibrium. I argue that the equilibrium-based scheme more plausibly represents a classification system for extraterrestrial life and shows that DNA-life is a subset of the more general class of Far From Equilibrium Dissipative Structures. In the traditional view, we pretend that there is a discrete defensible boundary between life and non-life (thick blank line) although we are not sure in which box to put viruses, prions, ecosystems and Gaia. If we (the traditional "life forms" of Earth) belong to any generic set, it will be to the set of Far From Equilibrium life forms, along with hurricanes, red spots on Jupiter and stars (bottom panel).

life forms in general are persistent structures that reduce the electrochemical potential gradient associated with reduction/oxidation pairs -- essentially electrons falling into deeper potential wells. They exploit the gradient of electron negativity in redox pairs (Nealson and Conrad 1999). Photosynthetic creatures are structures maintained by the dissipation of the energy associated with 6000 K photons in a 300 K environment. If these photons were coming from all directions and in equilibrium with a 6000 K environment, there would be no free energy available, and no far from equilibrium structure could exist: no plants and no hurricanes. With these thermodynamic

considerations, far from equilibrium dissipative structures (not just the carbon-DNAbased ones) are a broad category that can be used to define life in a way that makes sense on the planets orbiting Alpha Centauri or anywhere in the Universe. It is clear that DNA-based life belongs to this group of far from equilibrium dissipative systems. It is also clear that FFEDS is a larger more generic group that includes more than just DNA-based life.

But wait! In our hunt for generality couldn't we arbitrarily say hydrogen atoms are alive -- and since we've detected hydrogen everywhere in the observable universe, we could say: We have detected extraterrestrial life! That, however, would be a semantic game with no scientific content. I believe that there are many good physical, thermodynamic reasons to put traditional life into a more objective, more generic, more well-defined class of objects called far from equilibrium dissipative structures. When we get used to calling this category "life", I suspect that our previous definitions of life will seem as parochial as equating life with just flora, fauna and fungi.

If most alien civilizations are based on nuclear life on the surfaces of neutron stars (Feinberg and Shapiro 1980), what type of definitions for life would be required to call them life. A 'life=FFEDS' definition would work but a DNA-based definition would not. Far from equilibrium systems and their relation to life is discussed in Schneider and Kay (1994,1995), for an opposing view see Anderson and Stein (1986).

5. The Origin and Centralization of Information and the Prejudice against Non-DNA Life.

One argument against the idea of FFEDS = life, is that hurricanes and convection cells and stars contain no information within themselves that is passed on when they reproduce. Stars for example are far from equilibrium dissipative structures metabolizing the free energy made available by a nuclear potential energy gradient. A star has no DNA inside itself and no internal structure that is passed on to the next generation of stars. However, when a massive star dies, it explodes and infuses the surrounding molecular hydrogen with heavy elements that enhance the ability of the clouds to lose energy and collapse to form more stars. The shockwave from the explosion also plays a role by kick-starting gravitational collapse. Thus, there are important links from one generation of stars to the next. However, the information controlling and sculpting the next generation of stars is in the modifications of the stellar environment, not centralized in some coded molecule.

The information content of DNA came from the environment as generation after generation of organisms were selected and filtered. Does it matter whether the information to form another system is contained centrally or distributed? In our traditional view of life, just as we may be exaggerating the importance of whether we 'reproduce' or 'are reproduced', we may be exaggerating the importance of whether the information and conditions that affect reproduction are stored internally in DNA or externally in the composition of the material that will form the new FFEDS. Survival is the issue, not whether the gradient that led to a FFEDS has been set up artificially by centrally stored information or naturally by decentralized information.

6. The First Detection of Life as We Don't Know it.

I went to a conference on artificial life where there was a serious discussion of how to build a robot--essentially a mobile computer acting on it's own, making it's own decisions about where to go etc.

We all laughed at clips of battery powered robots stumbling over little obstacles. We had all walked into the room carrying laptop computers that we opened up and fed information to. At the end of the discussion we picked up the laptops and carried them efficiently out of the room. During the discussion I mentioned that our laptops were already doing everything that we were trying to get robots to do. Our laptops have co-opted our legs to move around. I was surprised that this idea seemed absurd to all the robot-building, laptop-carrying attendees.

Similarly the detection of extraterrestrial life claimed here, based on a more general definition of life may seem absurd to the army of biochemists invested in looking to manufacture traditional life in the lab. According to the new definition, life is easy to make – just let the water out of the tub or blow smoke rings or just boil water and watch the convection cells. With a shift in focus to the most general, universal features of life -- a redefinition of life -- we start to see life everywhere.

The non-prevalence of terrestrial life in the universe is becoming a data set that should give us pause and motivation for a more general view of life. I have argued that the traditional definitions of life are too narrow. These definitions don't include viruses and often include a meaningless statement about 'self-reproduction'. It is possible that the universe and the life forms in it are not usefully defined by our traditional definitions of life. Therefore we should take seriously a different more universal definition: life = FFEDS.

With this more universal definition of life, we can say with conviction that we have detected extraterrestrial life and that life on Earth is not alone in the universe. We are not alone! Somebody should let the SETI people and NASA (who are "following the water") know that they've been scooped.

7. References

- Anderson, P. W. and Stein, D. L. (1987) Broken Symmetry, Emergent Properties, Dissipative Structures, Life: Are They Related? In: F. E. Yates (ed.) Self-Organizing Systems: the emergence of order. Life Science Monographs, Plenum Press, NY, pp. 445-458.
- Bamford, D.H. Burnett, R.M. Stuart, D.I. (2002) Theoretical Population Biology. 61, 461-470.
- Bell, P. (2001) Viral Eukaryogenesis: Was the Ancestor of the Nucleus a Complex DNA Virus? J. Mol. Evol. 53, 3, 251-256.

Bergh, O. Borsheim, K.K., Bratbak, G. and Hudd, M. (1989) High abundance of viruses found in aquatic environments. Nature. 340, 467-468.

Bernal, J.D. (1949) The physical basis of life. Proc. of the Physical Society. 62, 10, 358B.

Chyba, C.F. and McDonald, G.D. (1995), The Origin of Life in the Solar System: current issues, Ann. Rev. Earth Planet Science. 23, 215-49.

Cleland, C.E. and Chyba, C.F. (2002) Defining Life, Origins of Life and Evolution of the Biosphere. **32**, 387-393.

Conway-Morris, S. (2003) Life's Solution: Alone in a Crowded Universe Cambridge University Press.

- Feinberg, G. and Shapiro, R. (1980), Life Beyond Earth: the Intelligent Earthling's Guide to Life in the Universe, Morrow, NY.
- Hedges, S. B., Blair, J.E., Venturi, M.L., Shoe, J.L (2004), A molecular timescale of eukaryote evolution and the rise of complex multicelllular life. BioMedCentral Evolutionary Biology. 4(2), 1-9.

Klein, H..P. (1999) Did Viking Discover Life on Mars? Orig. Life and Evol. Biosphere. 29, 625-631.

- Kostianovsky, M. (2000), Evolutionary Origin of Eukaryotic Cells, Ultrastructural Pathology. 24 (2), 59-66.
- Kuhn, T. (1962) The Structure of Scientific Revolutions, University of Chicago Press.
- Lehninger, A. L. (1970) Biochemistry, Worth Publishers Inc. NY.
- McKay, C.P., (1997) The Search for Life on Mars, Origins of Life and Evolution of the Biosphere 27 (1-3), 263-289.
- McKay, C.P. and Stoker, C.R. (1998) Gaia and life on Mars. In: S.H. Schneider and P.J. Boston (eds.) Scientists on Gaia, MIT press, Cambridge, MA, pp 375-381.
- Nealson, K.H. and Conrad, P.G. (1999), Life: past, present and future. Phil Trans. R. Soc. Lond B 354, 1923-1939.
- Pace, N.R. (1997) A molecular view of microbial diversity and the biosphere. Science. 276, 734-740.
- Paerl, H.W., Pinckney, J.L. and Steppel, T.F. (2000) Cyanobacterial-bacterial mat consortia: examining the functional unit of microbial survival and growth in extreme environments, Environmental Microbiology 2 (1), 11-26.
- Prigogine, I. (1947) Etude thermodynamique des phenomenes irreversibles Dunod, Paris.
- Prigogine, I. (1980), From Being to Becoming Freeman, NY.
- Sagan, C. (1970) Life. In Encyclopedia Britannica 15th edition Vol. 10, New York, Macropaedia.
- Schneider, S.H. and Boston, P.J. (eds.) (1991) Scientists on Gaia, MIT Press, Cambridge, MA.
- Schneider, E.D. and Kay J.J. (1994). Life as a manifestation of the second law of thermodynamics. Mathematical and Computer Modeling. **19**, No. 6-8, 25-48.
- Schneider, E.D. and Kay, J.J. (1995) Order from Disorder: The Thermodynamics of Complexity in Biology. In: M. P. Murphy and L.A.J. O'Neill (eds.), What is Life: The Next Fifty Years. Reflections on the Future of Biology, Cambridge University Press, pp. 161-172.
- Schrödinger, E. (1944), What is life? and other scientific essays Double Day Anchor, Garden City, NY.
- Simpson, G.G. (1964), The Non-Prevalence of Humanoids. Science. 143, 769.
- Woese, C. (1998) The Universal Ancestor. PNAS. 95, 6854-59.
- Xue, H. et al (2003) Transfer RNA paralogs: evidence for genetic code-amino acid biosynthesis coevolution and an archaeal root of life. Gene. 310, 59-66.