WE NEED A BIO-EINSTEIN

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We are celebrating the 100th anniversary of Albert Einstein's Theory of General Relativity, the theory that enabled the remarkable advancement of modern day physics. To match that progress in solving the mystery of life we need a Bio-Einstein. We need someone who will do top-down biological research, starting with bio-gedankenexperiments. By top-down I mean imagining some basic theory of how life begins, some Law of Life that commands inert components to organize and become a living cell, as in Fig. 1, some theory that is verifiable by a proposed experiment, as was Einstein's prediction of the bending of light by gravity.



Fig. 1. Single cell of Archeae – Can this simple life form be disassembled and then revitalized?

Many efforts have been made by biologists over the past two centuries to discern the origin of life, with such attempts increasing exponentially in the last few decades, for example Sidney Fox (Figure 2) who tried to coax amino acids into life assembly.



Fig. 2. Sidney Fox, 20th century pioneer in attempting to construct a living cell.

However, biologists have not been nearly as successful as the physicists. We now pretty much understand how particles and waves evolve and react to produce our physical universe. Of course, as with life, the question of origin remains. But the physicists are much further along the road to the beginning than are the biologists. However, we must acknowledge that the biologist's road is much harder. Biologists seek to discover how the physicists' particles, waves and products thereof somehow became assembled into the ill-defined, uniquely functioning thing we call "life." The commonly stated, "We can't agree on a definition of life, but, like pornography, we know it when we see it," remains true.

None of the many brilliant minds at work in laboratories around the world has succeeded in abiotically producing life, or even biological membranes. Louis Pasteur's pronouncement that life comes only from life remains intact. This seemingly leaves but three alternatives: 1. life has always existed, there was no beginning; 2. life resulted from the very spontaneous generation Pasteur ruled against, some *elan vital*; or 3. life is supernatural, invoking shades of "intelligent design." None of these alternatives is acceptable to the scientific mind we have cultivated over the last few centuries. But, the biologist is plagued with the

additional problem that, whatever logical explanation might be found to explain genesis, that explanation must include the reason genesis seems not to have occurred again. The logical approach to genesis thus requires that some environmental condition key to the process must have changed since life first began. Perhaps, searching for such possible changes over the history of the Earth or beyond (since there is no reason to believe that genesis occurred on Earth) might prove fruitful in providing a clue to geneses. However, any such change cannot have proved inimical to the continuation of life: the change must prevent new geneses, but not be harmful to survival of the first life form. This puts a strong constraint on any such change.

To pursue another famous quote by Einstein, "If at first the idea is not absurd, then there is no hope for it," I have conjured the following absurdity. Suppose that organic molecules produced in the big biological bang passed through a region of space having the conditions that organized them into living cells that eventually found their way to Earth and possibly to other habitable planets. This still leaves the problem of why this has not occurred again with new life forms finding their way to Earth over the more than four billion years since the first form arrived here. A possible counter to this would be to say it has occurred, but all life forms created by the Law of Life are necessarily identical and, therefor, not discernible as coming from another genesis. This highly unsatisfactory explanation seems the only possibility left for this far-out approach. But as Einstein also cautioned about absurd theories, "A scientific theory should be as simple as possible, but no simpler."

Darwin and Oparin tried to explain away the lack of a second form of life on Earth by saying that, once one form of life appeared, it would consume or out-compete any subsequent emergence of life. However that conclusion seems unwarranted. The preference of our form of life for D-carbohydrates and L-amino acids would seem to leave organisms with preference for the opposite enantiomers virtually unopposed. Should they nonetheless compete for space, water and light, Darwin's own argument might be used to indicate that, once appearing, such a form would evolve to survive the hostility of an existing life form, as have our present competitive species.

While representing a myriad of approaches, virtually all the efforts to unveil the secrets of life share one fundamental aspect in common. They work at the molecular or microscopic level. These efforts try to assemble life from its elementary components. The revelation of the citric acid cycle, the ubiquitous role of ATP, the startling discovery of DNA (Figure 3), and the mapping of genomes are examples of important achievements made at the molecular level.



Fig. 3. Strand of DNA – Would it reassemble with all other cell components?

However, this "bottoms-up" approach is in contrast to the post-Newton revolution that led to our understanding of the physical world. That insight began at the top. No teams of scientists with elaborate machines and equipment were required, just paper, pencil and thought. Einstein's gedankenexperiments opened the true nature of the universe to us. They created the milieu for the subsequent penetrating experiments performed with incredible instruments on Earth and in space explaining the universe in ever more detail. How do we get to this denouement of fundamentals in biology?

Biologists have made much progress, but, as stated above, fall painfully short of being able to create life. The role of DNA as master of the dance of life is explained, even to the extent of being able to transfer the nucleus of one cell into another, or to alter DNA to have it make new, unnatural products. But we cannot create a functional biological membrane (Figure 4, or a living cell (Figure 5) *de novo*. It seems the bottom-up endeavors, while revealing marvelous detail, might not provide the desired ultimate answer.



Fig. 4. The bacterial cell membrane – not a simple device.



Fig. 5. Key steps in reassembly of a bacterial cell – What drives this?

Why not try the top-down approach on biology? Some may contend it has been done, such as in the "Biological Big Bang" theory, that biology suddenly appeared very early after the physical Big Bang. This is intriguing, but without significant consequence in our search: the details of how life formed are missing. No experiment is cited to test that or any new theory even though we now have exquisite microscopes (Figure 6) and other instruments to aid in exploring the minutest details of the cell and its components.



Fig. 6. Images through the atomic force microscope – could this aid our quest?

Where is that office clerk, with an open mind? Obviously, the genius of an Einstein will be hard to find. But why not seek for him or her? Some will say any such genius will inevitably come to the fore, and need not be sought. But it seems likely that encouragement and support might help to find those gems of purest ray serene that might otherwise remain unseen. Why not have conferences inviting participants to present their top-down bio-gedankenexperiments? Perhaps a publication could be dedicated to the subject. Grants and prizes might coax forth the needed genius. The awards need not be large since no equipment or staff are needed. Only the P.I. need be supported to flesh out his or her theory into testable form. Thus many grants and awards could be made at modest financial investment. Government, industry and private parties could participate in the funding. We should try all of these things. The benefit-to-cost ratio is enormous.