Term paper 1 : Prebiotic RNA–Protein Co-evolution and the Origin of 'Life'

- Swarbhanu Chatterjee.

In Biology, life is defined as a "cellular phenomenon that perpetuates itself in suitable conditions". The theory that life evolved from lower unicellular organisms to more complex cellular organisms is a very plausible premise. More than 40 years ago scientists at the University of Chicago showed that amino acids can arise out of complex molecules in primordial conditions of heating, cooling and electrification < corresponding to lightning >. Other scientists showed that amino acids can form into simple proteins, the building blocks of terrestrial life, under primordial conditions. It has been shown that under primordial conditions, these thermal proteins < oligo/peptides > can then produce small, cell-like objects called microspheres. Microspheres do not have the internal structure that runs the living cells of today. But they do bear a resemblance to microfossils of Precambrian rocks and this has inspired some scientists to claim that these microspheres are only the first step towards the formation of proteinoid protocells from thermal proteins. If we have something like a proteinoid protocell, it is reasonable to assume that the protocell membrane would have to act in many ways similar to a living cell membrane. However, we don't know what the actual structure of the protocells may have been. The above idea challenges conventional thinking that nucleic acids needed to have existed before the arrival of any form of living cell. Proteinoid protocells may have been the first step in evolution. But it is still only a conjecture at present.

Bioinformational molecules

Evolution of terrestrial life is all about the evolution of the genome, because it's the genetic information that decides everything about the structure and functions of the proteins used in the cells. Therefore bioinformational molecules, the molecules which take part in storing genetic information, are essential for the evolution of life through genetic means. Whether proteinoid cells existed before the evolution of nucleic acids or not, its commonly believed that before DNA came into the picture, polyribonucleotides played the role of storing and passing on genetic information. There was coevolution of templates for RNA synthesis and protein < polypeptides > synthesis. While the evolution of polyribonucleotides was through RNA replication < where there were frequent mutations and miscopying >, the evolution of the proteins < polypeptides > took place simultaneously but independently through nonribosomal synthesis, i.e. alteration of side chains. In this way, the RNA-Protein world came into existence. The RNA took the role of storing and evolving genetic information while the proteins were synthesized either by ribosomal synthesis or through nonribosomal synthesis like folding and alteration of sidechains.

Therefore according to the above hypothesis, the first self-replicating systems associated with the origin of life consisted of both RNA and protein. RNA served to hold information whereas protein molecules provided all the enzymatic activities needed to make copies of RNA and to reproduce themselves. The cycle that developed a self replicating system out of the primitive soup of amino acids and nucleotides had therefore two radically different components – RNA and proteins.

There have also been efforts to describe how new RNA molecules can be synthesized directly from precursors and an RNA template without the involvement of protein at the beginning of biological evolution. If RNA could self replicate, it would evolve slowly by miscopying < mutations >. The self-splicing and insertion < transposon > mechanisms would enable genetic changes which are said to be equivalent to sex, which Gilbert (1986) defines as " the infectious transmission of genetic elements from one organism to another. " The latter may precisely be what viral infections are.

It is thought that after thousands of years, the RNA world evolved into the DNA world in which DNA came into center-stage as the most efficient way of storing and passing on genetic information while keeping the option of mutation alive.

This seems to be the most plausible hypothesis for the evolution of RNA, DNA and terrestrial life. If the above scheme is correct then life evolved from a highly determined chemical sequence and did not arise due to chance, which suggests that life is very likely to occur elsewhere in the universe. But its still only a hypothesis since we cannot do an experiment in which we start with a very large number of amino acids under primordial conditions and wait long enough till we get a small number of unicellular organisms because evolution takes a rather long time. The only clues as to what actually may have taken place are fossils.

A Thermodynamic Model for Prebiotic RNA-Protein Co-evolution

In their paper ' A Thermodynamic Model for Prebiotic RNA-Protein Co-evolution', < July 19, 2001 > authors Erkan Tuzel and Ayse Erzan have proposed an interesting scenario for the co-evolution of RNA and of fast folding proteins with large entropy gaps in porous rocks. A cross section of a porous rock containing the prebiotic soup of RNA, protein molecules, amino acids and water is shown in Figures 1 and 2. The surrounding rock serves as an infinite heat reservoir for these pores since their sizes will be small compared to the whole volume of rock. The channels between these pores aid in the transport of materials and the whole system might be thought of as a porous network.

One assumes that the amino acids are free to diffuse anywhere in the soup and every RNA molecule can find enough amino acid around to use in the synthesis of proteins. The RNA molecules string up the amino acids to make the proteins. The RNA molecule can be thought of as a power supply since it provides the information that determines the particular amino acid sequence, and therefore the interaction energies between neighboring monomers which in turn determines the energy of the chain.

In order to reduce the total free energy of the system, the hydrophobic residues are pushed away from water and tend to get hidden by adsorption on the rock surface while the polar residues stick out into the water. If the chain now adsorbs in a highly stretched conformation, it can slightly increase its entropy with the aggregation of the hydrophobic residues that will allow the intervening sections of the chain greater freedom. This provides an effective entropy driven attraction between the hydrophobic residues because if the hydrophobic residues come together, the total free energy is reduced. The above mechanism leads to a partially folded conformation of the chain with the polar residues on the outside and the hydrophobic residues on the inside. Thus the chain is guided by the rock surface into a partially folded state which now detaches from the rock upon folding around the hydrophobic core. Therefore a final state with lower energy is achieved when compared to the random coil in the soup. Energy is given out in the process to the rock surface that acts like an infinite heat reservoir. The folded proteins then get detached from the rock surface and unfold in the soup due to a higher ambient temperature. Heat is absorbed by the chain from the soup. The soup in turn takes heat away from the rock surface.

Therefore an entire refrigeration cycle is completed in three steps :

- Synthesis of proteins by RNA
- Partial folding of proteins on rock surfaces
- Unfolding of proteins on soup.

The refrigeration cycle is depicted in Fig 2.

The refrigeration cycle proposed by the authors is a possible way to cool down the prebiotic soup within pores. Nature would therefore favor the process because the energy is lowered and therefore the RNA would replicate more. The process works better for proteins having large entropy gaps and for those that can fold very quickly before the soup is again warmed up by the rock. Moreover the proteins should be small enough so that the rock surfaces can aid them in the folding. These best describe heat shock proteins that are small and perform their folding-unfolding transition at higher temperatures in a rapid way. It is also speculated that this is the reason for the presence of very fast folding proteins that are observed today under hot conditions. Since heat transfer depends strongly on surface-to-volume ratio, proteins will cool down only pores of appropriate sizes. Therefore the pore size is important in this scheme.

The partially folded proteins have a tendency to aggregate in order to reduce their hydrophobic surface. But this will hinder the efficiency of protein folding. Therefore, there have to be molecular chaperons that would have to bind reversibly to these partially folded chains to prevent their aggregation and to promote their passage into the soup. The authors speculate that in the course of evolution, these molecular chaperons have taken over the role of rock surfaces.

This is not the only mechanism that might have operated in the prebiotic earth. Eigen proposed a different mechanism affecting the coevolution of proteins and RNA, namely the catalysis of RNA replication by certain proteins.

A generic definition for 'living systems' ?

In my opinion the concept of life should be generalized beyond the cellular life that has evolved on earth, because the living organisms in some other galaxy may not be cellular in form. There should be a generic way of describing the origin of life in which one does not have to refer to RNA - DNA strands or amino acids, because protein-life may be specific only to the earth.

In my opinion, the most abstract definition of life would be the following - Life is a phenomenon in which a system evolves spontaneously into greater and greater states of 'orderedness and correlation between the units comprising the system' without requiring the active interference of a superior 'ordered' system.

By 'orderedness', I mean the following - When a man feeds in codes in a program, then there is a reason or logic behind every part of the string of letters entered. There is a correlation or interrelationship between every part of the code. However, if we let a not so intelligent animal like a monkey type in something, then the string of letters will be less 'ordered'. The 'orderedness' increases when the man feeds in codes of different types and makes them all fit into one big program. So the different kinds and larger number of units are made to have a relationship or correlation among each other and this corresponds to greater 'orderedness'.

A piece of computer software, and therefore the computer, becomes 'more ordered' due to the interference of a 'highly ordered system' like a computer user. But if one can think of a kind of software which becomes 'more ordered' without requiring the interference of a man, one can say that the computer with the software has living characteristics according to the above definition.

It would be nice if one can think of an appropriate universal measure for the 'orderedness' and then one can have a more universal theory of life because life may in reality not be only a cellular or only an organic phenomenon.

Bibliography < References relevant to the discussion >

1. 'A Thermodynamic model for Prebiotic RNA-Protein Co-evolution', E. Tuzel and A. Erzan, arXiv:cond-mat/0107315 v1 (July 14, 2001).
2. http://mccoy.lib.siu.edu/projects/bio315/section5.htm
3. Deamer, D. W. and G.R. Fleischaker, Introduction to Section V, Origins of Life : The central Concepts (1994).