

Nucleobase Peptide Protocells

by: Robert B. Login

During my retirement, I became interested in keeping up with organic and polymer chemistry; however, I also decided to study biology and biochemistry as I felt that I had a very limited knowledge of the current state of these disciplines. To my surprise the workings of the cell are now well understood. Even so called “simple” prokaryotes have been in essence revealed and the revelation of their fantastic complexity was for me a humbling experience. How could organic chemistry generate organisms that no man had a hand in?

The remarkable Dr. Venter and his institute were even able to synthesize DNA and commandeer prokaryote cells by replacing their DNA to generate bacteria to do their bidding. But he still needed the cells machinery and could not generate life from scratch; however, this is an example of “Synthetic Biology” with its potential to build “living cells” from parts available by synthesis or from dismantling prokaryote cells, for example. There is also another new discipline referred to as “Systems Biology” where the idea is to study how said parts can be put to work together generating a “living system”. For example E. Coli, if you could see it at the molecular level, is a fantastically complicated machine with 4000 genes and thousands of enzymes and protein with numerous feedback loops like a complicated computer program that could be fundamentally understood and recreated.

My problem is that I believe somewhat in “Holism” the doctrine that a biological system is more than the sum of its components. This is the opposite of “Reductionism” where its adherents believe that understanding how the parts of cells work together is all you need to understand living systems. By “Holism” I really mean that something is still

missing from our understanding of “life”.

Synthetic and Systems biology still left me unsatisfied as I wanted to know how life began. I found two schools of thought, the RNA first school and the metabolism first school. RNA because it was thought to both store genetic information and can reproduce itself and has been shown to catalyze reactions like enzymes (called ribozymes), hence avoiding the chicken and egg conflict because modern organisms need for enzymes and genetic information and reproduction. With the idea that RNA would do all gives it the lead in current protocell arguments. The metabolism school believes that the need for energy over rules the RNA first theory, however.

Numerous books and articles have been written covering abiogenesis and it is claimed currently to be the most important unknown in science. Obviously, the first living thing was very simple but it had to be able to undergo reproduction and evolution to be considered to be alive. The current state of affairs would make you think that this abiogenesis event happened only once. Suggesting the idea that one protocell started it all. When you look around and see that nature does not bet on single events but produces success by the millions nay billions; therefore, I believe the first living things were plentiful and that under the right circumstances life could be created in the lab., the problem is that we really don't know what life really is!

Present day organisms are based on not that many compounds. Twenty amino acids, five purines and pyrimidines, several lipids and sugars, the various metabolism intermediate compounds, several metal ions and from these the myriad of proteins, enzymes and nucleic acids are synthesized. It seems reasonable to me that these compounds and required metal ions were available at abiogenesis. Therefore, the first protocells must have also employed the same cast of ingredients. The problem is that current cell

biology is so complicated that its hard to see how to simplify it.

Mostly everyone can distinguish between the living and the dead. You know a dead anything when you see it, but I ask if you could go back in time would you see the first life as living. I believe you would because in reality it was in my opinion, no different than now. It had the “life-force”, this is what is missing in current abiogenesis theories, what is the “life-force”? Maybe that's the wrong word as it can bring simplistic religious thoughts into the discussion. What I'm looking for is the physics/chemistry that means life. For example is it some yet unknown physics such as unknown molecular orbitals where electrons are alive? On the atomic level biology is really about moving electrons which are governed by the strange rules of quantum mechanics. Who is not to say that life is another branch of physics yet to be explained? This is “Holism” as I previously explained. Modern biology is reductionist and does believe that science will create life in the laboratory from cell parts refuting holism. Presently, the generation of the molecules of life from simple precursors such as HCN, formaldehyde, and formamide for example seems very reasonable; however, this is a long way from life itself.

In the distant past the Earth has experience mass extinctions, with many branches of the tree of life extinguished. The survival of RNA/DNA in the eukaryote cell was all that was needed to repopulate the Earth regardless of the nature of where these cells came from. When catastrophe opens up niches in the biosphere, even rodents can become lions. However, the bacteria are so successful and numerous that they and other prokaryotes were never exterminated and are probably unchanged to this day.

This suggests that of all the molecules of life, the nucleic bases and their polymers are center stage in importance. Thus they must have existed in some form from the beginning. RNA could well be that beginning but I find that unsatisfying as RNA is a

very complicated polymer. If you believe nucleic bases hold somehow the “life-force” then nucleic derivatives that could do the basics of life must have existed in large amounts. I suggest that the bases, the purines and pyrimidines were very plentiful in the beginning. Many scientists have proof that derivatives of formaldehyde/formic acid/formamides easily generated these bases. The early earth they say was hot enough to do this chemistry, and that meteors and comets contained these simple chemicals. Life started shortly after the heavy bombardment where innumerable meteors and comets had hit the earth.

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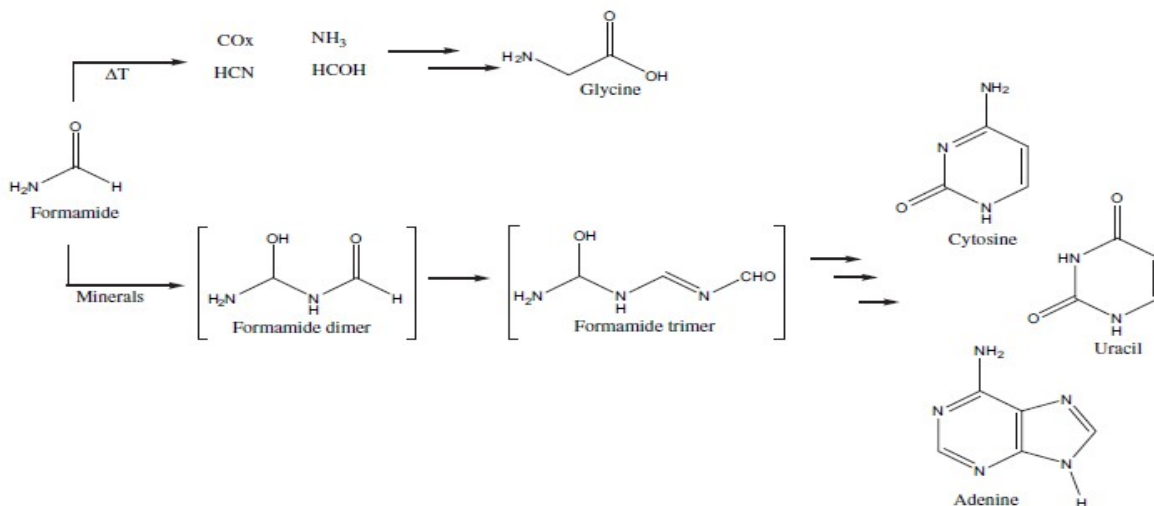


Fig. 1. Synthesis of nucleic acid bases and one amino acid from formamide in the presence of phosphate minerals.

I suggest that because amino acids were also present and that it might have been possible that amino acids or peptides having free amino groups could react with the formamides to produce derivatised nucleic bases. Such derivatives with amino acid or peptides would be hydrophobes with carboxylate head groups and nucleobase terminals that form surfactants that will spontaneously form protocells in water. The bases are arranged inside cell like peptide membranes. The inside is hydrophobic so that the bases could hydrogen bond to each other in familiar ways. Those

carboxylates are on the outside and in an aqueous environment. I believe the organization of the bases starts out randomly but eventually contains very pertinent sequences.

These sequences are in essence “alive”. They could be pi stacked with extended molecular orbitals in which electrons are in an environment of “life” and from which they are difficult to remove as the life-force will fight to survive. Survival is everything to present life forms....why? Organic molecules are just as happy to be in a bottle as they are in an organism! I know that vitalism is debunked because the molecules of life can be synthetically generated individually. Presently scientists suggest that life is nothing but a complimentary machine that requires as a minimum metabolism, heredity, and duplication. Once you have the components connected properly, the system is then alive. Obviously, this is reductionism and presently if you compare where we are in generating life in the laboratory, I think you could compare us to early astronomy where the earth was newly found to orbit the sun. Hopefully I'm being overly pessimistic as some very brilliant scientists are working in this field.

The early earth was bathed in much more energetic sunlight than today. This could have replaced the need for metabolism and primitive life would then need heredity and duplication. Nucleobase peptides, as self organizing entities, could easily reproduced by hydrogen bonding free nucleobase peptides to generate replicas. Hence we have the polypeptides and nucleobases in the same structures. How then does evolution occur?

Since the nucleobase peptides are not polymeric but associated in protocells, they can separate and reform. They could do this innumerable times until by chance a living

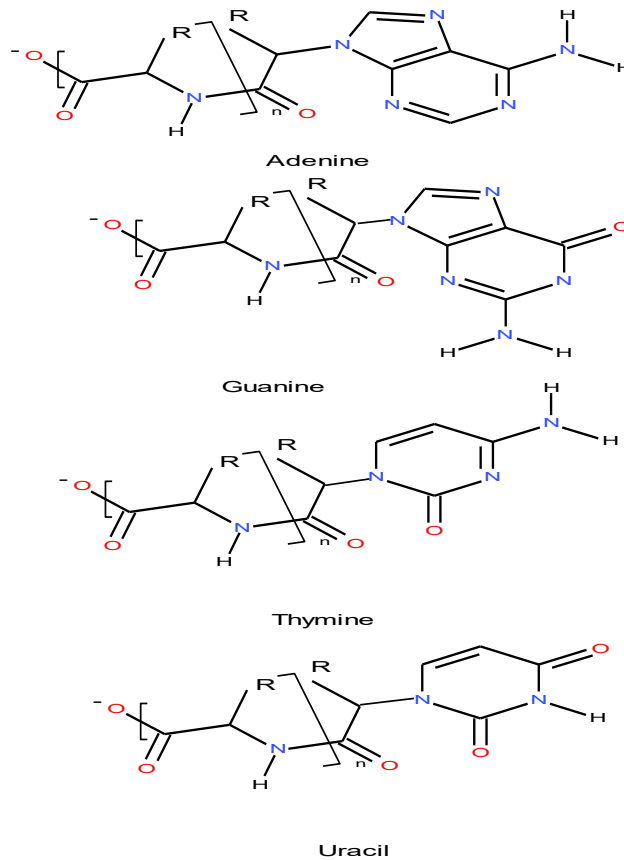


Fig. 1

entity resulted. This organization would persist as the hallmark of life is survival.

Examples of said nucleobase peptides are shown in figure 1. The peptide chain can also be attached at other positions of the nucleobase. For example:

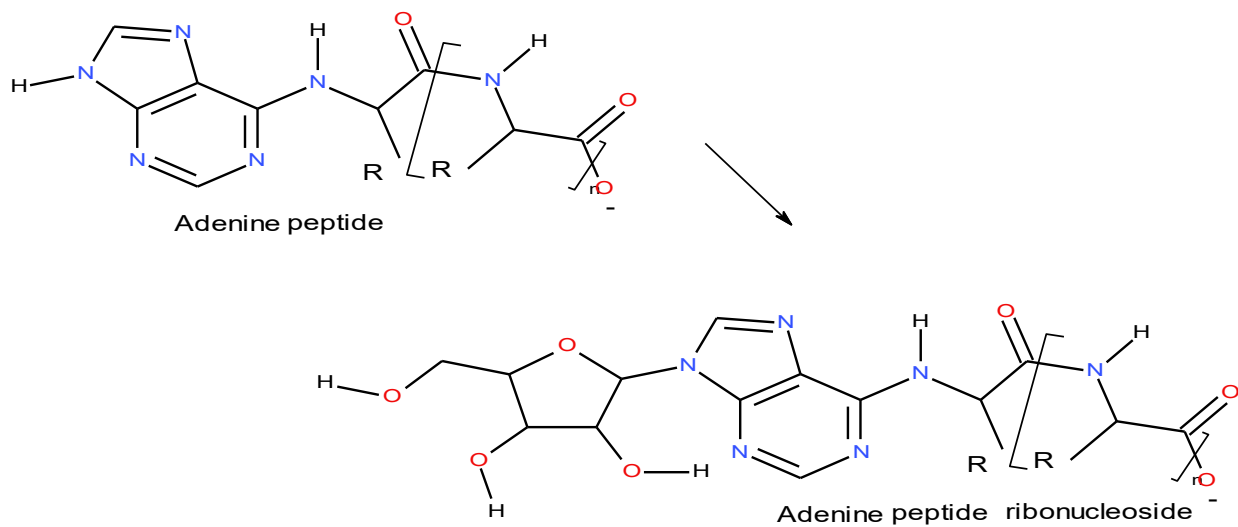


Fig. 2

Fig. 2 also illustrates that leaving the usual reactive nucleobase position free would allow for the addition of ribose. Thus paving the way for a route to primitive RNA structures.

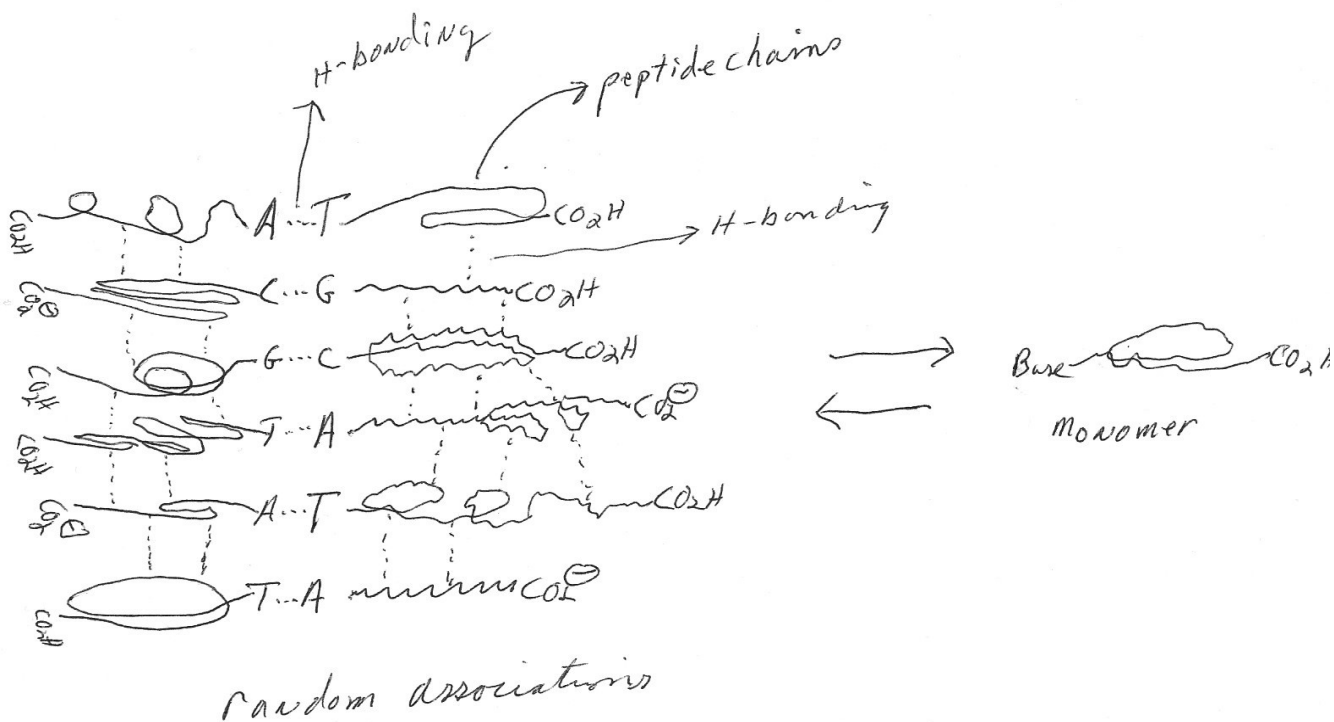


Figure 3

Figure 3 illustrates, in schematic form, how these nucleobase peptides could organize and depending on pH, the carboxylate end groups would be neutral or charged.

The complex shown in figure 3 is not only stabilized by the hydrophobicity of the peptides that are in each chain but by the hydrogen bonding of the nucleobases and between the peptide chains. Obviously much bigger structures can be visualized but I think the above affords the general idea. Now can I explain how the prokaryotes or the eukaryotes evolved ? No I can not as the above is just speculation but so is the immense abiogenesis literature which has only been able to show experimentally how the basic chemicals of life could have been generated from formamide for example.

The above peptide chains could grow larger because the associated monomers can return to their single status picking up more amino acids that would add to the caboxylic acid end groups upon dry down. They can then re-associate with other monomers when rehydrated. The peptide chains of the right structure would naturally fold and by chance become enzymatic. As the complexes grew bigger, the chance of splitting apart would increase, mimicking reproduction. In addition, metal ions could be embedded within the peptides which would act as ligands. This might have been how enzymes came about?

Remember it took billions of years for actual living cells to emerge. That's a lot of time for trial and error. Once a workable combination formed by accident it would do all it could to survive. Prokaryotes reproduce rapidly as a survival mechanism and can also form spores is this not a way to protect their genes. It seems that survival of DNA/RNA is all that matters.

The need for sunlight as a substitute for metabolism would have been a risky proposition because at night, disorder could occur. Those protocells that could substitute some

rudimentary metabolism would survive. It would take energy to maintain electrons in this privileged living state because of the right combination of nucleobase peptide monomers. I know this sounds bizarre but life could be a new state of matter; for example, we have no problem explaining aromaticity because we understand the quantum mechanics of this structure. Before quantum mechanics we had no real idea about it. I believe there is a quantum mechanical explanation of life. Since the nucleic bases play a pivotal place in life and are aromatic purines and pyrimidines, that are stacked up in cells, where they can have pi-pi interactions with electrons jumping around in macro-orbitals...is this like aromaticity, a more stable desirable set of orbitals, but with a hitch in that energy is required to be in this state? We know that at the subatomic level things are very strange why not explain life at this level. Why does life do everything imaginable to stay alive and since that eventually fails, reproduce protecting those nucleic base organizations so that they can be passed on from generation to generation for billions of years?

Modern biology presents DNA and RNA as just repositories of heredity. That RNA is the key to transcription and translation from the DNA repository of the information required to eventually form the proteins needed for current life. There is no idea for a physical reality beyond our current understanding. Why would organic compounds form an organism that fights for its existence. Is it all just a molecular machine? Religions explain this by vitalism and I don't accept this but can there be a scientific explanation?

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