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11.2.77

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Dear Dr. Bahadur,

thanks for your very suggestive letter. I knew, naturally, the bulk of your work, bus I was not avare of some important items which I would like to diskuss with you. But let me first answer your question.

The idea to study the entropy shift probably resulting from the formation of the spherical particles is certainly very interesting. Unfortunately I am not able to do the experimental work. I retired from the University a few years agot in order to awoid the administrative work related with the function of a director of a department, and I renonced also to experimental work, considering the theoretical biology as the domain requiring all my attention. Thus, I have not the technical possibility to do those measurements.

Nevertheless I can give you some information which seem to confirm your idea. Some years ago I worked on the mechanism of coacervation. The idea was, that the macromolecules in the coacervate are linked together by dipole forces, while the global charges - usually negative ones in most protein coacervates - provide a repulsing component, the macromolecule being in equilibrium between these antagonistic elecrostatic fields. In order to join the coacervate a macromolecule must thus overcome the negative barrier, and this requires a certain amount of kinetic energy, and this excludes the "cold" molecules from coacervation and accepts only the "hot" ones, exactly as would Maxwells demon.

A macromolecule joining the coacervate would be immobilized and loose its kinetic energie which is transformed into an increase of the electrostatic field, an event equivalent to reduction of entropy.

The experimental control was made by my assistant Wilhelm Linke (Protoplasma 52, 376 - 384, 1960) on coacervates from gelatin and arabic gum, which form very dense coacervate grains sedimenting rapidly and forming two sharply separated levels: the supernatant equilibrium liquid and the sedimented coacervate. As expected, the temperature of the supernatant layer dropped during coacervation, while the coacervate accumulated at the bottom, kept the initial temperature. Kinetik energy has been extracted out of a part of a initially homoenergetic medium and converted to a higher form of energy. Entropy had been reduced.

I strongly beleave that the globules you obtain are physicochemically related to coacervates. They are no amorphous masses

of isoelectric precipitates and certainly no cristals. They display sharp delimited phase boundaries so characteristic for the coacervate state, it seems not too far fetched to consider that entropy shifts observed during coacervation may arise also at the formation of your spherical particles.

There is another point of your letter which seems to me outmost important. We - that is a group of mostly young biophysicists in Berlin, working together with the perspective to write a book on the biophysical aspects of biogenesis - have studied the kinetics of the abiogen formation of amino acids under different energetic conditions. Let us consider e.g. a glycin molecule in which one of the two symmetrical hydrogen atoms is to be substitutend by CH_3 in order to form an alanin molecule. The substitution of one of them requires 2000 cal and yields an L-Alanin, or 2200 cal and yields a D-alanin. The difference ist experimentally well established and ist possibly due to the orientation of the electron spin.

If I try the synstesis by short wave UV with quanta energies about 10^0 cal, I must obtain the same output of L- and D-alanin. But in the primitive ocean the synthesis took place at about 38 to 40°C. The quanta energy distribution (at a logarythmic scale) is something like the courve drawn at the small leaflet. Quanta of 2000 cal or more, sufficient to produce a L-alanin, are somewhat scarce but still aviable; those of 2200 cal or more are more less numerous. Thus we must obtain an optically active substance with predominance of L-alanin.

I ignore the temperature at which you performe the synthesis, but it cannot be too high, because the resulting polypeptides loose their enzymatic activity by heating, and as this happens usually slightly above 70°C, I suppose that the temperature must be well below this limit, not so far away from 40°C. Logically you obtain an optically active solution, while other methods performed at higher energy levels produce only racemates. You may understand that I was quite happy reading your letter, and that I have mush respect for your achievement.

There is also another aspect to be considered. There is usually some gap between the activation energy required to form and to destroy a chemical bond. E.g. one needs some 4000 cal in order to make a peptide bond and some 12000 cal in order to break it. If I expose a mixture of amino acids to UV radiation, I shall break the bonds as quickly as I build them, and the yield of peptides will be small, whatever be the irradiation time. The same is true, with only slightly modified energy levels, for the abiogenic synthesis of all organic substances including amino acids.

At low temperatures the synthesis of a amino acid or a dipeptide is a relatively infrequent event, but if then things take place on the descending branch of the Boltzmann distribution, and the breaking of a bond will be an event even much less frequent than its formation. The product will therefore accumulate much quicker that at hig energy synthesis. This explains why, with relatively small amounts of energy and in relatively little time you obtain an astonishingly high amount of organis proteinlike substances.

We conclude, and your beautiful experiment confirms our opinion, that the perebiotic accumulation of organis substances did not take place in the atmosphere with a dramatic cooperation

of lightnings and hard UV rays, but rather under comfortable thermic conditions in the luke warm ocean, and that it took place in the whole mass of the water, heated mostly by telluric heat, than in the this superficial layer accessible to solar radiations. So far, your model of abiogenesis of peptides seems the best representation of what may have happened really.

I mentioned allready, that we prepare the publishing of a book on these problems. The work advances nicely and we hope to start writing at the beginning of 1978. May I ask you the favor to sent me all the available offprints related to this problem and for the other the necessary bibliographical referencies.

In order to give you an idea of the general orientation of this book, I sent you a paper upon the origin of membrane structures. It is, on a higher level of organization, the same problem; which events must happen necessarily under given conditions?

Very sincerely yours

(Prof. Dr. J. Segal)

Prof. em. Dr. JAKOB SEGAL

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My dear colleague,

with great joy I learned that your troubles are finished, and that you are in a good state of health and able to do more valuable scientific work. Meanwhile I have some informations which may interest you.

I just came back from a symposium on Natural Selection in Chekoslowakia, where I met Oparin. I had pfepared a lecture on organic synthesis at low energetical levels, in which I also spoke of optical active molecules you obtained. Oparin was very much interested by this possibility to explain the origin of chiralic amino acids. He will - or more correctly his main collaborator, Dr. Gladilin will proceed to some controle experiments at low temperatures, including your method. I just have sent to him a photostat of your paper in the J. Brit. Interplanet. Soc, 1970 with the description of the methods you used. I am perfectly avare, that in such a paper you can only give an outline of the methods, and you know perfectly that often the success depends on some detail. So, if you have any advice to give, please write it to Gladilin (K. L. Gladilin, Bach Institute of Biochemistry, Academy of Sciences of the URSS, Leninski Prospekt, 117 071 Moskow W - 71, URSS) and send a copy to me.

After my lecture I had different discussions with regards to your work. ~~Among~~ Besides positive appreciations I heard also expressions of mistrust, easy to understand as long as people do not understand, that under critical thermodynamical conditions chemical reactions take a course qualitatively different from the usual one. I also heard the opinion that such results may be due to bacterial proliferation in your vessels. This, I cannot agree with. First of all, when a scientist states, that he did sterilize his material anf later did make a bacteriological control, we must take it for granted as long as there is no contrary evidence. But in this case, the assumption of a bacterial proliferation appears completely absurd. In a vessel with 140 ml of liquid you add 10 ml of a 30% formaldehyde solution, thus establishing a 2% formaldehyde concentration. In such a medium ne bacterium can grow.

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So I must conclude that something happens in your experiment which, until now, we cannot fully understand from the physicochemical point of view, but its elements are accessible to analysis. Chiralic molecules are due to the low energetic level; macromolecules arise even in aqueous media, especially in the presence of phosphates; when these macromolecules have a global electrical charge and a dipole moment, they form liquid crystals, either in form of liquid coacervates or of linear threads of fibers, or even of membranes (I am sending you an offprint offering a hypothesis of the formation of membranes in coacervate systems); several authors (Linke and Segal, Fox, Gladilin) have observed budding or dividing of coacervates and microspheres; synthetic polypeptides always display some enzymatic activity, and this activity seems to increase, if the molecules are orientated in a multimolecular structure. The physicochemical mechanism of this biocatalytical activity can be explained by the energy liberated at the transition of peptide bonds from the keto to the enol form, an event likely to happen at any unspecific peptide bond (Segal and Kalaidjiew; Biophysikalische Aspekte der Struktur, Dynamik und Biosynthese der Eiweissmoleküle. Thieme, Leipzig, 1977).

Every single event in the jeewanu can be discussed on the basis of concrete physical knowledge. Put together they must produce a most complexe function which, by now, is not easy to be understood. A physicochemical approach seems to me still the best thing we can do about it.

I wish to you a good health to carry on this interesting work

Very sincerely yours

J. Segal