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CONFERENCE ON CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE: SELF-ORGANIZATION OF THE MACROMOLECULES OF LIFE

SUMMARIES

Trieste, 25-29 October 1993

CONFERENCE ON
CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE: SELF-ORGANIZATION OF THE MACROMOLECULES OF LIFE

25 - 29 October 1993

According to the standard scenario the formation of biomolecules was a necessary preamble to the emergence of life on Earth. This interdisciplinary conference will emphasize the role of replication in processes of self-organization of biological macromolecules. This will be inserted in a programme that will include molecular and biological evolution. We will also consider the evidence of early life from the oldest known fossils in the geologic record.

In this Internal Report we have gathered together the summaries of papers to be read at the conference which were available at the time of going to press. The meeting was possible thanks to the generous support of the European Commission, ICTP, the International Centre for Science and UNESCO.

Cyril Ponnamperuma, Director
Julian Chela-Flores, Local Organizer
19 October 1993

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THE PHYSICO-CHEMICAL BASIS OF SELF-ORGANIZATION

Dr. Cyril Ponnamperuma
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We have explored the possibility that there is a stereochemical basis for the origin of nucleic acid directed protein biosynthesis, a key circumstance in the transition from chemical to biological evolution. Using NMR as a probe of weak molecular associations in solution, we have found that there is an anticodonic bias to the genetic code; that there are preferred isomers and preferred phosphodiester bridges.

In related studies, we have explored the synthesis of polypeptides from phosphoanhydrides of amino acids. These give rise to peptides spontaneously in dilute solution. We have observed that the differential reactivity of the amino acids results in nearest-neighbor preferences and that the presence of complementary polynucleotides had no influence on the specificity. These results have implications for our understanding of the origin of the Genetic Code.

Energy, Matter and Self-Organization in the Early Molecular Evolution of Bioenergetic Systems

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Light, heat, energy-rich phosphates and thioesters, and/or compounds capable of undergoing oxidation-reduction reactions, may have been significant among energy sources for the self-organization of matter on the early earth, or to be more specific, for the process of molecular evolution which gave rise to the first life from which all known organisms appear to have evolved.

In living cells phosphate compounds play a well-known central role in the fundamental reactions of both bioenergetics and genetic information, and they may be assumed to have been of paramount importance also in connection with the origins of life and its first emergence. This presentation will focus attention on the possibility that inorganic pyrophosphate (PPi), which we have earlier shown to be formed at the expense of light energy in bacterial photophosphorylation as the first known alternative to the central carrier of biologically useful chemical energy in living cells, adenosine triphosphate (ATP), and to function as an alternative carrier and donor of energy, and which is now known, in contrast to ATP, both to occur in mineral form and to be produced in hot volcanic magma, preceded ATP as energy carrier. Examples will be given, where PPi serves a the predominant biological energy donor. A possible evolutionary pathway from a "PPi world" to an "ATP world" will be outlined. The concept that evolutionary pathways essentially have involved "anastrophic" rather than "catastrophic" steps will be discussed in some detail, as will the concept of "anastrophies" in not only biological but also chemical evolution.

Abstract for the Conference on Chemical Evolution and the Origin of Life: Self-Organization of the Macromolecules of Life, Oct. 25-29, Trieste

Archaebacteria: Key organisms for the study of the early evolution of life

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A kingdom called Archaebacteria (or Archea) was proposed as the third kingdom (or domain) of life by Woese and Fox based on sequence analysis of a ribosomal RNA. The phylogenetic tree constructed by molecular evolution techniques suggests that the primitive cell began to diverge into two groups, eubacterial and archaebacterial lineages. Eukaryote cells can be regarded as hybrids or chimeras of these two groups; chromosomes are derived from archaebacterial line and mitochondria from eubacterial line. The biochemistry of the common ancestor can be speculated from the comparison of biochemistry of eubacteria and archaebacteria. If a common biochemistry is found, this could be the biochemistry of the common ancestor. If different, the simpler or less efficient one would have been the biochemical property of the ancestor. The tree indicated that the closest organism to the primitive cell is either eubacterial or archaebacterial hyperthermophile. Hyperthermophiles are capable of growing at 90°C or higher, and produce extremely stable proteins. This suggests that the primitive cell was also a hyperthermophile and the proteins at the beginning are unusually resistant to heat.

The Initiation of Biological Processes on Earth: Summary of Empirical Evidence

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With the currently available geological record at hand, the existence of life on this planet as from at least 3.8 Gyr ago seems so firmly established as to be virtually unassailable. Specifically, various disparate lines of evidence have merged to indicate (1) that the surface of the Archaean Earth had hosted prolific microbial ecosystems as is testified by a quasi-continuous record of microbialites ("stromatolites") and associated microfossils of prokaryotic affinity over 3.5, if not 3.8 Gyr of geological history, and (2) that the sedimentary carbon record has preserved the isotopic signature of autotrophic (notably photosynthetic) carbon fixation over the same time span. With the observed enrichment of isotopically light carbon in sedimentary organic matter largely consonant with the bias in favor of ^{12}C during photosynthesis, the mainstream of the carbon isotope record can be best explained as geochemical manifestation of the isotope discriminating properties of the ribulose-1,5-bisphosphate (RuBP) carboxylase reaction of the Calvin cycle suggesting an extreme degree of evolutionary conservatism in the biochemistry of autotrophic carbon fixation. As a consequence, partial biological control of the geochemical carbon cycle was established already during Early Archaean times and fully operative by the time of formation of the Earths's earliest sediments.

THE WEAK FORCE AND THE ORIGIN OF CHIRALITY AND SELF-ORGANIZATION

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Summary

Pre-biotic homochirality (i.e. all molecules of one hand) may be a pre-condition for self-organization and life (rather than a consequence thereof), because polymerization to form the necessary stereoregular biopolymers does not proceed efficiently in racemic solution: a homochiral monomer solution is required. To get life started, therefore, a symmetry-breaker may be needed, and we believe this could be the weak force, which produces a small eneryy difference between enantiomers that could lead, by amplification processes, to homochirality. We present our calculations of this parity-violating energy difference or "PVED" for a range of biomolecules including amino acids, sugars, DNA and quartz, and in nearly all cases it is indeed the natural enantiomer (e.g. L amino acids) which is the more stable.

CONTRIBUTIONS

Electroweak Interactions and Chirality of Aminoacids

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August 1, 1993

Abstract

Systematic approach to the problem of possible connection between the electroweak interactions and chirality of aminoacids is presented. Successive reduction of the standard model of electroweak interactions down over 10 orders of magnitude is done: from the energies of more than 100 *Gev* (the elementary particle physics with presence of $W^{\pm}$ and Z bosons) to 10 *ev* (the energy of ionization of stable atom). The restrictions made are these: the virtuality of $W^{\pm}$ and Z bosons; projection of hadron states onto only proton and neutron states; nonrelativistic approximation. All terms of the parity violating weak interaction, which might be relevant to the atomic physics effects, were kept and no unjustified ommisions were made. The following classes of weak interaction were considered: electron-electron weak interaction; electron-neutron weak interaction; electron-proton weak interaction; and, at last, the "astrophysical" electron-neutrino weak interaction. The importance of the overlapping of wave functions of weakly interacting particles was thouroughly discussed and its crucial character for the weak interaction effects in atomic physics were demonstrated. The discussion of the previous work was given. The comparison showed that the electron-electron weak interaction for chemical bonds was unjustifiably neglected in favour of electron-neutron interaction. Evaluation for electron-electron weak interaction contribution to molecular energy was done. It was also shown that, for stationary states, the weak interaction in a chemical bond destroys the singlet spin state of chemical bond and leads to the appearance of small magnetic moment transforming therefore itself from the contact zero-range interaction into the long-range magnetic interaction. For transitions between atomic levels, the weak interaction leads to the appearance of non-zero diagonal electric dipole moment which must be detectable by conventional Mössbauer spectroscopy. The model Hamiltonian is formulated.

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In vitro intron splicing by T7 RNA polymerase of a polymerase chain reaction product containing the common bean (Phaseolus vulgaris) chloroplast trnL (UAA) gene and pseudogene.

O. Carelse(1) and M.V. Mubumbila(1,2).

Summary

A 600 bp product of a polymnerase chain reaction (PCR) amplification, containing the common bean chloroplast trnL (UAA) gene and pseudogene, was transcribed in vitro using E. coli, T7 and SP6 RNA polymerases. The in vitro transcription with E. coli RNA polymerase produced two tRNA-Leu (UAA) precursors which derived from the gene and pseudogene. Its in vitro transcription with T7 RNA polymerase resulted in the splicing of the tRNA-Leu (UAA) intron and the production of RNA transcripts that derived from the 5' and 3' exons of both the gene and the psudogene and from the ligated exons. The in vitro transcription with SP6 RNA polymerase did not occur. The splicing of a chloroplast group I intron by T7 phage RNA polymerase was quite unexpected. The different activities of these RNA polymerases, probably the successive intron loss from the SP6, E. coli and T7 genomes, through the evolutionary time scale. The fact that SP6 RNA polymerase did not transcribe the trnL (UAA) gene suggested that the SP6 genome diverged very early in time, and acquired stringent specificity for its own promoter. In contrast, the splicing of an ancient group I intron by T7 phage RNA polymnerase may have demonstrated the retention of an original function from the T7 genome, not yet altered by the recent loss of its introns. Although of very different phylogenetic origins, both E. coli and T7 RNA polymerases identified specific promoter sequences within the introns of the chloroplast trnL (UAA) gene and pseudogene. Such ability may reflect an ancestral relationship between the two genomes. It was proposed that protein-dependent splicing of some group I introns may be a control mechnaism for intron retention.

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ROLE OF NITRILES AND OTHER REACTIVE MOLECULES IN CHEMICAL EVOLUTION

by

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Some of the molecules which are relevent to Primordial Organic Chemistry and are highly reactive are HCN, HCHO, NH_3 and H_2O. There are others like H_2, N_2, CO and CH_4 which are also important but require inputs of energy (electric discharge, short wave UV radiation etc) to provide reactive species, which in turn lead to molecules with enhanced reactivities.

The formation or the presence of the above molecules is of primary significance as some of these have been shown to be precursors of amino acids, nucleic acid bases, sugars etc.

A review of their presence/formation in interstellar medium, comets and in the laboratory experiments will be presented. Their significance and that of some of their products in the formation of organic compounds which have been characterised in meteorites, in the primitive earth experiments and in the Jovian and Titan atmosphere experiments will be presented.

The role which compounds like HCN, its dimer and tetramers and aminonitriles may play as condensing agents, in addition to their significance as important precursors, will also be discussed.

CONFERENCE ON
CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE:
SELF-ORGANIZATION OF THE MACROMOLECULES OF LIFE
Miramare, Trieste (Italy) 25-29 October 1993

MOLECULAR RELICS FROM CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE

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ABSTRACT

The main hypothesis proposed in this work intends to remove the difficulty that arises from the conjecture that the RNA world may have left molecular relics that may still be extant in the angiosperms.

We discuss whether it is possible to envisage a possible evolutionary pathway of the RNA replicators spanning the vast time span separating the first appearance of the angiosperms, late in the Mesozoic era (the Lower Cretaceous), from the most likely suberas in which the RNA world may have occurred, namely the Hadean/Early Archean.

In order to address this question we suggest that through *horizontal gene transfer,* as well as through a *series of symbioses* of the precursor cells of the land plants, the genes of the replicases (RNA-directed RNA polymerases) associated with putative DNA-independent RNA replicators may have been transferred vertically, eventually becoming specific to the angiosperms.

MIRAMARE-TRIESTE. September, 1993

Key words:
RNA world, horizontal gene transfer, symbiosis, viroids, RNA plasmids

Comets as "Sowers"of Prebiotic Molecules in the galaxy

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The discoveries of prebiotic molecules in the cometary comae during the last 10 years by ground-and space-based observations increased hugely our knowledge on the organic chemistry occuring in cometary nuclei.

The discovery of HCO in comet IRAS-Araki-Alcock(1), of H_2CO, $(H_2CO)_n$ (Polyoxymethylene)(2), and $C_{14}H_{10}$ (Phenanthrene)(3) in Comet Halley by the GIOTTO Spacecraft and finally of CH_3OH (Methylene)(4) in 6 different comets showed that molecules, even more complex than those discovered in interstellar clouds, may be present in the cometary nuclei.

Moreover the observations made in February 1991, when Comet Halley was at a distance of 14.3 A.U. from the Sun, showing a strong cometary activity independently from solar irradiation, led to the conclusion that other internal sources of energy are available.

Exothermic reactions due to phase transitions from the amorphous to the crystalline structure of water ice(5) or chemical explosions produced by NH and NH_2 radicals or HCN polymerization(6) as well as decay of pre-solar isotopes entraped in the cometary ices: that kind of internal energy sources acting on the rich biogenic compounds could be responsible for the generation of an enourmous amount of prebiotic molecules.

Our planet was bombarded in the first 500 milion years from its origin by showers of comets coming from the outer solar system which deposited bilions od tons of organic material and water on its surface.
Since it has been calculated that the original amount of Carbon and water on our planet was not sufficient for the development of present life, astrophysicists are convinced that Comets are responsible for the origin of life on the Earth as well as on other habitable planets of the Galaxy.

References

1) Cosmovici,C.B. and Ortolani,S.,:1984, Nature, 310, 1992;
2) Hubner,W.F.:1987, Science, 237, 628;
3) Moreels,G. et al. 1993, IAU Symposium 160: Asteroids, Comets, Meteors, 221, Belgirate, Italy, June 1993;
4) Mumma,J.M. et al., idem, 227;
5) Prialnik,D. and Bar-Num A.: 1992, Astron. Astrophys., 258, L9-L12;
6) Rettig,T.W.:1992, Ap.J., 398, 293

Fluorescence imaging of replicating RNA in capillaries

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The experiment was conceived by Prof. John M^c^Caskill and observes travelling waves of colonies of self-replicating systems in thin polyethylene capillaries.

At present, it consists of 144 parallel capillaries with an inner diameter of about 0.4mm on an area of 14cm by 17cm. The capillaries are filled with a solution essentially containing nucleotides, the Qβ-polymerase and some RNA starter molecules.

A CCD-camera observes the fluorescent light emitted by ethidium bromide intercalating into the newly synthesized strands of RNA during replication.

Using a gated image intensifier and a pulsed Lasersystem, it is possible to do time-resolved imaging and to discard of the unwanted fluorescence of the unbound dye by selecting the time-window of detection for the longer-lived fluorescence of the intercalated dye. The setup also allows measurements of fluorescence lifetimes, which depend on the local environment of the dye and may be used to obtain additional information about the RNA-strands.

Taking pictures of the capillaries about every minute, the movement of the wavefronts of the emerging colonies can be monitored over the course of some hours. The velocity of the waves is of the order of 0.15mm/min. and allows the determination of the replication-rate of the system (with the diffusion constant known) with a resolution of about 100µm along a capillary. A change of the usually very constant velocity indicates a change in the replication-rate and thereby an evolution event.

By varying the environmental conditions such as the concentrations of nucleotides, enzyme, salt, dye, pH and by changing temperature and viscosity of the solution, the fitness parameters can be influenced and their effect on the development of the system can be studied. The great advantage of the capillaries lies in the fact that over a thousand experiments (= more than ten per capillary) can be performed at the same time, where different boundary conditions may be chosen for different capillaries.

On Attempts to Create Life-Mimicking Cells. 9/9/93

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Our searches so far for reproducing credible scenarios for the Origin of Life on planet Earth suffer from such fundamental difficulties that any understanding of how inanimate matter may have become "alive",lies still in the indefinite future. One might thus think of approaches other than trying to duplicate the Genesis of "our" Life, and attempt to study the possibility of creating other,simpler,artificial forms of life.

Such attempts are immediately confronted by other large difficulties, in particular, that we have no incling of possible forms of Life other than our own, which means also that we do not know of any other building blocks than those produced by our extant biological apparatuses. Theoretical biologists, mathematicians and engineers are therefore trying different routes,in particular that of creating robots,cellular units,and artificial intelligence that perform in a manner analogous to the characteristics of our Life. In parallel,I am going to argue for attempting to find simpler ways in which we might observe the transition from non-living to an "equivalent" of living matter.I emphazise chemistry and mimicking our biochemistry, because chemical units are more readily selfstarting than mechanical or electrical ones,and because we may then derive the needed blueprint as being ultimately a function of the atomic (molecular)structure of matter.

A rational approach along synthetic,constructionist lines seems to require a general definition of Life,actually a circularity, since we do not know other life forms to generalize from. Fortunately,for the course advocated, it is sufficient to formulate a definition that can be derived from life as we observe it. Learning from other attemps at a definition, the following can be postulated for our purposes: -"Living matter(on planet Earth) occurs in the form of identifiable cellular units which repair damage to,or regenerate,its constituents,and replicate themselves according to inherited blueprints, using material and extracting energy from its environment in the process,and respond to changes in their surroundings in ways that help the units' intact survival(adaptation)"-.

Since we do not try to create artificial life by routes that may have been followed 4 billion years ago, we are not restricted by uncertainties as to the nature of our Earth's atmosphere at the time of Life's appearance,or whether Life arose in hot,or cool, acid ,or neutral environments,and that only once ,or any number of times.Implicit in this approach is,on the other hand,that the arrival of Life and its character were pretty well determinate, but that the route which its evolution took was a matter of chance.

In any case,for rational modeling,one has to make an assumption about whether,and which part of,the essential chemistry evolved before or after cell formatipon, and how leaky and how chemically active the enclosing membranes were.The choice proposed is that the encapsulation occurred at an early state of metabolic evolution,allowing an early development of individuality. We avail ourselves also of the,under our circumstances permissable assumption that the membranes formed by accidental co-micellization of amphiphiles and multimers and subsequent liposome creation, were rather leaky,and yet retained then,and shall retain also in our model, small catalytically active polymers ("multimers"). We borrow further from reasonable assumptions that the enclosing membrans were at first chemically inert,but soon began to imbibe elements (rudimentary pigments) that responded to radient energy. This constitutes a compromise between current views.Further advantages of utilizing our best knowledge of biochemistry and plausible thoughts about the evolution of membrane structure are,that the inevitable osmotic pressure to which our model cells will be exposed will be low, and that diffusive material exchanges of small molecules through the membrane will be easy and permit a further evolution of the intracellular metabolism.

Combining the most plausible features of our present knowledge, this model also addresses the central problem of the "Non-living to Living Transition" in the following way:-- Just as no amount of external operation will cause the parts of a clockwork,thrown haphazardly into a box,to assemble themselves accidentally to a working clock (requiring a watchmaker to assemble the parts according to a blueprint),even intact constituents identical with those of a living cell,randomly thrown together,will never come to life.For units of chemical or mechanical nature to be essentially different and more than the sum of their parts,the latter have to be eenclosed together while growing and organizing themselves within a dissipative flux of energy.

Singular appearences of new properties and function occured spontaneoslyly during the evolution of our Universe.Instances are: the organization of photons into atoms ("matter"),the combination of atoms into molecules ("materials";it is not possible to derive,e.g., the properties of water from those of hydrogen and oxygen),the qualitative changes during polymerization and those due to polymer folding (the 10+6 -fold increase of their enzymatic-catalytic functions),the clustering of supra-macromolecules to become cellular scaffoldings and organs like tubules and ribosomes,and the organization of the brain that allowed intelligence to appear in multicellular, multi-organ animals. The apperance of life may then be seen as another instance of a jump in properties and functiones as the result of material organization within irreversible processes. Property alterations due to phase changes do not belong into this class,since they occur during equilibrium processe at zero change in Free Energy.Self-assembly processes like those of the fragments of sonicated viruses are different again: they follow instructions already inherent in the parts (morphogenesis), instructions which millions of years of evolution,i.e.,of synthesis and selection happened to build into long chain molecules,their supramolecular structures,and eventually into a specific repository of information,DNA.

Thus,when as chemists we try to fashion life-mimicking units, we can not help but model them after the only life that we know. It seems then reasonable to provide,in solution,the reagents for spontaneous organic-chemical reactions known from biochemistry for their synthetic and energy-capturing value, a solution which contains also the ingredients for the synthesis of amphiphilic molecules (e.g.,apolar peptides,fatty acids,glycerol and their phosphates)that allow an early encapsulation. A population of spontaneously formed cells exposed,e.g.,to ultraviolet light,heat,or acidity will be subject to selection pressures: cells of a higher metabolic rate of regenerating damage-resistant multimeric molecules will survive better.

It lies in the nature of this model that it allows,in principle, for a myriads of compounds such as must have arisen on primitive Earth under geologically conceivable conditions,but which also,under constant attack of destructive forces, must have become reduced to a,still very large,but finite number of compounds in dynamic equilibrium of synthesis and decay,as a function of the conditions that prevailed over the eons.In given locales, such as hot vents,acid pools,freezing or dehydrating exposures (including the effects of condensing agents),on surfaces or within interlayers,further selections to smaller numbers of componds that crowded-out others must have taken place.It remains then for the personal preference of todays' experimenter,which small number of self-synthezising and themselves mutually catalytically influencing and self-organizing, molecular weight-wise upwards-spiralling compounds he chooses for this constructionist approach that utilizes an arbitrary,but not improbable,set of starting compounds for an analgous simulation of (terrestrial) chemical evolution in a test tube.

Any combination of starting compounds that leads to a progressive synthesis of multimeric peptides,of keto-acids,of acyl-phosphates, PPi and/or ATP,and the addition of primitive synthetic reducing enzymes like ferrodoxins plus ferrous salts as electron donors,should provide a suitable choice. This represents, as far as the presumed history of Life on Earth is concerned, picking up at some midpoint of the continuous sequence of evolution prior to the appearence of RNA. Altough historically,the most likely nature of the energy flux would have been caloric or radient,one is,due to the nature of this approach free to introduce their likely energy-rich (storing) products,namely thioesters,or phospho- or-adenyl acylates,or add sugarphosphates as source of energy from fermentative glycolysis,to start desired anabolic and selforganzing reactions spontaneously. What is proposed here is really something like Spiegelman's, Eigen's,or Joyce's artificial evolution reactions with several important differences: (1) instead of biological enzymes,one employs in situ formed multimeric peptides,or introduces peptides that were surface-catalytically pre-synthesized (with their spontaneous indiginous sequences); (2) the synthesis aims at evolving higher polypeptides and their complexes and co-factors and later also nucleotides,eventually aiming at a peptide-nucleotide co-evolution, and (3) does so within liposomes! Utilizing Deamer and Oro's method of including polymeric reagents into liposomes, and following this by dialysis and the regulated addition of "nutrients",it should be possible to establish (e.g.,by consumption of the latter and resulting wastes)any progress of reactions and self-organization within the liposomes. An important goal would be to find the error rate of any replication

The above is the "hoped for" development.It includes anabolic reactions with the catalytic help of templates,or by multimeric complementarity (de Duve's nomenclature; I dubbed it: "molecular messages",information by contiguity),which lead to the formation of larger molecules which support life-mimcking reactions. Even more importantly,it should lead to selfsustaining reactions (fed by inward diffusing nutrients)or.better still,to their cycles(e.g.,primitive carboxylic cycles). Unfortunately,we do not know a any relevant reaction in non-biological organic chemistry, and in inorganic chemistry only the group of Zhabotinski-Belousov reactions which,though much quoted,are at best pointers for our purposes (except for their very existence). Having only the rudimentary structural self-organization through templates,the now most important quest must be for self-organizing reactions.It may well be that such reactions develop only in the confined space of small cells, originally under the influence of the inner surfaces of liposomic membranes. The latter,though the least specific of all (living) cell constituents,had been selforganizing through the processes of micellization and their extroverting variety: liposome formation.The upshot,and conclusion, of all the above is then the proposition that one should experiment with life-related organic reactions within liposomes of life-related coposition. If selforganizing,at first heterotrophic,reactions can be established, one would have thereby synthezised,even if only short-lasting, life-mimicking self-maintaining cells and opened the possibilty of their evolution.

PROFESSOR JULIAN CHELA - FLORES
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ICTP CONFERENCE ON CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE
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MEMBRANE PHASE SEPARATIONS, ASYMMETRY AND IMPLICATIONS IN THE ORIGIN OF LIFE

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ABSTRACT

Escherichia coli K 1060, an unsaturated fatty acid (UFA) auxotroph, grown in the presence of various UFAs was found to maintain membrane fatty acyl heterogeneity. The lipids of this membrane exhibited a broad gel-to-liquid crystalline phase transition during Differential Thermal Analysis. The broad transition showed lateral phase separation in which domains of gel phase lipid coexist with liquid crystalline lipid within the bilayer. The increased lateral compressibility in this membrane state favoured transport of solutes, and is the basis of homeoviscous (or homeophasic) mechanisms whereby microorganisms acclimatise to temperature fluctuations.

Heterogenous macromolecular composition results in membrane asymmetry, according to the Fluid Mosaic Model. This asymmetry is vital for membrane functions, and fine-tunes phase separation in the two halves of the bilayer.

The microsystem hypothesis assumes that the formation of coacervate droplets, and proteinoid microspheres as protecells is an integral part of chemical evolution of life. In the premordial ocean (i.e., "premevial broth") lipids would dope these microsystems to various levels, thus yielding protocells of varying stability. The most stable under the harsh conditions of temperature, etc., would "survive" as "the fittest", and proceed to evolve into higher structures. Thermostability would result from compositional heterogeneity resulting in thermotropic phase separations in same sense as stated by A. I. Oparin, and akin to that in the *E. coli*. This is related to evolution of the biomembrane.

Evidence from other sources (e.g., primitive Archaebacteria, and higher organisms) suggest asymmetry and lateral phase separation as underlying physical characteristics which have enabled the evolution of the living system. Experiments measuring phase transitions in doped microspheres are advocated.

Chiral Interaction in Molecular Systems

G. Gilat

ABSTRACT

Chiral interaction presents a new approach that may have certain dynamical advantages due to chirality. A few macroscopic examples, such as windmills, Crookes' radiometers and electric cells are discussed. A distinction between geometric and physical chirality is made. A simple model for chiral interaction between soluble proteins and ionic solvents is described. It is shown that two major structural features are required for chiral interaction, namely, chiral structure and an interface separating between two media. It is well known that all soluble proteins become globular before they can function as enzymes. The globular shape provides for an interface separating between the solvent and the molecular interior. Chiral interaction generates an intrinsic perturbation or current, flowing in a single preferred direction out of two possible ones. This mode of perturbation is time-irreversible but obeys PT-invariance. Such features may be related to a beginning of organization which, presumably, could be associated with a control mechanism of enzymatic activity. Two different experiments aimed to verify the validity of chiral interaction are proposed. One is a direct experiment, the other indirect. Chiral interaction in conjunction with terrestrial magnetic field might have also played a significant role in the evolutionary selection of the L-enantiomer of amino acids.

Computational Support for Origins of Life Research

for presentation at the
Conference on Chemical Evolution and the
Origin of Life

Trieste, Italy
October 25-29, 1993

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SUMMARY

The language of computer science has been pervaded by terms derived from biology: such terms as worm, virus, genetic algorithm, and others are now common. There is a natural affinity between these seemingly disparate disciplines, such that many developments in modern molecular biology and biochemistry would not have been possible without computational support.

Computers can be of similar significant aid in investigations of the origins of life, with particular emphasis on the topic of self-organization. Both analytic and synthetic investigations have already felt the benefits of computational tools. Whether one moves from the present backwards in time to examine the evolutionary pathways for development of organisms from common ancestors, or forward in time from the first moments of the creation of the universe to that same point, computers will continue to allow the human mind to explore realms outside the boundaries of everyday experience, and extend human senses into realms heretofore inaccessible with standard laboratory techniques. Ultimately, it should be possible to combine the best features of computational and "bench" chemistry to understand the processes whereby abiogenic molecules combine to produce structures that, by still as-yet-to-be-defined criteria, would be classified as living systems.

Examples of existing research supported by computational techniques will be provided, and the rationale for incorporating advanced techniques into research on self-organizing systems will be discussed.

FORMATION OF AMINO ACID PRECURSORS BY COSMIC RADIATION IN PRIMITIVE TERRESTRIAL AND EXTRATERRESTRIAL ENVIRONMENTS*

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ABSTRACT

It has been controversy that bioorganic compounds were formed on primitive earth or formed in space and supplied to the earth before the origin of life on the earth. In order to verify the possibility of the formation of amino acids under both primitive terrestrial and extraterrestrial conditions, several kinds of gas mixtures and ice mixtures ("simulated planetary atmospheres and cometary ices") were irradiated with high energy particles. We found wide variety of amino acids in the hydrolysates of the products. The present results strongly suggest that amino acid precursors could be formed by cosmic ray radiation at any place where carbon and nitrogen compounds exist such as in primitive earth atmosphere and in extraterrestrial environments such as cometary nuclei.

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COSMOLOGICAL SOURCES OF MOLECULAR CHIRALITY

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ABSTRACT

We address the old paradox in chemical evolution that chiral amino acids, rather than racemic mixtures, are abundant on Earth since they are universally present in proteins. Amino acids still have not been observed in interstellar space, in spite of the fact that cosmic organic matter is known to exist. We assume that the electroweak interaction is a truly universal chiral influence that may have induced a bias at a cosmological level of left-handed amino acids.

The minimal model we discuss assumes supercooling and that one-dimensional tunneling may have been possible between the two vacua of the Salam-Weinberg model of the electroweak interactions. We show that the electroweak phase transition may have been delayed due to supercooling and that subsequently tunneling may have occurred from an unbroken SU(2)XU(1) metastable symmetric-vacuum to the stable asymmetric-vacuum state. It is shown that for a certain choice of the parameters (the Higgs mass), the symmetric phase can persist long enough to strongly favour a definite homochirality of the primordial molecular clouds.

Thus, the model demonstrates that a cosmological source of chiral amino acids is not in contradiction with known cosmological constraints. One experimentally verifiable consequence is that there may exist interstellar clouds of amino acids which are optically active.

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Key words for information retrieval:

Chirality, chemical evolution, electroweak phase transitions, optical activity, spontaneous symmetry breakdown.

Hydrogen Cyanide Polymers: Prebiotic Agents for the Origin and Self-Organization of Proteins and Nucleic Acids

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Hydrogen cyanide polymers—heterogeneous solids varying in color from yellow to orange to red to black—may be among the organic macromolecules most readily formed within the solar system. Current studies of these ubiquitous compounds point to the presence of polyamidine structures readily converted by water to polypeptides.

Implications for prebiotic chemistry are profound. Primitive Earth may have been covered by HCN polymers through bolide bombardment or terrestrial synthesis, producing a proteinaceous matrix able to promote the molecular interactions leading to the emergence of life. Most significant would have been the parallel synthesis of polypeptides and polynucleotides arising from the powerful dehydrating action of polyamidines on available sugars, phosphates and nitrogen bases. On our dynamic planet, this polypeptide-polynucleotide symbiosis mediated by polyamidines may have set the pattern for the evolution of protein-nucleic acid systems controlled by enzymes, the mode characteristic of life today.

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Randomness, Determinism, Thermodynamics and Evolution

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Abstract

Nature is nonlinear. Life process is a form of nonlinear evolution and neither unique nor a matter of chance. Far from equilibrium nonlinear dynamics of driven dissipative systems produce self-organizations which are actually disorder systems as admixture of order and disorder of very generic types in a field of particle-like excitations and defects. Origin and evolution are not very disparte phenomena. Emergence and complexity occur at the interface between order and disorder. It is the functional connections between the parts that are important than the structured parts themselves.

Nonlinear dynamics does not consider fluctuations. But in real systems stochastic process should be added. Self-organization is necessary but not sufficient for the life process. In the real world, Darwin's principle of diversity, stability and selection are ideally suited for chemistry-in the strings of heterogenous polymers selecting intramolecularly better sequences and coevolution by intermolecular interactions which may also be responsible for the production of the first autocatalytic material. Complexity (fitness) is towards a better choice of folded polymers, result of self-organization and selection driving the system to adoptation in the region of kinetic phase transition.

The folded polymers are mesoscopic disordered dynamic systems with conformational substates or polymorphism with very little evidence for solitons. Complexity is an increasing process with time. Mesoscopic systems and coevolution systems can be studied by irreversible thermodynamics with complexity standing for efficiency.

The clue to understanding biological evolution is in the protein folding. Further bottom-up models in bilogical evolution are ribozymes, RNA, DNA and hypercycles. Recent work on ribozyme synthesis and selection-competition studies along with smallest size suggestions from cellular Automata are encouraging to witness a possible forerunner.

A PLAUSIBLE ROUTE FOR THE SYNTHESIS OF BIO-ORGANIC COMPOUNDS IN THE PRIMITIVE EARTH FROM MINERAL SALTS. AN OVERVIEW.

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There is no longer a consensus on the prevalence of reducing conditions on the early Earth. The primitive Earth atmosphere is now considered as a mixture of CO, CO_2, N_2 and water. On the other hand, it has been pointed out that the yields of organic compounds of biological significance in such gas mixtures are extremely low. For this reason, it is important to review the prebiotic synthesis of organic compounds and investigate those pathways that can yield organic compounds in a neutral atmosphere.

Carbonates are minerals widely spread on the Earth. They constitute carbon reservories. Carbonates were involved in a complex equilibrium with the carbone dioxide from the atmosphere as well as carbonate and bicarbonate dissolved in the oceans. Carbon would have been transferred from the fluid reservoir of ocean and atmosphere to the solid reservoir of carbonate minerals on the sea floor (Walker, 1985). Such minerals certainly seem widespread in the Archean period. Further, the amount of these sedimentary carbonates is enormous ($\approx 1.8 \times 10^{22}$ g) even when compared with other forms of carbon in the biosphere ($\approx 6.8 \times 10^{21}$ g) (Broda, 1975). Therefore carbonates may be possible sources of bio-organic compounds. As an energy source to carry out these synthesis, ionizing radiation may be a good candidate. Estimates of the natural radioactivity, 3.8×10^{9} years ago, only in carbonates shows that it was 1.92×10^{-8} Ci/Kg. This amount of energy from radioactivity is adequate to produce radiolysis.

The present study is a review of some possible radiation-induced reaction in carbonates that lead to the formation of reduced compounds. This synthesis may have been a prebiotic route for the formation of one or two carbon atoms. Some compounds detected are formic acid, oxalic, acetic, glycolic, and glyoxylic, also formaldehyde, and methanol.

Broda, E.: 1975, The evolution of the bioenergetic processes. Pergamon Press, London.

Walker, J.C.: 1985, 16, 117-127.

On Dyson's Model of the Origins of Life and Possible Experimental Verification

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Abstract

Some years ago F.J.Dyson put forward an interesting 'double-origin' hypothesis concerning the origin of life on the earth. His essential contention was that protein-based life capable of metabolism originated first, about three billion years ago, and that much later on RNA-based replication evolved in existing cells. Dyson based his hypothesis on the experimental evidence that amino-acids, which are the basis of proteins, are much easier to be synthesized in prebiotic primordial conditions than nucleotides the constituents of RNA and DNA. The purpose of this review paper is to examine critically Dyson's theory and consider recent experimental evidence for and against the theory.

GRADUAL RISE OF CELLULAR TRANSLATION

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Abstract. "RNA worlds", nowadays the most popular scenarios of life emergence, are obviously rich in polyribonucleotides. Here a hypothesis is presented for the gradual increase of the role of the polynucleotides in the biosphere, from mononucleotide-like molecules driving the condensation of amino acids, to polyribonucleotides acting as gene-messengers and transferers. The molecules involved are supposed to have changed from short to long, but also from variable and relying on chemical affinity, to constant and stereospecific. Accordingly, the genetic code changed from approximate to accurate.

Keywords or phrases

genetic code
organic phosphates
origin of cells
origin of life
origin of translation
primitive oligopeptides
primitive oligonucleotides
RNA worlds

ROLE OF INFORMATION PROCESSING IN THE EVOLUTION OF COMPLEX LIFE FORMS

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ABSTRACT

A mass of biological evidence suggests that introns, transposable elements, viroids and virtually all enzymes are involved in information processing. Diener found structural similarities between introns, transposons and viroids. In all three cases typical sequences were of the type XYYX and some direct repeats. In the Epstein-Barr virus (EBV) these segments are known to form perfect palindromes. Going a step beyond, our theoretical analysis shows that the nucleotide sequences having structure XYYX, XYYZ, XYYYX and XYYYZ, where X,Y and Z are any nucleotides C,G,U or T, and A ($X \neq Y \neq Z$) are omnipresent in ribozymes, introns and viroids. Such motifs are found especially near important sites, e.g. splicing and initiation sites. A combinatorial analysis shows that many mathematically interesting sequences, including the well-known Fibonacci and Morse-Thue, can be constructed from the abovementioned motifs. Both Fibonacci and Morse-Thue sequences contain palindromes. A theorem of Cobham relates sequences to information processing as follows: to each k-sequence, there exist a k-automaton which accepts/recognizes or generates this k-sequence. They are also known as *automatic sequences* and can be generated by rewrite systems, a computational model that is just as powerful as the Turing machine. This result and a further study of ribozymes' primary structure led us to the following hypothesis.

1) Introns, transposons, viroids, highly conserved TATA box, ALU sequences and ribozymes are involved in some aspect of information processing. Editing, proof-reading, error correction etc. are examples of this capability.

2) Information processing capability of ribozymes developed early in evolution and before the genetic code and transcription mechanism. Without such capability the evolution of the complex life forms would have been impossible.

3) Formation of these motifs is the result of prebiotic chemistry. Moreover, the principle of unavoidable regularity, a theorem of van der Waerden, asserts that it is impossible to produce long sequences of elements taken from a finite set of symbols that do not contain subsequences possessing some regularity. Thus we rule out formation of completely random sequences even if there were no constraints due to chemistry.

It is now known that an automaton or a finite-state machine can also be represented by a linear sequence of symbols. Nature has, it seems, used the linear structure of nucleotides not only to store information but also to encode processing instructions. It is like a long tape that contains alternatively data (exon) and corresponding program to process this data (intron), all "hard-wired" in a single genome. Furthermore, we show that there is a correspondence between the word-subword structure of an automatic sequence and its secondary structure. This clearly relates enzymes and automata.

A theoretical bonus of this approach is a plausible explanation of the C-value paradox. The complexity of species is not proportional to its DNA size, but to the number of intronic segments present in its genome. We predict, therefore, that primates are expected to have the largest number of introns in their genome.

A practical outcome of this approach is that it would be possible to predict critical segment(s)/determinants of specific ribozymes and thus an effective anti-sense strategy can possibly be devised to block the function of undesirable genes. Many oncogenes (e.g. suppressors and enhancers) as well as the HIV-1 virus are potential candidates for application.

General Crystal in Prebiotic Context

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General crystal is an extension of the crystal concept to any form of matter which exhibits neighbour structure determination. This extention makes many results of solid state physics applicable to heterogenous matter. Among others it includes the description of phase transition from random to unique structure. The advantage of the general crystal approach is demonstrated on globular proteins, one of the most important macromolecules of life, which are capable of adopting unique 3D structure spontaneously, regardless of the heterogeneous character of their chemical structure and conformation. It is suggested that the use of general crystal concept may help to find candidates among heterogenous matters capable to spontaneous self-organization on the same way as crystallization results in unique structure of homogeneous matter, and to apply some of the results of solid state physics to describe the phase transition and other behaviour of this matter. We comment on the possible relevance of these concepts to chemical evolution.

ORIGIN OF BIOCHIRALITY - A BEAUTIFUL THEORY, BUT NASTY EXPERIMENTS ?

by
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Anybody seriously studying the origin of life by whichever means will be puzzled by the phenomenon of biochirality: the fact that all living species show very strict handedness, quite in contrast to the organic chemist's experience in his laboratory who will produce only achiral or at best racemic compounds (without the help of biology !). Now we have been taught that we ought to understand the effect on theoretical arguments at least: Enantiomer amino acids, sugars, etc. are not energetically identical, - the one biologically preferred enantiomer is the one with the least potential energy (*MacDermott et al.*). This is what I call a beautiful coincidence between physics and biology, but it remains one flaw: The energy difference between both enantiomers is extremely small, in the order of magnitude of 10^{-14} kT at most. Nobody can verify such an effect in an experiment on the laboratoy bench at present; there have been attempts to prove such an effect by amplification through physicochemical processes though. However, there has been presented an independent hypothesis: the combined effect of (Earth) magnetic field and light in a (possibly !) stereoselective synthesis. Yet - we are still equally puzzled by the fact that experimental evidence of a preferred (bio)chorality has been very ambiguous so far, and by no means convincing. Is this due to the smallness of the effect as such, to rather carelessly controlled experimental conditions, or to the lack of a general support of such an endeavor which touches one of the most fundamental problems in science ? Or is it only misunderstanding: some physicists claim why do we bother in organic and biochemistry, that atoms at least are chiral is proven and accepted ?! As long as we have no answer to the missing experimental evidence of chiral bias in chemistry, life and its origin will remain covered with some mystery and present an ample playground for vitalists, creationists, and related prophets.

FINDING NECESSARY CONDITION AND SCOPE OF SURVIVING L-AMINO ACID UNDER BETA ELECTRON IRRADIATION

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ABSTRACT

According to the difference of inelastic scattering cross sections of D and L type molecules under irradiation of β electron, the necessary condition of L-amino acid surviving is: When $R_{n+} > 0$, $\sigma_D > q_L$. A new classification of 20 amino acid based on the rotatory strength sign of L-type was proposed. We suggest laboratory testing of these ideas by focus on looking for the surviving condition of first kind of amino acids --- alanine, valine, aspartic acid, Glutamic acid and serine.