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The Hypothesis of Condensation in Assessing the Role of Chirality in the Origin of Life

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These are preliminary lecture notes, intended only for distribution to participants.

GENETICS, EVOLUTION, AND THE ORIGIN OF LIFE

LECTURE 1

THE HYPOTHESIS OF CONDENSATION IN ASSESSING THE ROLE OF CHIRALITY IN THE ORIGIN OF LIFE

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THE FIRST UNIFYING PRINCIPLE IN BIOCHEMISTRY

Sometime during the long course of **chemical evolution** chiral asymmetry was set in molecules that were to be the precursors of the macromolecules of living organisms. I tend to agree with Alan Weiner and his colleagues (among them James Watson) with their statement in *The molecular Biology of the Gene* (3rd Edition):

The bias for the handedness of the main biological macromolecules may be due to the detailed enzymology of the first RNA replicase. This is an enzyme that is capable of forming, in an RNA world, as well as in current organisms. new RNA strands upon parental RNA templates. The initial bias may also depend on the first working translation system. These arguments treat the the homochirality of the nucleic acids and proteins as a frozen accident.

Before we discuss the alternative that will be presented in some detail by other speakers of the **Fifth College of Biophysics**, particularly the ideas of Abdus Salam, it is convenient first to review some elementary concepts from organic chemistry.

Two molecules are said to be **steroisomers** if the order in which atoms are bound to each other is the same in both compounds, but differ in the spatial arrangement of their constituent atoms. On the other hand, enantiomorphism is another name for the phenomenon of such mirror-image relationship exhibited by the molecular structure of two steroisomers (each partner is called an **enantiomorph**).

What is particularly striking - Francis Crick has called the phenomenon 'the first principle of biochemistry' - is that inside living organisms all synthesis and degradation of the macromolecules of life involve one enantiomorph alone. In other words, the key molecules - amino acids, sugars, and natural lecithins (phospholipids) - have the same handedness or chirality. Remarkably, this is true for all organisms with the exclusion of bacterial cell walls, which contain D-amino acids, as in the case of

Bacillus brevis , and
Lactobacillus arabinosus.

However, we may state in general that living systems translate their genes into proteins composed of twenty L-amino acids.We shall further hear during the ***Conference on Chemical Evolution and the Origin of Life*** the interesting work of Salam who has attempted a search for the physical bases of this principle in biochemistry. This work has been preceded by a long history of efforts investigating the chief cause of the molecular evolution from racemic mixtures of amino acids to enantiomorphous-biased L-amino acids This will be appreciated from the lectures of Lawrence Barron and Vladick Avetisov in this College and, during the Conference, in the lectures of Alexandra MacDermott.

In a substantial group of previous work, the parity-violating electroweak neutral current has been suggested as the main physical force inducing the observed biochirality. The new approach to the origin of chirality that concerns us here once again invokes the electroweak interaction, but is original in appealing to further physical concepts which we shall discuss in turn.

First of all Salam considers that at the end of chemical evolution a particular cooperative phenomenon did take place, namely, a phase transition beneath a certain critical temperature T_c : Amino acids that had been synthesised earlier from various precursors entered into a new phase which was a Bose condensed mode. Since this concept is well understood in physics, but has only been used a few times before in the context of biochemistry, we shall illustrate the main ideas to a reader whose background is in the life sciences.

2. COOPERATIVE PHENOMENA, CONDENSATION, AND PAIRING: POSSIBLE FACTORS IN CHEMICAL EVOLUTION

The work reported in this set of three lectures is based on the belief that biosystems, in spite of their complexity, may be described in simple physical terms by appealing to general analogies between the macromolecules of life and phase transitions that may occur in various forms of (non-living) condensed matter.

Thus, complexity of the living cell and its constituents (membranes, nucleus, chromosomes) should not be a barrier that prevents us from finding some general properties, subject to specific laws.This approach has been hinted at in the past by various authors, notable amongst which are Max Delbrück, Herbert Fröhlich, and Salam. The motivation to look at microscopic basis for biology goes back to ***Delbrück***, who was considering the question:

> **"whether or not something very peculiar**
> **from the quantum mechanical point of view, like superconductivity or superfluid helium, will come up.**
> **If strange cooperative phenomena can happen at room temperature in very special molecules...,**
> **then certainly life would have discovered this"**

Perhaps the deepest question now raised by ***Salam*** is whether microscopic cooperative phenomena, in terms of phase transitions may occur in biochemistry. It is this general question that we wish to discuss in these lectures, however, not restricted only to biochemistry, but also discussing genetics and the origin of life, as we have been doing systematically since 1985. A very broad set of references on the application of the analogy of macroscopic quantum mechanics on biological phenomena may be found in the recent paper of Miller, published last year in the Journal of Theoretical Biology.

The implications of considering the physical analogies on the mechanisms that may have led to the origin of life is left for our contribution to the Conference. In his study of amino acids Salam has done a service by arousing attention to a specific form of cooperative behaviour at the microscopic level: *Bose condensation.* This phenomenon is being proposed as a quantum mechanical enhancing factor in the molecular evolution from the initial racemic mixture to the present day chiral amino acids.

As we mentioned above, the concept of condensation is not new in biology.. In the context of *the origin of life* condensation in the nucleic acids was already suggested by us to have played a role in the origin of Darwinian evolution. However, in spite of these previous efforts the concept still remains unfamiliar in the life sciences, notwithstanding its extensive use made in studies of the cell membrane by Fröhlich.

The necessary conditions for condensation have been studied by Lev Landau, who distinguished between Bose superfluids and Fermi superfluids. It should be noticed that even for Fermi superfluids, like superconductors, the phenomenon of bosonic condensates still occurs; in this case the condensate consists of *Cooper pairs*, which is a further physical concept used by Salam.

The above three physical concepts: cooperative phenomena, condensation, and (Cooper) pairing have led Salam, with arguments developed in considerable detail, to suggest that the electromagnetic force is not the only force which can produce chemical effects: The Z^0 component of the electroweak force, in spite of the fact that its effects appear to be negligible at low temperatures, may play an active role in chemistry.The reasons for the proposed chemical role of the parity-violating weak interactions may be found in some calculations in quantum chemistry of George Tranter, Macdermott, and Barron.

The results of these calculations indicate that four amino acids, for which calculations have been completed, taken in aqueous zweitterionic conformation, are L-stabilized relative to their D-partners for configurations in aqueous media (the above-mentioned amino acids are alanine, valine, serine, and aspartic acid). This stability affects 1 out of 10^{17} molecules at room temperature, since

$$10^{-17} \approx (3x10^{-19}\ eV\ /\ 300Kk_B)$$

a small quantity that has deterred many chemists from accepting the effects of the electroweak interactions as a possible source of optical symmetry. We shall illustrate in the remaining part of these lectures how the hypothesis of (Bose) condensation may play the role of the amplifying factor. This is needed for Salam's theory to be valid.

IS CONDENSATION RELEVANT TO BIOCHEMISTRY?

In order to understand the condensation hypothesis-microscopic cooperation- consider the following argument :

There are many examples of structures that are ordered in position, such as crystals. Condensed matter ordered in momenta is less well known, in spite of the fact that such state of matter was discovered over eighty years ago. We will mention the phenomenon of superconductivity in metals and superfluidity in liquid helium four. Later on we shall comment on other such phenomena which is of more recent discovery.

When we consider ordinary condensation as temperature decreases, we may appreciate that atoms, for instance, in liquid water assume an orderly pattern in a crystal lattice. On the other hand, the less evident pattern of order observed in a superfluid is a pattern in motion rather than in position. The effect of the establishment of such new order is easy to observe, for it manifests itself macroscopically in spite of its origin is quantum-mechanical: The viscosity of helium flow through capillaries vanishes, hence the term 'superfluid helium'.

What Salam has done is to assume that as temperature drops from a given value T_2 to T_1 the amino acids which have some degree of spacial order, around the α-carbon, now assume a *new* order. This involves the motion of the electrons of the various atomic shells constituting the amino acid itself.

Salam maintains, as we shall learn from his talk at the Conference on Chemical Evolution and the Origin of Life, that electron-nucleus interactions may play an important role.

CAN PHASE TRANSITIONS OCCUR IN THE MOLECULES OF THE LIVING CELL?

Search for some evidence for phase transitions in the life sciences should not be limited to biochemistry, but a separate line of research in genetics may also suggest the possible occurrence of phase transitions:

A factor that may influence the onset of DNA replication is intracellular *ion concentration* . In fact, experiments with rat liver-cell nuclei may indicate that chromatin structure and nuclear volume display abrupt transitions as function of ion concentration in the nuclear environment. This experiment has suggested to its authors that the chromatin structural changes may be discussed in terms of phase transitions.

These comments lead us naturally to raise the question:

What direct evidence is there for a clear hallmark of the phase transition underlying the origin of chirality?

Some alternatives may be presented:

(1) **Melanin** - a dark brown pigment of many animals- is the product of tyrosine metabolism. It is often located in melanophores (cells with permanent radiating processes lying superficially in vertebrates).

Synthetic melanins may be produced by the enzymatic action of mushroom tyrosinase on tyrosine under certain conditions. It may also be produced by the auto-oxidation of L-dopa (3,4 dihydroxyphenyl-L-alanine). However, the following physical properties are analogous to some ordinary forms of condensed matter:

(i) Temperature-dependent linear term in the specific heat is larger than the corresponding crystalline state,

(ii) Data taken from natural melanins, as well as from melanosomes isolated from human malignant melanoma obtained at autopsy, clearly indicate that it undergoes a phase transition. In fact, its heat capacity shows a discontinuity near *1.9K*. This anomaly, though relatively small, is significant beyond the scatter of the data points. It is probably associated with a magnetic transition possibly from paramagnetism to antiferromagnetism.

In an analogous manner, a means of detecting the putative phase transition may be by measuring differences of specific heats and looking for anomalies in the curve

$$C = \gamma T + \beta T^3 + \ldots$$

as has already done for the above-mentioned case of melanin.

(2) The second alternative is a direct means of testing the new theory for the origin of chirality in amino acids: A 50-50 racemic mixture of crystalline L- and D-amino acids may be subjected to a gradual lowering the temperature. Salam has discussed such an experiment involving a 50-50 racemic mixture subjected to a temperature gradient ranging from the melting temperature for the amino acids to the absolute zero temperature.

(3) We would like to comment upon a third possibility. In view of the discovery of organic superconductors with critical temperatures similar to metals and alloys, an alternative experimental procedure may be to test directly for conductivity and magnetic (Meissner effect) properties of amino acid crystals: Salam makes the suggestion that a ***superconducting-like phase transition*** may actually occur in amino acids. Some possibilities should be kept in mind:

-The first class of (low-temperature) superconductors was discovered in 1911; these early superconductors were unlike any form of matter that occurs in living systems. In fact, they were metals and alloys.

-The discovery of a radically new class of superconductors had to wait some time: In 1986 a more interesting superconductor from the point of view of chemistry was identified in certain ceramics.

-The simple potassium-doped ***fullerine*** K_3C_{60} has been shown to be superconducting with a reasonably high critical temperature i.e., the onset of the critical temperature is 18K.

-***Organic superconductors*** have been known for some time, such as graphitic compounds with typical formulae C_8A (A = K, Rb, Cs) with values of T_c smaller than 1° K; another example is that of the organic superconducting metal bis(ethylene dithiolo)tetrathiofulvalene triiodide with formula $(C_{10}H_8S_8)_2 I_3$ with a value of $T_c \approx 1.5°$ K at normal pressure. Hence, testing for the phenomenon of superconductivity seems a valid experimental approach to test the validity of the Salam theory.

CAN CONDENSATION OCCUR IN CHROMATIN?

We are going to illustrate the relevance of condensation with examples taken from genetics. The state of matter that concerns us here is ***chromatin.*** This is DNA complexed with DNA-binding proteins. The most abundant such proteins are the histones, which are known to be of five different kinds. They are small, in the range 11-21 kDa, as shown in the table below:

Calf thymus histones	*Total residues*	*Mass (kDa)*
H1	213	21
H2A	129	14
H2B	125	13.8
H3	135	15.3
H4	102	11.3

DNA and histones form the bulk of the eukaryotic chromosome. Other proteins are, nevertheless, present and physiologically relevant such as the four types of highly-mobile group.

The packing density of chromatin requires some definitions.

The ***chromatin repeat length*** (λ) is the average amount of DNA wound around a core of histones. To be more precise, the λ parameter consists of two sections:

(i) The first one (L) consists of two full turns of DNA wound about the histone core, contributing a fixed number of base pairs to the overall value of λ.

(ii) The second section is called ***the linker DNA*** (l). It is a variable length of DNA; its average length varies with species, cell type and developmental stage. It links adjacent nucleosomes, contributing to the flexibility of the chromatin fiber.

We may summarize the above information in terms of a simple formula:

$$\lambda = L + l$$

A selection of values of λ is given in the following table for a wide range of eukaryotes, from sac fungi and true slime molds to cells from a variety of tissues from echinoderms and chordates:

Cell type	***(Division/ Phylum)***	***λ in base pairs***
Aspergillus	Sac fungus (Ascomycota)	154
Yeast	Sac fungus (Ascomycota)	165, 163
Neurospora	Sac fungus (Ascomycota)	170
Physarum	True slime mold (Myxomycota)	171, 173
Tetrahymena micronucleus	Ciliate (Ciliata)	175
Rat fetal liver	Vertebrate (Chordata)	193
Rat liver	Vertebrate (Chordata)	198, 196
Syrian hamster liver	Vertebrate (Chordata)	196
Chick oviduct	Vertebrate (Chordata)	196
Tetrahymena macronucleus	Ciliate (Ciliata)	202
Rabbit cerebellar neuron	Vertebrate (Chordata)	200
Chicken erythrocyte	Vertebrate (Chordata)	207, 212
Sea urchin gastrula	Echinoderm (Echinodermata)	218
Sea urchin sperm	Echinoderm (Echinodermata)	241

In other words, this parameter ranges from 154 to 241 bps. However, what is more interesting to notice is that for a given cell, λ also changes at different stages of ontogeny (cf., the examples of the rat liver cells).

Chromatin packaging may be studied in terms of the variable η parameter, just as the analogous phenomena in condensed matter may be studied in terms of the energy gap. To be more specific this possibility may be illustrated by emphasizing wo aspects of chromatin structure:

(i) The tight packing of chromatin yields DNA concentrations ρ within localized regions of interphase nuclei of :

$$\rho \cong 0{,}2 \ gm \ / \ cm^3$$

significantly higher values are expected for metaphase chromosomes, since the η parameter may be one or two orders of magnitude larger.

(ii) The ***packing ratio*** η or degree of condensation of chromatin is given by:

$$\eta = L_1 / L_2$$

where L_1 denotes DNA length in the fully extended state, and L_2 denotes the length of the coiled, or folded state achieved at any state of condensation. In the nucleosome we have 165 base pairs (bps) of DNA rolled over a histone core; in this case

$$L_1 \cong 600 \ \text{Å} \ \textit{and} \ L_2 \cong 55 \ \text{Å}$$

Thus:

$$\eta \ (nucleosome) \cong 10$$

In heterochromatin

$$\eta \ (\ heterochromatin\ ) \cong 4000 - 5000$$

If we define the the η parameter with λ substituting L_1, its value is only marginally larger, particularly recalling that nucleosomes provide only the first stage in the packaging of DNA, but η must be considered in this case to be a variable parameter.

The packing density of chromatin ranges from about 10^2 to 10^3 in the more dispersed state of **interphase nuclei**. The value goes up to 10^4 in the more compact **metaphase chromosomes.** Indeed, we can say that the basic level of organization is the 100 Å beads-on-string fibre. This is then coiled into a 300 Å fibre, possibly induced by histone H1 as a cross-linker, to yield a structure with packing density close to that of interphase chromatin. We have summarized some of these results in the following table:

DNA Organization	*Packing density*	*Density (mg/ml)*
100 Å beads-on-string fibre	10	
300 Å beads-on-string fibre	(25-40) X 10	
Interphase chromatin	10^2 - 10^3	>200
Metaphase chromosome	10^4	

From the 300Å fibre to the mitotic chromosome two orders of magnitude of compaction are generated by specific nonhistone proteins, which form the skeleton, or scaffold of the chromosome. We shall discuss a model of polymerase dynamics in Lecture 3. We assume as a working hypothesis that chromatin in interphase nuclei with *packing density higher than that of liquid helium four* (145 mg/ml), is condensed in the same physical sense of Salam. Thus the analogy with phase transitions will be accessible to the analytic formulation of mean-field theory. However, before approaching the central problem of polymerase dynamics, underlying the observed coupling of DNA replication and transcription, we shall discuss possible ways of testing the Salam theory.

CHROMOSOMAL SILENCING IN FEMALE MAMMALS

In order to appreciate the relevance of DNA packaging in gene expression we would like to emphasize a property of gene expression which will serve to further illustrate the coupling between transcription and replication, namely, *dosage compensation*. This mechanism is used by diploid organisms: Different degrees of DNA packaging occur in a pair of homologous chromosomes. This ensures that a large number of genes are not expressed in one of the partners (the inactive chromosome) while the other partner, in spite of being exposed to the same amount of metabolic energy, remains active. The silent, heterochromatic, densely-packed chromosome is called the Barr body in female mammals, while the other partner is the euchromatic, active chromosome.

Indeed, all female mammals are chimeras. In other words, inactivation of the X chromosome is random, so that the early embryo- at the level of the blastula- is a mosaic of two types of cells in each of which one of the two X chromosomes is inactivated. This has a very striking manifestation at the phenotypic level- *the tortoiseshell cat*- since genes coding for coat pattern are on the X chromosome; this cat is an example of a female heterozygous for a mutation for the coat colour which is coded on the X chromosome. In other words, the female does not have two equivalent genes for coat colour at a given locus of the active X chromosome and of the inactive X chromosome.

In the case of humans in a single step a large number of X-linked genes are inactivated in one or the other X chromosome in the female. This affects the expression of genes of an entire chromosome which, in the particular case of humans, involves more than 150 million base pairs (bps), amounting to several thousand genes. Although this was pointed out at an early stage by Mary Lyon, the underlying mechanism for gene dosage remains unknown.

CHROMOSOMAL SILENCING IN SCALE INSECTS

Scale insects are a large group of homopterans (Superorder Hemiptera -true bugs) belonging to several families, named for the waxy or horny scales under which most of the females live. Most females are wingless and have no legs. A few, such as the **mealy bugs** (in the family Coccidae), retain their legs and some mobility. Male scale insects have one pair of wings and resemble small midges, but they are rarely seen. Most species reproduce by parthenogenesis (i.e., from an unfertilized gamete). It is precisely the unusual reproduction of the mealy bug *Planococcus* which is of interest to us: These scale insects derive paternally a haploid chromosome set (i.e., a set with half as many chromosomes as in the somatic cells). This inherited set is **heterochromatic**, in spite of the fact that in the father such haploid set was euchromatic.

This is an extraordinary phenomenon if we keep in mind that in mammals it is just one X chromosome that is silenced. Instead in* Planococcus *the set consists of five chromosomes that have been simultaneously silenced.

This male coccid has a euchromatic haploid chromosome set derived from the mother. In male meiosis the paternal set disintegrates. This leaves only the maternal set to be packaged into sperm.

CONCLUSIONS

The relevance of testing Salam's rationalization of the origin of chirality cannot be overemphasized: Some of the same experiments that may test his original theory for the origin of amino acid chirality, are indeed experiments which suggest searching for superconductivity-like effects in one of the main carbon-based molecules constituting the living cell, namely, amino acids; earlier, this possibility was also raised for nucleic acids regarding the origin of evolution. One way to interpret Salam's contribution is as a proposal for a solid-state candidate for a superconductivity-like phenomenon in a novel class of organic molecules, namely, the amino acids.

We have also discussed the possibility that physical condensation may occur in chromatin. The control of replication and transcription are intimately related with DNA packaging. However we have shown that chromatin in certain conditions may assume a state of condensation. This suggests that the hypothesis of condensation may play a significant role as a controlling mechanism in DNA replication and transcription. These comments shall be expanded in the following lectures.

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Comments on a Novel Approach to the Role of Chirality in the Origin of Life

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ABSTRACT We review a recent paper[20] in which a specific enhancement factor (i.e., a phase transition into a condensed Bose mode) is proposed to account for the observed amplification of the ground state energies of the L- and D-amino acid enantiomers; the difference between these energies is assumed to be due to the neutral parity-violating electroweak interaction. This physical effect initially shifts the enantiomer energies by about 3×10^{-19} eV. The proposed phase transition is characterized by a critical temperature T_c, which may be studied theoretically by enlarging the standard electroweak theory to include either the top quark or supersymmetry.[21] Possible experimental means of finding T_c are discussed.

KEY WORDS: chirality, origin of life, Bose condensation, organic superconductivity, electroweak interaction

THE SOURCE OF BIOMOLECULAR HANDEDNESS

The first unifying principle in biochemistry is that the key molecules—amino acids, sugars, and natural lecithins (phospholipids)—have the same handedness or chirality.[5,24] Chiral molecules and their corresponding mirror images may be defined by left (L), or right (D) optical/rotatory dispersion. Remarkably, this is true for all organisms with the exclusion of bacterial cell walls, which contain D-amino acids, as in the case of *Bacillus brevis* or *Lactobacillus arabinosus*.[22] However, we may state in general that living systems translate their genes into proteins composed of 20 L-amino acids.

In a recent paper a search for the physical bases of this principle in biochemistry has been attempted.[20] This work has been preceded by a long history of efforts investigating the chief cause of the molecular evolution from racemic mixtures of amino acids to enantiomorphous-biased L-amino acids.[16] In a substantial group of previous work, the parity-violating electroweak neutral current has been suggested as the main physical force inducing the observed biochirality. The new approach to the origin of chirality that concerns us here once again invokes the electroweak interaction, but is original in appealing to further physical concepts which we shall discuss in turn.

First of all, Salam considers that at the end of chemical evolution a particular cooperative phenomenon did take place, namely, a phase transition beneath a certain critical temperature T_c: Amino acids that had been synthesized earlier from various precursors entered into a new phase, which was a Bose condensed mode. Since this concept is well understood in physics, but has only been used a few times before in the context of biochemistry, we shall use some simple examples drawn from the new publication, which illustrate adequately the main ideas to a reader whose background is in the life sciences.

COOPERATIVE PHENOMENA, CONDENSATION, AND PAIRING: POSSIBLE FACTORS INFLUENCING CHEMICAL EVOLUTION

In order to understand how the amino acids may behave as the temperature exceeds the critical value, it is somewhat simpler to consider with Salam[20] a well known physical system where analogous *cooperative phenomena* may occur:[1]

At absolute zero temperature the electron spins are aligned parallel to one another to give a resultant magnetization even in the absence of an external magnetic field. However, at a finite temperature thermal agitation is able to turn over some of the spins and the average magnetic moment in the direction of magnetization is thereby decreased. As soon as this process starts, an electron chosen at random is likely to have neighbours pointing against the direction of magnetization as well as with it and this reduces the energy needed to reverse the spin of the electron, so that, as the temperature increases and more spins are turned over, it becomes increasingly easier to turn over the remaining spins and the disordering process develops with ever increasing rapidity. At the Curie point (i.e., at the critical temperature) the disordering is eventually complete and the spins point equally in both directions, so that only a 50–50 racemic state survives.

In his study of amino acids, rather than of electron spins, Salam has done a service by bringing attention to a specific form of cooperative behaviour at the microscopic level: *Bose condensation*. This phenomenon is being proposed as a quantum mechanical enhancing factor in the molecular evolution from the initial racemic mixture to the present day chiral amino acids. The concept of condensation is not new in biology; indeed it goes back some 30 years.[7] In the context of the origin of life condensation in the nucleic acids was suggested to have played a role in the origin of Darwinian evolution.[3] However, since the concept still remains unfamiliar in the life sciences, in spite of its extensive use made in studies of the cell membrane,[9] we cite an interesting introduction to this singular phenomenon:[13,20]

Imagine that you are on a mountain top looking down at a distant city square. The crowd is milling around at random,

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and each individual is doing something different. Now suppose, however, that it is not market day but the day of a military parade, and the crowd is replaced by a battalion of well-drilled soldiers. Every soldier is doing the same thing at the same time, and it is very much easier to see (or hear) from a distance what that is. The physics analogy is that a normal system is like the market day crowd—every atom is doing something different—whereas in a Bose-condensed system the atoms (or, more accurately, the fraction of them which is condensed at the temperature in question) are all forced to be in the same quantum state, and therefore resemble the well-drilled soldiers: *"every atom must do exactly the same thing at the same time."*

The necessary conditions for condensation have been studied by Lev Landau, who distinguished between Bose superfluids and Fermi superfluids. It should be noticed that even for Fermi superfluids, like superconductors, the phenomenon of bosonic condensates still occurs; in this case the condensate consists of *Cooper pairs*, which brings us to the third of the physical concepts that we set out to introduce with simple examples. In this case Salam chose another analogy from the work of Goodstein:[10]

Imagine two people on an old sagging, nonlinear mattress. They tend to roll toward the middle, even if they don't like each other. That is, there is an attractive interaction. The cause of this interaction is that the people create distorsions in the mattress, and the distorsions try to merge. The electrons in the metal do not stand still but rather zip through the lattice at something like the Fermi velocity. The ions are attracted to the electrons but, owing to their large mass, move very slowly compared to the much lighter electrons. By the time the ions respond the electron is long gone, but it has, in effect, left behind a trail of positive charge, which is the lattice distorsion we mentioned above. Another electron, transversing the same path, would find that its way has been prepared with the positive charge it finds so attractive. We can imagine that the first electron created a phonon, which the second happily absorbs. Notice that the interaction is strongest if the two electrons (i.e., the Cooper pair) traverse exactly the same path—that is, if they have, say, equal and opposite momenta.

ALTERATIONS IN THE CHEMISTRY OF CHIRAL MOLECULES DUE TO THE PARITY-VIOLATING NEUTRAL WEAK INTERACTIONS

The above three physical concepts—cooperative phenomena, condensation, and (Cooper) pairing—have led Salam, with arguments developed in considerable detail, to suggest that the electromagnetic force is not the only force which can produce chemical effects: The Z^0 component of the electroweak force, in spite of the fact that its effects appear to be negligible at low temperatures, may play an active role in chemistry.

The reasons for the proposed chemical role of the parity-violating weak interactions may be found in some calculations in quantum chemistry.[16] The results of these calculations indicate that four amino acids, for which calculations have been completed, taken in aqueous zwitterionic conformation, are L-stabilized relative to their D-partners for configurations in aqueous media (the above-mentioned amino acids are alanine, valine, serine, and aspartic acid). This stability affects 1 out of 10^{17} molecules at room temperature, since

$$10^{-17} \approx (3 \times 10^{-19}\ \text{eV}/300\ \text{K}\ k_B),$$

a small quantity that has deterred many chemists from accepting the effects of the electroweak interactions as a possible source of optical symmetry; nevertheless, in Salam's most recent calculation[21] new work has been reported on the proposed phase transition, in which he has found sufficiently large effects by the inclusion of the top quark (t) and top antiquark $(\bar{t})$ in an enlarged version of the standard theory. He has also found evidence for the extinction of further macroscopic quantum mechanical effects below T_c, such as the value of the critical magnetic field **H** for the Meissner effect, which becomes extinct for temperatures above T_c. He finds that the phenomena of polarization will occur, as explained in the recent paper. For temperatures below T_c he finds no evidence for polarization (since $\mathbf{H} = \mathbf{O}$ and, therefore, $\mathbf{H}\cdot\mathbf{E} = \mathbf{O}$ inside the specimen, where **E** denotes the electric field).

In modelling the phase transition Salam used the condensate wave function as $\omega_D \exp(-2/gv)$, where ω_D is the Debye energy, p_F stands for the Fermi momentum, while g is the effective 4-Fermi coupling parameter for electrons and v is given by the expression $(p_F\ m/\pi^2)$. The approximation $gv \approx 1$ is important in the postulated phase transition. This needs justification. We now understand this approximation as follows (Salam, private communication): The g parameter contains the term $1/m_z^2$, so there must be a large mass coming in the picture in order to cancel m_z^2. This mass can only be $t\bar{t}$, or due to the supersymmetry partners of the old quarks and old mesons being heavier than the original ones by m_x^2, where $m_x \approx 1$ TeV. To sum up, Salam now believes that the approximate equality $m_x^2 \approx (1\ \text{TeV})^2$ is responsible for the very important approximation $gv \approx 1$.

POSSIBLE SCENARIOS FOR THE ORIGIN OF BIOCHIRALITY

An important aspect of the origin of biological chirality concerns the thermal conditions that may have existed in the Hadean Earth, when presumably the presently observed handedness of amino acids originated. Since the ambient temperature of the Earth's surface is approximately 300 K, if T_c is much smaller than this temperature, Salam's theory may not apply to the Earth, in which case at least three scenarios may be possible:

1. Presolar contributions may be necessary to get low enough temperatures.
2. Major contributions come from the more distant and cooler parts of the solar system with ambient temperatures less than T_c (typically all the outer planets have temperatures smaller than liquid nitrogen).
3. If T_c is found to be considerably less than 300 K, one would be led to accept that the Earth only acted as a junction place where L-amino acids came together with D-sugars and nucleotides, in a (field theoretic) self-consistent fashion, so as to give rise to early replication.

Salam feels that for the biotic alternative to prevail, it may be necessary to invoke a mechanism for delivering to the Earth the constituents of the biomolecules from the cooler locations (1) and (2). It may be reasonable to assume the following:[4,19]

The Earth did accrete prebiotic organic molecules important for the origin of life from impacts from cabonaceous asteroids

and comets during the period of heavy bombardment in the Hadean Earth.

Remarkably, we may also assume that the alanine molecules, for instance, could withstand temperatures as high as about 700 K for 1 sec, whereas the other amino acids could withstand temperatures in the range 600 to 800 K for a similar period of time, and remain stable and intact upon impact with the Earth.

CAN PHASE TRANSITIONS OCCUR IN THE MOLECULES OF THE LIVING CELL?

The Occurrence of Phase Transitions Is Possible in Biochemistry and in Genetics

Perhaps one of the deepest questions raised by Salam is whether phase transitions of the type of Bose condensation may occur in the living cell. To a certain extent the answer must be positive, since we may recall that in the case of certain specific macromolecules relevant to living processes, this subject has been studied in both biochemistry as well as in genetics during the last 30 years.

In biochemistry, the ability of lipids to adopt a variety of phases is well documented.[14] This has been called lipid polymorphism; an important aspect of this topic is that the macroscopic structure adopted by lipids depends on the experimental conditions; for instance, temperature is an important parameter which determines the macroscopic structure of hydrated membrane lipids.[6] At present a conservative position is still that the possible biological significance of some of the polymorphic membrane transitions is striking, but we have not yet bridged the gap between these transitions and physiological phenomena.[14]

On the other hand, evidence for phase transitions in the life sciences is not limited to biochemistry, but a separate line of research in genetics also suggests the occurrence of phase transitions: A factor that may influence the onset of DNA replication is intracellular *ion concentration*.[8,15] In fact, experiments with rat liver-cell nuclei may indicate that chromatin structure and nuclear volume display abrupt transitions as a function of ion concentration in the nuclear environment.[18] This experiment has suggested to its authors that the chromatin structural changes may be discussed in terms of phase transitions.

Experimental Tests of the Possible Occurrence of the Superconducting-Like Phase Transition in Amino Acids

These results from the biochemistry of the cell membrane and from the genetics of chromatin structure lead us naturally to raise the question: What direct evidence is there for a clear hallmark of the phase transition underlying the origin of chirality?

Salam's paper provides a sample of alternatives:

1. Melanin—a dark brown pigment of many animals—is the product of tyrosine metabolism. It is often located in melanophores (cells with permanent radiating processes lying superficially in vertebrates). Data taken from natural melanins, as well as from melanosomes isolated from human melanoma, clearly indicate that it undergoes a phase transition. In fact, its heat capacity shows a discontinuity near *1.9 K*. This anomaly, though relatively small, is significant beyond the scatter of the data points. It is probably associated with a magnetic transition possibly from paramagnetism to antiferromagnetism.[17] In an analogous manner, a means of detecting the putative phase transition may be by measuring differences of specific heats and looking for anomalies in the curve $C = \gamma T + \beta T^3 + \ldots$ as has already done for the above-mentioned non-amino acids.

2. One direct means of testing the new theory for the origin of chirality in amino acids is by taking a 50–50 racemic mixture of crystalline L- and D-amino acids and lowering the temperature. Salam has discussed extensively an experiment involving a 50–50 racemic mixture subjected to a temperature gradient ranging from the melting temperature for the amino acids to the absolute zero temperature. In Figure 1 we have illustrated the Salam picture for the evolution of the D/L ratio.

3. In view of the discovery of organic superconductors with critical temperatures similar to metals and alloys (cf. below), an alternative experimental procedure may be to test directly for conductivity and magnetic (Meissner effect) properties of amino acid crystals.

The suggestion has been made that a superconducting-like phase transition may actually occur in amino acids. Physics has been rather slow in studying alternative candidates for superconductors. The first class of (low-temperature) superconductors was discovered in 1911; these early superconductors were unlike any form of matter that occurs in living systems. In fact, they were metals and alloys. The discovery of a radically new class of superconductors had to wait some time. In 1986 a more interesting superconductor from the point of view of chemistry was identified in certain ceramics. Finally, this year, the simple potassium-doped fullerene K_3C_{60} [12] has been shown to be superconducting with a reasonably high critical temperature, i.e., the onset of the critical temperature is 18 K.

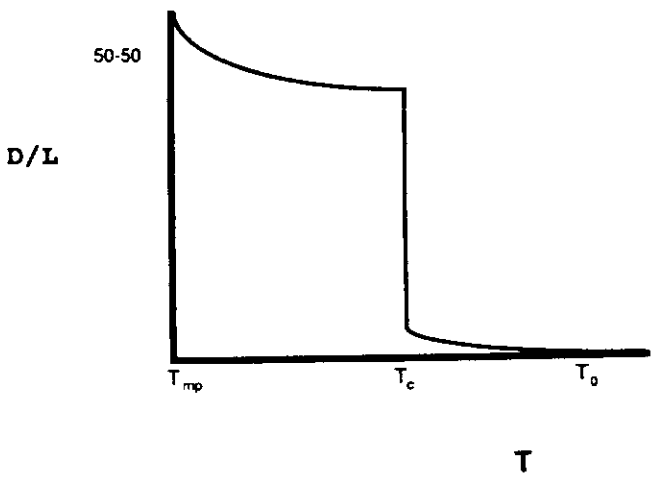

Fig. 1. Evolution of the D/L parameter in the Salam picture for an experiment involving a 50–50 racemic mixture subjected to a temperature gradient. The temperature T ranges from the melting temperature (i.e., melting point) for the amino acids (T_{mp}) to the absolute zero temperature (T_0 = 0 K). Here T_c denotes the critical temperature for the phase transition. The part of the curve from the melting point to the critical temperature has been conjectured in analogy with Atkins'[1] semiclassical treatment of ferromagnetism; this is not in disagreement with the expectation of Bada and Miller[2] that with increasing temperature the D/L ratio increases (as it does in the tail from T_0 to T_c). The phase transition has not been assumed to be of the "reentry" type, as it may happen in some superconductors, in which case the phase transition may occur only in a thermal range defined by *two* critical temperatures.

However, we should recall that organic superconductors have been known for some time, such as graphitic compounds with typical formulae C_8A (A = K, Rb, Cs) with values of T_c smaller than 1 K;[11] another example is that of the organic superconducting metal bis(ethylene dithiolo)tetrathiofulvalene triiodide with formula $(C_{10}H_8S_8)_2\ I_3$ [23] with a value of $T_c \approx 1.5$ K at normal pressure. Hence, the discovery of the most recent superconductor, K_3C_{60} in a simple organic compound of relatively high critical temperature, if confirmed in many laboratories, would be yet another small step in the direction anticipated by those of us who have maintained that superconductivity-, or superfluidity-like effects may occur in biology.

DISCUSSION AND CONCLUSIONS

The relevance of testing Salam's rationalization of the origin of chirality cannot be overemphasized. Some of the same experiments that may test his original theory for the origin of amino acid chirality are indeed experiments which suggest searching for superconductivity-like effects in one of the main carbon-based molecules constituting the living cell, namely, amino acids; earlier, this possibility was also raised for nucleic acids, as previously pointed out regarding the origin of evolution:[3]

To sum up, one way to interpret Salam's contribution is as a proposal for a solid-state candidate for a superconductivity-like phenomenon in a novel class of organic molecules, namely, the amino acids.

The essence of the analogy used by the author is that the "superfluidity" exhibited by amino acids is to "superfluidity" in superconductors and not to liquid helium. In the case of superconductivity, one has to apply an external magnetic field and look for the Meissner effect to determine T_c; likewise, the "superfluidity" of amino acids may, in principle, be measured by shining external light sources on these molecules. The calculation of critical temperatures in terms of an electroweak lagrangian including the top quark, as mentioned above, may serve to restrict the value of the critical temperature from the wide range of the ambient temperature of outer space and the dissociation temperature for amino acids. However, in view of the considerable theoretical difficulties still to be overcome, perhaps the best way to determine T_c may be by means of the experiments suggested above, or by other experiments that may have escaped our attention.

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