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Vol. 3 *Absolute is sentient thou hast proved, impersonal calamity thou hast removed.* *No. 3*

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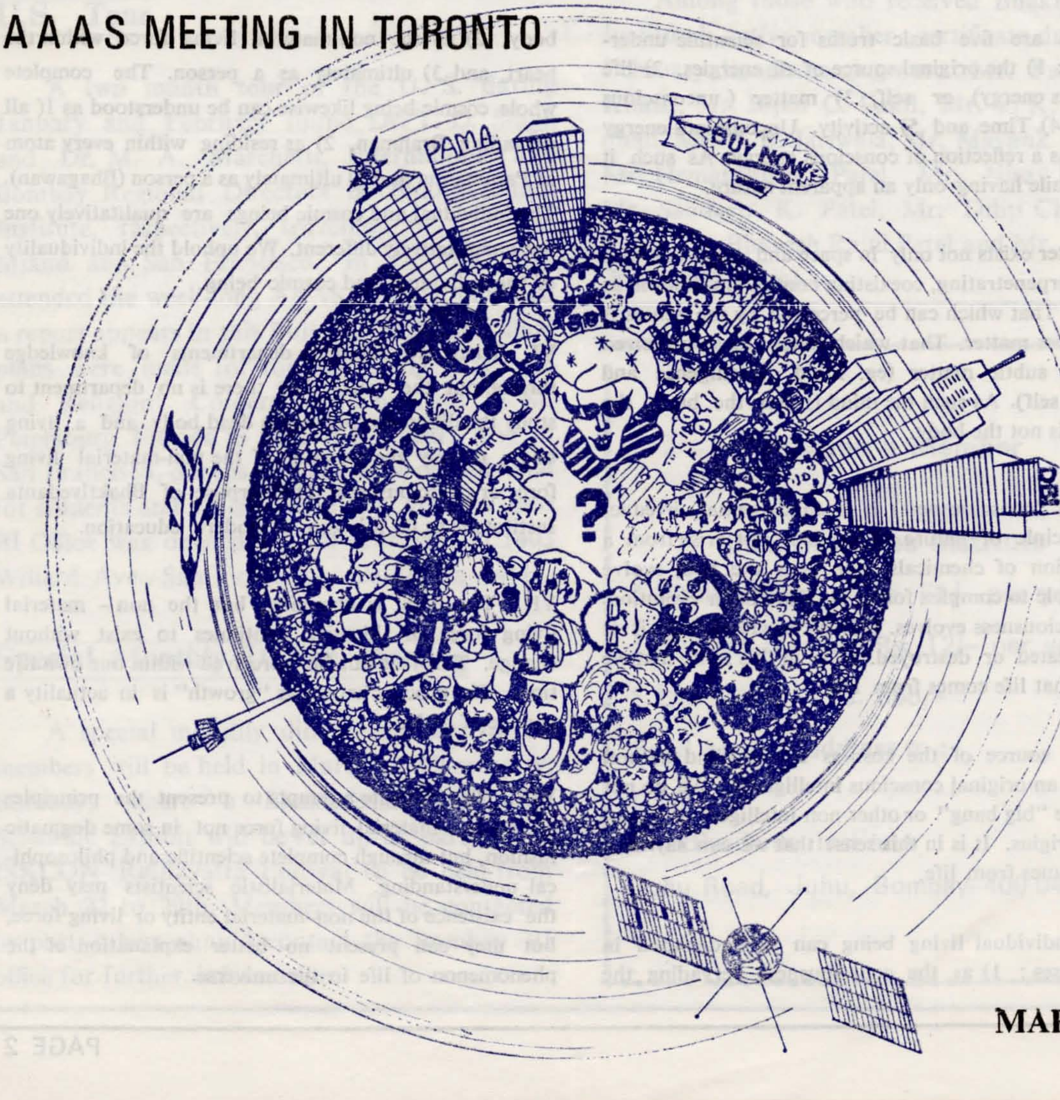

MARCH 1981

It is often claimed in books on the origin of life that life is bound to evolve from chemicals, given sufficient time. The idea is that even though an event may be highly improbable, if one waits long enough it is bound to happen. As one popular account has it.

> *The odds against the right molecules being in the right place at the right time are staggering. Yet, as science measures it, so is the time scale on which nature works. Indeed, what seems an impossible occurrence at any moment would, given untold eons, become a certainty. (1)*

Therefore, we shall briefly examine how chance applies to the form ation of biological macro-molecules.

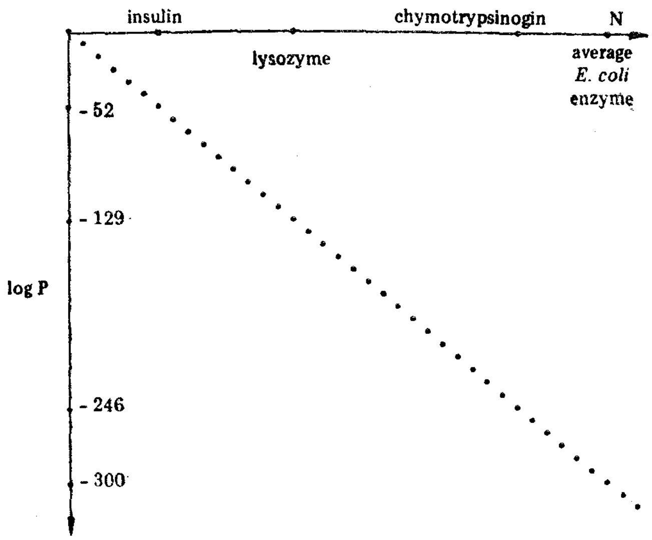

Fig. 1. The Probability, P, of randomly picking a specific protein of N amino acids with an error of 10% or less.

THE ROLE OF CHANCE AND THE LONG TIME SPAN

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Let us consider the probability of forming a particular chain of amino acids at random. Since there are 20 kinds of amino acids in living bodies, there are some 20N possible protein composed of N amino acids linked in a chain. Of

$$\binom{N}{N/10} 20^{N/10}$$

these, there are chains equal to a particular given chain for all but 10% of its amino acid links. If we pick an N link chain completely at random, the probability that 90% of it will match our given chain is therefore,

$$P = \binom{N}{N/10} 20^{-9N/10} = \frac{10^{-N}}{\sqrt{N/2}} \qquad (1)$$

Figure 1. illustrates these probabilities for a number of proteins found in living cells. These probabilities show that it is extremely unlikely that a particular protein will form by chance, even if we allow for 10% of its amino acid subunits to be in error. These conclusions are elementary and well-known. However, numbers such as 10^{-52} and 10^{-246} are not very meaningful by themselves. In order to see what these numbers mean, let us consider them in the context of a model for the chemical origin of a protocell. We would like to show that the necessary molecular components for a functioning protocell cannot be expected to come together by chance, even if thousands of billions of years are allowed.

For our model, let us postulate a "primordial soup" one kilometer thick, covering the entire surface of the earth. Let us suppose that this soup is so packed with protein molecules that there is an average of one protein in each $20 \times 20 \times 25\ \mathring{A}^{3}$ box throughout its entire volume. We shall assume that these proteins are continuously being created, destroyed, and moved about, so that their arrangement changes in each millionth of a second. We shall also assume that these arrangements are completely random and disorderly. This model is intended to provide more random arrangements of molecules per unit time than could ever have been produced in any actual situation on the primordial earth. As such it takes into account both the random creation and the random diffusion of molecules.

We are interested in seeing whether or not the necessary initial constituents of a self-sustaining protocell could be expected to come together by chance in this soup over a long period of time. In order to do this, we shall first review the molecular composition of living cells. The distribution of molecules in a cell of the bacterium Escherichia coli is outlined in Figure 2. We can see from this table that many thousands of very large protein molecules are involved in the metabolism of E coli, even though this is one of the smallest independent living cells. The average size of these proteins is about 300 amino acid subunits.

Cell Component	Approximate Number/Cell	Different Kinds.
Water	$4x10^{10}$	1
Inorganic Tons	$2.5x10^{8}$	20
Carbohydrates and Precursors	$2x10^{8}$	200
Amino acids and Precursors	$3x10^{7}$	100
Lipids and Precursors	$2.5x10^{7}$	50 (50)
Nucleotides and Precursors	$1.2x10^{7}$	200
Proteins	10^{6}	2000 to 3000
D. N. A.	4	1
t R. N. A.	$4x10^{5}$	40
m R. N. A.	10^{3}	1000

Fig. 2. The distribution of molecules in Escherichia coli.

An example of the function of such complex proteins in cells is the process of biosynthesis of L-isoleucine Figure 3. which is produced from L-threonine in five steps. Each step is catalyzed by a specific large protein molecule called an enzyme. Such enzymes have the property of greatly accelerating a particular chemical reaction, while not affecting other reactions at all. They also must be capable of interacting with other particular molecules to regulate their activity. In this example, the enzyme L-threonine deaminase, catalyzing the first step in the chain, is sensitive to the presence of the product molecule L-isoleucine, produced four steps later.

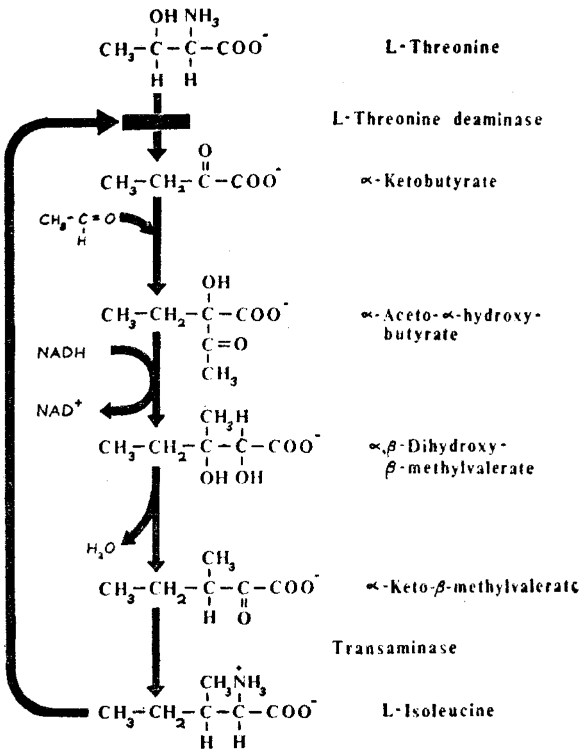

Fig. 3 : Enzymotic regulation in cellular synthesis.

When the concentration of L-isoleucine reaches a certain critical level, this enzyme ceases to function, insuring that no more than the necessary amount of the product is formed. We can thus see that a precise and integrated system of molecular interactions analogues to a sophisticated computer program is necessary for the harmonious functioning of a self-sustaining metabolic system.

Another example is the system of enzymes involved in the replication of DNA. Here we are indeed, faced with an intriguing problem. In order for D. N. A. to replicate, certain highly complex enzymes are needed which are themselves encoded in D.N.A. How could such an arrangement get started ? These are both examples in which many interdependent cellular components interact in such a way that the successful functioning of the whole cannot take place unless all of the components are present.

We do not know whether any kind of self sustaining metabolizing unit is possible with substantially fewer and smaller molecules than a small bacterial cell like E. coli. Yet, for the sake of argument, let us consider a protocell made with protein molecules no larger than insulin. We choose insulin for the sake of clarity. Its structure has been analyzed, and with only 51 amino acid subunits, it is one of the smallest known proteins. We should note that the arrangement of the amino acids in insulin has to be very precise in order for it to function properly in the human body. The British scientist Sanger demonstrated that a very slight modification of any one of its molecules - for example the removal or modification of any one of the amino acids - would spoil its activity as an anti-diabetic agent.

Even though a protocell might be less efficient than modern organisms, it would have to have a sufficiently sophisticated metabolic apparatus to enable it to continue functioning for a long period of time-long enough to give it the opportunity to evolve further by the accumulation of mutations and adaptations. Since many highly specific protein molecules are evidently needed in the functioning of present day living cells, it stands to reason that similar molecules should be required in our hypothetical protocell.

Let us compute the probability that k specific proteins of N amino acid units apiece will appear in a small volume in our "primordial soup" at some time in 1,000 billion years. We shall take this volume to be about 10^{12} A^{03} the approximate volume of an E. coli cell. Neglecting insignificant terms, this probability is no more than

$$P_r < 1.6 \times 10^{61} (10^{10} P)^k / k! \qquad (2)$$

where P is the probability for the random formation of one protein of N amino acids.[4] If we use equation (1) for P and let N=51, the number of amino acids in insulin, we find that

$$P_r < 10^{-21} \qquad (3)$$

even for k=2. This means that two specific molecules the size of insulin could not be expected to occupy by chance the same volume of E. Coli size anywhere in our super-concentrated soup at any time in billions of years.

Even if we let N=20, we find the similar probability of finding six specific peptides of 20 amino acids apiece in one volume the size of E. coli to be

$$P_r < :02 \qquad (4)$$

This probability indicates that there is only one chance in 50 for these six peptides to be found together even once in a thousand billion years.

These figures, and others which can be easily calculated, show that chance cannot be expected to bring together the initial components of k protocell, even though thousands of billions of years are allowed for this process. We should point out that these calculations are by no means limited to proteins. They also apply to the formation of the specifically ordered nucleotide chains that are believed to have been essential components of the protocells.

It is ironic that even though these calculations are both elementary and familiar to many scientists, students are nonetheless taught in schools and colleges that life has arisen by a chance combination of molecules over a long span of time. Evidently, however, chance will not suffice; some other cause must be invoked to account for the structures of living cells. The only alternative available within the limits of modern science is to suppose that the simple push-pull laws of molecular interaction can somehow bring cells together out of chaos. But how are they to do this? No explanation ever proposed has stood up under scrutiny. Yet the teaching that life has arisen from matter continues without reservations.

REFERENCES

1. Gore, R. **National Geographic,** 150(No. 3), 390 (1976)
2. Watson, J. D. **Molecular Biology of the Gene** p. 85
3. Lehninger, A. L. **Biochemistry,** 2nd ed. New York : Worth Publishers, Inc., 1975, p. 234
4. Watson, J. D. **Molecular Biology of the Gene.** p. 281
5. In this formula we assume that the "primordial soup" is divided into boxes 20 x 20 x 25 A3 in size. Molecules can be created and destroyed in each box at a rate of one per microsecond. They can also jump from box to box at a rate of not more than one jump per microsecond. It is assumed that their jumping, creation, and destruction are completely random. The term, $(10^{10} P)^k/K1$ is an estimate for the probability of finding at least k events out of 10^{10} opportunities, assuming that events occur randomly with probability P. There are less than $10^{10}/16$ 'boxes' in the volume of a typical *E. coli* cell ($10^{12}A^{03}$). The number, 1.6×10^{61}, is an upper bound for :

$$\frac{\text{(volume of "soup")} \times \text{(microseconds in } 10^{12} \text{ years)}}{\text{(volume of } E. coli \text{ cells)}}$$

Formula (5) thus gives a bound on the probability that k specific molecules will be found together in some *E. coli* sized volume in the soup at some time in a 10^{12} year period. By taking faster rates for the molecular events one can obtain the same results for proportionately shorter time spans.

● The Darwin theory of Evolution is based on the hypothesis that, without exception all the organisms in the world today came about by transformation of this kind starting with some primitive ancestral forms. If such transformations are always possible then the problem of evolutionary theory in to determine what event in the nature might cause them to actually take place. RICHARD L. THOMPSON in this context discusses THE NATURE OF BIOLOGICAL FORMS.

● Bhaktivedanta NEWS AND much more.

● In the foregone issues of the Bulletin, the well-known economist Mr. K. J. Jayaraman in his **"QUEST FOR NEW STRATEGIES FOR ENRICHMENT OF LIFE"** has discussed several aspects associated with the need to cast a new look in to the plans and implementation methods in order to overcome the ill-effects of the modern profit oriented economic system with a view to provide a viable basis which is essential for attaining the well - being of the masses. In this issue, the economist, however, seeks to lay stress on the **"SOCIAL THEORIES AND BEHAVIARAL PATTERNS VIS-A-VIS WANT BASED CONCEPTS".**