PROBABILITY AND LEFT-HANDED MOLECULES

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The mystery of stereo-selectivity in proteins is examined. The history of efforts to explain this strange phenomenon is traced from Pasteur to the present. Conversations with a number of prominent scientists regarding the current status of knowledge on this problem are reported. Probability theory is applied to the chance production of a minimum set of protein molecules for the smallest theoretically possible living entity with only left-handed protein components. The odds against this happening once among all the protein molecules that ever existed on earth are evaluated. Comparison of the naturalistic and creationist positions is examined regarding this mystery.

One of the strangest mysteries in biology is the fact that proteins are made of left-handed molecules. This remains without adequate solution after well over a hundred years of study.

Understanding Proteins—Complex Yet Built on a Simple Plan

To preface the mystery, we might review for those in other fields what proteins are like. They are, of course, a major class of the complex molecules of which all living things on earth are made. In primary structure, proteins are long, slender filaments or threads that are unbelievably small. In fact, Max Perutz of Cambridge University notes that they are 500 times thinner than the thinnest object a good optical microscope could reveal.¹ Although so tiny, they are by comparison to many other molecules positively gigantic. A single protein molecule may contain hundreds, and in some cases even tens of thousands, of atoms bonded together! The miniature long filament is often precisely folded into a globular shape.

Fortunately for our understanding, proteins are constructed on a simple plan, in one sense. They are made of smaller molecules called "amino acids." There are 20 varieties of these that are commonly used in proteins.† Each amino acid contains atoms of carbon, nitrogen, oxygen, and hydrogen. Two of these 20 have, in addition, a sulphur atom each. Separately, they range in size from 10 to 27 atoms. All of the 20 kinds of amino acids occur in proteins of all organisms.⁴ The number of these building blocks

An exotic new amino acid, "desmosine," has recently been investigated.² It is formed outside the cell from four units of lysine, another amino acid, and it functions as part of "elastin" in larger organisms. There are also many natural amino acids not ordinarily used in proteins. In the last few years, over a hundred of these have been discovered.³ in a single protein ranges from around 50^{**} to several thousand in the more complex proteins which have several subunits.

Though proteins are very large and complicated, it is encouraging that the amino acids (of which they are made) possess a degree of uniformity. In fact, when joined to others, each amino acid residue is practically identical in its main section with all the others.

The sole difference between the various types of the 20 amino acids is that each has a different "side group" of atoms, often called the "R" group. This is fastened to a central carbon atom. (In the amino acid proline, the side group loops back and attaches also to the adjacent nitrogen atom, replacing a hydrogen atom usually found there. Proline is therefore actually an "imino" acid.)

In the various amino acids, the distinguishing side group contains from 1 to 18 atoms. There is considerable diversity in these side groups. This makes possible many of the things proteins do.

Amino acids can be linked together, end to end, in long chains called "polypeptides." In proteins, the sequence in which the various kinds are arranged is of great importance. Different proteins are simply different orders of the 20 varieties of amino acids.

When the units of the protein chain are in any particular sequence, the resulting chain will coil or spiral and fold in a specific way. This final shape makes the protein able to do its unique job in the cell. Each kind of protein has a specific function. It may be a digestive enzyme, for one example, or a structural molecule, for another.

When two amino acids unite, a molecule of water is released. This is formed from atoms that were part of the amino acids, so they now are not quite as large. This is why amino acids in a protein chain are called "amino acid residues."

It takes energy to get the amino acids to bond together. It is quite difficult to bring this about outside of living things, but it can be done by special techniques in the laboratory.

In living organisms, on the other hand, protein chains are linked up rapidly (polymerized). Special enzymes bring this about with the help

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Various biochemists list 18, 20, 22, or even up to 27. The common universal ones are often totalled at 20 because of genetic coding considerations and convenience. Different totals arise if we combine or separate certain pairs that are similar and where one is derived from the other, or if we include those that are used only in special situations, as in collagen, etc. An exotic new amino acid, "desmosine," has recently

^{**}using the word protein in the non-technical sense.

of other unique molecules. The system used by living things for making proteins is very complex and efficient. It all takes place under instructions from the DNA code, the hereditary "language of life."

How Can a Molecule Be Left-Handed?

Amino acids can exist in both right-handed and left-handed forms. Your two hands show how this can be. They have the same components—fingers and thumbs—yet they are different. The thumb of one is on the left and of the other on the right. They are "mirror images" of each other. Some molecules are like that.

Let's imagine that we are able to look at an amino acid molecule. Remember each is built on the same simple plan. In the main part, there are three atoms which we could call the "backbone." These three atoms are in the direct line of the protein chain when the amino acid is united with others. Of the three, two are carbon atoms and the other is nitrogen.

Looking at it from a particular end,* we notice the center carbon atom. It appears to be elevated a bit compared to the other two atoms. That middle carbon atom is called the "alpha" carbon. It is said to be "asymmetric," that is, different on every side. This difference is not in the atom itself, but in the four items which are bonded to it.

As we view it from our vantage point at the carboxyl end of the amino acid, we note that this central carbon atom has two side projections which angle upward to the right and to the left. On one side, this extension is simply a hydrogen atom. Opposite it is the "side group" mentioned earlier, the group which differs for each of the 20 amino acid types.

If that identifying side group is on the left, the molecule is "left-handed." If instead it protrudes to the right, the amino acid is said to he "right-handed."

These two forms of the same chemical contain the exact same components and are called "isomers" or "stereoisomers" of that chemical. Their side groups are just positioned oppositely in space. Each form is the "antipode" of the other. They are "enantiomorphs" of each other.

We may note in passing that this difference was discovered in an accidental way.⁶ A French physicist named D. F. Arago in 1811 shined a beam of plane-polarized light through quartz crystals. He discovered to his surprise that the plane of the light was twisted or rotated as it passed through the crystal. In 1815, J. B. Biot found that some aqueous solutions also would cause this. Whether the light was rotated to the right or to the left depended on the substance used. Solutions which rotate light in this manner are said to be "optically active."

Pasteur, while investigating this strange phenomenon, in 1844 found that the optically active substance he was studying was made of onehanded molecules, all of the same "hand." (Solutions made of the opposite enantiomorph of such a chemical may rotate the light plane the opposite way. Both forms mixed together equally usually will not rotate the light plane at all.) One might suppose that left-handed molecules would rotate light to the left, but this is not necessarily so. There is no simple relation between configuration and optical rotation.⁵

Only Left-Handed Amino Acids in Proteins

Francis Crick, of Cambridge, tells the way living things are in nature:

It has been well known for many years that for any particular molecule only one hand occurs in nature. For example the amino acids one finds in proteins are always what are called the "L" or "levo" amino acids, and never the "D" or "dextro" amino acids. Only one of the two mirror possibilities occurs in proteins⁷

That is the mystery. English biologist John Maddox called it "an intellectual thunderbolt that natural proteins should contain only the left-handed forms of the amino acids."⁸

This is a special difficulty for those who believe that life originated from non-living matter by natural processes. A. I. Oparin, Russian biochemist, has perhaps had more to do with current evolutionary thought than any man since Darwin. He mentioned the subject in a recent book (1968) thus: "It is necessary to touch briefly on a problem which has been discussed in the literature for a long time."⁹

In an earlier book (1961) he went into more detail. The atoms involved in the different positions (right- and left-) are subject to the same forces. When amino acids are formed, the varying side group could just as easily be on the right as on the left. Oparin wrote:

The probability of the formation of one antipode or the other is therefore the same. As the law of averages applies to chemical reactions the appearance of an excess of one antipode is very improbable, and, in fact, we never encounter it under the conditions of non-living nature and in the laboratory syntheses.

In living organisms, on the contrary, the amino acids of which naturally occurring proteins are made always have the lefthanded configuration. . . This ability of protoplasm selectively to synthesize and ac-

^{*}from the "carboxyl" end. See, for example, illustrations in Barry, *Introduction to the Structure of Biological Molecules* (1969), on pages 99 and 116. An excellent small book on proteins, DNA, etc.⁵

cumulate one antipode alone is called the asymmetry of living material. It is a characteristic feature of all organisms without exception but is absent from inanimate nature.

Pasteur pointed out this fact as follows: "This great character is, perhaps, the only sharp dividing line which we can draw at present between the chemistry of dead and living nature."¹⁰

In modern times, many have expressed the same surprise as Pasteur. For example, Linus Pauling, Nobel laureate in protein chemistry:

This is a very puzzling fact. . . . All the proteins that have been investigated, obtained from animals and from plants, from higher organisms and from very simple organisms—bacteria, molds, even viruses—are found to have been made of L-amino acids.¹¹

He concludes: "No one knows why living organisms are constructed of L-amino acids."

Dr. Larry Butler, biochemist at Purdue University, has said, "In all respects chemically and physically (except for physical properties associated with asymmetry . . .) D- and L-amino acids are not only equivalent but indistinguishable."¹² He then refers to the interesting observation that some amino acids can be discerned by taste. This is not an exception, he notes, because taste is a subjective response rather than a fundamental property.

Professor Dennis Englin of Los Angeles Baptist College calls attention to an amusing experiment. Scientists now can hook up proteinlike chains which contain both the L- and Damino acids, and put such chains into a living organism, e.g., a bacterium. The organism immediately takes them apart, and in some cases rebuilds the amino acids in the left-handed form!¹³

It might be noted that D-amino acids do occur in nature, but not in regular proteins. As Ernest Baldwin and others have pointed out, the cell wall outside the cell of some bacteria uses righthanded amino acids as structural components, as one example.¹⁴ Since these are not proteins and are outside the cell, the rule holds, that only L-amino acids are used in naturally occurring proteins. (Other examples are antibiotics (such as penicillin, and a substance used in luciferin, the light-making chemical in fireflies.³)

Professor William Stokes of the University of Utah sums up what is actually known regarding this baffling question of the two forms as they occur in proteins:

They are as identical in all other respects as a pair of gloves. When amino acids are prepared artificially, both L- and D- varieties occur in statistically equal amounts. But living things can use and construct only the lefthanded type, probably for hereditary reasons going back to the first ancestors of all life on earth.¹⁵

Looking at it from the naturalistic standpoint for the moment, we may ask: How could living things have gotten started which use only lefthanded amino acids in proteins? A lot of research has been done to try to account for this. A brief review is instructive.

The first problem is to explain how any amino acids could begin. For this, the current explanation is to postulate a primitive atmosphere that was totally different from that known today. Then it is claimed that amino acids might have been formed from that prescribed atmosphere by the action of ultraviolet rays, lightning, and perhaps heat.

In a famous experiment at the University of California at San Diego, Stanley L. Miller tried to duplicate that supposed atmosphere in laboratory containers. He then subjected a heated mixture of its gases to an electric spark for a week. He succeeded in getting the two simplest amino acids, glycine and alanine, for sure. There were perhaps three others (that were of doubtful identity).¹⁶ The results, however, included both left- and right-handed isomers,¹⁰ just as in other laboratory syntheses mentioned above. Such a result, containing both forms, is called a "racemic modification."

Later, Sidney W. Fox, now at the University of Miami, obtained perhaps as many as 13 or 14 of the amino acids. His experiments were more complex, and involved the use of heat (quartz sand at around 1,000° C), pressure, use of an acid, and other laboratory-controlled conditions.¹⁷

Summarizing these efforts and others, we may refer again to Dr. Stokes' statement that when amino acids are prepared artificially, both L- and D- varieties occur "in statistically equal amounts."

So we still have the problem even if the amino acids could be accounted for at all.* If they had occurred naturally, these experiments indicate that the supply would have been racemic, instead of all L- or all D-.

Efforts to Account for Exclusive Use of Left-Handed Amino Acids in Proteins

Oparin gives a good summary of the many efforts that have been made to find a way in which one-handed amino acids might have been formed, in contrast to the racemic products just mentioned. Let us briefly follow his report.⁹

In 1904, 1925, and 1929, some German scientists reported the use of "circularly polarized

^{*}It is interesting to note that the hypothetical primitive atmosphere conveniently happens to contain methane, ammonia, hydrogen, and water vapor, from which it is a comparatively simple step to the amino acids.

light" to bring about a photochemical reaction. The impression is given that they managed to synthesize some one-handed molecules. Oparin's vagueness here leaves strong doubt whether they proved anything significant. (Light can be circularly polarized by reflection, and, as John Keosian points out, circularly polarized light may be present in moonlight.¹⁸) Natural circular polarization of light could at most be slight, however, and the activities that can be produced photochemically in the laboratory have usually been extremely small.⁶

In 1950, J. Bernal advanced another hypothesis. These amino acids, he says, may have been formed "on the surface of nonsymmetrical quartz crystals." Two Russian scientists (Terent'ev and Klabunovskii) claimed to have accomplished this in laboratory experiments.⁹ We may note, however, that when quartz crystallizes, its two mirror image forms are produced with equal probability,⁵ in contrast to living things.

Continuing Dr. Oparin's summary, we note that George Wald in 1957 "expressed doubt, however, that any of these abiogenic factors could create conditions for the emergence of stable asymmetry." Instead, Wald theorized, the selection of L-amino acids was made from both types "at the time of the selection of alpha spirals in proteins."

This idea must be examined. An "alpha spiral" is a special helical form of the protein chain. Pauling and his colleagues discovered this in 1950. Left-handed amino acids form a righthanded helix. If, by chance, a helix had gotten started, there is no adequate reason to suppose that only L-amino acids would link up at the end of such a chain. We will later discuss the idea that a helix may have some effect as to preference, but either L- or D- forms can and do join it in the laboratory. After both forms are used, the helical form may change or be discontinued, but the chain can continue to grow, with units of either hand.

Furthermore, "selection" cannot operate at all *unless there is a system for accurate duplication of all the needed parts.* This undeniable precept is stated by Theodosius Dobzhansky, now with Rockefeller University in New York, in these words: "For natural selection to operate there must be reproduction, and reproduction is the key property of life."¹⁹

The only system known for duplicating amino acid chains accurately in nature is the intricately complicated system used by all known living things on earth. It is the DNA-RNA-enzymestransfer-RNA-ribosome-protein system. Besides that fact, no model of any theoretical "primitive" system has yet been presented which is convincing, in spite of extensive attempts by Oparin and others following his lead.

Natural selection has been vastly over-rated. It would have been completely absent before there were self-replicating living systems. Logically, then, it becomes apparent that "alpha spirals" could not have been "selected" prior to complete replicating systems (even if an alpha helix could be formed).

Amino acid chains that use only one "hand" undeniably have some advantages. Dr. Fox among others, believes that a chain of lefthanded amino acids, for example, is "thermodynamically more stable" than one that is composed of both forms.²⁰ (In either right- or lefthanded helical form, the stability is increased by hydrogen bonds between the turns of the spiral.)

The big problem, which has no natural solution in sight, is how to get such a chain even the first time. It is important to keep in mind that selection could not have been operative at that stage, as we have seen.

Getting back to Oparin's summary of efforts to solve this mystery, we find that A. Pasynskii in 1959 suggested that "stereo-chemical proteins" may have been first formed by chance, and then these served as enzymes or catalysts to build the amino acid molecules in only the L- form.⁹ This is as if a complex factory machine happened by chance, and then it manufactured the exactly needed simpler products. It boils down to random link-ups that just happen to turn out in an exactly needed sequence. The likelihood of that occurring is beyond conceivable probability as we will see.

Keosian (1964) gives an excellent very compact summary of these and other attempts, though none of them is a real solution. 18

After considering all these, it is clear, then, that unless chance could do it, there is at present no adequate answer, from an evolutionary standpoint, which explains the mystery. As a result, there is little evidence of any agreement or consensus among scientists on the source of this stereo-selectivity. Oparin must presume it started without prior design. Any other belief would be inconsistent with his Communist philosophy. (Interestingly, that viewpoint—dialectical materialism—is not atheistic after all. Professor Claude Tresmontant of the University of Paris has pointed out with unanswerable logic that Communists are actually pantheists, worshipping matter-in-motion.²¹)

Oparin does not make clear which of all these ideas he prefers, as to the supposed natural origin of the exclusive use of left-handed amino acids in proteins, but he assumes it happened nevertheless. He is admirably straightforward in realizing the difficulty: Even when we know how the asymmetry arose, though, we still cannot answer the question of why one antipode, rather than the other, should occupy such a monopolistic position in the life of all the organisms inhabiting the Earth. This question is important for an understanding of the essential nature of life but it remains for future investigators to supply the answer.¹⁰

On that subject, Pauling made this imaginative comment:

The earth might just as well be populated with living organisms made of D-amino acids as with those made of L-amino acids. A man who was suddenly converted into an exact mirror image of himself would not at first know that anything had changed about him.

He could drink water, inhale air and use the oxygen in it for combustion, exhale carbon dioxide, and carry on other bodily functions, just as well as ever—so long as he did not eat any ordinary food. If he were to eat ordinary plant or animal food, he would find that he could not digest it.¹¹

He then reminds of a strange coincidence. Way back in 1872, Lewis Carroll's *Through the Looking Glass*, was published. In it, Alice said, "Perhaps Looking-glass milk isn't good to drink." (We have seen earlier that some organisms can convert some of the D-amino acids into the Lform. Similar conversion to the natural form does not seem to be possible, however, in the case of the "universal" energy food, glucose sugar⁶ This is true of other vital foods such as Vitamin C, which is L-ascorbic acid.²²)

Left- and Right-Handed Amino Acids Can Link

We may ask, "Are the two forms of amino acids shaped so that any of them could unite, whether they are L- or D- in type, as far as contour is concerned?" According to California Institute of Technology's veteran researcher, James Bonner (noted among other things for his discovery of the role of certain proteins in gene repression), the answer is yes.²³ Whether leftor right-handed, it seems that any amino acid can conceivably link with any other of either hand. Dr. Fox said he was inclined to agree with Bonner on this.²⁰ The resulting shape of the chain, whether it spirals and how it folds, will be entirely different, but numerous polymers or chains have been put together containing both L- and D-amino acids of a variety of types, including some with the largest side chains such as the amino acids tyrosine and phenylalanine.²⁴

Would both L- and D- forms hook up under the supposed conditions of primitive synthesis? Dr. Fox heated all the common amino acids at 200° C temperature under certain conditions. He obtained protein-like chains containing all the amino acids.²⁵ When asked if both left- and right-handed amino acids were included in the same chain, he replied that he was almost 100% certain that they were, but that there was no way to tell absolutely at the time.²⁰ At least both types were included cumulatively in the total of the various chains.

This question of whether there would be "steric hindrance" or difficulty of fitting together due to shape was put to Dr. Pauling, now at Stanford University. He mentioned that there was that possibility between opposite hands,²⁶ but for details he referred to a section in his 1964 book mentioned earlier. There he had written, "We have no strong reason to believe that molecules resembling proteins could not be built up of equal numbers of right-handed and left-handed amino acid molecules."¹¹

On the same matter, I questioned Dr. Arthur Elliott of the Biophysics Department at King's College in London.²⁷ He replied that he knew of none of the common amino acids that could not be connected to any other opposite isomeric form. Dr. Harry Block of the Chemistry Department, University of Liverpool, was of the same opinion—that he did not know of any exceptions.²⁸ In other words, it is possible for any of the 20 amino acids to connect with any other of the same or opposite hand. (Drs. Elliott and Block have authored several reports on experiments in this field.^{29,30})

Will Opposites Join with Equal Facility?

In the literature, there are hundreds of writeups of experiments where D- to L- link-ups were made, and vice versa. Almost never is any mention made of any more difficulty in joining opposite hands than the same isomers. There have been some rare exceptions to this general picture which we will look at in more detail, which seem to indicate a degree of stereo-selectivity in some particular joinings.

At the present stage of experimental knowledge in this field, there is nothing like complete certainty on whether there is an average preference for the same hand, or, if not, what degree of selectivity exists. Study of experiments to date seems to warrant this conclusion: the truth may turn out to be either equal probability *on the average*, or some limited degree of preference that is usually too small to be noticed.

For those who are interested in delving more deeply into the evidence, we will have to get a bit more technical. (Some may wish to skip over the remainder of this section, and to continue with the next main heading.)

An article in *Biopolymers* (April, 1971) by E. Klein, *et al*, is a good example of description of matter-of-fact linking of opposites.³¹ In this instance, the amino acid chains formed were

"poly-D, L-leucine, co-D, L-methionine." I asked Dr. Klein, a research scientist for Gulf South Research Institute at New Orleans, if he and his colleagues knew of any preference of L- for L- or D- for D- in their experiments. He said if there is any selectivity, they had not detected it in their work which often involves joining of pre-formed blocks of each isomer within the same chain.³²

There is great variety in the side chains of the 20 amino acids. This diversity was stressed by Daniel Levy at the University of Southern California in connection with the guestion whether there is equal ease of joining.³³ It depends on which amino acids you are considering.

One of the best ways to get an understanding of this matter is to work with models of the amino acid residues. If ready-made atomic models are not available, it is possible to get by with styrofoam balls or other round objects. These may be colored in order to distinguish the different kinds of atoms, and some may be glued together. It is very important to make the models to scale. Accuracy involves attention to comparative sizes of the different atoms, length of bonds, bond angles, and bonds which allow rotation.

A convenient source for most information needed is Pauling's *The Chemical Bond* (1967), available in most city or school libraries.³⁴. He gives tables of effective radii or size of the atoms (van der Waals radii), and bond lengths (pages 136 and 152). Angles and positions are shown on page 229.

It is interesting that the four bonds of a carbon atom usually point in the direction of the corners of a regular tetrahedron. Each bond is approximately 110° from each of the others (actually 109° 28' average). In making models, one discovers that the bond lengths will require him to gouge out quite a bit on the sides of various atoms in models so they can fit together at proper distance. In other words, their surfaces overlap considerably. There is some leeway in the van der Waals radii when atoms seem not to have room to fit next to others at the side. If the conflict is within a comparatively small angle from the direction of the bond,³⁴ a little of the edge may be trimmed to allow room for fit.

Some crafts-supply stores carry several sizes of styrofoam balls (in the range of 1 inch diameter or so), which are close enough to proper proportion to use in making approximate models.

In general, some rotation is allowed on single bonds. In the backbone of an amino acid chain, these bonds on which rotation is possible are on either side of the alpha carbon atom.³⁵ There is also rotation permitted on single bonds in the side chains (especially the "methyl" groups).³³

Where two amino acids are joined in "peptide linkage," the four atoms involved (C'O-NH) are "co-planar," and therefore more or less fixed or rigid.³⁴ The reason for this is that the C=O bond, which is a double bond, "resonates" back and forth between the oxygen and the NH group.

Two Part Construction

For this reason, we have found it logical to make the models in two separate parts. The peptide linkage group can be one separate model item (the co-planar C'O-NH just mentioned). The alpha carbon, with the hydrogen atom and R group, is the other. In this way, only a few of the peptide linkage units are needed, since they are all the same (except in the case of proline).

The alpha carbon group, however, requires a different model for each enantiomorph of each amino acid. A preliminary idea of this fact can be gained by experimenting with models of a few representative shapes of the 20 types. If the atoms of the side chains are glued into proper position, then one must keep in mind that rotation on single bonds is possible in real molecules. P. K. Ponnuswamy and V. Sasisekharan, of the University of Madras, India, give helpful information on positions of the atoms.³⁶

It is out of the question to try all conformations, for the number is infinite. It will be apparent, however, that some amino acids will link more easily with those of the same hand, and some more easily with those of the opposite hand. The general impression can be gained that the probability is approximately equal, on the average.

We might mention also, that electrostatic forces may in some cases restrict rotation to a degree, but this does not seem to be a barrier to more or less equal ease of fit.

Experiments on Preferential Linkage

In 1962, Dr. Akiyoshi Wada at the Department of Physics of Tokyo University discussed the implications of certain experiments in the 1950s by Doty, Lundberg, and Blout. These tests seemed to show that a preformed chain consisting of L-residues begins reaction more rapidly with another L- unit than with the opposite isomer, in the case of polymers of gamma-benzylglutamate NCA.³⁷ Important work on the same question was done by C. H. Bamford and Harry Block, who are now at the University of Liverpool.³⁰ Put in simplest terms, they found indications that an L-amino acid was five or six times more likely than a D- unit to connect at the end of a preformed L-chain, and vice versa, in certain circumstances.

The synthetic polymers used in much of this type of work are not simply amino acids. In-



Figure 1. The model to the left is L serine and the model to the right is D serine. This is an example of the "left handed" (L) and "right handed" (D) configuration of the same amino acid. On the models C refers to carbon, N to nitrogen, O to oxygen, and hydrogen is a white ball unlabeled. The L form, with the amine (NH₂) group to the left of the #2 carbon atom, is the form found in living protoplasm. The D form has the amine group to the right of the #2 carbon. Notice that attached to the #1 carbon atom of each molecule is an O and an OH group. The lone oxygen is double bonded to the carbon atom; whereas, the OH group is singly bonded to the carbon atom. The double bond is rigid, while the single bond is free to rotate, unless physically hindered. The differences between the linear arrangements of the carbon atoms of the molecules reflect this ability of the single bond to rotate. (Molecular models and figure caption by Dennis Englin. Photograph by George Howe).

stead, an attachment consisting of a carbon ring and several other atoms has been added to the usual side chain of glutamic acid (one of the 20 amino acids). It seems likely that this long and bulky extra portion of the side chain might cause more steric hindrance than a normal amino acid would have. (Glutamic acid and aspartic acid each have an acidic (COOH) group in their side chains, and this must be protected from reaction with other molecules in the solution. The "protection" of these and other reactive groups, including the ends of amino acids, is one of the main problems of peptide chemistry.³⁸)

Dr. Elliott called attention to other polymerizations that are done—e.g., poly-alanine—where extra attachments are not left on the amino acid residue in the chain.²⁷ I later asked Dr. Block if in cases of that kind any selective bonding of Lto L- as compared to D- to L- was observed. He indicated that experiments with the amino acids, alanine and phenylalanine did seem to show a preference. He had no data as to the degree of preference, but said there must have been some selectivity, because there were, in the resulting chain, blocks^{*} of L- and blocks of D- residues.²⁸

Such experiments by Doty, Bamford, Block and others led some to believe that this stereoselectivity was a result of steric hindrance or other conflict with the preformed helix. Dr. Fred

^{*}Applying probability theory to this matter of "blocks" would seem to lead to this result: As soon as, by chance, one isomer happened to get four in a row, probability would favor that type, by a certain factor. On the average, the opposite would finally show up, and there would be equal probability till one or the other got four in series. The final result would not favor either hand, as to total residues, with each having the same average number and length of blocks. On the question of whether the length of the helix of one isomer increased the preferences, Dr. Block said it did not.²⁸

D. Williams, with co-workers at Michigan Technological University, however, doubts that this is the cause. They report polymerization of monomers of the same glutamic acid complex in which results seemed to indicate a selectivity even before a helix was formed.³⁹ This was quite marked in degree, in the second stage of reaction. (This is another case where the bulky artificial side chain mentioned earlier may be affecting the outcome.)

Dr. Williams told me of quite opposite results in recent experiments with D, L alyl-isoleucine. These two amino acids exhibited a crosswise stereo-selectvity₄₀ (e.g., D- to L- instead of L- to L- preference).⁴⁰ Shröder and Lübke in West Berlin reported a similar reverse preference in "cyclo" polymers of glycine and D, L leucine.⁴¹

The picture is, hence, far from final on selectivity, at this writing. There are many variables which enter into the reaction potentials. The type of solvent used, temperature, pH reading, protecting attachments, all these can affect the linking. The activating intermediates which must be used to bring about the polymerization also complicate the picture. There is, moreover, a tendency of many chemical reactions to bring about "racemization" as a side effect—changing some amino acids themselves to the opposite isomers.⁴¹

Then there is the problem of trying to "read" the results. When we recall that biochemists are working with molecules far too small for the ordinary laboratory microscope, one must emphasize how hard it can be to tell exactly what happened in a reaction, and to what degree. The results must be discovered by indirect means. Sometimes a bit of guesswork is required. Later experiments may disprove the tentative conclusions of a certain experimenter.

A fairly good case might be made for the idea that there is equal probability of opposite antipodes linking, as an average of all types. Here are some facts which may be used to support this conclusion:

(1) Numerous reports of D. L chains with no mention of any stereo-selective factor; specific statements by experimenters such as Dr. Klein that they have not noted any such specificity.

(2) Reports of a reverse preference of L- for D- or vice versa in the case of some experiments. 40,41

(3) The evidence from models of amino acid residues.

(4) Opinions of prominent researchers such as Banner and Fox who make no mention of selectivity when commenting on the ability of all to fit.

(5) A mysterious reaction reported by Bam-

ford and Block,³⁰ in which the addition of lithium perchlorate to the reaction mixture *eliminated the optical specificity*, leaving both forms reacting at the same rate with a "15-mer" as would be expected with a "3-mer" chain. (This was part of experiments mentioned earlier which involved gamma benzyl glutamate N-carboxy anhydride, where reaction of the same isomer with a preformed helix was thought to be five or six times as fast.) It was thought that the lithium perchlorate reduced hydrogen bonding of the NCA to the helix. The result seemed to show "that the specificity may, in part, be connected with adsorption." (Adsorption is the attaching of one atomic or molecular entity to another through electrostatic forces.)

(6) It seems likely that in the presumed "primitive" environment prior to the existence of life, the numerous variables that might affect reactions would by chance be as likely to favor one type of hook up as another. Apparently, no steric reasons would prevent equal ease of fit. There is no reason to think "nature" would happen to provide the same highly specific reactant preparations and conditions that a biochemist might choose, from his artificially prepared supply.

The Odds Against Proteins Having Only L-Amino Acids

The "laws of chance," or principles of probability theory, are widely depended upon in science, industry, engineering, government, and everywhere. Since the advent of "quantum mechanics" in the 1920's, these rules of probability have been carefully verified. It is logical that they be applied to this question, since nothing other than chance has been found that could account for this mysterious left-handed phenomenon.

In order to be certain, probability reasoning should be applied to the two outer limits of what may be the real situation: (1) either there is equal probability, on the average, of opposites linking under natural conditions prior to life on earth, or (2) a preference of 6/7, at the most, in favor of joining with the same isomer. Because it is simpler, the odds regarding equal probability will be calculated first.

(1) Equal Probability Calculated

Dr. Harold Morowitz of Yale University has done extensive research for the National Aviation and Space Agency to discover the theoretical limits of the simplest possible autonomous selfreplicating entity.⁴² He took into consideration the hazards of thermal motion, electrical properties, and functional space. He concluded that the smallest conceivable such entity would require at the very least 45 different kinds of proteins averaging 400 amino acids each.*

Nothing simpler than that could meet the test of replication. As we have seen, there can be no natural selection without ability to duplicate all necessary parts. Chance alone, unaided by natural selection, would have to link up at least one complete set of 45 proteins with all-left-handed amino acids of the universal 20 kinds. (There is strong evidence that all 20 were in use from the time of the first living thing.)

Now consider just one of those average size proteins with 400 units. First, we must allow for the amino acid, glycine, which exists in only one form. Its side chain is just a hydrogen atom, the same as exists opposite it. If we assume that 1/20 of the chain will be glycine, that leaves 380 which could be L- or D-. There is 1 chance out of 2 that the first one might be left-handed. The same is true for each of the other 379.

Calculations of probability require the famous Multiplication Rule, the heart of probability theory. Physicist George Gamow once said it thus:

If you want several different things, you may determine the mathematical probability of getting them by multiplying the mathematical probability of getting the several individual ones.⁴⁴

To get the probability of all 380 of the isomeric amino acids of just one chain happening by chance to be all left-handed, we must multiply the "1/2" probability which is the case for each individual step. It is like flipping a coin 380 times expecting to get all heads. For each step, there is 1 chance in 2, so we must multiply the 2 by itself until we use the figure 380 times. That is 1 chance in 2^{380} .

It will be easier to work with this figure if we translate it to powers of 10 instead of powers of 2. Multiplying 10 by itself is just adding another zero. 2^{380} is about the equivalent of 10^{114} .**

The probability of one average-sized protein molecule of the smallest theoretically possible

living entity happening to turn out with only left-handed amino acids is, therefore, 1 in 10^{114} .

Professor Murray Eden at Massachusetts Institute of Technology estimated that the total number of protein molecules that ever existed on earth might be 10^{52} as an extremely liberal approximation.⁴⁵ If we assume for the moment that all these were the same size as the average protein in the smallest possible autonomous living thing, we can then calculate *the probability that any one protein that ever existed on earth would have only left-handed amino acids just by chance,* as follows:

That isn't all. Even if one *did* happen, many more all-left-handed ones would be needed to work with it, or all would be lost. The odds against each one would be the same. Those huge numbers would then have to be MULTIPLIED together, according to the Multiplication Rule. This would give the odds against the necessary group of proteins being all left-handed. The number is beyond all comprehension. And, if we had all such amino acids, they still could not duplicate themselves, so it would be the end of the line, unless chance could also produce the DNA code and enzyme system.

It is enough to remember that the number of inches across the known universe from one side to the other is less than 10^{28} . The odds against even one average-sized protein with all left-handed amino acids is a figure 10 million billion billion times that big, namely 1 in 10^{62} .

The foregoing were the figures if there is equal probability of either hand linking up each time. There remains the second outer limit to be computed on the basis of supposing the opposite extreme, namely a preference factor of 6 chances in 7 that the same isomer will link up next.

(2) Calculation of Preference Factor

Starting with the average number of 400 amino acids per protein, we subtract the 20 which are

^{*}Compare this with the smallest known actually living thing, which is the minuscule bacteria-like *Mycoplasma hominis* H39. It has 600 different proteins, averaging 400 amino acids each.⁴³ We have no real reason to believe anything simpler has ever existed, from present scientific knowledge. We will, however, use the much smaller total of different proteins from Morowitz' theoretical smallest autonomous self-replicating entity mentioned above.

^{**}For the non-mathematician, there is a simple way to change from 2 to 10 as a base. If you multiply 2 by itself until the total is about equal to a power of 10, you find that 2^{10} is about the same as 10^3 . The convenient formula, then, is .3 times the exponent of 2. That gives the proper power of 10 which is approximately equal to it. Applying it to our figure of 2^{380} , we get: 10^{380} X⁻³, which is 10^{114} .

presumed to be glycine, since it is not onehanded.

Of the 20 symmetric glycine molecules, on the average perhaps two of them would be together in the chain. We will assume that there are 18 glycines that are followed by another kind. In each such case, there would be no preference exerted on the one following the glycine, since it is neither L- nor D-. Those 18 would therefore be on a 1 in 2 probability, while the remaining 362 (380 less 18) would be figured at 6 in 7 probability of the same hand. (In this, a concession is being given to chance, in that calculations are based on the preference at 6/7 even before there are several of the same hand in a row.)

The 18 at 1/2 probability by the Multiplication Rule would result in $1/2^{18}$. The 362 at 6/7 probability (odds of 6 to 1) give rise to this result: $6^{362}/7^{382}$. Multiplying by the preceding figure which resulted from the other 18 at even probability, and translating to base 10, we arrive at 1 chance in 6 X 10^{29} (600 thousand million billion billion.) That is for one average protein chain. To get the absolute minimum needed for the smallest theoretical living thing, we need at least 45 such proteins. By the Multiplication Rule, the odds are around 10^{1334} to 1, after dividing by a million to allow for overlapping. That is the same as 1 with 1,334 zeroes after it. It would require the greater part of a column to print the number.

Going back to the total number of proteins that might have existed on earth, 10^{52} , that would be enough to make $10^{52}/45$ sets for the smallest conceivable living entity, which is 2.22 x 10^{50} sets. Dividing that into the big figure, we find that the odds against one set (they would have to be located together in order to work together) would be about 10^{1283} to 1 that no set of 45 proteins of all that ever existed would by chance have only L-amino acids.

One cannot comprehend such a number! Compare those odds $(10^{1283} \text{ to } 1)$ with the number of seconds since the universe supposedly began, which is 10^{18} seconds for the longest such estimate.

Even if the L-amino acids were 100 times as likely to link with L- as with D-, and considering all the proteins that ever existed on earth, the odds against one set of 45 together having all left-handed amino acids would be more than 10^{258} to 1. It would require saying the word "billion" 26 times. Each time, the entire preceding figure *is multiplied* by a billion.*

Conclusion

No natural explanation is in sight which can adequately explain the mystery that proteins use only left-handed components. There is little hope that it will be solved in this way even in the future. Even if such a result occured by chance, life still would not exist. The proteins would be helpless and non-living without the entire complicated DNA-RNA system to make copies for the future.

There is, however, no problem here for the person who believes in an intelligent Creator of living things. For reasons of his own, such an infinite Planner could have decided to use just L-amino acids in proteins. He would have placed the proper L-enzymes and coding in the cells which would form only left-handed amino acids for use in proteins.

These created enzymes would thereafter be replaced as needed at the "orders" of the DNA code. The same Creator would be the Author of that amazing code, a complete instruction book written in the genes of every cell of every living thing, incredibly comprehensive and detailed.

For those whose philosophy is evolution, this left-handed matter is an embarrassing problem. The efforts at solutions which Oparin catalogued are noteworthy for the questions they bring up rather than for answers. It is not likely that this mystery will ever be adequately explained, as long as the evidence of intelligent planning is ignored.

But what if some day we happen to find a really adequate natural solution to this question? It has frequently been the case that when we discover "natural" explanations for mysteries, at the same time we uncover other complex new problems which only deepen the underlying mystery of this amazing universe.

Finding that birds and other creatures use celestial navigation, for example, solved one question. It opened up much more intriguing mysteries that seem to add far more to the wonder of what exists about us. How can a bird instinctively navigate by the sun and stars, and how is this coded for inheritance?

It has been a mystery how bird eggs all hatch so close to the same time. Now scientists actually have tape recordings of quail eggs "talking" to each other by clicks and vocal sounds to synchronize hatching.⁴⁶ Thus, a greater mystery appears.

The left-handed amino acids are not the only one-handed molecules. The stereo-selective phenomenon is found throughout living nature. For example, vitamin C, which is L-ascorbic acid, is always left-handed in its natural form in foods. This compound can be made in the laboratory in

^{*}Word from Dr. Morowitz just prior to press time informed the author that the smallest theoretical living entity's requirements are now estimated at 124 instead of 45 different kinds of proteins!

both D- and L- isomers, but only L-ascorbic acid has Vitamin C activity. 22 Sugar molecules, conversely, are habitually D- or right-handed.

Remembering the weakness of chance is a necessary step in deciding which philosophy of origins one will believe: evolution or creation. Blind chance requires an average of ten billion tries in order to count to ten. Can this pathetic source account for the intricacies of the eye, or a beehive, the song of a mockingbird, or the metamorphosis and migration of the monarch butterfly? Natural selection is completely inadequate as a solution, since it cannot invent ordered and intelligent new material.

Final Thought

We find that there is no lessening of confusion until one accepts the logic that intelligent systems could not arise without an intelligent Designer.

In Genesis, chapter one, we are given the idea that God did the deciding how each living creature would be assembled. He apparently used L-amino acids, formed by himself, for reasons of his own. We may some day discover those reasons. It is the privilege of scientists to experiment in a well-equipped cosmic laboratory, try-

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ing to find out how the Creator put things together, trying to understand the wisdom built in.

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Relevant Quote

Pasteur, speaking of the "mysterious influence" in this "dyssymmetry" of living matter, said in 1860: "There are here mysteries which prepare immense labors for the future, and from this time invite the most serious meditations of science.'

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(Continued from page 161) **BOOK FOUR**

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For three generations, the theory of evolution has been dominant in the textbooks and teaching materials used in the public schools. This has been true, not only in the natural sciences, but also in the social sciences, and even in the humanities and fine arts. Man has been considered essentially as an animal or a machine, either implicitly or explicitly.

Many educators and scientists, as well as a great number of concerned parents and other laymen are convinced that the evolutionary philosophy is both scientifically false and sociologically harmful. However, the alternate approach, that of creationism, has been commonly rejected as "religious" and, therefore, unacceptable in public educational institutions.

Modern educators and jurists are now recognizing this practice as discriminatory and uncon-"religious" and both "scientific," so that if either is taught, then both should be taught, on as nearly an equal basis as possible. However, no textbooks presenting the scientific aspects of creationism, apart from any religious aspects, have heretofore been available. The "Science and Creation" series will now make it possible to teach creationism, on a purely scientific basis, as a valid alternative to evolution.