ENGINEERING AND SCIENCE
*March 1960, Volume XXIII, No. 6*

# The Place of Genetics in Modern Biology

*by George W. Beadle*

Twenty-five years ago Professor William Morton Wheeler, a distinguished and admired professor of biology and Dean of the Bussey Institution of Harvard University, wrote a small essay (*Science*, Vol. 57, p. 61, 1923) in which he said, " . . . natural history constitutes the perennial rootstock or stolon of biologic science . . . From time to time the stolon has produced special disciplines which have grown into great flourishing complexes . . . More recently another dear little bud, genetics, has come off, so promising, so self-conscious, but also, so constricted at the base." I am sure Professor Wheeler was convinced that this bud would be abortive.

A few months ago there appeared in *Science* (Vol. 130, p. 959, 1959) a related essay by a distinguished and likewise much admired biologist, Sewall Wright, who had been a graduate student at the Bussey Institution during Wheeler's time. After quoting Wheeler's words, Wright pointed out that, far from aborting, the little bud genetics has flourished mightily and has in many respects replaced natural history in the sense that it has become the rootstock of all biological science, and has bound ". . . the whole field of biology into a unified discipline that may yet rival the physical sciences."

Why such a change in 26 years? For, despite the fact that Wheeler was not above a bit of ragging of his friends and colleagues in genetics, he was basically serious. There has been a great change. We have come to recognize that genetics does in fact deal with the very essence of life. This is why at the present time in biology laboratories there are physical chemists, biophysicists, biochemists, microbiologists, virologists, zoologists, and other varieties of biologists devoting much effort to the study of genetic material.

*"The Place of Genetics in Modern Biology" has been adapted from the Arthur Dehon Little Lecture given by Dr. Beadle at the Massachusetts Institute of Technology on November 18, 1959.*

I should like to begin a development of the thesis that genetics is the keystone of modern biology by reminding you that every one of us starts development as a tiny sphere of protoplasm, and that somehow in this small sphere there must be contained the specifications, the directions, or the architectural blueprints for making one of us out of that bit of jelly-like material. Of course, the process by which this happens is enormously complex, and we do not yet understand very many of the details. But we do know that a substantial part of these directions is wrapped up in the centrally located nucleus of the cell. These directions are the material heredity that we received from our parents.

In addition to this set of directions in the nucleus, there must be more. There must be cytoplasm, adequate food, suitable temperature and so forth. The environment adds to the information in the original egg. This is particularly impressive in our own species, for in addition to all the other environmental information fed into us during development we are continually bombarded with cultural inheritance – language, art, music, religion, history, science and so on – that in man supplements biological inheritance to a far greater degree than in any other species.

What are the directions in the nucleus and how do they specify that from this minute cell one of us will come? I shall ask five questions about these specifications:

First, how do we get them and how do we transmit them? I shall dispose of this one, though, for it is answered by classical genetics – the Mendelian genetics now found in every elementary textbook of modern biology.

Perhaps you know less about the remaining four questions:

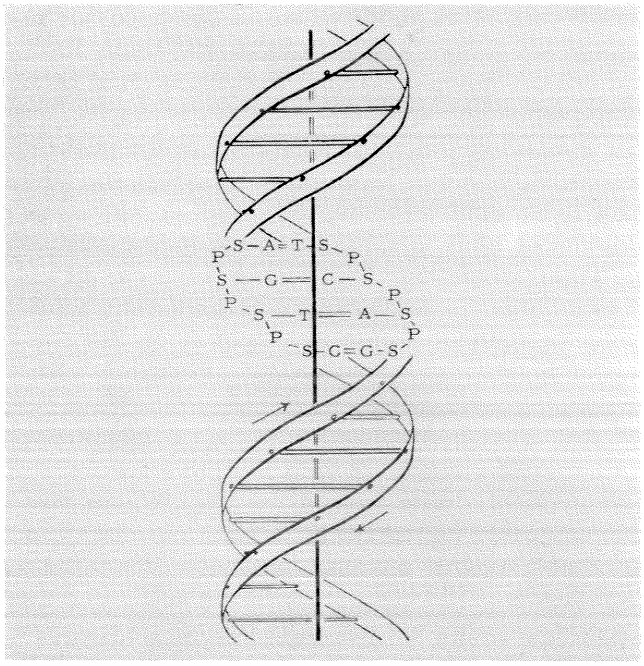
How are the specifications written – that is, what is the language of genetics?

How are the specifications replicated? From the time we start development as a fertilized egg until we transmit them to the next generation, there are perhaps 16 to 25 successive replications of these specifications, depending on whether the carrier is female or male. Each time the material is replicated it doubles, so 20 replications represent more than a million copies. How does replication occur with the precision necessary to avoid intolerable numbers of mistakes?

How are the specifications translated? This is an enormously difficult question and I shall say right now that we know very little about it.

How are specifications modified during the course of evolution? Most of us believe in organic evolution and we want to know how we come to be different from our ancestors? In other words, what is the nature of the mutation process?

A few years ago we would have had a very difficult time answering the four questions that I have just asked. But within the past half dozen years or so, excellent clues have turned up. In 1953 there occurred an important turning point in modern biology. By this time it had become quite clear to a number of biologists that a particular chemical substance called deoxyribonucleic acid (DNA) was important in transmitting hereditary information in bacteria and in viruses. Since the cells of all higher plants and animals contain DNA, it seems probable that it served to carry genetic specification in all living systems.



*Diagrammatic representation of the Watson-Crick structure of DNA (redrawn from Watson and Crick, 1953). The parallel spiral ribbons represent the paired polynucleotide chains. Hydrogen bonds are represented by transverse parallel lines. P=phosphate; S=deoxyribose (sugar); A=adenine; T=thymine; C=cytosine; G=guanine. Orientation of nucleotides is indicated by arrows.*

I shall attempt to explain how and why this substance is important. DNA has been known for a long time. And it was known that it consisted of long chain-like molecules made of four kinds of units called nucleotides. But it was not known exactly how DNA molecules were internally organized until in 1953 two investigators – James D. Watson, now at Harvard University, and Francis H. C. Crick of Cambridge University – succeeded in formulating a structure that has proved to be substantially correct.

From the information then available from classical chemistry, from x-ray diffraction studies, from analysis of the relative proportions of the four kinds of nucleotides, and through ingenious model building, Watson and Crick proposed the structure illustrated below. This structure was at once exciting to biologists because it suggested such plausible answers to the four questions: How is genetic information written? How is it replicated? How is it translated? And how does it mutate?

The key to the structure of DNA is that its molecules are double in a special way. There are two parallel polynucleotides wound around a common axis and bound together through specific hydrogen bonding.

You can more easily visualize the essential features of DNA if you will imagine a four-unit segment of it pulled out in two dimensions as follows:

A - T - C - G
: : : :
T - A - G - C

in which the four letters represent the four nucleotides and the pairs of dots represent hydrogen bonds. In fact you can very nicely represent such a segment with your two hands. Place your forearms vertically before you and parallel. Fold your thumbs against your palms and place homologous finger tips together as though they were teeth on two combs vertically oriented in a single plane, tooth tip to tooth tip. In this arrangement the two index fingers represent the A:T nucleotide pair and so on.

Imagine many fingers along your forearms – of four kinds, corresponding to the nucleotides A, T, C, and G. The four kinds of fingers or nucleotides can be arranged in any order on one arm but must always have the complementary order on the other; T opposite A, A opposite T, G opposite C, C opposite G. Thus, if one knows the sequence of nucleotides in one chain, the sequence in the other can be determined by the simple rule of complementarity.

This structure suggests that genetic information is contained in the sequence of nucleotides; in other words, DNA is a kind of molecular code written in four symbols. One can think of the code as a sequence of nucleotide pairs or of nucleotides in a single chain, for it is obvious that the double chain and the two single component chains all contain equivalent information. In essence, the two complementary chains are analogous to forms of a single message, one written

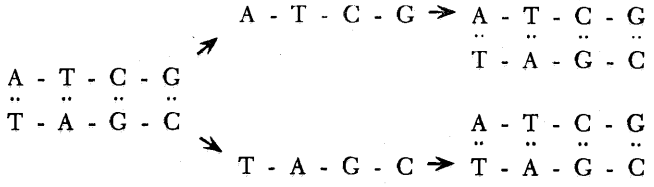
in conventional Morse code, the other in a complementary code in which each dot is changed to a dash and vice versa.

Let us now ask the question: How much information is packed away in the nucleus of a human egg? It is estimated that there are about five billion nucleotide pairs per single cell. How much information does this correspond to in terms of, say, information spelled out in the English language? Francis Crick has expressed it this way: If you were to make an efficient code for encoding messages in English in the four symbols of DNA, and then started encoding standard sized library volumes in this DNA code, you could get the contents of about 1000 volumes in the DNA of the nucleus of a single fertilized egg cell.

This is another way of saying that it requires the equivalent of about 1000 large volumes of directions in the egg nucleus to specify that a human being like one of us will develop properly from it.

That is supposedly the way the genetic information is carried from generation to generation – in a language we might call D-N-A-ese. Each gene is a segment of DNA of perhaps three or four thousand nucleotides.

Now let us ask about the replication. The double structure of DNA suggested immediately to Watson and Crick how this could happen. If, during cell division, the two chains were to come apart, obviously each could serve as a template for picking up additional units to make new half chains. And this is happening in each of us right now. In many cells nucleotides are continually being made from food components. The replication of DNA according to this scheme is illustrated as follows:




You can represent the process with your hands. Indicate the double molecule as already directed as paired hands. Take the two hands apart. Imagine free fingers (nucleotides) moving around at random. Each single hand serves to select in proper order the one-fingered units necessary to make a complementary hand. The right hand is a template for making a left hand, and vice versa. So, with a double molecule represented by a pair of hands, two single molecules arise by breakage of hydrogen bonds, with each then directing the synthesis of a new complementary single partner.

This process of replication takes place with every cell division and, as we shall see, with a high degree of precision.

This hypothesis by which two identical bipartite molecules arise from a single such double molecule is very satisfying in its simplicity and elegance. If true, it is presumably the basis of all biological reproduction at a molecular level. Can the hypothesis be tested? The answer is yes. In fact, several kinds of experiments have been made to see if the hypothesis agrees with observed facts.

## *Testing the hypothesis*

In one kind of experiment DNA units are labeled with radioactive phosphorus. Each nucleotide has one phosphorus atom, and a certain number of these atoms can be made radioactive by growing the organism, say a bacterium, in a medium containing radioactive phosphorus for several generations until it becomes equilibrated. Then both chains of its DNA molecules will be labeled. If the bacteria are then allowed to multiply in a medium in which there is no radioactivity, the two chains of each DNA molecule, both labeled, should come apart, each then directing the synthesis of an unlabeled partner. The new double molecules should then be labeled in one chain but not in the other. In the next generation the labeled chain should separate from the non-labeled one. With synthesis of non-labeled partners by these, there should be produced labeled and non-labeled double molecules in equal numbers. The observed results are consistent with this expectation.

Another way of doing essentially the same experiment is to replace the normal nitrogen atoms of DNA with "heavy" nitrogen, the stable isotope $N^{15}$, instead of the usual $N^{14}$ counterpart. DNA molecules so labeled become heavier but not larger. Hence they are denser. DNA containing only $N^{15}$ can be cleanly separated from that containing $N^{14}$ in an analytical centrifuge cell in which an appropriate density gradient is established. In such experiments it is found that bacteria containing DNA fully labeled with $N^{15}$, if allowed to multiply once (double in number) in a medium containing only $N^{14}$, give rise to descendants in which all the DNA molecules are "hybrid," (i.e. "half heavy"), as though one nucleotide chain of the double molecues contained $N^{15}$ and the other $N^{14}$. This, of course, is what is predicted by the hypothesis. In a subsequent generation, also in $N^{14}$ medium, half the DNA molecules are hybrid and half are fully light as predicted.

While experiments of this kind do not prove that the Watson-Crick hypothesis of DNA replication is correct, they do strongly suggest it. An even more dramatic way of testing the hypothesis is the one used by Professor Arthur Kornberg, now at Stanford University, and his associates. They have devised a test-tube system which contains the four nucleotides A, T, C, and G as triphosphates, a buffer solution, magnesium ions, and a polymerizing enzyme. DNA molecules added to this system appear to be replicated. Is the new DNA like the primer molecules added? One important observation suggests it is. The ratio of A:T nucleotide pairs to C:G pairs of

the product is like that of the primer DNA. It is not easy to see how this could be if the primer were not being copied in a precise way. On the other hand, if DNA having known biological activity (as determined by ability to transform the genetic constitution of a bacterium) is used as a primer, both the product and the primer added end up being inactive. Why this is so is not known, but it is strongly suspected that the polymerizing enzyme added contains a small amount of depolymerizing enzyme that breaks up DNA chains and thus destroys activity.

Again, the Kornberg synthesis does not prove that the hypothesis is correct. It is just possible that an unkind nature could have evolved a system that would do just exactly what the hypothesis predicts, but by a different mechanism.

## *Ribonucleic acid as messenger*

How is genetic information translated? These are enormously difficult questions, and we know relatively little in detail about the answers. They involve the whole of development, differentiation, and function. There are working hypotheses – widely used and useful ones – that suggest how some of the steps occur.

We know that in our bodies there are many thousands of kinds of protein molecules – large, long molecules made of amino acids, and very specific in their properties. One, for example, is hemoglobin. It is built of 600 amino acids strung together in a particular way. There are two kinds of chains of amino acids per hemoglobin molecule, each in pairs. Each chain is about 150 amino acids long. And we know that there are segments of DNA – two, we postulate – in our chromosomes that say how to build the two protein subunits.

A widely used working hypothesis assumes that around a double helix of DNA there is wound a helix of another kind of nucleic acid, called ribonucleic acid or RNA. RNA, like DNA, is built in four nucleotides. In this way the DNA code may be translated into a corresponding sequence of RNA. RNA then moves from the nucleus into the cytoplasm. There it is incorporated into microsomes, which are sub-microscopic structures in which protein synthesis occurs. In the microsome, RNA units are believed to serve as templates against which amino acids are lined up in proper sequence. Amino acids, derived from the proteins in our food, are first activated by enzymes and subsequently hooked to small carrier segments of RNA that serve to carry the amino acids to their proper places on the microsomal RNA templates.

Carrier RNA may be thought of as messengers carrying packages and addresses to which they are to be delivered. The messengers carry the amino acid packages along the RNA template until the address matches that on the template. There is a specific RNA messenger for each of the twenty kinds of amino acids. When all component amino acids are correctly ordered, they are linked together to form proteins which then peel off the templates and the process is set to be repeated. For hemoglobin, for example, there are assumed to be two DNA segments, one for each kind of protein chain, and two corresponding RNA templates. This in essence is believed to be the translation process.

A large number of proteins serve as enzymes or essential components of enzymes. Enzymes catalyze chemical reactions that would otherwise occur at rates so low that life processes would essentially cease. For each enzyme protein there is supposedly a segment of DNA information in the nucleus – a gene – and corresponding microsomal RNA templates in the cytoplasms of those cells active in synthesis of that particular enzyme protein.

An important question of present day biology is concerned with the nature of the mechanism by which the four-symbol code of DNA is related to the twenty-symbol code of proteins. It is obvious that single symbols of DNA cannot stand for amino acid for there are only four. Likewise, pairs of DNA symbols will not do, for there are only 16 such pairs if the DNA molecule is read in one direction. If one reads in one direction and uses three symbols per amino acid, there are 64 possibilities. However, only 20 of the triplets are useful if successive sets of three are used, for the overlapping sets of three must not encode amino acids or there would be confusion in the translation.

## *Mutations as a source of evolution*

Twenty is the minimum number required to encode all of the amino acids that occur in proteins – that is, if one reads the code in one direction. However, because the two parallel chains in a DNA molecule have opposite polarities as determined by the way the nucleotides are oriented in the two chains, the double DNA molecule is symmetrical and there is therefore no obvious way to know in which direction the information is to be read. Unless there exists some kind of marker, as yet undiscovered, that specifies in which direction to read, the number of three-symbol sets that can be used to encode amino acids unidirectionally is only 10. Four-symbol codes have accordingly been investigated. It turns out that there are 27 such four-symbol "words" that can be used without any of their overlaps making sense when read either forward or backward, and without the four-letter words themselves making sense when read in reverse. This is sufficient, but it is not known if this is indeed the correct coding mechanism.

My fourth question concerns the nature of mutation.

During DNA replication, occasional mistakes are made. Presumably during replication a nucleotide does not pick up a complementary partner as it should, but instead picks up a non-complementary one. It has been postulated that such mistakes result from an improbably tautomeric form in which a hy-

drogen atom is in an improbable position at the exact moment the nucleotide picks up a partner. A wrong partner is therefore selected. In the next round of replication the "wrong" partner will pick up what is its complementary partner and this will result in substitution of one nucleotide pair for another.

This is somewhat like a typographical error. In typographical errors it is possible to have extra letters, or too few letters; one letter substituted for another, or transposed letters. Presumably, similar kinds of mistakes can be made in genetic information during replication. In fact, there is genetic evidence that these four basic types of mistakes do occasionally occur.

How often do such mistakes occur? Quite infrequently, we believe. From the time one receives a set of directions in the fertilized egg, until one transmits it to the next generation (and remember this is perhaps 17 to 20 successive replications of information, equivalent to about 1000 printed volumes) a mistake is perhaps made about once in a hundred times – that is, a significant and detectable mistake. This is clearly a high order of precision.

What happens to such typographical errors as are made? First of all it is clear that the DNA molecule will replicate just as faithfully whether the information in it makes sense or not. Its replication is a purely mechanical one, it seems. Therefore mistakes in genetic information will be perpetuated.

## *Accumulated errors*

It is obvious that if there were no way of eliminating errors in such a process, such errors would accumulate from generation to generation. Perhaps an analogy will make this clear. If a typist types in a purely mechanical way, never proofreading, never correcting, and types successive copies of the same material always from the most recently typed copy, she will accumulate mistakes at a rate dependent on her accuracy until eventually the sense of the original message will be entirely gone. In the same way, this would have to happen with genetic information if there were no way of taking care of mistakes. With genetic information something does happen that takes care of mistakes. By extending the analogy, perhaps I can make clear what that is:

The typist, typing mechanically, can correct a mistake by a second random typographical error, but obviously the probability of this is extremely low. It is likewise so with genetic information, and it is clear therefore that this is not the principal way in which mistakes are prevented from accumulating. Let us pretend the typist has an inspector standing beside her. When she makes a mistake, he says, "Throw that one away and start over." If in the next try she makes no mistakes, he says, "All right, now you may type another from the one you have just finished." Each time she makes a perfect copy he allows her to go ahead, but each time she makes a mistake, he insists she throw the copy away. That is what happens with genetic information. The inspector is analogous to natural selection. Bad sets of specifications in man are eliminated by natural selection.

A more dramatic term for elimination of unfavorable specifications by natural selection is "genetic death," as used by H. J. Muller. Individuals developed from unfavorable specifications do not reproduce at the normal rate, and ultimately a line so handicapped dies out. To avoid progressive accumulation of mistakes from generation to generation, it is obvious that every error in replication that is unfavorable must be compensated for by the equivalent of a genetic death. That is why geneticists are concerned about factors that increase the mutation rates.

## *Mutations – favorable and unfavorable*

You may quite properly ask, "Are there no favorable mutations?" The answer is yes, there are occasional favorable mutations; they are in fact the basis of organic evolution.

However, because many mutations involve subtle changes that may be favorable under special circumstances of environment or overall genetic constitution it is not easy to estimate the proportion of favorable to unfavorable mutations. Theoretical considerations and a certain amount of experimental evidence agree in indicating that the great majority are unfavorable. Organisms are, in general, already so highly selected for success in their normal environments that the chance of further improvement by random mutation must be very small.

Perhaps an analogy with a fine watch will dramatize the point. Assume the watch is very slightly out of adjustment. A random change brought about, say, by dropping it, could conceivably improve the adjustment. Clearly, however, the chance of making it run less well, or not at all, is enormously greater. Now let us extend our typing analogy. Assume our inspector exercises judgment. When the typist makes an error that improves the original message, he passes it. Thus, improved messages will replace their ancestral forms and the improvement will be cumulative. Something like this happens with living systems. Specifications improved by occasional favorable mutations are preferentially reproduced and thus tend to replace their ancestral forms. This is natural selection.

In recent years many factors have been found to increase the frequency of mutations. High energy radiation that penetrates to the cell is mutagenic in proportion to its amount. A number of chemical agents are likewise mutagenic. It is now possible, for example, to alter nucleotides in known chemical ways that will produce mutations. Oxidation of amino groups of nucleotides with nitrous acid is one way. It is encouraging that biochemists and geneticists who study the mechanisms involved are beginning to be able successfully to predict the types of mutations

that are most likely to be produced by specific chemical agents. It is not, however, possible to do this specifically for certain genes only.

## *The sources of living systems*

Let us now turn to the general question of evolution. What do mutations have to do with the processes by which it occurs? It is especially appropriate at this time to discuss this aspect of my subject, for, as you know, this is the hundredth anniversary of the publication of Darwin's *The Origin of Species.*

Organic evolution is interesting and important in many respects. For one thing, it is not logically possible to accept only a small amount of it, for one cannot imagine a living system that could not have evolved from a very slightly simpler system. Starting with man, for example, and working backward toward simpler systems one sees no obvious stopping place. Our ancestors were presumably a bit simpler than we. Early in man's evolution there were primitive men. And before primitive man there were prehuman ancestral forms capable of evolving into true man.

This is true however one defines man. And so one can go backward in the evolutionary process to simpler and simpler forms until finally one begins to think of systems like present-day viruses, the simplest of which consists of little more than nucleic acid cores (DNA or RNA) and protein coats.

One can easily imagine that, before systems of this type, there were smaller and smaller system of nucleic acid and protein capable of replication and of mutation which in turn had ancestors consisting of only nucleic acid. We know that nucleic acids can be built up from nucleotides and these from simpler precursors. In a recent lecture, Melvin Calvin, professor of chemistry at the University of California, talked about the origin of some nucleotide precursors, and presented evidence suggesting that some such compounds, or their relatives, are found in certain meteorites. It is assumed that these were formed by natural chemical reactions that went on and are still going on outside living systems. Presumably through such reactions, precursors of nucleotides were formed. Professor Calvin also mentioned the evidence that amino acids are made from such simple inorganic molecules as methane, ammonia, hydrogen, and water under conditions assumed to have obtained on primitive earth.

It is, I believe, justifiable to make the generalization that anything an organic chemist can synthesize can be made without him. All he does is increase the probability that given reactions will "go." So it is quite reasonable to assume that, given sufficient time and proper conditions, nucleotides, amino acids, proteins, and nucleic acids will arise by reactions that, though less probable, are as inevitable as those by which the organic chemist fulfills his predictions. So why not self-duplicating virus-like systems capable of further evolution?

I should point out that nucleic acid protected with a protein coat has an enormous selective advantage, for it is much more resistant to destruction than is "raw" nucleic acid. Viruses can be stored for years as inert chemicals without losing the capacity to reproduce when placed in a proper environment. Of course, present-day viruses demand living host cells for multiplication, but presumably the first primitive life forms inhabited environments replete with spontaneously formed building blocks from which they could build replicas.

Before molecules like methane, hydrogen, water, and ammonia, there were even simpler molecules. Before that there were elements, all of which nuclear physicists and astrophysicists believe have evolved and are now evolving from simple hydrogen. That is why I say if you believe in evolution at all there is no logical stopping place short of hydrogen. At that stage I'm afraid logic, too, runs out.

The story can, of course, be repeated in reverse. When the conditions become right, hydrogen *must* give rise to other elements. Hydrogen fuses to form helium, helium nuclei combine to give beryllium-8, beryllium-8 captures helium nuclei to form carbon, and carbon is converted to oxygen by a similar process. In this and other known ways all the elements are formed. As one goes up the scale the number of possibilities rapidly increases. As elements begin to interact to give inorganic molecules, the number of possibilities rapidly becomes greater. I do not know how many inorganic molecules are possible, but I do know there must be a very large number.

## *The number of possibilities increases*

With organic molecules the number becomes truly enormous, particularly with large molecules like proteins and nucleic acids. For example, there are something like 4 raised to the 10,000th power number of ways that a modest-sized DNA molecule can be made. There appears to be no stage at which there is a true qualitative change in the nature of evolution. The number of possibilities goes up gradually, the complexity goes up gradually, and there appears to be no point at which the next stage cannot be reached by simple mutation.

Let us suppose that we have a small piece of DNA protected by a protein coat and capable of replication in the presence of the proper building blocks and a suitable environment. During replication, the system will occasionally make mistakes. It is a mutable system. Given sufficient time, there will eventually occur a combination of mutations of such a nature that the protein coat will become enzymatically active and capable of catalyzing the formation of a nucleotide or amino acid from a slightly simpler precursor. If this particular building block happens to be limiting in replication, the mutant type will obviously have a selective advantage. It can replicate in the absence

of an essential building block by making it from a simpler precursor. If two such units with protein coats, having different catalytic functions, combine to form a two-unit system, they will be able to make two building blocks from simpler compounds, and will be able to survive under conditions in which their ancestral forms would fail.

In the same way, it is not too difficult to imagine systems arising with successively three, four, five, and more units, with every additional unit serving a catalytic function. With each additional unit the total system would become one step less dependent on spontaneously preformed precursors. With perhaps ten thousand such units the system might be able to build all its necessary parts from inorganic materials as we know present-day green plants do.

## *Reaching the stage of man*

How many units to reach the stage of man? Perhaps 100,000 units carrying out 100,000 functions are necessary. However many it is, we know they carry the specifications for the development of a complex nervous system, by which we supplement blind biological inheritance with cultural inheritance. We reason, we communicate, we accumulate knowledge, and we transmit it to future generations. No other species we know of does this to anything like the same degree. We have even learned about organic evolution and are on the verge of learning how to start the process.

I pointed out that in the Kornberg system, with the four nucleotides present, nothing happens unless a primer is added. That is not entirely true. After a delay of some three or four hours something does happen even without a primer. What happens is that a DNA molecule is spontaneously formed. It differs from all naturally occurring DNA in that it contains only two of the four nucleotides.

Now, if this two-unit co-polymer is used as a primer in a new system, it immediately initiates the synthesis of co-polymers like itself. In other words, it starts replicating. Remember it arose spontaneously. If you believe in mutation, and you must if you accept scientific evidence, you must believe that if you start with a two-unit co-polymer and let it undergo successive replications, there will eventually occur a mutation with which a pair of nucleotides will be replaced by the pair originally excluded in the process. This conceivably could have been the origin of the four-unit DNA of all higher organisms.

Knowing what we now know about living systems – how they replicate and how they mutate – we are beginning to know how to control their evolutionary futures. To a considerable extent we now do that with the plants we cultivate and the animals we domesticate. This is, in fact, a standard application of genetics today. We could even go further, for there is no reason why we cannot in the same way direct our own evolutionary futures. I wish to emphasize, however, that whether we *should* do this and *how*, are not questions science alone can answer. They are for society as a whole to think about. Scientists can say what is possible, and perhaps something about what the consequences might be, but they are not justified in going further except as responsible members of society.

Some of you will, I am sure, rebel against the kind of evolution I've been talking about. You will not like to believe that it all happened "by chance." I wish to repeat that in one sense it is not chance. As I have said, the mutations by which we believe organic evolution to have occurred are no more "chance" reactions than those that occur in the organic chemist's test tube. He puts certain reactants in with the knowledge that a desired reaction will go on. From the beginning of the universe this has been true.

In the early stages of organic evolution, the probabilities were presumably very small in terms of time intervals we are accustomed to think about. But, for the time then available, they were almost certainly not small. Quite the contrary; the probability of evolving some living system was almost surely high. That evolution would go in a particular direction is a very different matter. Thus the *a priori* probability of evolving man must have been extremely small – for there were an almost infinite number of other possibilities. Even the probability of an organism evolving with a nervous system like ours, was, I think, extremely small because of the enormous numbers of alternatives. I am therefore not at all hopeful that we will ever establish communication with living beings on other planets, even though there may well be many such on many planets. But I do not say we should not try – just in case I am wrong!

## *Scientists and materialists*

Some of you will no doubt be bothered by such a "materialistic" concept of evolution. Ninety years ago in Edinburgh, Thomas Henry Huxley faced this question of materialism in his famous lecture on the physical basis of life. What Huxley said can be said today with equal appropriateness.

He said in effect that just because science must by its very nature use the terminology of materialism, scientists need not necessarily be materialists. A priest wears material clothes, eats material food, and takes his text from a material book. This does not make him a materialist. And so it need not with a scientist.

To illustrate, the concept I have attempted to present of the origin of life and of subsequent evolution has nothing to do in principle with the problem of ultimate creation. We have only shifted the problem from the creation of man, as man, to the creation of a universe of hydrogen capable of evolving into man. We have not changed the problem in any fundamental way. And we are no closer to – or further from – solving it than we ever were.