CHAPTER 13

FURTHER APPLICATIONS OF MATHEMATICS IN THE NATURAL SCIENCES

IN THIS CHAPTER I would like to give some additional examples of sophisticated mathematics used by physicists and biologists today. There are situations where classical mathematics, the solution of differential equations, which describe physical phenomena, are not obtainable in a closed form by the methods of standard analysis. A lot of numerical work of heuristic value was done in Los Alamos during and after World War II, and this is perhaps a novel feature of present day applications of mathematics, but the physicists there also used some very abstract mathematics. For example, some results of topology were of use in the design of accelerators.

At Los Alamos, just after the war, the fixed point theorems concerning transformations of a ring into itself were useful to obtain ideas of the behavior of orbits in a circular accelerator of particles. Some modern accelerators consist of a ring in which particles, such as protons or even electrons, go around a million or many millions of times in a very short period, inasmuch as their velocity is close to the velocity of light. These orbits in the torus have to satisfy certain properties — they should not get too close to the walls. It turns out that topology theorems concerning such transformations of a torus into itself have direct applications, probably something that a pure mathematician would not suspect *a priori*.

There was at Los Alamos from the beginning of the project a group devoted to the study of the effects of radiation, specifically the study of the health hazards of radiation. This group started with very specific problems concerning the effects of gamma rays, neutrons, and charged particles, which are very dangerous to the health of people working near accelerators with radioactive materials. People working with such have to wear film-badges that record the amount of radiation they are being exposed to. This group contained a number of biologists and medical people. In the beginning, it was a rather small group, but when the war ended it became a whole division where one studied not only the immediate practical problems of the hazards and dangers of radiation and its effect on tissues, but more fundamental biology in general. They studied problems of genetics, and in order to put the knowledge of these problems on a more general basis, they studied properties of cells and their reactions to external influences, in particular those of radiation.

Now to pursue this somewhat autobiographical vein, I should mention that in talking to some of the members of that division I became more and more interested in the problems of biology in general. This was in the late forties and early fifties, before the great discovery of Watson and Crick on the mechanism of replication and the role of the code that describes the development of living organisms. This discovery, by the way, besides its enormous direct import on biology in general, also had a psychological effect on biology. It revolutionized the aspects of molecular biology and even influenced more generally a whole field of natural sciences.

For a long time, I was interested, in an amateurish way, in biology. When I tried to ask general questions of some colleagues, at Harvard or other places, some 45 years ago, the answer was "Ah, you cannot say this because there is an exception. What you say is sometimes true, but there are such animals, or insects, or fish that are not that way." Even slight generalizations almost seemed to be resented in those days. The discovery of Crick and Watson which showed a certain universality, a great generality of a schema of replication, greatly changed the attitudes of biologists and people in natural sciences. As a consequence of these ideas, there is now much more willingness to talk about generalities, to speculate on generalities that might be discovered, and on the theoretical variations of what we, in a special case here on earth, call life. I cannot explain here or give examples of this revolution in attitude, but there certainly has been a change in the psychology of the researchers.

Some time after World War II ended and I returned to Los Alamos, I held discussions with biologists in the so-called H Division (H for health), and with some physicists and a mathematician or two. We organized a little seminar for laymen like ourselves with some professional biologists who were willing to tell us about the fundamental properties of the units of life and teach us about the morphology, behavior, and role of cells. I certainly did not know enough organic chemistry to discuss this thoroughly, but really was interested in the general conceptual problems, problems of the schemata of the organization of the cell and its functioning. We noticed that indeed some simple mathematics could be useful, not merely as a service function to help calculate by differential equations phenomena that were understood in principle or physically, but perhaps even in formulating the schema of the organization and functioning of the cell itself. To this day these schemata are not completely known, and fundamental questions remain unanswered.

Of course, one knows that mathematics, that is to say statistics, was always useful in biology. Even in the fundamentals of Mendelian theories one needs a little probability theory. There are the simple and nice observations of G. H. Hardy, a pure mathematician, a great number theorist. There are studies using differential equations to describe the flow of blood in veins and arteries; the idea of diffusion. In other words, classical mathematics had been used for a very long time. But it seemed to some of us, to myself certainly and I still feel it very strongly, that the time had come for a deeper involvment of mathematical work on a conceptual basis, on the basis of the formulations themselves, to the problems of biology.

I would like to talk now about the possibility of using abstract, more general mathematical ideas in the schemata of molecular biology, and in problems of genetics and evolution. I will also make a few remarks about the problems of organization of the nervous system and of the functioning of the brain itself. All this, of course, is quite different from the application of mathematics to theoretical physics, because much less is known about the facts of biology in the areas that I have mentioned; although during the last couple of decades exploration is proceeding in a most impressive way.

As I stated above, the discoveries of Crick and Watson involve the fact that a living organism is programmed, coded by a linear sequence of letters. Biologists denote it by *A, C, T, G.* This linear sequence and code is contained in the nucleus of a cell, in the chromosomes, and is very long. Now, instead of letters, we can again use symbols such as 0, 1, 2, 3, or for purposes of illustration that will not change the gist of the matter, just the two symbols 0 and 1, and consider the code consisting of a long sequence of binaries. In every organism, even in bacteria, this code in the nuclear tape is quite long. For a mammal, such as a human being, it is apparently some billion units long.

To impress mathematicians, who in general avoid complexity as such, we should point out that even a single bacterium has up to ten thousand different enzymes and proteins, each of which is coded by a lengthy expression of these symbols. The code involves not only the chemical substances, the hardware so to say, but also the coding of functional uses; not just sets of molecules, but something that corresponds to a higher logical order of instructions for motions for organization and such; this still is not understood very well.

Thousands of proteins are now decoded in the sense that one knows the linear sequence that defines them. What happens with the code is this: molecules go along the code or part of the code in a chromosome, to make a simile, in the fashion of a zipper.

These molecules read short segments of it, then travel from the tape to little spheres called ribosomes, which are in a sense factories. This transcript of a section of tape, when deposited in the ribosome, will start manufacturing the particular chemical molecule read from the code and deposit it. Substances like hemoglobin and myoglobin and many of the other important molecules are manufactured in this manner. Of course, this description of the process is much simplified.

I should point out here that there is one special substance, a protein called cytochrome *C*, that is present in mammals, fishes, insects, and in seemingly all living organisms. Although not identical in all organisms, large segments of the molecule are chemically homologous. Cytochrome *C* is important for the phenomenon of electrical conduction inside the living organism and is absolutely essential for life. The code for it is some hundred to hundred fifty units long. (When I speak of units I mean the DNA units, not just the 0's and 1's. In symbols reduced to 0 and 1, one needs a couple dozen times more units.) I also neglected to state that the code is formed by triplets of these letters, which can be thought of as forming "words." Combinations of these words, of which there are some twenty, form "sentences." These sentences then are the definitions of the proteins and enzymes and other substances that control the life processes. The universal occurrence of this protein in living organisms suggested to the biologist Margoliash the idea of trying to devise the sequence of evolution from hundreds of millions of years ago to the present, by looking at the variations in this protein. Margoliash assumed that the more complex or varied definitions of cytochrome *C* came later as a result of mutations. If there was a primitive original form, then one could conceivably follow its succession of changes until one arrived at its present variety. Margoliash's idea was to discuss the evolutionary tree for this molecule and to assume that it mirrored in a way the evolution of living organisms. In all, he analyzed the protein code for approximately 20 or 30 different species. Assuming the simplest one corresponded to a proto-organism, and noting the changes and differences between them, he ordered them in a tree that described successive mutations due, in all likelihood, to selective pressures. These led to different cytochromes in the more complex organisms, and the idea was to find an order in the tree based on the following assumption: small changes are more probable than large changes. Now what is small and what is large depends in our language on the distance or metric in the space of codes for this special cytochrome. One also had to assume that nonextant organisms were points in the tree. These junction points or vertices are conjectural. It is done in such a way that the sum total of the distances through the whole tree of the codes is as small as possible, that is, the sum of the distances in the sense of the metric in the space of codons. Therefore, mathematically the problem was: given a number of points in the space of codes how to construct a *binary* tree, a tree splitting into two branches at each node, corresponding to single mutations, in such a way that the sum of the distances of the edges between vertices, including of course those that do not exist any more, be as small as possible. At the end of the tree we have the existing species examined by Margoliash and his collaborators, about thirty points (theoretically one could have many more.)

It occurred to me at once that given an idea of distance (one which I will define below), the problem becomes a variation or a generalization of an old geometric problem of Steiner's, the nineteenth century geometer: what are the smallest, most economical connections in the form of a binary tree linking points lying in the Euclidean plane (with the distance being the Euclidean, normal distance used for measuring separation of points in two dimensions)? This problem is not yet completely solved even in this special form.

In our situation, we don't have a *plane*, but a general space, a space of codons, of sequences of 0 and 1, between which a special distance is defined. One wants to find new points and to connect all of them in such a way that the total sum of all the distances is as small as possible. This means that the total of the mutations was a least improbable one among the possible series of such.

Now, what kind of distance should we consider between the codes for DNA that define the organic substances? To simplify again, I will assume that the symbols are only 0 and 1, not the four letters used by biologists, although it makes no difference at all mathematically. One distance between two such sequences could be the well-known sum of the absolute value of the differences between the two sequences

$$\alpha = [\alpha_1, \alpha_2, \ldots, \alpha_N] \text{ and } \beta = [\beta_1, \beta_2, \ldots, \beta_N]$$

namely

$$\rho(\alpha, \beta) = \sum_{i=1}^{N} |\alpha_i - \beta_i|$$

used in mathematics and in physical applications. Sometimes, this distance is called a Hamming distance; really, it is a special case of the Minkowski distance, which is a more general one than the Euclidean distance between points in a plane (or for that matter, in three-dimensional space or *n*-dimensional space.) But this distance is not suitable for examining similarity (or dissimilarity), analogy, or the measure of "likeness" between biologically meaningful structures. The reason is this: having a code, if you imagine it as a physical object, then its position is not fixed, rigid, as is the case for physical objects lying in space. A tape can be twisted, shifted, curved, and the idea of similarity or closeness of form between two such tapes of codes would be different. For example, take the sequences

$$\alpha = 010101\ldots\ldots.1 \text{ and}$$
$$\beta = 101010\ldots\ldots0$$

the two sequences are really very similar. The normal "Hamming" distance between them would be very large, equal to N if there are N symbols in each, because they differ in every *place* or index, the index being rigidly fixed for each. However, by a *shift* and one or two *erasures* one can make them identical. The obvious thought then is to modify the idea of distance to incorporate such possibilities of allowing small changes of a different type in order to compare two given sequences of 0 and 1.

A new definition to satisfy this feeling could be, given two sequences,

$$\alpha = \alpha_1, \alpha_2 \ldots\ldots \alpha_N$$
$$\beta = \beta_1, \beta_2 \ldots\ldots \beta_N ,$$

operations of two types are allowed. Type I is to change 0 into 1 or vice versa, and each such step costs one unit. Type II is to erase a letter and then contract the rest so as to annul the symbol that we have gotten rid of, a sort of omission of a symbol (by mutation so to speak). This operation is allowed on the first or second sequence or on both. We have then steps of two types, and we can call a distance between the two sequences the minimum number of steps that will result in the two sequences being identical. This minimum number, it turns out, satisfies the property one wants to have for a distance or a metric. First of all, the distance has to be symmetric. When it is 0, it means the sequences are identical. Secondly, we have to have a triangle inequality, meaning that from a sequence A to a sequence C the distance between these two sequences is not less than any intermediate path going from A to B and B to C. The sum of these two is equal to or greater than the direct distance between A and C. It turns out that our definition satisfies this property. Of course the original attempts made by biologists did not necessarily satisfy this last postulate of the so-called triangle inequality.

Now I want to mention some mathematical problems that are suggested by that sort of definition of distance between codes or one-dimensional sequence problems that might amuse a pure mathematician.

The first problem is an elementary one. Suppose I have two sequences given at random of 0 and 1 each of length n. What is the average distance, in our new sense, between them? It is obvious that the classical, ordinary distance, the sum of absolute values of differences for two randomly chosen sequences of length n will be $n/2$, because on the average, the difference will be in half the places. In our distance, the number, the average will be different; it is clear that it will be less than $n/2$.

At first I was trying to prove a simpler statement that this average is a linear function of n. I did not find a proof of it, but a young mathematician, Joel Spencer, professor at Stony Brook on Long Island, proved that indeed for large n the average distance tends to behave linearly with n and in the limit it is a linear function of n with a coefficient less than ½. He does not know its exact value but has upper and lower limits for it. This theorem proves, as mathematicians would say, a weak law of large numbers for such random sequences.

For infinite sequences we may now proceed as follows: One way to define the distance between two sequences is to write them down, compare the first n segments of both, compute the distance between them and divide this by n. By virtue of the result of Spencer, this should be on the average a linear function of n. Then we go to the limit for n tending to infinity. In order to prove that it exists for almost all sequences, one has to identify any two sequences such that the distance between them, defined in the way I just indicated, tends to zero. Therefore, we will obtain a space of classes of sequences of 0 and 1, a rather interesting new type of space. I should mention here that Peter Sellers, a professor at the Rockefeller University in New York, proved nice theorems about distances between codes of this type.

What I have just said is extremely schematized and simplified. The operations we allow of changing letters and erasures are very specialized; in reality, we might make definitions more general. The changes of substitutions of letters should perhaps not be weighed equally. Some mutations are easier for certain symbols than for others. Also the mutations may involve a whole small block of letters together, not just a single one, and the cost of erasure of a block need not be equal to the number of letters erased, but could perhaps be smaller in some cases. Suppose we erase five letters, it should not cost five units, it could cost less, depending on which letters and which combinations they are. Let me also add that one can talk about additions, not only erasures of symbols, or intercalations in the middle. Mathematically, it would not make much difference. For the sake of simplicity it is easier and sufficient to talk about diminutions or erasures of symbols. To find the exact cost of erasure of a block would depend on the nature of the symbols, the biological facts, and chemical or physical properties. This has yet to be studied experimentally.

The trees of evolution that Margoliash and Fitch constructed seemed to satisfy zoologists. The zoologists have their own way to guess or estimate the possible succession of evolutionary changes among species. Recently, attempts have been made to use other proteins, not just cytochrome *C*, to try to define distances between corresponding sequences and use those proteins to construct a tentative or conjectural tree of evolution. There is some literature on those problems and I myself and collaborators have written some mathematical papers on such problems.

So here is just one illustration of a problem arising from the world of natural sciences that suggests mathematical schemata slightly different from some that have been considered in pure mathematics or in mathematical physics.

So far we have discussed briefly a space of codes, one-dimensional sequences of symbols. More general and more difficult analogous problems are suggested by similar considerations concerning objects in two or three dimensions, the real physical objects. A protein that is manufactured by the parts of the cell receiving the code is not a straight linear sequence but a three-dimensional object looking like a very contorted pipe. For several of these proteins, it has been possible to map the three-dimensional positions of the atoms forming them. This was much harder to obtain than the linear sequence of the DNA defining it.

Techniques of crystallography and X-ray diffraction have enabled the biologists to discover in some cases the position of the atoms forming the complicated large molecules corresponding to certain proteins. Some hemoglobins and myoglobins, for instance, were learned in this manner. Mathematically, the technique depends on the inversion of Fourier transforms, a very laborious analysis where computers are absolutely necessary to enable one to discover what the distribution of atoms is in some of these large assemblies. As I said before, the linear code is known for many hundreds or thousands of proteins. New techniques of cutting up the linear sequence are permitting an examination of the complicated sequence of symbols by various difficult chemical techniques. It is more difficult to study the three-dimensional structures, but a number of them are known now. A few years ago when I looked at an atlas of proteins there were less than 100 such spatial shapes.

Now one might try to discuss the possibility of defining the degree of similarity or dissimilarity or analogy between *spatial* objects of this sort. How does one measure quantitatively, or at least somewhat quantitatively, the degree of similarity between the shapes of organisms? In general, these are three-dimensional objects, and in mathematics, in pure mathematics, people have discussed for some time the ways to define distance between two sets. Suppose these sets are in the Euclidean plane or Euclidean three-dimensional space.

The mathematician Hausdorff defined a measure of distance; he made a metric space out of sets, say closed sets in a given metric space. I shall now briefly describe the Hausdorff distance between such sets A and B. We take a point on A, call it x and look for the closest y in B. We take the distance between these two points x and y. Distance is defined in the general metric space in which these sets are located. Then this y is the closest to x. We take the minimum for all y with respect to x. Then one considers the value of this minimum with respect to the original choice of the point x and we take the maximum of that. If the sets are closed and bounded this maximum exists. So the maximum of this minimum we define as distance. I should add that in order to make the distance symmetric we turn the expressions around, we start at a point belonging to B, look for the closest in A and take the maximum with respect to the initial point in B. The sum of these two we consider as the distance between the two sets A and B. It satisfies the common sense requirements for a distance between sets. All this assumes, however, that the two sets are fixed, rigid, positioned in a given metric space. Again, when it comes to objects that are organisms, i.e., sets that are not really fixed in space but are pliable, soft, malleable, deformable, and can possibly be twisted, this procedure is not the right one.

One should actually look not at a fixed set A, but at all the sets like A, be they translated, rotated, subjected to small deformation, and so forth. That is to say, we have a class $\mathcal{A}$ of sets that are "like" A. Then having another set B, we again do the same and have a class $\mathcal{B}$ of sets like B. What we want to define is a distance between two of these classes. In order to make it a bit extreme for illustrative purposes, suppose that A is a dog, B is a cat. I then consider something that I would like to define as the distance between a cat and a dog as species. It amounts to taking all possible sets like A, all possible sets like B, and attempting to define the distance between these two classes. This will be the Hausdorff distance. It turns out that this iteration of the Hausdorff distance leads to a rather reasonable idea, it seems to me, of distance and a metric space between closed classes of closed sets of a given type. I shall not go into details of how the classes are precisely defined but merely say that mathematically it amounts to allowing certain operations that deform or transform the given sets A and B. They are not groups of transformations, that would be too much, rather they are kernels or neighborhoods of unity of certain groups of transformations or distortions, and now we can define the distance as follows

$$\rho(\mathcal{A},\mathcal{B}) = \max_{B\in\mathcal{B}} \min_{A\in\mathcal{A}} \rho_H(A,B) + \max_{A\in\mathcal{A}} \min_{B\in\mathcal{B}} \rho_H(A,B) ,$$

where ρ_H denotes the Hausdorff distance in the space E where the sets are located, and

$$\rho_H(A,B) = \max_{y\in B} \min_{x\in A} \rho_E(x,y) + \max_{x\in A} \min_{y\in B} \rho_E(x,y) .$$

This gives another example of a mathematical technique, a mathematical point of view and a new type of construction suggested by a "real" problem of natural sciences other than physics or astronomy.

A similar technique or similar problem is found in an entirely different connection. The problem of recognition, let us say recognition by a machine, by a computer, of signs or objects on a screen or in three-dimensional space. It is of interest when we study the vast area of questions about the working of the nervous system and of the brain itself. I can only talk here about generalities. From the beginning of the construction of electronic computers one has talked about its memory, about the various programs that enabled one to execute a number of mathematical operations. By now we have a vast literature dealing with the similarities between some rudimentary properties of the nervous system and our thinking and the functioning of computers.

As everyone knows, a computer is vastly faster for all the operations that it is able to perform than the nervous system or the human brain. But it is very limited in what it can do compared to the human brain, or even to the brain of certain primitive animals, in the following way: computers that now exist work essentially in series, linearly, one step at a time. There seems to be no question that our brain, or even the brain of much simpler organisms, works differently in that the process operates in parallel, essentially simultaneously, independently on thousands or even millions of different channels. The retina of the eye has several million rods and cones connected to nerves. Behind the retina, there exist four or five layers where there is a rewiring. This scheme is not yet really understood in detail or perhaps even in a general combinatorial sense. This rewiring finally leads impulses to the brain, which contains, in the human case, an assembly of some ten billion or more elements, the neurons, and, perhaps even more impressive, hundreds of thousand times more connections between them. I remember discussing this with von Neumann years ago, and he said "It is fantastic, from each neuron there are maybe a hundred connections to other neurons and in the central part of the brain there must be several hundreds leading to other elements." By now these hundreds are known to be many thousands, and in the central part, apparently from a single element on the axon, there are perhaps a hundred thousand wires leading to other elements.

The problem of recognition, visual recognition of a pattern, is therefore to be studied in a vastly more general way than that of a linear mechanism for processing individual single impressions step by step. I should like to add that the problem of recognition does already exist on a different level. All the problems involving immunology, recognition of antigens by antibodies, involve some chemical schemata for finding spatial patterns or shapes by a method not understood to this day, but which undoubtedly involves a parallel gathering of information and a suitable code for action.

Such problems form a very fertile field for the intervention of mathematics on a general, abstract, conceptual scale. From the beginning of the construction of electronic computers there was talk of learning machines and speculation on how to imitate the workings of the brain on a very modest scale.

In this set of problems, again, it seems to me that it makes sense to talk about the problem of distances. Suppose we have a visual set of points on a screen of our visual field. I want to discuss how one such impression of a visual picture can be compared to other pictures, and how this comparison could involve again the idea of a distance between such sets of points. These sets are not rigidly, stiffly precise, but speaking mathematically, are modulo a number of transformations. It is obvious that the picture that I recognize need not have a fixed size — it can be large or small provided it is similar. If I am at a distance or close, the same object will appear in a different way as a set of points on the retina. We recognize it, however, as the same one. In addition, translation of a picture does not alter its recognition either. Small changes in shape also are neglected in the recognition of the class of the object.

For a simple example, consider the problem of recognizing a handwritten letter, *A* for example, from a handwritten letter *B*, independently of whether it is large or small, slightly shifted, turned or written by persons whose handwriting differ markedly. In order to give a mathematical setting to this problem of recognition, I would like to introduce again an idea of distance between classes of sets corresponding to the letter *A* and the letter

B, or for that matter any other letter. We tried this in Los Alamos on a computer, and it turns out that some types of distances, one of which is the Hausdorff distance discussed above, were very useful for setting up a program that enabled the computer to decide, with a probability that turned out to be very good, the distance between the two alternatives.

Let me give a brief account of this story. The work was done years ago in Los Alamos with Robert Schrandt, (in the mid-seventies, I believe.) We obtained a number of handwritten letters *A*, which were put in the memory of the machine. Actually, instead of writing the letter 128 or 256 times (we wanted to have that many examples in the memory), we did one or two by hand, and then performed small deformations by computer by iterating two given transformations in turn seven or eight times. These iterated transformations deformed in various ways the picture representing the letter *A*. We did the same with the letter *B* and had it also in the memory of the machine. Then the problem was given to the machine. Somebody wrote a new letter and the machine was to decide whether it was an *A* or a *B*. In order to render the machine able to do this we introduced a distance between pictures. This distance was different from the Hausdorff distance, but I will not attempt to describe it here. There are different types of distances, different types of metrics that one can introduce in the space of pictures which are suitable, and probably all independently used for recognition by the nervous system. I should not say that these distances, which we considered, are actually used by the brain, but distances somewhat like these I think may be involved in our recognition patterns, perhaps also in recognition by animals.

Now, given a new letter, the distances were computed by the machine between this new letter and all the examples of *A* on one hand and then all the distances between it and the letter *B* on the other. Whichever came out smaller in the average of these distances made the machine decide in favor of it. The program was quite successful. There was 80 or 90 percent success in recognition. This was just a first crude attempt to discuss recognition by a mathematical program, and no doubt more sophisticated and suitable distances are used by living organisms.

The above is only the simplest problem — it is recognition of a picture and not of an object. Assuming we should be able to do that for a large class of objects, the next stage is more sophisticated. We have not a single object and its variations, but rather a class of pictures. For example, we have a tree. It need not be a specific tree, like an oak, but rather the class of trees. On the other hand, we have examples of animals. The question is how to distinguish between these classes of objects? Classes for which elements are sets are not necessarily variations of each other. This is the next step in sophistication. Such a class can be called a concept. One can again iterate this procedure and imagine classes of classes, or collections of classes. Probably in the future one will be able to devise methods for such increasing abstractions, and perhaps people who now work in computer technology and theory will be able to devise ways to recognize and discern more than the mere arithmetical or Boolean operations computers are so good at now. We shall be able to define analogues, at first still modest for years to come, of some of our thinking processes and ideas obtained by abstractions, as a better way to study impressions. It seems to me that the idea of distance between sets, classes of sets, and so on, will play a role in this program. There are many mathematical problems relevant to this idea.

The thinking process involves the examination of analogies obtained from external impressions, visual and auditory, and from the other senses. I am reminded of Norbert Wiener's and von Neumann's debate of years ago. Von Neumann saw the analogies with computing machines and Wiener was for hormonal, continuous fluid type relations as the mainstay of our thinking process. No doubt future development of computers will involve all kinds of distances between sets of impressions and later an analysis of functionals of what the external world produces as our stimuli will form more abstractly what we call concepts or ideas.

To finish this point, I would like to stress again that mathematics not only applies itself, as it is and as it develops, to other sciences, but perhaps has a direct biological role for the human race. Mathematics, and perhaps other sciences like physics, have the mission to prepare or improve the human brain, be it the brain of an individual or the collective brain of mankind, for developments yet to come. Just as animals play when they are young in preparation for situations arising later in their lives, it may be that mathematics to a large extent is a collection of games. In this light, it has the same role and may be the only way to change the individual or collective human mind to prepare it for a future that nobody can now imagine.

As biologists now discuss it, life appears *inter alia* as a sequence of chemical games. Games played between individuals, or between groups of individuals are something that is essentially of a mathematical nature. I do not mean the von Neumann-Morgenstern theory of games, but more general games in the widest sense. This has perhaps, I will repeat it again, a direct biological role.

There appeared recently a book written by the German biologist, Manfred Eigen, entitled *Das Spiel* (The Game). It describes a number of mathematical games or puzzles and discusses the games molecules and groups of molecules play with each other.

Other interesting mathematical puzzles have appeared in the last twenty years — Conway's Game of Life, for example. In this connection we have already seen that starting with a simple pattern and simple recursive rules can lead to unbelievably complicated configurations. The configurations, though defined by a rule that a grade school child can understand, defy analysis *a priori*. There are many mathematical problems beyond just amusement or diversion that involve new combinatorial patterns and constructions. One can imagine a little branch of mathematics (and call it, perhaps, "Auxology") concerned with the geometric properties of recursively growing figures.