THE MOLECULAR LANGUAGES

by

Walter Gordy
Department of Physics, Duke University
Durham, North Carolina

It is a distinct honor for me to speak to such a bright group of young high school seniors as I understand you are. I hope that I can close the generation gap enough to communicate with you. In this effort I have great help from my son, who has just become eighteen. He has taught me much about this generation which may help me to understand you.

My confidence in my subject was shattered just a bit, though, by Professor Levy when he declared, "What is everybody's language is nobody's language." I am going to talk about a language that is not simply international but is universal, one which is common not only to man but to all the lower animals. One of the most compelling and exciting motives for space travel and explorations is to learn whether this same language is used by life forms on other planets - if we find any life on other planets. Whether this is nobody's language or not, I must inform Professor Levy that there is little doubt but that more information is stored in this universal language than in all the libraries of all the world, in all the diverse languages of the world. Therefore we need to try to understand this language, to learn how to read it.

More than two thousand years ago the Greek philosopher Socrates challenged man to know himself. Socrates presumably thought that man could control himself a little better, perhaps could improve himself a bit, if he could know himself. If we are ever to understand ourselves, our fellow animals, and other living systems on this earth, we must be able to read and understand the universal language in which the information content for all life processes is stored.

The information content is of three types. One type is genetic information, that which is passed from parents to children at conception and which serves for construction of living systems and for much of their functions and behavior. Another type is immunological information, that which our cells learn in order to fight disease. I suppose we could call the latter a military type of information which a CIA force of molecules obtains about viruses or germs invading the cells; it allows the cells to fight the invaders more effectively the next time they appear. If our cells did not have the power to acquire and store such information about potential enemies, we probably would never live to complete high school. Genetic information and immunological information are both essential to us; but the third type of information, that which we acquire through observation and study and store in the brain, is probably of more concern to you who have just completed the storage of your high school education and are immediately faced with the task of storing away four years of college learning. Learned information seems more important to us because we must work so hard to get it. Nevertheless, this information may well be the least significant of the three kinds. It is certainly not comparable in importance to the genetic information which we received free from our parents when we were conceived and which they had received from theirs. If you should be bitten by a rabid dog, you would probably regard the immunological information which could be injected into you with a needle as of paramount importance.

Let us consider the question of where we store the kind of information we get from teachers, from studies and observations. We have long known that in the higher species of animals learned information is stored in the head. If anyone still believed that we learn "by heart," his belief must have been shattered by the heart transplants which left memory unchanged. But where in the head is such information stored? If it is stored in the biological cells of the brain, in what part of the cells is it stored? You see a word on the blackboard that your teacher has written, and you learn to spell it. Suppose, for example, that it is the "deoxyribonucleic-acid." This is actually three words put together, a long organic chemical word, which is conventionally abbreviated to DNA. Suppose you examine this long word until you learn to spell it. The next week you teacher asks you to reproduce it, to write it on the board yourself. If you are as smart as you are supposed to be, you can do this trick easily, and I shall assume that you write the word correctly. Where has the word been stored for the week? In what form? Did you translate it into another language when you stored it and then re-translate it when your teacher asked you for a reproduction in the original form? You know where it was stored on the blackboard and that it was written in chalk. You know where it is stored in the library, on the pages of books, in printer's ink. You could write it in stone, as the Ten Commandments are supposed to have first been written. You might translate it into hundreds of different languages. You might write it in all these forms without changing the meaning of the word. The essence of the word is its information content, its meaning, not its particular form in a specific language. How did you store the information about this word for a week in your head? If you can answer this question, you should be able to explain how your entire high school education is stored.

Many people regard man's genetic information as essentially that which determines his physical make-up, not including any like the knowledge which man gains for himself after birth. Most people will agree, in varying degrees, that a man's ability to learn is largely inherited or, more correctly, is grown in him in accordance with inherited instructions. However, from comparisons with many lower life forms that operate rather impressively throughout their lives almost wholly by instinctive (genetic) information, it seems probable that much of what we think we learn and what we take credit for learning for ourselves is actually inherited information. Man simply supplements his inherited information by learning; some men supplement much more than others do; indeed, some men have much more ability to do so than others have. The distinction of man over the lower animals, the birds and the insects is his greater ability to supplement his inherited information. In recent centuries he has added to this advantage by developing auxiliary information storage places such as libraries entirely outside himself. Many of the lower species do not live long enough to acquire much education even if they had high learning power. Therefore they must come equipped with most of the information they require for their operations. A spider builds a web which must amaze and confound a structural engineer. A bee builds a honeycomb which is a marvelous chemical and architectural achievement by human standards. These insects do not have to go to school to learn their feats - they don't even have to watch their parents. I read about a biologist who put a just-hatched spider into a small container where he could not build a web nor see other spiders do so. There the spider remained until he was grown. He was then allowed to crawl out into the wide world where there was room to spin a web. The first web he made was a perfect reproduction of the pattern his ancestors had used before him. Although a man cannot alter the inherited information of a spider by teaching or propaganda, he apparently can do so with certain chemicals. Colonel Burton told me of reading about an experiment in which a spider was fed LSD. The webs the spider made thereafter were misshapen, structurally unsound, and unlike those of his ancestors. Thus in a given individual it is possible with certain drugs to destroy information inherited from the ancestral establishment. Unfortunately, it is not likewise possible by use of drugs to create information of value comparable to that collected over millions of years by the evolutionary process.

Men speak often about the mystery of life or the secret of life. Life has always been very mysterious to man, just as the sun was mysterious to man. There are two common human attitudes toward anything mysterious.

One is to fear it; the other is to worship it. These two attitudes are connected closely: if you fear something, you reason that it, assuming that it has understanding, will appreciate your bowing down and will reward you by being kind to you. And so you do this as an act of appeasement, a safety precaution. To fear and to worship the unknown are thus natural and complementary processes. Man once worshipped the sun, but he doesn't bother to worship it any more because he understands how it shines.

I shall describe briefly the passing of the mystery of the sun to give you a better understanding of what is happening to the mystery of life. The mystery of the sun largely disappeared before you were born, but in this century. Up until 1905 no one had any understanding of how so much energy could pour out continuously from this one source, without seemingly being diminished. There was no basis whatever for understanding it until Einstein developed his special relativity theory, which predicted the equivalence of mass and energy and, what is more, predicted the very, very, very great amount of energy that is contained in a very small mass. This equivalence is expressed in his now famous equation, $E = mc^2$. Even before Einstein predicted the colossal amount of energy contained in matter, Madame Curie, Becquerel, and others discovered that certain atoms in disintegration were throwing out enormous amounts of energy in so-called radioactivity. These discoveries brought the key to the mystery of solar energy within sight, but it took some fifty years for man to work out the particular nuclear reactions responsible for the conversion of mass energy to radiant energy within the sun. Only three years ago Bethe, at Cornell, received the Nobel Prize for finally wrapping up this problem, for deriving the particular mechanism of the nuclear fire that burns in the sun. After it became apparent that there was so much energy in the nucleus of the atom, that this energy could be released, and that it was entirely adequate to power the sun for hundreds of millions of years without being noticeably diminished, people no longer had cause to fear the whims of sun gods.

How can the enormous amount of information required for man to move about and survive in the complex world be stored in the small space of the head? How can the vast architectural information required for the construction of man, or even the simplest animal or plant for that matter, be stored in the small space of the biological cells united at conception? The sperm which comprises all the information which you received from your father has dimensions of the order of eighty-thousandths of an inch, much too small to be seen with the unaided eye. Although the egg of the human female is about one two-hundredth of an inch, barely visible to the unaided eye, most of this egg is food for the growth of the new life. The nucleus of the egg, which contains the information passed on from the mother is as small as the sperm with which it combines. How can the very great amount of instinctive information evidenced by some species be transmitted from generation to generation through these small cells? These are some of the most puzzling aspects of the mystery of life.

The first break in the wall which encloses the mystery of life came about the time of the ending of World War II when scientists recognized that the genetic information adequate for the construction and operation of all known living things could be coded in atomic groups of molecules known to be constituents of all life forms. This recognition was aided by a number of clever experiments as well as by the theoretical calculations of the amount of information that could be thus stored. In 1944 three scientists - Avery, McLeod, and McCarthy, working at the Rockefeller Institute - found that the chemical deoxyribonucleic acid (DNA for short) extracted from a particular strain (S bacteria) of a pneumonia-causing bacteria could transform a different strain (R bacteria) to the S bacteria. Earlier, in the thirties, scientists had found that dead bacteria of the S strain when added to a brine containing living R bacteria converted the R bacteria to living S bacteria. The three scientists working at the Rockefeller Institute found that a particular molecular compound DNA was responsible for this amazing resurrection. This chemical which was first discovered in the nucleus of pus cells a hundred years ago (1869) by a German chemist is now known to be a vital component of all biological cells.

The second break came in 1954 with the discovery by Watson and Crick of a specific molecular model which provided a mechanism for replication of this vast information of life and for its transmission from parents to children, from generation to generation. We might say that Watson and Crick really closed the generation gap! At the same time their model revealed beyond reasonable doubt that the vast library of life is inscribed in molecules, molecules of a specific kind called DNA. Since that time scientists have been excited and busy, trying to learn to read the molecular language of this library. Much progress has been made in this endeavor. In 1968 Nirenberg, of the National Institutes of Health, was granted a Nobel Prize for his progress in cracking the genetic code. Nevertheless, we are still in the primer stage of this new language course, still learning our DNA's. Learning to read the molecular language of life is perhaps the most exciting adventure ever undertaken by man, and most of this adventure is still ahead. It will engage the efforts of some of the ablest members of your generation.

The alphabet of the DNA language consists of only four letters. These letters are the organic chemical groups cytosine, thymine, adenine, and guanine - abbreviated as C, T, A, and G. They are attached to a long strand - long as compared with the size of the letters - which is made up of repeating links of phosphate-deoxysugar groups. The phosphate-sugar strand is the "blackboard" on which the DNA language is "written" by various sequential arrangements of the four organic chemical groups. The order of the arrangements of the chemical groups determines the information content of DNA just as do the arrangements of the letters of the alphabet determine the meaning of words and sentences in our English language.

In the nucleus of the cell two such strands are found to be coiled together. According to the Watson-Crick model the arrangement of the letters and hence the information contained in each strand is not entirely independent of the mate strand. In the coiling of the helix the A must be matched with the T, and the C must be matched with the G. The coiled strands thus constitute a complementary pair. This complementary character of the strands is of great importance for the replication and the preservation of genetic information through succeeding generations.

The information content in DNA can be readily transferred by chemical processes within the cell to the molecule RNA (ribonucleic acid). Although closely similar to DNA, ribonucleic acid does not form the dual helix of the Watson-Crick model. Except for the change of cytosine to the very similar uracil group, the information groups of RNA (its alphabet) are identical to those of DNA. Thus the RNA language is more correctly regarded as a dialect of DNA rather than as a separate language. For the cell, translation from one to the other is simple chemistry. There is, however, still another language of nature, the protein language, which has an alphabet entirely different from that of DNA. In the protein language the alphabet consists of some twenty different "letters," comparable in number to the letters in the alphabet of our English language. These "letters" are the different types of organic chemical groups, the various amino acid groups, which are attached to the polypeptide chain of the long protein molecules. Although the protein language with its different alphabet must be considered an entirely different language from that of DNA, the biological cells seem to have no difficulty in translating information from DNA language to protein language. The translator is RNA. Through it, genetic information contained in DNA can flow to the proteins.

Many experiments on worms, rats, fish, birds, and monkeys - about which I have not time to tell you - suggest that learned information retained in the memory is stored in the proteins or in RNA molecules. Perhaps for really long-range memory the learned information is transferred from protein to RNA and eventually to the more stable DNA molecules. Whether memory storage takes place in one or in all three of these molecular species is yet to be proved, but it would be surprising indeed if nature uses entirely different mechanisms for storage of the three kinds of information - genetic, learned, and immunological.

The organic chemical groups which comprise the letters of the molecular languages have dimensions of the order of one ten-millionth of an inch. If the total information stored in the library of the West Point Academy were translated into a molecular language, it could be contained in a library so small that it could scarcely be seen with the unaided eye. Thus much of the mystery of life is in the small size of the atomic groups that make up molecules, just as much of the mystery of solar energy was found to be wrapped in the still smaller nucleus of the atom.

However, there are other big questions about this almost sacred mystery. How has this genetic information been accumulated? According to modern evolutionary theory, it has come through billions of selections from mutated forms over millions of years, selections which must survive the test of environment. A faulty bit of genetic information is eliminated in much the same manner as an incorrect postulate is eliminated in the test of experiment in the laboratory. The instinctive information thus accumulated by a species on the basis of survival value may be similar in another important way to that which is learned by a given member of a species and retained as long-range memory. The two kinds of information may be stored in the same manner in the cells so that it may be very difficult to be aware of their difference. Furthermore, it is difficult to distinguish between inherited and acquired information on the basis of their consequences. Man is probably the most complex and unpredictable of all animals because he is controlled by a mixture of inherited and acquired information, with large but uncertain proportions of each. In fact, the proportions may vary over a wide range depending on the situation or stimulation which motivates him to action. The behavior of the lower animals, determined mainly by one form of information (genetic), although perhaps not so clever and interesting, is more dependable and predictable.

As a result of man's increasing knowledge of nature his fears of things animate and inanimate have been greatly reduced. In early times men were afraid of the trees, the wind, the sun. They tried to appease the sun god; they tried to appease the weather gods, the thunder god. Fears of such gods and the forces they purportedly controlled no longer haunt mankind. With man's increasing knowledge of science, his dominance over the earth has become increasingly secure. He no longer fears the lions or the tigers or any of the lower animals. His fears of many microbes and viruses have been greatly reduced by vacines and antibodies. However, as his dominance over the earth increases, as his power through knowledge accumulates, as his fears of other species fade away, man is becoming increasingly afraid of himself and of his own kind. His greatest need now seems to be to improve the nature and quality of man and to curb the overly rapid increase of the human species on the limited earth. Can the new knowledge of the information molecules be used to achieve these goals? The answer seems to be yes. Will it be used for these purposes? Regretably, at this time the answer seems to be no.

As an example of what is being done with the genetic information encoded in the universal language of nature, let me tell you about the work of a geneticist friend of mine, Professor H. S. Perry, who has spent many years of his life in developing a hybrid corn with improved flavor and texture. For many summers he has provided me with delicious corn, better than any I have eaten before. He uses me and my family along with many other friends in Durham as corn tasters. Each corn-taster has two numbered ears of corn at a time which he rates for flavor and texture on a form provided for the purpose. Each summer for the past several years the corn has been getting better and better. Now it is really delicious.

One Sunday morning when I was on my way home from my laboratory and feeling a little guilty about not being in church, I passed the botony department. There was Professor Perry watering his corn in the greenhouse. I could not resist the temptation to stop and chat with him. As I looked at all the different kinds of corn he was growing I asked him, "Dr. Perry, why can't we use the kind of information you are applying to corn to grow a sweeter person - one with a finer texture?" He is a very solemn type of quiet-speaking man; he thought for a while before replying, "Well, we probably could, but it would be easier to start with monkeys because we would be freer to experiment with them." It is apparently the sad plight of man that he can use genetic knowledge to improve the corn, to improve the pigs, to improve the beef cattle, the milk cows, the race horses, - but he cannot use the similar knowledge to improve his own kind.

The youthfulness of the men who have contributed to the discovery of these secrets provides some justification, perhaps, for the claim some college students are making that people over thirty can't understand life! Friedrick Miescher was only twenty-five years old when he discovered DNA in the nucleus of the cell a hundred years ago. Watson, who is still a young professor at Harvard, was only twenty-five when he and Crick worked out the double helix of DNA which is essentially the key to life. Einstein was twenty-five when he developed the theory of special relativity, which is necessary for comprehension of solar energy - of atomic power. Mosely, who discovered the secret of the atomic table through his X-ray studies, did this when he was about twenty-three; he was killed in World War I, when he was twenty-five. Mosely really laid the foundation for understanding of the atomic table.

However, those who achieve greatness in youth, or at any other age, are exceptional. Just being young is not being great. I could tell you of many, many other young people, twenty-five or under, who had wrecked their own lives by the time they were twenty-five. I remember a very bright young member of my high school class who ended his life at the age of twenty-one by driving off a bridge while drunk. Some young people become dope addicts by the time they are seventeen; some become criminals before they are seventeen. Many waste their youth simply frittering away their time, achieving nothing. Don't get cocky and think that mere youth is a ticket to success. Those young people who made discoveries are exceptions, and those who make such notable achievements will continue to be exceptions.

Some six years ago, a distinguished and famous Russian chemist, V. V. Voivodskii, member of the Russian Academy of Sciences and professor in the University of Moscow, was attending a Gordon Research Conference in New Hampshire which I was also attending. While there, he received a message from home, one sent by his wife, who is herself a professor of biochemistry. This message told him that their daughter had been declared valedictorian of all the city schools of Moscow. I congratulated him, "This is wonderful. Your daughter will follow in the footsteps of her parents. She will achieve great things." "Not necessarily," he replied, "this means that she has a fifty-per-cent- chance of achieving great things." He explained, "We have found in Russia that only half of the valedictorians reach excellence; the others decline after graduation."

Therefore, I should say that I am honored to speak to half of you today! I hope that in our country our valedictorians achieve that fifty-per-cent average. It is, actually, a high average. Many brilliant young people do not do well. To achieve greatness, one must have other exceptional qualities besides a high intellect, and one must have a measure of that which we call good luck.