THE PHYSICS AND CHEMISTRY OF LIFE

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a SCIENTIFIC AMERICAN book

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INTRODUCTION

This book is concerned with life as a physical process. The questions raised here are the kind that can be answered wholly within the disciplines that explain the behavior of nonliving atoms and molecules. The first chapter advances an explanation of how life was originally ignited in the elements of the earth. The last chapter describes the beginning of our understanding of the electrical basis of thought. The speculations of these two authors are sustained by the work in a dozen different fields of investigation reported by the other contributors to the book. There are gaps and unknowns in the picture. But it is a connected one, and it is increasingly worthy of the attention of priests, philosophers and poets.

It is to these and other nonscientists that this book is primarily addressed. Its contents are the product of a unique collaboration between its scientist-authors and the editors of the magazine SCIENTIFIC AMERICAN, *in which the eighteen chapters were first published as articles during the past several years. Assembled in book form, each article gains in relevance from the others. Together, they present a synthesis of the state of knowledge of life that is not to be found between the covers of any other book.*

The "Origin of Life," by George Wald, is itself a synthesis of a good deal of the material in the succeeding chapters. To reconstruct the beginning of life, a scientist must marshal what we know about the processes of life as they go on today: how complex living material is built up from the simple molecules of nonliving matter; how it is endowed with the properties we associate with life; how living things reproduce themselves and transmit their *characteristics to their offspring. The fact that Wald is able to account for the main issues involved in the primordial experiment is a measure of the recent vigorous progress of the life sciences.*

However it began, life continues to originate on earth. Living things are constantly bringing into the processes of life the inert substances of their environment. In the great closed circle of the interdependence of life, all creatures ultimately depend upon plants. Through photosynthesis, mediated by sunlight, plants compound air and water into the elementary organic molecules of carbohydrates. The energy of sunlight, thus stored in the chemical bond, is the energy that is expended in living by the entire kingdom of life. For structural material plants and, in turn, animals depend upon hosts of obscure bacteria which have the capacity to incorporate atmospheric nitrogen into organic compounds and thus lay the foundation for the synthesis of proteins—the principal stuff of life.

The protein molecule, Joseph Fruton says, "is the noblest piece of architecture produced by nature." It is chiefly architecture—the infinitely various and intricate ways in which their component atoms are assembled—that gives proteins their richness and diversity in form and function. Linus Pauling and his colleagues describe the work that has now elucidated the main plan. It yields direct insight into the characteristics and behavior of the molecules as we encounter them in bone and muscle, in the bloodstream and in the nucleus of the cell. The next article describes one of the major recent triumphs of biochemistry, principally the work of Frederick Sanger of Cambridge University. This is the first complete description of a protein—the molecule of insulin—with the location of its every sub-unit and atom established.

The function of protein which perhaps has been most illuminated by this new understanding of protein structure is the central process of life: reproduction and the transmission of hereditary characteristics. Alfred Mirsky tells of the subtle work that has identified the molecule of heredity. He and other investigators have succeeded in subjecting chromosomes to chemical analysis, both in the intact cell and delicately separated from the cell. They have determined that the prime carrier of heredity is a constituent of the nucleoprotein of which the chromosome is composed. This constituent is desoxyribonucleic acid, referred to as DNA. The recent unraveling of the structure of DNA, which resembles the general plan of the protein, is described by F. H. C. Crick. From its structure, Crick shows us, we can begin to see how DNA .. endowed with the capacity to reproduce itself. We can thereby begin to account for the same capacity, in much more elaborate and complex form, in the cell. The structure of DNA also provides our first clue to the manner in which it encodes the information that determines whether the dividing cell will eventually yield a billion identical amoebas or a man.

The rich endowment of these fundamental materials of life is well demonstrated by the virus. Outside a living cell, the virus is simply an elaborate molecule of nucleoprotein. Inside a cell, as Gunther Stent shows, the virus merges itself in the chemistry and substance of its host and generates therefrom a multitude of replicas of itself. Whether viruses should be regarded as living or nonliving is a moot question. It is more interesting to ask whether they are precursors of cells or the end point of a degenerate evolution. In either case they are parasites, obliged to obtain ready-made from the cell the substances that go into their construction. For the investigator, now that virus diseases are coming under medical control, they are of interest principally as providing nucleoprotein in its handiest form.

A higher order of parasite, able to manage a somewhat broader range of life processes, is the tiny organism known as the rickettsia. It is a little bigger and more complex than a virus, but less complex than a cell. Rickettsiae are able to metabolize some substances and thus to generate a portion of their own life energy. Aside from their *interest as the agents of such diseases as typhus and Rocky Mountain spotted fever, they fascinate investigators as subjects for research into life processes.*

The comparative self-sufficiency of a rickettsia is explained by the fact that it is able to synthesize the enzymes necessary to its limited metabolism. Enzymes are the important topic of the next section of the book. These are substances, principally proteins, which act as catalysts in living systems; they speed up the otherwise slow reactions of organic molecules to the pace of life. Since each enzyme mediates but a single step in a reaction, hundreds of different ones are required to conduct any reasonably high order of existence. For example, in the metabolism of sugar, from which animals derive a major portion of their energy, no fewer than a dozen enzymes are involved. As the comparison between rickettsiae and man might suggest, the capacity to synthesize enzymes is among the characteristics transmitted by heredity. George Beadle has investigated this process in the bread mold, Neurospora. *He finds that the presence or absence of a single gene will account for the presence or absence of a particular enzyme. This work strongly supports the hypothesis that the nucleoprotein material of the gene synthesizes the enzyme by some sort of replication, not unlike self-replication.*

The theater for all this immense variety of biochemical activity is the microscopic living cell. Since even a virus or rickettsia depends upon the cell for reproduction, the cell may be fairly described as the irreducible unit of life. Daniel Mazia describes the still far-from-comprehended process of mitosis by which a single-celled organism divides to reproduce its kind. He and other workers have recently succeeded in isolating the mitotic apparatus and have begun the long analysis of its substance and structure. The next frontier is the question of how a single cell elaborates and differentiates into the distinct and various tissues of the multi-celled organism. C. H. Waddington reports that, while this process is held under exquisite control by organizer substances produced by *the evolving organism, it is also subject to manipulation and derangement by a wide variety of common chemicals.*

In the higher organisms, we come now to two vital processes which are better, if still not completely, understood. A. Szent-Györgyi tells how the elastic protein of muscle fiber converts the chemical energy yielded by sugar metabolism into the mechanical energy of action. It works like a spring in reverse: the muscle does its work when it relaxes; its contraction is the discharge of the energy it has stored. Bernhard Katz explains the ingenious electrochemistry of the nerve fiber, which provides the body with its communication system. Like a transcontinental telephone cable, it employs repeater stations, each firing the next, to conduct its messages.

The electrical activity of the brain is still an undeciphered code which scientists have just begun to read. But W. Grey Walter has been able to relate the patterns drawn by electroencephalographs and cathode-ray tubes not only to pathology but to learning, personality and emotions.

THE EDITORS *

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The structure of proteins goes far toward explaining how these substances reproduce themselves and transmit hereditary characteristics in the cell. Viruses and rickettsiae, being scarcely more than naked nucleoproteins, provide powerful tools for investigation of this process.

4. ENZYMES AND ENERGY

One of the main functions of heredity is to equip individuals with their complement of enzymes. These are proteins that catalyze, or accelerate, the chemistry of life. The breakdown of sugar and fats by enzymes completes the energy cycle of life, converting the energy of sunlight, stored in the chemical bond, into the heat, growth and motion of living things.

5. CELL AND ORGANISM

Because a single cell can grow only to a limited size, cell division is the key process of growth. The complex apparatus that conducts this process has now been isolated from the cell. In the growth of higher organisms, the dividing cells must also differentiate into a variety of specialized tissues. Differentiation is controlled by chemicals, called organizers, still unknown.

6. MUSCLE, NERVE AND BRAIN

Muscle is a protein that converts chemical energy into mechanical energy. The basis of the activity of the nerve fiber which provides the communication system of the body is found in electrochemistry. And the activity of the brain can be read in the variation of electrical voltages.

PART 1 THE ORIGIN OF LIFE

I. THE ORIGIN OF LIFE *by George Wald*

One of the world's leading authorities on the chemistry of vision, George Wald is professor of biology at Harvard University. After considering careers successively in engineering, law and medicine, he found what he wanted in science—"a way of life that would always run far ahead of my capacities." It was as a graduate student at Columbia University under Selig Hecht, "a superb scientist and a great personality," that Wald developed his interest in vision, a field of research he has pursued with tenacity and increasingly rewarding discovery for some twenty years. He went to Germany on a National Research Council Fellowship, discovered Vitamin A in the retina while working in Otto Warburg's laboratory in Berlin and obtained a first view of the function of the rhodopsin cycle in rod vision in Otto Meyerhof's laboratory at Heidelberg. He received the Eli Lilly prize of the American Chemical Society in 1939 for his fundamental work in biochemistry.

II. PHOTOSYNTHESIS *by Eugene I. Rabinowitch*

The community of science identifies the name of Rabinowitch with two major enterprises. The first is the subject of this chapter, on which Eugene Rabinowitch wrote the definitive treatise under the same title. Born in St. Petersburg (Leningrad) in 1901, he became a botanist after having been trained (at Berlin, Goettingen, Copenhagen, London and M. I. T.) in biochemistry and physics. This diverse background fitted him particularly for work in photosynthesis, which breaks down into a series of biochemical and physical problems. The other half—it is perhaps more than half—of his double life is occupied by the *Bulletin of the Atomic Scientists,* which Rabinowitch and his Manhattan District colleagues founded as a mimeographed newsletter in the first hours after the apocalypse of Hiroshima. Largely through his devotion and fortitude, the *Bulletin* continues publication today, reaching an increasingly numerous and influential audience, as an independent forum "for science and public affairs."

III. NITROGEN FIXATION *by Martin D. Kamen*

When Martin D. Kamen, at the age of sixteen, matriculated at the University of Chicago in 1930, he planned to concentrate in music and literature. A freshman course in chemistry, however, diverted him to the sciences, and he emerged six years later with a Ph.D. in physical chemistry. The University was then planning to build a cyclotron, and he was despatched to the University of California for training under E. O. Lawrence, inventor of the instrument. There Kamen teamed up with Samuel Ruben, a young scientist pioneering in the new field of radioactive tracer analysis in biology. Together, in 1940, they discovered Carbon 14, which has proved to be the most valuable of all the tracer isotopes. Their partnership was ended by the war, Kamen going into the Manhattan District and Ruben into the laboratories of the Chemical Warfare Service, where he lost his life in a research accident. Kamen is now associate professor at Washington University, St. Louis, where he is winning distinction as an investigator of problems in photosynthesis and metabolism.

THE ORIGIN OF LIFE

by George Wald

ABOUT a century ago the question, How did life begin? which has interested men throughout their history, reached an impasse. Up to that time two answers had been offered: one that life had been created supernaturally, the other that it arises continually from the nonliving. The first explanation lay outside science; the second was now shown to be untenable. For a time scientists felt some discomfort in having no answer at all. Then they stopped asking the question.

Recently ways have been found again to consider the origin of life as a scientific problem—as an event within the order of nature. In part this is the result of new information. But a theory never rises of itself, however rich and secure the facts. It is an act of creation. Our present ideas in this realm were first brought together in a clear and defensible argument by the Russian biochemist A. I. Oparin in a book called *The Origin of Life*, published in 1936. Much can be added now to Oparin's discussion, yet it provides the foundation upon which all of us who are interested in this subject have built.

The attempt to understand how life originated raises a wide variety of scientific questions, which lead in many and diverse directions and should end by casting light into many obscure corners. At the center of the enterprise lies the hope not only of explaining a great past event—important as that should be—but of showing that the explanation is workable. If we can indeed come to understand how a living organism arises from the nonliving, we should be able to construct one—only of the simplest description, to be sure, but still recognizably alive. This is so remote a possibility now that one scarcely dares to acknowledge it; but it is there nevertheless.

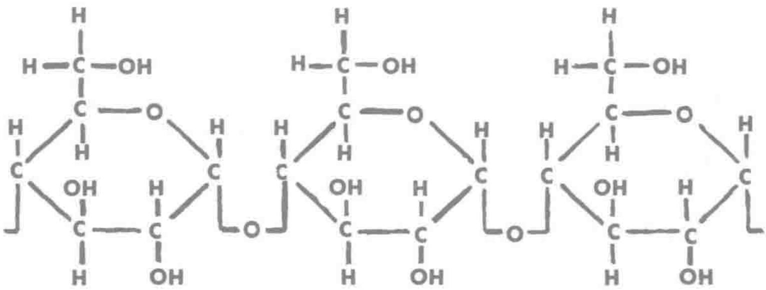
One answer to the problem of how life originated is that it was created. This is an understandable confusion of nature with technology. Men are used to making things; it is a ready thought that those things not made by men were made by a superhuman being. Most of the cultures we know contain mythical accounts of a supernatural creation of life. Our own tradition provides such an account in the opening chapters of Genesis. There we are told that beginning on the third day of the Creation, God brought forth living creatures—first plants, then fishes and birds, then land animals and finally man.

The more rational elements of society, however, tended to take a more naturalistic view of the matter. One had only to accept the evidence of one's senses to know that life arises regularly from the nonliving: worms from mud, maggots from decaying meat, mice from refuse of various kinds. This is the view that came to be called spontaneous generation. Few scientists doubted it. Aristotle, Newton, William Harvey, Descartes, van Helmont, all accepted spontaneous generation without serious question. Indeed, even the theologians—witness the English Jesuit John Turberville Needham—could subscribe to this view, for Genesis tells us, not that God created plants and most animals directly, but that He bade the earth and waters to bring them forth; since this directive was never rescinded, there is nothing heretical in believing that the process has continued.

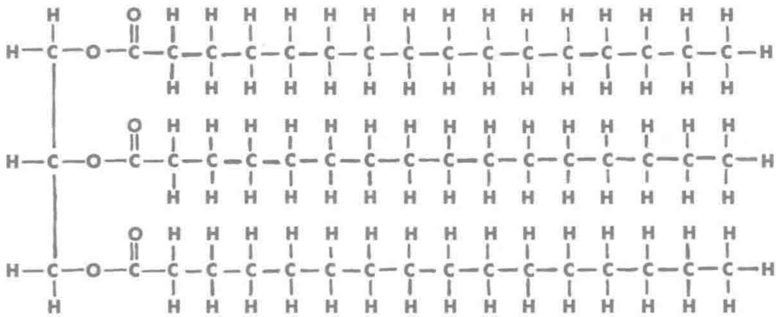
But step by step, in a great controversy that spread over two centuries, this belief was whittled away until nothing remained of it. First the Italian Francesco Redi showed in the seventeenth century that meat placed under a screen, so that flies cannot lay their eggs on it, never develops maggots. Then in the following century the Italian abbé Lazzaro Spallanzani showed that a nutritive broth, sealed off from the air while boiling, never develops microorganisms, and hence never rots. Needham objected that by too much boiling Spallanzani had rendered the broth, and still more the air above it, incompatible with life. Spallanzani could defend his broth; when he broke the seal of his flasks, allowing new air to rush in, the broth promptly began to rot. He could find no way, however, to show that the air in the sealed flask had not been vitiated. This problem finally was solved by Louis Pasteur in 1860, with a simple modification of Spallanzani's experiment. Pasteur too used a flask containing boiling broth, but instead of sealing off the neck he drew it out in a long, S-shaped curve with its end open to the air. While molecules of air could pass back and forth freely, the heavier particles of dust, bacteria and molds in the atmosphere were trapped on the walls of the curved neck and only rarely reached the broth. In such a flask the broth seldom was contaminated; usually it remained clear and sterile indefinitely.

This was only one of Pasteur's experiments. It is no easy matter to deal with so deeply ingrained and common-sense a belief as that in spontaneous generation. One can ask for nothing better in such a pass than a noisy and stubborn opponent, and this Pasteur had in the naturalist Félix Pouchet, whose arguments before the French Academy of Sciences drove Pasteur to more and more rigorous experiments. When he had finished, nothing remained of the belief in spontaneous generation.

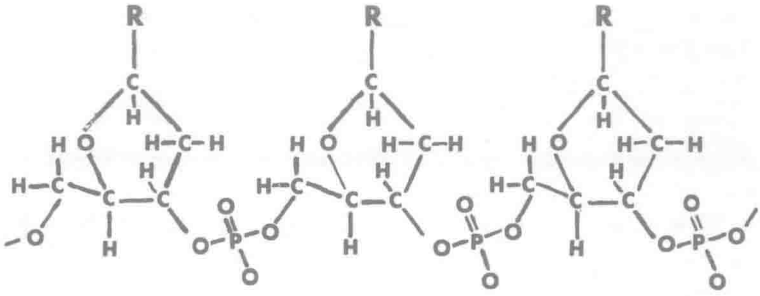
We tell this story to beginning students of biology as though it represents a triumph of reason over mysticism. In fact it is very nearly the opposite. The reasonable view was to believe in spontaneous generation; the only alternative, to believe in a single, primary act of supernatural creation. There is no third position. For this reason many scientists a century ago chose to regard the belief in spontaneous generation as a "philosophical necessity." It is a symptom of the philosophical poverty of our time that this necessity is no longer appreciated. Most modern biologists, having reviewed with satisfaction the downfall of the spontaneous generation hypothesis, yet unwilling to accept the alternative belief in special creation, are left with nothing.



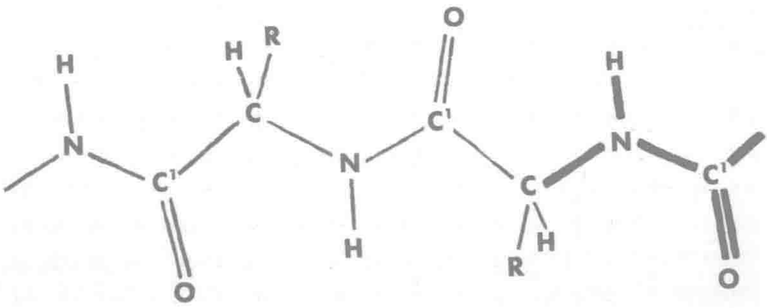
Carbohydrates comprise one of the four principal kinds of carbon compound found in living matter. This structural formula represents part of a characteristic carbohydrate. It is a polysaccharide consisting of six-carbon sugar units, three of which are shown.



Fats are a second kind of carbon compound found in living matter. This formula represents the whole molecule of palmitin, one of the commonest fats. The molecule consists of glycerol (the 11 atoms at the far left) and fatty acids (the hydrocarbon chains at right).



Nucleic acids are a third kind of carbon compound involved in life processes. This is part of desoxyribonucleic acid, the backbone of which is five-carbon sugars alternating with phosphoric acid. The letter R is any one of four nitrogenous bases, two purines and two pyrimidines.



The fourth major carbon compound involved in life processes is the protein. The basic structure is the polypeptide chain shown here. The structural unit of the chain, in turn, is an amide group, isolated by the heavy lines at right. The same unit may repeat down the length of the chain, as here, or alternate with other groups.