BIOLOGY, MOLECULAR AND ORGANISMIC

THEODOSIUS DOBZHANSKY

The Rockefeller Institute, New York City

It is customary for presidents of scientific societies to address those who saw fit to elect them. The wise course is to choose a safe and noncontroversial topic; for a postprandial address, a mildly humorous topic is preferable to enable the speaker to display his wit, if he has any. I am following neither the custom nor the council of wisdom. This address has been postponed long enough for me to achieve the obscurity of an ex-president, and my topic is controversial and not particularly amusing. However, the relationships of molecular and organismic biology, zoology and botany, are most certainly of current interest; I am probably not far wrong to surmise that this topic is the most often discussed one among zoologists. I expect that what I am going to say may seem provocative to some of you; I do not expect it to seem boring.

Indisputably, molecular biology has achieved in our day advances of signal importance. Suffice it to mention the elucidation of the chemistry of heredity, the breaking of the genetic code, studies on protein structure and synthesis, and the unraveling of the sequences of chemical reactions in metabolic processes. All this has brought biology considerably closer than it was a generation ago to understanding the phenomena of life. Although it is equally indisputable that this understanding is nowhere near complete as yet, it is fair to say that we are the living witnesses of a great efflorescence of biological sciences. The modern advance is perhaps comparable in magnitude, although probably not in the depth of the philosophical repercussions, to that which occurred roughly a century ago under the stimulus of Darwin's theory of evolution. Every biologist feels gratified by this advance, and hopes that further research in molecular biology will be pursued with all possible vigor. What is debatable is the situation of the organismic biology vis-a-vis its molecular sibling.

Nothing succeeds like success. In molecular biology, one spectacular discovery has followed closely on the heels of another. Molecular biology has become a glamor field. It has attracted many able young students as well as older investigators. Glamor and brilliance generate enthusiasm and optimism; they may also dazzle and blindfold. The notion has gained some currency that the only worthwhile biology is molecular biology. All else is "bird watching" or "butterfly collecting." Bird watching and butterfly collecting are occupations manifestly unworthy of serious scientists! I have heard a man whose official title happens to be Professor of Zoology declare to an assembly of his colleagues that "a good man cannot teach zoology." A good man can teach, of course, only molecular biology.

Such pronunciamentos can be dismissed as merely ridiculous. They are, however, caricatures of opinions entertained by some intelligent and reasonable people, whose views deserve an honest and careful consideration and analysis. Science must cope with new problems that arise and devise new approaches to old problems. Some lines of research become less profitable and less exciting and others more so. The progress in a given field of study may slacken because the approaches used have already yielded most of what they are capable of yielding. Probably every thoughtful scientist can give examples of research efforts

It is a pleasure to acknowledge here the kindness of my colleagues Messrs. W. Anderson, A. G. Bearn, E. Bösiger, R. J. Dubos, H. G. Frankfurt, A. E. Mirsky, and B. R. Voeller, who have read this address in manuscript and have contributed valuable suggestions and corrections. The responsibility for the ideas expressed, as well as for the errors of commission, or omission, is nevertheless entirely my own.

[This address was presented at the summer meeting of the American Society of Zoologists, Boulder, Colorado, August 27, 1964.—Ed.]

which have bogged down, and of types of inquiry which seem to have run into at least temporarily impassable obstacles. If such researches and inquiries are not abandoned altogether they usually drift into more and more narrow specializations and uninspired repetitiousness. On the other hand, an apparently depleted field may burst into renewed fertility when a new idea or a new technique is invented.

Is it, then, possible that biology other than molecular biology has entered upon a period of doldrums? It is good for any scientist from time to time to re-examine and to re-think his aims, purposes, and approaches. Intellectual laziness has been the undoing of many a capable scientist, who rested on the comforting assumption that what was good a generation ago is good enough today. A line of research is not necessarily good because it is traditional, and it is not necessarily worth pursuing because it has become an ingrown habit. But neither is newness and fashionableness a valid enough reason to choose one's line of work. Let us face the problem squarely and honestly.

Biology is structured rather differently from other natural sciences. Since this is equally true of zoology and botany, I prefer to use here the inclusive word, biology, covering both. A biologist, more than, for example, a physicist or a geologist, is faced with several hierarchically superimposed levels of integration in the objects which he studies. Life presents itself to our view almost always in the form of discrete quanta —individuals. But unlike the atoms of classical physics, individuals are conspicuously divisible, and, unlike the atoms of modern physics, divisible into great numbers and a great variety of component elements, cells. Cells are, in turn, complexly structured and well-integrated entities. They contain chemical substances of numerous, probably thousands, molecular species. It is, however, a gross error to think of a cell simply as a mixture of chemicals, like a mixture that can be made in a test tube. The chemical components are arranged in cells in series of intricately built organelles. Chromosomes and genes have that extraordinary chemical substance, the DNA, as the key constituent. But the DNA in the chromosome is something more than the DNA in a test tube. A chromosome is an organized body, and its organization is as essential as is its composition.

The supra-individual forms of integration seem less tangible in a spatio-temporal sense than the infra-individual ones, but just as interesting and significant. Mankind is less clearly perceived by our sense organs than an individual man, but it is nevertheless as meaningful a biological entity as it is a cultural entity. The sexual mode of reproduction connects individuals into reproductive communities, Mendelian populations. Mendelian populations are united by reproductive bonds into inclusive reproductive systems—biological species. An isolated individual, especially an individual of a sexual species, is at least as clearly an anomaly as a cell isolated from a multicellular body. With asexual modes of reproduction, the bonds which integrate individuals in Mendelian populations and biological species are absent. Other bonds operate, however, in sexual as well as in asexual organisms. Individuals and species belong to ecological communities and ecosystems. An individual taken out of the system in which it normally occurs is incomplete and it may be inviable.

The hierarchy of levels of biological integration may be represented schematically as the following sequence: molecule, cellular organelle, cell, tissue, organ, individual, Mendelian population, species, community, ecosystem. This sequence is, to be sure, not everywhere rigorously adhered to. There are unicellular (or acellular) as well as multicellular organisms; the sexual and the asexual modes of reproduction impose, as indicated above, different modes of integration. Even the level of an individual is not always unambiguously distinct. Consider a colonial form, such as a siphonophore; an individual of the higher order (colony) is composed of several individuals of the lower order which are incapable of independent existence. Among social insects, the colony becomes an entity for which the designation "supraorganism" has been suggested.

Biologists have studied the manifestations of life at all levels of integration. It would therefore be logically possible to distinguish molecular biology, cell biology, individual biology, population biology, community biology, etc. This is neither necessary nor convenient in practice. It is, however, desirable to have a simple dichotomy of molecular and organismic biology, the latter name subsuming studies on all levels above the molecular one.

The designation "organismic" is an appropriate one, notwithstanding the fact that this adjective was utilized by the so-called "holists" for some of their special, and now almost completely forgotten, notions. This should not, I think, make the word forever ineligible for use in a context which renders its different meaning unambiguously clear.

Organismic biology, dealing with biological integration levels above the molecular one, has in recent years been referred to, sometimes pejoratively, as the classical or traditional biology, or as natural history. The opinion forcibly expressed by some molecular biologists is that, to be "modern," or even "scientific," organismic biology must be reduced to molecular biology. All that this means in most cases is that many molecular biologists are so excited about what they are doing that they are unable to see why their organismic colleagues can find excitement in something else.

There are, however, also more rational arguments with which the claims of a supremacy of molecular biology are sometimes supported. One reason is simply the acceptance of the mechanistic hypothesis and rejection of vitalism. Biological phenomena are complex patterns of physicochemical ones; there is nothing in living bodies, no special form of energy or any other agency, that is not potentially analyzable into physicochemical components. More than three centuries ago, Descartes wrote "That I do not accept or desire any other principle in Physics than in Geometry or abstract Mathematics, because all the phenomena of nature may be explained by their means, and sure demonstration can be given of them." Descartes also wrote "that the body of a living man differs from that of a dead man just as does a watch or other automation (i.e., a machine that moves of itself), when it is wound up and contains in itself the corporeal principle of those movements for which it is designed along with all that is requisite for its action, from the same watch or other machine when it is broken and when the principle of its movement ceases to act."

Most present-day biologists accept the Cartesian view of the nature of living bodies. Three centuries of research in biology have yielded abundant evidence in favor of this view. Time and again, processes and phenomena which appeared distinctive of living matter were shown to be compounds of chemical and physical constituents. Driesch was probably the last outstanding biologist to espouse the classical vitalist doctrine. He believed that a special force or energy, which he called by the Aristotelian name "entelechy," was active in living bodies. Vitalism is now not only very much a minority view but, and this is characteristic, its present adherents are loath to admit that they are vitalists. For example, Sinnott is convinced that the development of the organism is presided upon by a "psyche," but, if I understand him aright, this psyche neither substitutes for, nor enters into any give-and-take with, ordinary physical corporeal processes.

The reason why mechanism has triumphed in biology, and vitalism has faded out of the picture, must be made unequivocally clear. Far from all life processes have been, or for that matter are ever likely to be, exhaustively described in chemical and physical terms. A universal negation is notoriously hard to substantiate; there is no irrefutable proof that some sort of an entelechy may not be lurking somewhere. The point is rather that vitalism has turned out to be unnecessary and unprofitable, while mechanism has vindicated itself as a guide to discovery. For this and for no other reason, the contest of mechanism versus vitalism has been a dead issue in biology for at least half a century. Not even the few surviving vitalists deny that physical and chemical processes occur in living bodies, and more examples would not impress them greatly. To do research for the purpose of invalidating vitalism is at present a height of futility. It is not unlike using heavy artillery to kill mosquitoes.

Reduction of the organismic biology to the molecular level may, however, be urged also on different grounds. This is the proposition that chemistry and physics are sciences more "advanced," more exact, and hence superior to biology. More than a century ago (1830-1842), the positivist philosopher Auguste Comte set up an hierarchy of sciences. In his opinion, the most basic science was mathematics; less basic were, in a descending order, mechanics, astronomy, physics, chemistry, biology, and sociology. The progress of scientific inquiry consists of reducing the description of the phenomena studied by the less basic sciences to the more basic ones. The aim of biology is, then, to describe life in terms first of chemistry, and eventually of physics and mechanics, and thus to dispense with biological concepts and ideas altogether. The greatest conceivable success of biology would be to make itself obsolete and unnecessary.

The Comtian positivism had a powerful influence on the world view of nineteenth century scientists, but its reputation has not fared well among philosophers. Some of the greatest modern works on philosophy of science (e.g., Nagel, 1961) do not mention Comte at all. At present not all scientists know his name either, and fewer still have read any of his works. The belief in the Comtian hierarchy of sciences, and the faith in reduction as the intent of scientific inquiry, nevertheless persist and are seldom questioned among scientists, especially among biologists. The matter is, however, far from simple; it deserves being considered with care and caution.

Nagel (1961) defines reduction as "The explanation of a theory or a set of experimental laws established in one area of inquiry, by a theory usually though not invariably formulated for some other domain." Reduction of organismic to molecular biology, and of the latter to chemistry, would be effected if biological laws and theories, such as for example Mendel's laws of the theory of inheritance, were shown to be deducible as consequences of the laws and theories of chemistry, physics, or mechanics.

The reductionism is a more sophisticated notion than the simple, and often a little naive, wish to prove that biological phenomena are not manifestations of some sort of vital force or psyche. It must, however, be understood that, while under some conditions the reduction is useful and enlightening, under others it merely detracts from the research effort better applied elsewhere. This is a question of research strategy, not of some sacred and immutable law of scientific development. To be profitable, the reduction should open up new possibilities of using some powerful theories or concepts of a more advanced, or if you wish, more basic, science. It must help making discoveries in the field of science undergoing reduction, and at that, discoveries which could not otherwise be made or not made as easily. Such advantages have accrued, for example, when thermodynamics was reduced to statistical mechanics. In biology, at least some chapters of physiology are being successfully reduced to biochemistry, chemistry, biophysics, and physics. However, here I must again quote Nagel, whose philosophy is, let this be made clear, quite favorable to reductionism. According to Nagel, "The question whether a given science is reducible to another cannot in the abstract be usefully raised without reference to some particular stage of development of the two disciplines. . . . The possibility should not be ignored that little if any new knowledge or increased power for significant research may actually be gained from reducing one science to another at certain periods of their development, however great may be the potential advantages of such reduction at some later time."

Nagel's analysis has not been made especially with biology in view, but it describes splendidly the present situation of the biological sciences. The progress of biology would not be furthered by frenetic efforts to reduce organismic biology to chemistry or physics. This is not because there is anything in living things that is inherently irreducible. It is rather because a different research strategy is more expedient. Those who urge an immediate absorption of the organismic into molecular biology neglect the simple but basic fact that life has developed several levels of organization. These are levels of increasing complexity, and they are hierarchically superimposed. The elementary phenomena and regularities on each succeeding level are organized patterns of those on the preceding level. Organismic biology can be said to be a study of patterns of molecular phenomena. Such a definition of organismic biology is correct as far as it goes, but it does not go quite far enough. It is a study not only of the molecular patterns but also of patterns of patterns.

Some examples should make the meaning of this clear. A gene, or at least its key constituent, is a double-stranded DNA molecule, or perhaps a part of such a molecule. A chromosome is, however, not a heap of genes, but a configuration of genes arranged in a certain way which proved to be adaptively advantageous in evolution. A cell is not a conglomeration of chromosomes but a supremely orderly contrivance consisting not of chromosomes alone but also of many other organelles. An organ and an individual body are, in turn, not simply piles of cells but beautifully designed and often highly complex machines, in which the cellular components are not only diversified but often have lost their separate identities. Mendelian populations and species of sexually reproducing organisms are not throngs or medleys of individuals, they are reproductive communities of interdependent members. Species are categories of classification, but they are not only that. Evidence is rapidly accumulating to show that the gene pool, the collective genotype of a species, is an organized system of coadapted constituents. Biotic communities or ecosystems are not miscellanies of species which happen to live side by side or in the same general region; they are structured associations of more or less mutually interdependent forms.

A follower of the philosophy of Francis Bacon could perhaps hope that if one accumulates an abundance of accurate chemical and biochemical observations, then all biological phenomena on all integration levels could easily be deduced from these observations. Indeed, we have admitted that what the organismic biology studies are patterns, and patterns of patterns, of chemical and physical processes. In actual fact, the development of biology has followed a quite different path, and really no branch of science has trod the way which Bacon, who was not himself a practicing scientist, imagined it would. In biology, research was and is being carried on simultaneously, and discoveries are being made on all organismic and molecular levels.

The discoveries in one branch of biology often suggest work to be done, and stimulate discovery in other biological disciplines. It is, however, not at all a general rule that these discoveries are made by simple deduction. It was, for example, biochemistry and spectroscopy that yielded the celebrated Watson-Crick model of the structure of DNA. This represents a very important advance in our understanding of what the genes are and how they work. But the existence of genes was discovered with the aid of the methods of hybridization and of statistical analysis of hybrid progenies, not of chemical methods. Even now, given the entire present day knowledge of the chemistry of DNA, one could hardly deduce from this knowledge that the genes exist and behave as Gregor Mendel found them behaving in inheritance.

A suggestion has also been made that biologists should exercise a kind of restraint, and leave the problems of organismic biology in abeyance until the time should come when these problems could be reduced to the molecular level. This suggestion has at least the merit of a kind of ruthless logic behind it, but like so many other ruthlessly logical proposals, it is a practical impossibility. It is like the advice, also logically impeccable, that a moratorium ought to be declared on all scientific research, to give time for mankind to absorb the knowledge already available. Both proposals are futile, not to say silly, and for the same reason. Man's intellect will not tolerate such shackles, not even were it convinced that these shackles would be good for it.

To make the situation ironic, some of the same people who would declare a moratorium on organismic biology until such time when it can be reduced to molecular terms, also argue that organismic biology is largely a finished business, worthy neither of much attention nor support. Now, it is true that a method of investigation or a line of research may be productive at one time, and become like a squeezed-out lemon afterwards. However, he is a reckless, rather than a courageous man, who wraps himself in a prophet's mantle. The history of science often deals roughly with fortunetellers. Consider the discipline of human anatomy. It should have been dead four centuries ago; after Vesalius not many new organs can be found in the human body. Yet we find anatomy prospering and forward-looking. Microscopes have opened vistas which were not accessible to Vesalius. Polymorphisms and variations, normal and pathological, individual and racial, have acquired new meaning in the light of genetics and evolution. Finds of fossil human and prehuman remains create such excitement that some discoveries are reported in the daily press before they are buried in weighty monographs.

What is predictable about most discoveries is that they are unpredictable. If they were predictable, they would be made sooner, but making them would be a less inspiring occupation than it is. We have been discussing the methodology and the strategy of modern biology. No synopsis of major or outstanding problems of either the molecular or the organismic biology will be attempted here. Even if I had the wisdom, or the brashness, needed for such an undertaking, it would require a book, instead of an address or an article. I hope, however, that it is not out of place to venture here a very general characterization of the subject matter of biology, both organismic and molecular.

The world of life can be studied from two points of view—that of its unity and that of its diversity. All living things, from viruses to men, have basic similarities. And yet there is an apparently endless variety of living beings. Knowledge and understanding of both the unity and the diversity are useful to man. I like, however, to stress here not the pragmatic aspect, not the applied biology, but the aesthetic appeal. Both the unity and the diversity of life are fascinating. Some biologists find the unity more inspiring, others are enthralled by the diversity. This is evidently a matter of personal taste, and a classical adage counsels that tastes are not fit subjects for disputation (although this is what most disputations are about). The consequence of the polymorphism of tastes is that there always will be different kinds of biologists and different subdivisions of biology. Some of the subdivisions may be offering more fleshpots than others, and hence will be more popular, especially among those for whom the fleshpots are the prime consideration. Other subdivisions will, however, continue to attract some votaries.

The number of described species of animals is estimated to be not less than one million, and of plants about one-third as many. The total number of existing species of organisms may only be guessed—from two to four million. It is, however, not only the great number of yet undescribed species that gives the lie to the oft-repeated contention that the systematic and descripive biology have already fulfilled their functions and may be relegated to amateurs and to museum drudges. Species identification and description is an indispensable preliminary, but only a preliminary, to other, and perhaps more exciting and significant inquiry. The ferreting-out of new species belongs to what Mayr has called the "analytical stage," and what is sometimes referred to also as the "alpha-taxonomy." This is followed by the "synthetic stage," and finally by the study of causes and regularities of the evolutionary process. Birds are the group of animals which is attracting the greatest number of workers relative to its size (i.e., to the number of species in the group); the species of birds are, however, so well explored that the chances of finding a new one are probably smaller than in any other group of animals of comparable size. Ornithologists are interested surely not so much in finding new species as in understanding the old ones. So are many, if not most, other systematists.

Remarkably, even paradoxically, the fundamental unity of all living things makes possible an understanding of their prodigious diversity. Nutrition, respiration, irritability, and reproduction are found everywhere. Some of the enzymes in my body are similar in function to the enzymes in the lowly yeast and bacterial cells. My genes are different sequences of the same four "letters" of the "genetic alphabet" which also compose the genes of a fish or of a corn plant. Genes reproduce themselves generally with an astonishing accuracy; the sequences of the four "letters," the nucleotide bases, are usually identical in hundreds of billions of cells of the bodies of the parents and of their progeny. Occasionally, there occur, however, changes, "misprints," mutations. Self-reproduction plus mutation make possible natural selection. Natural selection makes possible evolution. Evolution is not always, and not necessarily, but sometimes, progressive.

The enterprise of biology rests chiefly on two patterns of explanation. One is the organism-the-machine theory, stated quite clearly by Descartes. The other is the theory of evolution, creditable, despite some predecessors and anticipators, to Charles Darwin. Both mechanistic and evolutionary explanations are pertinent to, and are made use of, in molecular as well as in organismic biology. These explanations are not alternative or competing; they are complementary, without, however, being either deducible from or reducible to each other. It is nevertheless possible to say, as a broad generalization, that the molecular biology is preponderantly Cartesian and the organismic biology is basically Darwinian. I utter this generalization not without misgivings; it should not be misunderstood as creating a dichotomy, for such a dichotomy would be a false one. Both the Cartesian and the Darwinian approaches are essential for understanding the unity and the diversity of life at all levels of integration. Nevertheless, at the lower levels of integration the type of question most frequently asked is "how things are," while at the higher levels an additional question insistently obtrudes on the mind of the investigator—"how things got to be that way."

Perhaps the most significant and gratifying trend during the last two decades or so has been the increasing unification of biology as a field of knowledge. Of course, we are all specialists in some particular line or even technique of research. But now more than ever before one can discern the meaningful relationships between all these specialties and techniques. The spectacular progress in molecular biology has surely acted as a unifying agent. To treat molecular biology instead as a bludgeon with which to destroy, or to reduce to insignificance, the organismic biology is to basically misunderstand the nature of life and the requirement for its study.

I venture another, and perhaps equally reckless, generalization—nothing makes sense in biology except in the light of evolution, *sub specie evolutionis.* If the living world has not arisen from common ancestors by means of an evolutionary process, then the fundamental unity of living things is a hoax and their diversity is a joke. The unity is understandable as a consequence of common descent and of universal necessities imposed by common materials. The diversity is intelligible as the outcome of adaptation of life to different environments, or, if I may use this unfortunately ambiguous and yet indispensable concept, to different ecological niches.

If one could imagine a universe in which the environment would be completely uniform in space and in time, then in such a universe a single kind of living inhabitant could conceivably be all that an evolutionary process might produce. The real universe is certainly not uniform. The living matter has responded to the diversity of physical environments by evolving a diversity of genotypes able to survive and to reproduce in a variety of environments. Organic diversity is necessary because no single genotype can possess a superior adaptedness in all physical environments. This is, if anything, even more true with respect to the biotic environments. The more different organisms inhabit a territory, the greater becomes the variety of ecological niches. In a sense, the growth of the organic diversity is a self-accelerating process.

Although there is again no sharp dichotomy here, the concepts of adaptedness and adaptation occupy a more important position in organismic than in molecular biology. The existence of several hierarchically superimposed levels of organic integration is in itself understandable only as an adaptation. Living beings survive and reproduce sometimes in apparently most hostile environments. One can argue that all environments are hostile, and that death and extinction are probable events, while survival is improbable. Just how life has managed to overcome this improbability is a problem which many biologists find challenging and fascinating. In my opinion, this problem may well be used as the framework on which to build the teaching of biology. At least I found it so, both as a student and as a teacher.

I am, of course, not unaware of dissenting opinions about adaptation. It has been argued that adaptation is either a tautology (what can survive, survives), or a teleology (a belief that organisms are shaped by or for a purpose). Such opinions reveal a basic misconception. Darwin has, once and for all, taken the sting out of teleology. For example, the statement that the hormonal mechanisms in a mammalian female serve the purpose of reproduction does not imply that these mechanisms were contrived by some kind of entelechy which knew what it wanted to accomplish. Nor does the statement that a wasp seeks a prey in order to provide food for its offspring mean that the wasp is conscious of the purpose of its activities. Reproduction is accomplished, and the offspring is fed, by a great many methods other than those used by the mammalian and by the wasp females.

The meaning of the above statements is really simple and straightforward. When certain hormones are produced in the body of a mammalian female, and produced in a certain delicately balanced sequence, then and only then the chain of events takes place which eventuates in the birth of a viable infant. The wasp goes through a series of complex actions, which result in her progeny's feeding and developing, instead of starving to death or being poisoned by unsuitable food. A logical analysis of pseudo-teleological statements like the ones above has been made with a great discernment by Nagel in his admirable book "The Structure of Science." This pseudo-teleological language can only be avoided by means of ponderous circumlocutions, which are superfluous to a biologist acquainted with the modern evolutionary thought.

It is a striking and profoundly meaningful fact that organisms are so constructed, so function, and so behave that they survive and perpetuate themselves in a certain range of environments frequently enough for their species not to become extinct for long periods of time. Furthermore, the ranges of the environments propitious for survival and reproduction are widely different for different forms of life. A biologist who chooses to ignore this widespread adaptedness overlooks a fundamental and very nearly universal characteristic of all that can be meaningfully studied on every level of biological integration, from the strictly molecular to the highest organismic —the ecosystem level. Even the exceptional failures of the adaptedness, the phenomena of extinction, constitute an obviously meaningful and important subject of study.

Zoologists, and in fact all biologists, should never lose sight of this one highly peculiar, and yet remarkably interesting, animal species—*Homo sapiens*. The worth and utility of biology, and, indeed, of science and of intellectual endeavor as a whole, will perhaps, in the fullness of time, be judged by the contribution they will have made to man's understanding of himself and of his place in the universe. I do not wish this statement to be misconstrued as urging that we jettison our zoology and all strive to become anthropologists or philosophers. By being good biologists, we may make a real contribution to the Science of Man, if not to anthropology in the strict technical sense. It is a hoary fallacy to think that man is nothing but an animal; however, man's nature is in part animal nature, and man's not-so-remote ancestors were full-blown animals. Man's humanity and his animality are not independent or kept in isolated compartments; they are interdependent and connected by reciprocal feedback relationships.

The parts played by the molecular and the organismic biology come out with extraordinary clarity when viewed against the background of the Science of Man. Like that of any other living body, the physiological machinery of the human body is compounded of chemical and physical ingredients. Certain diseases, particularly hereditary ones, are molecular diseases. The elucidation of their etiologies makes some splendid pages in the story of modern biology. Let me cite just one example—that of the sickle-cell anemia. This usually fatal disease is due to homozygosis for a single gene; the heterozygote for this gene and its normal allele is healthy or only mildly anemic. The hemoglobin in the blood of homozygous individuals is chiefly the so-called S hemoglobin; the heterozygote has both S and the normal hemoglobin A. Ingram and others found that hemoglobin S differs from A in the substitution of just a single amino acid, valine in place of glutamic acid in the beta chain of the hemoglobin molecule. The mutational change in the gene responsible for the synthesis of the beta chain must have involved the substitution of just a single nucleotide, a single "letter" of the "genetic alphabet." At least 14 other abnormal hemoglobins, in addition to S, are known to have single amino acids substituted in certain definite positions in the molecule.

Man is, however, an organism, and a highly complex and remarkable one. I suggest to you a single reason, but in itself a sufficient reason, why organismic biology will always occupy a leading place in the enterprise of science. Man seeks to understand himself. The pursuit of self-understanding is a never-ending quest. Darwin's work marked a turning point in the intellectual history of mankind because it showed that mankind was a product of a biological history. The evidence for this is now overwhelmingly convincing, except to a few antievolutionists. But just how and why man's bodily structures, physiological functions, and mental capacities have developed as they did is by no means well understood. The working hypothesis now in vogue is that the process of adaptation to the environment is the main propellant of evolutionary change. Evidence is rapidly accumulating which, in my opinion, substantiates the hypothesis. It remains, however, not only to convince the doubters but, what is more important, to discover just how the challenges of the environment are translated into evolutionary changes.

Man is interested in his future no less than in his past. Evolution is not only a history, it is also an actuality. Of course, *Homo sapiens* evolves culturally more rapidly than it evolves biologically. Man must, however, face the problem of adapting his culture to his genes, as well as adapting his genes to his culture. Man is being forced by his culture to take the management and direction of his evolution in his own hands. This is perhaps the greatest challenge which mankind may ever have to face, and this is far too large a problem to be more than mentioned here. It is childish to think that it is solely a biological problem; the entire sum of human knowledge and of human wisdom will be needed. Biology is, however, involved, and this necessarily means both the Cartesian and the Darwinian, the molecular and the organismic biology. Fashions and fads come and go in science as they do in dress and in head gear. The big question remains: What is Man? It remains not because it is hopelessly insoluble, but because every generation must solve it in relation to the situation it faces.

Biology is here relevant; a solution based only on biology may well be wrong, but, surely, no solution ignoring either the organismic or the molecular biology can be right and reasonable.

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