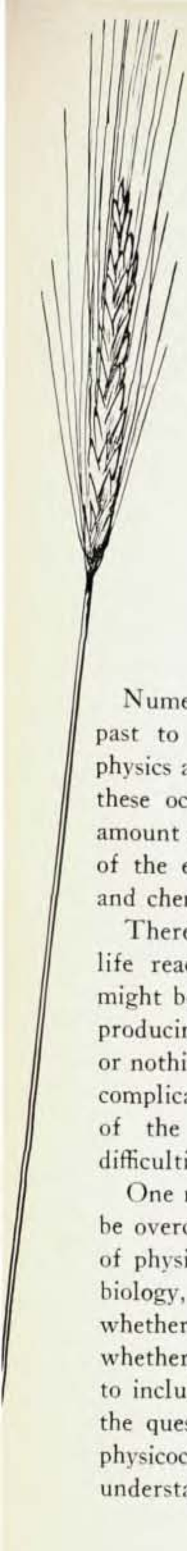

LIVING MATTER and PHYSICAL LAWS

by John R. Reitz and Conrad Longmire

The biologist is perhaps as skeptical of the help the physicist can offer the life sciences as the physicist is confident that he has something to offer. But physical concepts are being applied to the study of life both with humility and with prospects for progress.

Numerous attempts have been made in the recent past to apply the laws and the methodology of physics and chemistry to the life processes. Although these occasionally have been marked by a certain amount of success, biology as a science retains much of the empirical quality that characterized physics and chemistry in their early days.

There is good reason for this. The chemistry of life reactions appears exceedingly complicated, as might be expected in any mechanism capable of reproducing itself. Large molecules, about which little or nothing is known, are involved. Furthermore, the complicated and delicate nature of the mechanisms of the life process adds to the experimental difficulties.

One may expect that many of these obstacles will be overcome or circumvented, and that the domain of physics and chemistry will be extended far into biology, but it is still too early to say with certainty whether present physical laws will suffice, or whether they will have to be modified or extended to include a new "life" principle. Without arguing the question further, we shall review some of the physicochemical studies that offer hope for a greater understanding of biological processes.

Thermodynamics of Life

Most living organisms contain such very large numbers of atoms that it is natural to ask whether physical statistics holds for living organisms. Specifically, are the first and second laws of thermodynamics obeyed? There is no doubt that the first law, which states that energy is conserved, holds. The sources of energy are apparent and the energy of reactions that take place in the cell can be shown to balance exactly, as in ordinary chemical reactions.

The second law states that in any system left to itself the entropy either increases or remains constant but will not decrease. This statement may be interpreted roughly in terms of order and disorder: any system left to itself tends to become more disordered or remains the same; it will not become more ordered. The system will definitely become more disordered if an irreversible reaction takes place.

Now consider a glass box containing some earth and water and air, and a flower seed. Only the flower seed may be said to have a high degree of order, or low entropy. The earth, water, and air are at equilibrium in a rather comfortable state of disorder. Two things, of pertinence here, may happen to our system. First, the seed may rot. This is certainly an irreversible reaction, and as required by the second law, the disorder and entropy of our system increases. On the other hand, the seed may grow and produce a flower and many other seeds like itself (though we may need to introduce a cooperative bee). The growing is also an irreversible reaction, but this time the order has increased for some of the

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disorderly earth, air, and water has been converted into orderly seeds.

At first sight, because the entropy has thus decreased, our glass box may seem to contradict the second law. Actually there is no contradiction, since the box was not really left to itself as required, but was invaded by a large amount of sunlight during the growth of the flower. So we must consider as our system the box and the sunlight, which we may imagine to be enclosed in a long pipe ending in the box. If the radiation in our system were in complete disorder it would consist mainly of heat waves corresponding to the temperature of the box and there would be no visible light to speak of. Since there is a lot of visible light in our pipe, the radiation is obviously not in its most disordered state. When the seeds are grown, and the sunlight has been used up, some of the order once possessed by the radiation is gone, but in its place is the order of the new seeds. To satisfy the second law, it is required only that the order of the new seeds be less than the order initially present in the sunlight.

It is apparent, then, that our flower has increased its degree of order by feeding on energy in a high degree of order, or by feeding on what Schrödinger has called "negative entropy." The source of the negative entropy for plant life is the sun. Though the radiation emitted by the sun is in equilibrium with the very hot surface of the sun (6000°C) and is therefore in complete disorder at that place for that temperature, the order comes about when this high temperature radiation enters our low temperature box.

Not all living organisms depend upon the sun for their negative entropy. The more highly developed forms of life have learned to feed upon other living matter, where it is already stored up. Although nature perhaps did not intend that dog should eat dog, she apparently did intend that dog should eat rabbit, and that rabbit should eat clover.

It is thus possible for living organisms to increase their degree of order without violating the second law but it has not been proven that the second law is actually obeyed. The reason is that it is too difficult to measure or calculate exactly the entropy of a living organism. We cannot then say as experimental fact that the decrease in entropy of a living organism is less than the increase in entropy of its food energy. We shall have to learn much more about the detailed structure of living organisms before we can answer the entropy question completely. For example, we shall have to learn how to calculate the entropy of a man's brain.

Ontogenesis and Metabolism

The development of an organism during its lifetime (ontogenesis) is supported by the metabolism of the cells making up the organism. Certain metabolic processes have been studied in great detail by the biochemists, and it is in this field of research that the application of physical and chemical laws has been most helpful.

The metabolic reactions which occur in the cell are mainly a series of oxidations and reductions, as evidenced in respirations, fermentation, and photosynthesis. Photosynthesis will be discussed later in more detail. In respiration oxygen is reduced to water; in fermentation several oxidation-reductions may occur. The metabolites come in as fuel, are oxidized or fermented, and leave as waste products. As in the case with any fuel, energy is liberated during the reaction; however, the reaction does not always proceed spontaneously. The metabolites, as in the case of fuel-gas air mixtures, represent a state of higher energy than the reaction products, but there may be a potential barrier which prevents the reaction from occurring. In other words, the metabolites (or fuel mixture) would have to go through a region of higher energy in order to react. In the case of the fuel mixture, combustion is achieved by raising part of the mixture to the ignition point. The cell, on the other hand, makes use of specific catalytic agents in order to make the metabolic reaction proceed. These catalysts, or enzymes as they are called, have been identified as protein molecules, and they are vital agents in most of the metabolic reactions. In some cases they act in the following way: the enzyme adsorbs the metabolites together, and so distorts them that the potential barrier is lowered and the reaction proceeds.

Although the enzymes often perform their function in an ingenious manner, the reactions described above in which energy is given off (exothermic) are not the most miraculous functions performed by the cell. The cell can also perform reactions in which energy is absorbed (endothermic) known as phosphorylations. During phosphorylation, the energy from an exothermic reaction is simultaneously used to create an energy-rich phosphate group from inorganic phosphate. The molecules containing these energy-rich phosphate bonds serve as a supply of energy for the work performed by the organism. For example, ATP (adenosine triphosphate) has three phosphate linkages containing 11,000 calories per link per mole, and its splitting is the source of all muscular energy. This exothermic reaction, coupled to a phosphorylation, will not proceed in the absence of inorganic phosphate. Further, for every molecule oxidized or reduced in the exothermic reaction, exactly one phosphate linkage is formed.

As mentioned above, sunlight is the original source of energy and negative entropy for living organisms. In photosynthesis, the green plant cell reduces carbon dioxide to carbohydrate when the energy for the reaction is obtained from the absorption of light. This is an endothermic reaction which needs about 160,000 calories per mole for each carbon dioxide molecule reduced. Now the light quanta have various energies depending on their frequency, but it has been found by experiment that the energy per quantum which can be made available for the reaction is the same for all frequencies of light throughout the visible spectrum. The reason for this is that the chlorophyll molecule has a metastable state which is higher in energy than the ground level (or normal state of the molecule), and the energy difference between this state and the ground level is equal to the energy of a red quantum. When excited by light of any frequency greater than that of red light, the molecule slides by a radiationless transition into this metastable level. Here it can either fluoresce, use the energy to heat up other molecules, or use the energy to make photosynthesis take place.

Thus for each quantum absorbed there is available the energy of one quantum of red light. In order to get 160,000 calories per mole of carbon dioxide, four quanta would have to be absorbed for each carbon dioxide molecule reduced. Actually about ten to twelve quanta are absorbed per molecule and the efficiency is therefore around forty percent. We see, then, that the cell converts the energy of sunlight to its own purposes at a quite high efficiency. It should, however, be noted that the high efficiency quoted occurs only at low light intensities when the reaction is light limited; if some other process limits photosynthesis, the efficiency will be considerably lower.

Photosynthesis manifests itself in a variety of forms throughout the plant kingdom. Certain microorganisms which grow in the dark reduce carbon dioxide to carbohydrate (in this case the metabolites must be such that the overall reaction is exothermic), which means that the carbon dioxide reduction in normal photosynthesis does not have to be sensitized by light. The light energy in some not well understood manner gets picked up from the excited chlorophyll molecules and is fed into the metabolic chain.

Cells as a rule are situated in a fluid which supplies the metabolic fuels and also carries away the waste products. Thus metabolism is to some extent governed by the physical laws of diffusion. A spherical cell in an infinite medium presents a simple geometry, and the diffusion equation can be solved quite simply for this case. This situation can be approximated experimentally for the case of eggs or bacteria immersed in a fluid. The relevant experiments have been made on the metabolism of both arbacia eggs and luminous bacteria, specifically for the case of low oxygen concentrations. The experimental results on oxygen consumption as a function of oxygen concentration are fairly well represented by the theoretically calculated curves, while the diffusion coefficient inside the cell and the permeability of the cell membrane are given reasonable values by the experiments.

Two other fields of research to which physical and chemical techniques are being applied should be mentioned. They are the behavior of muscles and the mechanism of nerve conduction. Much of the knowledge about muscle behavior has come from the work of the biochemist, A. Szent-Gyorgyi. As mentioned above, the energy for muscle contraction is supplied by the phosphate linkages in ATP. It is also known that potassium plays a vital role with regard to the electrical properties of the muscle; the basic reaction in contraction of muscle involves a loss of electric charge by certain molecules.

When a nerve fiber is stimulated, the excitation travels along the fiber in the form of small electric currents. Since the phenomenon is essentially an electric one, knowledge supplied by physics can be used, and several mathematical treatments of excitation and conduction have been proposed. One of these is based on the Ostwald-Lillie iron wire model which is an inorganic system resembling the nerve in many respects.

As was emphasized above, enzymes play a fundamental role in practically all life processes. If we understood completely how enzyme action depends on its structure, and how enzymes are generated, we would have gone a long way to find many of the answers to the life riddle. The enzyme is a protein molecule made up of perhaps 10,000 atoms. This is a small number from the statistical point of view, especially since all atoms are not the same and since they are arranged in specific groups which act essentially as units. On the other hand, the detailed structure of the molecule with all its atoms seems too complicated to be calculated by a straightforward application of quantum mechanics. There are no methods known to physics at the present time for calculating these intermediate-sized aggregates; but one might conjecture that if such a method were discovered, it would allow great advances in biology.

Genes and Mutations

The science of genetics started with the experiments on the garden pea by the Augustinian abbot, Gregor Mendel, although it was not until the rediscovery of his work half a century later (about 1900) that the science began to develop. Genes, the entities responsible for passing hereditary characteristics from parent to offspring, at first were considered merely hypothetical carriers. They have since been identified as a physical part of the chromosome, which exists in pairs in the nuclei of the cells making up the organism. One of the pair is an exact replica of the chromosome transmitted by the mother, the other an exact replica of the chromosome transmitted by the father. During normal cell division each chromosome reproduces itself, and thus each daughter cell gets an identical set of chromosomes and therefore identical sets of genes.

An important fact for the physicist is the permanence of the gene; this structure faithfully transmits the hereditary traits over many generations. This great stability means that a gene is certainly a molecule. An approximate size for the gene can be obtained from the observed domain of influence in the chromosome and from x-ray experiments to be described later. The gene molecule is made up of about 10,000 atoms and is perhaps very similar to the enzyme molecules described in the last section.

Although the gene displays its permanence over many generations, it is not completely permanent. and it is this slight impermanence which is essential for evolution. Mutations were discovered about fifty years ago by the Dutchman, deVries. He found that occasionally the offspring of pure bred stock showed small but discontinuous changes in certain of their characteristics, which were subsequently inherited. Apparently the gene which governed this characteristic had been altered. It is of course upon these mutations that natural selection and evolution depends.

If a gene is a molecule, how do we explain the mutations which are apparently due to some alteration of the gene? Quantum mechanics gives us the answer; it explains both the strong forces which give the molecule its essential permanence, and also the quantum transitions which cause a slight lack of permanence. These quantum transitions occur between isomeric gene-molecules, i.e. they convert the normal gene-molecule into the mutated isomer. Isomers are quite familiar to the chemist, being molecules which have the same numbers and kinds of atoms, but with different molecular structures. It thus follows that the physical and chemical properties of isomers are different.

Molecules the size of a gene can, of course, have many isomers. Not all will represent the same degree of organization as a gene, but it is certainly conceivable that a large group of them will be genes which transmit definite but different hereditary characteristics. These isomers correspond to minimum energy configurations since they are stable structures; this does not mean that they all have the same energy, but it does mean that they all have low energies, and to get from one stable state to another it is necessary to distort the molecule, thereby going through a region of higher energy. It is something like the situation on a rollercoaster; here the track is made up of hills and valleys. The valleys correspond to the stable molecules, since it takes energy to leave the valley; the hills correspond to the potential hills (or barriers) which separate the stable configurations. During a mutation the gene molecule receives energy from some source (heat energy or cosmic rays), is lifted to the top of the potential hill, and drops into another stable configuration. Of course not all mutations will be equally good; in some cases the mutated gene may be so disrupted that it cannot perform the proper vital functions, and death to the individual will result. Natural selection picks out the fortunate mutations and uses them to change species.

The quantum theory of mutations, the work of the physicist M. Delbrück, has been subjected to certain experimental verifications. First of all, the percentage of mutations in the offspring can be increased artificially by irradiating the parents with x-rays. It is found that the increase in mutation rate is proportional to the x-ray dosage, and also that all wavelength rays from soft x-rays to hard gamma rays are equally effective as long as the dosage is the same measured in r-units, an r-unit corresponding to a definite amount of secondary ionization. This leads to the conclusion that a mutation by x-rays is not an accumulative effect due to many quanta, but is a single event due to the chance hitting of a particular gene by a single quantum. The gene, therefore, applies the energy of the quantum (more exactly the energy of one of the secondary ions produced by the quantum) to lift itself over the potential hill. Since we know quite well the amount of ionization produced by x-rays, these x-ray induced mutations allow us to estimate the size of the gene.

A second set of experiments is concerned with temperature induced mutations. The atoms in the molecules always have a certain amount of thermal motion at any temperature above absolute zero. It is known from statistical mechanics that the probability that thermal energy will raise the system over a particular potential hill is proportional to an exponential quantity involving the potential barrier, the absolute temperature, and Boltzman's constant. The law was tested by rearing fruit flies at various temperatures. Not only did the mutation rate follow the exponential law within experimental error, but the value of the potential barrier determined by the data turned out to be of such an order of magnitude as to make mutation a rare event, although not an impossibility. Thus Delbrück's theory of mutations stands the experimental tests fairly well. This theory is discussed at considerable length in the book by E. Schroedinger, What is Life? (Cambridge University Press).

The actual mechanism by which a gene reproduces, or exercises its controls, is not known. It has been suggested that gene reproduction may be an autocatalytic process, i.e., a type of reaction in which one of the reaction products catalyses the reaction.

Finally, we should say a word about viruses. A virus is a small independent structure which can reproduce itself under suitable conditions. Again it is about the size of an enzyme molecule. It appears as if enzymes, genes, and viruses are all very similar both in their structures and in their behavior. The viruses present one of the best opportunities for studying living reactions, since they are relatively simple structures, not having to support a metabolism. Their reactions are not bound up with and dependent upon a much larger and more complicated structure, as is the case with genes and enzymes in the cell.

Intelligence

If physics and chemistry are capable of explaining the various aspects of life, it is likely that intelligence will be the last aspect to be explained. First, one must discover the physicochemical equivalent of an idea which, it must be admitted, is likely to be difficult. If the problem is solved, one should then be able to understand memory, the storage and classification of ideas for ready use, and learning, the formation of new ideas. The next step would be to find how the brain weighs ideas and decides among them. It does not seem that psychology in its present form is apt to help much along these fundamental lines, for it is a completely phenomenological science which tries to learn how the brain works as a brain and not how it works as a highly specialized grouping of physicochemical substances. In order to get at the fundamental questions one must take the brain apart piece by piece. The difficulty here, as in all biological research, is that dissection changes the specimen to such an extent that the properties which the researcher seeks to explain are destroyed.

Niels Bohr has suggested that there may exist a principle of complementarity between life and physical science. The principle says that the two modes of description of a system, one on the basis of its aspects of life, the other on the basis of physical processes, cannot both be applied simultaneously. This is analogous to the principle in wave mechanics that the wave aspects and particle aspects of a system cannot be observed simultaneously. According to the principle, an attempt to follow the physical processes in a living organism exactly will necessarily kill the organism.

Whether or not the complementarity principle is fundamentally true, it apparently has a certain practical truth, as is made evident by the difficulties encountered in biological research. Those who do not subscribe to the complementarity principle may say that now that we know what questions to ask, ways will soon be found to answer them.