THE MEANING OF BIO-ELECTRIC POTENTIALS*

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Design in living things is the most important problem in biology for not only are the patterns which plants and animals exhibit the cornerstones upon which rest description and classification, but also they are the expression of those underlying forces which impart stability in the midst of chemical flux. The search for the origin of that design is the province of genetics and of embryology, but it must necessarily be guided by a fundamental philosophy as to the nature of things. Fortunately, the forces by means of which the design is worked out in the matrix of protoplasm are matters which are capable of analysis by the experimental method. Exception to this statement has been made by certain biologists who have sought to explain the mechanism through the medium of some indefinable causal principle, such as the teleology of Aristotle and the entelechy of Driesch. Modern investigators have sought the answer in living things themselves and have proceeded, in general, along two lines. One of these begins with the assumption that the total pattern is the consequence of the summation of innumerable and often different entities. This point of view asserts that if all the building blocks could be neatly isolated and labelled, the form could be compounded from the shape and properties of the units. By contrast, the second avenue of approach starts from the assumption that the ultimate design is a function of the possible relationship between entities rather than the characteristics of the units themselves. Investigators starting with this premise lay emphasis upon the dynamic properties of the living system rather than on the chemical constituents. In modern science the atomistic approach is exemplified by the encyclopedic work of Needham, who, in his Chemical Embryology and in his more recent Morphogenesis and Chemistry, reviews the very interesting story of the search for the ultimate chemical constituents to be found in every part of a living organism. Needless to say, information of this kind is essential. No final answer can ever be given without it. It tends, however, to ignore the fact that there are important describable relationships between the units no less significant than the entities themselves. The proponents of the

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relational approach have been stimulated greatly by the experimental biologists in general and, more particularly, by the great experimental embryologist, Spemann. The discovery of the important relationship between two different tissues resulting in the organization of the nervous system through the infolding of the dorsal lip of the blastopore, and the phenomenon of induction following upon the impact of one kind of tissue on another, has emphasized the significance of the interaction between parts of the system and to some extent of the action of the whole upon its constituent parts. Childs has used this approach very effectively in his development of the theory of physiological gradients. This has shown that an area of high metabolic activity seems to exert some kind of a dominating influence over areas of lesser activity.

The great difficulty with the second line of attack lies in the many obstacles to quantitative measurement of the relational properties. This has led many investigators to believe that further search in this direction is not likely to be fruitful. Fortunately, however, there is another way of attacking this problem which may yield significant results. It is well known that in the inanimate world a valuable way of studying relationships between entities is through the analysis of electrical properties and forces. The development of the modern vacuum tube has made it possible to apply some of these methods to the study of living things. In 1932 Burr, on the basis of an analysis of the development of the nervous system in the salamander, proposed a solution to the problem of the patterning of the nervous system through the use of electrical technics. He proposed the assumption that every living thing had as one of its characteristics an electrodynamic field. This field was to be thought of as a primary property of protoplasm; just as significant a property as its irritability, its metabolic capacities, and similar attributes. Such an assumption requires experimental validation in the laboratory of the existence of the field in measurable form, of the relationship of this field to the design of the whole organism, and the modification of development through change in the field of the organism by an applied external field. A more complete formulation of this thesis was made by Burr and Northrop (1935).

In order to make a study of this kind possible, it is necessary to have at hand a reliable technic by means of which some significant property of the field can be measured accurately. Fortunately, a standing potential difference is such a measurement. Using vacuum tubes it has been possible to develop a microvoltmeter and a technic for its use which gives a fairly adequate picture of the potential difference between any selected pair of points in the living system. By means of this procedure, the existence of relatively steady-state standing potentials have been demonstrated in the frog and salamander. These exhibit a characteristic pattern and constitute an electrical field. One particular finding is of importance. During the course of an investigation of the standing potentials of the frog's egg, it was shown that the animal pole of the egg has a characteristic electrical pattern. In spite of its uniform appearance, electrical differences could be recorded which define a pattern in the unfertilized egg. This pattern could be seen in eggs before and after fertilization, and through all the stages of segmentation and gastrulation, including the formation of the neural plate. The axis of this pattern was found to coincide with the longitudinal axis of the embryo.

These findings suggest very strongly that the field, indicated by these patterned electrical differences, is a constant concomitant of development. In other words, the evidence points to the conclusion that the field is present before visible structural differentiation occurs and is in some measure a determiner of the pattern of the differentiation. The most satisfactory evidence for the validity of the assumption would appear if it were possible to change development by modifying the field of the embryo through the impact of an external field. A number of attempts have been made to do this, notably by Gray, without success. The failure of these experiments does not constitute any refutation of the electrodynamic theory. A little elementary calculation shows that by no stretch of the imagination could the electrical field derived from a battery of low voltage applied to a developing chick embryo create thereby an external field of anything like the magnitude of that of the embryo. The field intensities of the organism far transcend those of any other known field except the gravitational field. The voltage gradient, for example, across a cell wall of molecular thickness, runs from 50 to 150 mvs. If this is calculated in the more familiar volts per centimeter, it reaches an astronomical figure. It is, therefore, highly improbable that a DC field of sufficient intensity can be set up in such a form that it might be expected to modify a biological field.

Further evidence supporting the field theory has been found in a study of the electrical correlates of form in the cucurbits. In collaboration with Sinnott, a positive correlation has been recorded between the long and short dimensions of three races of cucurbits and the potential difference corresponding to these axes. Moreover, in the "elongate" form the gradient of the potential difference in the long axis increases with age. Conversely, it decreases in the "flat whites" and remains practically unchanged in the "rounds." This close correlation between potential difference and form suggests very strongly a highly significant relationship.

It is clear that these studies arise from two sources. The first of these is the working hypothesis of the field theory. This theory was derived from numerous reports in the literature. It has been customary in the past to look upon all electrical manifestations of living things as by-products or consequences of chemical processes. The primacy of the forces which are measured by electrical devices throughout the material universe raises the possibility that in living organisms these same forces might operate with the same primacy. From this standpoint then, living beings like inanimate material things, would depend for their pattern of organization upon electrical forces.

The second source of these studies is a body of data collected by means of a technic which, while not uniquely new, yet possesses at least three significant attributes. One of the great difficulties of earlier measurements lay in the fact that the majority of them were made with current drain devices. In other words, they required power for their operation, drawn from the system measured. The vacuum tube microvoltmeter was developed to reduce the current drain to an insignificant minimum. As a result, it has been possible to measure potential difference more or less independent of current and resistance. Under normal operating conditions the current drain varied from 10^{-10} ampere to 10^{-12}. Changes in resistance in the system measured have no effect on the final reading except where, either in the electrodes or in the living organism, the resistance exceeded 5 megohms. This last value could of course be increased significantly by increasing the input impedance of the microvoltmeter. In addition, the instrument was so designed as to operate at free grid potential. This was introduced into the design as a means of controlling the power requirements of the measuring device. Finally, by means of non-polarizing and reversible electrodes it has been possible to make the great majority of determinations on the intact living organism with virtually no disturbance of either structural or physiological mechanisms. This last is a highly important point. Much of the experimental work done in the biological field involves more or less serious disruption of the living organism. So-called units have been isolated from the rest of the organism and examined with meticulous care without regard to the fact that the unity of the whole organism has been seriously disrupted. While many biological processes seem to carry on fairly effectively for short times when removed from the total organism, there is always the very grave possibility that the recorded data are both incomplete and not a true picture of what happens in the intact being.

The argument here presented is an example of the application to the field of biology of the well-established methods of science used most successfully in the field of physics. Since the time of Aristotle, biology has been almost exclusively a descriptive science. This is, of course, a basic requirement of our understanding of the world about us. However, there comes a time when the major descriptions and classifications are completed; when the mind of man no longer asks, "what?" but "how?" and "why?" This is the point at which meaning enters the picture as a significant element.

The ultimate goal of science is an adequate understanding of the meaning of the Universe and more particularly the meaning of man and his relationship to that Universe. This is a problem which every human being must solve sooner or later. Any consideration of the meaning of observed differentiations in the external environment always involves an examination of the relationships between the describable entities. While many of these relationships can be expressed in feet and inches, or in minutes and seconds, the ultimate design involves far more than this. To recognize the design is fairly easy, but to understand it is extremely difficult. It is here that one of the unique properties of the human mind becomes most significant. Sometimes through conscious discriminations, but perhaps more often from intuitive syntheses, new and unexpected relationships are imagined. This is the stuff from which a theory or a working hypothesis is constructed. Tentative formulation must follow and then a complete and rigorous set of logical consequences must be prepared. The experimental laboratory then becomes the seat of an exciting effort to determine whether or not the logical consequences are true. If, in other words, there is a correspondence or an epistemic correlation between the logical consequences of a theory and the experimentally determined facts, it is safe to assume that the theory is true, although of course not necessarily the only theory which those facts may support. If the correspondences do not exist, the theory either must be discarded or rigorously modified.

Application of this procedure to the determination of the meaning of potential differences yields not only a validation of the electrodynamic theory but also a number of new ways of regarding the electric manifestations of life. If, as a starting point, it be assumed that electrical forces are as primary in living as in non-living things, then it must follow that protoplasm, the physical basis of life, must exhibit meaningful electrical manifestations. These are as fundamental as those other properties of protoplasm, descriptively designated as irritability or metabolism, or reproduction.

From such a viewpoint, the electrical properties of living things are given a primary attribute of life. The pattern of the potential differences, which in some measure is an evidence of an electrical field, is a correlate of the design in protoplasm. A set of potential difference measurements provides a picture of the magnitude and direction of those electrical forces which determine the position and movements of all the charged units in the system. At best, however, these measurements are only a gross statistical average of innumerable local cellular potential differences. Hence, only in single cell systems, as Lund and Osterhout have shown, is there found any accurate picture of the field intensities.

Potential difference measurements provide clues, not only to the pattern of the field forces but also to the energy content of the field. This is important because the living process itself requires energy. It has been generally assumed that the chemical reactions of metabolism meet this requirement. Energy is stored in chemical form within the substance of the protoplasmic matrix. Since a living system is never at equilibrium, some energy must be continuously expended. When protoplasm is stimulated by change in the external or internal environment, and the propagated change results in some form of response, greater amounts of energy are required. Moreover, much of this energy must be immediately available. The propagation of a neural impulse, or the contraction of a muscle unit is rapid and hence the energy drain must be equally fast. The potential difference can be thought of, then, as an index of the amount of energy present in the system, as a reservoir from which energy can be drained rapidly to meet the exigencies of activity. At this point the chemistry of metabolism steps in to re-establish the energy levels so that the cycle can be repeated. The electrocardiogram and electroencephalogram are records of such cycles repeated rhythmically. To some extent, then, potential differences measure metabolic activity, since a record of the latter reports the amount of work required to refill the electrical reservoir. The chemistry of the cell is, therefore, of major importance. However, attempts to explain the standing potential on chemical grounds alone nearly always result in confusion and disagreement. Studies of ionic mobilities, concentration gradients, and the like, provide important information, but there remains a body of phenomena which they do not explain. From the standpoint of the argument presented here, it is the unexplained phenomena which can be understood best as electrical manifestations of a field and its stored energy. Specifically, this would mean that each kind of biological activity, such as muscle contraction and nerve impulse propagation, would present its own characteristic electrical correlate. Thus, it is possible to differentiate the activity of the brain from that of the heart. The change in standing potential which accompanies the phenomenon of ovulation is another example of a specific tissue activity. In all probability, all forms of biological activity will be found to possess characteristic electrical signs. It must be emphasized that the point of view here presented requires consideration primarily of relationships. It is not concerned with the entities themselves, but with those forces which bind the units into an organic whole. By virtue of the fact that only relationships are studied, a significant datum is the potential difference between two points. Willard Gibbs pointed out long ago that in fluid systems there is no meaning to potential at a point. This is exactly the opposite to what is true in the material universe, for potential at a point is there defined as the energy necessary to transport a unit charge from infinity to the point in question. In fluid systems the charges are not electrons but are to be found associated with ions. Hence, potential measurements in fluid systems show only the relationship between two parts of that system. The significance of this is clear, because to ascribe meaning to a potential at a given point on or in any living system is an obvious fallacy. Recent criticisms by Rock and his associates, of the changing potential during ovulation, are an example of this fallacy. There is no reason to expect some magic potential in the ovary. There is none and there cannot be one. Iso-potential points have meaning only when measured against a particular reference point which in itself may be changing. It follows, then, that the geometry of electrode placement becomes a matter of major importance. In living systems, therefore, any reports of standing potentials or changes in the potential differences must refer only to the pair of points described in the given experiment. The meaning lies in the potential difference, not in the location.

What, then, is the meaning of standing potentials in living systems? Following the argument here outlined, the recorded potential differences are measures of a store of electrical energy which can be drawn upon by biological activity and, hence, they provide valuable evidence of the nature and range of those activities. Moreover, the pattern of the potential differences defines an electrodynamic field whose forces critically influence growth and development and determine the pattern of living things.