DESIGN IN THE NERVOUS SYSTEM [1]

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Human behavior, the unsolved problem facing mankind, is the consequence of the activities of the nervous system, the result of the structure and function of its component parts. It is not the pink pill taken before breakfast, or how your endocrines have been stimulated the week before, or what vitamins you have been taking, that determine behavior. They contribute to it, because all these chemical phenomena are, in the last analysis, the source of energy with which the nervous system operates; but that energy is undirected. It is the job of the nervous system to direct that energy in specific directions. This pattern of organization of the nervous system, at the heart of behavior, is an exceedingly complex piece of machinery of such precision that man, even in his modern vanity, has not yet been able to duplicate it. It is a piece of machinery, however, a physical-chemical system which exhibits certain properties and certain structural foundations for those properties. If ever we are going to be able to understand what human behavior is like, one of the requirements is understanding of the structural and functional components of the nervous system. We know that the nuclear masses within the neural mechanisms occupy positions which have extraordinary constancy over the whole vertebrate scale. It has been shown that the ocular motor nucleus, for example, the third nucleus, occupies the same relative position in the vertebrate nervous system, in all vertebrates, with a variability of less than 2%. Some forces must be operating power-

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fully in the living system to establish this necessary relatedness, especially when we stop to think of the incredible flux of chemicals that is going on in the living system at all times. We know, furthermore, that the axis cylinders of the neurone in the ocular motor nucleus move out to their peripheral connections in the extra-ocular muscles with precision and accuracy and certainty. There must be directive forces which determine the position of the nucleus in the first place, and the distribution of its processes in the second place. What is the nature of the forces that can do this kind of thing in the nervous system?

When you think about this at all, it will be clear that this is a very special case of the general problem, characteristic of all living systems and of the universe itself, for that matter, of the origin of pattern in nature. What are the forces that impose this design on nature? This is a problem which goes back to Aristotle who first posed it. He asked the question: Why does an acorn always grow into an oak tree and not into a fig tree? You remember he listed a number of causes — the material cause, the formal cause, the final cause — which were fairly adequate descriptive terms but were not things capable of being subjected to any kind of scientific analysis. Down through the ages since then, a few people have attempted to answer the question. The dualism of Descartes and the entelechy of Hans Driesch, among others, maintained that this is an insoluable problem. All we know is that something "sits" on the living system and guides and directs its growth and development from fertilization to death. This is one aspect of the mind and body problem. It is also the problem of the relationship between man and his soul that most of us, at one time or another, have to face. Descartes placed the soul in the pineal body; at Harvard it has been reported that the pineal body from fifteen beasts, given to mentally deranged people, has straightened them out.

Most people who have been interested in living things have dodged the issue. It can be argued, nevertheless, that the soul is a qualitative attribute of the functioning nervous system. Where, then, does the living system get its pattern of organization? It is a pattern so precise that we can classify animals on the basis of it. The majority of us have pushed it into the darkest corner of the darkest shelf of the darkest closet of the darkest part of the attic and left it there, deciding it was an insolvable problem. Some of us, however, have an incurable curiosity about these problems and are not content to leave it in the darkest corner of the attic shelf, but rather want to find out whether there is any possible solution to this question: — What is the nature of the forces which define design in the nervous system in particular, and the living system in general?

To solve a problem of this kind, the scientific method should be employed. The method has been deified to some extent and surrounded by a lot of obscurantism which is quite unnecessary, because the procedure is that by which you and I live all the time — betting on the horseraces, a bridge hand or poker hand; in general, solving perplexities of existence.

The method of science involves, basically, three things. All the information about the background of the area in which you are interested is collected. This has been called the natural history of science. Who else has looked at this problem, and what has been found? Obviously, in this day and generation, no one man can cover all the evidence. One has to read as widely as possible, take bits of information here and there and pile it up somewhere in the back reaches of the mind to let it soak until one day — it happens to all of us — an idea appears suggesting some unsuspected relationships in the components of the natural history background of the problem. If it is your idea, it is a brilliant idea; if it is the other fellow's idea, it is not so smart — maybe naive. Nevertheless, it is an idea. At one time Einstein was discoursing on the method of science. He called attention to the fact that no one could legislate an idea. It comes out of the blue into the here without any hinderance. You cannot call it when you want it, you cannot define the conditions which elicit it; it just turns up. Sooner or later some unsuspected relationship in the things which are observable is seen; or a relationship which has not been conceived by other people. This idea is then formalized — technicians call it an hypothesis, a theory — but actually it is just a hunch, like horseracing and bridge played. The question is asked, Have I a good bridge hand? If you have one, then certain things will follow logically. So, if you have a hunch or an idea, certain things should follow logically. Thus, in the method of science, an hypothesis is erected from which the logical conclusions are deduced. Then comes, of course, the third component of the scientific method, the test of the logical conclusions under the controlled conditions of the laboratory.

How this is done is not too hard in the inanimate world. It is much more difficult in some aspects of the living world. The controlled experiment must be set up in such a fashion that the possible artifacts are reduced to a minimum. In laboratories, if your logical conclusions demand certain results, and you find them in the laboratory under controlled conditions (these are what Northrop calls "epistemic correlations," and Margenau calls "correspondences"), it is the tendency of all of us to say, "Aha! I have proved it." Nothing is further from the truth, of course. This is the fallacy of assuming the logical consequence, because there may be other hypotheses, the logical consequences of which will yield the same laboratory results.

If this method of attack is applied to the problem of the origin of design of the nervous system, some interesting results emerge. This is not the time or the place to review all the natural history, the evolution and the ontogeny of the nervous system of vertebrates from amphioxus to man, but there are certain things that can be selected from the available information which are useful. One of these is this:— If you spend any time studying embryos, as Dr. Davenport Hooker, Dr. John Nicholas, and Dr. Samuel Detwiler, among many others, have done, some very interesting facts appear. It was a habit for awhile, at least, to assume that working with embryos at certain stages of development, significant answers to questions about the origin of design might be forthcoming. I doubt very much if this is so. Some interesting facts have been reported which contribute much to the basic problem but have, as yet, told us little about the origin of design.

The nervous system of a salamander, for example, has a pair of cerebral hemispheres and a brain stem similar to that found in man. On each side of the head are a pair of thickened patches of ectoderm which are the source of the neurones which make up the olfactory system. These are the olfactory placodes and under normal conditions a neurone, a cell body, lies in this placode and sends its axis cylinder into the primitive cerebral hemisphere. This is the normal story. What happens when you remove this placode? Little happens. The hemisphere with a placode continues to grow; the other does not. One is smaller than the other. This change in size of the hemisphere occurs about the time the animal begins to eat, begins to use his smelling organs as a method of acquiring food. So it is not too hard to guess that the reason why one is larger than the other is because one side of the brain is smelling and the other is not. So the old problem of nurture versus nature appears. As a matter of fact, by a variety of tests, it has been demonstrated that this is not true. It is not function that resulted in the size differences; rather it was the actual presence of ingrowing axis cylinders.

If a smaller hemisphere is found when its placode is removed, what happens when an additional placode is placed beside that of the host? There should be twice as many olfactory stimuli coming into the hemisphere and, as a matter of fact, there is about a 30% increase in the number of cells in the hemisphere under these conditions, but not twice the number. Hence, function was not the answer. On the contrary, it was the telodendria of the additional neurones that produced the hyperplasia.

Not all the fibers from these cell bodies grew into the normal area in the primitive forebrain. It once was said that the reason the fibers grew into the forebrain was because of some chemical agent which attracted the growing axis cylinders. In a certain number of cases, however, the new neurones grew caudally past the hemisphere, finally penetrating the wall of the diencephalon, ending about a mass of cells which are undergoing rapid cell division, in the wall of the thalamus. What made the axis cylinder from this transplanted cell body (supposed to be an olfactory unit) leave its normal distribution in the forebrain and travel back to end in the thalamus, a part of the nervous system which is concerned largely with visceral and visual functions? This raises a peculiar and exceedingly pertinent question. Here is a neurone in a strange position, developing a strange process and going to a strange place. A study of a series of sections made from such an experimental embryo suggests that this strange neurone knew where it was going, not just wandering around through the tissues of the head, but headed for this particular area. A search through this region of the embryonic head reveals a mass of rapidly growing cells in the wall of the hypothalamus at the stage when the axis cylinders reach this area. In the literature there is evidence that rapidly growing masses of cells give rise to chemical substances which attract a growing axis cylinder. Detwiler reported this in limb transplants.

This cannot be the solution even though many modern chemists talk about short range or contact forces, never of long range forces. Many will not admit the existence of long range forces; forces, rather, are contact forces, where two things are in actual apposition. It is difficult to imagine a chemical substance which could seep through the wall of the neural tube only at this point, thereby leading the growing nerve to this particular group of cells. Examination of the whole length of the neural tube reveals, on the other hand, as Herrick and Burr have pointed out, that there is a mass of rapidly dividing cells opposite the point of entrance of every sensory component of the cranial nerves. This suggests that an actively growing mass of cells provides an attractive force operating over a distance on the growing axis cylinder. But what could be the nature of this force? It is not a contact force and it is not a short range force; it operates over a distance.

In the natural history background it will be found that a Russian botanist named Gurwitsch, a good many years ago, made the observation that if an onion root tip in which mitosis was evident, was directed at the side of another onion root where there was no mitosis, the cells in the second onion root suddenly started to divide. Gurwitsch postulated that the dividing cells gave rise to mitogenetic rays. I do not know whether or not there are any such things as mitogenetic rays. Very competent people have said that they exist and have determined the length of such rays in angstrom units. Other equally competent students have denied their existence. But if such phenomena exist, it follows that rapidly dividing cells may exhibit properties which can be measured by electrical instruments. The electrical activity of living systems then becomes interesting and important.

Early in the 1920's Ingvar came to this country to work with Dr. Ross Harrison and set up a laboratory experiment in which he subjected the growing axis cylinder of neurones in tissue cultures to an electric environment. He demonstrated that an axis cylinder growing out of a cell body could be diverted from its normal course to grow toward the negative side of the imposed field. This implies that there is an electrical component in the picture, not just a chemical one. An extensive literature has developed in this field, sparked by the important work of Lund and his associates and students. Evidences of this kind suggested that a careful study of the electrical phenomena to be found in growing things might yield interesting facts. At a meeting of the American Association of Anatomists, at Columbia, in 1929, therefore, Burr suggested that examination of the development of the pattern of organization in the nervous system of the salamander might reveal some electrical properties which could be considered to be measurable attributes of an electrodynamic field. Ingvar's work suggested this, as did Lund's work with lower forms. With ths natural history background it seemed pertinent to ask, "What do we know about the electrical properties of living systems?" Back in the 1920's EKG's were just beginning to be important; EEG's were recognized, as well as action current potentials in the nerve fiber, potentials of contracting muscles, and potentials in secreting cells, etc. A lot of scattered information was available with no single basic assumption which would tie them all together. If field properties could be demonstrated, a common basis for all the electrical phenomena would be at hand, since all the electrical phenomena could be variations in the relatively steady state standing potential of the electrodynamic field. A very cursory review of the natural history of the electrical properties of living systems — from Galvani with his frogs' legs down to the development of the string galvanometer and the appearance of EKG and EEG — suggested further study, in part because the results were often exceedingly contradictory. It seemed probable that the reason for the variability in results might be due to the fact that all the methods of observing the electrical properties of living systems in the past had made use of current drain instruments — meters — meters which require current for their operation, current which must be taken fom the system being measured. In other words, the measurement disturbed the thing being measured. This makes accurate determination difficult, if not impossible. It seemed necessary, therefore, to develop a procedure which would disturb the living system electrically minimally, or not at all.

About that time, in the early 30's, I had the great good fortune to discuss this problem with F. S. C. Northrop, one of the best minds this country has produced. An extraordinarily able man, he had worked on some aspects of this problem while a student of Lawrence Henderson at Harvard. He had spent a good deal of time trying to work out a reasonable basis for the origin of pattern in material universe, the position and movement of the stars in their courses and of form in nature. The results of that study were published in a book called, "Science and First Principles" which is recommended as an exercise of major importance to every thinking person. As we talked, I asked, "What would you think of a field theory for living systems?" because, in his study, he had been unable to find any evidence in biology for the existence of an electrical field such as exists in inanimate nature. It has always been assumed that the EEG and EKG and the rest, were the consequences of physiological activity, and that all electrical phenomena were, therefore, a by-product of the living process. The net result of our talk was that in 1935 he and I collaborated on a paper published in the Quarterly Review of Biology — Raymond Pearl was the editor at that time — called, "The Electrodynamic Theory of Life."

One technique that could be used in a study of electrical field properties is the quadrant electrometer, since it draws virtually no current from the system under study. This is a precision instrument of great sensitivity but with many drawbacks. After a few trials it was discarded, since it could not be readily adapted to the measurement of relatively steady state potential differences in living beings. A healthy respect for the modern radio tube led to the development, with the invaluable aid of Professor Cecil Lane of the Physics Department of Yale, of a vacuum tube microvoltmeter. With adequate sensitivity and workable stability, this instrument, under normal conditions, draws less than 10^{-9} amperes. Thus there was available an instrument which made it possible to make measurements on living systems without disturbing the system under study; that is, without drawing current from the living system and which was, therefore, independent of resistance changes in that system.

Good biologists usually are wary of theory, though they admit to two theories — evolution and genetics. Those are largely statistical theories, neither of which provides much information as to the mechanisms involved. The electrodynamic theory, on the other hand, provides a single basic assumption — logical deductions from which would require answers to questions capable of laboratory analysis.

With the voltmeter, Northrop's help, and the very great help of Leslie Nims who perfected proper electrodes, 4 questions were asked of Nature:

1. Are there electrical properties in living systems which can be measured with certainty and accuracy?
2. Are these measurable electric properties of the living system chaotic, or do they exist in a pattern?
3. If these electrical properties, measured with certainty and accuracy were obtained, is there any sense in which they may be said to constitute a fundamental electrical field?
4. Finally, if these electrical properties exist in a pattern and constitute an electrical field, is this field a by-product of the living process or is it, in any sense of the word, a determiner of it?

Very close to 200 papers have been published providing affirmative answers to the 4 questions. Of these studies, three groups have specified reference to the nervous system. That the human nervous system exhibits certain fundamental patterns is well known. It has first of all a longitudinal axis — a head-tail axis — around which is hung a bilateral symmetry, a right side and a left side. What forces determine this symmetry? One clue emerges from electrical measurements. In the salamander egg, with an electrode at the north pole of the egg and another at 4 succesive areas around the equator of the egg, it turns out that there is a voltage drop — a gradient — between the north pole and each one of these 4 points. The magnitudes differ and show no symmetry. Observationally, the egg is a radially symmetrical system; but electrically it is not. There is one point on the equator where the voltage drop is greater than it is at any other point. If this point is marked and followed through development, it is found that the plane of this voltage drop establishes the longitudinal axis of the embryo, or at least is correlated with it. This suggests that these electrical properties are of considerable interest because the longitudinal axis maintains itself throughout all the life of the individual. It is a constant in development; a measurable constant in development.

These observations, together with Lund's, Ingvar's and others, suggested that there might be a significant relationship between the physiological activity of a nerve fiber and the voltage drop along its path. For example, anaesthesia of a nerve, such as the ulnar, and a measure of the voltage drop along its path, results in a complete reversal in polarity of the field. As the anaesthetic wears off there is a return to the normal pattern. This occurs not only in anaesthesia but also in section of the nerve. Conceivably, this could have practical consequences of some importance in peripheral nerve surgery.

Another very interesting phenomenon occurs in the excised frog nerve. If a frog nerve is placed in a proper chamber, with stimulating electrodes and a ground, then with a pick-up electrode which can be moved toward the nerve fiber or away from it in the air surrounding it, measurements can be made of the field surrounding the nerve fiber at rest and during a propagated impulse. Working with Dr. Alexander Mauro, the action potential in this nerve was measured at varying distances up to at least a millimeter from the nerve, in the open air. If this action current potential in the nerve fiber could be recorded outside of the nerve fiber, but not in contact with it, the nerve fibers must be surrounded by a field, just as Farrady's wire is surrounded by a field when a current passes along it.

Thus, electrical studies of bacteria, teleosts, amphibia, reptiles, birds, and man have demonstrated the existence of a quasi-electro-static field. This field is primary. The forces in it are of such a nature that they can, and probably do, determine the position and movement of all the entities in the living system. It constitutes a set of forces which establishes pattern and is, therefore, a determiner of the design of living things in general, and of the nervous system in particular.