Neural Theory and Modeling

Proceedings of the 1962 Ojai Symposium

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Edited by **Richard F. Reiss**

Associate Editors: H. J. Hamilton, Leon D. Harmon, Graham Hoyle,
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Preface

Various developments in science and engineering have in recent years combined to produce a surge of activity in neural theory and modeling. As in other interdisciplinary fields, research has been carried forward by a very mixed company of biologists, chemists, engineers, physicists, mathematicians, and computer specialists; these men have brought with them the research philosophies and methodologies peculiar to their own disciplines. The result has been a potpourri of partial theories and models, ideas and data, that is difficult to comprehend. The numerous studies have not in general been coordinated, and communication between individuals has often been confounded by jargon and conflicting attitudes. The confusion has been further amplified by the immense complexities of the research subject: the nervous systems of man and animal.

In the Spring of 1962, Dr. Harvey Savely, of the Air Force Office of Scientific Research, suggested to me that a small symposium be organized to facilitate communication between diverse types of theorists and modelers scattered over the United States and Europe. It was hoped that such a symposium would mitigate the present confusion by producing some agreements on aims, problems, and methods.

Under the joint sponsorship of the Air Force Office of Scientific Research and General Precision, Incorporated, a symposium was duly held at Ojai, California, on December 4, 5, and 6, 1962. The main objective in the organization of the Ojai symposium was to bring together the greatest variety of theorists and modelers possible under existing restrictions of size, time, place, and so on. As deliberately planned, the participants were almost evenly divided with respect to their backgrounds; slightly more than half of them were professional biologists, the remainder coming primarily from various fields of engineering and the physical sciences. There were twenty-four formal papers presented at the symposium, of which twenty-one appear in this volume. The subject matter of these papers ranges from highly speculative theories to rather detailed reports of physiological experiments thought to be particularly suggestive in the further development of theory.

All the papers in this volume were put into their final form after the symposium was over. Some of them have been modified in varying degrees as a result of discussions at the symposium. However, none of the discussions themselves have been preserved here.

The papers have been divided into two distinct groups. Part I is composed of papers which are predominantly theoretical or general in nature; with the exceptions of Pringle and Rall, all of their authors are non-biologists. The papers in Part II are concerned with theories and data derived from very specific nervous systems; with the exception of Fender, the authors of these papers are all biologists. The emphasis on invertebrate nervous systems in Part II is largely the result of an invitational policy followed in organizing the symposium. Invertebrate systems are simpler and generally more accessible than the much-publicized vertebrate central nervous system, and, in the opinion of the organizers (not to be confused with the sponsors), they are more promising subjects for detailed theoretical analysis in the near future.

Because of the rather sharp differences in subject and approach, the two parts of this volume have received separate and independent introductions. In the introduction to Part I, I have concerned myself primarily with the methodologies and objectives of papers which present formal theories and physical models. Since a few of these papers are in Part II, my introduction is not strictly limited to Part I.

The introduction to Part II has been written by a biologist, Donald Kennedy, who is an associate editor of as well as a contributor to this volume. The majority of papers in Part II are so closely connected with the experimental techniques and data of biologists that it was desirable to have this material reviewed by a professional biologist. Although Kennedy's specific comments are confined to the papers in Part II, his general remarks are relevant to the volume as a whole.

Thus to some extent both introductions are concerned with both parts of this volume; on a small scale they reflect the differing interests and criteria of the biologist and the non-biologist that are commonly met in the field of neural theory and modeling.

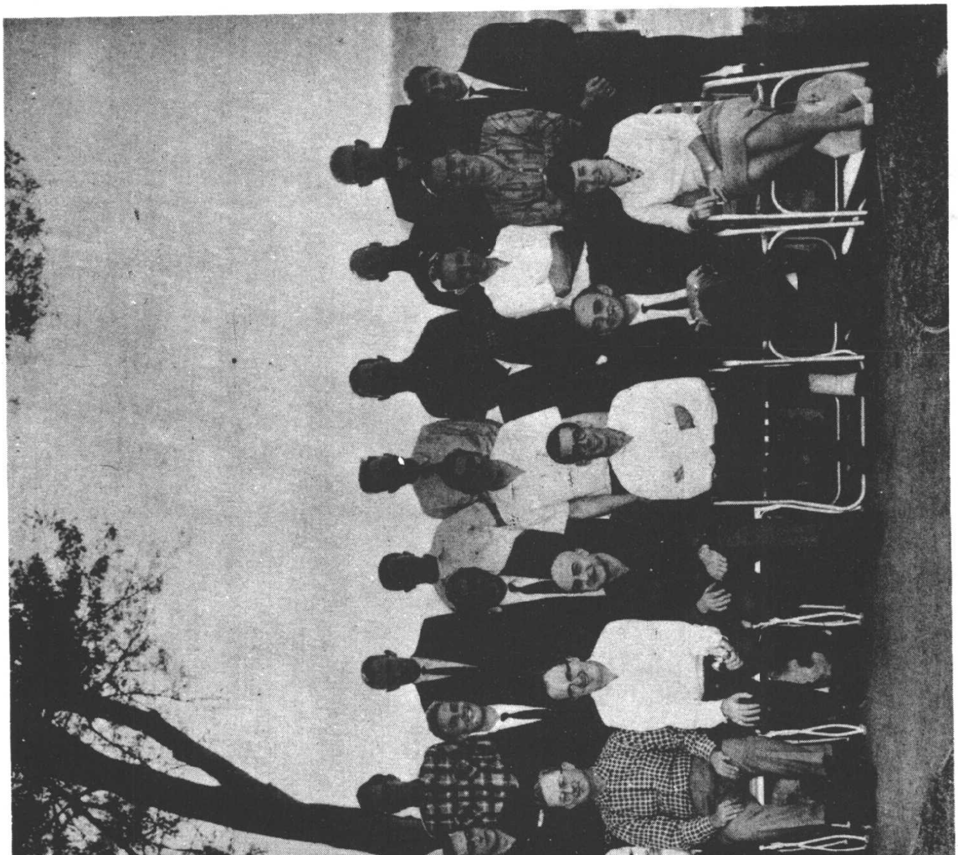
I wish first to acknowledge the invaluable assistance rendered by the associate editors, each of whom carefully edited a subset of papers. I also wish to thank the authors for their efforts and patience in revising their papers subsequent to editorial review.

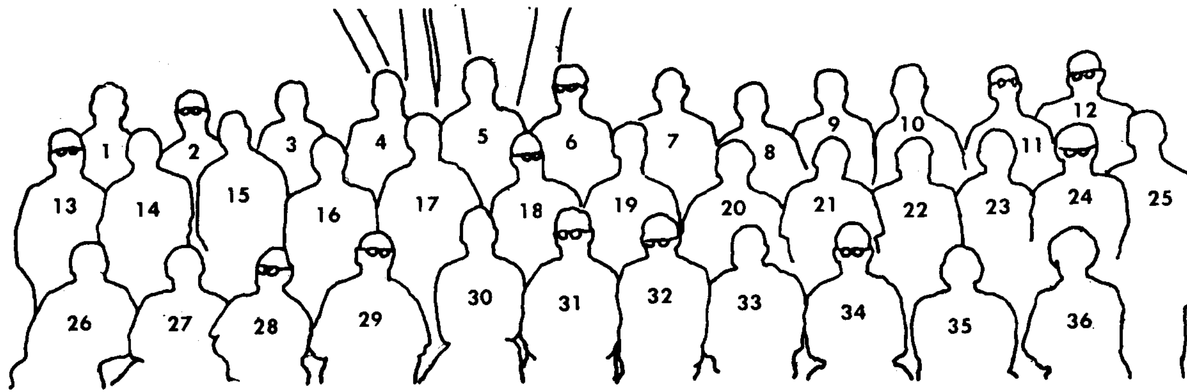
Although no transcripts of discussions are included in this volume, all formal presentations and discussions at Ojai were recorded by R. Vinetz; these recordings supplied valuable documentary support for editing.

It is fitting that I acknowledge here the services of T. H. Bullock; he provided aid in organizing the symposium and acted as a constant, effective, and tireless catalyst throughout the long and exhausting days at Ojai.

Finally, without the financial and moral support of the sponsors, the Air Force Office of Scientific Research and General Precision, Incorporated, the production of this volume would have been impossible, and their support would have been fruitless without the guidance and extensive aid provided by the staff of the Stanford University Press.

RICHARD F. REISS





Participants in the Ojai Symposium, December 4–6, 1962

1. E. R. Lewis, General Precision, Incorporated
2. R. Vinetz, General Precision, Incorporated
3. Lawrence Stark, Massachusetts Institute of Technology
4. Wilfrid Rall, National Institutes of Health
5. Charles Molnar, Cambridge Research Laboratories, USAF
6. Harvey Savely, Air Force Office of Scientific Research, USAF
7. Robert K. Josephson, University of Minnesota
8. James C. Bliss, Stanford Research Institute
9. Belmont G. Farley, Massachusetts Institute of Technology
10. H. D. Crane, Stanford Research Institute
11. M. R. DeLucchi, Air Force Office of Scientific Research, USAF
12. J. Thorson, University of California, Los Angeles
13. H. Mittelstaedt, Max-Planck-Institut für Verhaltensphysiologie
14. Ervin J. Nalos, Boeing Aircraft Corporation
15. H. J. Hamilton, General Precision, Incorporated
16. Leon D. Harmon, Bell Telephone Laboratories
17. Melvin J. Cohen, University of Oregon
18. Peter Kunze, Universität Freiburg
19. G. E. MacGinitie, California Institute of Technology
20. Derek H. Fender, California Institute of Technology
21. W. Van Bergeijk, Bell Telephone Laboratories
22. B. S. D. Raj, University of Oregon
23. Donald M. Wilson, University of California, Berkeley
24. G. D. McCann, California Institute of Technology
25. F. Jenik, Technische Hochschule, Darmstadt
26. Richard F. Reiss, General Precision, Incorporated
27. D. M. Vowles, University of Oxford
28. T. H. Bullock, University of California, Los Angeles
29. Otto Schmitt, University of Minnesota
30. J. W. S. Pringle, University of Oxford
31. L. Butsch, Aerospace Medical Laboratory, USAF
32. Graham Hoyle, University of Oregon
33. E. R. Caianiello, Università di Napoli
34. Donald Kennedy, Stanford University
35. C. A. G. Wiersma, California Institute of Technology
36. Ann Biederman, University of California, Los Angeles

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Part I

General Theory and Modeling

Introduction to Part I

RICHARD F. REISS, *General Precision, Inc.*

Although man's knowledge of his own and other animal nervous systems is still quite limited, the diversity of neural structures and functions already uncovered has led to the creation of similarly diverse theories and models. Like the fabled blind men who examined an elephant, each observer tends to generate a theory which reflects the particular type, level, and function of the nervous system which, for one reason or another, has attracted his attention. Thus it is not surprising that current neural theories and models, taken together, present a confusing and often exasperating jumble of logical forms and empirical correlations; many generations may pass before a remotely satisfactory unified picture of the whole beast or beasts can be constructed.

The present disorder is not entirely due to the chameleon-like qualities of nervous systems, the fragmentary experimental data, or the necessarily limited perceptual grasp of the individual human observer. In recent years there has been an accelerating increase in the number of neural theorists who initially trained and worked in nonbiological fields. These poachers in the domain of biology bring with them a wide variety of research attitudes, habits, prejudices, and analytic tools developed in their other occupations. Some of this baggage may prove to be a liability rather than an aid—it is too early to say—but it is clear that the influx of nonbiologists is contributing to the ferment and confusion. Speaking as a poacher myself, I believe that the confusion is a transient disturbance which will soon subside into well-ordered research; professional biologists are beginning to absorb the poacher's methods and ideology, and the poachers themselves are gradually being initiated into the often painful mysteries of biology. The chief short-term danger is that narrow enthusiasms in one faction will inadvertently mislead members of the other faction into wasteful or inappropriate projects.

As noted in the Preface, these factions are represented here by almost equal numbers of papers which have accordingly been organized into two groups. I have implied sharp factional differences which, in many individual cases, do not in fact exist. However, in general attitude and methodology, the papers in Part I are noticeably different from those in Part II. The nonbiologist modelers usually prefer to risk irrelevance by postulating universal principles which will satisfy their needs for economy and logic in model building. The biologists in Part II, on the other hand, tend to be conservative empiricists who are haunted by the diversity and variability of neural processes; their discussions are tied closely to specific experimental data obtained from particular neural preparations.

As a poacher, a nonbiologist, I shall confine most of my remaining remarks to the papers in Part I. Donald Kennedy's introduction to Part II provides a balancing commentary from the standpoint of a biologist.

There is a semantic difficulty inherent in both the title and many papers of this volume: What is the difference between a "theory" and a "model"? A physical device intended to explain or predict some aspect of neural behavior is, by more or less general agreement, called a "model." Such physical models are based, explicitly or implicitly, on some "theory" of neural behavior. The difficulty arises when the two terms are used interchangeably. On the one hand, a theory is often called a model, meaning a *conceptual* or *mathematical* model; for brevity the adjectives "conceptual" or "mathematical" are dropped. On the other hand, a physical model is sometimes considered to *be* a theory, i.e., it is the *definitive* description of a "theory." This viewpoint is most often taken when a physical model, although it may be constructed from components whose behavior is well understood, is so complex in structure or behavior that the human mind is incapable of "understanding" it in any detail.

Thus there are no hard and sharp criteria for the use of "model" and "theory"; these terms remain ambiguous in their usage, and the reader must determine from the context in each particular case what the author intends.

The initial paper of Part I outlines a number of problems which are of great importance in the construction of neural models (under any definition of "model"). With a background in communications engineering coupled with extensive experience and knowledge of neural modeling, L. D. Harmon is a good example of the nonbiologist who has become deeply involved in a study of biological systems. Both his detailed remarks and general attitude are of special interest because they are the result of a sustained clash between the ideology of engineering, with its emphasis on formal precision and free-wheeling synthesis, and the harsh realities of biological research: fragmented, incomplete, uncertain data acquired by painfully slow experiments on systems of bewildering complexity.

In the latter half of his paper Harmon rapidly surveys a wide variety of current and recent neural models. Although he has not attempted an exhaustive survey, with its accompanying bibliography the paper provides an excellent introduction for newcomers to the field of neural modeling whether they are biologists or otherwise. A careful reading of Harmon's paper will also provide a general framework for evaluating much of the remainder of this volume.

The following paper by the eminent zoologist J. W. S. Pringle concentrates on one aspect of the problem of achieving realism in neural models. In the context of specific types of sensors and effectors he examines certain general properties that a model's input and output should have; he argues that without these properties, the inputs and outputs constitute arbitrary simplifications which may destroy the value, or at least the biological relevance, of the model as a whole. This possibility has often been ignored in the past, presumably because many modelers have concerned themselves with very tentative models of fragments of central nervous systems. Even though a central nervous system, from one viewpoint, exists only to serve the organism's sensors and effectors, it is tempting to make a few hasty, simplifying assumptions about these peripheral elements in order to get on with the ostensibly more exciting business of analyzing central networks. Perhaps this research strategy is, and for some time will remain, legitimate owing to our extensive ignorance of *all* parts of the nervous system, but it must eventually lead to folly.

Both Harmon and Pringle have directed their attention to problems of establishing correlations between current neurophysiological data and models; by contrast B. G. Farley has approached the problems of model validity from an entirely different direction. Starting with a more or less positivistic conception of the nature of scientific theory, he argues that it will ultimately be possible, if not desirable or necessary, to develop a formal schema for defining and evaluating biological "theories," this schema to be based on the "theoretical properties of ideal computers." Since our ignorance of the future capabilities and properties of computers, ideal or real, is perhaps as great or greater than our ignorance of neural mechanisms, Farley has been forced to engage in hazardous speculations; but whatever his errors may be, he has here opened a subject that has received little consideration among modelers.

In order to illustrate some of his points, Farley describes recent digital simulation experiments he has carried out on a large, special-purpose machine. A similar application of digital computers to network analysis is outlined by R. K. Josephson in Part II of this volume. There is this marked difference, however: Farley's experiments were conceived as explorations of the possible behavior, under various assumptions, of cortical networks—at the highest level of the vertebrate central nervous system—whereas Josephson's simulation experiments were aimed at testing very specific hypotheses regarding the behavior of particular coelenterate networks—at one of the lowest levels of the invertebrate peripheral nervous system. It is interesting to note that systems at two extremes of organizational level have suggested similar conceptual models, hence similar simulation programs.

This curious methodological and formal similarity of models at opposite extremes of the organizational spectrum is also apparent in the following two papers. In both cases rather elaborate mathematical techniques, involving equations taken from the physical sciences, are applied to neural problems. Wilfrid Rall analyzes one of the smallest elements of cortical systems, the dendritic structure of an individual neuron, whereas E. R. Caianiello is concerned with the cortical mass as a whole, a system estimated to contain from 10^9 to 10^{10} neurons. At both extremes the behavior of the subject appears to be sufficiently continuous and linear in form to permit the application of well-known mathematical techniques; at many intermediate levels of organization the behavior is so nonlinear as to generally defy mathematical description.

Rall's paper is but one of the latest in his exceptionally consistent and methodical series of studies of the individual neuron. He presents a persuasive argument to the effect that the behavior of a cortical neuron can be dominated by dendritic synapses in certain spatial distributions of a type that has been observed; if this is true, then any cortical network model which ignores the peculiar properties of dendritic structures (and most such models have to date been guilty of this simplification) is likely to be in serious error.

Rall is one of those still rather rare physiologists with a good grounding in mathematics. In order to get a grip on dendrites with his differential equations he makes use of a "compartmental model" which he has "borrowed" from the fields of chemical and radioactive tracer kinetics. Caianiello, a theoretical physicist, has similarly borrowed equations from the field of thermodynamics and modified them in a manner which, he believes, will make them applicable to masses of cortical neurons. However he does not go into details here; he mentions them only as examples of a methodological approach that he champions.

The next two papers also have much in common. Both authors are connected with the computer field, and both use combinations of simple logical, numerical, and physical arguments to explore possible signal-processing mechanisms that could be theoretically realized by small networks of neurons. R. F. Reiss argues that by means of "resonant networks," a nervous system could take advantage of valuable pulse interval coding techniques which would be forbidden to it if only the commonly assumed statistical decoding mechanisms are available. He examines several types of hypothetical network that could perform various switching, filtering, and decoding tasks; deduces the ranges of neural parameters required; and suggests how the presence of such networks may be detected by physiologists.

In his introductory section Hugh Crane provides the reader with a glimpse of the line of reasoning that has drawn a computer engineer into neural modeling. He shows why he has been led to examine the possible roles of axon–axon interactions in neural signal processing, a subject that has received very little attention from other theorists. Such interactions may occur quite naturally in ganglia, and Crane proposes several kinds of switching and frequency-modulation functions that could result. As in Reiss's paper, Crane's material is highly speculative but predicts patterns of neural behavior which, if detected, would indicate the existence of the hypothesized networks.

The papers by Lewis, Jenik, and Hamilton describe existing physical models of all or parts of the individual neuron. Working within the framework of the ionic hypothesis and guided specifically by the experimental data of Hodgkin, Huxley, and others, E. R. Lewis has developed an electronic circuit which is capable of reproducing most of the subliminal responses that have been observed in neurons. His results suggest that the ionic hypothesis may be sufficient to account for somatic behavior as well as spike initiation and propagation in axons; one need only vary a few parameters to transform the model's behavior from that of an axon membrane, through a variety of semi-active membranes (including the pacemaker type), to that of electrically inexcitable synaptic membranes.

Franz Jenik's model is based on the Hodgkin-Huxley mathematical theory, and it has several features in common with the Lewis model. However, Jenik has focussed his attention on the spike initiation process as it affects the statistical relations between trains of input and output pulses; he displays a very tidy method for characterizing the behavior of a neuron in terms of ratios of mean input and output frequencies.

The circuits of Lewis and Jenik are probably the most flexible and realistic neuron models yet devised. Although they were both intended primarily for use in the study of individual cell behavior, groups of them can be connected together to simulate networks of neurons. They are too costly for use in large quantities, but they could well lead to a new era in the study of small networks. Even if they were cheap, there is reason to doubt that a network containing a dozen or more such complex and protean models could be rationally managed at the present time.

Looking forward to the time when we can manage large systems of realistic model neurons in meaningful experiments, H. J. Hamilton has been developing a special type of analog device which he believes will serve as a realistic model that is both small and cheap. There appear to be some striking similarities between the behavior of gas ions, under certain conditions, and the evident behavior of sodium and potassium ions in a neural membrane. Hamilton describes a class of simple gas-ion devices which, though still in an early stage of development, have several of the most important properties required in a model neuron. If these devices can be further refined and mass produced in convenient and flexible organizations, then they may provide serious competition for digital computers in the simulation of large neural networks.

But even if gas-ion or other special types of device turn out to be superior vehicles for neural modeling, the digital computer is likely to be the best tool for controlling and analyzing the behavior of large simulation systems. The problem of managing experiments on complex systems appears to be exceedingly difficult, and digital computers offer the only promising means of solution in the foreseeable future. From the standpoint of the computer there may ultimately be little difference between the management of experiments on real nervous systems and on realistic models of nervous systems. Thus if the problem can be solved for either type of experimental subject, it may be largely solved for the other.

For this reason efforts such as that described by G. D. McCann are of interest to the modeler as well as the experimental biologist. In his paper McCann outlines the organization of a rather elaborate system composed of digital computers, measuring instruments, and special machines which can control certain types of physiological experiment, make and record observations, and perform data-reduction tasks which will facilitate the analysis of results. As an example of one of the first applications of this system he reports some automated experiments on opto-motor responses of the fly.

This type of control and recording system has to date proven most useful in the study of semi-independent servomotor mechanisms in various nervous systems. The "cybernetics" approach to biology has been influential in drawing attention to such mechanisms and in developing appropriate conceptual models. These are often called "black-box" models because the neural mechanism is represented by a set of interconnected units—the "boxes"—whose functions are typically defined in mathematical terms. The specific neural sub-systems responsible for the generation of these functions may not even be postulated, much less known, and therefore the boxes are "black."

The black-box model is an important and increasingly popular type of theory which is not discussed in any detail in Part I of this volume. However, two examples may be found in Part II. H. Mittelstaedt outlines a family of equations which can be considered black-box models intended to explain orientation responses to various kinds of stimuli observed to occur in certain insects. D. H. Fender not only presents a black-box model of the eye movement control system in humans; he also gives a step-by-step account of how this model was developed. Here we see explicitly what kinds of questions and answers are entertained by a man who entered into neural modeling from the field of engineering. It might be noted in passing that black-box models are a stock in trade of electrical engineers; as more such persons enter the field of neural theory we can thus expect to see a great proliferation of black boxes.

The note by James Bliss is connected with a black-box model, but is essentially a brief summary and introduction to the literature of a special mathematical function which has been proposed to explain certain opto-motor responses in insects.

1. Problems in Neural Modeling

LEON D. HARMON, *Bell Telephone Laboratories, Inc.*

The making of models is universal in the search for a consistent and instructive picture of nature. Models of neural action have been frequently employed in the past; their relative importance, however, has been minor. Early neurophysiological research was oriented principally to experimental investigation of gross structure, metabolism, and relatively simple electrochemical stimulus–response properties. Now, as greater emphasis is placed on the view of the nervous system as a processor of information, theoretical models assume greater importance and have become increasingly numerous.

In this paper I shall attempt to sketch out several fundamental considerations and problems which seem to me particularly relevant to an understanding of signal processing in the nervous system. This will be followed by a survey, illustrative rather than exhaustive, of the principal types of neural models. I hope to show how experimental and theoretical neurophysiology now stand in relation to each other and where concentrated effort can be significantly applied in both areas to produce a more satisfactory elucidation of nervous action.

Problems in Experimental and Theoretical Neurophysiology

Single Units

In recent years the discovery of increasing numbers of single-unit properties, many of which are apparently nonlinear besides being continuously variable, has greatly intensified a number of traditional problems. One especially difficult question is the following: To what extent does a particular response depend on a *given* stimulus and to what extent does this response reflect the influence of *preceding* stimuli? Moreover, in what ways does response depend not only on instantaneous values of the stimulus parameters but also on their directions and rates of change?

A well-known example of sensitivity to past events is to be found in postsynaptic inhibition. If a neuron's postsynaptic membrane potential at a given time is at or near the resting level because the unit has been inactive for a long while, then an applied excitatory stimulus will have one particular effect. If, however, this present membrane potential results from a conductance change due to a recent inhibitory stimulus (clamping the membrane to or near the