

PACEMAKERS IN RELATION TO ASPECTS OF BEHAVIOR

By

HUDSON HOAGLAND

*Professor of General Physiology
Clark University*

NEW YORK
THE MACMILLAN COMPANY
1935

COPYRIGHT, 1935,
By THE MACMILLAN COMPANY

ALL RIGHTS RESERVED—NO PART OF THIS BOOK MAY BE
REPRODUCED IN ANY FORM WITHOUT PERMISSION IN WRITING
FROM THE PUBLISHER, EXCEPT BY A REVIEWER WHO WISHES
TO QUOTE BRIEF PASSAGES IN CONNECTION WITH A REVIEW
WRITTEN FOR INCLUSION IN MAGAZINE OR NEWSPAPER

Published March, 1935.

SET UP AND ELECTROTYPED BY T. MOREY & SON
PRINTED IN THE UNITED STATES OF AMERICA

To
Wendell T. Bush
and
Mary L. Bush

ACKNOWLEDGMENTS

It is a great pleasure to express my gratitude to Dr. W. J. V. Osterhout and to Dr. Gregory Pincus for their critical reading of the original draft of the manuscript. I am, of course, alone responsible for the text and for any errors that may appear in it, especially since I have added several sections in a later draft of the manuscript. I wish also to thank Mr. Franklyn G. Palmer for valuable assistance in proofreading. In addition I am much indebted to the following publishers for their kind permission to use figures and quotations: The Clark University Press, *The Journal of General Physiology*, *The Journal of Physiology*, *The American Journal of Physiology*, *The Journal of Comparative Neurology*, The Macmillan Company, J. B. Lippincott Company, The Cold Spring Harbor Biological Laboratory, and The University of Pennsylvania Press.

HUDSON HOAGLAND

TABLE OF CONTENTS

CHAPTER	PAGE
I. INTRODUCTION	1
The Limitations of Behavioristic Empiricism	3
II. KINETICS OF THE STEADY STATE	6
Bioelectric Potentials	15
Stimulation	18
Some Applications of the Conception of the Steady State to Animal Physiology	20
III. RHYTHMICITY OF RESPONSE AND RELAXATION	
OSCILLATORS	23
Relaxation Oscillators	26
The Iron Wire Receptor-Nerve-Fiber Model	28
IV. EFFECTS OF TEMPERATURE ON PACEMAKING	
"MASTER REACTIONS"	33
V. LATERAL-LINE RECEPTION IN FISHES	45
The Lateral-Line Organs as Tactile Receptors	45
Physiological Analysis of the "Spontaneous" Discharge	52
The "Spontaneous" Discharge and the Central Nervous System	64
Responses of Lateral-Line Receptors to Tones	66
Thermal Reception in Fishes	67
Kinetics of the "Spontaneous Discharge"	71
VI. PERIPHERAL INHIBITION (ACCOMMODATION), AND THE STEADY STATE	79
Adaptation in Nerve	81
Adaptation of Tactile Receptors	83
Adaptation of Muscle Spindles	95
Phylogenetic Significance of Efficient Mechanoreceptors	99
Inhibition within the Central Nervous System	101
Photochemical Adaptation	103
A Steady State Maintained by Motor Nerve Impulses	104

CHAPTER	PAGE
VII. THE CHEMICAL BASIS OF OUR SENSE OF TIME .	107
VIII. RECAPITULATION AND CONCLUDING REMARKS	121

APPENDIX

AN EQUATION FOR THE STEADY STATE . . .	125
CITATIONS	127
INDEX	135

PACEMAKERS IN RELATION TO ASPECTS OF BEHAVIOR

CHAPTER I INTRODUCTION

In the following pages are discussed certain studies of behavior which imply the existence of continuous controlling mechanisms which may be called pacemakers. The examples selected are diverse and are merely representative, no attempt having been made to present even a partly complete picture of this extensive subject.

The point of view which we wish to stress is that much of the overt behavior of organisms is determined by the interrelations of chemical events within cells and groups of cells, quite independently of external environmental factors. This effect is especially shown by rhythmic spontaneous cycles of activity of organs and of the organism as a whole.

A number of physiological processes will be discussed in some detail in order to illustrate the role of pacemaker mechanisms. We shall have occasion in Chapter II, to review work from Osterhout's laboratory and to consider how the behavior of plant cells (permeability, growth, and bioelectric effects) is determined by chemical dynamics. In this same chapter we shall review applications of similar dynamic considerations to certain problems of animal physiology. Since rhythmic activity is so very characteristic of protoplasmic action, in Chapter III we shall discuss relaxation oscillators and show, with the aid of a model, how rhythmic activity might be expected in tissues as a sort of corollary to the type of kinetics discussed in Chapter II.

Chapter IV consists of a description of the temperature method of analysis of master reactions controlling rhythms

of behavior with special application of the analysis to problems of pacemakers of the central nervous system.

In order to illustrate the role of the dynamic steady state in the behavior of receptors, the lateral-line receptors of fishes will be discussed in some detail in Chapter V and comparisons will be made between these receptors and those of the ear and of the skin. In connection with the physiology of the receptors, the nature of the production of relaxation oscillations set up in nerve fibers by continuous excitatory processes in receptor cells will be considered.

In Chapter VI we shall discuss the general physiology of sensory adaptation or accommodation and present a physicochemical hypothesis to account for it. To do this we shall review the phenomena of adaptation as they are observed in nerve itself and in rapidly adapting "phasic" tactile receptors (free nerve endings) and finally in slowly adapting "postural" receptors such as muscle spindles. We shall also consider points of similarity between sensory adaptation and inhibition within the central nervous system.

Lastly (Chapter VII), in connection with central nervous pacemakers, we shall consider the physiology of the sense of time and endeavor to show how the dynamics of the steady state may serve as a sort of "chemical clock."

Although considerable space is devoted to reviewing published work from several laboratories, certain points of view are, I believe, presented here for the first time. For example, in Chapter V an hypothesis concerning the receptive behavior of groups of cells of the lateral-line organs is advanced and discussed in connection with certain general problems of mechanoreception. In Chapter VI a new general chemical hypothesis to account for the phenomenon of accommodation or sensory adaptation of mechanoreceptors is advanced. Discussions of the role of pacemaker master reactions in connection with a wide variety of problems at very diverse levels of the biological sciences, make, as far as I know, their first synthesized appearance here.

THE LIMITATIONS OF BEHAVIORISTIC EMPIRICISM

Since the rise of behaviorism in 1912, a vast amount of data has been collected, largely in psychological laboratories, describing what animals do. Behaviorism arose primarily as a revolt against anthropomorphism and current conceptions of the animal mind and of consciousness. Interpretations of behavior based on the results of introspective psychology were rejected and a militantly objective vocabulary was developed for use in behavioristic laboratories. With all of this self-conscious objectivity it was natural that behaviorists should look to physiology for their interpretive principles. But most professing behaviorists were, and curiously enough, still are, trained in psychology, and hence, with certain notable exceptions, seldom are in a position to relate effectively their experimental results to specific physiological mechanisms. The result of all this has been the development of a great number of "stimulus-response" relationships as descriptions of behavior with, for the most part, little or no effective analysis of underlying physiological determinants.

The implicit faith of many behaviorists, as revealed by their writings, seems to be that somehow the collection of a sufficiently extensive body of empirical correlations of behavior with a diverse group of environmental variables will yield an understanding of such phenomena as learning, discrimination, "drives," etc. Much of this work involves the designing of experiments for the investigation of loosely preconceived events which, despite their objective nomenclature, may in themselves be extremely complicated, relatively incommensurable processes, difficult to analyze. The host of elaborately contrived experiments to investigate learning is a case in point. It is generally assumed that there is "a learning process" and that *this process* may be measured by maze techniques, conditioned reflex procedures, the memorizing of nonsense syllables, and the determination of the speed of acquisition of various skills. The unitary character of

learning is often tacitly taken for granted, it being assumed that learning is a sort of universal characteristic of organized nervous systems. The unsatisfactory character of this point of view is immediately apparent if one tries to formulate a precise definition of learning. The difficulty of separating learning from such phenomena as sensory adaptation and a variety of events, such as hysteresis, occurring in purely inorganic systems, at once becomes apparent (Rashevsky, 1931).

To escape from such dilemmas certain behaviorists have ceased to try to work with conceptions derived from psychology and have contented themselves with the establishment of purely empirical stimulus-response relationships, contending that such descriptions of behavior must precede general interpretations and that interpretive conceptions must grow and develop inductively from quantitative descriptive correlations. Skinner (1931, 1934) has formulated this point of view in regard to the reflex. He points out that a reflex is a stimulus and a response correlation at a level of restriction of experimental conditions marked by the orderliness of changes in the correlation. His definition is independent of presuppositions concerning even such widely accepted physiological mechanisms as the reflex arc.

This emphasis on empiricism has, in my opinion, served to obscure certain important problems by shifting attention in many laboratories away from behavioral mechanisms with roots in the natural sciences to verbal constructions either deduced from, or induced by, the experimental data. The question of the role of intrinsic physicochemical dynamics of groups of cells in maintaining certain behavioral response patterns independently of the external environment has been overlooked by many students of conduct largely because of this empirical faith. This, combined with a tendency to use oversimplified physiological notions, such as the naïve conceptions of the reflex arc (decried by Skinner, 1931) as a sort of inert conducting pathway between receptors and effectors, has been misleading. This oversimplification of

reflex physiology, as is clear from the writings from Sherrington's laboratory, is not due to the principal investigators of reflex phenomena. It seems rather to have grown up as a by-product of the faith of the behaviorists in stimulus-response empiricism, coupled with their desire for physiologically simple interpretations.

In the following pages we shall discuss certain traditional problems of complex behavior in the light of chemical events in cells which occur in a relatively constant internal environment. In terms of selective modifications of this internal environment we shall consider the kinetics of controlling pacemaker mechanisms, and endeavor, by the use of a variety of examples, to demonstrate how certain general dynamic conceptions of protoplasmic action may be applied to aid the understanding of a very diverse group of behavioral phenomena. We shall attempt to show how certain principles of general physiology may be useful in investigations of problems of traditional interest to psychologists, but usually interpreted by them in terms devoid of physicochemical meaning.

CHAPTER II

KINETICS OF THE STEADY STATE

It is an interesting commentary on the potentialities of general physiology that one of the most effective quantitative analyses of vital processes, of value to all students of behavior, has been carried out on simple plant cells. The work of Osterhout and members of his laboratory has given us a picture of cellular kinetics which appears to be of very wide application to biological problems. This work not only embraces the extremely important specific problem of cellular permeability with respect to substances composing the cell's environment, and hence regulating its metabolism, but also contributes to the understanding of phenomena of great general interest, such as protoplasmic excitability, bioelectric potentials, and cellular growth.

The earlier work of Osterhout has been summarized in his monograph of 1922. He there points out that the electrical resistance of a simple plant or animal is an excellent quantitative index of what may be called its normal condition of vitality. Injurious agents always change its electrical resistance. He says (*op. cit.*¹), "For example if the marine plant, *Laminaria*, is taken out of its normal environment of sea water and placed in a solution of pure NaCl it is at once injured, and if the exposure be sufficiently prolonged it is killed. During the whole time of exposure to the solution of NaCl its electrical resistance falls steadily until the death point is eventually reached; after this time there is no further change. A study of the time curve of this process shows that it corresponds to a monomolecular reaction (slightly inhibited at the start). This can be expressed as an equation which can be utilized to predict the curve of death

¹ From Osterhout, 1922, *Injury, Recovery, and Death in Relation to Conductivity and Permeability*, Lippincott.

under various conditions. We find that in testing these predictions we must ascertain where the death process reaches a definite stage (*i.e.*, when it is one-fourth or one-half completed). This can be determined experimentally with a satisfactory degree of accuracy."

Osterhout goes on to show how the process of death may be followed quantitatively in the same manner as one may follow the progress of a chemical reaction *in vitro*. The death process is apparently always going on as a normal part of the life process "producing no disturbance unless unduly accelerated by an injurious agent which upsets the normal balance and causes injury so that the life process comes to a standstill."

The acceleration of the death process by NaCl may be inhibited (*i.e.*, antagonized) by adding a little CaCl_2 to the solution. An optimum ratio of NaCl/ CaCl_2 is found in which the death process is maximally inhibited. On the assumption that both Na and Ca combine with a constituent of the protoplasm forming a compound which inhibits the death process as revealed by the electrical resistance of the tissue, an equation (to be presented below) was formulated, by means of which it is possible to predict the death curve of simple plant cells in any mixture of Na and Ca with considerable accuracy.

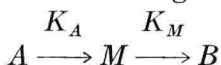
From these investigations Osterhout was led to look upon recovery from injury as not merely the reversal of a reaction which produces injury. The life process appears to be dependent upon a series of balanced reactions, injury and recovery differing only in the relative speeds at which the sequence of processes takes place. To quote again (*op. cit.*), "The experiments . . . lead to the view [earlier emphasized by Loeb, 1912] that life depends upon a series of reactions which normally proceed at rates bearing a definite relation to each other. If this is true it is clear that a disturbance of these rate relations may have a profound effect upon the organism, and may produce such diverse phenomena as stimulation, development, injury and death. Such a disturbance might be produced by changes of temperature (if the temperature coefficients of the reactions differ) or by chemical

agents. The same result might be brought about by physical means, especially where structural changes occur which alter the permeability of the plasma membrane or of internal structures (such as the nucleus and plastids) in such a way as to bring together substances which do not normally react."

In a later chapter we shall consider in detail how the effect of temperature on rhythms of behavior may be used as a tool for investigating aspects of their chemical determinants. Let us now examine more specific aspects of Osterhout's work with *Laminaria*.

In solutions of NaCl of the same osmotic pressure and pH as sea water, the electrical resistance of *Laminaria* falls according to the exponential equation for a monomolecular reaction, except for slight inhibition at the start, until an asymptotic value of resistance is obtained for the dead tissue equal to about 10 per cent of the resistance of normal tissue in sea water. In a corresponding solution of CaCl₂, the resistance at first rises sharply to a maximum of 150 per cent of the normal and then declines. By making up solutions of equal osmotic pressure (*i.e.*, to that of sea water) containing different ratios of NaCl and CaCl₂, a family of curves varying systematically between these two extremes was obtained. The ratio of these salts producing the minimal injury effects as measured by the resistance, exists in a solution composed of 97.56 mols per cent NaCl to 2.44 mols per cent CaCl₂ (*i.e.*, a solution of 955 cc. of 0.52 *M* NaCl plus 45 cc. of 0.278 *M* CaCl₂). Figure 1 shows the family of curves.

To account for these results Osterhout assumed that at the surface of the cell there is a substance, *M*, forming a continuous layer the thickness of which determines the amount of resistance. This substance may be increased by the breaking down of a substance *A* to form *M* according to the monomolecular reaction $A \rightarrow M$, but *M* also breaks down simultaneously to form *B* according to the paradigm



where K_A and K_M are velocity constants.

In such a system, when $A = M$, the amount of M will remain constant if K_A and K_M are equal, since M will decompose as fast as it is formed and a dynamic steady state will result. An increase in K_A alone will correspondingly

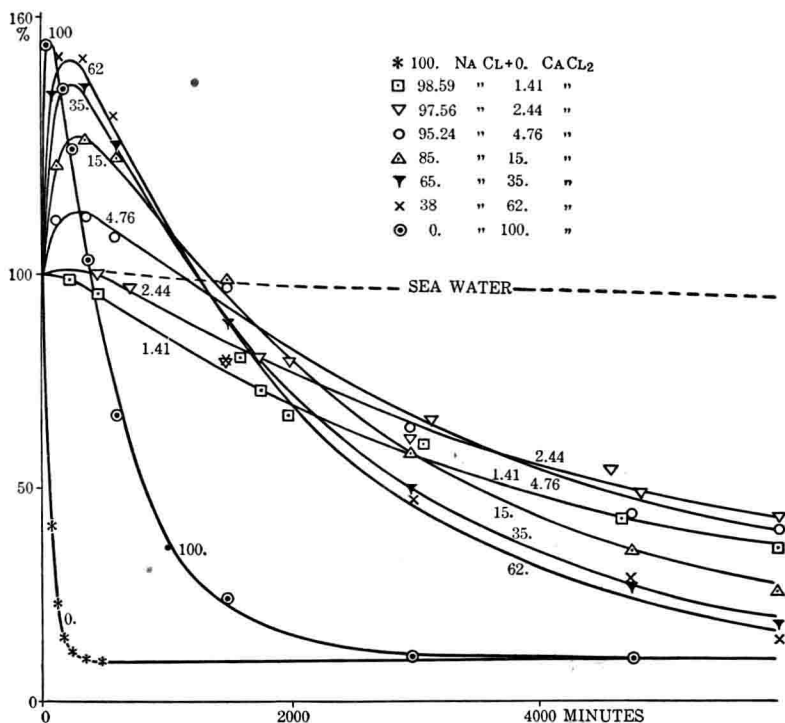


FIG. 1. Curves showing the net electrical resistance of *Laminaria agardii* in 0.52 M NaCl in 0.278 M CaCl₂ and in mixtures of these (the figures attached to the curves show the molecular per cent of CaCl₂ in the solution). The curves show the calculated values (from constants obtained by trial); the points show the observed values (some are omitted in order to avoid undue crowding); each represents the average of six or more experiments. Probable error of the mean < 10% of the mean. (From Osterhout, 1922, *Injury, Recovery, and Death in Relation to Conductivity and Permeability*, Lippincott.)

cause M to increase while an increase in K_M alone will correspondingly cause M to decrease.

A hydraulic analogy to a system of this type has been presented by Osterhout (1922, cf. Figure 2). The following quotation (*op. cit.*) describes this model. "If the reservoir

A be filled with water while M and B are empty and if water be allowed to flow from A into M the amount of water in M (for convenience this amount is called y) will first increase and then decrease. The rate of increase and decrease and the maximum attained will depend on the relation between the two outlets K_1 and K_2 . We may suppose that if K_1 is equal in diameter to K_2 we get the upper curve shown in the figure, while if K_1 is less than K_2 we get the lower curve (in the latter case both outlets are supposed to be smaller than the former). This is analogous to what occurs in the re-

action $A \rightarrow M \rightarrow B$ if K_1 is the velocity constant of $A \rightarrow M$ and K_2 is the velocity constant of $M \rightarrow B$.

In sea water it is assumed that A is renewed

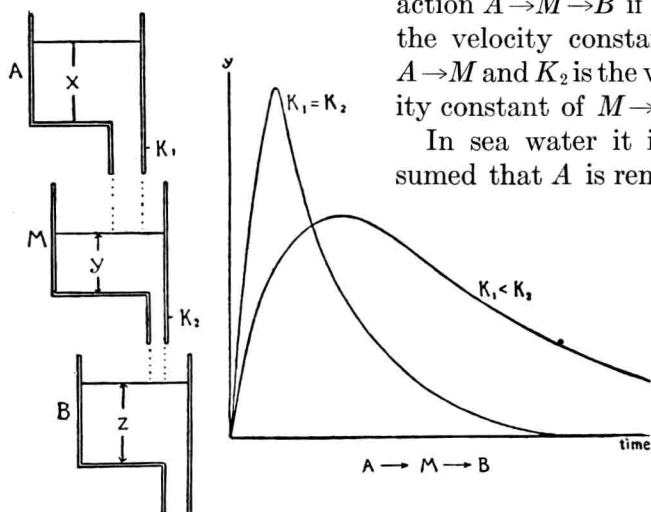


FIG. 2. Diagram illustrating consecutive reactions in which a substance M is formed by the reaction $A \rightarrow M$ and decomposed by the reaction $M \rightarrow B$. (From Osterhout, 1922, *Injury, Recovery, and Death in Relation to Conductivity and Permeability*, Lippincott.)

as fast as it is decomposed and that M is therefore constant. In 0.52 M NaCl the production of A ceases but it continues to break down to M and B . The equation for this kind of catenary chemical system is well known (cf. appendix for derivation) and may be written

$$M_T = 2700 \left(\frac{K_A}{K_M - K_A} \right) (e^{-K_A T} - e^{-K_M T})$$