Waves, Pulses, and the Theory of Neural Masses

Walter J. Freeman

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I. Introduction

It is a truism that systems as complex as vertebrate nervous systems are more than the sum of their parts. What is meant is that the interconnection of numbers of neurons gives rise to collective properties belonging to the neural populations and not to the neurons taken one at a time. The purpose of this essay is to explore some facets of the nature of neural collective properties.

Conventional wisdom holds that such properties emerge from the interconnection of finite numbers of neurons in discrete chains and networks, which are logical and anatomical counterparts of the Jacksonian-Sherringtonian heirarchy of reflex arcs. According to a popular analogy, neurons are like the electronic components of a television receiver which can be connected in a certain way or set of ways to give the properties of the receiver. The central thesis of this essay is the idea that, when neurons strongly interact in sufficiently large numbers (on the order of 10' or more), new collective properties emerge that demand a different kind or level of conceptualization.

An analogy equivalent to that given above is the notion that temperature and pressure exist only for a mass, in contrast to the thermal kinetic energy of molecules in the mass. The suggestion is that certain interactive phenomena in vertebrate brains occur only as broadly distributed and continuous events or waves across masses of neurons, and that in some instances these cooperative phenomena may be essential aspects of normal brain function. The task is to describe some of these wave phenomena in terms of underlying collective properties, and to do so in such a way as to minimize confusion between observables and principles. Again by analogy, brain potentials (EEG waves) appear to have somewhat the relation to wave activity of neural masses that flow patterns have to temperature and pressure waves in atmospheric storms. They are observable side effects that are of interest mainly because they give access to the internal dynamics.

The approach used is to review the historical interplay between ideas concerning neural networks and masses, to develop a set of rules for describing neural masses as dynamic entities, and then to discuss some of the implications of those rules for neurophysiology.

Throughout the development the emphasis is placed on the idea of graded neural synaptic interaction, because it is interaction of neurons that gives rise to something more than the sum of parts. Neurons are connected to each other by structural synaptic linkages. For each neuron there is a certain density of these anatomical connections, referring to the number and size of contacts of each neuron with its neighbors within each unit volume of neural mass. But the significant quantity is the momentary functional or effective connection density, which denotes the level of transfer of influence across a given set of connections at a given time and place. If, for example, a volley arrives on an afferent path to a neuron that is in an absolute refractory state, the functional connection density is zero, even though the anatomical connection density is nonzero.

Two kinds of massive connections are distinguished. The first is a one-way or forward connection from one neuron to neurons in another mass; the second is feedback connection of one neuron with many others in the same mass. Both types give rise to mass actions of many neurons, but only the second gives rise to the collective properties of interest in the present context. That is, neural interactions based on functional interconnection densities give rise to wave phenomena, and, as is shown for some of the neural masses in the

mammalian olfactory system, the observable effects of wave patterns in turn provide the means for measuring the intensities of interactions.

II. Comparison of the Hypotheses of Reflex Centers and of Pulse Logic

A. THE ORIGINS OF REFLEX CENTERS

The basic assumption required for a theory of neural masses is that there can exist across an interactive mass of neurons a continually changing state of activity, which is manifested in several forms of unit and field potentials, and in muscle contraction and hormone secretion, but which is not identical with any of them. The precursors of this assumption can be traced (Brazier, 1959, p. 33) to an idea first proposed in 1784 by George Prochaska, a Bohemian philosopher-physician, who used the term vis nervosae in direct analogy to Isaac Newton's vis gravitans (see note 1*). He used it to connote an elemental form of energy, which was unobservable except through its effects (such as "reflexions" or reflexes), and conformed to natural laws that could be quantitatively described (as could the energies of optics and gravitation), but which could not be "explained." By mid-nineteenth century the terms "nerve energy," "nerve force, " and reflex were in common use. Spencer, for example, in 1863 stated (quoted from Darwin, 1872, p. 71) as an "unquestionable truth that, at any moment, the existing quantity of liberated nerve-force, which in an inscrutable way produces in us that state we call feeling must expend itself in some direction . . . must generate an equivalent manifestation of force somewhere." Darwin (1872) remarked: "This involuntary transmission of nerve force may or may not be accompanied by consciousness. Why the irritation of nerve-cells should generate or liberate nerve force is not known; but that this is the case seems to be the conclusion arrived at by all the greatest physiologists such as Muller, Virchow, Bernard, etc." (p. 70).

Two developments terminated the general acceptance of these terms. One was the popular confusion of "nerve force" with "vital force," such that neither survived the revulsion against vitalism by the beginning of this century. The confusion was inevitable, because with better understanding of thermodynamics the term "nerve energy" became oxymoronic; for example, whereas the law of conservation of energy developed by Helmholtz in and after 1847 became fundamental in physics, "conservation of nerve energy" remained meaningless.

The other was the widespread acceptance, largely owing to the work of Ramón y Cajal (1911), of the neuron doctrine as the central dogma of neurophysiology.

The concept of the neuron as a discrete structural and functional entity had earlier been proposed by Deiters in 1865 and by Waldeyer in 1891 (who coined the word neuron), on the basis of microscopic dissection and staining of cells in the nervous system. This hypothesis was, in fact, an extension to the nervous system of the cell doctrine of Schwann and Virchow developed in the 1830's, which asserted the cellular basis for the organization of all living tissue. The concept did not seem immediately valid for the nervous system, because neurons had "bizarre" radiating filamentous shapes, unlike the cylinders, discs, and spheres of almost all other cell types (Peters et al., 1970). The most compelling kinds of evidence for its validity through the first four decades of this century were the patterns of degeneration and regeneration of neurons following experimental injury to central and peripheral tracts and nerves (Ramón Cajal, 1928) ; the physiological differences distinguishing transmission inside neurons along fibers and between neurons across synapses (Sherrington, 1906) ; and the electrical properties of the nerve membrane (Katz, 1939). So strong was this accumulated indirect evidence that confirmation under the electron microscope of the anatomical integrity of the nerve cell membrane at the synapse (Palay, 1956) was received with little fanfare.

* Notes to the text appear at the end of the chapter on pp. 152-161.

Throughout the last six decades most neurophysiologists have inferred that, because the neuron was the unit of growth, metabolism, and structure in the nervous system, it was also the unit of function. When "function" meant the action of generating and transmitting synaptic current and the nerve impulse, this inference was quite satisfactory. But when the term "function" contained reference to the mechanism of reflex operations (Sherrington, 1925, 1929) and animal behavior (Hebb, 1949) or even to the physiological operations of multineuronal parts of the nervous system (Lorente de Nó, 1938), there were difficulties. They stemmed from the anatomical facts that the numbers of neurons in vertebrate central nervous systems were known to be astronomically large, on the order of 10^7 to 10^{11} and that the numbers of synapses on the surface of each neuron, ranging from 101 to 104 or more, set the levels of possible interactions between neurons beyond the range of numerical evaluation or sequential observation.

The question has been, Can patterns of animal or reflex behavior be described or accounted for in terms of finite and discrete networks of single neurons as in reflex arcs? Or is it necessary to work with some intervening level of neural organization consisting of interconnected neurons forming a mass? This general question can be more sharply put in neurophysiological terms of connectivity. Granted that there are large numbers of neurons and anatomical connections in the neural masses of the brain, these facts do not state how many are obligatorily active during a behavioral event. The proper question is, What is the level of functional connection density among the neurons in a mass? If it is generally low but with high transmission effectiveness across a selected few synapses at any moment, then the network description is appropriate, because the neural mass exists anatomically but not functionally. If it is generally high, then the network is an illusion, and the appropriate level of analysis of neural "function" must be, in some sense, the neural mass and not the single neuron.

The need for some kind of organizing concept or principle between lie level of the neuron and that of the whole brain was met empirically for or many years by the idea of the "reflex center." The "center" originated in the 1870's (Brazier, 1959; Freeman, 1961) as the notation for the structure or anatomical location in the brain, at which electrical stimulation yielded a reproducible motor response. Under the influence of the doctrine of specific nerve energies then prevailing, the concept was broadened to the extent that the behaviorally related functions of the brain were commonly described in terms of a mosaic of "centers," which were cortical or nuclear masses of neurons thought to control some motor or sensory pattern of behavior, whether autonomic (respiration, body temperature, etc.) or psychic (speech, vision, rage, etc.). Each center was conceived to be the focus of nerve activity or energy, which on release in the form of action potentials in response to an appropriate sensory trigger would excite motor neurons to generate a specific pattern of behavior. Connections were conceived on the model of the telephone switchboard. Experimental verification was by use of the implanted macroelectrode. The effect of electrical stimulation was artificially to excite neurons in the center and cause them to produce the specific behavior. The electrode was also used to record the electrical activity generated in the center during normally induced patterns of behavior, and, by use of very strong electrical current, to destroy the center and prevent its energy release and the appearance of its controlled output.

Sherrington (1906, 1925, 1929; Denny-Brown, 1940) devised an explicit model for the dynamics of the "center" by treating it as a pool of neurons receiving converging sets of afferent nerve fibers and transmitting pulses over a compound efferent nerve tract. The state of activity of the pool was described as the sum of the central excitatory and central inhibitory states (c.e.s. and c.i.s.) induced by afferent volleys. These hypothetical energy states were graded in proportion to input intensities between the limits of threshold and occlusion imposed by refractory periods. They were added "algebraically" by processes of convolution in both time and space, termed temporal and spatial summation. (In the narrowest of several senses, Sherrington's famous title in 1906, "The Integrative Action of the Nervous System," implied literally the summation of infinitesimals.) The resultant determined the magnitude of pulse output from the pool, which was estimated by measuring the magnitude of muscle contraction. In subsequent work by others (see Note 2) the c.e.s. was identified either with pools of action potentials (Lorente de Nó, 1938) or with pools of synaptic potentials (Eccles, 1957, 1964).

This model was widely disseminated in textbooks of the period, and its main use was to spur the study of the mechanisms in synaptic transmission and of the electrotonic properties of neurons underlying processes of spatial and temporal convergence and summation. Despite the concomitant discovery and reportage of the electroencephalogram (EEG) by Berger in 1929, Sherrington's model did not lead to the development of understanding of wave phenomena in the nervous system. The reason appears in retrospect to have been that his model treated neural events within masses only in terms of forward actions of one set of neurons on another, and it did not allow for local reactions or interactions within pools, but only between pools, as the basis for recurrent or cyclical neural events. It was a statistical mechanical model of neural mass action, in which each neuron in a pool was assumed to be identical to all others and topologically to lie in parallel with them. Graded response properties emerged from the all-or-none characteristics of the parts by virtue of distributions of thresholds and refractory periods. The actions of immense numbers of neurons could be sampled, measured, and modeled by means of lumped circuit or block flow diagrams. The required conceptual bridge was thereby established between the single neuron as the element of neural "function" and highly organized reflex response patterns involving very many neurons as the element of behavioral "function."

But wave actions were not intrinsic to the model and had to be initiated by synchronized afferent volleys. Repetitive response patterns such as clonic afterdischarges, pendular reflexes, the scratch reflex, and respiration could be dealt with only in terms of bulk interactions of neuronal pools forming reciprocal centers (flexion-extension, inspirationexpiration, heat-cold, etc.). In brief, Sherrington's model made it possible to "explain" global neural response patterns in terms of the properties of single neurons, but his neural masses were internally noninteractive. Reciprocal antagonisms and facilitations were between masses and not within masses.

His model could account for the continuous gradations and algebraic additivity (what is now called linearity or superimposibility) of the neural input-output relations of masses of highly nonlinear elements (the neurons), but only if continuity were imposed by the input, owing to the absence of interactive terms. This accounts for the supreme importance in the doctrine of centers of the use of the inductorium and the focal stimulating electrode, which was the commonest means for imposing synchronous volleys on numerous spatially contiguous axons.

B. THE RISE OF PULSE LOGIC

After 1940 the widespread use of the microelectrode and its appurtenant technology (electronic amplifiers, oscilloscopes, etc.) had a revolutionary impact on neurophysiological theories of behavior. The nerve impulse was observed in almost all parts of the peripheral and central nervous systems and came to be regarded as the universal currency, whether it was induced by electrical stimulation or afferent sensory stimulation or occurred "spontaneously" (see Note 3).

For some microphysiologists the microelectrode was merely the means for observing the unit pulse correlates of neurons in centers in relation to the appropriate forms of behavior, as, for example, the bursts of firing of neurons in the medullary reticular formation in relation to respiration. For others a much more exciting range of analysis was opened to view by the work of McCulloch and Pitts (1943), which showed that pulse generators connected in networks could in theory perform certain logical operations and gave rules for constructing such networks. They and others (Householder and Landahl, 1945) rapidly extended this concept to networks containing erratically firing units without precise time relationships among them. In 1949 Hebb, with the aid of neuroanatomical concepts of Lorente de Nó (1938), used these operations for the analysis of human and animal. behavior (see Note 4). Owing largely to his work, and with the concurrence of neuroanatomists and neuroembryologists, who like Sperry (1951) strongly emphasized the meticulous detail with which neural connections are laid down, the hypothesis of the nervous system as a pulse-logic device superseded the older concept of the brain as a switchboard of centers (see Note 5).

The payoff from this change in theory was rapid and continuing, especially in the visual system (H. B. Barlow, 1953; Jung, 1961; Hubel and Wiesel, 1963), and to lesser extents in the somesthetic (Mounteastle, 1957) and auditory (Kiang, 1968) systems of vertebrates, the eye of Limulus (Hartline, 1938; Hartline and Ratliff, 1958), and a variety of invertebrate preparations (Bullock and Horridge, 1965). It is now well established that transmission through each stage in a sensory channel is not simply by forward relay but involves some logical operations, which can be conceived as the addition and subtraction of pulses on adjacent lines (axons), selective delay, clipping by thresholds, etc., performed by interneurons and recurrent collateral axons. In some channels these processes have been shown to have precise spatial localization and very fine-grain texture. Among the most compelling neurophysiological demonstrations of the past decade have been the remarkable specificities of the input configurations that serve optimally to drive selected neurons in the visual and somesthetic pathways.

These patterns have been termed "trigger features" (H. B. Barlow, 1953) ; the operation of the neural nets has been termed "feature" abstraction (Lettvin et al., 1959). Logical calculi have been devised (e.g., Rosenblatt, 1962) to simulate the behaviorally related functions of such nets in terms of the selected storage, recognition, and recall of "features." A series of statistical procedures has been developed to obtain useful in formation from neural pulse trains (Gerstein and Kiang, 1960; Rodieck et al., 1962; Perkel and Bullock, 1968). H. B. Barlow (1969) and Marr (1969) have taken the theory to its logical culmination, as McCulloch and Pitts did earlier (1943), in proposing that perception and motor action are based on serially ordered neural nets, such that single neurons at successive removes from primary receptors and effectors have progressively more complex input or output connections and trigger features or motor correlates, until, at the highest level, a single neuron can "encode" a unique percept, memory, or action, which McCulloch and Pitts (1943) termed the "psychon." Current experimental work is directed toward defining the trigger features of higher-order cells, analyzing the simpler networks of lower-order neurons to determine how the operations are performed, and determining how the networks are embryologically laid down with the requisite degree of anatomical specificity.

C. TO THE FUTURE: DIVERGENCE AND CONVERGENCE

It is proposed that the most fruitful development will next occur as a fusion of the concepts of reflex centers and pulse logic, which are alike in several important ways. Each in its time has been an attempt to conceive and understand brain function in terms of brain properties. Neither is an analogy in the way of the telephone

switchboard, the Faraday field, the servo system, the digital computer, the correlograph, or the holograph. Each has been very fruitful as the stimulus and guide to experimental work, because it has been so directly tied to a technique of observation on the brain. Each has been developed around the idea that an on-going pattern of animal behavior can be identified with an on-going pattern of cerebral activity, which is observable through patterns of neuroelectrical activity. But each has suffered the limitations of its technique. The description of the operation of centers was never extended past the global summation of Sherringtonian central excitatory and inhibitory states, largely because the macroelectrode did not give access to the rich texture of neural events within "reflex centers." With the microelectrode it is very difficult to make effective observations on more than one neuron at a time, and still more difficult to make or test effective inferences concerning the operation of large numbers of neurons surrounding the one under observation.

Herein lies an important limitation of pulse-logic models of the nervous system. The microelectrode as conventionally used is a tool for the study of convergence in the nervous system, whereas the operations of the system are based on divergence. As such, the tool gives a deceptively deterministic view of neural events. Each neuron in the brain at any moment must have some set of effective input connections (including the null set) from other parts of the brain, including sensory receptors. It must have some instantaneous pulse rate (including zero). Corresponding to the set of input connections there must be some configuration of afferent stimuli, which serves maximally to enhance or decrease the pulse rate. That is its trigger feature. On the other hand, of all possible motor actions there must be one that is associated with maximal firing rate. That is its motor correlate or psychon under the designated conditions of observation.

Each stimulus is invariably a surface event over an array of receptors. Even where elaborate precautions are taken to restrict input to a single receptor, the input configuration must be specified as "this neuron on" and all others "off" or "at background level." Each afferent axon characteristically branches 'repeatedly, and if its own spatial divergence is minimal the divergence at synaptic stages is prominent. Each motor response consists in timed sequences of muscle contractions and relaxations in response to space-time patterns of motor neuron firing. These patterns can also be conceived as surface events in the array of neurons sustaining axons to the periphery. No one denies that even the simplest stimulus-response event consists in surface-to-surface transmission of pulses from arrays of receptors through intervening synaptic layers to arrays of motor neurons.

However, the numbers of neurons in neural arrays characteristically are extremely large, and the degree of overlap of the fibers of each neuron with its neighbors is very high. Microelectrodes cannot be used to sample more than a very few neurons among the thousands or millions of neurons constituting a typical mass. Pulse-logic concepts do not in themselves yield rules for spatial and temporal sampling through a neural mass. It is true that experimenters devise probability distributions, topographic maps, homunculi, and other continuous patterns to describe the most probable locations of neurons in arrays triggered by or associated with certain classes of stimulus or response, but these are based on past experience and on anatomical analysis, not on the theory.

It is proposed that these "arrays" of neurons might not merely be describable in terms of continuous distributions, but in many cases might actually function that way. Concepts of mass action might take the form of probability distributions of pulses, which would allow description of the activity of single neurons in the context of the mass.

D. ANALOG -TO-DIGITAL AND DIGITAL-TO-ANALOG CONVERSIONS

It is well-known that neurons are not pulse-logic devices (Bullock, 1959). They transmit over long distances (that is, distances greater than a few tens or hundred of microns) by means of pulses, but the significant interactions within neurons at synaptic junctions in masses are not impulsive. They occur in the form of continuously varying synaptic currents, which determine from moment to moment whether or not a neuron will fire a pulse. Each neuron is a two-stage converter. It receives pulses and converts them at synapses into synaptic currents. It filters these currents through the distributed resistance and capacitance of its dendritic tree and adds the weighted sum. It converts this to a pulse train, or, more accurately, to a probability of pulse formation at some site or multiple sites of optimal sensitivity, termed trigger zones. The pulse is transmitted to other neurons in (usually) all-or-none fashion, but with logical processing in the form of translation, delay, dispersion, and "multiplication" over successively branching axon terminals (see Note 6). The identity of manifold input pulses on dendritic trees is lost in terms of their times and locations. Discrete values are smoothed by the cable properties of dendrites, and the output of any one neuron can. only represent the weighted, smoothed sum of afferent pulses over its entire surface and for some uncertain period of time. That is, the control of the pulse rate is invested in an analog signal, which varies continuously and not discretely in its

temporal and spatial dimensions.

The combination of divergence in neural transmission with two-stage conversion by each neuron brings an uncertainty. A sensory stimulus evoked neural discharge runs out over diverging axons leaving one neuronal array and approaching another array. The neurons of the next array are activated by the volley, but their output pulse trains contain little information about which axons in the now converging array were necessary and sufficient to produce the output. If the involved axons are described as a set, and the neurons of which the axons are a part are collectively described as a neural mass, there are (for present purposes) two modes of transmission by the mass with differing implications for the observer.

If the behaviorally related neural transmission conforms to Hebb's (1949) view, then on each of several parallel axons the message is complete. A record of the pulse train on any one axon will provide the observer with all the information that was sent and received. But if the transmission occurs partially on each of several axons in random order, uncertain and indifferent in number, location, and timing within not well defined limits, as envisioned by Lashley (1942), then the observer cannot know from a record of one pulse train what message was sent. He must either back up in time and repeat the transmission again and again, until '-,he axon he observed has (presumably) displayed on the average the same behavior as all the other axons during any one transmission, or he must record simultaneously from all the active axons. Because he cannot know their identities, locations, or number, he cannot logically achieve either of these ends, unless he records from all the axons in the set, nonactive as well as active. If there are more than 100 or so, he is forced to express his findings in the form of a probability distribution around the neuron under observation, which is a continuous function locally across both space and time.

How is an observer to know whether he is recording from a Hebb neuron or a Lashley neuron? Within the present context of neuropsychology and electrophysiology he cannot, because he has the unrestricted freedom to structure the experimental situation to yield whichever answer he desires. He usually desires dramatic bursts of pulses and strives for them. But the list of possible neural pulse codes is long and still increasing (Perkel and Bullock, 1968), and there is no a priori reason given by pulse logic to prefer some over others. The identification of pulse rate with psychon intensity is appropriate for first-order sensory neurons (Fulton, 1949), but beyond that level it is merely a plausible analogy. The aim of a higher level of analysis should be to describe the properties of cooperative activity as they appear in neural masses in analog form, to deduce the equations governing an alog-to-digital and digital-to-analog conversions, and then to predict the admissible forms of pulse codes.

E. MUTUAL INHIBITION AND MUTUAL EXCITATION

Another limitation of the pulse-logic hypothesis is its failure to incorporate the property of excitatory feedback among neurons. The defining characteristic of an interactive neural mass is the functional interconnectivity of a large enough number of neurons to make feasible a continuum as an approximation to their function. How large that number might be is not important; elsewhere it has been suggested that the numbers from 101 or 101 to 101 or 101 are useful guidelines (Freeman, 1972). The definition must also include a statement on the kind of interaction, whether excitatory, inhibitory, or a mixture of both.

An array of sensory neurons interacting by mutual inhibition and giving rise to the phenomenon of "lateral" or "surround" inhibition has been described for the retina of an invertebrate, Limulus (Hartline and Ratliff, 1958; Knight et al., 1970). This pattern of interaction leading to contrast enhancement along lines and edges has become virtually an archetype for the interpretation of interactions of neurons in the vertebrate retina, even though the latter contain both excitatory and inhibitory neurons. That is, emphasis has been laid on the inhibitory actions of neurons, such that each neuron is thought primarily to inhibit its neighbors and, by reciprocal release from the inhibition exerted by its neighbors, to enhance its own activity.

This analysis fits well with the conception of each neuron as a separate information channel. There is minimal channel cross talk, confusion between adjacent channels, or loss of topographic specificity at the readout end, and yet each neuron has the local cross-connections demanded for local logical processing.

A very different pattern of function emerges from neurons that are interconnected by excitatory synaptic contacts. There is strong evidence in the olfactory system (Freeman, 1968a,b) and possibly other parts of the brain that dense interconnections occur among excitatory neurons. That is, excitatory neurons excite each other and are re-excited in return. This kind of interconnection has, been modeled in terms of pulse logic as the reverberating circuit, the two-neuron or multineuron closed loop with a periodically circulating pulse (Lorente

de Nó, 1938; Hebb, 1949). In neural masses the recursion of an impulse of a neuron back to itself through its neighbors can be modeled in terms of a one-dimensional diffusion process (Freeman, 1964). That is, the recurrent event is dispersed by Gaussian distributions of conduction, synaptic, and cable delays and is smoothed by the resistive-capacitative properties of the membrane. A large number of such interconnected neurons cannot "reverberate" (generate periodic pulse trains) in the steady state, for the output of each is desynchronized at each passage around the loop. If left to itself such a mass can only approach some steady level of activity, each neuron generating a random pulse train at a mean rate peculiar to itself. This condition is evident in the "spontaneous" or background pulse trains of central neurons, which characteristically are aperiodic and cannot be attributed to "pace-makers" or to discrete loops.

If a pulse is introduced into such an excitatory mass by way of an afferent volley on a set of input axons, to have a detectable effect on any one neuron it must be carried on enough axons and arrive within a short enough period of time that the arrival is distinct from a random surge of background activity delivered to that neuron. That is, multiple afferent neurons in the local domain must be coherently active to achieve an effect on any one neuron, and (in such a mass) the same effect must take place in more than one neuron, if it takes place in any, owing to afferent divergence, though to varying degrees. Recurrent excitation in the activated region of the mass must lead to further coherent activity (dispersed in time as well as divergent in the surface), which is an increase in probability of aperiodic firing of neurons over the domain of interconnection. The transmitted event to other neurons in the mass is a spatially and temporally distributed set of pulses on the axons of those neurons that were likely in any case to have fired. Owing to the smoothing of a spatiotemporal distribution of pulses by the dendritic membranes of the recipient cells, the transmitted event is a continuous variable. That is, it cannot be treated as a pulse or sum of pulses. It is a wave.

The probability of firing of each neuron is determined by the local value of this wave, superimposed on background activity, but the same wave occurs in many neurons in the same domain. The sum of probabilities of firing over those neurons gives rise to an actual pulse density (number of pulses per unit area per unit time), which is the output. Owing to temporal dispersion and divergence of axons this event must likewise undergo smoothing within an axonal tract, so that the output not only can but must be treated as a duality. In terms of its accessibility to observation with a microelectrode, it is a pulse function-that is, a set of near-random pulse trains with some coherence in terms of mean firing rate in relation to an afferent stimulus. In terms of its effect on the next succeeding synaptic layer, the output is a wave function-a continuous event in space and time (see Note 7).

F. SUMMARY

The earliest attempt to represent neural dynamics in the abstract led to the concept of "nerve energy" as the basis for neural action in relation to sensation and motion. The term fell into disuse with the advent of the neuron doctrine, but the concept persisted as Sherrington's central excitatory state. Reflex actions were conceived to result from the sum of concerted actions of like neurons wired in parallel, so that neural masses could be treated as lumped elements in block diagrams. Subsequently the technology of the microelectrode gave access to the pulse trains generated by single neurons, and conceptually the networks of centers were replaced by networks of single neurons. By logical extension the operation of neurons within masses was conceived as encoding behaviorally significant information ("psychons") into the pulse rates of single neurons, in much the way that the discharge magnitudes of "centers" were previously related to specific behavioral functions.

It is proposed that pulse logic can be fused with the doctrine of centers in such a way that the chief virtue of each can be preserved and extended. This is the identification of a behavioral event with a pattern of neural activity, which is accessible to electrophysiological observation. Three areas are identified for extending pulse logic into the domain of continuously varying quantities. One is the description of divergence of neural activity in terms of spatial pulse probability distributions. A second is the description of the rules governing wave and pulse conversions. The third is the description of dense excitatory neural interactions in terms of temporal pulse probability distributions.

It is suggested that the fusion of these two modes of thinking will impose a duality of conception onto the neural pulse train, viewed with respect to the neuron as a pulse function and with respect to the neural mass as a wave function.

III. State Variables of Neural Masses

An observed pulse train of a neuron in an internally interactive mass can be treated experimentally in either of two ways. The conditions of the observations can be adjusted to optimize the probability of firing in relation to an afferent stimulus, which leads to the designation of the trigger feature or "psychon" in the context of pulse-logic analysis. Or for a known stimulus configuration the complex covariation can be observed between the pulse train and the activity patterns of other neurons in the local domain. Generically speaking, the search can be made for the structure of the higher-order wave event, of which the pulse train is a manifestation. Because the wave event is sustained by uncertain numbers of neurons firing unpredictably in unspecified volumes of neural tissue, that search must undertake the description of neural masses in terms peculiar to their own properties, arising out of but distinct from the properties of single neurons.

These properties include the types, levels, and densities of interconnections; the gross geometries and dimensionalities of neural masses; the state variables of neural masses, which serve to describe their levels of activity; the observed events manifesting the state variables in the forms of pulse trains and field potentials; and the system parameters, both fixed and variable, consisting mainly of rate, space, and gain coefficients.

Experimental freedom of choice conveys the right to choose preparations optimal for the end in view. The retina (both vertebrate and invertebrate), the mammalian geniculocalcarine and lemniscal systems, and a variety of invertebrate visceral ganglia have been found well adapted to network analysis. On the other hand, the system best adapted to studies of neural masses is the vertebrate olfactory system. The high numbers of neurons, degrees of divergence, and density of interconnectedness are exemplary, whereas the degrees of topographic specificity and specialization of cell types are minimal. Most of what now follows applies directly although not uniquely to the mammalian olfactory bulb and cortex.

A. THE HIERARCHY OF COMPLEXITY

The assumption of the possible existence of an active state across a neural mass means that widespread cooperative activity, not necessarily uniform, synchronous, or intensive, is assumed to occur among its neurons. Such cooperation can result either from a common driving source or from internal interaction, In either case the active state is based on a form of neural connection. Analysis of the active state requires the specification of the approximate numbers of neurons involved, the size and limits of their domain, the types and densities of connection, and the level of complexity of connection.

The simplest type of neural mass is a set of neurons which have no internal interactions among them, but which have a common source of input as the basis for cooperative activity. This type is hereafter called an "aggregate." An example is the aggregate of olfactory receptors. These are specialized sensory neurons having cell bodies in the olfactory mucosa in the nose. The input end of each neuron maintains cilia projecting into the pituitous surface of the nasal cavity. The output end is an unbranched axon, which does not send collateral axons to other receptors. There is no neural basis for interaction among the receptors, but there is a possible basis for covariant activity in responses to olfactory stimuli, which are delivered to the receptor surface in a continuous air stream.

It is convenient to subdivide aggregates into three subtypes. That containing all excitatory neurons is called an excitatory aggregate; that containing all inhibitory neurons is an inhibitory aggregate; that containing roughly equal numbers is a mixed aggregate.

This example illustrates a basic rule, that the defining characteristic for a neural mass is a possible set of cooperative active states rather than any one active state. Obviously this definition makes it possible to define the entire brain as a neural mass, which is reasonable, but the definition is made more useful by some restrictions, such as the rule that they have a common input. In this manner the olfactory receptors can be conceived as a neural mass, even though it is unlikely that they are either all covariant with each other at any moment, or all independent of other brain neurons.

In the case of cooperation based on interconnection, the simple form of interactive mass is that in which all the neurons are either all excitatory or all inhibitory. This type of mass is called a "population." Each neuron need not be connected with all others in the mass, but it must be densely connected with many neurons in its vicinity. By "dense"' connection is meant that each neuron is connected to a large but unspecified fraction of the neurons within the radius of its own processes, and that no small number of such connections dominate the whole set. By "many" neurons is meant that it is inconvenient or impossible to count them, but that the numbers can be estimated by an appropriate volumetric sampling procedure, and that the active states of that

number of neurons can be reasonably approximated by some continuous average across them.

The outer limits of the mass are set by the anatomical extent of the neurons having that kind and density of connectivity. Additionally, because the essential characteristic of the mass is the possibility of cooperative activity, it is reasonable to impose the requirement that the interconnected neurons receive direct (monosynaptic) input in common from another previously defined mass, whether interconnected (a population) or not (an aggregate). This ensures the possibility of cooperative activity. The outer limits of these two defining characteristics would define two sets, and the mass would be the union of the two sets.

There are two types of interactive masses or "populations." One is composed of densely interconnected, mutually inhibitory neurons, which have some common source of input, and which coincide with a locus for possible states of cooperative activity. These form an "inhibitory population." The other is similarly composed of excitatory neurons. It will be shown that the dynamics of excitatory and inhibitory populations differ in a characteristic way, so that it is essential to distinguish them at the outset as being each composed of neurons having a common sign of output: all excitatory or all inhibitory.

The dynamics characteristic of a neural mass containing both types of population densely interactive without regard to type are far more complex than the dynamics of either simple interactive mass. At this juncture it is desirable to introduce a series of four levels of complexity intervening between the neuron and the whole brain, and a new vocabulary to label them.

The first level is that of the aggregate (the noninteractive mass), which is either excitatory, inhibitory, or mixed. The second level is that of the population (interactive mass), for which the two types are excitatory and inhibitory. The third level is that of the compound interactive neural mass, which can be treated (for analytic purposes) as resulting from the dense interconnection of excitatory and inhibitory populations. (Populations containing scattered single neurons of unlike sign of output, such as inhibitory neurons within an excitatory population at insufficient density to establish detectable interactions with each other, need not be reclassified, but the disparate neurons are not members of the population, even though embedded within it. Alternatively, if the numbers of disparate neurons are appreciable, but not their density of interconnection, the mass might he described, for this example, as an excitatory population in parallel or in series with an inhibitory aggregate.)

Each mass existing as some combination of populations has properties unique to itself, depending on the nature of the interactions, which can be "explained" in terms of the properties of the populations, but which transcend them. In all their variety and specificity the entities deserve a class name that has not been applied to lesser masses of neurons. It is proposed that they be called neural "cartels," from the same root as "chart" or "charter." The dense connection of an excitatory with an inhibitory population is a simple cartel. A complex cartel is formed by the dense connection of a simple cartel with an aggregate, population, or some combination of them in series or parallel topology.

This third level of organization, that of the neural cartel, is of greatest importance in respect to observation. Populations and covariant aggregates naturally function within cartels. Nerve tracts normally activate complex cartels, and they can be isolated from certain input by cutting the tracts. Surgical ablation is most practically performed on the whole of a cartel. Therefore, a model of neural masses must aspire to predict and describe at this level- of complexity.

Although recording yields electrophysiological data produced by aggregates and populations, the data cannot be understood or explained without recourse to the cartel of which they are parts. The state or the output of a cartel must be represented by multiple neural activity distributions, at least one for each component population and covariant aggregate. Examples from the olfactory system are described below.

The fourth level of complexity results from interaction among complex cartels. This is the level of "brain systems." Familiar examples are the sensory and motor systems of the vertebrate brain. The dynamics at this level have not yet been modeled in terms of linear analysis, as have the dynamics of the first three levels (Freeman, 1972).

To summarize, the neural mass is defined as the set of neurons lying within a locus of domains of cooperative activity supported by them. Depending on the type, density, and complexity of neural interconnections, a four-level hierarchy of masses within masses can be defined.

1. The aggregate is a mass of neurons which have some common source of input, but which do not interact with each other. There are three subtypes depending on the sign of output: all excitatory, all inhibitory, or mixed.

2. The population is a mass of neurons which have some common source of input and a common sign of output, and which are densely interconnected. There are two kinds of populations, excitatory and inhibitory,

3. The simple cartel is formed by the dense interconnection of two populations, one excitatory and the other inhibitory. The complex cartel is formed by the combination of a simple cartel with a population or an aggregate.

4. The brain system is a modality-specific chain or network of neural cartels.

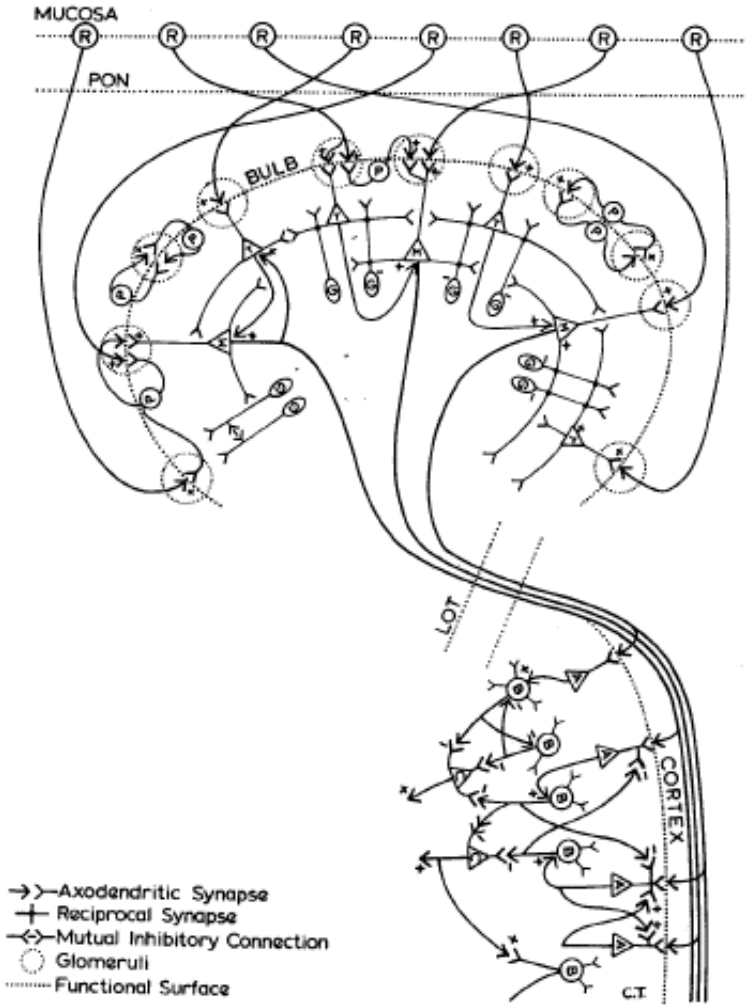

FiG. 1. This is a diagram of the neuron types of the olfactory system and their connections. All types of connections and feedback loops are shown. The levels of neural mass (aggregate, population, cartel, and system) are based on these connection types. Although each schematic neuron is shown making a few connections, each neuron in the bulb and cortex makes the indicated types of connection innumerable times.

B. TOPOLOGY OF OLFACTORY BULB CONNECTIONS

The vertebrate olfactory system can be divided into three gross parts and two connecting nerves. Each of the parts and the nerves is accessible to stimulation, recording, and surgical ablation. They are the mucosa, the primary olfactory nerve (PON), the olfactory bulb, the lateral olfactory tract (LOT), and the prepyriform or primary olfactory cortex (see Fig. 1). The neural masses within these gross parts display clear organization into sequential layers (Ramón y Cajal, 1955; Valverde, 1965).

The first part of the olfactory system, the layer of mucosa, contains the receptor cell bodies. Their axons extend from the mucosa without branching and form the PON. Electrophysiological measurements imply that the receptor neurons are all excitatory. This, plus the fact that they are not interconnected, means that these neurons form an excitatory aggregate.

The second part is the olfactory bulb. The bulb can be conceptualized simply as a kidney bean-shaped body made up of several layers. The PON axons terminate in the outer layer, which is made up of the periglomerular cells (P) and the glomeruli. The glomeruli are spherical nests of synaptic endings. Within the glomeruli the PON terminals connect with the mitral cells (M) and the tufted cells (T). The periglomerular cells are excitatory and densely interconnected; thus they form an excitatory population (P+P).

The convention (Freeman, 1967) adopted for representation of a population (a densely interactive mass of neurons which are all excitatory or all inhibitory) in a flow diagram (Fig. 2) is a pair of circles, each with a horizontal arrow to the other. The plus sign (+) represents excitation, and the minus sign (-) denotes inhibition. The first circle represents the subset of neurons in the population which receives a given input, in this case from the PON by way of the glomeruli. This subset will excite another subset which may include all or part of itself. One can imagine an indefinite replication of successive excitations, but two groups interacting among themselves will suffice for modeling purposes. The second circle represents the subset of the neurons acted on by the first subset. The output is represented diagrammatically as taken from the first subset, though in precision work a correction term is required to predict the output of the whole population. An aggregate is represented by one circle (for example, R).

The next inner layers of the bulb are made up of the mitral and tufted cells. They have two kinds of dendrites. The apical dendrites for both cells are perpendicular to the bulbar surface and end in thick brushes in the glomeruli, where they receive input from the PON and the periglomerular neurons. The basal dendrites extend for long distances in all directions parallel to the bulbar surface. The axons of both neuron types give off collaterals ending on the cell bodies of the other type which are excitatory (Nicoll, 1971). Thus they form an excitatory population (M++T).

The innermost layer of the bulb is made up of granule cells (G), the most numerous type of cell. They are slender neurons with sparsely branched dendrites oriented perpendicular to the bulbar surface. They have no axons. They are densely studded with small bulbous projections called spines or gemmules (Valverde, 1965), which form two-way or reciprocal synapses with the basal dendrites of mitral and tufted cells (Rall et al., 1966). Indirect evidence from electrophysiological recordings implies that they are densely interconnected, and that effectively they are inhibitory to each other (Freeman, 1972) as well as to mitral and tufted cells (Rall and Shepherd, 1968). It is inferred that the granule cells form an inhibitory population (G = G).

The dense interconnection of the mitral-tufted excitatory population with the granule inhibitory population forms the bulbar cartel. The conventional form representing a simple cartel in a flow diagram is the diagonalized square (T++MG = G).

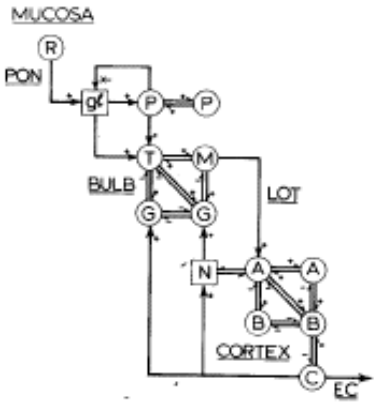

FIG. 2. This is a lumped-circuit diagram showing the main functional connections within the two olfactory complex cartels located in the bulb and cortex, and the polarities of connection: +, excitation; -, inhibition; x-, multiplicative inhibition (related to presynaptic inhibition). For symbols, see text. From Freeman (1970).

The serial-parallel cascade of the periglomerular excitatory population into the bulbar simple cartel forms the bulbar complex cartel (P++P)(T++MG = G). Together with terminal parts of the PON and the origins of the LOT this complex cartel constitutes the olfactory bulb.

Although the axons of the tufted cells end predominantly if not exclusively within the bulb, the axons of the mitral cells project from the inner layer of the bulb out to the surface of the cortex, where they form the LOT.

The LOT axons terminate in the third gross part of the olfactory system, the cortex, so that the mitral cells are the readout neurons of the bulb.

C. THE TOPOLOGY OF CORTICAL CONNECTIONS

The cortex contains three main types of neurons (Valverde, 1965; O'Leary, 1937), which have been categorized also in respect to their physiological properties (Freeman, 1968a). The superficial pyramidal cells (A) form a dense sheet of cell bodies lying parallel to the cortical surface. Their dendrites receive the axons of the LOT. Each neuron has a multiply branched axon, which terminates on other superficial pyramidal cells as well as on deeper cells. They are excitatory (Freeman, 1968a), so that these neurons from an excitatory population (A++A).

The cortical granule cells (B) occur in the layer deep to the superficial pyramidal cells. Their dendrites radiate in all directions. Their axons terminate on each other as well as on other neuron types. They are inhibitory (Freeman, 1968a) and form an inhibitory population (B = B).

The dense interconnection of these two populations forms the cortical simple cartel (A++AB = B).

The third mass is made up of deep pyramidal cells (C). They are relatively large and sparse in number. Their dendrites radiate in all directions and form connections mainly if not dominantly with the cortical granule cells. Electrophysiological evidence indicates that they are excitatory. Their axons give off collaterals to the cortical granule cells before leaving the cortex and entering that part of the white matter known as the external capsule (EC). They are the cortical readout neurons. The connections between deep pyramidal neurons appear to be much less dense than their connections to and from granule cells. Therefore the set is provisionally classified as an aggregate (C).

The serial cascade of the cortical simple cartel into this excitatory aggregate forms another complex cartel, (A++AB = B)(C), which (together with parts of the anterior olfactory nucleus) constitutes the functional prepyriform cortex. There is some evidence from EEG recording (Freeman, 1963) that the cortical mass should be subdivided into two or more complex cartels, each receiving input from the LOT and transmitting to the EC in parallel, but this is still uncertain.

D. NEURAL ACTIVITY DENSITY

The single neuron embedded in a mass is (with few exceptions) a one-directional four-stage transmitter, which generates activity in two forms. The dendritic tree receives pulse trains from afferent axons at synapses and converts them to hyperpolarizing or depolarizing dendritic current. This is transformed by weighted algebraic summation within the dendrites to the dendritic current acting on the trigger zone. There it is converted back to a pulse train. Finally, the axonal tree distributes its impulses in accordance with the location of its branches. Characteristically, the dendritic responses to two or more inputs are superimposable; that is, they are additive and proportional to the input, so that they are susceptible to linear analysis. Characteristically the axonal response is all-or-none, discontinuous, and highly nonlinear.

The activity of the single neuron at any given location in time and space can be specified experimentally by intracellular recording to determine two variables: the degree of membrane polarization related to synaptic current, and the presence or absence of a pulse at any time. Similarly, the activity of a neural mass can be observed experimentally by extracellular recording to determine two variables, which are the relative density of synaptic current (V) generated by the dendrites and the number of pulses per unit time and volume (P) on the axons of the mass.

In reality an intracellular recording from the soma of a neuron does not specify its entire state. The mitral cell, for example, has output through basal dendrodendritic synapses with granule cells, axon collaterals to tufted cells, and widely distributed axon terminals in the anterior olfactory nucleus and cortex. It is doubtful that the level of transmembrane potential in the soma can serve fully to specify the magnitudes of those outputs at any moment. It is not possible to measure the transmembrane potential at many points in the neuron, so rules are adopted (for example, an action potential is all-or-none for the entire axon; synaptic conductance changes are nonpropagating; membrane specific capacitance is invariant) to permit an observer to infer the state of the whole neuron from a single measure. The validity of such rules is continually subject to challenge and review, but they are widely used.

Similarly, it is not possible to measure neural responses at all points in a mass, and rules are needed to extrapolate from a limited set of measurements to the active state of the mass. But the two cases differ in regard to dimensionality. The state of a single neuron can be inferred from one of the two variables changing with time at some fixed point, but the active state of a mass must be inferred from one of these variables changing in space as well as in time.

The neural masses of the olfactory system occur in layers, which lie orthogonal to the main trajectory of axonal trunks connecting them. Interactions (when they occur) take place in the layers, and neurons vertically separated in the same part of a layer often have similar response patterns. One of the rules applied to masses is that the active state can be adequately described in the two surface dimensions of the layer containing a neural mass, so that the activity of any neuron or set of neurons in the vertical column (Mounteastle, 1957; Hubel and Wiesel, 1963) at or around a point on the surface of that mass serves to represent the active state of that part of the surface. By means of this rule the neural activity at or in the near vicinity of a point can be referred to as an activity density.

The size of the "near vicinity" in which a single value for one of the variables, V or P, can represent the activity density of the surface is larger than the size of a single neuronal soma and less than the radius of its dendrites. In a mass containing an excitatory population, both P and V are continuous. This is unlike the case for measures of activity of single cells where only one variable is continuous-that which measures membrane potential, V. Both P and V are continuous across the surface because the many branches of the many neurons are interwoven and the neurons are densely interconnected. It is continuous in time, because there is temporal dispersion across the large number of axon terminals, and because the dendritic membranes exert a smoothing action. Owing to this trait the activity distribution of a neural mass can be specified by many fewer measurements than the numbers of its neurons (see Note 8).

This continuity must hold for populations but need not hold for aggregates (noninteractive masses), owing to their lack of internal interconnectedness, unless it is imposed by continuity in some input function, such as an electrical stimulus.

Because a functional surface is defined as the entire cross section of a population or aggregate orthogonal to the transmission trajectory, it may coincide with the anatomical surface of the mass. But it need not. Typical functional surfaces are indicated by dotted lines shown in Fig. 1. The mucosa is a representative surface for the receptor cell aggregate, but so also is any cross section through the PON. All surfaces have limits or boundaries. The three populations of the bulb share a common functional surface, a common anatomical surface, and a common boundary. The boundary is determined by the distribution of the terminals of the PON. Activity in the mitral cell population can also be represented at any cross section through the LOT. This is an example of a population for which more than one functional surface can be defined (none of which, obviously, is the anatomical surface of the LOT). The populations of the cortex share a common functional surface, a common anatomical surface, and a common boundary, which is determined by the distribution of axon terminals of the LOT (LeGros Clark, 1956, 1957, White, 1965; Heimer, 1968).

E. EXPERIMENTAL INPUT-OUTPUT VARIABLES

Although each population performs all four transformations and sustains both wave and pulse activity, this activity is not always detectable.

Pulses can be recorded from any type of cell in the olfactory system except the granule cells (G), because they do not have axons and do not produce extracellularly detectable action potentials.

Waves can be detected only for the bulbar granule cells (G) and for the superficial pyramidal cells (A) (Freeman, 1970). This is due to the individual and collective geometries of the neurons of the populations. The waves of potential which are recorded are the result of extracellular spread and summation of dendritic current in a volume conductor. This current is produced by the dendrites of large numbers of neurons. Populations whose neurons have dendrites oriented radially with respect to their cell bodies generate a closed or monopole field of potential, which is low in amplitude and restricted to the anatomical limits of the cell processes. Populations whose neurons tend toward axial symmetry generate dipole fields, which are high in amplitude and extend for greater distances. In the olfactory system the granule cells (G) and the superficial pyramidal cells (A) have dendrites oriented on an axis perpendicular to the population surfaces, so that their dipole fields greatly overshadow the monopole synaptic current fields of the mitral-tufted cells (M, T) in the bulb and the granule cells (B) in the cortex.

The activity of a population can be observed in two experimental conditions-during normal unstimulated operation characterized by "spontaneous" or background activity, and during electrical stimulation characterized by evoked activity. The spontaneous activity for single neurons for the great majority of bulbar and cortical neurons takes the form of seemingly random pulse trains (Freeman, 1968a). The mean pulse rate is designated P,. The expectation density or autocovariance is usually nonoscillatory. Spontaneous wave activity, which is the EEG (electroencephalogram) of the bulb or cortex, takes the form of a randomly varying potential having one or more characteristic frequencies of oscillation. The wave amplitude histogram almost always conforms to a Gaussian curve. Mean pulse rate for the single neuron, P., is usually less than one-fourth the characteristic frequency of the EEG.

The other type of activity is caused by single-shock electrical stimulation of the PON or the LOT. The former superimposes a volley of action potentials onto the spontaneous or background activity of the PON and activates the bulbar complex cartel (P++P)(M++TG = G) orthodromically (in the normal direction of transmission). The latter superimposes a volley of action potentials on the background activity of the LOT which runs in two directions: orthodromically to the cortex, where it activates the cortical complex cartel (A++ AB = B) (C), and antidromically (or in the reverse of normal direction of transmission) to the bulb, where it activates the bulbar simple cartel (M++TG = G) but not the periglomerular population (PTP).

The resulting wave responses of the granule cell populations (G = G) or of the superficial pyramidal cell population (A++A) are known as evoked potentials, and the pulse responses of single neurons (P, M, or TI A and B) are known as the induced unit responses. Sets of evoked potentials and induced unit responses are averaged to remove background activity. The results are known as the averaged evoked potential (AEP) and the post-stimulus time (PST) histogram. These averaged responses are the prime working data for mass analysis.

To estimate a pulse density distribution, spontaneous pulse trains or induced unit responses are sampled at many points under the surface, but to estimate a wave density distribution, the EEG's and evoked potentials are best taken from epicentral regions on the surface to represent the activity of masses determined from the spatial distribution of the dipole fields.

F. THE ACTIVITY DENSITY FUNCTION (A.D.F.)

To recapitulate, the assumption is made that a neural activity distribution exists across an interactive neural mass, for which the magnitude of each point in the surface is an activity density. The activity density is reflected in the pulse trains and EEG waves recorded at and about each point. The next question is: How can one determine the relationship between the observable events and the underlying events of interest?

In answer, it is inferred that the activity distribution arises from the cooperative interactions of many neurons by means of their functional interconnections. It is feasible to describe the known dynamic characteristics of single neurons by means of nonlinear differential equations an further, to describe the proposed topologies of their massive interconnections in their surface dimensions by the same means. The equations can be solved for initial conditions corresponding to known or suspected input to a neural mass. The solution takes the form of an equation for a time-varying surface, which is an activity density function (a.d.f.), and which describes the neural activity distribution. Next, the time dependent value of the a.d.f. at each point in the surface can be transformed in accordance with the predicted relation between the neural activity density and an observable event such as a pulse train or EEG wave. The comparison of observed waveforms with predicted waveforms derived from the a.d.f. determines whether the image constructed for the neural activity distribution is admissible. Such comparisons are demonstrated in Figs. 3-6.

The a.d.f. is defined only for aggregates and populations or parts of them, and it holds only for aggregates when continuity of function is imposed in both spatial and temporal dimensions by the input. The dynamic properties of simple and complex cartels must be predicted by generating an a.d.f. for each population and aggregate constituting them. This is because the observable events and averages of them are manifestations of activity by single neurons or groups of neurons of the same kind, which is in the definition of the population. The observable outputs of the olfactory bulb, which contains a complex cartel, are action potentials from neurons in two populations, EEG waves from another, and action potentials from the LOT, which is the real output to the cortex producing cortical responses to bulbar events. The "output of the bulb" does not exist except in relation to these observables, and in each case a complete set of population a.d.f.'s is required for prediction and description.

The concept here expressed as the activity distribution of an aggregate or population is basically equivalent to

the representation of an active state by Sherrington (1929) for pools of motorneurons in the spinal cord as the central excitatory state (c.e.s.). The term a.d.f. is introduced in part to avoid the unnecessary dichotomy between c.e.s. and c.i.s. (inhibitory) ; in part to avoid an ambiguity in usage of the term c.e.s. between "state of excitation" and "state of excitability" to the exclusion of the latter- and in part to introduce explicitly the notion of a mathematical, continuously varying surface density representing the activity distribution maintained by the neurons in a population, which exists only as an attribute of the mass (see Note 9).

Distributions exist before and after each transformation effected by a population. When the successive transformations of the component neurons are lumped into four types (a pulse-to-wave conversion, a wave-to-pulse conversion; a wave-to-wave transformation; and a pulse-to-pulse transformation), there is a pulse a.d.f. or wave a.d.f. to describe each input and each output. Further, a pulse a.d.f. can be defined for each surface orthogonal to the trajectory of an axonal tract or compound nerve. That is, an a.d.f. can be defined for cross sections of the PON and LOT as well as for the olfactory mucosa, the olfactory bulb, and the cortex. These a.d.f.'s are the state variables of the equations describing the neural dynamics.

The main task for population analysis is to estimate the a.d.f. before and after each successive trans formation, and from each pair to describe the essential nature of each transformation.

The method of analysis proposed here and elsewhere (Freeman, 1963, 1972) for the dynamic properties of neural masses logically parallels that used to analyze the Properties of nerve axon and axon bundles. One side of the analysis involves the measurement of observables. First, the electrical output of a population, when it is a functional part of a cartel is measured in a broad range of conditions, particularly in relation to behavior, so that a physiological dynamic range of function can be defined for both "spontaneous" and evoked activity. Second, by paired shock stimulation and the application of the superposition principle a linear dynamic range is established. This range is extended by piece-wise linear approximation, and the limits of nonlinear performance are clearly defined. Third, within the linear and piece-wise linear ranges the responses to electrical stimulation, AEP's, and PST histograms are fitted with curves generated from the sum of exponential terms having both real and imaginary coefficients. This constitutes the process of measurement (Freeman, 1972.).

The other side of the analysis is the formulation of mathematical equations describing three aspects of each population functioning within a cartel-namely, the dynamics, the state of activity, and the observed responses. First the dynamics of the mass are described by a linear differential equation having state-dependent coefficients formulated from the known or suspected physiological, pharmacological, and anatomical properties of the cartel. Next, the distribution of neural activity is described by an a.d.f., which is a solution to the differential equation for boundary conditions corresponding to the stimulus conditions. Finally, predicted waveforms are derived from the a.d.f. by transformations which are specified by the rules relating the active states of neurons to the electrophysiological events observed by recording, including the recording sites.

The resulting transformed a.d.f.'s (the predicted waveforms) are compared with the curves derived from measurement (the observed wave forms). Congruence implies that the differential equation is an admissible formulation of the dynamic properties of the cartel; noncorrespondence gives reason for another try, either at observation or at formulation. Because some of the coefficients in the differential equation can be evaluated only by comparison with the measured response, mere congruence for single responses is not difficult to achieve. It is more difficult to formulate the differential equation, so that a change in one coefficient representing an appropriate physiological parameter will change the solution to the equation in the same way as a physiological change in the animal (or a change in the input) will change the output of the cartel. A still greater challenge is to observe a pattern of change in the cartel response, replicate it by changing a coefficient in the equation, and verify by independent observations that the necessary (predicted) condition or property exists in the cartel.

As with membrane studies, it is convenient at the outset to separate the time, distance, and amplitude dependencies of the activity density, and to treat either static or lumped-circuit properties in terms of ordinary differential equations. Experimentally this is done by recording from central regions of active zones in populations, and expressing the active state as a variable in time, t, x, y, or V or (in the linear case) in the operator, s.

Elimination of the spatial dimensions reduces representation of the cartels to a flow diagram (Fig. 2). The a.d.f.'s represented by the arrows are reduced to single-valued functions of time and amplitude, and in this form they are the state variables of the equations describing the dynamics of the cartels.

G. SUMMARY

It is assumed that widespread configurations of neural activity exist in neural masses, which are collective properties of the masses existing by virtue of dense connections within and between masses. Masses can be conceptually isolated, defined, and classified at four levels according to the complexity of their connections. The simple, internally unconnected mass with common input is an aggregate. The simple, densely interconnected mass with common input and common sign of output (excitatory or inhibitory) is a population. An excitatory population densely interactive with an inhibitory population forms a simple neural cartel. The combination of an aggregate or population with a simple cartel forms a complex cartel, which minimally suffices to represent observable masses in the vertebrate brain. Cartels in series and parallel configurations form brain systems.

The distributed active states sustained by cartels give rise to observable events such as pulse trains, evoked potentials, and EEG waves. After appropriate averaging, those observables can be treated as more or less direct representations of the distributions of massive activity. The relation between observed and assumed real events is established by representing the functional interconnections within the masses by differential equations. Each solution to the equations for specified input yields a theoretical or predicted activity configuration, which is termed an activity density function (a.d.f.). The a.d.f.'s for a given neural mass, whether in distributed or jumped circuit form, comprise the state variables representing the active state of a neural mass under designated input conditions. From the a.d.f.'s are calculated the predicted waveforms of responses to specific inputs. The predicted waveforms are fitted to observed waveforms to' evaluate the equations.

IV. The Parameters of Neural Masses

At the outset it is feasible conceptually and experimentally to separate three independent variables of the activity density function (a.d.f.). These are response amplitude (described in Sections IV, A and B), time or frequency (Sections IV,C-E), and space or the surface dimensions (Section IV,F-H). This results in three sets of linear differential equations, each with its own set of coefficients, which are gain coefficients, rate constants, and space constants. The mathematics and essential numerical results of these approaches have been summarized elsewhere (Freeman, 1967, 1968a,b, 1972). The present description is restricted to qualitative aspects.

The numerical evaluation of interactive properties of neural masses, which are dependent on input and output magnitudes, requires two types of gain coefficient. One is forward gain and the other is feedback gain. Forward gain is a measure of the one-way functional connection density between aggregates, populations, and cartels. It can go from zero (when the formation of spontaneous action potentials is suppressed by anesthesia or surgical trauma) up to the limit of the anatomical connection density. Feedback gain is a measure of interconnection or the functional interconnection density within populations and cartels. Since aggregates have no anatomical interconnections, they never have feedback gain. Thus, functional interconnection density within a neural mass is the defining characteristic by which to distinguish a population or cartel from an aggregate. It is the attribute most heavily responsible for the ways in which the dynamics of a neural mass differ from the dynamics of the component neurons. Therefore, the problems of quantitative measurement of this attribute are fundamental in the study of neural masses.

A. FORWARD GAIN

The forward gain of neurons in a mass can be treated as the product of two conversion factors. Each describes one of the two conversions that are carried on by each neuron in the aggregate or population. One is the conversion from. a pulse density function for afferent axonal pulse trains to a wave function for dendritic current; the other is the reciprocal conversion of dendritic current to efferent axonal pulse trains. Therefore the forward gain is dimensionless, but the two stages require reciprocal conversions of units-for example, from pulses/sec/unit area Of neural mass (pps) at the input of the dendrites to amp/unit area of neural mass (a) at the output of the dendrites, and from amp/unit area of the neural mass (a) at the input of axons to pulses/sec/unit area of the neural mass (pps) at the output of. the axons.

The conversion factor of each stage is given by the ratio of the instantaneous magnitudes of output to input in units of a/pps and pps/a. In principle, all that is needed for estimation of forward gain is the measurement of the population wave amplitude over its range of variation and the concomitant pulse densities at the input and output for the designated range. The former can be taken from a set of instantaneous values for the amplitude

of the EEG waves generated by a population, provided the field geometry is correctly mapped. (The units of measurement may be in <?>volts rather than amp, because the transverse cortical resistivity in ohms-unit area is invariant.) The pulse densities can be inferred from the- probability of pulse occurrence conditional (Parzen, 1960) on the amplitude of the EEG corresponding to the time of pulse occurrence (Freeman, 1972). In practice the analysis is limited to those neurons for which the requisite state variables are accessible. Moreover, recognition must be given to the time delay between the occurrence of a pulse and its manifestation in the wave, and vice versa. The delay appears constant for any neuron but varies from one neuron to another.

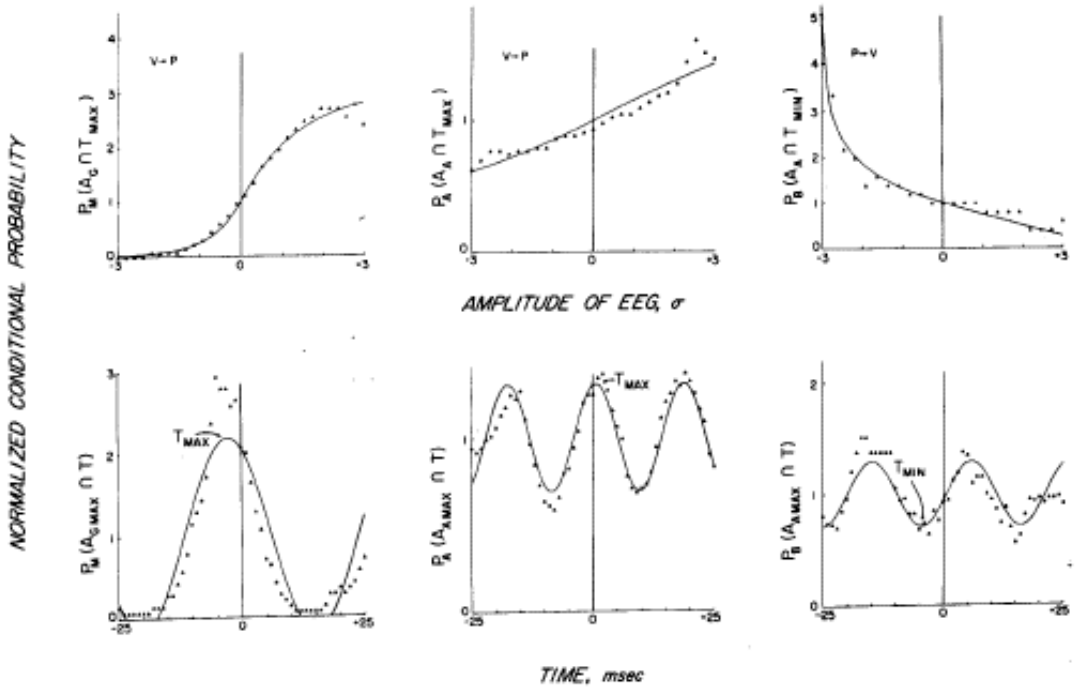

FIG. 3. The three lower frames show the probability of pulse occurrence (triangles) for three single cells of types M, A, and B, conditional on the time delay from the EEG wave maximum (+ 1σ to + 3 σ). The fitted curves are pulse probability waves. The three upper frames show the pulse probability (triangles) for the same three neurons, conditional on the amplitude of the EEG at the optimum time lag determined from the frames below. The fitted curves are the input-output conversion curves, from which forward gain and feedback gain are calculated. Equations for the curves are given elsewhere (Freeman, 1972).

The method for calculating experimental conditional probabilities is as follows. A random pulse train is sampled from a single cell simultaneously with the EEG for 1 to 5 minutes at intervals of I msec. The amplitude range of the EEG is divided into 64 segments or bins. For each value of amplitude as it occurs, the question is asked, Does a pulse occur now or at any of the preceding or following 25 msec? Tabulations are put into a table (64 X 51). For each block in the table the total number of pulse occurrences is divided by the total number of wave amplitudes, each block representing a certain time delay between the occurrence of pulse and a particular wave amplitude. Each fraction is multiplied by 1000 to express it in units of pps and is divided by the mean pulse rate, P_o, to express it as the normalized conditional pulse probability, P. The result is a table of conditional probabilities, P(T∩A), each block specifying the probability that a pulse occurs given a certain time delay from a certain wave amplitude.

The amplitude histogram showing the distribution of the wave amplitudes is Gaussian, with the mean equal to zero amplitude and the standard deviation equal to a. Whenever the EEG is taken from the surface, negative values of potential are due to excitation and positive values to inhibition of the neural populations generating the EEG. The reverse is true for depth recordings. To surmount these sources of confusion, the range of wave amplitude representing the increased excitation is denoted "positive," and the range from +σ to +3σ is designated A.., The corresponding ranges for inhibition (from -1σ, to -3σ) are called "negative" and A_{min}.

The conditional probabilities in the table are averaged within these two amplitude ranges for A .. in and A max at each value of T. Examples of graphs of the probabilities of pulse occurrence conditional on the time delay from the amplitude maximum, P(A ∩T), are shown in Fig. 3 (bottom, small open triangles). These

curves are oscillatory, with the same frequency as the on-going frequency of the EEG. They show the optimum time lag for the three conversions represented. This time lag is denoted T_{ma}. for the excitatory neurons, types A and M, and T_{mi}. for inhibitory neurons, type B. For example, in the graph at the left it is seen that the mitral cell is most likely to fire 4 msec prior to the maximum of the granule cell wave (T_{m}.. = -4 msec). This is because the mitral cells excite the granule cells, and the rise in their firing probability is followed by a wave of granule cell activity.

It has been found that each individual mitral cell has its own characteristic time delay from the EEG, but on the average it is one-fourth of a cycle at the on-going frequency. This is the basis for proposing the existence of a. phase code by which this part of the nervous system operates, about which more will be said later.

Examples of graphs of the probabilities of pulse occurrence conditional on the optimal time delay and the wave amplitude values, P(A∩T...) and P(A T_{mi}.), are shown in Fig. 3 (top, small open triangles). These are the experimental input-output curves of pulse-to-wave and wave-to-pulse conversions. The slopes or derivatives of these curves give the instantaneous output to input ratios or the conversion factors.

Three important generalizations emerge from these input-output curves. First, the curves are sigmoidal (s-shaped) ; thus it is seen that I the conversion factor is maximal at zero wave amplitude and decreases exponentially as amplitude increases from zero owing to excitation, or decreases from zero owing to inhibition. [The graph for B (Fig. 3, right) must be rotated 90' counterclockwise for proper viewing (Freeman, 1972). The reason is that both the theory and the experimental method for determining the relation of pulse, P, to wave, V, require that V be the independent variable, whereas the process of pulse-to-wave conversion in dendrites requires that P be the independent variable.] There are both upper and lower saturation levels for both conversions. Second, for each stage the conversion is linear over a central range of input-output amplitudes. Third, both sigmoidal curves have sharper curvature on the inhibitory side.

For dendritic pulse-to-wave conversion the sigmoidal pattern is immediately intelligible in terms of the ionic mechanisms of postsynaptic potentials of single neurons. For a given ion-specific conductance change induced in the membrane by an afferent pulse volley, the magnitude of the dendritic potential wave depends on the difference between the existing membrane potential and the equilibrium potential of the conductance, change. The magnitude of the second response superimposed on an earlier response is smaller than the first, because the driving force is less (Eccles, 1957). This inherent dependence of forward gain on response amplitude can be described with a pair of first-order linear differential equations, the solution to which yields the input-output curve shown in Fig. 3, right upper frame.

The same type of amplitude-dependence of the conversion factor occurs at the sites of wave-to-pulse conversion in neurons, the trigger zones. The typical wave-pulse relation for a population (Fig. 3, left upper frame) is not identical to that for a single neuron (e.g., Granit et al., 1963). The former is sigmoidal; the latter is linear between threshold (zero firing rate) and a high maximal rate, which can be sustained for brief periods of time but not indefinitely.

There are two reasons for the differences between these input-output curves for the population and the single neuron. The asymptotic approach to zero of the foot of the population curve can be attributed to a distribution of thresholds and of firing times with respect to the population means among the neurons making up the population. The asymptotic upper limit at three times the mean firing rate for each neuron can be attributed to the requirement that the upper limit hold for the neuron over an indefinitely long time-space, or (according to one form of the ergodic hypothesis) over the entire population at any one time. That limit clearly must be-lower than the upper limit on the maximal firing rate accessible to a neuron firing in bursts over short time intervals.

The operation of these two population properties yields a sigmoids wave-to-pulse conversion curve which is asymmetric. The curvature on the inhibitory side is twice that on the excitatory side, and the range is half. The implication is that the distribution of thresholds and firing times is directly related to or dependent on the maximal population mean firing rate and the central mean, Po, so that the single process occurring in membranes at the trigger zones (denoted by the conversion coefficient) controls the sensitivity or gain for wave-to-pulse conversion. This factor has not been identified at the cellular level, nor has it been adequately described at the population level. On the other hand, there are three processes in membranes at synapses controlling the factor for pulse-to-wave conversion: the two ionic equilibrium potentials, which are presumably fixed, and the conversion coefficient for the conversion process. Like the conversion coefficient for wave-to-pulse conversion, it has not yet been identified with known cellular mechanisms.

The forward gain, being the product of two conversion factors which are amplitude-dependent, is similarly amplitude-dependent. Increasing activity in either direction from zero results in decreasing forward gain.

Transmission is amplitude-limited normally at one of the two stages, activity at the other stage thereby being restricted to the quasi-linear range, so that, unless large-scale jumps in amplitude occur, the amplitude dependency of the forward gain for the two stages in series is normally determined by one stage and by one rate constant. Thus in the bulb the limits on wave-to-pulse conversion are dominant, whereas in the cortex the reverse holds.

B. FEEDBACK GAIN

Dense interconnection implies the possibility of feedback of activation (excitation or inhibition) onto that part of a mass initially perturbed by an afferent volley. For this reason analysis of the dynamics of interconnected neural masses requires measurement of the parameter of feedback gain as well as forward gain.

The level of interaction within an excitatory population is "positive excitatory feedback gain." That within an inhibitory population is "positive inhibitory feedback gain." That between excitatory and inhibitory populations within cartels is "negative feedback gain." (Interactions between cartels cannot be "dense" within the meaning of the term used here. It is likely that such interactions will best be described in terms of bias controls, as defined below, but the level of experimental analysis has not yet been advanced far enough to cope with this problem.) Within a population the feedback gain is the square of the forward gain, and it is positive. Between populations in a simple cartel the feedback gain is the product of the two population forward gains, and it is negative. In all cases the gains are dimensionless coefficients.

Two methods have been devised for estimating the values of negative feedback gain in simple cartels. The first method is by taking the product of forward gains from measurements of "spontaneous" activity. The necessary observed activity is accessible for both conversion curves for the A population, so that the forward gain for the A population has been calculated from the product of the derivatives (Freeman, 1972). Because the average phase lag between the conditional pulse probability waves for A and B neurons is about 90â€¢, it is inferred that the forward gain for the B population is equal on the average to that for the A population. Therefore the feedback gain of the cartel formed by them is given by the square of the forward gain for either. The second method is based on measurements of AEP's in response to electrical stimuli varied over a range of magnitudes, as described below. The close agreement in numerical values 'for gain derived from these two independent sets of data and analysis on the olfactory cortical cartel have provided a check on the validity of the methods (Freeman, 1972).

A population generates a characteristic pattern of response for its neural activity distribution upon impulse activation, depending on which level in the hierarchy it is functioning in. The measurement of observed waveforms from each response pattern yields a set of closed-loop rate constants or frequencies. These in turn serve to evaluate the magnitudes of the feedback gain coefficients, which express the mean densities of interaction within the neural mass. Experimentally it is found that on the average the feedback gain coefficients are related as follows. Feedback gain for the two kinds of population, the square of the forward gain for each population, is denoted by KE and Ki, Negative feedback gain, K_N, in a simple cartel is equal to the square root of their product, $K_N = (KEKI)^{1/2}$, provided the amplitude of the response to a test signal exceeds the amplitude of the background activity. If the test response is smaller than the background activity, then $K_n = (K_g K_i K_o)^{1/3}$, where K_o is a fixed reference gain equal to the gain at zero wave amplitude (Freeman, 1967).

The aggregate occupies a position of special importance in the hierarchy, because it is to this "open-loop" state that populations and cartels are reduced by very deep anesthesia. When interactions are reduced to zero by this method, so is the feedback gain, and the neural mass is a functional aggregate having only forward gain, even though the anatomical connection density is unchanged. In this state the open-loop rate constants of the component neurons, which express the fixed time delays of the component neurons, become accessible to measurement, Values obtained by measuring open-loop responses serve as the basis for computing the values for closed-loop feedback gain from the rate constants of the closed-loop responses.

The essential mathematical tool used for measuring these sets of rate constants and from them deriving estimates of gain is linear systems analysis. The experimental and theoretical bases and conditions for using this tool on neural masses have been described elsewhere (Freeman, 19641 19671 1972).

There are three main difficulties in its use in the present context. First is the separation of neural delays encountered outside a given neural mass (that is, those between the input site for stimulation and the first junction point within the mass) from those encountered inside the mass (those between the first junction point for the re-entry of feedback in the closed-loop state and the site of output for recording). For example, on electrical stimulation of the PON, the afferent axonal delay of the path stimulated is part of the total delay measured of the bulbar cartel $\wp\}$ the open-loop state, but it does not occur within the bulbar loop when the loop is closed. Second is the interpretation of the rate constants of the neural mass in terms of the delays of the component neurons. Third is the compilation of evidence that the open-loop rate constants do not vary when the loop is closed or when the gain otherwise changes. These problems have been considered in detail in the references cited above and in other work not yet published. As experimental problems they are both challenging and intriguing, and the proposed solutions strongly influence the details of the hypothesis of neural masses here being outlined. However, the prior questions must be dealt with here-whether the neural activity distribution of a population can exist in a closed-loop mass as a continuum, and, if so, what its time course might be when the population is functioning independently or as part of cartels of increasing complexity.

C. MONOTONIC RESPONSE PATTERNS OF POPULATIONS

The experimental results show unequivocally that wave responses can be observed and measured as the output of closed-loop masses. The excitatory population can be modeled as a positive feedback loop, in which, for both forward and feedback limbs of the loop, the response to an impulse input is a rapid rise in a.d.f. and a monotonic fallback to the baseline level without an overshoot. (A ripple with a frequency near 200 Hz may be observed to ride on the main transient.) The rate of rise is more rapid and the decay rate is less rapid than the corresponding rates for the open-loop response. The disparity increases with increasing feedback gain KE. As closed-loop feedback gain increases from zero and approaches the value of unity, the response decay rate approaches zero, which implies that the closed-loop response to a pulse may last many hundreds of milliseconds. Such long-lasting impulse responses are commonly observed in the central nervous system.

The same response configuration holds for the inhibitory population with an important exception. Whereas the a.d.f. of the forward limb increases on impulse excitation and then monotonically decays, the a.d.f. of the feedback limb decreases and then monotonically decays in mirror image to the a.d.f. of the forward limb. This is because the subset of neurons initially excited inhibit the second subset, which (being inhibited) disinhibit the first, which are free to be excited by spontaneous activity. Thus, this pattern cannot occur unless there is sustained or steady-state background activity of "bias" to the neurons in the inhibitory population, against Which the inhibition of the feedback limb can occur. This bias cannot be generated internally by mutually inhibitory neurons. It must come from excitatory neurons, either as an excitatory aggregate or as an excitatory population.

In the olfactory system the total removal of the olfactory receptors does not silence the activity in the bulb or the cortex. Transection of the bulbar stalk silences the cortex but not the bulb. Therefore, the bulb contains its own internal source of an excitatory bias, which has been traced to the population of periglomerular neurons (P++P in Fig. 2).

The mechanism by which this population is thought to operate is of crucial importance to the study of neural masses, so it must be considered in some detail. The anatomical connection density of these neurons is very high and must exceed the level sufficient for unity gain. The neurons do not have inhibitory input, so the only effective functional limits on their activity are the upper saturation limits on their P-V and V-P input-output curves. Therefore, provided those upper limits are sufficiently high to permit firing of each neuron at or above some minimal mean rate, each pulse emitted by each neuron will in effect recur upon that neuron (in smoothed form) with sufficient excitatory potential to excite that neuron at a shorter mean interval than the preceding interval. In effect, the closed-loop feedback gain can exceed unity, so that any random event will cause the population a.d.f. to rise exponentially.

But if the a.d.f. rises above the running mean pulse rate (in the excitatory direction), the forward gain of each limb of the loop diminishes, so that the feedback gain, which is the product of the two forward gains, must decrease until it reaches unity. Thereby the excitatory population is self -stabilizing in the absence of direct inhibitory input. Any additional transient input that increases the a.d.f. must further decrease the feed back gain and increase the decay rate of the impulse response, so that the a.d.f. returns to the unity gain level of activity (Fig. 4, left). Conversely, any sudden decrease in the background level of excitatory input from the aggregate of receptors must increase the gain above unity, so that the impulse response increases with time, and the a.d.f. returns to the level for unity gain.

The periglomerular excitatory population is the key to the study of neural masses in the olfactory system in two major respects (as well as several minor ones). First, the dense interaction at the local level provides a basis for the continuum of the a.d.f. in the spatial domain, which the olfactory receptors in the aggregate cannot. Second, its continuing output provides the excitatory steady-state bias required by inhibitory populations and cartels for operation within linear and quasi-linear ranges.

So crucial is this set of functions to the hypothesis being developed here that it cannot be expected to apply to other systems in the brain, unless excitatory populations are found in them as well. It seems likely that such populations will be identified for the somesthetic system in the substantia gelatinosa Rolandi (Wall, 1962), which has properties similar to those of the glomerular layer of the olfactory bulb. Whether they occur in the retina, the cochlear ganglion, or some other stages of the visual and auditory systems or in the spinocerebellar pathways is at present unclear. The identification and functional analysis of excitatory populations early in the transmission sequence of sensory systems is a major unsolved problem in the development of a theory of neural masses.

D. OSCILLATORY RESPONSES OF POPULATIONS WITHIN CARTELS

The existence of two interconnected aggregates, one excitatory and the other inhibitory, is conceivable and would be modeled as a simple negative feedback loop. The response to an impulse input would be a simple damped sine wave. The frequency of the oscillation would depend on the negative feedback gain; the higher the gain, the greater the frequency and the slower would be the decay rate of the "ringing."

This arrangement has not yet been found in the vertebrate brain. It would seem unlikely, because it would require that each neuron be densely connected exclusively with the other kind and not with its own kind, a pattern that could easily be identified and has not been. Where negative feedback is found and properly measured, it occurs between populations and not aggregates. Therefore the output, which is that of each population functioning within a simple cartel, consists in two parts or components: one (the dominant component) is the damped sine wave of the negative feedback loop; the other (the minor component) is a monotonic or nonoscillatory wave, which is the combined output of the two positive feedback loops.

The impulse response (triangles) of the granule cell population within the bulbar complex cartel (P++,P)(M++ T G = G) is oscillatory (frames at right, solid curves). The dominant oscillatory component (dashed curve) due to the negative feedback loop is a damped sine wave. It is superimposed on the minor monotonic component (dashed curve) due to the combined output of the two internal positive feedback loops (M++T) and (G = G). These two loops are driven by the monotonic output of the periglomerular population (P++P), as well as by the stimulus pulse. That is why the minor component is upward. In the output from a simple cartel it is downward.

As the stimulus intensity increases (from top frames to bottom) the observed waveform amplitude (triangles) increases, and its shape changes. The rate coefficients of the predicted waveform (fitted curves) also change. The changes can be accounted for solely by the amplitude-dependent pattern of change in functional interconnection densities (feedback gains) within the cartel, which is predicted by the curves in Fig. 3 (upper frames). From Freeman (1970).

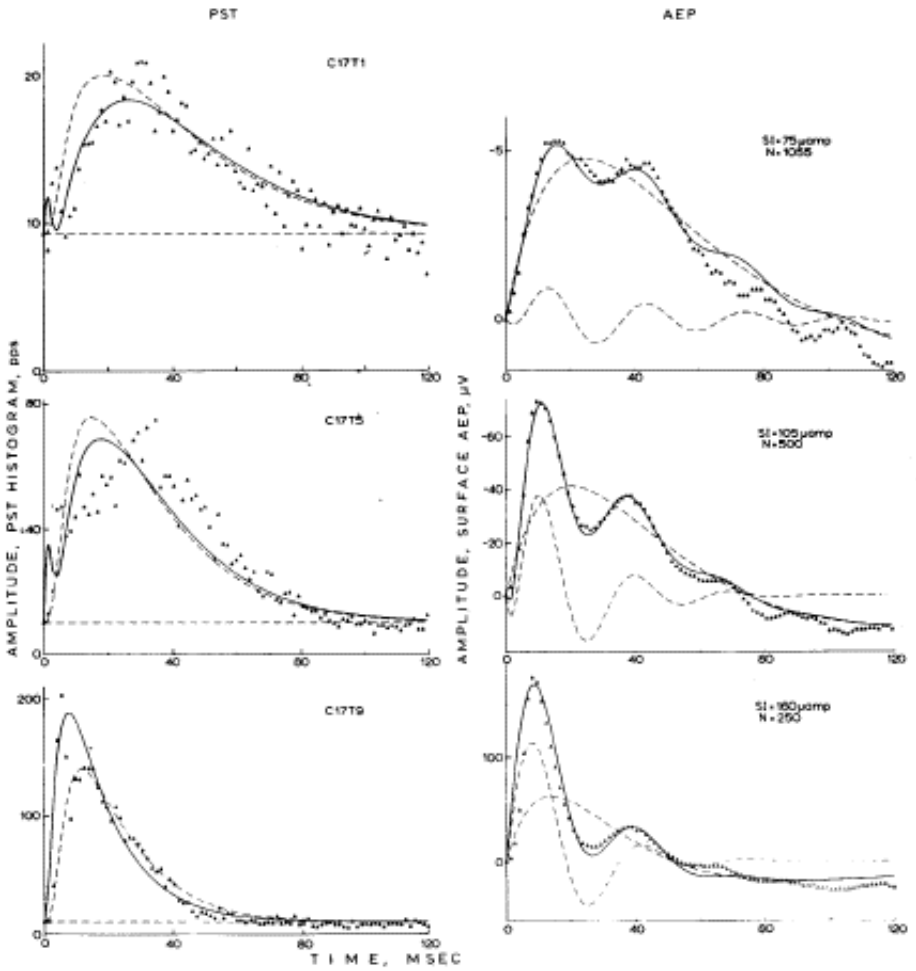

FIG. 4. The impulse response (triangles) of the periglomerular excitatory population (P++P) is monotonic (frames at left).

The minor component for a population in a simple cartel constitutes an "internal bias" on the operation of the oscillatory mechanism, which has a profound effect on the frequency and decay rate of the damped sine wave. Owing to the asymmetry of the conversion curves of the component neurons (Fig. 3), the internal bias is characteristically inhibitory. This is manifested by a downward monotonic base-line shift superimposed on the initially upward damped sine wave response to an impulse. The granule cell population functioning as part of the simple bulbar cartel on antidromic invasion from the LOT typically generates this waveform.

The orthodromic response through the PON is that of the granule cell population functioning as a part of the bulbar complex cartel, because the input is cascaded through the periglomerular population. The sustained excitatory input from this excitatory population following on the initial input causes the population to display an excitatory base-line shift; that is, the initially upward damped sine wave is superimposed on an upward minor component (Fig. 4, right). This is the manifestation of an "external bias" from the periglomerular population operating into the cartel in parallel to the transmission line for the original activating pulse.

The significance of external bias on simple cartels lies in frequency control. All neural populations functioning separately and as part of cartels have in common the amplitude-dependence of feedback gain. As the response amplitude of a population increases above mean, the feedback gain decreases, with the result that response frequency decreases and response decay rate increases. The effect of internal inhibitory bias is to augment the sensitivity of frequency to amplitude changes. The effect of external excitatory bias is to stabilize the frequency and to augment the sensitivity of decay rate. Thereby in the typical bell-shaped surface distribution of the bulbar focal response to PON stimulation, the response amplitude at the center of the focus decays faster than it does in the surround, but all parts decay at the same frequency irrespective of initial amplitude.

It will be seen shortly that the oscillatory responses of populations in the bulbar cartel following electrical stimulation of the PON or of the olfactory mucosa not only have a common frequency of oscillation, typically

between 40 and 80 Hz, but also have a common phase after the first cycle, despite prolonged conduction delays in activation across the surface. The external excitatory bias mechanism explains the common frequency but not the common phase. That can result only from dense interconnection among neurons in the cartel.

E. FEEDBACK IN THE TWILIGHT ZONE

The concept of pure excitatory feedback in networks of neurons was familiar to nineteenth century neurophysiologists and was described by Ramón y Cajal (1955, p. 11) with the term "avalanche conduction"; by Ranson and Hinsey (1930) with the term "reverberating circuit"; and by Lorente de Nó (1933) with the phrase "closed self-exciting chain." Lorente de Nó (1938, p. 233) later disavowed use of the last two terms to describe activity of "internuncial" neurons, because they omitted explicit reference to inhibitory actions. He also stated that his network diagrams based on Golgi stains. were heuristic schematics and were not adequate to describe the complexity of neural masses. Specifically he viewed the activity sustained among "internuncials" in response to impulse activation as a continuous barrage. The periodic firing of a motor neuron subjected to the steady level of excitation was owing to the refractory period of the motor neuron, he said (p. 241), and not to the circulation of a volley within the mass. Nevertheless the term "reverberatory discharge" (Hebb, 1949) has remained in general use for the concept of circulating impulses as the basis of short-term memory.

The tenacity of the concept, in the absence of any valid physiological evidence for it, is highly significant. Reverberation is the only basis on which the pulse-logic hypothesis can deal with excitatory feedback in networks. The experimental fact is that regularly periodic firing is characteristic of isolated neurons or injured neurons. It is progressively less common as the number of neurons in a mass increases. Among mammalian central neurons, periodic firing is the exception and not the rule. This does not preclude the possibility that such neurons are part of fixed circuits required by learning theory, which might have variable circuit times, but the analysis becomes cloudy. Therefore, while pulse-logic analysis is effective for describing forward transmission, it fails on application to feedback, primarily because recurrent neural action with few exceptions is a mass action, and as such it is continuous and not impulsive.

The difficulty has not lain in the lack of adequate mathematical formalisms to handle discrete-valued feedback system. It has stemmed from the experimental fact that feedback in a neural mass cannot be reduced to a discrete-valued variable. Two syllogisms follow. If the brain is a pulse-logic device, then local feedback is a trivial part of its operation, and continuous events such as evoked potentials are second-order epiphenomena. If local feedback is essential, then theories of neural function must provide a continuum as the basis for measurement of feedback gain, using wave events such as AEP's and PST histograms as the raw data.

Failure to comprehend this dilemma has led some neurophysiologists into a twilight zone, in which feedback, especially negative feedback, is accepted as an experimental fact, but it is considered to occur at such low gain that responses are overdamped.

The empirical evidence of this 'failure can be found in most electrophysiological studies of complex mechanisms such as the spinal cord (Eccles, 1957) ; the cerebellum (Eccles et al., 1967) ; the visual cortex (Bartley, 1959) ; the hippocampus (Kandel and Spencer, 1961); and the olfactory bulb (Phillips et al., 1963; Shepherd, 1963). Typically the effect on these structures of anesthesia, surgical isolation, or prolonged drug-induced immobilization of the body is the reduction in complexity of interactions among neurons (feedback gain) and the enhancement of forward transmission (forward gain), which can be studied one synaptic layer at a time.

Typically the response of neurons in an obtunded mass consists in an initial burst of excitation followed by a prolonged inhibitory overshoot, especially if the input intensity is high. This is commonly regarded as due to recurrent inhibition and therefore as a closed-loop response. In fact, it is only marginally so. Recurrent inhibition in a neural mass is more characteristically directed by each neuron to others in the mass than itself, so that true recursion would require more than the one cycle of excitation followed by rebound inhibition. What happens is that input is delivered along many parallel lines to many excitatory neurons. These excite inhibitory neurons, which spread their effects widely. Any one excitatory neuron therefore receives excitatory input from the afferent lines and inhibitory input mainly from other afferent lines through the intervening excitatory and inhibitory neurons. This is predominantly parallel feed-forward inhibition and is closer to the open-loop than to the closed-loop case.

There is a normal physiological range of operation for the cortex and bulb. Stimulation near threshold evokes activity having the same amplitude range and frequency range as does the normal EEG activity evoked by

odors. But, the evoked potentials must be averaged to be seen over the background activity. This procedure yields closed-loop responses having more than one cycle of excitation followed by inhibition. The two reasons for the failure of normal responses to occur are that anesthesia and surgical trauma depress background activity and thereby remove or diminish normal operating bias, and that typically neurophysiologists raise the stimulus intensity until the response waveform to a single shock stands out over the residual background level. But this is a distorted waveform. It no longer has the characteristic frequency of the EEG. Neural responses of this overdamped type, which are the most common electrophysiological response to artificial stimulation in surgical preparations, are unsatisfactory as the basis for measuring either the open-loop or the closed-loop rate constants.

Closed-loop response patterns have been measured in a number of complex systems such as Limulus eye (Knight et al., 1970) and the hippocampus (Horowitz, 1972), when the logic of the continuum has been used.

F. THE DISTANCES OF MASSIVE INTERACTIONS

The quantitative study of dense functional interconnection requires answers to three questions: How strong? of what duration? and over what distance? By far the most difficult to answer experimentally is the third, because the input and output functions are so inaccessible.

It should be recalled that the property of dense interconnection implies the convergence of input from many neurons to each neuron, the divergence of output from each neuron to many others, and the recurrence of that output through many others back to each neuron. The output of the convergence operation is a pulse train (or its equivalent) of one neuron in a mass, and the distances of convergence through the mass can be measured easily by determining the surface dimensions over which stimulation by the input function alters that point process. It might be supposed that divergence is the simple inverse of convergence in geometric terms. This is not usually true. In most systems it is not feasible to reduce the input function to a pulse train of a single neuron or receptor. That input is lost in the background activity of the neurons to which it is transmitted.

Some neural masses exist, as in the mammalian geniculocalcarine and lemniscal systems, for which the main function appears to be the detection and amplification of activity in single sensory neurons, or very small numbers of them. One can argue that the amplification of activity in one sensory neuron by a factor of 101 or 104 to the cooperative activity of that number of cells in a cortical column is essential, before the neural event is thrown into the boiling turbulence of distributed computation, and that the divergence in the cartels of these systems is superbly adapted to the requirement for preservation of information about precise spatial location. These systems also display a high degree of topographic localization and are the best proving ground for the pulse-logic hypothesis.

But at and after the first synapse in these systems the event must be considered multineuronal, and attempts to map that divergence have not been successful (Armett et al., 1962). In the vertebrate auditory and olfactory systems the organization of receptor mechanisms is such that the activation of single receptors is not possible. The impossibility of activating by sensory stimulation a single neuron selectively is by no means incompatible with the pulse-logic hypothesis of neural function (H. B. Barlow, 1969), but the blunt experimental fact is that the measurement of divergence requires a distributed input function and not a point process.

This constraint does not apply to the evaluation of the anatomical basis for divergence. Sholl (1956), for example, estimated the number of possible connections of the branches of single neurons in cortex from the number of apparent fiber crossings in Golgi preparations. He expressed the results in terms of the density of possible connections as a function of distance from the cell body of each neuron. To illustrate his results he showed plots for two stellate cells, which had exponentially diminishing densities of fiber crossings with distances from the somas. The length constants can be estimated as on the order of 35 to 50 microns. Such data as these are of great value for studies of neural interactions, and it is astonishing that so few of them have been published. They provide some essential structural constraints and guidelines to physiological measurements. But they cannot supplant the dynamic measurement, because the anatomical synaptic connection is necessary but not sufficient for transmission to occur.

On these grounds the study of divergence demands that an input a.d.f. and an output a.d.f. each be postulated, and that sampling be undertaken of neural activity across both surfaces to validate the functions and evaluate the parameters of the functions. The divergence is then expressed in terms of the relationship between the two a.d.f.'s. The nature of the relationship depends on the nature of the divergence. There are two basic classes of divergence, tractile and synaptic, and for each class there are three kinds.

G. TRACTILE DIVERGENCE

Tractile divergence is between cartels and is based on the geometric properties of neural surfaces, compound nerves, nerve tracts, and their axonal terminals. The simplest form is called dilative and is due to the change in the packing density-of a constant number of axons, as from the cross section of a tract through which axons pass to a neural surface on which they end. The second is called interspersive and is the result of interweaving of axons in the manner of diffusing particles, independently of any branching. The third is called collateral divergence and results from repeated branching of an axon along its main trajectory or over the surface at its terminals-that is, parallel or orthogonal to the main axis of transmission.

Neural fibers can be treated as lines or curves with or without branching, and transmission of pulses can be treated geometrically or analytically as the movement of particles or points. In sufficient numbers they can be treated by using continuous approximations related to diffusion or the heat equation. The key to proper design of the equations lies in expression of the particular geometries of the axonal beds. Each tract or nerve carries out a specific spatiotemporal transformation on its input, depending on the nature of the tract geometry. This is why a detailed catalog of nerve tract geographies is needed.

The continuous curves used thus far experimentally to describe divergence have been the exponential curve (Sholl, 1956) and the normal density curve (Kirschfeld and Reichert, 1964; Rodieck and Stone, 1965; R. Barlow, 1969) each requiring two parameters for evaluation of distance from the center of the distribution in the surface. Characteristically the distributions of neural activity observed experimentally are less regular than these curves would imply. The use of the second curve implies that the irregularities in observed distributions are chance departures from the normal distribution. Essentially this is the null hypothesis. So little is known about neural divergence that there is as yet no experimental reason to reject it for describing the tractile divergence displayed by responses to electrical stimulation.

Examples of tractile divergence can be taken from the olfactory system. Electrical stimulation of the PON activates a distribution of axons around the stimulating microelectrode, which can be fitted with the normal input density function with the standard deviation, a,,, to represent the input a.d.f. of the PON in the stimulus plane orthogonal to the PON axons. The value for σ_a from measurements of the compound action potential across the distribution averages about 200 microns. The surface dimensions of the volley which is delivered by the PON axons to the surface of the bulb can also be expressed in terms of normal density function with standard deviation, σ_i, to represent the output a.d.f. of the PON. The latter can be evaluated from recordings of the evoked neural pulse trains and field potentials in the bulb. The variance of the output a.d.f., σ_i^2, exceeds the variance of the input a.d.f., σ_a^2, minimally by a factor of 11. This is equal to the ratio of the cross-sectional area of the bulb on which the PON ends to the cross-sectional area of the PON at the site of stimulation. Therefore, in this minimal case where each a.d.f. is expressed as a normal density function, the divergence operation is expressed by the multiplication of the variance of the input function by the ratio of the two areas. This is dilative divergence.

The overall divergence from the receptors in the mucosa to the first passage through the mitral cells is very large. Measurement of a,, in the PON implies that the 95% effective stimulus radius of a microelectrode is about 0.5 min on the average. If this holds for the mucosal surface for about the same stimulus intensities, the region of activation encloses about 0.75 mm', or 0.2% of the receptors in the 1600 mm^2 of mucosal surface. The zone of activation of bulbar granule cells for this stimulation is estimated to cover between one'-sixth and one-third of the 176 min' of the bulbar surface, from measurement of the surface size of the bulbar AEP field. Most of this divergence is due to the extensive reorganization and interspersion of axons between the mucosa and the PON (LeGros Clark, 1956). In terms of the ratio of surface areas of mucosal activation (0.75 mm^2) to bulbar input (30 to 60 mm^2), the divergence is by a factor, P, of 40 to 80. In terms of the percentage of neurons involved, the increase is from 0.2% of receptors to about 20% of bulbar neurons, or by a factor of 100. If surface boundaries are ignored, this means that the standard deviation of the activity of a normally distributed subset of receptors is multiplied by six to ten times to give the standard deviation of the subset of granule cells to which those receptors transmit through the glomeruli and mitral cells.

This statement stands in stark contrast to the better-known "convergence ratio" for the olfactory bulb, which for the cat is 140 million receptors to 80 thousand mitral cells, or roughly 2000 to 1. Furthermore, each PON axon branches only within a part of one glomerulus and makes contact maximally with only the few dozen mitral cells having apical dendrites within that glomerulus; that is, collateral divergence in the PON is negligible. The tractile divergence of the PON becomes apparent only when the distribution of receptors in

some local domain of the input surface is mapped into the whole of the bulbar surface.

Collateral divergence is paramount in the LOT, because each mitral axon gives off repeated branches in its trajectory across the cortex. These are strongly interspersive, so that dilative divergence is negligible; the surface areas of the bulb and of the cortex are approximately equal.

The quantitative degree of collateral divergence over the cortex has not been determined with adequate precision. White (1965) commented concerning his histological findings: "These observations indicate the absence of a point to point relationship within the projection area of the olfactory bulb via the LOT and tend to indicate that minimal activation of the bulb could readily activate the entire cortex" (p. 473). On the other hand, Heimer (1969) wrote: "The classical anatomical and physiological observations by LeGros Clark (1951) and Adrian (1950), both suggesting a certain degree of spatial localization in the primary olfactory projections, continue to excite our curiosity. Degeneration, localized to certain parts of the lateral olfactory tract, has been observed in animals with restricted lesions in the olfactory bulb in several pilot studies, and the time seems ripe for a more serious attempt to unravel a possible topographic organization within the secondary olfactory connections . . ." (p. 144). These contrasting statements suggest that bulbocortical axonal projections might also be modeled using the bivariate normal density function, which would be continuous across the full extent of the surface, have a -maximum density at one location on the surface, and approach zero with increasing distance from the peak.

A unique feature of collateral divergence is the precise and reproducible delay in transmission of pulses at terminals in the surface along the axis of transmission. The velocity of a wave front would not in general be constant, because branching axons taper and the conduction velocity of branches is lower than that of parent fibers, but arrival times are sequential and fixed along the axis. Wave fronts also occur for input by way of the PON, but because the divergence is interspersive rather than collateral, the precision of succession cannot be as great.

H. SYNAPTIC DIVERGENCE

Divergence within cartels (specific configurations of interactive populations) is by means of both pulse propagation and electrotonic conduction. The former is characteristic of axons and the latter of dendrites, but either may occur in both. Departures from this rule are of no apparent importance in population analysis, because it is the overall sequence of conversions that matters and not the number of trigger zones in each neuron. Because sequential time delays are expressed in terms of sequential synaptic transactions, it is logical to express the successive steps of synaptic divergence by lumping together the axonal and dendritic components of the spread at each stage.

Corresponding to the three types of feedback interaction, there are three kinds of synaptic divergence. Excitatory divergence consists in the excitation of excitatory neurons by other excitatory neurons. It is monotonic in distance across the surface, as it is in time. Inhibitory divergence results when excited neurons inhibit their neighbors and these disinhibit and thereby excite their neighbors in turn. The pattern is monotonic in time but oscillatory in distance. Negative feedback divergence occurs when excitatory neurons excite inhibitory neurons, which inhibit other excitatory neurons; these in turn disexcite (inhibit) other inhibitory neurons yet further removed from the initial focus of excitation. The event is oscillatory in time, but it is monotonic in distance, because each new subset of neurons is recruited in phase with the damped sine wave established at the center of the focus.

An apparent instance of excitatory divergence is the spreading cortical depression of Leão (1944; Grafstein, 1956), in which cell-to-cell transmission of excitation is the mechanism. However, this is a pathological process and is not a good model for normal interactions. As yet in the olfactory system no evidence has been found for the occurrence of either excitatory or inhibitory divergence. The former has been sought particularly among periglomerular neurons after PON electrical stimulation, and without success. The reason appears to be the anatomical fact that the length of cell process of periglomerular cells and especially of granule cells in directions parallel to the. surface is small in comparison to the dimensions of the input divergence.

This can be shown as follows. Suppose that the distribution of effective branches around each periglomerular cell conforms on the average to a Gaussian distribution, with σ_p = 100 microns. A focus of excitation on the PON of the same form with σ_a = 200 microns will arrive at the glomeruli with or, 11 â€¢σ_a^2)$^{1/2}$ or 665 microns, owing to a dilative divergence. For each successive synaptic action among periglomerular neurons the Gaussian input distribution must be convolved with the distribution of the processes of the periglomerular cells.

The convolution can be described quantitatively by the addition of the variance. After one = $(\sigma_a^2 + \sigma_a)^{1/2}$, or 670 microns. After twenty interactions the expected size of the focus $\sigma_a 20$ = 800 microns) would be augmented by less than the size of one glomerulus (about 150 microns). At a cycle duration of about 5 msec for each transaction, this is about as long as a single-shock response lasts. The implication is that small neurons in long serial chains cannot contribute significantly to divergence.

Divergence of evoked neural activity does occur within the bulbar cartel by negative feedback. It is based on the very long basal dendrites of mitral and tufted cells, which extend parallel to the bulbar surface for distances up to 900 microns in all directions. This is shown diagrammatically in Fig. 5, summarizing the results of measurement of PST histograms of mitral-tufted units within an elliptical focus activated by single-shock electrical stimulation of the PON on the lateral surface of the bulb. The initially activated mitral cells (represented by + symbols) lie within an ellipse, the area of which is determined by the axonal divergence at the input. This area does not increase during the next succeeding period of re-excitation of mitral and tufted neurons by their interconnecting axon collaterals, which are relatively narrowly distributed (White, 1965, p. 469). The diameter of the elliptical zone of granule cells excited through reciprocal synapses on the mitral-tufted basal dendrites (Rall and Shepherd, 1968) is calculated from the distribution of the initial surf ace-negative peak of the surface AEP. It is larger than the zone of initially excited mitral-tufted neurons, but smaller than a surrounding zone of initially inhibited mitral-tufted neurons, which show inhibition at and after the crest of the granule cell response.

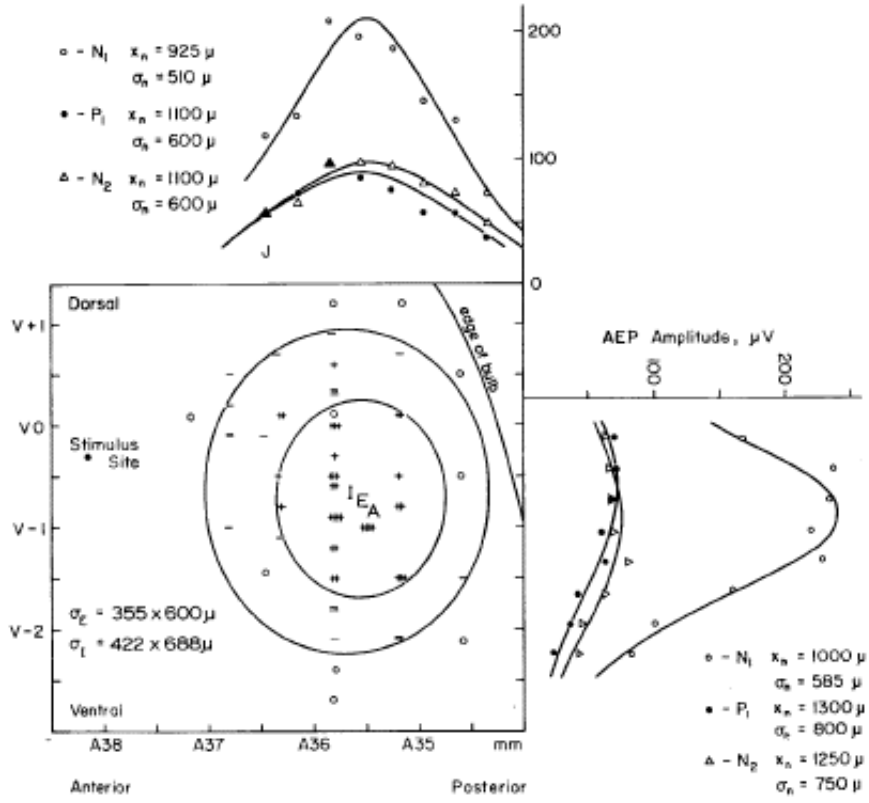

Fig. 5. The frame at lower left shows the locations of mitral cells initially excited (+), inhibited (-), or not affected (0) by single-shock electrical PON stimulation at the site indicated. The insets above and at right show the surface distribution of potential of the AEP across the center of the response focus at the crests of the first negative peak (ND, the first positive peak (Pi, inverted), and the second negative peak ∩,). The epicenter of the AEP is shown by A, and the centers of the ellipses by E and I. X. is half-amplitude radius for the AEP. The values for σ are those for bivariate normal distributions of the a.d.f.'s. Symmetrical radial spread in anesthetized animals does not occur after the first cycle of oscillation of the AEP.

This pattern of divergence also can be described mathematically by the addition of variance. The several successive regions of excitation or inhibition can be fitted each with the normal density function having the measured standard deviation, σ_i Beginning with the initial region of excitation, for which all is determined by the variance of the input a.d.f., the predicted variance of the next stage, σ_j^2, is equal to the sum of σ_a^2 and σ_i^2,

where a. = 382 microns is the mean standard deviation of the anatomical connection density (as a function of distance) of the mitral-tufted basal dendrites.

This simple formula holds through the establishment of inhibition among mitral-tufted cells surrounding the initial zones of excitation. It predicts that, with each successive quarter-cycle of the oscillatory interaction between mitral-tufted and granule cells, another increment in variance will occur. Provided the initial input variance is not excessive (and in many experiments it is not), this successive widening should be readily observable in both PST histograms and surface AEP's. After the first full cycle of oscillation, further radial spread has definitely not been observed (Fig. 5). Once the oscillatory focus has been established, it tends to remain as a standing wave within the confines of the focus. Therefore, the simple addition of a variance is an inadequate representation for the mechanism of negative feedback divergence.

At present there is no replacement. Metaphorically speaking, this is momentarily the end of the road, and beyond this point there are only tenuous paths for further advance.

I. SUMMARY

Equations representing the dynamics of neural masses can be formulated as sets of ordinary differential equations in three independent variables-response amplitude, time, and space.

Amplitude-dependency is expressed in the form of two types of gain coefficients. Forward gain is the numerical value for the functional connection density between aggregates, populations, and cartels. It is measured from the instantaneous ratio of neural output to input. The slopes of experimental and theoretical curves show that the values for forward gain are functions of output magnitudes. Functional interconnection density is expressed as feedback gain. For populations it is the square of forward gain and is positive. For simple cartels it is the product of the two forward gains and is negative.

The time- and space-dependent properties of neural masses are described by means of linear equations with variable gain coefficients representing the nonlinearities. In this formulation the open-loop rate coefficients are invariant- the closed-loop rate coefficients, which are the coefficients of the a.d.f.'s for neural masses, are amplitude-dependent. For an excitatory population the a.d.f. for impulse input is monotonic in time and in space. For an inhibitory population it is monotonic in time and oscillatory in space. For a simple cartel it is oscillatory in time and monotonic in space. Beyond these general rules, the temporal and spatial transformations effected by neural masses conform in detail to the geometry and topology of the component neurons.

V. Some Implications for Neural Information Processing

Three areas of observation and analysis have now been examined, in which concepts from the doctrines of centers and of pulse logic can be fused, so that cooperative and interactive neural phenomena can be described. (1) Divergence is an open-ended process described more appropriately in terms of a continuum than by means of discrete pulses for the immense numbers of neurons and synaptic connections in vertebrate central nervous systems. (2) Neural transmission involves alternating, conversions between pulses and electrotonic currents. It is appropriate to, describe pulse trains in terms of probability continua in order to relate them to synaptic currents. (3) The dynamics of feedback, especially excitatory feedback in populations, are most effectively described in terms of probability continua, owing to the experimental fact that central neural pulse trains characteristically are aperiodic.

Most proponents of the pulse-logic hypothesis have emphasized the "statistical character" of neural events, but they have not devised criteria for determining the spatiotemporal distributions, sample domains, or combinatorial laws for those events. This is the most compelling reason to look beyond the data on single cells and centers to the performance characteristics of great numbers of cells. When one does so, the striking ,experimental fact is that neural masses have properties that cannot be predicted from the properties of single neurons. Among these are continuous waves of activity in time and space at varying frequencies and amplitudes. The waves can be explained in terms of distributions of single-neuron properties-for example, thresholds, connection distances, synaptic delays (Rall, 1955; Ten Hoopen and Verveen, 1963; Calvin and Stevens, 1968), but because the distributions are properties of the masses, the waves cannot be predicted from single-neuron properties alone.

A. WHAT IS THE WAVE-PULSE DUALITY?

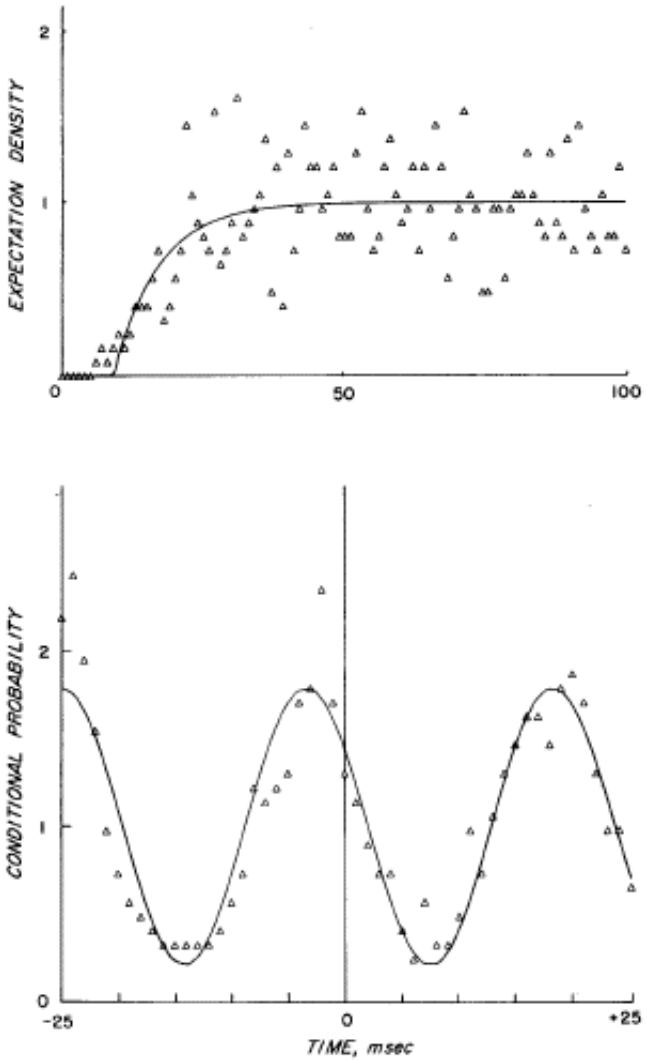

FIG. 6. The expectation density (closely related to the autocovariance), which is a property of the single neuron, is nonoscillatory, whereas the pulse probability conditional on the amplitude and phase of the EEG oscillates at the frequency of the EEG, which is a property of the bulbar neural mass. The phase and modulation amplitude of the pulse probability wave. $P(A_{max}\cap T)$, determined the "vector" of the neuron signal. Mitral cell. P, = 12.3 pps. ∩= 80,000.

This conclusion is illustrated in terms of the properties of single mitral cell pulse trains (Fig. 3, lower left, and Fig. 6). The typical, almost invariant pattern of firing is nearly at random intervals at different mean rates averaging 10 pps or less. The rates typically drop to half the mean between inspiration and increase two- or threefold during each inspiration. The interval histograms conform to an exponential curve with no intervals between pulses shorter than 2 or 3 msec. The. expectation density (Gerstein and Kiang, 1960; Rodieck et al., 1962; Poggio and Viernstein, 1964) of the trains rises exponentially from zero after 2 or 3 msec to a nonoscillatory level after the first 10 or 20 msec (Fig. 6, upper frame) ; only those pulse trains having mean firing rates approaching the EEG frequency at 40 pps or more show oscillatory autocovariance or expectation density.

The pulse-logic hypothesis asserts from such data that each neuron signals the rate of airflow or the concentration of some substance in the inspired air in terms of the numbers of pulses occurring over some reasonable time span, perhaps 200 to 400 msec.

A different picture emerges from a graph of the pulse probability conditional on the amplitude and time (or

phase) of the EEG recorded at a site epicentral to the single cells. The experimental curve, $P(A_{max} \cap T)$, characteristically conforms to a sinusoidal oscillation, for which the frequency is the peak frequency of the EEG. -The fitted curve, $P(A_{max} \cap T)$, varies from one neuron to the next in a manner that, while not random, is not at present satisfactorily predictable. The range for phase is at least 60Â° from the mean for the neuron type, and the range for modulation amplitude is from zero to a magnitude in excess of P_o, clipping then being obvious.

The result implies that each neuron in the readout population of a cartel transmits a wave as well as a pulse. The wave is the sinusoidal oscillation in probability of pulse occurrence at the characteristic frequency of the neural cartel. Being determined by a phase (with respect to the mean phase for the mass given by the EEG) and an amplitude at the momentary frequency characteristic of the mass, the transmitted signal can be described as a vector. Owing to the property of continuity of the a.d.f. over the local region around each neuron as well as in time, the signal transmitted by the LOT can be described as a vector field in the surface, either at the mitral cell layer or at the root of the LOT in cross section, prior to operation of tractile divergence in the LOT, or in the cortical surface after that operation.

The vector for each axon and the vector field for the LOT are properties of the cartel, because the phase and amplitude are determinable only as functions of a signal of the cartel, the EEG. The expectation density of pulse trains (Fig. 6, upper frame) does not usually show the oscillation, because the frequency of the EEG and/or its phase vary randomly in time, though they are the same at any one time across the surface, and the pulse on the average occurs only once in every four or five cycles of the EEG. Even when the mean pulse rate is fast enough to reveal an oscillation, the phase cannot be determined from the expectation density or from the autocovariance.

This is the wave-pulse duality. Certainly, the bulb transmits to the cortex only by means of pulses on axons, but the neural mass hypothesis asserts that information is conveyed by the pulses in the phase and amplitude of an oscillating probability wave of pulse occurrence, having four or more times the frequency of the mean pulse rate. The duality does not refer to the action potential per se. In physics, for example, the wave-particle duality refers to an uncertainty regarding position and energy level of an electron. There is no a posteriori uncertainty about the time, location, or magnitude of an action potential. The duality refers to the signal of a neuron, which is both a pulse and a wave (Fig. 6). With respect to the single neuron it is a pulse, and with respect to the neural mass it is a wave.

In this duality the fusion of the doctrines of centers and of pulse logic should now become clear. According to the doctrine of masses, neural information is transmitted and stored only in pulse trains (or the synaptic equivalent for granule cells) generated by specific neurons at specific times and places (see Note 10). Many neurons are required in parallel to transmit each message. The "center" is represented by a cooperative domain having a common phase reference. The EEG gives access to that phase reference, and by means of this key to the pulse timing, the information in the pulses can be extracted. But the EEG contains little or no information in itself. Neither waves nor pulses can be read without the other.

B. HOW MIGHT NEURAL VECTOR FIELDS BE GENERATED AND RECEIVED?

If it is known that a nerve tract can transmit a vector field, then it is important to determine how a sensory stimulus such as an odor might be encoded in that manner. This is a difficult question in olfaction for two reasons. First, too little is known about the nature of the olfactory receptors: whether there are basic types as for color in vision, and, if so, how many (Amoore, 1971); whether their locations with respect to airflow are important as for auditory receptors with respect to distance from the oval window; what their pulse train characteristics are, etc. Second, a mathematical description combining the time-, amplitude-, and space-dependent properties of the bulbar and cortical relays has not been developed. This will require the use of partial differential equations, either quasi-linear with state-dependent gain coefficients (Freeman, 1972) or nonlinear (Wilson and Cowan, 1971, 1972). Without them quantitative prediction cannot be made with adequate precision for experimental testing, while verbal descriptions tend to bog down in ambiguous referents and double negatives.

Even so, the main outlines of the process can be sketched. It is widely accepted that olfactory receptors differ among themselves in respect to sensitivity to different odors, and that an odor drawn into the nose by a sniff elicits a unique spatial pattern (LeGros Clark, 1951, 1957; Adrian, 1950, 1953) of excitation and inhibition among some but not all receptors scattered over the mucosa .(see Note 11). The anteroposterior rate of stimulus

activation in the mucosa is presumably determined by the rate of airflow and is about that of the mean conduction velocity of the PON axons (Dravniecks, 1964; Freeman, 1969). An afferent surge composed of action potentials and the absence of expected action potentials leaves the mucosa during a sniff and undergoes temporal dispersion and spatial transformation by tractile divergence. It is gated into the bulb by the periglomerular population, which closes the gate by a process related to presynaptic inhibition in the spinal cord (Wall, 1962; Eccles, 1964; Voronkov and Gusel'nikova, 1968; Freeman, 1970) beginning 10 to 20 msec after the start of the efferent surge and lasting several hundred milliseconds. This much is obvious from records of pulse trains from mitral-tufted and periglomerular cells and from AEP's.

Also, through glomerular synapses the PON axons activate mitral and tufted cells, which initiate oscillatory wave activity in the bulbar cartel. The periglomerular population serves to shut off the PON input at the end of the first half-cycle of the oscillation (10 to 12 msec), so that continuing PON input does not cancel the effect of that preceding. By this means the amplitude of oscillation in pulse probability of each mitral cell is determined by the density of PON action potentials in the leading edge of an afferent surge delivered to its glomerulus.

The phase of the oscillation in pulse probability for each neuron (with respect to the surface AEP as the reference signal) has three determinants. First, there is a systematic delay in arrival times of PON action potentials from anterior to posterior (the direction of conduction) amounting to about one half-cycle in length. But, by the end of the first full cycle of oscillation, the AEP at all points on the surface has the same phase and of course the same frequency of oscillation. The mechanism is obscure, but it involves coupling of the neurons in the bulbar cartel. It cannot be explained simply as an artifact of the bulbar volume conductor. Second, the pulse-generating mitral-tufted neurons lie in the forward limb of the negative feedback loop, whereas the field potential generators (the granule cells) lie in the feedback limb, so on the average the oscillation in firing probability leads the oscillation in field potential by about 90Âº. These two factors determine the mean value for phase across the mitral-tufted population.

Third, the value of phase for each neuron depends on the ratio of the forward gain to the feedback gain in its part of the loop. These gains are determined by the amplitude of the induced activity and by the bias levels in the forward and feedback limbs, which determine the degrees of saturation in the two limbs. When saturation by inhibitory bias is dominant in the forward limb of the cartel, $P_m(A_{Gmax} \cap T)$ leads the EEG by less than 90Âº, and when it is dominant in the feedback limb, P. (A.... ∩T) leads the EEG by more than 90Âº.

The bias levels are nonoscillatory in time, and the bias level within the excitatory population is nonoscillatory with respect to the surface dimensions. But the bias level of the inhibitory population is more complex, owing to the characteristics of inhibitory divergence. Inhibitory neurons initially excited tend to remain so, and those surrounding them ,hat are secondarily inhibited also tend to remain so. The sustained differences in activity level tend to bias some parts of the cartel in one direction and other parts in the other direction. This feature implies that for focal inputs the bias levels within the cartel must vary with distance across its surface, and so also must the value for the phase. Specifically, in those areas of the bulbar surface in which granule cells are initially excited, it is predicted that the mitral-tufted pulse probability waves will show relative phase lead less than 90'. In those areas in which granule cells are initially inhibited (disexcited), the mitral-tufted pulse probability waves are expected to show phase lead more than 90Âº. With respect to their own population mean (Fig. 7), initially excited mitral-tufted neurons will have phase lead (light domains), whereas those initially inhibited will have phase lag (dark domains). By this means the irregularities in the surface amplitude distribution of PON input must lead to corresponding phase irregularities in the vector field of the mitral cell output. Thereby an odor can be encoded into a vector field.

Readout of the vector field in the LOT by cortical neurons is by vector summation of the pulse probability waves, rather than by scalar summation of pulse trains as usually conceived. The possibility of vector summation is predicated on the existence of a common signal in the cortex, which is detectable in the cortical EEG (Boudreau and Freeman, 1963). For transmission to occur from bulb to cortex, the two EEG's must be coherent, and, in fact, a fluctuating and sometimes high degree of coherence has been observed between bulbar and cortical EEG's in normally behaving cats with implanted electrodes (Boudreau, 1964). With respect to the common phase, each cortical neuron can be regarded as computing a running Vectorial sum of input waves on its 101 input lines and generating a vector of its own in the same code, irrespective of changes in the system carrier frequency and amplitude, which are observed to undergo continual changes (Freeman, 1963).

C. DO TRAVELING WAVES EXIST IN NEURAL CLASSES?

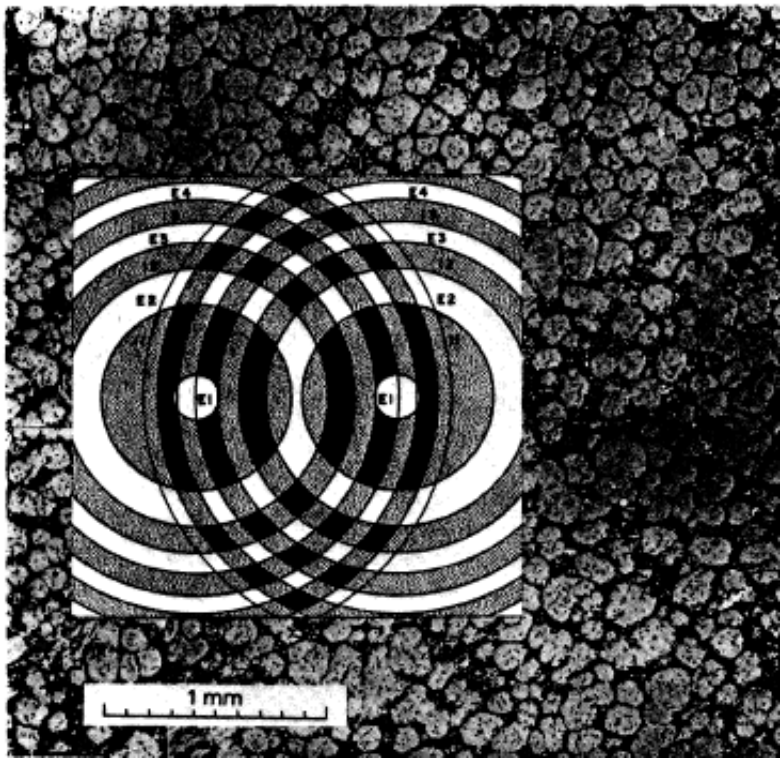

FiG. 7. This is a predicted form of the mitral-tufted population a.d.f. within the bulbar cartel on activation of two glomeruli separated by 900 microns, in the presence of a traveling wave condition. It is a phase interference pattern, in which light areas denote phase lead and dark areas denote phase lag of mitral-tufted probability waves, relative to the population mean phase. E, excitation; I, inhibition; 1, . . . , 5, successive peaks of the AEP. Inset: a histological section through the glomerular layer. Cresyl violet, 50X. In anesthetized cats the spread of activity is not beyond I.

Two kinds of traveling waves are commonly known to occur in cortex. One is the spreading depression of Leão (1944) for which a theoretical model has been developed by Beurle (1956), and which is here classified as based on excitatory divergence. The other is the spreading wave of dendritic potential upon direct cortical stimulation first described by Chang (1951) as owing to axonal transmission delay, which is here classified as based on tractile divergence, and which has been modeled by Horowitz and Freeman (1966). Either or both of these mechanisms can be invoked to account for the evoked and spontaneous spreading waves of cortical surface potential first mapped in detail by Lilly and Cherry (1954).

Neither of these processes has yet been shown to play any role in neural information processing, and for the olfactory system there is some evidence that neither does. On the contrary, in the case of the bulbar response to electrical stimulation of the olfactory mucosa or the PON, one is hard pressed to explain how a standing wave is generated in the face of tractile divergence and excitatory divergence in <?> input stages and synaptic divergence within the bulb.

Part of the answer may be that negative feedback divergence so greatly exceeds the excitatory divergence within the periglomerular and mitral-tufted populations that Beurle's type of wave cannot and in fact does not occur. The common occurrence of the "inhibitory surround" phenomenon for units elsewhere in the nervous system suggests that this negation holds rather generally. What cannot be explained by intuitive logic is the discrepancy between (1) the fact that synchrony in AEP oscillation develops within the first cycle across the whole of an active focus, which implies widespread interaction among the bulbar neurons, and (2) the fact that outward spread of the focus stops after the first cycle (Fig. 5).

The problem is nontrivial for the following reason. These observations on spatial distributions were made on anesthetized animals and with artificial stimuli. One can conceive a mathematical model for the bulbar complex cartel, which has the stability property of a high spatial damping factor in the presence of a low temporal damping factor to account for the discrepancy described above. But suppose for some combination of spatial and temporal damping factors in the model one were to reduce the spatial damping factor. One can expect outward spread of the focus in successive alternating steps of excitation and inhibition, as suggested in Fig. 7. The successive steps are based on summation of variance as described in Section IVA If two stimuli were delivered to glomeruli 900 microns apart, a phase interference pattern would occur as indicated in less than 100 msec, owing to the superposition of alternating rings of initial excitation and inhibition. The predicted

wavelength between initial amplitude deflections would average about 200 microns; the predicted wavelength between phase maxima would average about 400 microns, because the alternating peaks of reinforcement would themselves alternate between initially excitatory or inhibitory. By this means the vector field of the bulbar output would acquire spatial periodicity, as well as the temporal periodicity already demonstrated to exist. The predicted periodicity is approximately two times that of the diameter of the glomeruli in the bulb as shown in Fig. 7. It corresponds approximately to the diameters of proposed cortical columns in the visual neocortex (Marshall and Talbot, 1942; Hubel and Wiesel, 1963; Blakemore, 1970) and the somatosensory cortex (Mountcastle, 1957).

This configuration is the neurophysiological counterpart of Lashley's prediction in 1942 "that for any pattern of stimulation a stable resonance pattern, not unlike the interference effects of simple wave motion, would be established" (p. 315). It has not been found in anesthetized animals. It is proposed that, if it occurs, it will do so in waking animals, in which the activating stimuli also evoke either an orienting reflex or some subsequently developed conditioned reflex.

Neurophysiologists will see at once that this prediction will not be easy to test. The surface and depth field potentials cannot be expected to reveal spatial periodicities having so fine a grain. It will be necessary to record and process the pulse trains from single neurons at ten or more sites simultaneously in waking animals, and the ten sites must lie along a line (for example) in the mitral cell layer at intervals of no more than 100 microns.

Prior to such a prodigious undertaking, it would seem prudent to carry out some preliminary studies. The equations describing the bulbar cartel should be constructed, and the values of parameters necessary for a traveling wave condition should be determined. These values should be translated into the equivalent neurophysiological properties, to determine whether it is reasonable to expect the traveling wave to exist. Perhaps it will be possible to show that the necessary conditions can be imposed in anesthetized animals by surgical or pharmacological manipulation of the bulb (see Note 12). Tests of the bulbar AEP can be made by using repeated single-shock stimulation to determine whether the surface field of potential overlying a focus undergoes radial spread in the proper conditions. This is a necessary event for the development of a phase interference pattern, and while the pattern itself should not be and has not been detectable in surface AEP's, the radial spread should be.

Finally, further study must be devoted to the properties of the LOI and the response configurations of superficial pyramidal cells in the cortex, to determine in what conditions it is possible for these systems, respectively, to transmit and receive a vectorial interference pattern in the form of a phase front.

The traveling wave condition is not essential to the theory of neural masses, nor is it the only prediction of its kind (Perkel and Bullock, 1968). However, it is immediately relevant to many current questions concerning neural information processing (Adey, 1966; Caianiello, 1967; Weirsma, 1967; Liebovic, 1969; Schmitt, 1970; Campbell and Maffei, 1970; Pollen et al., 1969), (see Note 13) and it is directly accessible to experimental disproof, so it appears at present to be a promising avenue for further work.

D. ARE NEURAL MASS ACTIONS FIRST-ORDER, SECOND-ORDER, OR EPIPHENOMENAL EVENTS?

The assertion has been made that odors might be encoded in vector fields of neural pulse activity generated in the bulb and transmitted to the cortex. This offers an alternative to the assertion that odor is encoded in the discharge of a. small number of characteristic neurons. But it does more. It offers the means for strengthening the experimental investigation of the pulse-logic hypothesis in applications to those systems, where it is most likely to continue to be the most effective means for description. Even where rhythmic fluctuations in firing probability of single neurons exist, they may be no more than the idling discharge of immense numbers of neurons, each keeping its lines open for days, weeks, or years by transmitting and receiving random test pulses, and each waiting for some specific burst of pulses on two or more input lines signifying the presence of its "psychon," upon which it will emit a burst attesting to that fact. But which other neurons will read that burst? What are the mechanisms for providing the background activity in millions of idling neurons? What maintains each neuron in an optimal dynamic range? What are the burst rates and coincidence intervals that distinguish a "signal" from a random jump in background input? What are the a priori functional connection densities, and how much greater than these must the effectiveness of each single activated line become to qualify as a Hebb connection? These and related questions refer to the mechanisms for establishing the "ground" against which the "figure" of single-unit activity must be detected or maintained. They are questions requiring population studies. Therefore, neural masses are of interest not merely as phenomena in their own right, or as the possible

vectors of neural information in relation to behavior, but as an essential aspect of the pulse logic hypothesis.

On the other hand, there is a peculiar skeletal dryness about strict forms of pulse logic, which explain neural operations by discarding so much going on as merely epiphenomenal.

Neural activity in lightly or moderately anesthetized animals or in immobilized animals is relatively quiet, regular, and even stately. It is most suitable for the analysis of the basic topologies of connections, evaluation of fixed parameters, specification of state variables and observables, identification of intrinsic and extensive degrees of freedom, etc. In the waking animal the activity becomes more lively, especially in the presence of sensory stimuli and motivating antecedents such as food deprivation (Freeman, 1962). The activity comes dramatically to the foreground when the sensory or electrical stimuli are directed into the olfactory system, from which the recordings are being made (Freeman, 1960; Emery and Freeman, 1969). Above all, when the animal is in a state of learning with respect to the stimulus evoking the recorded activity (Freeman, 1968a), that activity comes to seem cataclysmic. Great waves of potential roll off each stimulus at wildly fluctuating frequencies as though immense numbers of neurons in the masses of the telencephalon were brought to focus on the primary cortex. Yet these waves are only the surface ripples of events within (Adey, 1966; John, 1967). When the full scope of the neural event in learning is eventually brought to view, it will be an awesome spectacle, even as it occurs in the brain of a mouse learning to run a maze for food. Hypotheses which express this phenomenon in terms of Pavlovian switching circuits and coincidence detectors of pulse trains may logically be correct, but their rectitude is that of the statement, "The brain is made of neurons." Of course that is true, but it is not the whole truth.

E. PROPOSITIONS FOR A THEORY OF NEURAL MASSES

This essay is intended to be propaedeutic toward the formulation of a theory of neural masses. Such a theory is not yet achievable, partly because observation at the requisite level of sophistication has not been extended much past the olfactory system, and partly because the theoretical investigation of the statistical properties of single neurons is incomplete. As an additional step toward the organization of a theory, a set of propositions is listed in logical sequence, but without the structural tightness that will be required for a theory.

1. It is assumed that an active state can exist across large numbers of neurons, which is represented by covariant (not necessarily cooperative) activity of those neurons.

2. A "center" is an anatomical domain of neurons maintaining a given active state.

3. The neural mass is the inclusive locus of domains of possible active states of a certain kind. The kind of active state is predicated on a certain kind of massive functional neural connection.

4. There are two elemental types of functional connection. One is forward or one-way, and the other is reciprocal or two-way. Their large scale numerical values are designated forward gain and feedback gain.

5. The local magnitudes of connection are expressed as functional connection density and functional interconnection density. Each may range from zero up to the limit set by anatomical connection density. High functional interconnection density confers the dynamic property of superposition and the topologically derived properties of convergence, divergence, and feedback.

6. There is a hierarchy of level of neural masses based on the complexity of neural connections, ranging from the internally unconnected mass to the whole brain, with a corresponding range in complexity of cooperative neural activity.

7. The aggregate is a neural mass with common input and zero functional interconnection density, even if anatomical connections exist within it. Its parameters are forward gain, a set of rate constants, and a set of space constants.

8. The population is a set of densely interconnected neurons with common input and the same sign of output. It is represented by a positive feedback loop. In addition to the parameters of an aggregate it has feedback gain. There are two kinds of populations: excitatory having positive excitatory feedback gain, and inhibitory having positive inhibitory feedback gain.

9. It is feasible to separate conceptually and experimentally three sets of independent variables for population function: amplitude, time, and space. Owing to the superposition property the transformations of populations

are susceptible to description using ordinary linear differential equations in each of these dimensions.

10. Each population (and aggregate, if the input imposes covariation) maintains a continuous activity distribution, which has at each point in time and space a certain density. The solution to the differential equations for the population dynamics is an activity density function (a.d.f.) . There are as many a.d.f.'s for each population as there are transformations by the population. Any one or two of these can serve as the state variable of the population.

11. The activity density at each point is reflected in pulse trains and field potentials. After appropriate spatiotemporal averaging, the latter became the observed waveforms. Following appropriate transformation the a.d.f. gives rise to predicted waveforms. Parameters in the differential equations are evaluated by fitting predicted waveforms to observed waveforms.

12. The amplitude conversions of the a.d.f. are from waves to pulses (V-P) and from pulses to waves (P-V). Input-output curves (derived from properties of single neurons) are sigmoidal but asymmetric, with sharper curvature on the inhibitory side.

13. The product of the derivatives of the two input-output curves equals the population forward gain. It is amplitude-dependent.

14. The population open-loop rate constants (measured by using models derived from properties of single neurons in the aggregate) are invariant. The same values serve to describe the five populations in the olfactory system.

15. The population closed-loop rate constants are gain- and amplitude dependent. The impulse response is monotonic in time, with decay rate approaching zero as feedback gain approaches unity.

16. The simple cartel results from the dense interconnection of an excitatory with an inhibitory population. The active state of a cartel cannot be expressed in a single a.d.f., state variable or predicted waveform. There is at least one for each component population.

17. The impulse responses of populations in cartels oscillate with an average quarter-cycle phase lead between the a.d.f.'s of the forward and feedback limbs. The phase, frequency, and decay rate of the oscillation are gain- and amplitude-dependent, both on the negative feedback gain and on the two types of positive feedback gain.

18. In general, the positive inhibitory feedback loop in the cartel contributes internal inhibitory bias and at unity gain determines the stability characteristics of the cartel. A source of external excitatory bias is required for normal operation.

19. In the olfactory bulb, the cascade of an excitatory population into a simple cartel forms a complex cartel. The population contributes normal de operating bias to the assembly, frequency stabilization against changes induced by variation of amplitude, and an input gate. The a.d.f. conversions are dominated by the limits on (V-P) conversion.

20. In the olfactory cortex a complex cartel is formed by the cascade of a simple cartel into an aggregate. It displays powerful external inhibitory bias, possibly because the limits on (P-V) conversion seem to dominate the a.d.f. conversions. This stabilizes the decay rate of oscillatory impulse responses, at the expense of strong variation in frequency and phase with response amplitude.

21. Divergence between cartels is tractile and takes three forms dilative, interspersive, and collateral-depending on the geometric patterns of the axons.

22. Both cortical and bulbar cartels have prominent tractile divergence in their input pathways. The open-loop space constants of cartels are independent of electrical stimulus intensity and response amplitude. In this they resemble the open-loop rate constants (cf. proposition 14).

23. Divergence within cartels is synaptic. The three types are cognate with the three types of feedback. For both excitatory divergence and negative feedback divergence the response configurations are monotonic in space. For inhibitory divergence the response configuration is oscillatory in space, even though it is monotonic in time (cf. proposition 15).

24. The bulbar cartel generates a standing wave field potential on impulse activation; that is, the phase and frequency are everywhere the same.

25. The pulse probability of single bulbar neurons conditional on the phase and amplitude of the field potential of the cartel has the same .,,Sinusoidal frequency of oscillation as the field potential, but the modulation amplitude and phase vary from neuron to neuron.

26. The cortical cartel generates a traveling wave field of potential at a frequency determined by the cortical cartel and a phase determined by the tractile divergence of the input tract, the LOT.

27. The pulse probability of single cortical neurons conditional on the phase and amplitude of the cortical field potential likewise oscillates at the common frequency but with variable phase and modulation amplitude.

28. It is concluded that each LOT axon transmits a wave as well as a pulse train, which is the sinusoidally oscillating probability of pulse occurrence. The phase and modulation amplitude of the wave convey a signal, which can be expressed as a two-dimensional vector for that axon.

29. It is proposed that olfactory information can be encoded in the form of a vector field established and maintained in the surface of the bulbar cartel by the population of mitral cells.

30. It is predicted that in animals oriented to an olfactory stimulus (chemical or electrical), a traveling wave condition will be found, such that the bulbar vector field will have the configuration of a phase interference pattern.

VI. Summary

From 1784 to 1940, coinciding approximately with advances in the technology of the gross electrode, the operation of the nervous system was conceived in terms of "nerve energies" or "central excitatory states," which were sustained by pools of nerve tissue forming networks and were related to specific forms of behavior. Since 1940 and the advent of microelectrode technology, conceptually the single neuron has replaced the "center" as the element of neural coding, and the nerve impulse has replaced the c.e.s. as the carrier of neural information in networks. It is proposed that with the advent of computer technology in electrophysiology it is possible to fuse these two systems of analysis. The new tools make it possible for the first time to "see" certain neural events occurring as continuous spatiotemporal distributions of nerve impulses or "waves," which reflect widespread cooperative activity among neurons in "masses." The neural information constituting the particulars of these events is conveyed only in pulse trains of many single neurons, but that information is observable only with respect to certain running averages or moments of activity across great masses. In selected cases these collective properties are accessible by recording the electroencephalogram (EEG). The information then appears in the form of pulse probability waves transmitted by single axons at the frequency of the EEG.

Such cooperative activity is conceived as arising only by virtue of certain forms of dense neural connection. Rules are given here for defining neural masses in relation to a hierarchy of complexity in connections, ranging from the "aggregate" (with no internal connections) through the excitatory or inhibitory "population" (having dense interconnections), to the neural "cartel" (consisting of densely interconnected populations of both kinds), and then to the familiar modality-specific neural systems (consisting of networks of cartels). Each level of organization can be recognized by characteristic response configurations, and each can be described by an appropriate set of differential equations. Such equations are in one of the three independent variables (amplitude, time, and space), and they have one of the corresponding three sets of parameters <?> (multitude, time, and space), and they have one of the corresponding three sets of parameters (gain, rate, and space coefficients). The solutions for specified input conditions are shown to yield the state variables, as well as predicted response waveforms. The comparison of predicted and observed response waveforms provides the basis for evaluation of the parameters and for provisional acceptance or rejection of proposed explanatory equations. On the basis of results thus far, specific predictions are made concerning the manner in which the bulb encodes olfactory information.

NOTES

1. Albrecht von Haller, the founder of modern physiology, used (1776, p. 320) the term vis nervosae to describe an agent that forced nerve fluid from the brain to the muscles to serve as a trigger for the local release of muscle force (vis insita). He subscribed to the Aristotelian-Galenic-Cartesian view of the brain as the seat or source of nerve fluid, of neural activity, and of behavior. For Jiri Prochaska (1749-1820), a professor of "morbid anatomy of the eye" in Prague, this tradition broke with dramatic force, when he observed the

behavior of anencephalic monsters as reported in 1784. How (p. 188) could a human infant without a brain be capable of movement? All parts of the nervous system including the spinal cord and nerves must have intrinsic nerve force (pp. 51, 78). He subdivided the lower nervous system into three parts: sensory systems, motor systems, and, intervening, the common sensorium in the medulla oblongata, in which nerve force released by sensory stimulation could be reflected suddenly and violently ("Subito et violenter" -p. 52) into the motor nerves. He conceived the operation of this nerve force in Newtonian mechanistic terms (p. 29) and thereby introduced the concepts of homeostatic and protective reflexes (p. 116): "The reflexion of sensorial into motor impressions, which takes place in the sensorium commune, is not performed according to mere physical laws, where the angle of reflexion is equal to the angle of incidence, and where the reaction is equal to the action; but that reflexion follows according to certain laws, writ, as it were, by nature on the medullary pulp of the sensorium, which laws we are able to know from their effects only, and in nowise to find out by our reason" (Prochaska, 1784, translated by T. Laycock, 1851, p. 430).

Prochaska was a mechanist in a time when vitalism was both rampant and politically prudent. But by 1812, following the discoveries of Galvani and Volta, he had thoroughly confused "nerve force" with "animal electric tension" (Prochaska, 1812). In so doing he committed the same error as Köhler (1940), who identified perceptual fields with electrical fields of current in the cortex (see Note 10), and as those investigators at present who would identify the "waves" of neural activity here being discussed with EEG waves.

2. Sherrington (1925) made an explicit distinction between the dependence of response magnitude on the number of active neurons and on the degree of activity of each: "From the standpoint which the diagram illustrates, reflex actions offer two discriminable attributes, quantity and intensity, quantity being expressed as the number of neurones engaged, i.e. the number activated in excitatory reflexes, and the number inhibited in inhibitory reflexes; intensity, on the other hand, being the excess of supraliminal state or the 'surcharge' exerted from up-stream on the individual downstream neurons and 'all-or-none' mechanism, whether that 'surcharge' be excitatory, or inhibitional, or, as usually, some algebraical resultant of the two together" (p. 542).

He proceeded almost apologetically to describe an "agent" (subsequently in 1929 named central excitatory state, abbreviated c.e.s.) for this dependence: "Reverting to the schema above proposed, one weakness lies admittedly in its assumption of the existence of an agent simply as inferred from reactions of which that agent could be the cause; and that agent, moreover, one, whose existence lies outside the intrinsic properties of pure nerve-fibre and with a, so to say, more chemical mode of origin and function than the nerve impulse per se" (pp. 542-543).

However, he was not explicit as to whether the "agent" was a property of each neuron, or of the population of neurons, or of both. Lorente de Nó (1938) identified the "agent" with swarms of neural pulses: "Internuncial bombardment . . . has all the properties of c.e.s. . . . and since a motoneuron despite any possible lowering of threshold due to previous, intrinsic or extrinsic activity does not fire unless impulses are delivered to its synapses . . . there is no doubt that the central excitatory state' leading to, motor discharge is due to internuncial activity and bombardment. Furthermore, it has been shown in this paper that subliminal c.es., i.e., excitation demonstrable only by its ability to facilitate the response to an intercurrent stimulus, is always accompanied by internuncial bombardment, which under the conditions of the present experiments overshadows the effect of any other factor capable of lowering the threshold of the neurons" (p. 227). Electrophysiologists with few exceptions after the development of intracellular recording identified the "agent" solely with the single neuron in the form of the dendritic postsynaptic potential. Granit (1967) wrote: "In his intracellular work on the postsynaptic excitatory and inhibitory potentials in the spinal cord Eccles may be said to have run out the course that Sherrington set, beside adding many new and significant observations to those briefly reviewed. The concepts of Sherrington (Chapter 3) have now been verified and reformulated in terms which for postsynaptic excitation and inhibition agree almost word for word with those of the old Master's, as was pointed out by Sir John Eccles himself in a review of Development of Ideas on the Synapse (1959). [Cf. Eccles, 1964.1 Postsynaptic inhibition is a stabilization of the potential of the cell membrane; it can be neutralized by postsynaptic excitation, the two processes being represented by potential changes of opposite direction; both events can be subliminal from the point of view of the firing mechanism and both are capable of being nicely graded; specific sensitivity to either of the two is likely to be localized in the cellular membrane rather than at the terminals themselves, etc."

Yet the level of postsynaptic potential (PSP) of one cell (Eccles, 1964) is not the same as the c.e.s. or c.i.s. of many cells, nor are their pulses; each is part of the mechanism. The questions for population analysis are: How do the PSPs of single cells relate to their active states? how do the active states sum to give the c.e.s.? and how does the c.e.s. relate to some measured quantity such as pulse firing or muscle tension?

3. Adrian (1947) wrote: "There would be no point in discussing the artificially produced nerve impulse ... if it

were not reasonably certain that impulses of the same kind are the basis of all nervous communication" (p. 12). Fulton (1949) wrote: "Since an end organ must convey its messages to the nervous system by the all-or-nothing nerve impulse, the only possible way of communicating differing intensities of stimulation from a single end organ lies in differing rates of discharge" (P. 12). Eccles (1952) wrote: "We may say that all 'information' is conveyed in the nervous system in the form of coded arrangements of nerve impulses" (P. 1).

The march of technology hag been crucial in this historical sequence. The macroelectrode made it possible to observe and manipulate the neural "center." The microelectrode likewise made the neuron and its pulse accessible. It is computer technology that has opened the neural mass and its wave properties to observation.

4. Hebb (1949) incorporated Lashley's (1929) data in his imaginative and very influential theory, -but his critique of Lashley's concepts of mass action contained an equivocal paraphrase of Lashley's position on stimulus equivalence. According to Lashley (1942): "The principle involved is that the reaction is determined by relations subsisting within the stimulus complex and not by association of a reaction with any definite group of cells.... An indefinite number of combinations of retinal cells and afferent paths are equivalent in perception and in the reactions which they produce.... Here is the dilemma. Nerve impulses are transmitted over definite, restricted paths in the sensory and motor nerves, and in the central nervous system from cell to cell through definite intercellular connections. Yet all behavior seems to be determined by masses of excitation, by the form or relation, or proportions of excitation within general fields of activity, without regard to particular nerve cells. It is the pattern and not the element that counts" (pp. 304-306). Hebb (1949) stated: "'Equivalence of stimuli has a double reference. It may mean only (1) that different stimuli can arouse the same response. This is an observed fact of behavior, whatever one's interpretation of the fact. But Lashley has also used the term to mean (2) that it does not matter what sensory cells are excited in order to get a certain response . . ." (p. 39). This Lashley did not say. Further, "Lashley has concluded that a learned discrimination is not based on the excitation of any particular neural cells. It is supposed to be determined solely by the pattern, or shape, of the sensory excitation. . . . This suggests that the mnemonic trace, the neural change that is induced by experience and constitutes 'memory', is not a change of structure. . . . If it is really unimportant in what tissues a sensory excitation takes place, one finds it hard to understand how repeated sensations can reinforce one another, with the lasting effect we call learning or memory. It might be supposed that the mnemonic trace is a lasting pattern of reverberatory activity without fixed locus, like some cloud formations or an eddy in a millpond . . ." (p. 12). Hebb acknowledged the effort made by Lashley to reconcile the mass action hypothesis with the necessity for specific structural synaptic changes as the basis for learning: "Lashley's (1942) hypothesis of interference patterns is the one explicit attempt to solve this difficulty and to deal adequately with both perception and learning. As such it deserves special mention here, although we shall see that in other respects it faces great difficulties" (p. 15). But the "other respects" of the difficulties stemmed from behavioral data, which were equally consistent with both Hebb's and Lashley's premises and conclusions, and Hebb concluded merely that "the fundamental difficulty with configuration theory, broadly speaking, is that it leaves too little room for the factor of experience" (p. 58). In so doing Hebb failed to meet Lashley's argument.

Hebb's development of his own discrete network hypothesis was inconsistent on precisely those points here at issue. His "neurophysiological postulate" (pp. 62-69) was developed in terms of networks of single neurons. In describing his synaptic hypothesis he stated: ". . . structural connections are postulated between single cells, but single cells are not effective units of transmission, and such connections would be only one factor determining the direction of transmission . . ." (p. 61). He stated the inference: "When impulses in one such path are not effective, those in another, arriving at a different time, could be" (p. 76). Thus he began.

Eventually the cell assembly became not merely "irregular" but "diffuse" (p. 86) and capable of sustaining "liminal or subliminal excitation" (pp. 86-87)-that is, a graded and continuous response variable. However: "At each synapse there must be a considerable dispersion in the time of arrival of impulses, and in each individual fiber a constant variation of responsiveness; and one could never predict a determinate pattern of action in any small segment of the system. In the larger system, however, a statistical constancy might be quite predictable" (p. 76). Hebb stated concerning his graphic models that "such neat connections" in a "three-dimensional lattice" (P. 72) of neurons forming an assembly were "of course statistical: the neurons diagrammed were those which happen to have such connections, and, given a large enough population of connecting fibers distributed at random, the improbable connection must become quite frequent, in absolute numbers" (p. 74).

The concept of uncertainty about the location of a specific effective connection in a random set of connections is not compatible with the concept of the continuous ("diffuse") distribution of effectiveness across the same set. Clearly Hebb did not weaken Lashley's case. On the other hand, there was no neurophysiological evidence put forward for "interference patterns" by Lashley (1942). He seems to have been the T. S. Eliot of his generation of neuropsychologists, and his writings often seem as bleak as "The Wasteland."

5. Sherrington's model was not unique, though it has stood alone in terms of the extent of its neurophysiological documentation. Several other mass action theories of the nervous system have been proposed, based on behavioral data, such as the spatial properties of pattern perception (Köhler, 1940), or the effects of brain lesions on learned behavior (Lashley, 1929), or on neuroanatomically based modeling (Cragg and Temperly, 1954; Beurle, 1956; Sholl, 19%; von Neumann, 1958). This evidence has been reviewed and up-dated recently, with the addition of new evidence based on electrical recording of field potentials in the brain (John, 1967) and on Skinnerian techniques (Pribram, 1969, 1971).

These anatomical and behaviorally derived data did not address or answer the question being raised here, concerning the nature of neural mass action, because they did not yield estimates of functional interconnection density. Suppose that the performance of a given task such as maze-running were shown by destructive lesions to depend on the quantity of a certain mass of neural tissue (such as cortex) and not on any specific part of the mass (Lashley, 1929). There were in principle two ways in which the neurons in the masses might operate. Either they; formed discrete, specific networks of selected connections that transmitted pulses along axons from neuron to neuron across synaptic connections, but with many distributed parallel or redundant channels for reliable transmission (von Neumann, 1958; Cowan, 1967). Or they formed cooperative domains by synaptic interactions over large regions, in which the pattern of activity was specific, but within certain limits the neurons sustaining it were not.

Networks and masses constructed according to. these two hypotheses shared the same properties of (1) transmission between neurons solely on the basis of pulses acting at synapses; (2) immunity of stimulus-response patterns to fairly large destructive lesions; (3) the occurrence of coherent activity among many neurons in correlation with a stimulus-response event; and (4) modification of transmission at specific synapses in the process of learning. Neither lesions nor recording of coherent activity could answer the question: Was the single neuron pulse train sufficient as well as necessary to carry the message, or was the message conveyed in mass action?

6. Bullock (1959) has argued persuasively that "all-or-none" pulse transmission phylogenetically is relatively new in comparison to graded wave-like events occurring in primitive and not-so-primitive nerve nets. Werblin (1971) has shown that transmission occurs though bipolar neurons 'in the retina of the salamander by graded events. In the olfactory bulb the granule cells have no axons and do not generate extracellularly detectable action potentials. These observations imply that it is not true that the nerve impulse is the "only basis for transmission" either' between neurons or within neurons. However, they are not relevant to the question at issue here, because the mode of transmission (pulse or wave) by one cell does not determine the content, nor does it preclude reduction of description of the operation to pulse logic.

McCulloch (1951) was explicit on this point: "Now, why have I chosen to quantize in nervous impulses? Well, let's say the human brain is of a general order of complexity of something like 10' if we think of it in terms of its ultimate particles. One might split this at the level of the atoms, or one might split this at the level of the neurons, and so on. The question is: At what level can one split the behavior so as to define a set of units in terms of which to work? And, obviously, the nervous impulse at the level of the neurons is a fairly nice unit for working. . . . "I look on . . . a field . . . as an analogy device when we disregard the unitary composition, or definite structure of our elements, and treat them as wholes, which means that we are dealing with their parts, if you will, at best, statistically. We have, with respect to them, thrown away the information that goes into their construction, and have retained only the overall picture of their behavior. Now, I do not like to treat something like the cerebral cortex in this 'field' manner. First, and foremost, I will admit unquestionably that it has some statistical properties. But what I am looking for is something that will perform a logical task. I like to look for it in a thing that has a grain, and I like to take that grain as my unit, because then I can see what degrees of freedom the system has and to what extent they are bound in any given job of handling information. I believe that there are many things in the nervous system that. smear the results ....

"They rob the system of some of its degrees of freedom without conveying information. They are the kinds of things that would arise if we had to build our electronic devices and keep them in tubs of salt water.... Now, the reason for making this distinction as sharp as possible in the face of plenty of evidence that the smearing occurs, is that we are dealing with something that has a field-Eke property. My-reason for treating it in the manner in which I have treated it is this. It compels one so to state his theory that he can account for these changes by the digital mechanisms; that is, so that he can contrive a digital device to account for each of these.... It was clearly shown in our first paper, I believe, that these field-like processes--facilitation and extinction-could be handled by sticking in hypothetical nets, because once a system is, in this sense, quantized anywhere, it might as well be quantized everywhere. This keeps the theory clean" (pp. 132-134).

7. By "wave function" is meant a continuously and often periodically varying probability of pulse occurrence in

both time and the surface dimensions of the neural mass and not a wave of polarization along the axon, as the action potential is sometimes referred to.

8. Mere size of mass and number of neurons are insufficient grounds for invoking the continuum; it is the topology of interconnection density that is important (Maynard, 1967). Bullock and Horridge (1965) wrote: ". . . there appears to be a general difference between the brain waves in invertebrates and vertebrates (Bullock, 1945). From fish to man . . . the brain exhibits smooth, low-frequency, sinusoidal waves dominated by rhythms of less than 50 per second and mostly less than 10 per second.... But in all invertebrates examined, including annelids, arthropods, and molluscs, activity recorded by surface electrodes is spiky. . . . Comparing the large cephalothoracic ganglionic mass of Limulus and the brain of a small frog, it can be concluded that size of ganglion is not the critical difference, and on similar grounds it seems possible to rule out size of axons. Apart from the spikes, invertebrate ganglia do show slow waves, and in some cases these appear to demand something beyond an envelope of individual spikes to account for them . . ." (p. 318). Certain molluscs and insects such as squid, wasps, and bees have massive central ganglia. with patterns of anatomical organization similar to the laminated neuropil (cortex) of higher vertebrates. These animals also show learning behavior involving pattern recognition similar to that in vertebrates. Wave activity has been reported in recordings from these structures (Bullock, 1945; Mislin, 1955; Bullock and Horridge, 1965) but not in sufficient detail to determine whether neural populations and cartels exist in these exceptional masses.

9. The point must. be re-emphasized that the a.d.f. is a mathematical description of an active state which is neither identical with nor reflected directly in the EEG or single neural pulse trains but reflected only in statistical averages of them. The rules for obtaining averages are as yet strictly empirical. It is known that the averages may be temporal, spatial, or both. Typically the EEG and the evoked potential are already spatial averages, owing to the fact that they manifest the sum of extracellular dendritic current from many neurons. They are also time averages, because of the smoothing action of the resistive-capacitive property of the dendritic membranes. Whereas the peak of the energy spectrum of the action potential is near 1000 Hz, that for the AEP or EEG rarely exceeds 80 Hz. Therefore in contrast to single neuron pulse trains, a short period of experimental time-averaging suffices to yield a defined activity pattern.

Well-defined and reproducible AEP's from the bulb or cortex require the sum of 30 to 100 trials. Relatively noise-free PST histograms from single neurons require 1000 to 10,000 trials. Recordings from an optimally placed extracellular EEG electrode in the bulb reflect the summed dendritic current of about 600,000 granule cells within a radius of half a millimeter. The same surface area encloses about 1500 mitral and tufted cells. The spectral and amplitude probability densities of the EEG can be defined adequately from records 2 to 3 seconds in duration with a sample rate of 200 per second (400 to 600 samples). The statistical properties of background pulse trains from single neurons become reasonably clear only after 100 to 300 seconds of recording while sampling for pulses with a sample rate of 1000 per second (100,000 to 300,000 samples).

Proportionately fewer samples are needed when pulse trains are recorded simultaneously by the same electrode from multiple (3 to 5) neurons, which is a form of spatial averaging of the pulse trains. These figures from anesthetized animals show that the amount of averaging required either within or outside the experimental preparation is prodigious. The reason is that the shared variance among neurons in the population is an exceedingly small fraction of the total variance of activity of each neuron within the population. The necessity for computers here is obvious.

The hypothesis underlying the procedure of experimental time-averaging of pulse trains is that the sampled neuron will reflect the state of all the neurons of the same population in its vicinity, if the sample period is long enough, which is in essence the ergodic hypothesis. But the ergodic hypothesis seems not to hold in any simple sense or over the designated time range, because the mean pulse rates, Po, differ from different neurons in the near vicinity. Largely for this reason a reliable method for estimating the overall mean pulse rate of the population, Po, has not yet been devised.

More fundamental than the experimental sampling problems is the question, How does the nervous system read the a.d.f. for the unique sensory event? Time-averaging over more than 100 msec seems unlikely; spatial averaging would seem to be essential. The bulb reduces the activity of 100,000,000 granule cells to that of 80,000 mitral cells, and 176 mm' of bulbar surface area to about 1.0 mm', the cross-sectional area of the LOT. The number of readout lines (80,000) still far exceeds the number of recording channels available to this experimentalist (1 to 64), so that his access to the uniquely distributed sensory event without recourse to repetition and time averaging is not yet possible. It may never be.

10. The possibility has been entertained for many years that the currents of the EEG (including very low frequency or "de" potentials) might have direct "ephaptic" effects on cortical neurons (Köhler and Wallach,

1944; Terzuolo and Bullock, 1956; Adey, 1966, p. 34). This mechanism is specifically excluded from the neural mass hypothesis here proposed on the following grounds: (1) It is not needed to account for cooperative domains. (2) Synaptic inputs not only are demonstrably more effective in most contexts as the basis for neural interactions but are more likely to be sites for specific changes associated with learning; and, as Lashley and Hebb stated (see Note 4), such sites must be anatomically specific. (3) The effects of widespread ephaptic interactions would be to promote synchronous pulse discharge, but to the extent that ephaptic synchronization occurred, with each EEG wave activity would be desynchronized on each subsequent passage through synaptic loops.

Although it is conceivable that ephaptic effects might be responsible for second order cooperative phenomena, despite psychophysical evidence to the contrary offered by Sperry and Miner (1955) and by Lashley et al. (1951), it is important to divorce that question from the problem of describing the dynamics of neural masses, and to answer it separately. The author wishes to add that each of his own experimental attempts to demonstrate a significant role for ephaptic transmission in masses has ended with a strong negative answer. These efforts have included (1) application of exogenous sinusoidal currents having spatial and temporal amplitude distributions resembling those of the EEG to animals that were trained to be exquisitely sensitive to brain electrical stimulation, whereupon such currents had no behavioral effects (Freeman, 1962); (2) measurement of cortical impedances to within 0.1% relative magnitude and 0.1Â° phase angle (Freeman, 1963) and finding no changes associated with behavior other than sleep and death; (3) measurement of temporal dispersion among action potentials in the PON, which was precisely in accord with predictions based on axon diameter distribution and allowed for no ephaptic synchronization (Freeman, 1969); and (4) measurement of the effects of applied transcortical direct currents on the shape of the AEP, which indicate that the current densities required to induce even modest changes in AEP waveform were one or two orders of magnitude greater than those physiologically present (Freeman, unpublished data, 1968). The author has concluded that the mechanism of ephaptic transmission should not be introduced into a theory of neural masses until all reasonable synaptic alternatives have been exhausted.

11. LeGros Clark in 1957 wrote: ". . . The sharply circumscribed nature of the glomerular formations and of their connexions suggests very forcibly some degree of individualization in their olfactory functions (in other words, some degree of functional localization) . . . . In fact, there is some reason for supposing that there may be two modes of localization in the olfactory bulb, a topical localization in the sense that certain local areas of the olfactory epithelium are projected to local regions of the bulb, and another kind of localization whereby fibres derived from receptors of different physiological significance are predominantly concentrated on correspondingly different glomeruli. . . . However, there is another possible explanation of the olfactory nerve plexus in the surface of the bulb-that it serves precisely the opposite purpose of ensuring complete randomization of fibres so that each glomerulus receives impulses from every type of receptor; in other words, that each glomerulus is in itself a functional unit concerned with the total range of olfactory discrimination. . . . The possibility has occurred to me that a purely random distribution of fibres from different specific types of receptors might itself confer some degree of functional specificity on individual glomeruli if one could suppose that in a normal distribution the proportion of fibres from each type terminating in each one of the two thousand glomeruli varies over a sufficiently wide range. But, assuming that the different types of receptors are distributed at random in a population of fifty million, statistical computations show that the existence of several hundred types would need to be postulated to allow the expectation that the range of variation in the number of fibres from any one type reaching individual glomeruli would be likely to have importance from the functional point of view. . . . There is at present no warrant for supposing that so many different types of receptors do exist; on the other hand, the possibility is not to be excluded, and it is also possible, of course, that such receptor types as do exist are not distributed at random in the olfactory epithelium. . . . The restriction in mammals of the main dendrite of each mitral cell usually to a single glomerulus suggests rather forcibly that this is part of a progressive evolutionary development in the specificity of the glomerular system associated with an enhancement of the capacity for olfactory discrimination. . . .

". . . The question arises, then, whether the impulses relayed from the different glomeruli are delivered in some sort of spatial pattern to different loci in the main olfactory centres or whether, as seems more likely, the mitral axons which convey them are distributed in such a way as to give rise to different patterns of excitation centrally" (pp. 310-314).

Since this was written, Amoore (1971) has collected a large body of data concerning the steric configurations of odorous molecules, odor similarities, and specific anosmias. He hypothesizes that particular molecules fit into receptor sites on olfactory cilia as does a key into a lock. From his present evidence he believes that there are at least sixty-two specific anosmias; this number approaches the requirement proposed by LeGros Clark for an olfactory model based on random connectives between the receptors and neurons in the first synaptic relay.

However, Amoore has also concluded that the number of "primary odors" in man "may be reduced to twenty-seven through grouping of likely redundancies" (p. 255).

12. For example, the application of polarizing direct current to the surface of the prepyriform cortex modifies the of polarizing direct current to the surface of the prepyriform cortex modifies the frequency and decay rate of the AEP in the same manner as does external excitatory or inhibitory bias (Freeman, unpublished results, 1968). It has also been possible by this means to cause a nonoscillatory AEP (open loop) to become oscillatory (closed loop), but it is not known whether this induced a traveling wave condition as well. Some slow or "dc" cortical potentials (Rowland, 1968) undoubtedly are manifestations of population a.d.f.'s and of the bias levels they represent. The close association of "dc" shifts with learning events suggests that a change in a population bias level might accompany or even be a. necessary condition for such events, and that "dc" polarization might mimic the effect of a change in bias level, leading to the formation of an orienting or a conditioned reflex (Rusinov, 1953; Morrell, 1961).

13. The dramatic properties of holograms have suggested the use of optical analogies for their predictive value. The possible relevance of the holograph (Gabor, 1947) to brain function has been noted frequently in the past decade (van Heerden, 1963; Lettvin and Gesteland, 1965; Longuet-Higgins, 1968; Pribram, 1969; Westlake, 1970; Pollen et al., 1971), as distinct from interactive networks (Willshaw et al., 1969; Anderson, 1970). There is an attractive but superficial plausibility about this. In a generic sense holography is the study of waves, their modes of propagation, their transformations to form distinctive patterns, and the nonlocalized storage and regeneration of information in such patterns (Caulfield and Lu, 1970). The neural populations of the olfactory system, owing to their vast numbers and the densities of their interconnections, provide the continuous media and the equivalent of energy density functions required to sustain waves of neural activity. The neural cartels generate the requisite carrier frequencies and phase standards. Excitatory populations provide the bias controls needed to make those frequencies invariant with respect to input amplitudes, and possibly to adapt them to as-yet-unspecified standard frequency values under central control. Inhibitory populations determine the stability properties in both time and space dimensions. The broad divergence of interconnections, established by both anatomical and physiological measurements, provides the basis for surface convolution and wave propagation at velocities precisely dependent on axonal propagation delays. The superposition properties of populations provide the basis for linear summation and the development of surface interference patterns.

The essential feature of the application of holography to the sensory process is the conversion of a sensory distribution (a pattern of light, a manifold of odors, the sound of a word, etc.) into its Fourier components prior to processing and storage. One may, in addition, postulate the inverse transform as the basis for image reconstitution, or further integral transforms into a manifold of motor patterns on the output side of the brain. It seems undeniable that, if distributed interactions are in some places the basis for neural information processing, then, irrespective of the mechanism, the processing can be described for some purposes in terms of the Fourier transform. So can speech.

The difficulty with this approach is to know whether it has predictive value or merely provides a change in variables, as spectral analysis does for the EEG. The most attractive feature of optical holography as an analogy is the mathematical simplicity of the classical Fourier transform; without this the explanatory mechanisms become objects of study in themselves. But this simplicity holds only for the case of far-field (Fraunhofer) diffraction. For near-field (Fresnel) diffraction the quadrature terms cannot be neglected; and this holds when, as in the olfactory system, the aperature is probably too small with respect to wavelength to permit neglect of edge effects, and the output of each element in the object plane is to some part and not all parts of the image plane. Considering such neurophysiological complexities as the multiple types of feedback, the nonlinearities of pulse-to-wave and wave-to-pulse conversion, and the broad nonlinear coupling that must underlie the phenomenon of bulbar hypersynchrony, the Fresnel diffraction approach seems more like a Procrustean bed than a working conceptual tool.

An alternative analogy of great interest is offered by thermodynamics of irreversible processes applied to "dissipative structures" (Katchalsky, 1971, and personal communication, 1971). The risks are appreciable of once again confusing neural massive activity with energy and neural waves with electromagnetic or fluid waves, but the usefulness of partial differential equations in both domains seems overriding, particularly as the means for predicting and measuring those properties of a system at a higher level, which emerge from the strong interaction of massive numbers of parts at a lower level in a multilevel hierarchy.

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