Meetings

Neural Communications: Experiment and Theory

Twenty years, more or less, have gone by since the pioneering work of Ashby, McCulloch and Pitts, Wiener, and others drew the attention of communication engineers to the diversity of problems offered by the neural communication system of the body. Initially the appeal was simple. Neurons were reported to be all-or-none devices, capable of functioning as elements in a switching or digital computing network; it seemed obvious that the Boolean algebra of such networks must help the neurophysiologist to understand the behavior of networks of real neurons. Nervous systems were self-regulating; it seemed obvious that the calculus developed by servo theorists must help to explain bodily regulation and its pathology. Brains enabled people to think (sometimes) logically and arithmetically; it seemed obvious that the theory of digital computers must illuminate the functioning and malfunctioning of the human brain. All living organisms were characterised by a vital traffic in information; it seemed obvious that the mathematical theory of information must bring the kind of precision needed to analyze and elucidate the information-processing functions of the nervous system.

Up to a point, this was indeed both obvious and true. The question, then and now, has been how far such methods could go before getting bogged down in the sheer complexity of real (as opposed to idealized) neural processes. Must the nervous system be caricatured beyond recognition before any mathematical technique can get a grip on it? Is it true, as many (though not all) neurophysiologists maintained 20 years ago, that only trivial problems could prove amenable to the newfangled techniques publicized by Wiener's *Cybernetics* and the flood of literature that followed in its train?

Twenty years might seem a reasonable experimental period on which to base some tentative answers to these questions. A proposal to hold an international working party on the subject last September at Keele University (Staffordshire, England) met with an enthusiastic response. The sponsorship of the International Brain Research Organization, with generous additional support from the Royal Society, the U.S. National Institute of Neurological Diseases and Blindness, and the U.S. Office of Naval Research, made it possible to bring together over 30 leaders in the neural, behavioral, and information-processing sciences for 4½ days of concentrated private discussion in an informal atmosphere. A total of eight countries were represented, although four invitees from the Soviet Union were regrettably prevented from attending.

The conference was planned with the assistance of an informal committee consisting of J. C. Eccles, R. Jung, J. Szentagothai, and H.-L. Teuber. Its core consisted of three full-day sessions devoted, respectively, to: (i) Neurons as information-processing elements, (ii) vertebrate sensory information processing, and (iii) functional organization of movement. These topics were chosen as typical sample areas of past and current interaction between experiment and theory. The object of each session was to take note of the most important recent (or neglected) experimental findings that may guide or set bounds to theoretical model-making, to evaluate existing models in the light of these findings, and to assess future prospects. A final day was set aside for methodological stocktaking and consideration of the kinds of theoretical training that experimentalists in brain research would find most profitable.

Experiment and Theory: The Present Position

Considerable interest, and some catalytic controversy, was aroused by the opening after-dinner speeches on the first evening. Under the chairmanship of H.-L. Teuber, four neurophysiologists of long standing, J. C. Eccles, A. E. Fessard, R. Jung, and D. Whitteridge, were invited to give their candid impressions of the past two decades of cybernetic theorizing, and of the present need for theory in neurophysiology. Each admitted to an initial skepticism 20 years ago which had by now been eroded to varying degrees, and all found the chief weakness of most theorizing to lie in oversimplification, due largely to a lack of firsthand acquaintance with raw experimental material and problems. The specificity of neural connections, for example, was seldom done justice in "neural net" models (Whitteridge). Uncritical use of informational jargon yielded mere restatements rather than solutions of problems (Jung).

All four speakers were encouraged (again in varying degree) by signs that theorists were increasingly keen to work alongside experimentalists and to be disciplined by physiological realities. Consultation at long range was not enough. Ideally, as Eccles and Jung emphasized, the marriage of experiment and theory must take place in one and the same individual if their partnership is to be creative.

What then of the future? New techniques of brain research were generating an exponentially growing pile of facts for which we had no adequate principles of classification. Jung suggested a parallel with the situation of chemistry in the mid-19th century, before the great theoreticians brought order into chaos with a few simple generalizations. The data for great discoveries might be with us already, lacking only the theoretical framework in which to see their significance. Eccles emphasized the necessity for theory and bold conjecture in the design of a worthwhile experiment, so as to give point and piquancy to the outcome. Refutations (if nontrivial) should be welcomed as steps forward in our knowledge. Fessard stressed the need for quite different kinds of theory at different levels of "coding," psychological as well as physiological.

In discussion W. A. Rosenblith warned against current misconceptions of cybernetics as some general theory purporting to solve all biological problems rather than as a collection of techniques for dealing with organized complexity. Used intelligently, these could not fail to benefit neurophysiology, but they were no substitute for data. Most participants seemed to agree that neurophysiology was already permeated by control-system thinking, and that the disappointment and confusion created by initial overselling was giving way to a growing confidence that this was fundamentally the right approach. General theories of the nervous system were deemed still remote possibilities, and there was a hint of frustration at the lag in this respect between biological and physical sciences. But this seemed to be something which must be lived with through many more decades of thoughtful experimentation, in which the theories of communication and control could contribute usefully to the building of working hypotheses.

Neurons as Information-Processing Elements

Theories of neural information-processing can hardly be better than their doctrine of what neurons are and do. Already, by the 1940's, simple and standardized all-or-none units were dubious as models of the real neuron in all its various forms. The famous propositions derived by McCulloch and Pitts for "neural nets" could at most be regarded as limiting cases or existence theorems to encourage the physiologist in search of a realistic theory. The last two decades have seen the electron microscope add new orders of complexity to our ideas of neuronal interconnections, and microelectrical and microchemical techniques of recording and stimulation are revolutionizing our understanding of interneural signaling. How much then remains of the ideas embodied in the "formal neuron"? What form of neuron doctrine is appropriate for theory-building today? This was our next question, which was considered under various heads.

1) First, the "all-or-none" law. Nobody doubts that this holds for neurons whose job is to signal over long distances; but in densely packed central neural networks, is it at all safe to assume that information is transmitted only by discrete impulses, and combined only by summation at thresholds? Such questions were being asked in the 1940's; but only recently has firm evidence begun to emerge that the assumption is not only unsafe but false. Outstanding in this connection—and outstanding as an elegant combination of theory and experiment—was the contribution of W. Rall, reporting work in collaboration with Shepherd, Reese, and Brightman. Starting with data recorded by Phillips and co-workers from the olfactory bulb, he showed how a quantitative analysis of firing patterns and potential waveforms led to the postulate that axonless granule cells must be involved in nonimpulsive interaction with neighboring mitral cells, through two-way, dendrodendritic synapses. Using a "compartmental cable" model of the mitral dendritic system, he was able to calculate speeds of propagation of nonimpulsive signals along dendrites and show that addition of granule activity would account quantitatively for the waveforms observed.

2) Second, what of the notion of the synapse? In the electron micrograph a synapse is identified by a thickening of the membrane on one side of a contact zone and an accumulation of "synaptic vesicles" in its vicinity. On this basis, evidence was presented by several participants suggesting that synapses of some kind could form not only between an axon and a soma or dendrite, but also with the axon of another cell (for example, in ciliary ganglion) or between one dendrite and another dendrite (for example, in lateral geniculate) or soma (for example, in the sympathetic system). Physiological evidence of their respective functions was incomplete, but Rall's work for example suggested that synaptic paths might even exist in opposite directions between the same two dendrites. These should not be viewed as a short circuit, because synaptic action can be brief and the opposite actions can be separated in time. In this case, the postulated synaptic actions provide a negative feedback that might account for adaptive inhibition and lateral inhibition.

The main question for the model-maker is how widespread such awkward complications may be throughout the central nervous system. Amacrine cells and (presumed) dendrodendritic synapses are well known in the retina, and similar situations were reported in other regions such as the optic tectum of the frog (somatodendritic synapses) and the cerebral cortex of mammals; but it seemed too early to generalize as to their distribution.

3) What of the assumptions so often made that connections between neurons are "randomly" distributed? It may be granted that visual inspection could not distinguish between the sort of "randomness" shown by a column of numbers in the telephone directory, where every entry is in fact precisely determined, and that of a stochastic process, where only certain statistical parameters are determined. But do neurons grow and interconnect randomly in either sense? Szentagothai produced impressive evidence to the contrary for a number of regions of the nervous system where "compartmentalized" growth is the rule. Dendrites may even be seen to turn back upon themselves in such a way as to respect the boundaries of their own "compartment." Curiously enough, although the cerebellum of most animals illustrates this phenomenon in an extreme form, it is only in the primates, and especially in man, that the idea of a "proper space" for dendritic trees finds clear expression in the cerebral cortex.

In this connection, V. B. Mountcastle offered the fascinating suggestion that certain neurons (such as the horizontal cortical cell of Cajal, which migrates from the outer layer during ontogeny and finally disappears) might have a part to play in controlling the development of the rest of the cortex.

4) To what extent can processes other than synaptic be ignored for informational purposes? Do neuroglia, for example, show any signs of information-processing activity? K. Krnjevic presented recent evidence that although neuroglia were inexcitable they responded to certain chemicals such as γ-aminobutyric acid and acetylcholine, suggesting the hypothesis that they might act as "scavengers" for transmitter substances. If so, it was pointed out that they could strongly influence the integrative time-constant of synapses in their vicinity, so affecting the time-resolving power of any neurons acting as coincidence-detectors. It was evident that we needed much more information before the possibilities of chemical signaling in the central nervous system, chemical secretions during learning, and the like could be evaluated.

5) What of the customary notion that a neural net can be adequately specified by a schematic connection chart in which geographical details are ignored? If the "weight" of a synapse is known, does it matter whereabouts on the neuron it lies? Are dendrites merely spatial integrators of distributed inputs? Here again material presented by Rall on the spinal motoneuron typifies a disturbing trend for the simple-network theorist. It seems all too likely that in a dendritic arborization the effectiveness of a synapse near the tip could be grossly modified by activity nearer the soma. Krnjevic reported evidence that where inhibitory and excitatory synapses converge on the same neuron, the former tend to lie close to the soma and the latter out on the dendrites. This might have functional significance.

There seemed to be general agreement with Eccles' view that at least the fields of current flow in the vicinity of dendrites have no physiological significance. However, Krnjevic was concerned that the possibilities of electrical transmission should not be neglected by theory-builders. Altogether it seems inevitable that more attention should be paid in future to the physical layout as well as the connectivity of dendritic and axonal circuits.

6) Finally, there is the vexing question of the sensitivity of the neuron to different parameters of an input array. Granted that frequency modulation rather than digital encoding is the typical mode of peripheral signaling, and is found also in many central areas, how well could a central neuron function for example as a coincidence detector? Here the answer seemed to depend very much on the sample chosen. Inhibitory effects could easily last for 200 milliseconds, making such inhibition virtually useless for fine timing purposes; but summation of excitation could require coincidence of impulses within a few milliseconds. It was pointed out that in parallel networks of n elements the time-resolving power could in principle be sharpened by a factor of the order of $\sqrt{n}$, so that the transmission time along quite short axons could become functionally important. The majority view seemed to be that timing was smoothed out too much by synaptic integration to be significant. Fessard, however, reported that in *Aplysia* the same fiber might even have excitatory and inhibitory effects on the same cell, according to the impulse frequency.

It was generally agreed that in sufficiently complex parallel networks there might be little meaning in speaking of the information-bearing variable for a single neuron. Fresh techniques were needed to study the activity of many neurons simultaneously, and G. L. Gerstein and D. H. Perkel described two promising computer methods of analyzing interactions between different impulse trains. The difficulty of simultaneously recording from really large numbers of neurons was felt to be a serious limitation by the theorists present. An interesting theoretical approach to the problem of interaction between sufficiently large populations of neurons was suggested by J. D. Cowan, who showed that this could be formally treated by methods already developed in statistical physics. Bursts of neuronal activity following statistical laws similar to those found in ecology and population genetics were among the possibilities predicted. However, the crucial experiments that would distinguish this theory from others remain to be done.

Vertebrate Sensory Information Processing

Sensory neurophysiology is just now reaching the end of a major transitional stage. As V. B. Mountcastle put it in opening the second main session, interest has almost completely shifted from static to dynamic properties of sensory systems. So we now face new, and perhaps still more difficult, questions in terms of process rather than product. Instead of asking how percepts are represented by neural configurations, we are having to learn to ask how perceiving is represented by neural activity.

Two examples may help to show that this change of emphasis involves more than a mere shift of language.

1) Twenty years ago an accepted problem in sensory pyschophysiology was to explain how the various nuclei along the afferent pathways (conceived of as "relay stations") managed to preserve the sharpness of the "neural image" on its way to the cerebral cortex. The ubiquitous overlaps and lateral interactions between sensory elements were thought of as merely introducing blurring, and some restoring process was supposed to be needed before the input was projected to the final "sensorium." The presupposition embedded in such thinking was that perception amounted to some kind of internal inspection of a static pattern delineated by neural firing.

2) It was also in line with this idea to interpret the then accepted logarithmic relation (Fechner's law) between the physical and perceived intensity of a stimulus as confirmatory of the accepted logarithmic relation between physical intensity and receptor response. The subject of a psychophysical experiment was assumed to be simply "looking at" and reporting the level of activity of some sensory neurons.

Today things are different, although the latter Cartesian assumption still had echoes at our meeting. In the first place many lateral interconnections have been recognized as mediating simple computing operations that enhance informationally significant features of the sensory input. Thus in the visual system the work of Hubel and Wiesel, Lettvin, and others has populated our picture of the cortex and lower centers with cells responding selectively to gradients and rates of change of brightness, directions of contour, motion of the image and the like. Second, in the field of psychophysical measurements S. S. Stevens has stirred us from dogmatic slumbers with repeated discoveries of power-law rather than logarithmic relations between physical and subjective intensity in many modalities. Physiologists in turn, notably Mountcastle, have found power-law transfer functions in a number of sense organs.

The time seems to have come to ask questions which take less for granted about the way in which sensory experience and brain physiology are related. For the organization of perceptive behavior, automata theory has taught us that no sharply reconstituted internal image of the external world need be projected within the controlling information system, so long as the relevant information in sensory stimuli has been extracted and signaled to guide the appropriate ongoing activity. Similar considerations indicate that no simple numerical relation need hold between the firing frequencies of sensory nerves and the magnitudes attributed to sensations by the subject of a psychophysical experiment. A logarithmic receptor characteristic is perfectly compatible with a power law for "sensaton," for example.

How then is sensory information represented, and how transformed, at different levels of the central nervous system? This was our first question of the second main session. Special interest was aroused by Mountcastle's elegant cross comparison of human sensitivity to vibratory stimulation with physiological data from the sensory system of monkeys subjected to the same stimuli. Results indicated not only a good correlation between psychophysical and physiological data (on a plausible cross-species assumption), but also that vibration at certain frequencies might be clearly represented by the synchronous entrainment of cortical neurons without giving rise to any perceived sensation. Eccles suggested that such unperceived information might be utilized by the cerebellum or other centers dissociated from awareness.

Workers on both somatic and auditory systems reported cases where the frequency of a single fiber was related more closely to the frequency than to the intensity of stimulation, suggesting

that intensity might be represented by the number of fibers active. R. F. Schmidt pointed out that in some preparations significant responses could be evoked by a single afferent impulse. No simple ideas of "frequency modulation" could be generalized to the whole sensory system.

The relationship between signaling processes of this kind and "feature extraction" systems seems as yet unclear. Granted that, as H. B. Barlow indicated, features such as moving contours might be detected and signaled even at the retinal ganglion cell level (in rabbit), how is such information integrated with that from other types of retinal cell? Barlow suggested some reasons for associating the rabbit's directionally sensitive units with the control of reflex eye movements rather than with visual perception; but what of the "complex" and "hypercomplex" cortical cells found by Hubel and Wiesel in cat and monkey? Are their outputs, as Barlow suggested, the triggers of pattern recognition and clues to binocular depth perception; or do they supply only collateral cues to higher neuronal mechanisms, perhaps including those that facilitate or inhibit whole classes of recognitive process? There appeared to be little firm evidence on such questions, but it seems healthy that they were raised at a time when the connection of feature detectors with pattern recognition is often taken for granted.

Evidence was also sparse regarding the precise transformations borne by sensory signals at different processing stages. For example, sensitivity of single neurons to rate of change of frequency is enhanced in the higher levels of the auditory system, as reported by E. F. Evans and I. C. Whitfield; but does this indicate the function of these levels, or is it only a by-product? Again, Jung pointed out that in the visual system the level of spontaneous activity is progressively lower at each stage on the way to cortex, typically dropping from 40 per second in optic nerve to 20 per second in lateral geniculate to 5 per second in visual cortex. Information on "brightness" and "darkness" is separated in the retina and signaled to cortex in two antigonistic systems, and enhancement of contrast is present at all levels. But whether these facts reflect the principal function of the different stages is still unknown.

For the lateral geniculate W. A. Richards proposed the unsuspected function of size-transformation, partly on the basis of evidence that single geniculate units in unanesthetized monkeys change their firing rate with the approach or withdrawal of objects. A neural "zoom lens" at this level, it was suggested, might serve to maintain size and distance constancy. Here again, simultaneous microelectrode recording from many cells would be necessary to demonstrate such "remapping" directly.

Another hard question which produced few answers was whether temporal patterning of impulses, as distinct from mean firing rate, carried significant sensory information. W. M. Siebert had calculated that if all temporal information in the observed activity of the auditory nerve in response to a tone burst were exploited, human frequency discrimination could be orders of magnitude better than it is. In practice it seemed to be roughly what one would expect if our performance were based only on the overall statistical distribution of cochlear cell activity. A few exceptional cases are of course well known in binaural localization, for example, where interaural time differences of a few tens of microseconds can be detected. Again, in *Aplysia*, a train of pulse-pairs of constant frequency has been found to have different effects according to the interval separating each pair. By and large, however, evidence for rhythm coding of information in single fibers is as yet negligible.

Between the impulses in convergent fibers, small intervals of time can have large effects, but we have still no direct evidence that significant sensory information is represented by the relative temporal patterning of impulses in parallel channels. One reason for interest in the question is that if this principle were used in the nervous system, differential changes in the speed of propagation of convergent fibers could modify the response of the system to different input rhythms. This would offer an additional possible mechanism for the long-term retention of adaptive changes. A second advantage of rhythm codes, illustrated by the Morse code call system used in many hospitals, is the possibility they offer of specific selectivity without specific connections to the central office.

Two warnings emerged from discussion which may be worth reporting here. The first concerns the drastic effects of different anesthetics, even in liminal amounts, on the picture obtainable of cortical unit sensitivity to sensory stimuli. Techniques of implanted electrodes enabling single units to be studied in unanesthetized animals promise to revolutionize many accepted ideas of sensory information processing. The other warning arose in connection with the use of computers to estimate the information content of sensory signals, when it was emphasized that what an observer can extract from a neural signal may bear very little relation to what the organism can do with it. Computer analyses only determine upper bounds, which can be ludicrously unrealistic as estimates of performance.

A third topic of great interest but of frustratingly small information-content was the central regulation of sensory information processing. Whitfield and Jung indicated that in most sensory pathways efferent fibers have been found which are presumed to lay open peripheral mechanisms to central control. What purpose might be served by such central regulation?

Automatic or voluntary gain control is one obvious possibility; but for this one would scarcely need the large number of efferent fibers observed in the auditory and visual pathways. Control of resolving power, differential control of sensitivity among members of a neuronal population, and even code-switching according to the current perceptual task, were among other suggestions. However, apart from the hint that receptive fields in unanesthetized animals are not fixed in shape, little relevant evidence was adduced.

A somewhat different class of efferent signal discussed by H.-L. Teuber and others is the corollary discharge presumed (though not yet unequivocally demonstrated) to run from motor to sensory centers, to prevent misinterpretation of the sensory effects of voluntary movement. If this hypothetical device were to operate by suppressing incoming signals (for example, from the eyes during voluntary eye-movements) this could employ some of the efferents in the optic pathway; but it was not clear that the suppression need take place at such a peripheral level, or even that it must take place at all. There seemed to be general acceptance for the view that only re-evaluation and not cancellation of sensory changes is required during voluntary movement.

It will be evident that from a theoretical standpoint sensory psychophysiology was felt to be in a rather precarious state. Old presuppositions are being upheaved, but their last traces have not disappeared (and perhaps rightly) from much of current experimentation. The need for clearer thought about the relation between physiological and psychological phenomena was urgently felt. It was generally agreed that with proper cross linkage the study of perception could supply useful clues to the design of fruitful physiological experiments, and vice versa. The role of the theory of information processing seems promising in this connection, since it belongs in a sense to both areas, and offers a kind of "interlingua" in terms of which data from one can be expressed so as to suggest or discipline ideas in the other.

On the other hand, the conceptual structures "ready-made" on the theoretical side today were felt to be woefully inadequate for all but the simplest of sensory situations. R. B. Livingston particularly emphasized the lack of any clear logical link between sensory experience and functional anatomy, suggesting that the "central gray core" of the central nervous system might be most relevant to the search for correlations. There was a general feeling that the simpler problems should be tackled first. As Mountcastle put it, with the strong concurrence of Eccles and Phillips, it is still from simple experiments, done well, that we shall learn what we most need to know in sensory physiology today.

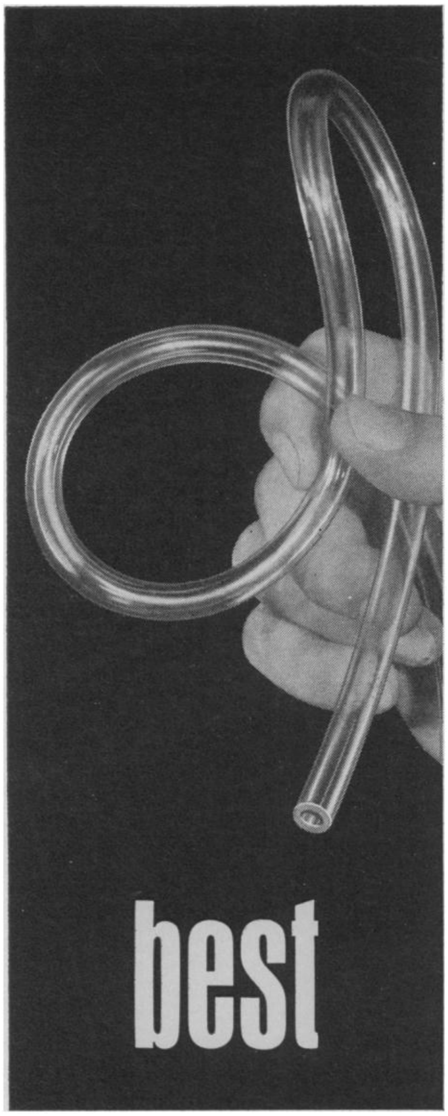
Functional Organization of Movement

The shift of emphasis from static to dynamic system properties was amply illustrated in the third session (chaired by C. G. Phillips) where we were concerned with the preparation and control of ongoing action. What physiological signs may there be of the planning of voluntary action? How should we conceive of sensory-motor integration at a neural level? Have we enough circuit information on the cerebellum—or even on the spinal cord—to attempt a mathematical theory? These were typical of the questions that troubled us, tempered by Phillips' admonition that only problems with a reasonable prospect of solution were worth discussing.

One of the early triumphs of neural communication theory was the elucidation of the α-γ muscle control system as a follow-up servo. Now, it seems, there is some doubt whether the γ loop gain available is sufficient, and Phillips quoted evidence of Evarts and others that in higher mammals effective feedback loops extend up to cortex. Does cortex then compute the mismatch between the action realized and the action intended, and use the result to initiate corrective force? If so, one could expect to record two kinds of cortical activity: one concerned with corrective action and the other reflecting the setting of the goal, as it were, before each action was initiated.

Data presented by E. V. Evarts supported this suggestion and aroused great interest. Electrodes recording from pyramidal cells of unanesthetized monkeys allowed cortical signals to be monitored during a highly motivated, learned movement. These signals were found to match closely the activity of the spinal motoneurons with which they were associated, varying according to the load against which the limb was working rather than merely specifying its position. Neighboring units were found to differ considerably and nonrandomly in their activity patterns, raising the question whether the motor cortex might not be compartmentalized in its organization in much the same way as the sensory cortex, so as to enable motor goals to be spelled out in fine detail. The fact that human subjects can quickly learn to control individual units selectively in their own motor nerves was cited as confirming the astonishing degree of detailed specificity present at least in the human motor-cortical population. The notion of reflex fields first introduced by Sherrington now seems to have a cortical counterpart, which may be considered to correspond to the idea of receptive fields on the sensory side. As was pointed out by Sherrington, such fields could change in size and shape. In discussion it was generally agreed that this area had reached a stage at which collaboration between control theorists and physiologists might be particularly fruitful in suggesting crucial experiments.

And so we turned to the cerebellum, most invitingly schematic of all vertebrate neural systems. Here, if anywhere, said Eccles, the computer engineer should come into his own. In the last few years, thanks largely to work in Eccles' own laboratory, our knowledge of cerebellar physiology has reached an unprecedented level of detail, backed by the anatomical work of Szentagothai and others. High hopes have been expressed that we now know enough for the mathematicians to be set to work on a realistic theory. We know which of the main components are excitatory and which are inhibitory.

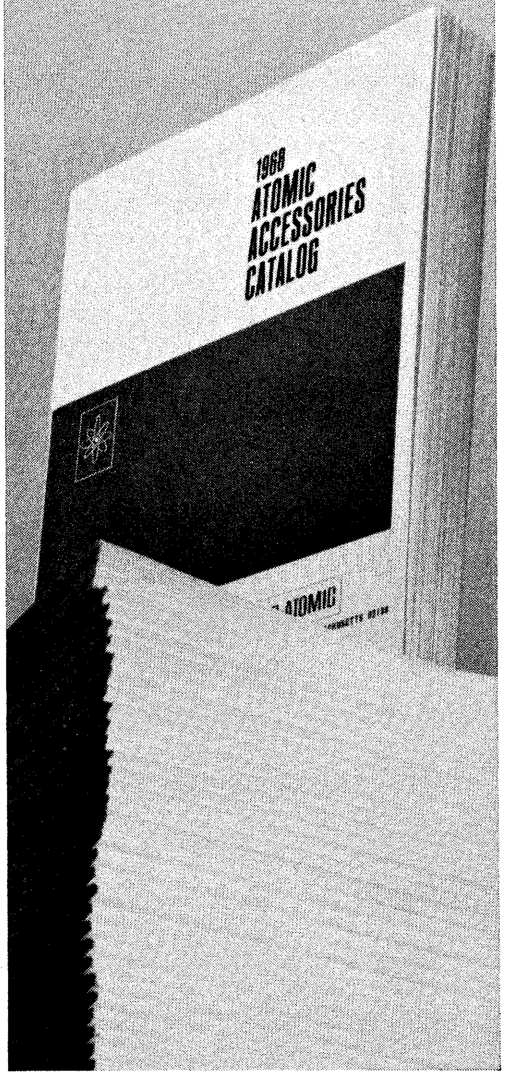


Because of the astonishing regularity of cerebellar structure we can generalize about the directions in which excitatory and inhibitory signals run, as well as about their cells of origin and destination. Transmission times, synaptic time constants, thresholds—almost all key parameters are known. What then is lacking? Why did our discussion echo the feeling, expressed at other recent meetings on the cerebellum, that detailed theoretical modeling may still be premature?

The reason, I think, was twofold. First, at a neuronal level, a vital part of the functional circuit of the cerebellar system lies outside the well-mapped cerebellar cortex, in the deep nuclei and other regions less well known. Indeed, as Eccles pointed out, some of its most important integrative feedbacks come from the evolving movement itself. Moreover, although cortical connection patterns have been carefully established, the quantitative implications of multiple reciprocal innervation, by populations with differently shaped arborizations, involve too many still-undetermined quantities to be easily tabulated at this stage. In any case it is clear that the experimental and natural conditions are not strictly comparable.

Second, at a functional level, we lack any clear idea or even a sharp hypothesis, as to what the cerebellum is there to do. To be sure, the effects of cerebellar lesions, both clinical and experimental, give a general picture of its function as a modulator, integrator, and stabilizer of the components of voluntary action. But whether it stores learned patterns, or merely insures obedience to those stored elsewhere; whether it functions as a timing organ or merely as a smoothing device; what use it makes of the sensory information projected to it from all modalities—these and a host of other clues to a sensible theory are still missing or highly debatable. Our discussion, stimulated by a perceptive summary of the contrast between cerebellar and cerebral cortex by V. Braitenberg, left the theorists among us soberly encouraged that, in this area at least, there was plenty of scope for good ideas as well as good data.

The role of sensory signals in the regulation of movement, it was suggested by H. H. Kornhuber, offers as yet the most promising field for the application of systems analysis to neurophysiology. But there are serious snags, due to the adaptive nature of neural systems. The Nyquist analysis of the



oculomotor system, for example, works well for periodic stimuli; but with unpredictable stimuli the system constants change in ways too complex for theoretical treatment. Only for lower forms such as insects and crabs has exact cybernetic analysis of sensorimotor coordinations been successful.

Qualitatively, however, some quite complex sensorimotor relationships have been clarified, particularly in the control of eye movements, and of limbs under cutaneous feedback. Evidence was mentioned that the cerebellum participates in the planning as well as the execution of saccadic eye movements; and Teuber reported the discovery by E. Bizzi at M.I.T. that the position of the eyes, rather than the force in the eye muscles, is represented in neural activity of the frontal eye field. Convergence of different sensory modalities on single motor cortical neurones is common, but how this sensory information is used is far from clear.

Intriguing clues which are emerging from studies of adaptation to sensory rearrangements were also reported by Teuber. Distortion of visuomotor coordination by prism spectacles, as in the work of Held and Hein, can be overcome more rapidly and completely if the corrective information is gained from the sensory results of active movements rather than from passive observation. The same movements imposed passively, in such a way as to generate no corrective information, of course produce no improvements. The suggestion was made that readaptation here requires, or is facilitated by, the presence of the hypothetical corollary discharge, but more direct evidence is still lacking.

Methodological Stocktaking

As may be imagined, a good deal of stocktaking went on in the concluding discussions under each of the foregoing heads; but as the last half-day was expressly devoted to methodological topics it will be convenient to report the substance of all these discussions together. Broadly speaking, we asked ourselves three questions:

(1) What types of investigation seem most promising as sources of bridge-building material between experiment and theory?

(2) What trends do we feel to be most profitable in theoretical model-making today?

(3) What implications are there, if any, for the training of research workers in this area?

Bridge-building material. Even if the best bridges between experiment and theory are those formed in one and the same head, different types of experimental study obviously vary in the suggestiveness, precision, or manageability of their material for the theorist. What the theoretical model maker wants most of all is the kind of data that enable him quickly to narrow down his range of options: to decide that a whole class of alternatives "won't do." It may easily happen that some of the most important studies for this purpose become relatively neglected, either because of the intrinsic physiological interest of some other types of experiment, or because of mere tryanny of fashion.

Thus a severe restriction on any neural theorist is that the system he postulates must have been capable of growing that way. Some genetic, embryological, and developmental data may be more crucial to the early stages of his theorizing than many measurements on mature brains.

Similarly, the fact that more primitive animals can employ simpler neural structures to do a given job may help considerably to identify the more essential features of a complex system like the cerebellum; and the abilities lacking in these simpler animals may offer clues to the functions of the elements they lack.

The effects of brain lesions, both experimental and clinical, have similar potentialities, though fraught with difficulties of interpretation, especially in clinical cases. There was particularly strong agreement with the views expressed by Teuber and Mountcastle as to the growing value of psychophysical studies for sensory physiology, both under normal conditions and those of stimulus deprivation or distortion.

The growth of small neural nets in tissue culture, and neural transplantation experiments, were mentioned as useful ways of isolating small enough systems to tackle mathematically. This was also a point in favor of studying animals such as *Aplysia* with ganglia having very few and easily identified neurons.

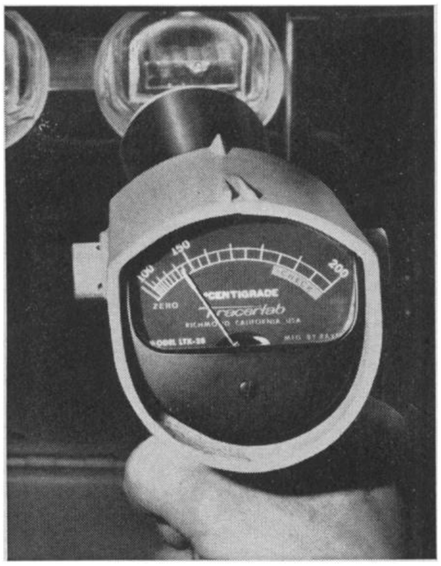
The theoretical importance of simultaneous multiunit records was frequently stressed, as a necessary complement to the single-unit studies favored by some participants. The brain, as Gerstein put it, is a parallel system, in which most of the information is carried by the ensemble of neurons rather than the single unit. We must find ways of studying the ensemble if progress is to be made. Stochastic multichannel stimulating and recording techniques were described by D. G. Lampard and S. L. Redman which may point to one way ahead here.

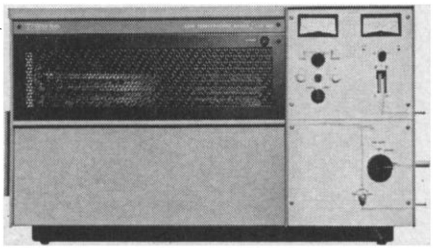
Sequential records from different sites are of limited value as a substitute; for (i) in an adaptive system it is not possible to assume that responses to the same stimulus recorded successively from different units are equivalent to simultaneous recordings; and (ii) to discover statistical dependencies between many units on the basis of sequential recordings is virtually impossible.

What we most lack is any means of identifying the significant elements of signal traffic in large cell masses—of passing from the single cell level to the level at which the slow-traveling waves of cortical activity are our data, for example. What would constitute a simple, well-done experiment at that level? Does the study of cortical surface potentials, or of evoked electroencephalogram potentials in human subjects who can report their perceptual correlates, offer a useful way in? Some of us felt that these techniques, now greatly sharpened by the advent of powerful computing methods and used in conjunction with single-unit studies, hold considerable promise. Others were not so sure. All were agreed on the special care needed in the design and interpretation of EEG experiments, with proper regard to individual differences in cortical anatomy, if the literature were not to be flooded with results of little generality.

Neuronal biochemistry, especially with the development of multibarrelled micropipette techniques, is opening up a whole new dimension for the neural theorist. The importance of axonal transport phenomena and other dynamic aspects of neuronal metabolism was emphasized by F. O. Schmitt and other participants. On the whole, however, it seemed too early to assess the relevance to the theory of neural information-processing. Current speculations as to the possible storage of information in neuronal RNA were not discussed.

Present trends in model-making. What then has happened to "neural net modeling" over the past 20 years? Cowan, in introducing the topic, felt that the most noticeable shift had been from Boolean formalisms postulating switch-like McCulloch-Pitts "formal



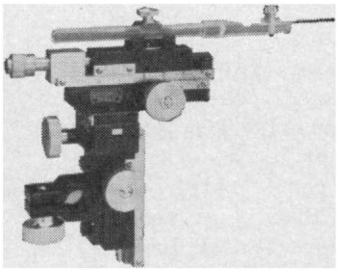


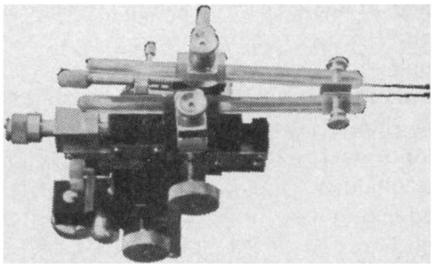
neurons" to powerful stochastic process techniques for the analysis and prediction of pulse-interval distributions and mass activity. He and others emphasized that different kinds of mathematical approaches are required for different purposes. To handle the problems of neuronal potential fields there would always be a need for biophysical models of the sort elegantly developed by Rall. To deal with local system properties differential equations were useful, as in the models of R. L. Beurle; to handle global properties the possibilities of multidimensional topology were being explored—with what value remained to be seen. Between the two extremes there is a gap at present unfilled.

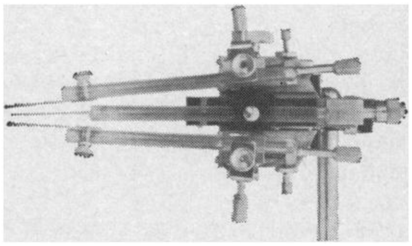
H. C. Longuet-Higgins spoke in favor of trying to design automata to perform brain-like functions, in the hope that the unsuspected problems we would encounter might force us to discover solutions that the brain also may have had to employ. It was generally agreed that mere imitation of function could be a snare unless the solution had a reasonable chance of being unique; but it was suggested that information-flow-modeling on the principles of automata theory did offer a most appropriate conceptual framework for the design and interpretation of experiments on large-scale behavior. As G. C. Quarton put it, "loyalty to structure" and "loyalty to function" may call for quite different kinds of model-making. A. M. Uttley pointed out that by looking at a neural network simply as a conditional probability machine and imposing a very general criterion of informational efficiency, one could arrive at predictions leading to fruitful experiments.

The usefulness of model neuromimes was illustrated by a neat and remarkably successful simulation by G. Szekely of the spinal circuit controlling a salamander's leg movements; but the pros and cons of hardware models versus computer simulations versus mathematical analyses were not much discussed. Generally it was felt that the nature of the problem, rather than dogmatic prejudice, must be allowed to dictate the choice of method. It seemed clear that the kind of insight offered by each would have a different appeal to different temperaments.

This bears upon the whole question of what constitutes an explanatory theory—a question raised more than once, but not resolved. From observation of the contemporary scene, and of







our 33 various reactions to theories proffered during the week, it seems woefully possible that the releaser of the "aha!" feeling for a mathematician may sometimes be quite different from that for an experimentalist. "Reduction to the familiar" for the theorist may mean the discovery that a barbarous physiological situation can be reduced to formal order by a familiar mathematical technique. For the experimentalist it may mean the recognition of a qualitative analogy between a new and a familiar situation, both equally intractable mathematically. Each may be tempted to reply "so what?" to the protestations of the other that he now "understands." Once again, we face Eccles' reminder that it is problem-centered rather than technique-centered investigation that makes good science.

What to teach. This perhaps brings us naturally to our concluding topic. How can we train research biologists to take advantage of what both theory and experiment have to offer in this area? Should every physiology student have courses in information theory, servo theory, automata theory, and high-powered mathematics, for example?

The general feeling among physiologists was that at the undergraduate stage at least there was too much essential biology to be learned for anything so ambitious to be added. Enough acquaintance with mathematics (including geometry) to give some idea of its scope and limitations; familiarity with the qualitative ideas of feedback theory and communication theory; and a working knowledge of statistics and computer programming as applied to experimentation: these seemed to be as much extra as we could expect a good physiology-degree course to include. The general principles of experimental design—for example, that an experiment gives most information when the probabilities of its various outcomes are equal—should also be covered, as a standard part of any science course.

Nor was there much support for the idea of hybrid undergraduate degrees in brain science. People should concentrate on mastering the facts of anatomy and of animal behavior by the age of 20, said Whitteridge; other things can follow in due course. Other participants urged that the more mathematical disciplines should be taught early, perhaps even in high school. It was thought best to accept the fact that only a proportion of students will be suited to both theoretical and experimental thinking. As Barlow put it, one should strengthen people at their strong points rather than their weak points. They can then choose the specialist theoretical techniques (stochastic process theory, hierarchic automata theory, advanced computer techniques, servo system analysis were mentioned) to be acquired later according to their abilities and the research problems that come to interest them. Inasmuch as educational experiments of this sort are now being mounted on different lines in various countries, it was pointed out that we should have more concrete evidence to go upon in the near future.

Perhaps the greatest unanimity was on the human and personal aspects of a good interdisciplinary research training. To have a "feeling" for several disciplines cognate to one's own, so that one knows roughly the shape of questions that can be sensibly asked in case of need, may be far more important than to have a rusting armament in one of them which one seldom uses. But knowledge of this kind is best acquired through personal contact between specialists in each discipline who are prepared to give time to listen to one another on favorite topics. Similarly, it is through regular personal contact with the older hands who can pass on their enthusiasm in research to the next generation. Their job, as Teuber and Eccles particularly emphasized, is to exhibit attitudes as much as to teach facts and techniques: to stir imagination and curiosity and to convey that combination of critical power with humility that marks the true scientist. Perhaps personal contact is also the best way to convey two other qualities suggested as desirable—the ability to express thoughts with precision in ordinary language, and an ability to profit from the history and the philosophy of science.

Who then is sufficient for these things? Perhaps it is as well for our peace of mind that we disbanded without any formal resolutions, other than one of gratitude to the supporting bodies who made possible this unusual and rewarding inquiry.

The present report, compiled with the assistance of E. F. Evans, J. C. G. Nicholson, D. Regan, and J. P. Wilson, is of course a personal and highly condensed sample, but has benefited from the comments of all participants.

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