19. Physiology

Academic and Research Staff

Prof. J.Y. Lettvin, Prof. C.L. Searle, Dr. L.A. Kamentsky, Dr. G. Plotkin, Dr. S. Weisner, G. Geiger

Graduate Students

A.C. Grant, B. Howland, G. Pratt, H. Secker-Walker

19.1 Peripheral Vision

Gad Geiger, Jerome Y. Lettvin

We have performed a set of experiments to show that the tachistoscopic presentation of a form at the point of fixation makes an identical form salient where it occurs in the peripheral visual field during the same flash. We call *demasking* the induced saliency of forms that are laterally masked within a horizontal string of forms that lie away from the fixation point. We call *eccentric enhancement* the induced saliency of eccentric forms that are presented alone on a blank field. In contrast, eccentric enhancement operates in all directions from the direction of gaze. Demasking, however, is contingent on the following conditions: a) the forms (one at the fixation point and an identical one at the periphery) should have the same orientation; b) the forms should have complex shapes, like an E or O, not just a single bar; c) the identical forms should be parts of two distinct aggregates of forms.

In addition, preliminary experiments show that dyslexics, and persons who had prolonged dyslexic episodes, have an extended central vision (for resolution of form) which is wider than central vision of readers. As a consequence, lateral masking is not as effective as with readers.

Moreover, present detailed investigations show remarkable patterns of interactions between lateral masking and demasking.

These experiments raise the question of whether lateral masking and compromise in clarity that so characterize peripheral vision is intrinsic to the visual system or is a learned way of visually attending. In addition, it questions the existence of multi-state visual attention. Our data regarding dyslexics also supports these notions. We argue that dyslexics merely fail to learn how to narrow their visual attention at a critical period as readers do.

19.2 Electrophysiology as an Anatomical Technique

Arthur Grant, Jerome Y. Lettvin

We have continued electrophysiological probing of frog optic tectum with the following question in mind: from what kind of element is one recording in the superficial tectum? There is a marked paucity of tectal cell bodies and their axons in this region, certainly not enough to account for the typical vivacious and dense activity. The shortage of cells, together with the observation that signals in tectum resemble qualitatively those in the optic nerve and are usually triphasic, was persuasive evidence at first that such signals were recorded from the retinal ganglion cell (RGC) terminal arbors (Lettvin *et al.*, 1959). George and Marks (1974) subsequently examined other electrophysiological properties of these fibers and confirmed the earlier claim.

Nevertheless, there remain inconsistencies. For instance, many optic fibers sweep across a great distance of tectum before they arborize, yet one can record from them only in the restricted area of arborization. The precise retinotopic map (Gaze, 1958; Lettvin *et al.*, 1959) would not exist if one could record fibers in passage, for then the mapping of the visual field onto the tectum would appear relatively disordered and diffuse. The traditional explanation of this phenomenon is that since the RGC terminal arbors are quite branched, only there is the extracellular current magnified enough to raise the signal above the noise level.

Now, however, the electrophysiology, in particular that from the binocular region of tectum, suggests a new model for the recording site and synaptic configuration of frog optic tectum and by analogy, of central nervous system neuropil in general.

The indirect, ipsilateral retinotectal pathway maps the binocular region of each eye onto the ipsilateral tectum, in register with the direct input from the contralateral eye (Gaze and Jacobsen, 1962). In fact, when recording just below the tectal surface one often encounters small ($<5°$) and distinct overlapping receptive fields (RF) from both eyes (Gaze and Keating, 1970; Gruberg and Lettvin, 1980; Finch and Collett, 1983). Much of the intertectal communication is through the nucleus isthmi, a small, paired nucleus of 8000 cells in the dorsal tegmentum just caudal to the colliculi (Gruberg and Udin, 1978; Gruberg and Lettvin, 1980). Each nucleus receives signals from only the ipsilateral tectum, but projects back bilaterally to both tecta. To account for these overlapping RF's, and maintain that recording is from terminal arbors, means supposing that fibers of both retinal and isthmic origin, corresponding in their receptive fields, regularly arborize in such close proximity that one can record simultaneously from both. Additionally, with both eyes uncovered, one would then expect to record simply the sum of the independent activities from the two eyes. But that is not observed. Consequently, Finch and Collet (1983) remarked, "The upper layers of the tectum contain few cell bodies and we suspect that we have been recording from dendritic processes." However, a triphasic dendritic spike would endow dendritic

membrane with a regenerative property for which there is little support.

We propose a different scheme which is consistent with both the anatomy and the electrophysiology. Specifically, we imagine that in superficial tectal neuropil the extracellular electrode is responding only to current generated in small "sub-synaptic" regions. Here the RGC and isthmic terminal arbors make connections with the bead-like dendritic appendages of tectal cell dendrites. Furthermore, the dendritic membrane is presynaptic as well as postsynaptic (Szekely and Lazar, 1976) and we suspect that the signal is positively fed back to the input. With an electrode adjacent to such a synaptic arrangement one need not resort to an electrically active dendrite to account for a triphasic spike. After all, the activation of Na^+ channels by a transmitter produces much the same local sink of current as does electrical invasion.

To test this hypothesis, we looked for and found that precisely the same spike can be recorded in superficial tectum from independent stimulation of either eye. The probability that two adjacent fibers anywhere in the central nervous system have identical spikes is essentially zero. Therefore, if an electrode held at one spot in the tectum records the same spike from stimulation of either eye, the spike must be generated at only one location and by one generator. Skarf and Jacobsen (1974) used the same reasoning to identify binocularly driven cells in the deep tectal layers. We have been able to find, without great difficulty, examples of this phenomenon in several frogs. Our latest achievement was to obtain the same spike activated at either eye at five separate locations in the same frog tectum. Since the number of isthmic cells connecting one tectum to the other is only 2000, five examples found in one frog implies that many isthmo-tectal connections are of this type. We imagine that a retinal fiber and an isthmic fiber form neighboring synapses on the dendritic appendages. Szekely and Lazar (1976) frequently found serial dendritic synapses and commented that this arrangement produced positive feedback to the incoming signal. A simpler synaptic arrangement, such as the reciprocal synapse (as occurs between amacrine cells and bipolars in the frog retina), could also produce positive feedback.

The other consequence of this view is that inhibitory synapses should be relatively silent, since it is not a Na^+ conductance that is increased, so giving a large transient current flow, but rather a K^+ conductance which only provides a shunt at about membrane potential. Evidence for this has been had inadvertently by Gruberg and Lettvin (1980) who, on stimulating n. isthmi, were unable to record pulses in the tectum from the massive ipsilateral isthmo-tectal connections. These connections, for other reasons, are presumed inhibitory.

In our next set of experiments we will stimulate electrically in the nucleus isthmi, and look for evoked activity in the optic tectum. In this way we will test further our theories of isthmotectal interaction and the mode of extracellular recording in neuropil. Although a great many isthmotectal fibers will be stimulated, we expect to find no evoked potentials in the ipsilateral tectum since we propose that: 1) these fibers are exclusively inhibitory, and 2) it is possible to record only at the "sub-synaptic" region, where inhibitory fibers do not produce a spike. This

experiment will make explicit that only "excitatory" signals are recorded extracellularly in neuropil. We suspect that isthmi fibers which project to the contralateral tectum are excitatory, and therefore spikes should be found only just below the tectal surface where these fibers terminate.

References

D.J. Finch and T.S. Collett, "Small-Field, Binocular Neurons in the Superficial Layers of the Frog Optic Tectum," Proc. R. Soc. London B217, 491–497 (1983).

R.M. Gaze, "The Representation of the Retina on the Optic Lobe of the Frog," Quart. J. Exp. Physiol. 43, 209–214 (1958).

R.M. Gaze and M. Jacobson, "The Projection of the Binocular Visual Field on the Optic Tecta of the Frog," Quart. J. Exp. Physiol. 47, 273–280 (1962).

R.M. Gaze and M.J. Keating, "Receptive Field Properties of Single Units from the Visual Projection to the Ipsilateral Tectum in the Frog," Quart. J. Exp. Physiol. 55, 143–152 (1970).

S.A. George and W.B. Marks, "Optic Nerve Terminal Arborizations in the Frog: Shape and Orientation Inferred from Electrophysiological Measurements," Expl. Neurol 42, 467–482 (1974).

E.R. Gruberg and J.Y. Lettvin, "Anatomy and Physiology of a Binocular System in the Frog Rana Pipiens," Brain Res. 192, 313–325 (1980).

E.R. Gruberg and S.B. Udin, "Topographic Projections between the Nucleus Isthmi and the Tectum of the Frog Rana Pipiens," J. Comp. Neurol. 179, 487–500 (1978).

J.Y. Lettvin, H.R. Maturana, W.S. McCulloch, and W.H. Pitts, "What the Frog's Eye Tells the Frog's Brain," Proc. IRE 47, 1940–1951 (1959).

B. Skarf and M. Jacobson, "Development of Binocularly Driven Single Units in Frogs Raised with Asymmetrical Visual Stimulation," Expl Neurol. 42, 669–686 (1974).

G. Szekely and G. Lazar, "Cellular and Synaptic Architecture of the Optic Tectum," in R. Llinas and W. Precht (Eds.), Frog Neurobiology, (Springer–Verlag, Berlin 1976), pp. 407–434.

19.3 Generation of Coding that Resembles That of Nerve

Gill Pratt, Jerome Y. Lettvin

The neuron, despite our incomplete understanding of its characteristics and function, remains a seductive device. Utilizing only its active cell membrane for the multiple purposes of generation, propagation, and distribution of pulse sequences, it is certainly the most fundamental of information processing elements.

And yet, although first order models now exist for the membrane itself, very little is known about the neuron's function. Theories of spatial organization have been popular until now, due, in part, to their straightforward nature, the relative ease of gathering histological evidence, and, in cases of gross destruction, to correlations between loss of function and affected brain area. But it is as if after examining the physical architecture of a modern computer, noting the effect of snipping a few wires, and perhaps experimenting with a signal generator and oscilloscope, we were to declare an understanding not only of each component's function, but of the programs processed

within. This attitude is clearly ridiculous in the context of our relatively simple creation[5], yet it prevails in neurophysiology where design complexity knows no human bounds. As a result, the neuron has naively been reduced to an op-amp, adding and subtracting, as it were, its excitatory and inhibitory inputs, using a sort of noisy frequency modulation to relay the resultant value down the axon, and then simply fanning this signal out to other neurons. "What" the neuron says is thus determined solely by its spatial instantiation, whereas "how much" is quantified by the frequency of its signaling.

Our research centers about the study of axonal interval sequences. In 1970, Chung *et al.*[1] uncovered the multiplexing of messages in the frequency domain within a single dimming fiber of the frog's optic nerve. Clearly a code, if only the simple mixing of long and short intervals, was being used. Using modern computer instrumentation, I have since verified their discoveries. Lettvin has demonstrated the use of two channel frequency multiplexing along the single fiber controlling the large claw of the lobster. Raymond, in his 1969 Ph.D. thesis[2] and subsequent papers, proposed a function for the bifurcations of the axonal arbor, namely, that of a parser of time encoded messages arriving from the parent axon.

It is with this background that I presume a finer structure to axonal messages than is described by average impulse frequency. My research is progressing along four avenues:

1. Development of a theory of blocking logic.

2. Gathering and analysis of further experimental evidence.

3. Event driven simulation of dendritic and axonal arbor models.

4. Construction of a programmable "neural network" sensitive to single impulses.

19.3.1 Theory

The excitable membrane can be thought of as a nonlinear, regenerative, blocking, pulse amplifier. Made spatially continuous (as in an axon), we have a digital pulse transmission line of finite bandwidth. The variable of electrical interest on any particular patch of membrane is the voltage threshold above which an incoming impulse will be regenerated. Due to the blocking nature of the membrane, this threshold becomes very large immediately after an impulse is regenerated and gradually decreases (with some variation, dependent, in part, on past history) to its resting value. Along a stretch of membrane, and particularly at "regions of low conduction safety" such as are found at bifurcations of the axon, the time constant of the blocking function is found to vary. Without question, the fine twigs of the terminal arbor (whose thin diameter give them a very long recovery time) cannot sustain the pulse frequencies found in their parent axon.

19.3.2 Axonal Arborization

One is thus lead to the captivating idea that the very same mechanism which transmits pulse intervals may also be used to discriminate among them. If one were to hypothesize a logic discipline where "events," distinguished only in their time of arrival, were propagated rather than the logic values of conventional digital circuits, how could one use this most basic construct of a finite bandwidth channel to perform useful transformations?

In the conventional digital electronics realm, a blocking pulse amplifier (although simpler than any of the following components) would be described in terms of a timer, an arbiter, and a gate. After every successful regeneration, the timer would be reset. When a second pulse arrived, the arbiter would sample the timer's value to determine whether a sufficient blocking interval had passed. If so, the new pulse would be regenerated; otherwise, ignored. Two fundamental problems arise when arbitrations such as these are done on continuous variables (in the digital example, time, in the actual nerve, voltage). As the values to be compared approach each other, not only does the result become more indeterminate, but the time required for the comparison becomes unbound. Raymond noted the effect of cross coupling from other neurons on the blocking function's arbitration point. The increased propagation delay associated with "barely triggering" a membrane is well known.

If time encoded messages are to be reliably parsed without indeterminate, continuous variation of the newly created intervals, incoming messages must endeavor to stay away from the arbitration points of the axonal tree. Thus, if messages are parsed as Raymond believes, there must be a continuous set of forbidden messages that leave noise and arbitration margins around the parser's arbitration points.

19.3.3 Dendritic Generation

If a code, rather than a simple frequency, is generated on the axon, then some mechanism must exist in the neuron to generate it. Due to the difficulty of stimulating its various parts, the dendritic tree is less well characterized than the axonal arbor. It is known that certain (excitatory) synapses, upon stimulation by presynaptic fibers, increase the postsynaptic neuron's average firing rate. On the other hand, other (inhibitory) synapses effect an opposite response, lowering the neuron's mean firing rate.

Professor Lettvin has likened the generation of codes from the dendritic tree to the warbling tone resulting from a novice's attempt to play the flute. The resulting pattern of frequencies, in some sense, explores the various modes of the flute's cavity, giving the listener information, albeit in a very complex form, about the position of each of the player's fingers. In such a fashion, Lettvin asserts, the axonal code gives information, with increased definition as one continues to listen, about all of the dendritic tree's synapses. Of course, the activity of the synapses are changing while one listens, so one can only learn so much.

This analogy, while plausible, is not specific. A simple model of the dendritic tree which agrees with observed facts and hints of Lettvin's flute player is to suppose that a synapses' effect on a neuron is better described by phase modulation than frequency modulation, the difference, of course, being nothing but a convention as to the relative frequencies of modulating signal and carrier. If each firing of a pre-synaptic excitatory fiber hastened the generation of the next impulse, while the firing of a pre-synaptic inhibitory fiber postponed it, a resulting code would emerge which I feel to be quite in agreement with what one sees in the live animal. The degree and relative timing of excitation, inhibition, and self-blocking of the axonal cone (where the impulse starts) would determine the sequence so generated.

19.3.4 Experimental Work

Using sophisticated recording instrumentation, I am taking long, detailed, recordings from the optic nerve, tectum, and cerebellum of the frog. The cerebellum, in particular, is interesting because of its great activity even in an immobilized frog, as well as its regular physical structure.

Employing data analysis techniques similar to those used to test the merit of a random number generator, I am searching for apparent syntax within the recordings. By syntax, I mean structure both imposed by the arbitrations done in the axonal tree (i.e., forbidden sequences) as well as any other patterns which seem prevalent.

19.3.5 Simulation

Recent years have seen the fantastic development of efficient tools for simulating very large digital circuits. These simulators (in particular, those developed by Prof. C.J. Terman)[3] take advantage of the digital abstraction in voltage to gain huge leaps in efficiency. Thus, instead of linearizing a circuit's behavior through many small increments of time, the simulator can predict, based on a relaxation model, when a circuit node will cross a digital threshold. Simulated time can thus jump in leaps to the next threshold crossing, rather than crawling towards it by integration (as would be necessary in an analog simulator).

In the realm of purely time domain logic, such as I have described, the simulation task is even simpler. Relaxation equations are still necessary to represent the state of various blocking amplifiers, but the time events are pure, having no associated logic value. I am developing an event-driven simulator for blocking logic, based on the ideas contained in Terman's VLSI simulators. With it, I hope to flesh out theories of how such logic discipline might be put to use.

19.3.6 Neural Network

After a long hiatus following the Perceptron's demise, there has been a resurgence of interest in simple network structures for pattern recognition, associative memory, and problem solving. While the Perceptron did not deserve further investigation, these new "neural networks," whose

trajectory in state space depends not only on their input, but also their current position, are very promising. By initializing the set of "axon's" to a particular point in their collective state space, a tendency is found, with appropriate programming of connective parameters, for the system to migrate to one of many stable states. Thus, an associative memory can be built, where partial information is given, and the system migrates to a "near" state, being the associatively requested piece of data.

Most current neural networks are loosely based on the McCulloch/Pitts[4] neuron model whereby the firing rate of a neuron is not only averaged over time, but quantized to one bit (high rate/low rate). Thus, a digital amplifier can be used to represent a particular neuron's state, and the resulting state space is described by a boolean hypercube. Various methods of dithering the network so as to achieve interesting state transitions are used, such as the injection of noise into the "dendrites" or the use of a random sampling interval.

In collaboration with Chris Musil, I am engaged in the design of two VLSI chips that will allow experimentation with neural networks much more isomorphic to real nervous systems. In the first, actual pulses will be routed and mixed rather than voltages representing the frequency of abstracted pulses. Aside from making the network easier to construct than its voltage-summing counterpart, we will be able to experiment with high loop gains as are achieved by placing a phase modulator in the feedback path from dendrite to axon. The configuration of the network (i.e., which axonal pulses are routed to which dendrite, and with what sign) will be writable by computer. The excitatory and inhibitory dendritic outputs of the chip will be fed to an external charge pump, then to the phase modulator or VCO. Thus, the charge pump can be modified so as to change the speed of network convergence, as well as the nature of the axonal code generation model.

The second chip is a multiple frequency counter/interval timer with a computer interface which will allow us to record the axonal pulse frequencies or intervals with high efficiency.

References

1. S.H. Chung, S.A. Raymond, and J.Y. Lettvin, "Multiple Meaning in Single Visual Units," Brain, Behaiv. Evol. 3, 7–15 (1970).
2. S.A. Raymond, "Physiological Influences on Axonal Conduction and Distribution of Nerve Impulses," Ph.D. Thesis, Department of Biology, M.I.T., 1969.
3. C.J. Terman, "Simulation Tools for Dicital LSI Design," Ph.D. Thesis, Department of Electrical Engineering and Computer Science, M.I.T., 1983.
4. W.S. McCulloch and W. Pitts, "A Logical Calculus of the Ideas Immmanent in Nervous Activity," Bull. Math. Biophysics 5, 115–133 (1943).

19.4 Auditory Primal Sketch

Campbell L. Searle, Hugh Secker-Walker

We are searching for the auditory equivalent of Marr's "Primal Sketch," or, more precisely, the primal sketch for speech and music perception. The mechanical filters in the cochlea, while clearly the first step in the processing chain, do not appear to provide, by themselves, an invariant enough representation to act as a primal sketch. Spectral shapes, for example, vary considerably from speaker to speaker. Hence we are searching for a physiologically plausible neural primal sketch. Three avenues are being pursued: generalized automatic gain control and more robust representations derived from either a second set of filters, or linear combinations of the cochlear filter outputs.

19.4.1 Automatic Gain Control

There is now clear evidence that the gain of the auditory channels can be reduced by as much as 50 dB by efferent pulses.[1] Thus, it makes sense to study the possible use of this measured physiological function in the formation of a robust primal sketch. Computer simulation of the simplest possible gain control loop around a hyperbolic tangent hair-cell transducer showed that the simulated hair cell did not saturate (except for the first few cycles) over a range of input signals in excess of 60 dB. This indicates the potential normalizing power of some very simple neural structures. We plan to modify our software speech analysis system to include some form of physiologically realizable AGC. The key research questions are how to arrange the interconnections, and how to choose the time constants. The benefits of wide-band AGC (as in an AM radio) are well known, but the benefits of individual channel AGC, or some combination, must be determined experimentally.

19.4.2 Second Level of Filtering

We are also exploring the possibility that a second level of filter banks, operating on the temporal outputs of the primary filters, could provide a more robust primal sketch. Tansley's adaptation work,[2] as well as the more recent depth modulated FM detection thresholds results from Rees and Kay at Oxford,[3] suggest center frequencies and bandwidths for such filtering. Our preliminary work has shown that filtering provides additional cues for speech recognition from visual displays.

The work of McAdams[4] with synthetic musical instruments suggests that a second level of filtering could also play a role in the identifying and tracking of individual voices in noisy or multivoice signals. Changes in the spectral information from a single voice are correlated in both time and frequency; filtering of spectral samples allows the changes occurring in one voice to be characterized and followed.

19.4.3 Linear Rotations of Spectral Magnitudes

As a second method of deriving a robust speech representation, we are continuing to examine a linear rotation of the spectral magnitude information based on principal components analysis. The mathematics of such rotations is well understood, but the perceptual consequences of reducing the dimensionality of the new space has not been systematically explored. A computer program to delete components in the rotated space and to generate the corresponding modified speech (based on the Ph.D. Thesis of Bustamente, 1986)[5] is now operational.

References

1. J.J. Art and R. Fettiplace, "Efferent Desensitization of Auditory Nerve Fibre Responses in the Cochlea of the Turtle Pseudemys scripta elegans," J. Physiol. 356, 506–523 (1984).
2. B.W. Tansley and J.B. Suffield, "Time Course of Adaptation and Recovery of Channels Selectively Sensitive to Frequency and Amplitude Modulation," J. Acoust. Soc. Am. 74, 765–775 (1983).
3. A. Rees and R.H. Kay, "Delineation of FM Rate Channels in Man by Detectability of a Three-Component Modulation Waveform," Hearing Research 18, 211–221 (1985).
4. S. McAdams, "Spectral Fusion and the Creation of Auditory Images," in M. Clynes (Ed.), Music, Mind, and Brain, (Plenum Press 1982).
5. D.K. Bustamente, "Principal Component Amplitude Compression of Speech for the Hearing Impaired," Ph.D. Thesis, Department of Electrical Engineering and Computer Science, M.I.T., 1986.