A Model of the Anuran Retina

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COINS Technical Report 81-35
November 1981

Abstract

Knowledge of the anatomy and physiology of the vertebrate retina exists in sufficient detail for brain theorists to begin to be able to develop models which are capable of capturing its structure as well as its function. A preliminary retinal model is presented which is based upon a detailed account of the fine structure and current electrophysiological data, and which formalizes these data as a system of simultaneous differential equations which are subject to further formal study or simulation. In the course of the development of the model, a principled attempt is made to identify the assumptions which the modeller must make in the absence of requisite experimental data.

This research was funded in part by NIH grant NS17941-02, Michael A. Arbib, principal investigator, whose assistance the author gratefully acknowledges. The author also wishes to thank D. Nico Spinelli for valuable discussions of the literature. This material also appears in the author's master's thesis,

1. Introduction

This document represents an attempt to develop a formal mathematical model of the anatomy and physiology of the anuran retina which could be used for further mathematical analysis or computer simulation.

A premium has been placed on achieving structural validity; for this reason the biology of the retina is extensively reviewed before any formalisms are introduced. Also of interest is the philosophy of the modelling process itself, particularly with respect to the presence and nature of the assumptions that underly the chosen formalisms. An attempt has been made to make explicit these assumptions by clearly labelling them as such insofar as is possible, in order to make them available for the reader's scrutiny. Where insufficient data exist for anurans, we will rely on the available data on related vertebrates such as Necturus.

Early research on the retina resulted in the introduction of a wealth of anthropomorphic terminology that in retrospect has greater basis in fiction (i.e., inadequate models of the animal's teleological world) then fact (i.e., "scientific" observation). We shall eschew such terms as "feature detector" (except where reference to the literature would introduce them), and instead shall address only the electrophysiological phenomena, leaving questions of perception and cognition in anurans to future research.

2. General Morphology and Physiology

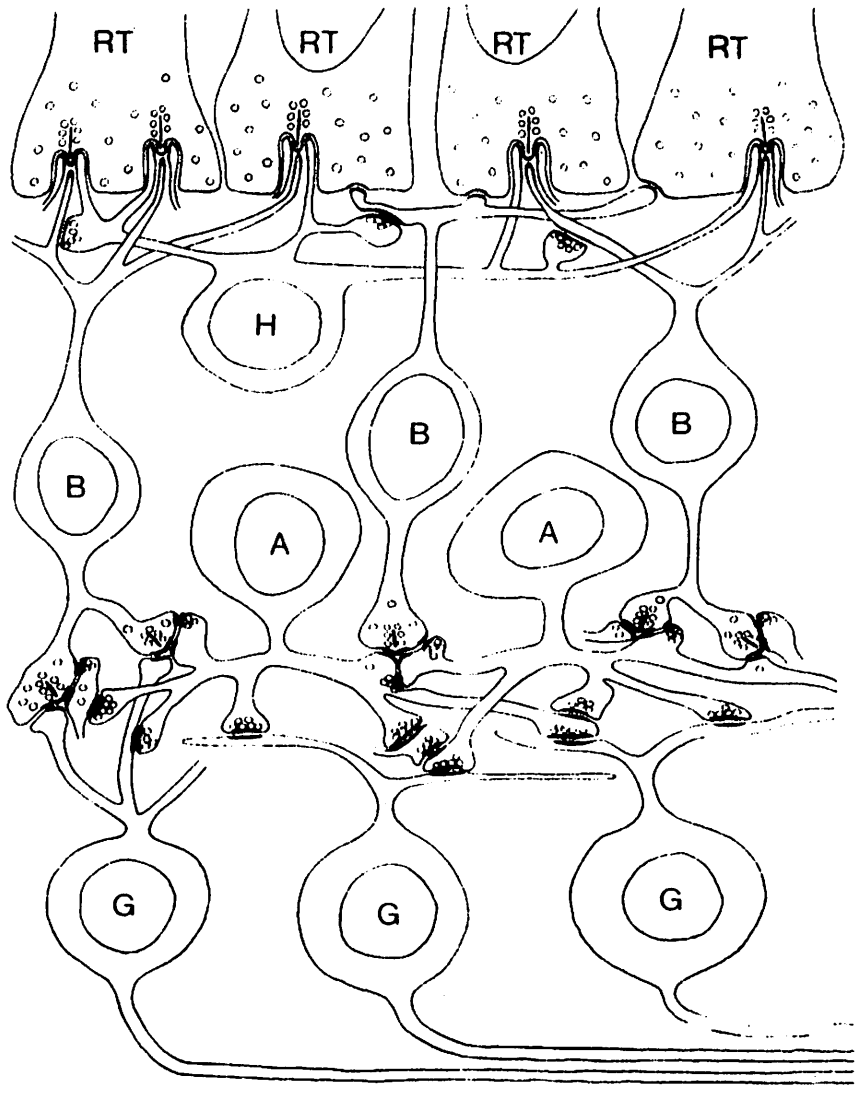
In this section we describe the known anatomy of the anuran retina, its electrophysiological behavior, and current views on its synaptic organization.

2.1 Gross Neuronal Structure

The gross morphology of vertebrate retinae varies little across species boundaries. Researchers currently recognize five principal types of neurons (receptor, horizontal, bipolar, amacrine, and ganglion cells), one neuroglial cell (the Mueller cell), and more recently an interplexiform cell which appears to transmit information centrifugally (that is, away from the brain). (See [13] for an extensive review of retinal morphology.)

Retinal neurons are organized in characteristic layers (see Fig. 1). Most distal (from the brain, in the synaptic sense, or from the lens in the spatial sense) are the photoreceptors, the perikarya of which are located in the outer nuclear layer and which synapse in the outer plexiform layer (OPL) with horizontal and bipolar cells. Both horizontal and bipolar soma are located in the inner nuclear layer; the horizontal processes ramify widely throughout the OPL but do not pass through the inner nuclear layer, whereas the bipolars send efferent processes into the inner plexiform layer (IPL) where they synapse with amacrine and (probably) ganglion cells. The amacrines themselves have no anatomically identifiable axons; the ganglion cell axons traverse the proximal aspect of the retina and pass through it at the "blind spot", joining to form the optic nerve, which in amphibians undergoes incomplete decussation at the optic chiasma and continues on to the optic tectum and thalamus.

Fig. 1. Synaptic contacts in the frog retina



A summary diagram of the synaptic contacts in the frog retina. Receptor terminals RT; horizontal cells H; bipolar cells B; amacrine cells A; ganglion cells F. (From [13], p. 289.)

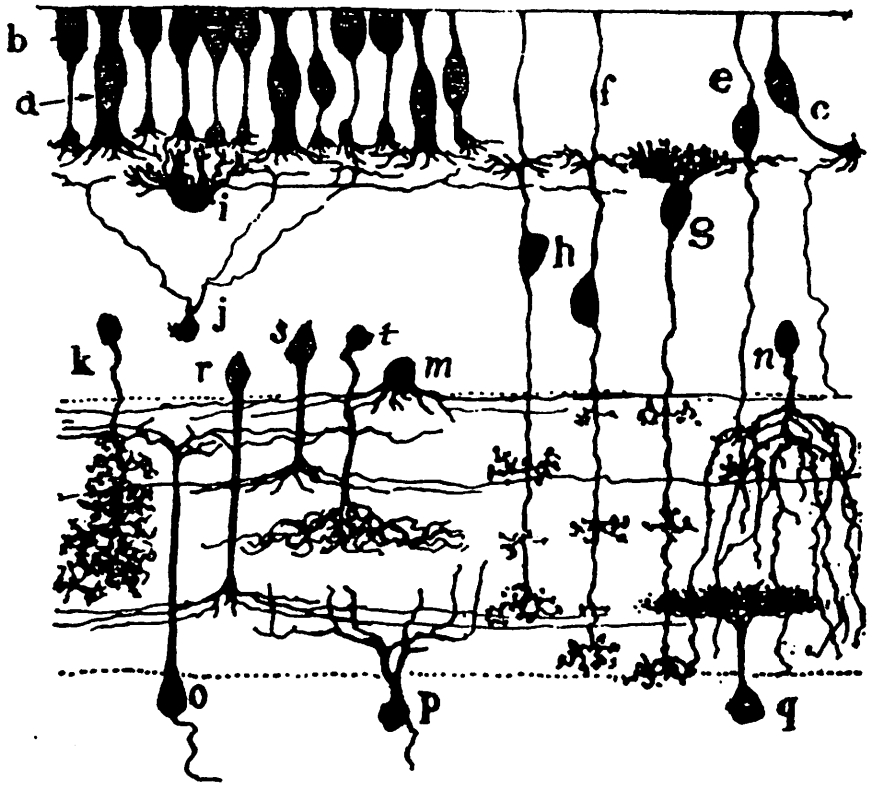
Most of the fundamental anatomical work in the vertebrate retina was, of course, performed by Cajal [7, 8], who identified numerous subclasses of retinal neurons (see Fig. 2). For example, he found two classes of horizontal cells: "outer" (the smaller and more distal) and "inner" (larger soma but smaller dendritic fields).

Similarly, Cajal discerned two types of bipolars: large (distal) bipolars with thick, bushy dendrites and small (proximal) bipolars with more slender dendrites, often associated with rods and cones, respectively, in many species. Within the IPL Cajal noted five distinct layers of dendritic contact; an individual bipolar cell might send processes to one or several of these layers. The morphological distinctions among various amacrine and ganglion cell types are in general beyond the scope of this paper (Cajal distinguished 24 types and believed his taxonomy to be incomplete), except to note the major subdivision of these cells into "stratified" and "diffuse" on the basis of their dendritic arborization patterns among the layers of the IPL. He was unable to find centrifugal fibers, although he suspected that they exist; evidence for them was not found until the last fifteen years (see [12] for a recent study of one type of interplexiform cell). As for the Mueller cells, which are located near receptor cells and exhibit slow "b-wave" potentials, information is scant; however, it has been hypothesized that they are involved in neurotransmitter synthesis or regulation [3].

2.2 Receptor Structure and Function

The anuran retina contains four classes of visual receptors: the "green" rods, "red" rods, single cones, and double cones (see Fig. 3 and Table 1). These receptors are maximally stimulated at different spectral wavelengths and are distributed unevenly throughout the retina. All seem to hyperpolarize as

Fig. 2. Frog retina: ultrastructure



Drawing showing typical cells in the frog retina (R. esculenta) stained by the Golgi method. Slightly modified from [8]. Cone a; rods b, c; horizontal cell i; large bipolar cell g; small bipolar cells h; displaced bipolar cell e; Landolt Club process f; stratified amacrines r, s, t; diffuse amacrines k, n; displaced amacrine q; stratified ganglion cell o; diffuse ganglion cell p; unidentified, partially stained cell j (perhaps an interplexiform cell). (From [13], p. 279.)

a result of (1) quantal light reception that evokes conformational changes in a pigment molecule and subsequent closing of channels for Na+ influx, or (2) electrotonic effects induced by nearby receptors which have themselves hyperpolarized via the extensive system of processes connecting adjacent receptors [16]. The cones are generally smaller and more pointed than the cylindrical rods; both have a lamellar structure in the outer segment (distal portion of the receptor), wherein the pigments reside. The cone terminals are usually larger than those of the rods [13]. (For an extensive review of receptor organization, distribution, and behavior, see [10].)

The "green" rods absorb light maximally ($lambda_{max}$) at approximately 432nm.[1] They occur more frequently in the area centralis of the retina (the central third or so in anurans); although reports vary, 432nm rods seem to constitute about 14% of the area centralis and 9% of the total retinal

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Table I. Rod and cone absorption data

Name	$lambda_{max}$	% in Centralis	% Total
green rod	432nm	14	9
red rod		51	57
larval/aquatic	522		
adult	502		
single cone		21	20
tadpole	620		
adult	580		
double cone		14	14
principal	620/580		
secondary	502		

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1. This is what humans perceive as violet light; the name "green" rod is used because these receptors reflect maximally in the spectral range that appears green to us.

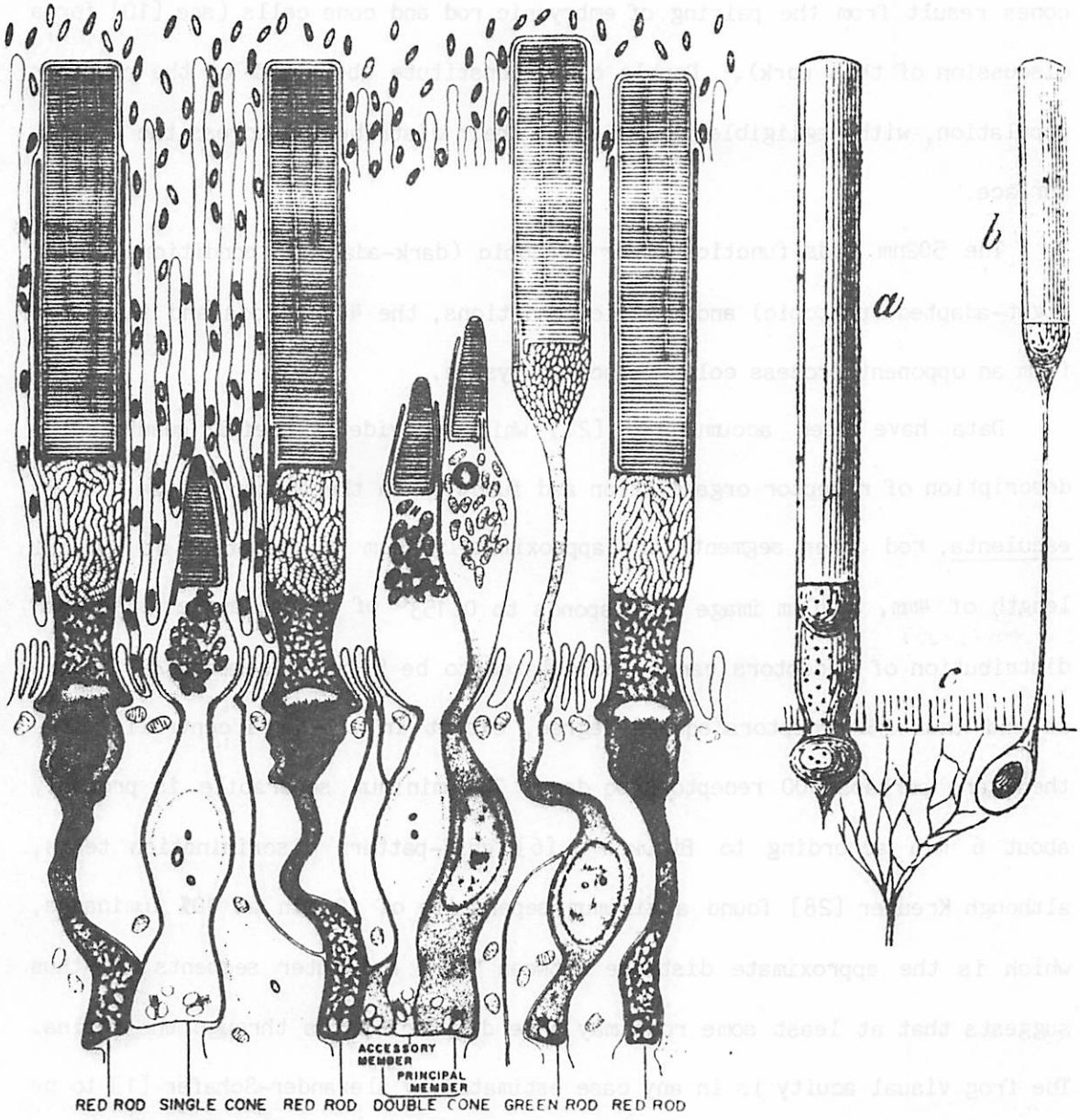
receptor population.

The "red" rod in fact contains different pigment chromophores and exhibits different $lambda_{max}$ depending on the age and habitat of the animal: the pigments of freshwater vertebrates, including larval and aquatic amphibians, contain 3-dehydroretinal and are called porphyropsin ($lambda_{max}$= 522nm), whereas those of adult frogs and toads contain retinal and are called rhodopsin ($lambda_{max}$=502nm). The pigments also differ in the amplitude (porphyropsin is weaker) and kurtosis (porphyropsin is broader) of their spectral responses. "Red" rods comprise about 51% and 57%, respectively, of the central and total receptor populations. (The bullfrog R. catesbiana is an exception in that its retinal receptors contain both rhodopsin and porphyropsin; the relative frequency of occurrence throughout the retina is seasonally-dependent, and there is a marked spatial division of the two populations with respect to their distribution above and below the horizon of the visual field.) Red rod pigment seems to regenerate more slowly upon bleaching than do the other pigments.

The structure of the single cones is more or less typical of that of vertebrate cones in general; their $lambda_{max}$ is 620nm in tadpole Ranids and 580nm in adults. Single cones make up approximately 21% of the central and 20% of the total visual field receptor populations. (Note that cone absorption spectra data are somewhat less reliable than rod data, due to the small size of the cone.)

Double cones consist of a pair of receptors: a "principal" cone, essentially identical in morphology and spectral response to the single cone, in apposition to an "accessory" member having a $lambda_{max}$ of 502nm. The observant reader will note that the accessory cone $lambda_{max}$ is identical to that of the adult "red" rod, and in fact there is much evidence that double

Fig. 3. Frog retina: fine structure



Left: schematic drawing, based on electron microscopy, of the receptor layer in the frog retina (R. pipiens). The picture shows three red rods, one single cone, one double cone, and one green rod. The receptors are separated from each other sclerally by means of pigment epithelium processes (some of which have been omitted) and vitreally by means of glial elements (Mueller cells), which form short processes at the level just sclerall to the red rod nuclei. Right: A red (a) and green (b) rod as drawn by Schwalbe. The Mueller cell processes (c) can be seen also in this picture. (From [10], p.252.)

cones result from the pairing of embryonic rod and cone cells (see [10] for a discussion of this work). Double cones constitute about 14% of the receptor population, with negligible variation in their distribution across the retinal surface.

The 502nm rods function under scotopic (dark-adapted) conditions; under light-adapted (photopic) and mesopic conditions, the 432nm rods and the cones form an opponent-process color detection system.

Data have been accumulated [21] which provide a useful quantitative description of receptor organization and function in the anuran retina. In R. esculenta, rod outer segments are approximately 10ùm in diameter; at a focal length of 4mm, a 10ùm image corresponds to 0.153° of visual angle. The mean distribution of receptors can be calculated to be 5 outer segments/23 square um and thus 35 receptors/square degree, except in the area centralis where there are perhaps 100 receptors/sq deg. The minimum seperabile is probably about 6 min according to Birukow's [6] grid-pattern discrimination tests, although Kreuger [28] found a minimum seperabile of 10 min at 10% luminance, which is the approximate distance between "red" rod outer segments and thus suggests that at least some rods may have distinct paths through the retina. The frog visual acuity is in any case estimated by Alexander-Schafer [1] to be "about 20 times lower than that of human foveal vision" [22].

2.3 Electrophysiological Classification and Behavior

Electrophysiological recording techniques have probably been the single most important source of information on the function of the retina in the last half-century. The initial research of interest here is the well-known work of H. K. Hartline [23, 24, 25] in which he determined that: (1) ganglion cells exhibit "on", "off", or "on-off" responses (that is, they fire at onset, or

disappearance, or both, of a stimulus); (2) ganglion cells have a receptive field (in the sense of Sherrington) within the total visual field, such that the image of an object can only produce a response in the ganglion cell when in its receptive field; (3) ganglion cells summate the excitatory responses produced by multiple stimuli within their receptive fields. (Also at this time, Granit developed the technique of extracellular retinal recording.) Several years later, Barlow [4] noted that expansion of the image beyond the size of the excitatory receptive field (ERF) caused a decreased neural response, but further enlargement resulted in an increase in response; this prompted Barlow to suggest that the system producing this paradoxical response could constitute a "fly-detection" system. At the same time, Kuffler [29] found evidence of concentric center-surround organization in the cat retinal ganglion cell receptive field. Lettvin et al.'s famous paper [30], in which they identified five classes of ganglion cells on the basis of their response characteristics and the depth of their axonal terminals in the tectum, provided us with the ganglion cell taxonomy that we use, with little alteration, to this day. (For an interesting historical perspective, see [5] or [39].)

In the following sections, we will consider the electrophysiological behavior of each retinal cell type in turn and choose a taxonomic scheme for each consistent with current recording data and contemporary classification methods. (Figure 4 shows the intracellular response observed during electrophysiological recordings of the five principal classes of retinal cells in the mudpuppy retina in response to spot and annular stimuli.)

Fig. 4. Intracellular recordings from Necturus Retina

Intracellular recordings from neurons in the mudpuppy retina. Responses were elicited with a spot of light focused on the electrode (left) and with a small and large annulus (center and right). (a) ganglion cells; (b) Retinal, horizontal, bipolar, and amacrine cells. (From [13], p.291.)

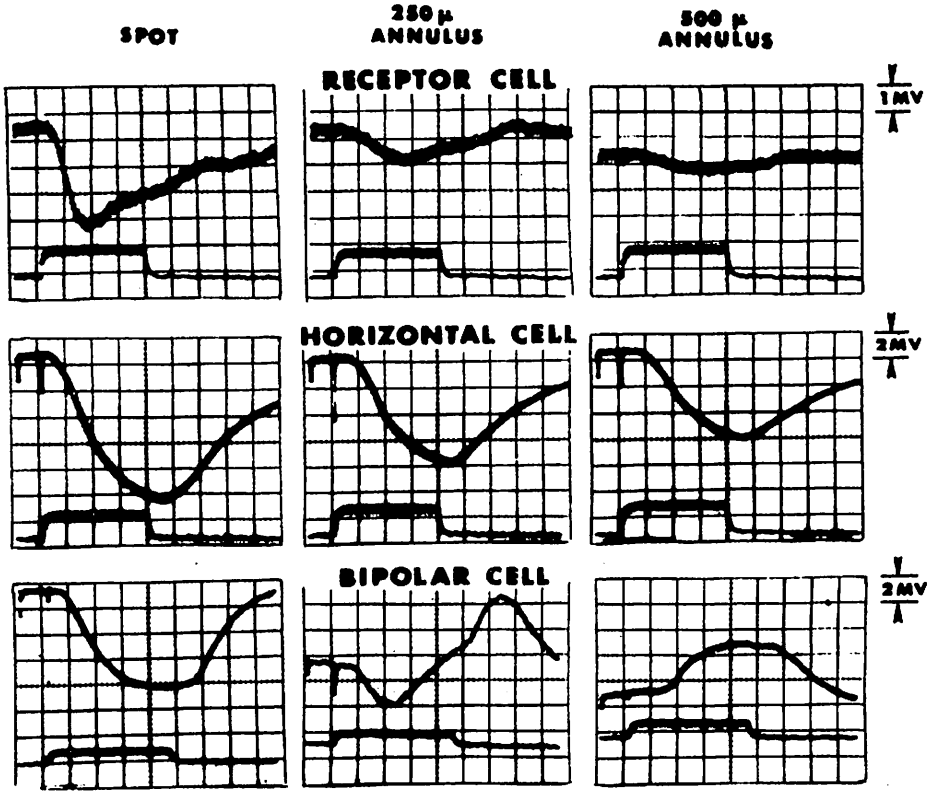
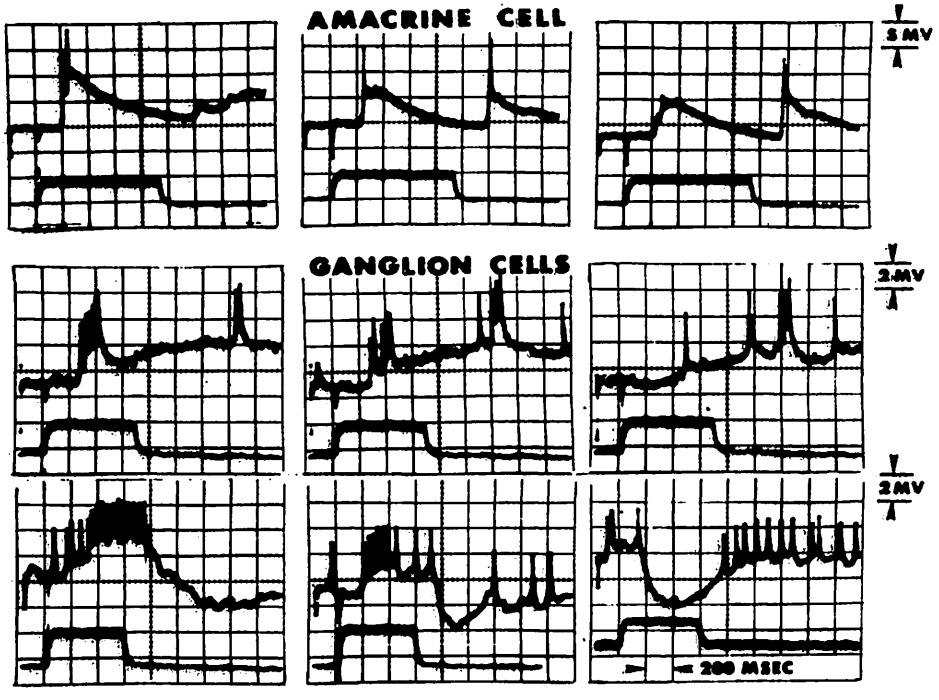


Fig. 4 (continued)



2.3.1 Receptors

The most striking physiological feature of all retinal neurons having processes extending into the OPL is their lack of classical action potentials: they exclusively exhibit graded potentials, most often hyperpolarizations. The receptor hyperpolarization seems to occur, as previously mentioned, when a single photon striking a pigment molecule causes conformational changes[1] that ultimately result in the closing of Na+ channels, halting sodium ion influx and thus producing a hyperpolarization of the receptor membrane. (See [42] and especially [3] for a thorough treatment.) Evidence is accumulating [20] that this hyperpolarization signals a decrease in receptor transmitter release; for example, receptor uptake of HRP is much higher in the dark than in partial light.

Fain [16] has demonstrated a second mechanism for production of these receptor hyperpolarizations: in the toad rod, he found that at least 85-90% of the shift in membrane potential for a given photoreceptor was attributable to quantal light reception in neighboring rods, passively spread through gap junctions at the terminals of interreceptor filaments. The toad rods summate activity over an area as large as 800μm.[2]

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1. The conformational changes apparently take 11-cis, 12-s-cis chromophore to all-trans retinol through several steps and, probably, more than one pathway — see [10].
2. This effect is absent in Necturus, but it is important to note that the visual system does not play as significant a role in the mudpuppy's behavior as it does in the toad, and furthermore the retina in Necturus is "developmentally that of an animal in the larval stage" lacking the additional growth of functionality that occurs at metamorphosis in other species [22].

2.3.2 Horizontal cells

In the mudpuppy (Necturus) retina, horizontal cells only hyperpolarize in response to light; in species with color discrimination, however, some horizontal cells are observed to depolarize as well, in a spectrally-dependent manner. These two physiological subclasses of horizontals are termed L-cells and C-cells (for "luminosity" and "chromaticity") respectively. No spikes have ever been observed in either L-cells or C-cells [13]; the time-constant for horizontal cell membranes is rather long, on the order of one second [22].

Their apparent color discrimination not withstanding, frogs seem to have only hyperpolarizing horizontals for light anywhere in the cell's receptive field, according to Gordon and Hood [20], who suggest that the maximal response of frog horizontal cells to 570nm light may indicate input mostly from cones, even in dim light.

2.3.3 Bipolar cells

As is the case with the other distal cell types, bipolars have never been observed to generate spikes; all responses are graded potentials [13]. Two physiologically discernible classes of bipolars are observed: those that hyperpolarize in response to spot illumination in their ERF (type a), and those that depolarize to such stimuli (type b) [43]. In both cases, presentation of an annulus in the surround has an antagonistic effect and in some species can even drive the membrane potential beyond its resting state (but not in Necturus; see [13]). This strongly suggests that the center-surround organization must be

mediated by horizontal cells. Additionally, Shepherd [42] argues that we can infer the existence of direct contacts between receptors and bipolars from the similarity of latency until onset of potential shift in bipolar and horizontal cells (about 100msec for both; see also [22]).

Within the two classes of bipolars, further categorization is possible on the basis of their dendritic field characteristics and their receptor contacts [43, 17]. For example, Stell et al. found in carp that type-a bipolars, which terminate in the more proximal "a" IPL sublamina corresponding to Cajal's strata 1, 2, and 3, can be further subdivided into a1 cells having an average dendritic field of 65um by 25um and receiving no "green" receptor input, and a2 cells having an average field size of 44um by 37um and receiving "green" receptor input; type-b cells have three subdivisions: b1, with 41um by 31um dendritic fields and no "green" receptor input; b2, with 56um by 48um dendritic fields and "green" receptor input; and b3, with 105um by 71um fields and "green" receptor input. There are always more connections observed with scotopic rods than with all other receptors combined, sometimes by an order of magnitude or more. Note that, while these data are from a non-anuran vertebrate (carp), the same bipolar classification also applies to cat bipolars "despite the very distant phylogenetic relationship of carp and cat" [17], and thus it is not unreasonable to suggest such a classification scheme for anuran bipolars as well.

2.3.4 Amacrine cells

Amacrine cells are the first cells in the visual system to exhibit action potentials; typically these spikes are superimposed on graded depolarizations. The membrane time constant also seems to be much smaller than that of the more distal units [42], although it appears to be larger than that of the ganglion cells judging from most published photographs of retinal unit responses. Amacrine cells can spike at onset, offset, or both onset and offset of the visual stimulus, which immediately suggests a possible role in Hartline's original classification of ganglion cell responses. Dowling [13] notes that in some species other than mudpuppy, amacrines are observed to hyperpolarize as well as depolarize, often in a spectrally-dependent fashion, and that unlike ganglion cells the amacrines only generate one or two spikes at "on" and/or "off", raising the question of "whether it is the slow potential part of the response or the spikes which is the most important component for signal transmission by amacrine cells". It may be that the function of spikes is simply to assist the electrotonic spread of amacrine response over the great lateral extent of their dendritic field [42].

2.3.5 Ganglion cells

Ganglion cells are doubtless the best-studied units in the vertebrate visual system; this is to be expected, since they occur in all vertebrates, have long accessible axons in an isolated bundle (the optic nerve), and ramify widely throughout the brain, apparently terminating in different brain regions depending on their

electrophysiological behavior and, within those regions, in different locations depending on the position of their ERF within the total visual field (see, for instance, [18, 41]).

It appears that stimulus intensity determines both the latency until onset of firing and the firing rate of ganglion cells [22] in logarithmic fashion:

$$R = k_1 \log \left[\frac{I}{I_s} \right] = \frac{k_2}{l} \qquad (1)$$

where R is the impulse rate, I_s is the threshold intensity, L is the latency, and k_i are constants which vary not only between neurons but within on-off neurons as well for their on- and off-activation phases. Gruesser and Gruesser-Cornehls suggest that the sigmoidal intensity function is "better described by the following hyperbolic equation:

$$R_i = \frac{I}{I_s + k_i} I \qquad (2)$$

(in impulses/sec)."

There are numerous classifications of ganglion cell activity (for example, [20, 24, 30]); we shall rely largely on that of Gruesser and Gruesser-Cornehls [21]. Note that throughout this discussion the usual caveat obtains: the behavior of these units is not neatly divisible into categories, but rather represents the peaks of a continuous distribution. Further, as Gordon and Hood [20] discuss at length, the usual assignment of "feature-detector" categories to the various

physiological classes of ganglion cells probably requires an unjustifiable leap of faith, and indeed we shall proceed cautiously in this regard. (Consider, for example, that all classes of ganglion cells respond to changes in contrast, and only classes 3 and 4 respond maximally to the features they are generally alleged to detect -- all other classes respond better to some other "feature", and all respond in any case to several "features". Rowe and Stone [Stone, personal communication] have even argued that the use of feature detection labels has stifled rather than assisted research on ganglion cell activity, at least in the mammal.)

2.3.6 Class 0 Neurons ("on"-neurons):

These units correspond to Gordon and Hood's [20] Class 6 unit and probably to Hartline's "on" cells; that they do not appear in Maturana et al.'s original classification is doubtless due to the fact that Maturana was recording from units in the optic tectum, while Class 0 cells project to the lateral geniculate and nucleus of Bellonci within the diencephalon [37, 38]. These units exhibit a strong transient response to red light and a much more prolonged response to blue light (up to two minutes). Stimulation in the IRF (inhibitory receptive field), where such a surround exists, evokes transient hyperpolarizations of the cell membrane; simultaneous stimulation of the ERF and IRF cause a weak depolarization. Receptive field size is 4–15° of visual angle, and maximal response occurs for 450–480nm stimuli, although the spectral response distribution is bimodal (a smaller peak occurring, obviously, at about 600nm). Some toad Class 0 units seem to respond well into the ultraviolet range.

2.3.7 Class 1 Neurons:

Class 1 ganglion cells are Maturana *et al.*'s "sustained edge detector". These units do not respond to changes in diffuse illumination, but a small spot projected onto the ERF produces a sustained "on" response, as do moving or stationary edges. The ERF is approximately 1-4° and is surrounded by a weakly inhibitory receptive field, often oval in shape. White-on-black and black-on-white stimuli of equal contrast produce equivalent responses. The sustained response to stationary stimuli is slightly decreased but still extant after darkening and relightening of the field [20]. A 1° stimulus of contrast >0.7 must be moved at least 0.03-0.05° in order to produce a shift in the unit's activity [22]. Class 1 cells project to the tectal dendrites within the superficial layer of the contralateral optic tectum.

Some Class 1 units receive input from 432nm rods and 575nm cones in opponent-process fashion; Gruesser and Grüesser-Cornehls [22] suggest that these correspond to Cajal's AII cells, which are stratified ganglion cells terminating in layers 2 and 4 of the IPL, and that non-opponent Class 1 units correspond to Cajal's AI cells terminating in IPL layer 4 only. These authors further suggest "red" rod input under both photopic and scotopic conditions.

2.3.8 Class 2 Neurons:

Maturana *et al.* refer to these as "convex edge detectors". A large (20-45°) IRF surrounds their 2-5° ERF. Maximal response is to small stationary spot illumination or moving contrast stimuli, with centripetal motion the preferred direction. Rapid habituation with a

10-30 sec recovery period is observed for successive small light stimuli in local areas of the ERF; this occurs regardless of background illumination and is not solely due to photochemical effects. (Note that Gordon and Hood [20] claim that Class 2 units do not respond to light stimuli at all.)

Inhibition effects from IRF stimulation are quite strong, which accounts for the lack of response to larger edge stimuli; IRF image motion direction need not be the same as that of the image in the ERF. Gruesser and Gruesser-Cornehls demonstrate convincingly that, despite popular folklore, these units are not at all selective for convex edges but rather respond equally well to all stimuli of equal size and contrast for images restricted to their ERF. Interestingly, these authors find Class 2 response to be more strongly inhibited by expansion perpendicular to the direction of motion than by expansion in the direction of motion for images large enough to affect both ERF and IRF, which could shed some light on the quite similar "worm/antiworm" behavioral response noted in toads by J.-P. Ewert [15 and personal communication]. Gruesser and Gruesser-Cornehls further suggest that black-on-white stimuli are more effective than white-on-black, although there are differences between, for example, frog and toad responses to black-and-white stimuli, and the authors do not specify the time of year for these experiments (many anurans exhibit a seasonally-dependent black/white preference -- see, for example, [27, 36]).

When the stimulus illumination is suddenly removed, Class 2 units will immediately cease their activity; however, unlike Class 1 units, Class 2 units do not resume firing when the stimulus illumination is restored. (This phenomenon was termed "erasability" by Maturana et al.)

While "on" and "off" responses are not generally observed, occasional units exhibit an "off" response with an unusually long (2-15 sec) latency.

Class 2 units often seem to receive spectrally opponent input; some may receive both cone and 432nm rod information. As is the case with Class 1 units, their response at low light levels implies some "red" rod input as well.

2.3.9 Class 3 Neurons:

These are Maturana's "changing contrast detectors" and probably Hartline's "on-off" cells; they are also referred to as "event detectors" (see, for example, [35]). Their ERFs of 6-12° have 12-20° inhibitory surrounds somewhat weaker than those of Class 2 units; stimulation of the IRF can inhibit ERF activation, but will not itself evoke a response. These units spike both at onset and termination of the stimulus; in both cases the cell membrane is observed to depolarize, yielding a burst of axonal impulses which is sometimes preceded by a brief hyperpolarization in the case of the "on" phase. Maximal response occurs for stimuli centered in the ERF, and white-on-black and black-on-white stimuli are equally effective. Directionally-selective responses have been observed, although simple asymmetry of the RF is apparently more common. Gruesser and Gruesser-Cornehls suggest that the incomplete habituation that is characteristic of these units could implicate them, in conjunction with Class 0 and some Class 1 units, as the source of the anuran's stationary environmental contrast information.

In those Class 3 units that show a spectrally-dependent response, "on" responses are seemingly 432nm dependent, while "off" responses occur for red stimuli in the spectral range that excites cones. The observation of a Purkinje shift with dark-adaptation again implies "red" rod input, and in fact the spectral response function of some Class 3 units seems to track quite well with the rhodopsin absorption curve, according to Gruesser and Gruesser-Cornehls.

2.3.10 Class 4 Neurons:

Class 4 ganglion cells are Lettvin et al's "dimming detectors", so named because they respond to small spots of light centered in their (up to 15°) ERFs with "off" activation and to ERF dimming by more than 10-30% with an increase in impulse rate. Some of these units are observed to show "on-off" activation for peripheral regions of the ERF, and bursts of impulses synchronized with the volleys of neighboring ganglion cells are typical.

A 2 to 5° moving object that dims the ERF evokes a response, as in general will any image that causes the ERF to dim, regardless of the image's size. Some units respond maximally at low levels of illumination; these have been referred to as "half-dimmers".

It appears that some Class 4 units have an opponent-process spectral response, with "off" activation maximal at 560nm and "on" activation possibly dependent on shorter-wavelength light.

2.3.11 Class 5 Neurons:

Maturana et al. labelled Class 5 units "dark detectors"; they "are continuously active and this activity increases as ambient illumination decreases" [20]. They respond slowly to changes in background illumination and "not at all to moving dark stimuli.... Reuter and Virtanen attribute a cone-dominated off-response to Class-5 neurons" [22]. Maturana et al. recorded Class 5 units from the same layer of the optic tectum as Class 3 units. Information on these units is scant, as they are rarely observed.

2.4 Retinal Synaptology

It seems likely that much of the function of the retina, especially as viewed from the anthropomorphic "feature detector" perspective, is critically dependent on the precise nature of the synaptic connections within the inner and outer plexiform layers. Until about two decades ago, little was known of the fine structure of the retina; most of this work necessarily awaited the advent of the electron microscope and its widespread application to the study of synaptic structure in particular. Fortunately, considerable effort has been expended recently to determine the nature of the retina's synaptic organization [2, 11, 14, 19, 34, 40], and while accounts still differ somewhat, a picture -- albeit subject to dispute -- is beginning to emerge. Much of the material in this section is derived from [13] and [42], but other sources will be relied upon as is appropriate.

In addition to the interreceptor-filament gap junctions previously described, two kinds of synapses seem to account for the majority of neuronal connections observed in the retina: "ribbon" synapses and conventional synapses. The latter are typical of chemical synapses found throughout the nervous system; the former are distinguished by the presence of a synaptic "ribbon" oriented perpendicular to the presynaptic membrane, surrounded by synaptic vesicles and apposed to a region of moderate densification of the plasma membrane. Such junctions are found in the OPL, where receptors often form synaptic complexes with a bipolar and several horizontal cells. It appears that the bipolar dendrite is generally surrounded by horizontal processes; the membranes of these processes lie close to the receptor membrane within an invagination into the cone "pedicle" or rod "spherule" (receptor base), whereas the bipolar dendrite can be as far as 1 um from the receptor in higher vertebrates. The question of whether the receptors directly or indirectly induce bipolar cell polarizations is thus an issue of current research and debate; however, as the distance from the central postsynaptic element to the presynaptic receptor membrane is only about 200-300 Angstroms in frog, we shall assume that receptors do, or at least can, directly effect changes in bipolar membrane potential in the anuran retina.

In addition to ribbon synapses, receptors also exhibit narrow- and wide-cleft junctions [43]; it appears that narrow-cleft and/or ribbon junctions provide input to type-a bipolars, whereas wide-cleft junctions synapse on type-b bipolars.

Shepherd indicates that lower vertebrates exhibit conventional synapses from horizontal cells to bipolars and other horizontals, that there are gap junctions as well between horizontals at least in fish, and that in some preparations synapses are observed to exist from horizontal cells back onto

receptors (interestingly, this may be the only place in the body where such a structure is found). It also seems likely that the interplexiform cells, which were observed by Dowling and Ehinger [12] to make conventional synapses in fish OPL, are present in the anuran OPL as well [13], probably presynaptic to horizontal cells.

The IPL is considerably more dense with synaptic connections than the OPL, especially in anurans. Most researchers believe bipolar cells to be distinguishable from the processes within the OPL on the basis of their synaptic ribbons, which are similar to those found in cone pedicles and rod spherules (if somewhat shorter, especially in frog). Allen [2] has shown that a single process may contain nearly two dozen ribbons, at each of which several postsynaptic processes may be found.[1] A striking peculiarity of IPL synapses is the evidence of vesicles on both sides of the membrane; Dowling calls this arrangement a "reciprocal synapse". The frog differs from higher vertebrates [13] in that the IPL processes of frog are typically "quite small and more uniform in size" and most seem to contain vesicles. In fact, over 70% of frog IPL ribbon synapses are observed to have vesicles in both postsynaptic processes (there are typically two, called a "dyad"), as against only about 20% of those in the primate retina. Where one or both postsynaptic processes in primates do not contain vesicles, they are generally observed to contain ribosomes instead, which Dowling takes as evidence that these cells are ganglion cells. This suggests that bipolar-to-ganglion contacts in the frog are rather rare, and that amacrines filter and transmit to ganglion cells

1. Stone [Stone, personal communication] reports that Wong-Riley has found that 30% of bipolar synapses observed in one study had no synaptic ribbon; one is tempted to ask whether these alleged "bipolars" could be interplexiform cells.

the information provided by bipolar neurons.

In addition to the ribbon junctions, the IPL contains numerous conventional chemical synapses (about 78% of frog IPL synapses for area centralis), and cascaded chemical junctions known as "serial" synapses (about 12% of frog IPL connections) [13]. The human IPL contains perhaps 3–4 times as many ribbon junctions as the frog and virtually no serial synapses.

It is instructive to consider the incomprehensibly large number of connections within the retina which must be accounted for when one attempts to understand retinal function through an analysis of the fine structure. Dowling draws upon data from a number of studies to suggest that there are approximately 3 million synaptic contacts in a square millimeter of human IPL, which is still relatively few in comparison with the 10–11 million such connections in an equivalent patch of the frog's inner plexiform layer.

3. The Retina as an Information Processor

In this section we shall develop a plausible neural model of the retina that we believe can account for the behavior of retinal neurons and especially ganglion cells. We shall rely upon the following assumption regarding the function of ganglion cells as information processors as a mainstay:

Assumption 1:

The ganglion cell functions principally as a simple integrator of amacrine and bipolar information.

Thus we take the perspective that the ganglion cell does not "process" the data provided by amacrine and bipolar cells in any profound way beyond performing (possibly nonlinear) sampling and summation of its inputs and producing spikes in accord with the resultant ganglion cell membrane potential. That is to say, the ganglion cell is assumed to deviate from the classical neuron little or not at all; it is strictly postsynaptic to other retinal neurons, has a rather standard morphological structure, is strictly presynaptic to the neurons of the brain regions to which its axon projects, and is in general not remarkable in structure or function. This naive caricature of the ganglion cell will hopefully prove to be a useful and not altogether inaccurate simplification of the "real" neuron and should serve us well.

Where, then, does the "information processing" occur? The following assumptions account for what we will take to be the most profound physiological processing of the light "data" striking the photoreceptors.

Assumption 2:

The "center-surround" response to visual stimuli corresponts to OPL activity exclusively and is mediated by the effects of horizontal cells on the receptor-to-bipolar pathway.

Assumption 3:

The "on", "off", and "on-off" responses to visual stimuli that are observed in ganglion cells correspond to IPL processing of bipolar membrane potential shifts and are mediated by bipolar-amacrine and amacrine-amacrine synapses.

This clearly characterizes horizontals as functional interneurons which act laterally on the information passing in parallel from the receptors to the brain. The characterization of amacrines is intentionally somewhat less clear, as they probably serve both the function of a lateral information processing "filter" and that of a transmitter of parallel centripetal information as well. Indeed, we shall see that this somewhat more complex behavior of amacrines follows rather directly from their great numbers in the IPL and the striking diversity of their synaptic junctions.

Given this skeletal representation of retinal information processing, our task becomes that of finding anatomical and physiological evidence to suggest or justify methods for "fleshing out" these few assumptions. But first we must have a structured perspective on neuronal functioning in general.

Assumption 4:

The significant physiological features of neurons will be taken to be the following:

a. They accumulate information by sampling and summing the PSPs (postsynaptic potentials) locally induced at their membrane surface by other neurons.

b. They encode information as changes in their membrane potential.

c. They transmit information to other neurons, either through direct electrotonic coupling or by chemical coupling, by producing membrane potential shifts in the postsynaptic neuron.

This multiple assumption allows us to talk more or less interchangeably about a neuron's electrophysiological state or the information it carries; similarly, we can now consider synapses to be the smallest structural element of interest when viewing the neural network as an information processing system, and the membrane polarization as the fundamental unit of information.

We note immediately that the receptors are trivial exceptions to these rules in that they are not postsynaptic to other neurons in general and their membrane potential shifts occur due to photochemical effects; however, unless otherwise stated, we shall allow these generalizations to stand as an explicit statement of our understanding of what Shepherd [42] refers to as the "neuron doctrine". Note that we deviate slightly from the norm here in not requiring unidirectional information flow; while in general we expect this to be the case, such a constraint would introduce definitional problems into our use of the word "synapse", given the observation of "reciprocal synapses" in the vertebrate retina.

There have been numerous retinal models in recent years, each concerned with a different problem or taking a different perspective on the structure and function of the retina [9, 13, 31, 35, 42, 44]. We shall take Dowling's anatomically-influenced approach as our point of departure, but will also develop a rigorous mathematical formalization of the proposed structures.

3.1 The Outer Plexiform Layer

Our analysis of the outer plexiform layer will be guided by Assumption 2; thus the questions we must answer here become:

(a) What local effects yield bipolar cell "center" activation?

(b) What lateral effects yield "surround" responses?

Implicit in these questions is the following assumption.

Assumption 5:

"Center" and "surround" effects are separable and are due respectively to local and laterally extensive networks within the OPL.

First we shall consider question (a). How, indeed, can receptor hyperpolarizations yield hyper- and depolarizations in bipolar cells? Our answer to this question relies on the work of Stell et al. [43] already cited regarding the synaptic organization at the receptor base. We note that type-a bipolars hyperpolarize when receptors hyperpolarize, whereas type-b bipolars depolarize under these conditions. We also recall that there is evidence to indicate that receptors release transmitter in the dark and that type-a and b bipolars exhibit different kinds of synapses with receptors. This leads us to the following conclusion.

Assumption 6:

The polarization behavior of bipolar cells is a function of their synaptic connections with receptors. More specifically, transmitter release at wide-cleft receptor junctions serves to induce EPSPs in type-a bipolar cells, whereas transmitter release at narrow-cleft and/or ribbon synapses serves to induce IPSPs in type-b bipolar cells.

Given that transmitter release decreases when light is absorbed by the receptor, we can infer that in the absence of a light stimulus in the ERF, the receptor's transmitter release has the effect of depolarizing a type-a unit or hyperpolarizing a type-b unit; when the transmitter release drops due to the presence of light in the receptor's RF, the bipolar cell reestablishes equilibrium -- that is, the type-a hyperpolarizes and the type-b depolarizes with repect to their membrane potentials in the dark.

This understanding can be formally represented by a system of first-order differential equations, where the membrane is regarded as a resistive capacitance. This model of the membrane is nowhere more appropriate than in the OPL of the retina, where all membrane polarizations are electrotonic (that

is, no nonlinearities due to action potentials are observed). Designating V_a as the type-a bipolar membrane voltage, V_b as that of the type-b cell, I as the stimulus intensity, I_s as the receptor threshold intensity, k_r as a (receptor) constant, k_a and k_b as the type-a and type-b bipolar membrane time constants, and finally V_{x0} as the RMP (resting membrane potential) for a type-x bipolar, we have from eq. (2):

$$\frac{d V_a}{dt} = \frac{I}{k_a(I_s+k_r I)} - \frac{V_a-V_{a0}}{k_a} \qquad (3)$$

and

$$\frac{d V_b}{dt} = \frac{I}{k_b(I_s+k_r I)} - \frac{V_b-V_{b0}}{k_b} \qquad (4)$$

We have finessed a few considerations here; for example, the "receptor input" is actually that of many receptors even for a single synapse, since 85-90% of a given receptor's hyperpolarization is due to light received by other receptors, as previously described (see section 2.3.1). Also, we have not treated the possible interactions when more than one receptor synapses on a given bipolar cell; for the moment we shall "wave our hands" and pretend that this interaction is linear.

A third extension which we have not yet addressed is that of the antagonistic "surround" effects on the bipolar cell's membrane potential. Here equations (3) and (4) are clearly incomplete. But first we must answer question (b): What structure can account for "surround" responses?

We recall that the frog contains only L-horizontals; that is, frog horizontal cells are only observed to hyperpolarize to a stimulus. We shall assume this to be true in general.

Assumption 7:

Anuran horizontal cells are strictly of the L-type, and do not depolarize to stimuli in their receptive field.

This implies that the L-horizontal's behavior is quite similar to that of the hyperpolarizing type-a bipolar but for the somewhat larger time constant of the former; we shall in fact start with the same form of equation.

$$\frac{d V_h}{dt} = \frac{I}{k_h(I_s+k_r I)} - \frac{V_h-V_{h0}}{k_h} \qquad (5)$$

It is clear, however, that this is insufficient in that the horizontal cell necessarily receives input from numerous receptors surrounding the central one that synapses upon the bipolar cell; thus we must augment eq. (5) to reflect multiple simultaneous input. Further, this summation is non-linear: the larger the annular diameter stimulated, the smaller the incremental hyperpolarization. Van de Grind *et al.* [44] note that this effect can be described by a hyperbolic equation like our eq. (2), but they offer no substantive anatomical basis for their equation, and thus it holds little interest for us. Instead we shall postulate the following:

Assumption 8:

The effect of local dendritic polarization on the membrane potential of a cell is inversely proportional to the logarithm of the distance from the synapse to the perikaryon.

This assumption is sufficient to afford us a "space constant" analogous to our "time constant", in the sense of the cable equation (see [33] for a discussion) to weight the contribution of each receptor in determining the horizontal cell's V_h. This also suggests that experimentalists should find that the closer an IRF annulus is placed to the ERF, the stronger the antagonistic effect, controlling for equal stimulus area. In fact, this phenomenon is noted for the ganglion cell ERF: more central stimuli usually have a stronger effect on, for example, Class 3 ganglion cells, than do more peripheral stimuli, possibly corresponding to the spatial constant for interreceptor filaments. Also related may be the observation that motion in the centripetal direction evokes the strongest response in Class 2 ganglion cells.

We shall use the "space constant" r_{li} proportional to the distance from receptor synapse i to the horizontal cell perikaryon; we then have that

$$\frac{dV_h}{dt} = \text{SUM} \frac{I_i}{k_h(I_{si}+(k_{ri}\ I_i\ r_{li}))} - \frac{V_h-V_{h0}}{k_h} \qquad (6)$$

We are now in a position to return to the bipolar cell and consider the antagonistic "surround" effect of the lateral horizontal cell network on the "center" effect already discussed. We note that (1) there are likely to be several horizontals impinging upon a given bipolar (at least 2 per "dyad"); (2) the potential shift induced in the bipolar does not actually equal its inputs, but rather is proportional to them, and in fact it is likely that there is an "offset" value such that beyond some non-zero V_h, a given horizontal-bipolar synapse sees no further increase in effect. This suggests

several extensions to our (already lengthy) formulae (3) and (4):

$$\frac{dV_a}{dt} = \max\left(\frac{I}{k_a(I_s+(k_a\ I))}, k_{r0a}\right)$$

$$- \text{SUM}\ \frac{\max(V_{hi}, k_{h0i})}{h_{1i}} - \frac{V_a - V_{a0}}{k_a} \qquad (7)$$

and

$$\frac{dV_b}{dt} = \max\left(\frac{I}{k_b(I_s+(k_b\ I))}, k_{r0b}\right)$$

$$- \text{SUM}\ \frac{\max(V_{hi}, k_{h0i})}{h_{1i}} - \frac{V_b - V_{b0}}{k_b} \qquad (8)$$

Here k_{r0x} is a receptor reference voltage beyond which the type-x bipolar will not be polarized and hli is the space constant for horizontal cell i which synapses on the bipolar cell at a distance 1 from the bipolar perikaryon.

Note that we are simplifying matters here by assuming that only one receptor synapses on a bipolar. This is actually rather unlikely; however, it is a painless simplification since (1) we already account for many receptors in the "center" through interreceptor filaments; (2) the extensions of the bipolar cell equations would be obvious and yet make them even more unwieldy than they already are. We thus choose to finesse this issue as well in the interest of clarity.

To recap, then, we have formulae (eq. (7) and (8)) for each of the two types of bipolars to show that the bipolar membrane potential is a nonlinear combination of a receptor input corresponding to a "center" effect, several horizontal inputs antagonistic to the receptor input and corresponding to a "surround", and a term to establish a resting membrane potential and specify that this RMP is achieved in logarithmic time after a (temporary) steady state for the inputs has been reached. Similarly, the horizontal cell membrane voltage (eq. (6)) is the sum of its receptor inputs scaled for the distance of their synapses to the horizontal cell perikaryon, plus a term for the horizontal RMP under no-change illumination. The implications of this OPL model are as follows:

1. The "surround" effect is antagonistic to the "center" effect with respect to their relative influence on the bipolar potential.
2. The bipolar and horizontal cells do not scale the receptor input differently (there is no equivalent of the k_{h0i} term for receptor synapses), in agreement with the observation that their response latencies are the same, as discussed in section 2.3.3 .
3. By postulating more synapses (either interreceptor filaments or receptor-horizontal synapses) we can alter the relative efficacies of "center" vs. "surround" stimulation; as noted in section 2.3.5, this ratio varies for different ganglion cell classes.

4. We would expect to see "on" and "off" effects in bipolar cells given only hyperpolarizations in both receptors and horizontal cells; this is precisely what is observed in recording experiments (see sections 2.3.1 and 2.3.2).

3.2 The Inner Plexiform Layer

The inner plexiform layer is much more dense with synaptic connections than the OPL; we shall start with some simplifying assumptions to make the anatomy manageable.

Assumption 9:

"On" and "off" responses observed in ganglion cells are the product of minimal processing of the "on" and "off" responses occurring in bipolar cells.

Assumption 10:

An important function performed by amacrine cells is that of a differentiator of input waveforms.

This pair of assumptions is quite powerful; they buy us an explanation of Class 0, 4, and 5 neurons and, with little more trouble, Class 3 units as well. It is important to stress that these are merely approximations to the true behavior; further work will be required to account for many of the subtleties each cell type exhibits. The equations for the IPL also may not be as "well-behaved" as those of the OPL — that is, they will require the introduction of substantially more nonlinearity in order to account for their diverse functional capabilities.

It is not at all clear how the amacrine cell performs the function asserted in Assumption 10; it could have to do with its complex synaptic structure, or possibly with its strange morphology (recall that amacrines are strictly dendritic). It does, however, seem quite likely to be the case that

they are indeed differentiators (in the circuit-theoretic sense); this can be inferred from numerous published photographs of their electrophysiological behavior (see, for example, [13]) and the facts that (a) they are the first neurons in the centripetal visual pathway to exhibit spiking behavior and (b) they are often observed to spike at onset or disappearance of the stimulus. This is not as clear a conflict with Assumption 1 as may seem to be the case at first blush: temporal scale and different levels of abstraction allow us to consider the neuron's function to be integration at one level, and differentiation at another. We shall employ Occam's Razor in modelling this phenomenon, keeping in mind that alternative underlying physiological mechanisms are possible, and suggest the following simple explanation:

Assumption 11:

The amacrine "on" and "off" units appear to differentiate their input because they have a very fast membrane time constant; a rapid change in presynaptic PSP is necessary in order for the amacrine cell to achieve threshold before the charge on the amacrine's membrane "leaks away".

Thus by assuming that the amacrine cells have a much faster membrane time constant than the bipolars with which they synapse, we have an explanation for "on" and "off" amacrine cells; and further, by invoking Assumptions 3 and 9, we have a viable explanation of the gross behavior of Class 0, 2, and 4 ganglion cell units. The equations for the amacrine cells are then:

$$\frac{dVA_a}{dt} = \frac{\Theta(V_a - VA_a)}{A_{at}} \qquad (9)$$

$$\frac{dVB_b}{dt} = \frac{\Theta(V_b - VB_b)}{A_{bt}} \tag{10}$$

where VA_a is an "on" amacrine (receiving input from a type-a bipolar) and V_a is as defined in eq. (7), and similarly for the VB_b amacrine, type-b bipolars, and eq. (8). The A_{xt} constants are the time constants for the A_x amacrine; it is assumed that $A_{at} >> k_a$ and $A_{bt} >> k_b$ (see eq. (7) and (8)). Note that a threshold function Θ has been applied to the integrand, to reflect the action potential that the neuron will generate.

The equations are equally simple for the corresponding ganglion cells:

$$\frac{dV_{c0}}{dt} = \frac{\Theta(V_a - V_{c0})}{c_{0t}} \tag{11}$$

$$\frac{dV_{c4}}{dt} = \frac{\Theta(V_a - V_{c4})}{c_{4t}} \tag{12}$$

Here V_{cn} is the membrane potential for a Class "n" ganglion cell; V_a and V_b are as defined in equations (7) and (8) respectively, and c_{nt} is the membrane time constant for a Class "n" unit.

It seems likely that the equation for V_{c2} is essentially the same as that for V_{c0}, but for the much faster time constant of the former (and, of course, the fact that the receptors which provide input to the associated bipolar cells are different).

The Class 3 ganglion unit can probably be adequately described mathematically as simply the sum of VA_a and VB_b inputs:

$$\frac{dV_{c3}}{dt} = \frac{\theta(VA_a+VB_b-V_{c3})}{c_{3t}} \qquad (13)$$

There are a variety of possible mechanisms by which we could account for the continuous activity of Class 5 units; for example, they may be continuously active because they receive input from amacrines having reciprocal synapses, or alternatively they may be among the few (if any) ganglion units that receive direct bipolar input. As was noted in section 2.3.5, information on these units is slim since they are rarely encountered; rather than choose arbitrarily among the possible explanations, we will allow this problem to remain unaddressed for the purposes of the current study.

4. Conclusion

We have developed a formal model in which the anuran retina is viewed as an information processor that encodes information electrochemically (and possibly temporally); hopefully, we have also been able to stay close to the known biology of the system and to explicitly indicate those times when we were forced to make an assumption that was based on epistemological or pragmatic grounds rather than on "hard scientific evidence". The model seems capable of replicating the known observations for this system, although only through simulation can its predictive validity be tested.

Future research can proceed along several lines. There is a great need in this field for a method of studying fine structure on an even larger scale without becoming swamped in anatomical detail; it seems likely that computerized anatomical analysis systems will be necessary before the huge quantity of data to be studied can be sifted through in a meaningful and organized fashion. Such a system would obviate the need for many anatomical assumptions that must be made regarding the synaptology of this system, which was indicated in section 2.4 as being critical in our understanding of the retina. Also important is the development of more sophisticated physiological techniques so that researchers can, for example, trace a whole pathway through the retina from receptor to ganglion cell, labeling units for later histological identification. Finally, a more comprehensive model is possible even given the current state of the art; in particular, a model using this one as its point of departure should attempt to address the retinal topology within the equations themselves rather than in the accompanying text, making the necessary assumptions regarding connectivity and physiology of the units involved.

References

1. Alexander-Schaefer, G. (1907), Vergleichend-physiologische Untersuchungen ueber die Sehschaerfe. Pfluegers Arch. ges. Physiol. 119:571-1079.

2. Allen, R. L. (1969), The retinal bipolar cells and their synapses in the inner plexiform layer. In: Straatsma, B. R., et al, The Retina: Morphology, Function, and Clinical Characteristics. Univ. Calif. Press, Los Angeles.

3. Arden, (1962), The retina — physiology. In: H. Davson (ed.), The Eye, Vol 2A. Academic Press, NY.

4. Barlow, H. B. (1953), Summation and inhibition in the frog's retina. J. Physiol. (Lond.) 119:69-88.

5. Barlow, H. B. (1970), Detection of form and pattern by retinal neurones. In Conrad, M. et al, Physics and Mathematics of the Nervous System. Springer-Verlag, Berlin.

6. Birukow, G. (1937), Untersuchungen ueber den optischen Drehnystagmus und ueber die Sehschaerfe des Grasfrosches (R. temporaria). Z. vergl. Physiol. 25:92-142.

7. Cajal, S. Ramon y (1894), Die Retina der Wirbelthiere (R. Greeff, transl.). Bergman, Wiesbaden.

8. Cajal, S. Ramon y (1911), Histologie du systeme nerveux de l'homme et des vertebres, vol. 2. Maloine, Paris.

9. DeValois, R. L. (1973), Central mechanisms of color vision. In Jung, R. (ed.), Handbook of Sensory Physiology, Vol. VII/3A. Springer-Verlag, N.Y.

10. Donner, K. O., and Reuter, T. (1976), Visual pigments and photoreceptor function. In Llinas, R., and Precht, W. (eds.): Frog Neurobiology,. Springer-Verlag, Berlin.

11. Dowling, J. E. and Boycott, B. B. (1966), Organization of the primate retina: electron microscopy. Proc. Royal Society B 166:80-111.

12. Dowling, John E., and Ehinger, Berndt (1975), Synaptic organization of the amine-containing interplexiform cells of the goldfish and Cebus monkey retina. Science 198:270-273.

13. Dowling, J. E. (1976), Physiology and morphology of the retina. In Llinas, R., and Precht, W. (eds.): Frog Neurobiology,. Springer-Verlag, Berlin.

14. Dubin, M. (1970), The inner plexiform layer of the vertebrate retina: a quantitative and comparative electron microscopic analysis. J. comp. Neurol. 140:479-1006.

15. Ewert, J.-P. (1976), The visual system of the toad: Behavioral and physiological studies on a pattern recognition system. In Fite, K. (ed.), The Amphibian Visual System: A Multidisciplinary Approach. Academic Press, Inc., New York.

16. Fain, Gordon L. (1975), Quantum sensitivity in the toad retina. Science 187:838-841.

17. Famiglietti, Edward V., Kanero, Akimichi, and Tachibana, Masao (1977), Neuronal architecture of on and off pathways to ganglion cells in carp retina. Science 198:1267-1269.

18. Fite, K. and Scalia, F. (1976), Central visual pathways in the frog. In Fite, K. (ed.), The Amphibian Visual System: A Multidisciplinary Approach. Academic Press, Inc., New York.

19. Goodland, H. (1966), The ultrastructure of the inner plexiform layer of the retina of Cottus bubalis. Exp. Eye Res. 5:198-200.

20. Gordon, J. and Hood, D. C. (1976), Anatomy and physiology of the frog retina. In Fite, K. (ed.), The Amphibian Visual System: A Multidisciplinary Approach. Academic Press, Inc., New York.

21. Gruesser, O.-J., and Gruesser-Cornehls, U. (1976), Neurophysiology of the anuran visual system. In Llinas, R., and Precht, W. (eds.): Frog Neurobiology,. Springer-Verlag, Berlin.

22. Gruesser-Cornehls, U. and Himstedt, W. (1976), The urodele visual system. In Fite, K. (ed.), The Amphibian Visual System: A Multidisciplinary Approach. Academic Press, Inc., New York.

23. Hartline, H. K. (1935), Impulses in single optic nerve fibres of the vertebrate retina. Amer. J. Physiol. 113:59-60.

24. Hartline, H. K. (1938), The response of single optic nerve fibres of the vertebrate eye to illumniation of the retina. Amer. J. Physiol. 121:400-415.

25. Hartline, H. K. (1940), The effects of spatial summation in the retina on the excitation of the firers of the optic nerve. Amer. J. Physiol. 130:700-711.

26. Ingle, D. (1976), Spatial vision in anurans. In Fite, K. (ed.), The Amphibian Visual System: A Multidisciplinary Approach. Academic Press, Inc., New York.

27. Ingle, D. (1976), Behavioral correlates of central visual function in anurans. In Llinas, R., and Precht, W. (eds.): Frog Neurobiology,. Springer-Verlag, Berlin.

28. Kreuger, H., Moser, E. A., and Zrenner, E. (1973), Influence of defocussing on retinal images of test patterns calculated with the modulation transfer function (MTF) by analytical functions. Vision Res. 5:331-341.

29. Kuffler, S. W. (1953), Discharge patterns and functional organization of mammalian retina. J. Neurophysiol. 16:37-68.

30. Lettvin, J. Y. et al (1959), What the frog's eye tells the frog's brain. Proc. I.R.E.

31. Marr, David (1974), An essay on the primate retina. MIT Artificial Intelligence Laboratory Memo 296, Cambridge, Mass.

32. Maturana, H. R., et al (1960), Anatomy and physiology of vision in the frog (R. pipiens). J. Gen. Physiol. 43, Suppl. 2, 129-175.

33. McGregor, Ronald J., and Lewis, Edwin R. (1977), Neural Modelling. Plenum Press, New York.

34. Misotten, L. (1965), The Ultrastructure of the Retina. Arscia Uitgaven, N. V., Brussels.

35. Moreno-Diaz, Roberto (1965), An Analytical Model of the Group 2 Ganglion Cell in the Frog's Retina. MIT Instrumentation Laboratory Report E-1858, Cambridge, Mass.

36. Mueller, Hk. (1976), The Frog as an Experimental Animal. In Llinas, R., and Precht, W. (eds.): Frog Neurobiology,. Springer-Verlag, Berlin.

37. Muntz, W. R. A. (1962), Microelectrode recordings from the diencephalon of the frog (Rana pipiens), and a blue-sensitive system. J. Neurophysiol. 25:699-711.

38. Muntz, W. R. A. (1962), Effectiveness of different colours of light in releasing the positive phototactic behaviour of frogs, and a possible function of the retinal projection to the diencephalon. J. Neurophysiol. 25712-720.

39. Muntz, W. R. A. (1977), The visual world of the amphibia. In: Crescitelli, F. (ed.), Handbook of Sensory Physiology, Vol. VII/5. Springer-Verlag, N.Y.

40. Raviola, G. and Raviola, E (1967), Light and electron microscopic observations on the inner plexiform layer of the rabbit retina. Amer. J. Anat. 120:403-426.

41. Scalia, F. (1976), The Optic Pathway of the Frog: Nuclear Organization and Connections. In Llinas, R., and Precht, W. (eds.): Frog Neurobiology,. Springer-Verlag, Berlin.

42. Shepherd, Gordon M. (1976), The Synaptic Organization of the Brain. Oxford University Press, London.

43. Stell, William K., Ishida, Andrew T., and Lightfoot, David O., (1977), Structural Basis for On- and Off-Center Responses in Retinal Bipolar Cells. Science 198:1269-1271.

44. van de Grind, W. A., et al (1973), Temporal transfer properties of the afferent visual system: psychophysical, neurophysiological, and theoretical investigations. In Jung, R. (ed.), Handbook of Sensory Physiology, Vol. VII/3A. Springer-Verlag, N.Y.