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Computations in the Vertebrate Retina: Gain Enhancement, Differentiation and Motion Discrimination

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Abstract. An understanding of brain function will ultimately require an understanding of the elementary information processing operations performed by synapses, membranes and neurons. Such knowledge, in addition to its intrinsic interest, will be instrumental for a full comprehension of the algorithms and computational procedures used by the brain to solve visual and other perceptual problems. The vertebrate retina is a very attractive model system for approaching the question of the information processing role of biological mechanisms of nerve cells. The retina provides the visual input to the brain and its main interface with the outside world. Its anatomy and physiology are relatively well known. We also have a fairly good idea of some of the information processing operations --- the computations --- performed by the retina. It is as yet impossible to provide a complete circuit diagram of the retina. But it is now possible to identify a few simple computations that the retina performs and to relate them to specific biophysical mechanisms and circuit elements, on the basis of theoretical work, computer simulations and experimental data. In this paper we consider three operations carried out by most retinae: *amplification, temporal differentiation and computation of the direction of motion of visual patterns.*

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Amplification and Temporal Differentiation

Visual systems are capable of measuring very low light intensities. Indeed, Hecht, Schlaer and Pirenne (1942) have shown that humans can detect fluxes of photons causing as few as four photoisomerizations in the retina, i.e. conformational changes in the rhodopsin caused by the capture of single photons. In this sense, the visual system is a remarkable photodetecting device with an almost optimal performance. Electrophysiological recordings from different species have shown that this large gain is already obtained in the retina (Barlow, Levick and Yoon, 1971).

Another surprising property of our visual system is the sluggish time course of the electrical signals in the very early stages of vision compared with our quick visual reactions. The time course of the electrical events in the photoreceptors is very slow because of phototransduction mechanisms that we now begin to understand (Lamb, this issue). The long time course of photoreceptor signals is likely to be related directly to their sensitivity. In all species rods are 20 to 50 times more sensitive to light than cones, but respond 5 to 10 times slower. In the turtle retina the cone sensitivity is approximately 25 μV per photoisomerization (Rh*) and the time to peak of voltage response to dim flashes is about 120 msec (Baylor and Hodgkin, 1973). In the same retina, rods have a sensitivity of about 1 mV/Rh*, but the time to peak of the voltage response to the absorbance of a few photons is about 1 sec (Baylor and Hodgkin, 1973). In primates, the time scale of electrical events is approximately four times faster (Baylor, Nunn and Schnapf, 1984). Thus, two important goals of retinal processing are a sophisticated amplification of the photoreceptor signal and some kind of temporal differentiation.

Gain

Figure 1 (kindly provided by D.R. Copenhagen and T. Reuter) shows the intracellular signal from a rod photoreceptor, a horizontal cell and a ganglion cell in the toad retina in response to a diffuse light stimulus. The rod voltage response is about 3 mV and has a time to peak of about 1.3 sec but is capable of eliciting in the ganglion cell a synaptic potential of about 87 mV and a quick discharge of spikes. Observe that the first spike is initiated 250 msec after the flash of light, when the rod voltage response has not reached its peak and is only 1 mV. When the light intensity is further reduced by 10 - 20 times the voltage response in rods is almost undetectable but it is still able to elicit action potentials in the ganglion cell.

The voltage gain between rods and horizontal cells is about 8 in the turtle (Schnapf and Copenhagen, 1982; Copenhagen, Ashmore and Schnapf, 1983) and about 11 in the tiger salamander. The voltage gain in the salamander retina between rods and on-center bipolar cells and off-center bipolar cells is 6 and 11 respectively (W. G. Owen, personal communication). Ashmore and Falk (1979) have estimated a considerably higher gain (~ 50) between rods and on-center bipolar cells in the dogfish retina. Another amplifying step occurs in the inner plexiform layer at the synapse between bipolar cells and amacrine or ganglion cells (Marchiafava and Torre, 1978) where the gain may be of the order of 5 (Copenhagen and Reuter, 1986).

Possible Mechanisms for Gain

In the retina, a high gain seems to be mostly achieved by synaptic transduction and only to a minor extent by regenerative properties of the neurons. Indeed, under physiological conditions, only ganglion cells and some amacrine cells produce action potentials. High gain between presynaptic and postsynaptic voltage can be obtained in two main ways: intrinsic synaptic properties or convergence of many synapses onto the same postsynaptic element.

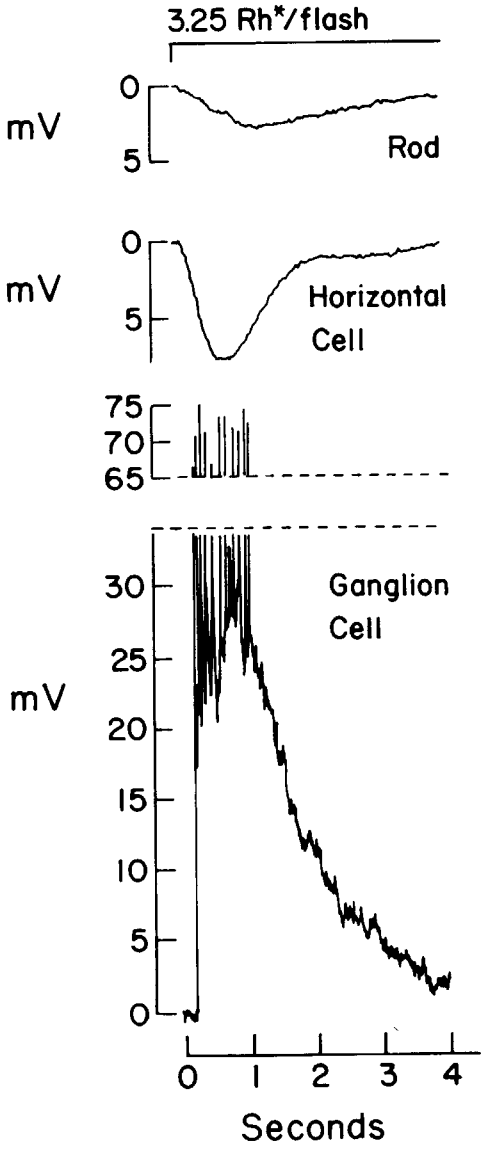


Figure 1. Intracellular recordings from a rod photoreceptor, horizontal cell and ganglion cell in the dark-adapted turtle retina (*Bufo Marinus*). Diffuse flashes of light were 13.5 msec in duration eliciting 3.25 photoisomerizations (Rh*) per flash. Full field stimuli (700 μm diameter), covering the entire receptive field of each of the neurons were used. The figure was kindly provided by D. R. Copenhagen and T. Reuter (1986).

One way of characterizing chemical synapses is to measure the synaptic amplification, also called sensitivity or dynamic gain, by recording the change in postsynaptic voltage in response to a small change in the presynaptic voltage (i.e.dV_{post}/dV_{pre}). As we have seen above, the synaptic amplification can be quite high at retinal synapses where only graded changes in potentials and no action potentials, are transmitted. Interestingly, the gain at impulse transmitting non-sensory synapses is considerably lower, 0.3 at lamprey central synapse and about 4 at the squid giant synapse (see Koch and Poggio, 1986).

A second mechanism of obtaining high gain is via a large number of converging synapses onto a single postsynaptic neuron. Since each synapse contributes to the postsynaptic potential, an arbitrarily small presynaptic voltage can be amplified to any degree if a sufficient number of synapses participates in transmitting the signal onto the postsynaptic cell, provided that synaptic saturation (due to the nonlinear interaction between the synapses) can be avoided. However, if an excitatory synapse is activated in the presence of a second, nearby excitatory synapse, its effectivness in generating an EPSP will be reduced in general in comparison to the case when the second synapses is not activated. This phenomenon, termed synaptic saturation, is due to the fact that synaptic inputs are changes in the membrane conductance (in series with a ionic battery) and not simply current inputs. Simple electrical considerations show that this postsynaptic saturation can be reduced if the synaptic input is distributed at many, relatively isolated, sites within the dendritic tree (Koch, Poggio and Torre, 1982). Thus in a cell with many dendritic branches synaptic saturation may be minimized and the synaptic gain therefore enhanced.

In conclusion, the recurrent retinal feature of massive divergence and convergence of signals may reflect the attempt of maximizing gain.

Temporal Differentiation

The time course of the change of photocurrent when a photon is absorbed in the rod outer segment is about 1 sec. With double recording techniques, it is possible to observe that in a rod voltage leads current (Baylor, Matthews and Nunn, 1984) in such a way that the time course of the photocurrent appears differentiated or accelerated. At both the rod-horizontal cell synapse (Schnapf and Copenhagen, 1982; Copenhagen *et al.*, 1983) and at the rod-bipolar cell synapse (W. G. Owen, personal communication), presynaptic potentials have a longer duration than postsynaptic events. In the inner plexiform layer, voltage responses in transient amacrine and ganglion cells have a duration shorter than the excitation in bipolar cells (Marchiafava and Torre, 1978).

The processing of signals in cones presents similiar but less pronounced features. Stimulating cones with diffuse flashes of light, leads to a discharge of action potentials in the ganglion cells before the voltage response of cones has reached its peak. However, since the photoresponse in cones is faster than in rods, temporal differentiation is less pronounced in the cone pathway.

Mechanisms of Temporal Differentiation

A major role of temporal processing in the retina is to accelerate the slow signals coming from the photoreceptors outer segments by a series of steps similar to temporal differentiation. Temporal differentiation can be performed using different biophysical mechanisms. A delayed negative feedback is an obvious and well known candidate mechanism that is present in the retina (Baylor, Fuortes and O'Brian, 1971).

Temporal differentiation can also be performed by active electrical properties of the cell membrane. If a voltage- and time-dependent current, which activates with increasing levels of depolarization, acts so as to counterbalance an increase in voltage it can best be described, within a certain voltage range, by a so-called phenomenological inductance. An example is the time-varying, voltage-dependent K^+ conductance turned on by depolarization, such as the delayed rectifier found in squid axon (Detwiler, Hodgkin and McNaughton, 1980; Owen and Torre, 1983) and its equivalent electrical circuit (see figure 2a) will contain an inductance (see also Koch, 1984). Therefore, if a steady synaptic current is fed into the circuit, the voltage will appear as a sort of temporal differentiation of the synaptic current (see figure 2c). Such a mechanism appears to be present in the rod (Owen and Torre, 1983; Baylor *et al.*, 1984). A recent patch-clamp study of isolated bipolar cells in the goldfish retina (Kaneko and Tachibana, 1985) has revealed the existence of a K^+ conductance, that may be involved in the bandpass properties of the rod-bipolar synapses.

An alternative mechanism for temporal differentiation is synaptic inactivation (Katz and Miledi, 1974). In this case, a steady presynaptic voltage is transformed into a transient post-synaptic current (see figure 2d). The equivalent electrical circuit is shown in figure 2b and has an equivalent capacitance, which is not the physical capacitance of the passive membrane itself. This mechanism can be involved at synapses in both the outer and inner plexiform layer. In the inner plexiform layer, where voltage responses of transient amacrine and ganglion cells have a shorter duration than the excitation in bipolar cells, the transient responses cannot be accounted for by a negative feedback or active properties of the membrane and are likely to be caused by synaptic inactivation.

Direction Selectivity

Numerous nerve cells in the visual system of both invertebrates and vertebrates respond differentially to motion. Moving a visual stimulus, say a dark bar on a light background, in a particular, the *preferred*, direction elicits a vigorous response from the cell while movement in the opposite direction, termed *null direction,* yields no significant response (figure 3d). *Directional selective* cells, described in the frog's retina in a classical paper by Maturana, Lettvin, McCulloch and Pitts (1960), have subsequently been identified, among others, in the third optic ganglion of the house fly, the retina of the rabbit, squirrel and cat, the optic tectum of frogs and pigeons and the visual cortex of both cats and monkeys (Hassenstein and Reichardt, 1956; Maturana and Frenk, 1963; Barlow and Levick, 1965; Hubel and Wiesel, 1962; Cleland and Levick, 1974; Hausen, 1981).

Early Experiments

Barlow and Levick (1965) systematically explored directional selectivity in the retina of the rabbit using extracellular recordings. About 20% of the ganglion cells in the visual streak give On and Off responses to stationary, flashed stimuli and are direction selective for moving stimuli. Two important conclusions can be drawn from their paper. First, inhibition is crucial for direction selectivity. On the basis of this evidence Barlow and Levick proposed, similar to the correlation model first devised by Hassenstein and Reichardt (1956; figure 3a), that sequence discrimination is based upon a scheme whereby the response to the null direction is vetoed by appropriate neighbouring inputs (the AND NOT gate in figure 3b). Directionality is achieved by an asymmetric delay --- or by a low pass filter --- between excitatory and inhibitory channels from the photoreceptors to the ganglion cell. Second, this veto operation must occur within small subunits

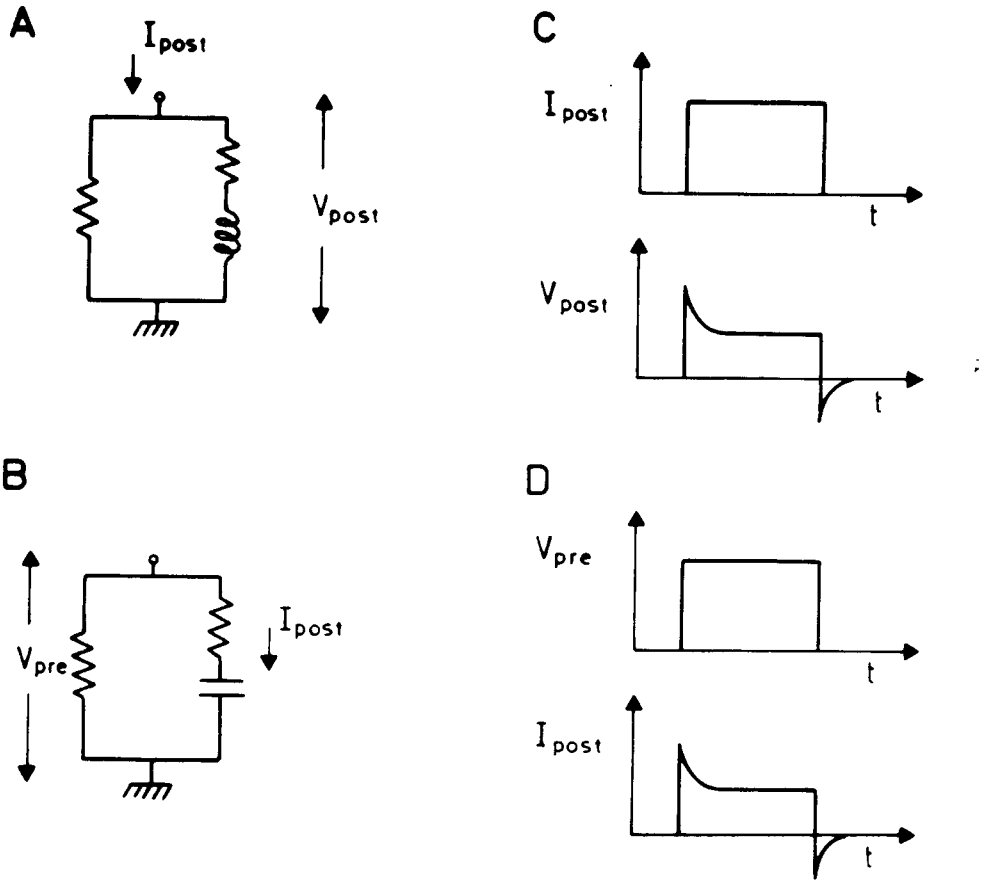


Figure 2. (a) Equivalent electrical circuit of a membrane with a time-varying voltage dependent K^+-conductance turned on by depolarization. (c) Post-synaptic current and voltage with a membrane with inductive-like properties. (b) Equivalent electrical circuit of synaptic inactivation. (d) Presynaptic voltage and postsynaptic current at synapses with synaptic inactivation.

distributed throughout the receptive field of the cell, since movement of a bar over 0.25^o to 0.50^o elicits a direction selective response (whereas the whole receptive field subtends 4.50^o; Barlow and Levick, 1965). Thus, the site of the veto operation is extensively replicated throughout the receptive field of the direction selective cell. Confirming evidence for the critical role of inhibition comes from experiments where inhibition is blocked using pharmacological agents (Caldwell, Daw and Wyatt, 1978; Ariel and Daw, 1982; Ariel and Adolph, 1985) resulting in an equal response for both preferred and null directions (see below).

A Biophysical Model

We can now ask how this operation is implemented at the level of the hardware, i.e. at the level of retinal cells. Torre and Poggio (1978) proposed a specific biophysical mechanism implementing the neural equivalent of a veto operation (figure 3c). When two neighboring regions of a dendritic tree experience simultaneous conductance changes --- induced by synaptic inputs --- the resulting postsynaptic potential is in general not the sum of the potentials generated by each synapse alone;

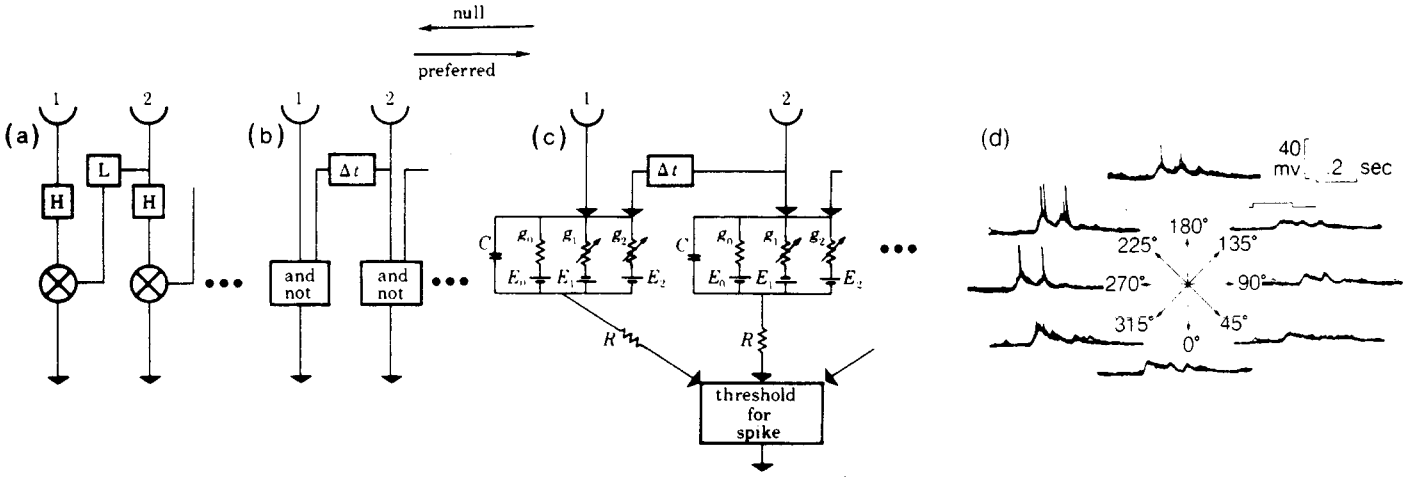


Figure 3. (a) A part of the model of movement detection of Hassenstein and Reichardt (1956). The two inputs are multiplied after low pass filtering with different time constants. If an average operation is made on the output, the overall operation is equivalent to cross-correlation of the two inputs. (b) The functional scheme proposed by Barlow and Levick (1965) to account for direction selectivity in the rabbit retina. A pure delay Δt is not necessary: a low pass filtering operation is sufficient. (c) The equivalent electrical circuit of the synaptic interaction assumed to underly direction selectivity as proposed by Torre and Poggio (1978). The interaction implemented by the circuit is of the type $g_1$alpha-g_1g_2. From Torre and Poggio (1978). (d) Intracellular recording from a directional selective turtle ganglion cell. The time of illumination is indicated by the line above the upper right record. Notice the absence of any hyperpolarization. Adapted from Marchiafava (1979).

that is, synaptic inputs may interact in a highly nonlinear fashion. This is true in particular for an inhibitory synaptic input which increases the membrane conductance with an associated ionic battery which reverses at, or very near to, the resting potential E_{rest} of the cell. Activating this type of inhibition, called *silent* or *shunting* inhibition, is similar to opening a hole in the membrane: its effect is only noticed if the intracellular potential is substantially different from E_{rest}. Torre and Poggio (1978) showed in a lumped electrical model of the membrane of the cell that silent inhibition can cancel effectively the EPSP induced by an excitatory synapse *without* hyperpolarizing the membrane. Pairs of excitatory and inhibitory synapses distributed throughout the dendritic tree may compute the direction of motion at many independent sites throughout the receptive field of the cell, in agreement with the physiological data. Since nonlinearity of the interaction is an essential requirement of this scheme, Torre and Poggio (1978) suggested that the optimal location for excitation and inhibition are fine distal dendrites or spines on the directional selective ganglion cells. Since this analysis left out the conditions required to produce effective and specific nonlinear interactions in a dendritic tree, Koch, Poggio and Torre (1982, 1983; see also Poggio and Torre, 1981) used 1-dimensional cable theory to analyze the interaction between time varying excitatory and inhibitory synaptic inputs in a morphologically characterized cat retinal ganglion cell (of the ∂ type; see Boycott and Wässle, 1974). They were able to prove rigorously in the case of steady state synaptic conductance inputs, that in a passive and branched dendritic tree the most effective location for silent inhibition --- most effective in terms of reducing an EPSP --- must always be on the *direct path* between the location of the excitatory synapse and the soma. Detailed biophysical

simulations of highly branched and passive neurons (like those shown in figure 6) show that this *on-the-path* condition can be quite specific. If the amplitude of the inhibitory conductance change is above a critical value (roughly between 10 and 50nS depending on the morphology of the cell and its input impedance), inhibition can reduce excitation by as much as a factor of 10, as long as inhibition is either very close to excitation or between the excitatory synapse and the soma. Inhibition more than about 10μm behind excitation or on a neighboring branch 10 or 20 μm off the direct path is ineffective in reducing excitation significantly. This specificity in terms of spatial positioning of excitatory and inhibitory synapses carries over into the temporal domain. For maximal effect, inhibition must last as least as long as excitation and their time courses should overlap substantially (Segev and Parnas, 1983; Koch *et al.*, 1983). Finally, the on-the-path condition is also valid in the presence of action potentials: in order for a shunting inhibition to block the propagation of a spike past a branching point on the dendritic tree, it must be located within at most 5 μm from the branch point (O'Donnell, Koch and Segev, 1985). This is especially relevant since recent observations by Jensen and DeVoe (1983) suggest that direction selective turtle ganglion cells may occasionally show dendritic spikes. The specificity of silent inhibition contrasts with the action of an hyperpolarizing synaptic input (i.e. a conductance change with an associated battery below E_{rest}). In this case, the interaction between excitation and inhibition will be much more linear, that is, the inhibitory synapse will reduce the EPSP generated by the excitatory synapse by an amount roughly proportional to the inhibitory conductance change with less regard to the relative spatial positioning of excitatory and inhibitory synapses (Koch *et al.*, 1983; Poggio and Torre, 1981; O'Donnell, Koch and Poggio, 1985; Koch and Poggio, 1986).

Critical Predictions of the Model

How does the model fare against experimental evidence? Table 1 lists some of the most important predictions. Currently, the main support for this hypothesis derives from intracellular recordings in retinal ganglion cells from the turtle (Marchiafava, 1979) and the bullfrog (Watanabe and Murakami, 1984). Moving a spot or a bar in the preferred direction gives rise to a somatic EPSP with superimposed action potentials while null direction stimulation results in a smaller EPSP *without* an hyperpolarization (figure 3d; see also Baylor and Fettiplace, 1979). The reduced somatic EPSP in the null direction appears to be caused by an inhibitory process which increases the membrane conductance with an associated reversal potential at or very near to the resting potential of the cell. This silent inhibition is revealed by injecting a steady-state depolarizing current into the soma, giving rise to an hyperpolarization (see figure 4). Preliminary evidence from rabbit ganglion cells indicates the presence of a similar inhibitory input (F. Amthor, personal communication).

Within the last years, two groups recovered the morphology of On-Off direction selective ganglion cells. Using a fluorescent stain, Jensen and DeVoe (1983) visualized these cells in the turtle retina and Amthor, Oyster and Takahashi (1984), used horseradish peroxidase (HRP) in the rabbit. The overall morphology of these cells appear to bear many similarities. Rabbit direction selective ganglion cells may be identified on purely morphological grounds because of several distinct features (figure 5): (1) these cells have two levels of dendritic ramification, corresponding to the On and Off laminae (Famiglietti and Kolb, 1976); (2) the dendritic branches of the direction selective cells are of very small diameter relative to other rabbit ganglion cells. Moreover, the dendrites carry spines or spine-like structures; (3) the dendritic branching pattern is quite complex, with dendrites forming apparent loops. Thus, the morphology of directional selective cells agrees well with our previous predictions (Koch *et al.*, 1982).

Table 1: Postsynaptic, silent inhibition model: predictions.

- On-Off Direction selective cells receive distinct excitatory and inhibitory synaptic inputs. The reversal potential of the inhibitory input is close to the resting potential of the cell (probably acting via a $GABA_A$ receptor).
- Bicucculin should abolish direction selectivity.
- Inhibitory synapses are not more distal to the soma than excitatory synapses.
- Direction selectivity is computed at many independent sites in the dendritic tree before spike initiation at the axonal hillock.
- The direction selective cell should show a ∂-like morphology, with a highly branched, bistratified dendritic tree with small diameter dendrites or possibly spines.
- On-Off direction selective cells are expected to show little interaction between dark bar/spot and light bar/spot moving in opposite directions within the receptive field because the correct functioning of this mechanism requires separate interactions within ON and OFF pathways.

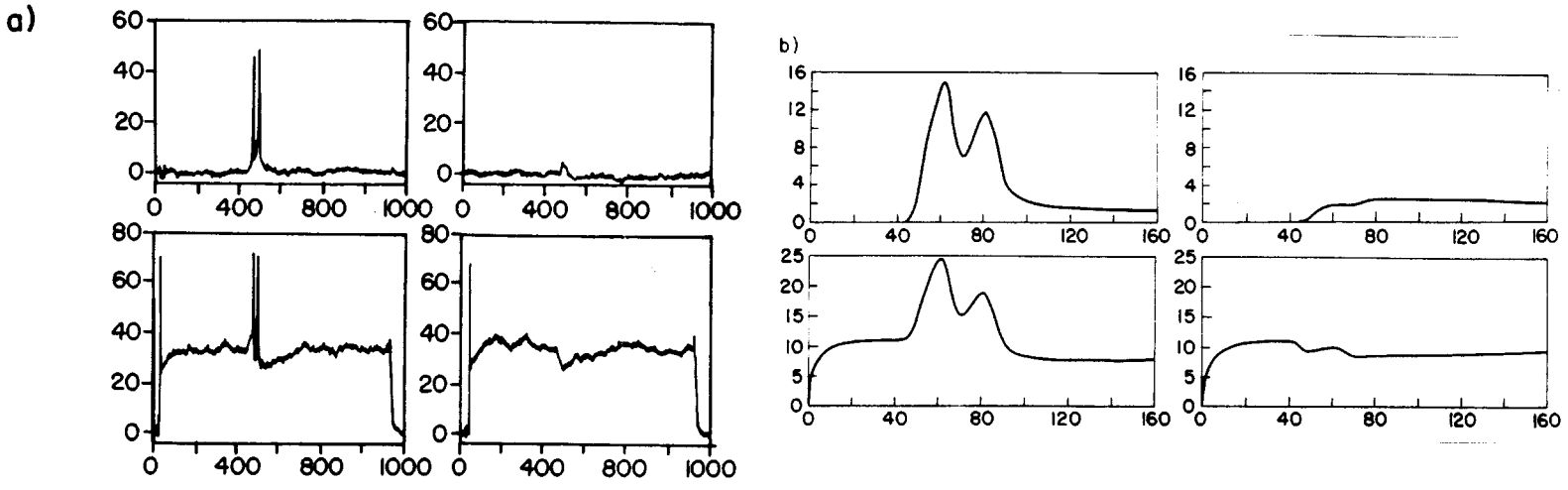


Figure 4. (a) The effect of intracellular current injection upon the photoresponse in an intracellular recorded directional selective turtle ganglion cell. The response in the preferred and null directions are shown in in the left and right part of (a). The lower record shows the photoresponse while 0.23 nA current was being injected into the soma. Adapted from Marchifava (1979). (b) Simulated intracellular potential at the soma of the reconstructed rabbit On-Off directional selective ganglion cell shown in figures 3 and 4 assuming a purely passive membrane. The two distinct peaks correspond to the leading edge, receiving On input, and the trailing edge, receiving Off input. (There is probably no connection with the fact that there are two spikes in (a).) In the bottom half, a step current of 0.091 nA was being injected into the soma. Preferred direction is left and null direction right.

In order to model massive synaptic input to a direction selective ganglion cell, we simulated (O'Donnell *et al.*, 1985; Mistler, Amthor and Koch, 1985), on the basis of 1-dimensional cable theory, the passive electrical properties of the anatomically reconstructed cell shown in figure 5. Our computer program allows the user to symbolically draw an electric circuit representation of a neuron with an arbitrarily complex dendritic tree, using certain graphic primitives like cables and synapses. The actual computation of the voltages is carried out by a common circuit simulation program, SPICE, first applied for biophysical circuit modeling by Segev, Fleshman, Miller and Bunow (1985). Figure 4b shows the resulting somatic depolarization in the absence and in the presence of a depolarizing current step injected at the soma, in comparison with experimental records obtained from turtle ganglion cells (Marchiafava, 1979; figure 4a). Figure 6 shows the intracellular potential throughout the whole cell --- coded in color --- in the preferred and in the null direction at two different times.

Presynaptic Circuitry

How much do we know concerning the origin and the properties of theexcitatory and inhibitory inputs to direction selective cells?

As presented elsewhere (Masland, *TINS*, **9**, 1986), there is evidence implicating acetylcholine (ACh) as the excitatory neurotransmitter underlying direction selectivity in both the rabbit (Ariel and Daw, 1982) and the turtle (Ariel and Adolph, 1985) retina. Recently, Masland and colleagues (Masland, Mills and Cassidy, 1984; Tauchi and Masland, 1984) identified two unique populations of cholinergic amacrine cells, which transiently release AcH at the onset and offset of light. These "starbust amacrine" cells appear to be presynaptic to bistratified ganglion cells with the morphological attributes of the direction selective cells of Amthor *et al.*, (1984).

The inhibitory input for motion discrimination is believe to be mediated by the neurotransmitter gamma-aminobutyric acid (GABA). Caldwell *et al.*, (1978) and Ariel and Daw (1982) infused picrotoxin, a potent antagonist of GABA, into the rabbit retina. Within minutes after the start of drug infusion the response of direction selective cells in the null direction increased dramatically, so that the cell becomes equally responsive to movement in both directions. A few minutes after drug infusion is discontinued, the cell becomes again direction selective. In the turtle retina during blockage of synaptic transmission via a low calcium concentration and EGTA, direct application of ACh leads to spontaneous firing in direction selective cells (Ariel and Adolph, 1985). This ACh--induced spike activity can be suppressed by GABA, indicating that both ACh and GABA receptors must coexist on the membrane of turtle direction selective ganglion cells. Thus, it appears that --- at least in the turtle and rabbit retina --- the excitatory and the inhibitory input to direction selective ganglion cells derive from cholinergic and GABAergic amacrine cells. This does not exclude, however, direct input from bipolar cells which may be responsible for instance for the center-surround organization of direction selective cells.

Alternative Models

What are the alternative models for the neuronal operations underlying motion discrimination? Although both Werblin (1970) and Marchiafava (1979) have failed to record direction selective responses in bipolar or amacrine cells, the possibility that the critical computations occur presynaptic (to the ganglion cell) cannot be excluded. Indeed, DeVoe and his collaborators (DeVoe, Guy, and Criswell, 1985) have recorded from directionally selective amacrine and bipolar cells in the retina of the turtle. Their evidence points towards an alternative or coexistent presynaptic site for the critical computation underlying direction selectivity in the turtle . A second

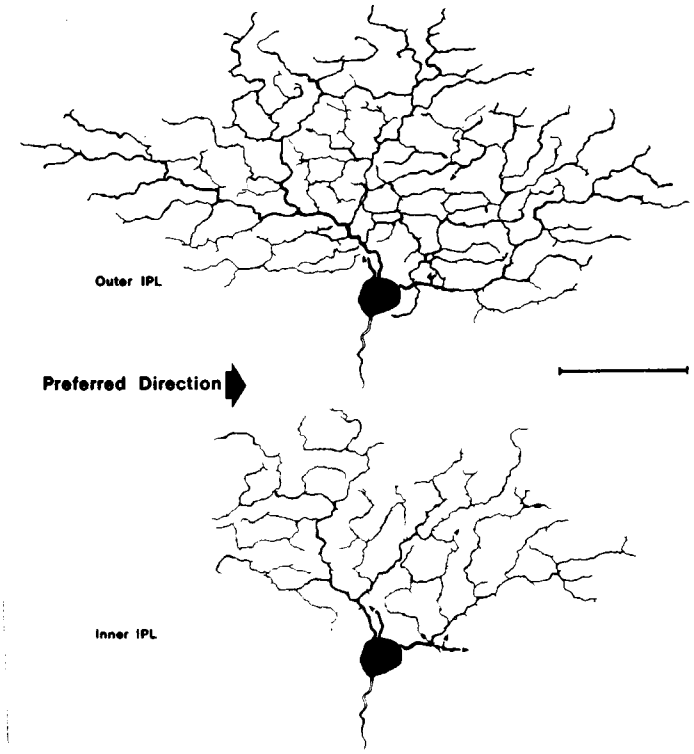


Figure 5. Camera lucida drawing of an HRP-injected On-Off direction selective cell in the visual streak of the rabbit retina. The dendritic fields have been drawn in two parts: "outer" refers to the part of the inner plexiform layer (IPL) closest to the inner nuclear layer, where the cells of the Off pathway make synaptic connections, while "inner" is the layer closest to the ganglion cell layer where the the On pathway is connected. There are no obvious asymmetries in the cell that are correlated with the preferred direction. Adapted from Amthor *et al.*, (1984).

Table 2: Biophysical models for the computations underlying direction selectivity in the rabbit retina. The inhibitory input derives in all models from a population of GABAergic amacrine cells.

Postsynaptic models

- Nonlinear interaction between excitation and silent inhibition at the level of ganglion cells dendrites.

Presynaptic models

- Nonlinear interaction between excitation and silent inhibition at the level of distal dendrites of the cholinergic starburst (amacrine) or bipolar cell.
- Linear interaction between excitation and hyperpolarizing inhibition followed by synaptic rectification at the level of the bipolar-starburst or starburst-ganglion cell synapse.

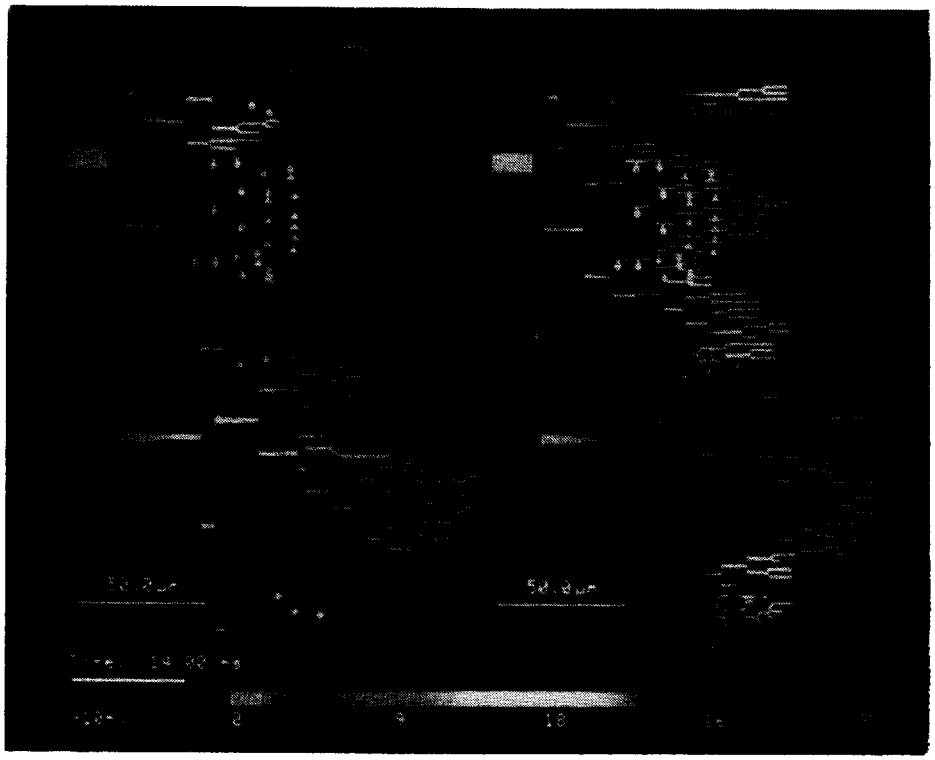
piece of evidence favoring a presynaptic arrangement is the influence of GABA on ACh. GABA inhibits the light evoked release of ACh in the rabbit retina (Massey and Neal, 1979; see figure 7 and table 2).

Other classes of presynaptic models for direction selectivity have been proposed (Dowling, 1979; Koch and Poggio, 1986) : Since GABAergic processes synapse onto bipolar, amacrine and ganglion cells, the site of the critical computation underlying direction selectivity could either be a bipolar cell exciting the star-burst amacrine cell or the star-burst amacrine cell itself. Starburst amacrine cells have dendrites that are probably decoupled from each other and the soma (Miller and Bloomfield, 1983). Only the distal most portion of the dendrites give rise to conventional chemical synaptic output, while the bipolar and amacrine cell input is distributed throughout the cell (Famiglietti, 1983). Thus, each dendrite may behave from an electrical point of view as an independent subunit, acting as the morphological basis of Barlow and Levick's subunits (1965). At least two biophysical mechanisms could underly direction selectivity: 1) the AND NOT veto scheme, now implemented at the level of bipolar or amacrine cells or 2) a linear interaction between an excitatory synapse and a hyperpolarizing synapse followed by synaptic rectification (Koch and Poggio, 1986). In this case, the nonlinearity essential for direction selectivity (Poggio and Reichardt, 1973, 1976) would be implemented by a rectifying synapse. For these presynaptic models, the release of neurotransmitter, whether from the bipolar or from the amacrine cell, would in itself be direction selective.

Beside the intracellular evidence cited above (see figure 4), two additional points, however, argue against the presynaptic hypothesis. First, if the release of ACh is already direction selective, the application of an ACh potentiator may have little effect on the direction selective response of the ganglion cell. Physostigmine does however eliminate direction specificity (Ariel and Daw, 1982; Ariel and Adolph, 1985). Second, Sakai, Naka and Dowling (1985) have recently reported that distal dendrites of ganglion cells in the catfish retina filled with HRP make conventional chemical synapses back onto dendritic processes in the inner plexiform layer. Although a partial EM reconstruction of a putative direction selective rabbit ganglion cell (Famiglietti, 1985) has failed to reveal any dendro-dendritic synapses, a possibility which has to be entertained is that direction selectivity is computed at the level of the ganglion cell and subsequently relayed backwards onto either bipolar or amacrine cells.

We would like to point out that both pre- and post-synaptic models may turn out to be simultaneously correct. As suggested by N. Grzywacz to one of us (CK), the directional selective bipolar and amacrine cells recorded by DeVoe *et al.* (1985) have a smaller velocity range than direction selective ganglion cells. Thus, a rough estimate of the direction of a moving stimuli could be computed at the level of bipolar/amacrine cells while ganglion cells would perform similar but finer measurements.

Acknowledgements: We would like to acknowledge the helpful discussions concerning direction selectivity with Lisa Mistler and especially Norberto Grzywacz. Frank Amthor kindly provided the data for the reconstructed cell shown in figures 3 and 4. David Copenhagen kindly provided figure 1. Thanks to Linda Ardrey for drawing the figures. Frank Amthor, David Copenhagen and John Dowling commented on the manuscript. Since we are thanking everybody here, we might as well thank Carol Bonomo, who, as usual, took out our commas and put her own in. Note that this is a corrected and better version of the TINS article. Also note in particular the changes in the last paragraphs (by TP) from TINS article.



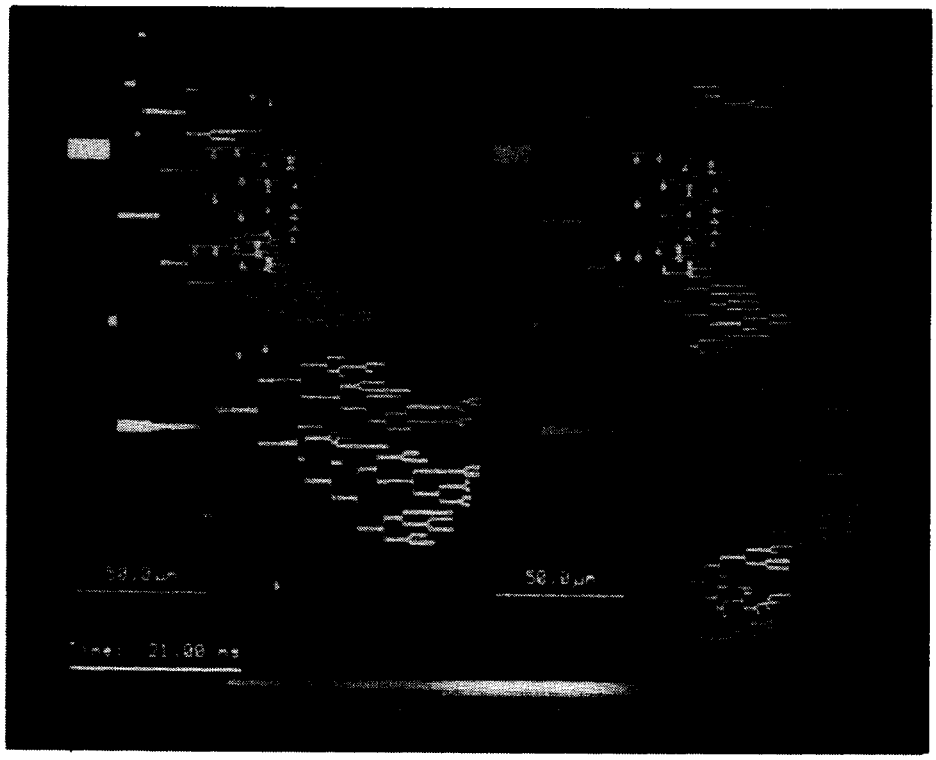


Figure 6. (opposite) Intracellular potential in the computer reconstructed cell shown in figure 5 in response to massive synaptic input. The cell was modeled with the aid of an integrated circuit simulation package (SPICE). The passive properties of the neuron, i.e. R_m, C_m and R_i, were inferred from the measured somatic input impedance (about 110 M-Omega) and membrane time constant (about 7 ms) --- under the assumption of a homogeneous membrane resistance. The color code for the intracellular potential is shown at the bottom of the image (relative to E_{rest}). For the simulation shown here, we assume that 6 groups of 5 to 7 excitatory synapses (indicated by a triangle) and 2 to 3 inhibitory synapses each (marked by a circle) provide the input to the dendritic tree, 3 groups in the On and 3 groups in the Off layer (see figure 3). Thus, these 6 groups of synapses would correspond to the "subunits" of Barlow and Levick (1965). Time to peak of the excitatory and inhibitory conductance changes are 20 and 25 ms respectively, in accordance with intracellular recordings (Baylor and Fettiplace, 1979). The peak inhibitory conductance change is about 20 times larger than the excitatory one (g_{ipeak} = 10nS versus g_{epeak} = 0.5 nS). The colors within the synaptic symbols code for the relative conductance change (similar to the voltage scale). Thus a green synapse is barely activated while a red one is maximally activated. The synapses in the On layer are switched on 20 ms after the onset of the synapses in the Off layer. In the preferred direction (right pane), the inhibitory synapses are delayed by 20 ms with regard to the activation of the excitatory synapses, while for the null direction (left pane) both synaptic inputs coincide. The bottom part of figure 4b diagrams the resulting somatic potential. For more details see O'Donnell *et al.*, 1986.

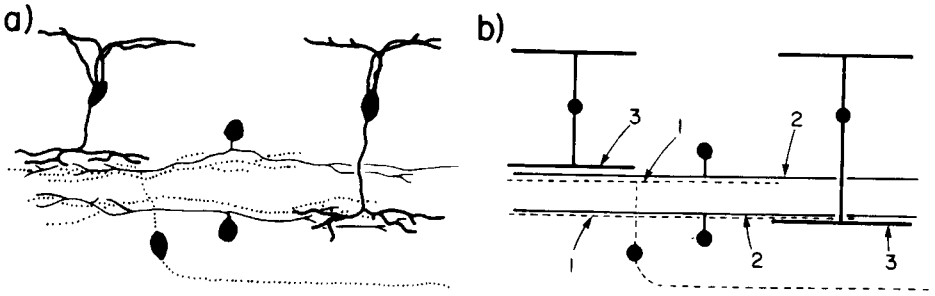


Figure 7. (a) A schematic view of the likely excitatory pathway from the outer plexiform layer (OPL) to the On-Off direction selective ganglion cell in the rabbit. Depolarizing (On) and Hyperpolarizing (Off) bipolar cells convey the visual information from the OPL to the On or Off part of the IPL. Here they most likely synapses either directly --- possibly using glutamate or aspartate as excitatory neurotransmitter --- or indirectly --- via other amacrine cells --- onto the cholinergic starburst amacrine cells. These amacrine cells feed in turn directly onto the bistratified On-Off ganglion cells. (b) Possible sites for the computations underlying motion discrimination. GABAergic amacrine cells can veto the excitatory pathway either at the level of the ganglion cell (1), at the starburst amacrine cells (2) or bipolar cells (3). The On and Off pathways are segregated up to the cell body of the On-Off direction selective cell.

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