Computations in the vertebrate retina: gain enhancement, differentiation and motion discrimination

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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 is 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, i.e., the computations, performed by the retina. A complete circuit diagram of the retina is not available, 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.

Amplification and temporal differentiation

Visual systems are capable of measuring very low light intensities. Indeed, Hecht, Schlaer and Pirenne[1] have shown that humans can detect fluxes of photons that cause as few as four photoisomerizations in the retina, i.e., conformational changes in 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 generated by the retina[2].

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 photo-, receptors is very slow because of phototransduction mechanisms that we are now beginning to understand (see 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 ms (Ref. 3). In the same retina, rods have a sensitivity of about 1 mV per Rh*, but the time-to-peak of the voltage

response to the absorbance of a few photons is about 1 s (Ref. 3). In primates, the time scale of electrical events is approximately four times faster[4]. Thus, two important goals of retinal processing are a sophisticated amplification of the photoreceptor signal and some kind of temporal differentiation.

Gain

Fig. 1 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 s, but is capable of eliciting a synaptic potential of about 27 mV and a quick discharge of spikes in the ganglion cell. The first spike is initiated 250 ms 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 to 20 times, the voltage response in rods is almost undetectable but 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[5,6] and about 11 in the tiger salamander. In the salamander retina the voltage gain between rods and on-center bipolar cells and rods and off-center bipolar cells is 6 and 11 respectively (Owen, W. G., pers. commun.). Ashmore and Falk have estimated a considerably higher gain (around 50) between rods and on-center bipolar cells in the

dogfish retina[7]. Another amplifying step occurs in the inner plexiform layer at the synapse between bipolar cells and amacrine or ganglion cells[8] where the gain may be of the order of 5 (Copenhagen, D. R. and Reuter, T., unpublished observations).
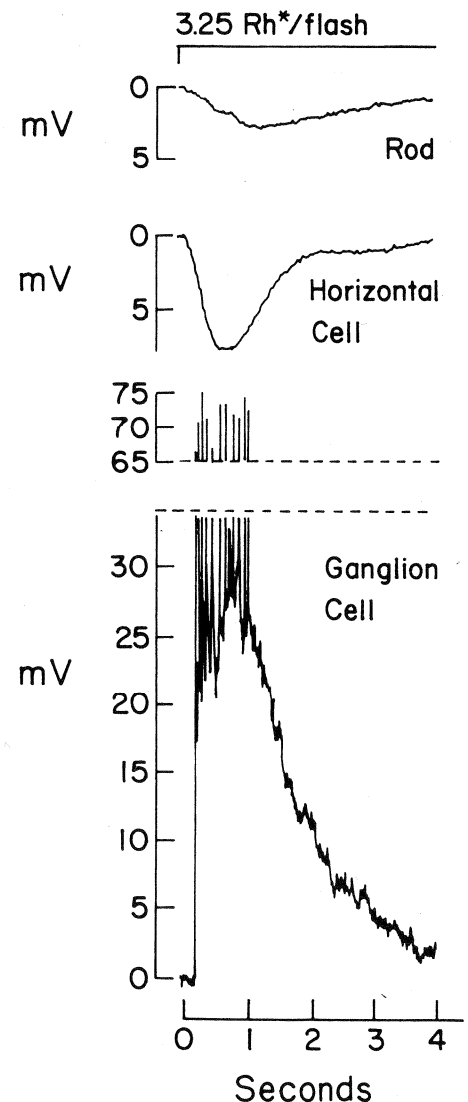
Fig. 1. *Intracellular recordings from a rod photoreceptor, horizontal cell and ganglion cell in the dark-adapted turtle retina (Bufo marinus). Diffuse flashes of light were 13.5 ms in duration eliciting 3.25 photoisomerizations (Rh*) per flash. Full field stimuli (700 µm diameter), covering the entire receptive field of each of the neurons were used. This figure was kindly provided by D. R. Copenhagen and T. Reuter.*

Possible mechanisms for gain

In the retina, a high gain seems to be achieved primarily 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 pre- and postsynaptic voltage can be obtained in two ways: intrinsic synaptic properties or convergence of many synapses onto the same postsynaptic element.

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. This amplification is due to a chain of active, non-linear processes underlying chemical synaptic transduction, from the activation of voltage dependent calcium channels in the presynaptic fiber to the kinetics of enzymatic degradation of the neurotransmitter at the postsynaptic membrane. 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[9].

A second mechanism for 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 non-linear interaction between the synapses) can be avoided. If an excitatory synapse is activated in the presence of a second, excitatory synapse nearby, its effectiveness in generating an EPSP will be reduced in comparison to the case in which no second synapses is 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[10]. Thus in a cell with many dendritic branches, synaptic saturation may be minimized and the synaptic gain therefore enhanced. Thus, 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 s. With double recording techniques, it is possible to observe in a rod that voltage leads current[11] in such a way that the time course of the photocurrent appears differentiated or accelerated. At both the rod–horizontal cell synapse[5,6] and at the rod–bipolar cell synapse (Owen, W. G., pers. commun.), presynaptic potentials have a longer duration than postsynaptic events. In the inner plexiform layer, voltage responses in amacrine and ganglion cells have a duration shorter than the excitation in bipolar cells[8].

The processing of signals in cones presents similar 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

One major role of temporal processing in the retina is to accelerate the slow signals coming from the photoreceptor 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[12]. Richter and Ullman[53] describe one model in which the dyad synapse (bipolar–ganglion–amacrine) implements a temporal derivative of the bipolar input.

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
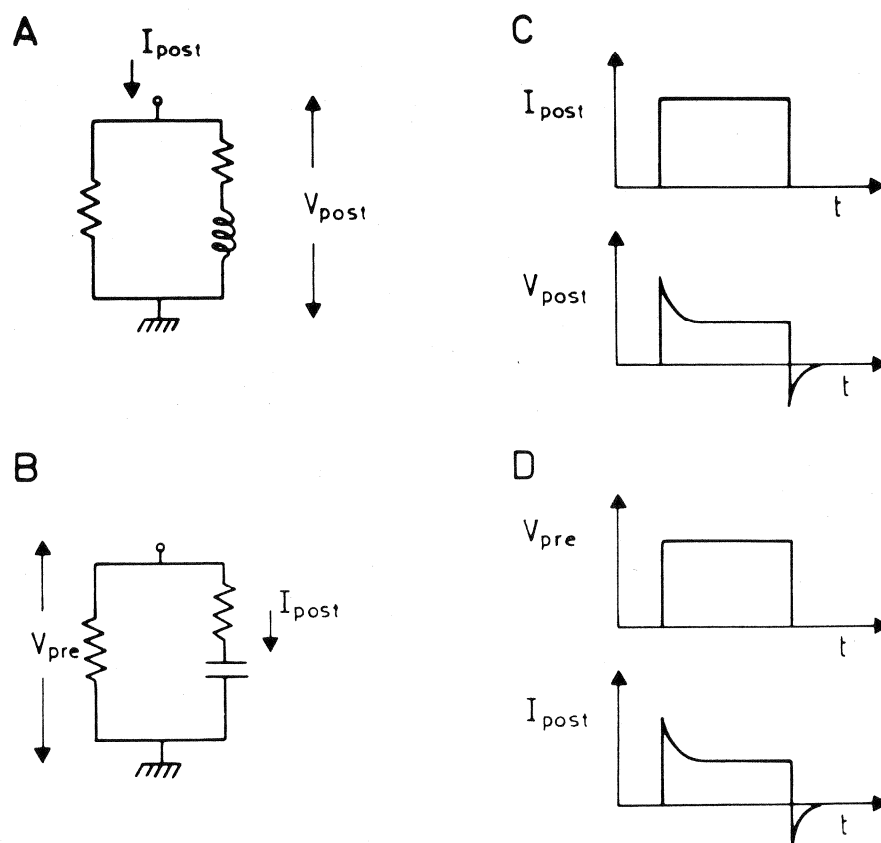

Fig. 2. (A) *Equivalent electrical circuit of a membrane with a time-varying voltage dependent* K^+ *conductance turned on by depolarization.* **(C)** *Postsynaptic current and voltage with a membrane with inductive-like properties.* **(B)** *Equivalent electrical circuit of synaptic inactivation.* **(D)** *Presynaptic voltage and postsynaptic current at synapses with synaptic inactivation.*

best be described (within a certain voltage range) by a so-called pheno-menological inductance. An example is the time-varying, voltage-dependent K^+ conductance activated by depolarization, e.g., the delayed rectifier found in squid axon[13,14] – its equivalent electrical circuit (see Fig. 2A) – will contain an inductance (see also Ref. 15). 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 Fig. 2C). Such a mechanism does seem to be present in the rod[11,14]. A recent patch-clamp study of isolated bipolar cells in the goldfish retina[16] has revealed the existence of a K^+ conductance that may be involved in determining the bandpass properties of the rod–bipolar synapses.

An alternative mechanism for temporal differentiation is synaptic inactivation[17]. In this case, a steady presynaptic voltage is transformed into a transient postsynaptic current (see Fig. 2D). The equivalent electrical circuit is shown in Fig. 2B and has an equivalent capacitance that 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 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, for example a dark bar on a light background, in a particular 'preferred' direction, elicits a vigorous response from the cell whereas movement in the opposite direction, termed 'null direction', yields no significant response (Fig. 3D). Directionally-selective cells, described in the frog's retina in a classical paper by Maturana, Lettvin, McCulloch and Pitts[18], have subsequently been identified in the third optic ganglion of the house fly, the retinae of the rabbit, squirrel and cat, the optic tecti of frogs and pigeons, and the visual cortex of both cats and monkeys[19–24].

Early experiments

Barlow and Levick systematically explored directional selectivity in the retina of the rabbit using extracellular recordings[21]. About 20% of the ganglion cells in the visual streak give ON and OFF responses to stationary, flashed stimuli and were found to be directionally-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[19] (Fig. 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 Fig. 3b). Directionality is achieved by an asymmetric delay (or by a low pass filter) between excitatory and inhibitory chan-

nels from the photoreceptors to the ganglion cell. Second, this veto operation must occur within small independent subunits distributed throughout the receptive field of the cell, since movement of a bar over 0.25° to 0.5° elicits a directionally-selective response [whereas the whole receptive field subtends 4.5° (Ref. 21)]. Thus, the site of the veto operation is extensively replicated throughout the receptive field of the directionally-selective cell. Confirming evidence for the critical role of inhibition comes from experiments where inhibition is blocked using pharmacological agents[25–27] resulting in an equal response for both preferred and null directions.

A biophysical model

We can now ask how this operation is implemented at the level of the

TABLE I. Predictions of a postsynaptic, silent inhibition model.

ON–OFF directionally-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).

Bicucullin, a specific antagonist of $GABA_A$ receptors, 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.
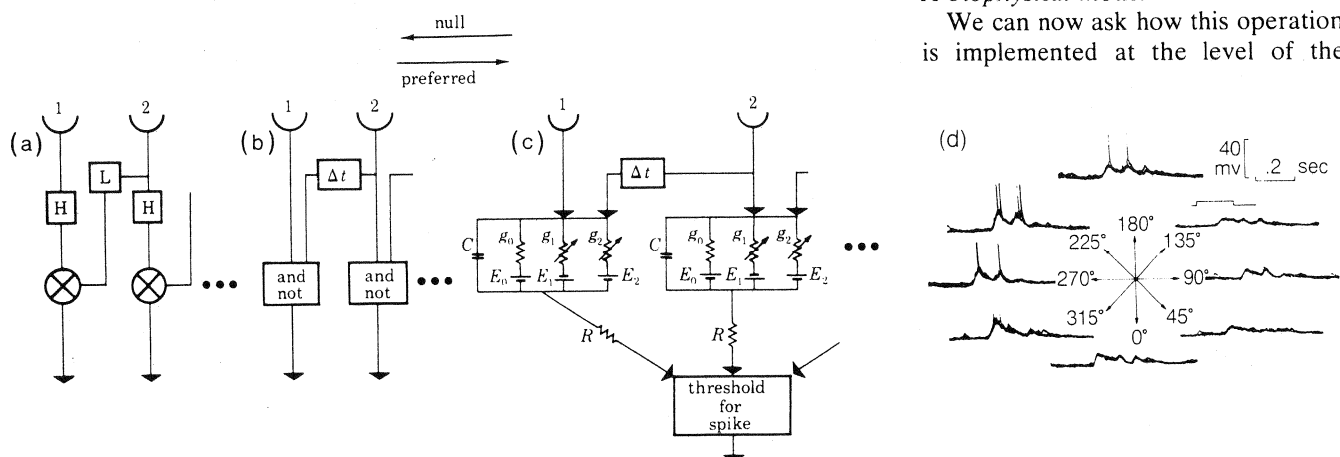
The directionally selective cell should show a δ-like morphology, with a highly branched, bistratified dendritic tree with small diameter dendrites or possibly spines.

ON–OFF directionally-selective cells are expected to show little interaction between dark bar/spot and light bar/spot moving in opposite directions within the receptive field.

Fig. 3. (A) *A part of the model of movement detection of Hassenstein and Reichardt [19]. 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 to account for direction selectivity in the rabbit retina[21]. 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[28]. The interaction implemented by the circuit is of the type $g_1 - \alpha g_1 g_2$.* **(D)** *Intracellular recording from a directionally-selective turtle ganglion cell. The time of illumination is indicated by the line above the upper right record. Notice the absence of any hyperpolarization. (A–C taken from Ref. 28; D taken from Ref. 35.)*

hardware, i.e., at the level of retinal cells. Torre and Poggio[28] proposed a specific biophysical mechanism implementing the neural equivalent of a veto operation (Fig. 3c). When two neighbouring 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; that is, synaptic inputs may interact in a highly non-linear fashion. In particular this is true for an inhibitory synaptic input that increases the membrane conductance with an associated ionic battery that reverses at, or very near, 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 showed that in a lumped electrical model of the membrane of the cell silent inhibition can effectively cancel the EPSP induced by an excitatory synapse without hyperpolarizing the membrane[28]. 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 non-linearity of the interaction is an essential requirement of this scheme, Torre and Poggio suggested that the optimal location for excitation and inhibition are fine distal dendrites or spines on the directionally-selective ganglion cells.

Since this analysis omitted the conditions required to produce effective and specific non-linear interactions in a dendritic tree, Koch, Poggio and Torre[10,29,30] used one-dimensional cable theory to analyse the interaction between time-varying excitatory and inhibitory synaptic inputs in a morphologically characterized cat retinal ganglion cell (of the δ type, see Ref. 31). In the case of steady state synaptic conductance inputs, they were able to rigorously prove 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 Fig. 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 50 nS 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 10 μm 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 at least as long as excitation and their time courses should overlap substantially[29,32]. Finally, the on-the-path condition is also valid in the

presence of action potentials: in order for a silent inhibition to block the propagation of a spike past a branching point, it must be located less than 5 μm from the branch point. This is especially relevant since recent observations by Jensen and DeVoe suggest that directionally-selective turtle ganglion cells may occasionally show dendritic spikes[33]. 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 would be much more linear; the inhibitory synapse would 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[9,29,30,34].
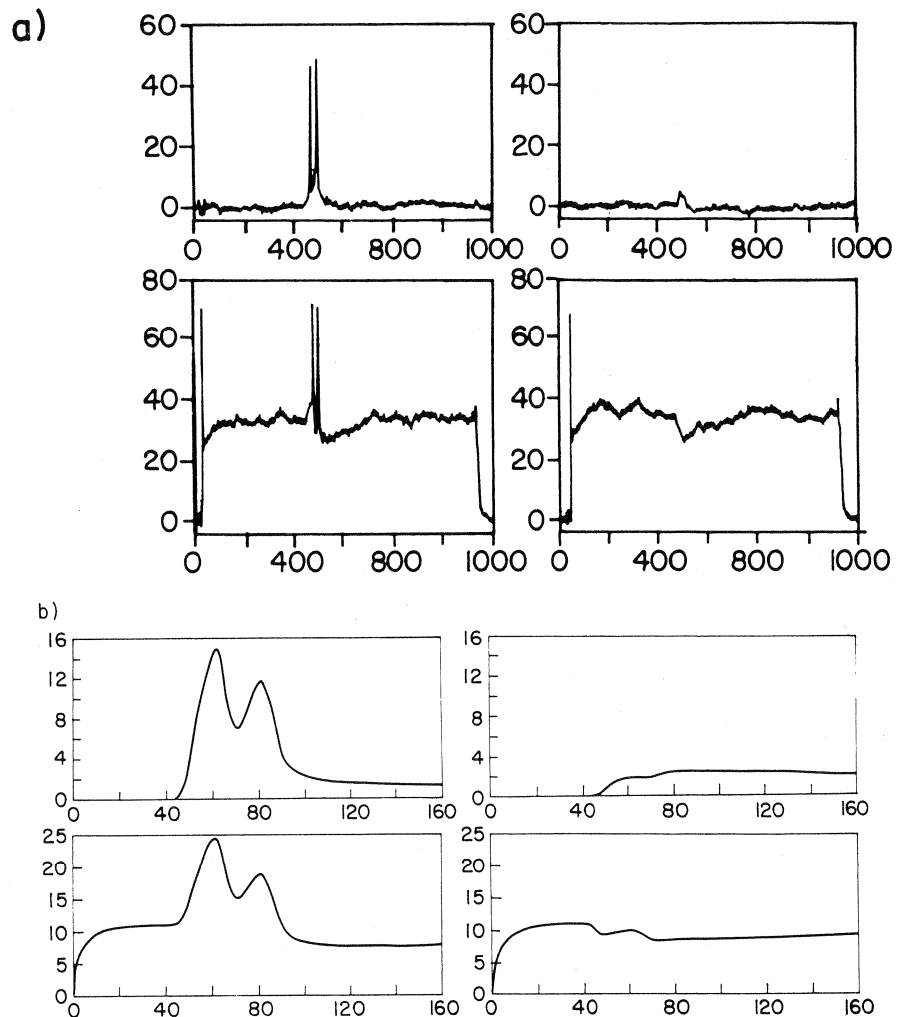

Fig. 4. (A) *The effect of intracellular current injection upon the photoresponse in an intracellularly recorded directionally-selective turtle ganglion cell. The response in the preferred and null directions are shown in the left and right part of (A). The lower record shows the photoresponse while 0.23 nA current was being injected into the soma.* (Adapted from Ref. 35.) **(B)** *Simulated intracellular potential at the soma of the reconstructed rabbit ON–OFF directionally-selective ganglion cell shown in Figs 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. In the bottom half, a step current of 0.091 nA is being injected into the soma. Preferred direction is left and null direction right. Scale is in mV (relative to E_{rest}) versus ms.*
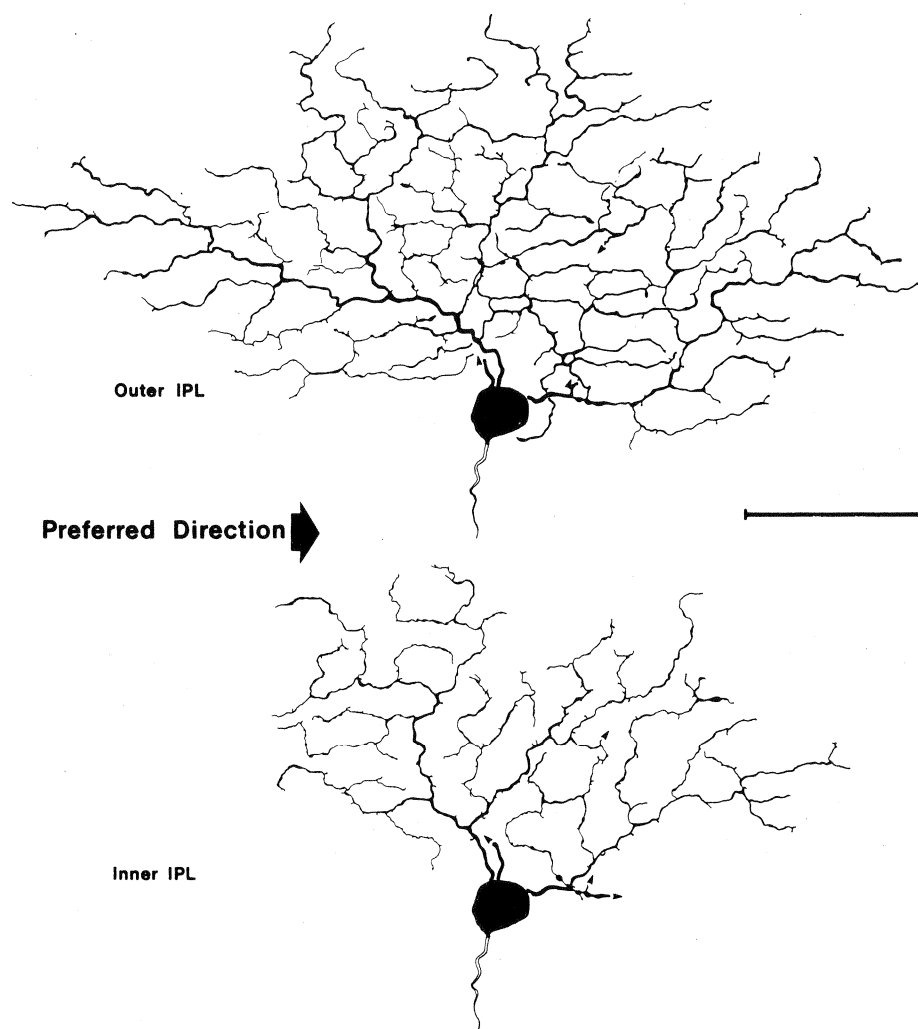
Fig. 5. *Camera lucida drawing of an HRP-injected ON–OFF directionally-selective cell in the visual streak of the rabbit retina. The dendritic fields have been drawn in two parts: 'outer' refers to the part of the inner plexiform layer (IPL) closest to the inner nuclear layer, where the cells of the OFF pathway make synaptic connections, whereas 'inner' is the layer closest to the ganglion cell layer where the ON pathway is connected. There are no obvious asymmetries in the cell that are correlated with the preferred direction. Bar is 50 μm. (Adapted from Ref. 38.)*

Critical predictions of the model

How does the model fare against experimental evidence? Table I 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[35] and the bullfrog[36]. Moving a spot or a bar in the preferred direction gives rise to a somatic EPSP with superimposed action potentials, whereas null direction stimulation results in a smaller EPSP without an hyperpolarizaton (Fig. 3d; see also Ref. 37). The reduced somatic EPSP in the null direction appears to be caused by an inhibitory process that increases the membrane conductance with an associated reversal potential at or very near the resting potential of the cell. This silent inhibition is revealed by injecting a steady-state depolarizing current into the soma, which gives rise to an hyperpolarization (see Fig. 4).

Preliminary evidence from rabbit ganglion cells indicates the presence of a similar inhibitory input (Amthor, F., pers. commun.).

Within the last years, two groups have recovered the morphology of ON–OFF directionally-selective ganglion cells. Using a fluorescent stain, Jensen and DeVoe visualized these cells in the turtle retina[33] and Amthor, Oyster and Takahashi used horseradish peroxidase (HRP) in the rabbit[38]. The overall morphology of these cells shows many similarities. Rabbit directionally-selective ganglion cells may be identified on purely morphological grounds because of several distinct features (Fig. 5): (1) these cells have two levels of dendritic ramification, corresponding to the ON and OFF laminae[39]; (2) the dendritic branches of the directionally-selective cells are of very small diameter relative to other rabbit ganglion cells, and 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 directionally-selective cells is compatible with our previous predictions[10].

In order to model massive synaptic input to a directionally-selective ganglion cell, we simulated the passive electrical properties of the anatomically reconstructed cell shown in Fig. 5 on the basis of one-dimensional cable theory[34,40]. Our computer program allows the symbolic drawing of 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 modelling by Segev, Fleshman, Miller and Bunow[41]. Fig. 4B shows the resulting somatic depolarization in the absence and presence of a depolarizing current step injected in the soma, in comparison with experimental records obtained from turtle ganglion cells (Fig. 4a; Ref. 35). Fig. 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 the excitatory and inhibitory inputs to directionally-selective cells? As presented elsewhere (see Masland, this issue), there is evidence implicating acetylcholine (ACh) as the excitatory neurotransmitter underlying direction selectivity in both the rabbit[26] and the

TABLE II. Biophysical models for the computations underlying direction selectivity in the rabbit retina. In all models the inhibitory input derives from a population of GABAergic amacrine cells.

Postsynaptic models
Non-linear interaction between excitation and silent inhibition at the level of ganglion cells dendrites.

Presynaptic models
Non-linear 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.
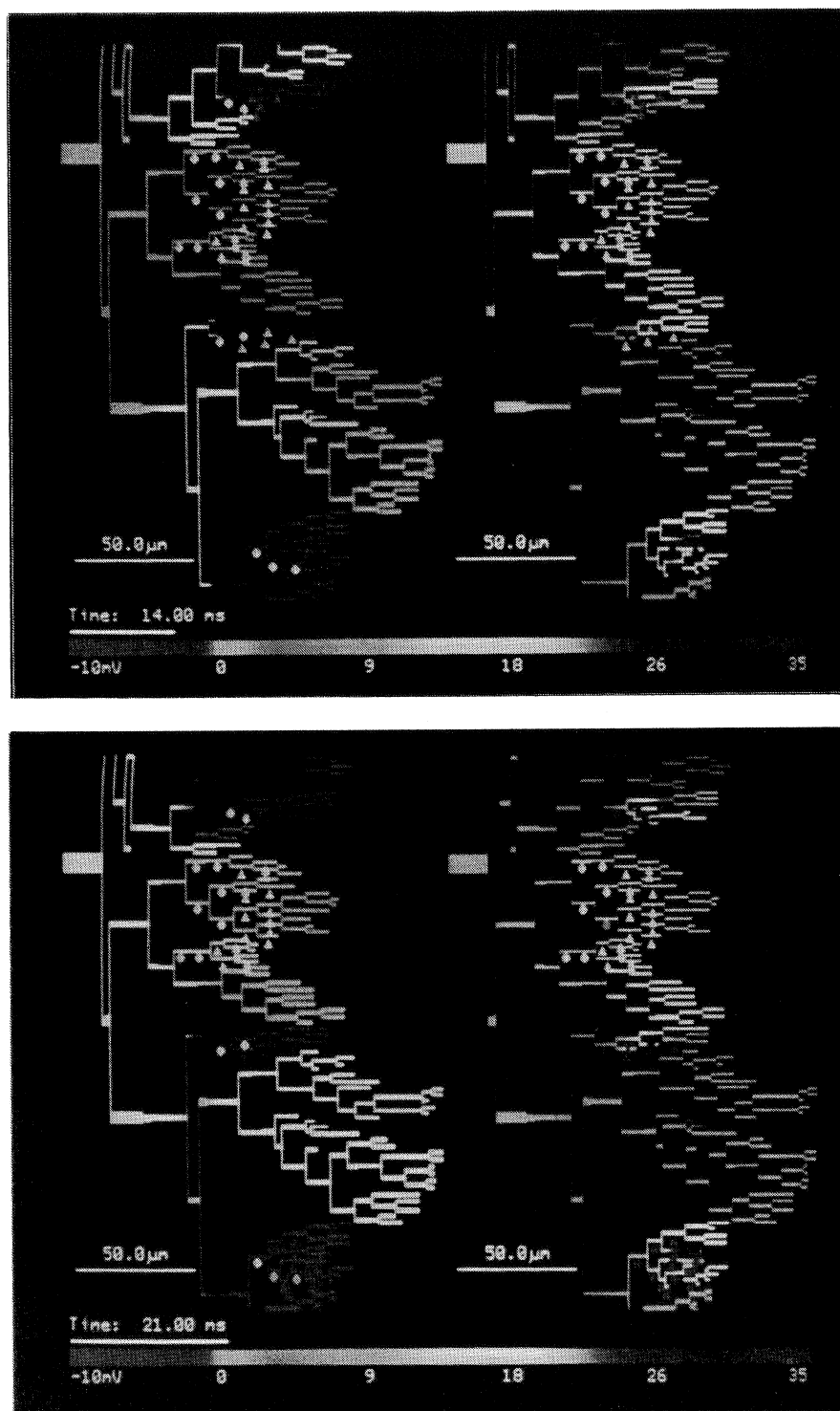
Fig. 6. *Intracellular potential in the computer reconstructed cell shown in Fig. 5 in response to massive synaptic input. The cell was modelled with the aid of an integrated circuit simulation package (SPICE). The passive properties of the neuron, i.e. R_m, C_m and R_i, were inferred from the measured somatic input impedance (about 110 $M\Omega$) and membrane time constant (about 7 ms), assuming 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 six groups of five to seven excitatory synapses (indicated by a triangle) and two to three silent inhibitory synapses each (marked by a circle) provide the input to the dendritic tree, three groups in the ON and three groups in the OFF layer (see Fig. 7). Thus, these six groups of synapses would correspond to the subunits of Barlow and Levick[21]. Time-to-peak of the excitatory and inhibitory conductance changes are 20 and 25 ms respectively, in accordance with intracellular recordings[37]. The peak inhibitory conductance change is about 20 times larger than the excitatory one ($g_{ipeak} = 10$ nS 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 overlap substantially. The top part of Fig. 4B diagrams the resulting somatic potential.*

turtle[27] retina. Recently, Masland and colleagues identified two unique populations of cholinergic amacrine cells that transiently release ACh at the onset and offset of light[42,43]. These starburst amacrine cells appear to be presynaptic to bistratified ganglion cells with the morphological attributes of the directionally-selective cells of Amthor *et al.*[38].

The inhibitory input for motion discrimination is believed to be mediated by the neurotransmitter γ-aminobutyric acid (GABA). Caldwell *et al.*[25] and Ariel and Daw[26] infused picrotoxin, a potent GABA antagonist, into the rabbit retina. Within minutes after the start of drug infusion the response of directionally-selective cells in the null direction increased dramatically, so that the cell became equally responsive to movement in both directions. A few minutes after drug infusion was discontinued, the cell once again became direction selective. During blockage of synaptic transmission via a low calcium concentration and EGTA, direct application of ACh to the turtle retina leads to spontaneous firing in directionally-selective cells[27]. This ACh-induced spike activity can be suppressed by GABA indicating that both ACh and GABA receptors must coexist on the membrane of turtle directionally-selective ganglion cells.

Thus, it appears that the excitatory and the inhibitory input to directionally selective ganglion cells derive from cholinergic and GABAergic amacrine cells, at least in the turtle and rabbit retina.

However, this does not exclude direct input from bipolar cells, which may be responsible for the center–surround organization of directionally selective cells.

Alternative models

What are the alternative models for the neuronal operations underlying motion discrimination? Although both Werblin[44] and Marchiafava[35] have failed to record directionally-selective responses in bipolar or amacrine cells, the possibility that the critical computations occur presynaptically (to the ganglion cell) cannot be excluded. Indeed, DeVoe and his collaborators have recorded from directionally-selective amacrine and bipolar cells in the retina of the turtle[45]. Their evidence points towards an alternative or coexistent presynaptic site for the critical computation underlying direction selectivity in the turtle. A second piece of evidence favoring a presynap-
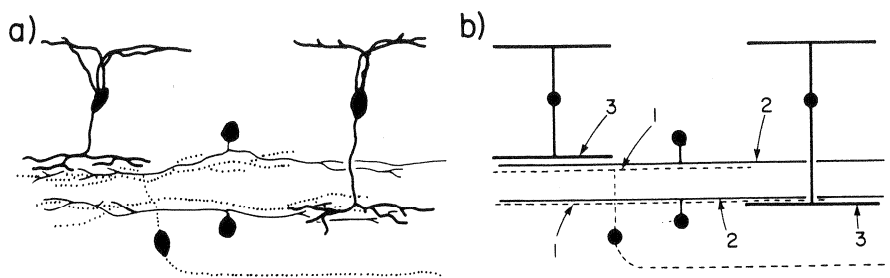
Fig. 7. (A) *A schematic view of the likely pathway from the outer plexiform layer (OPL) to the ON–OFF directionally-selective ganglion cell in the rabbit. Depolarizing (ON) and hyperpolarizing (OFF) bipolar cells convey the visual information from the OPL to the ON or OFF part of the IPL. Here they most likely synapse 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 in turn feed directly onto the bistratified ON–OFF ganglion cells. (B) Possible sites for the computation 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 directionally-selective cell.*

tic arrangement is the influence of GABA on ACh: GABA inhibits the light-evoked release of ACh in the rabbit retina[46] (see Fig. 7 and Table II).

Other classes of presynaptic models for direction selectivity have been proposed[9,47]. 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 starburst amacrine cell or the starburst amacrine cell itself. Starburst amacrine cells have dendrites that are probably decoupled from each other and the soma[48]. Only the distal-most portion of the dendrites give rise to conventional chemical synaptic output, whereas the bipolar and amacrine cell input is distributed throughout the cell[49]. 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[21]. At least two biophysical mechanisms could underly direction selectivity: (1) the 'and not' veto scheme, now implemented at the level of bipolar or amacrine cell; or (2) a linear interaction between an excitatory synapse and an hyperpolarizing synapse followed by synaptic rectification[9]. In this case, the non-linearity essential for direction selectivity[50,51] would be implemented by a rectifying synapse. For these presynaptic models, the release of neurotransmitter, whether from the bipolar or the amacrine cell, would in itself be direction selective.

In addition to the pharmacological and electrophysiological evidence cited above (see Fig. 4), two additional points argue against the presynaptic hypothesis. First, if the release of ACh is already direction selective, the application of an ACh potentiator should have little effect on the directionally-selective response of the ganglion cell. However, physostigmine does eliminate direction specificity[26,27]. Second, Sakai, Naka and Dowling 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[52]. Although a partial EM reconstruction of a putative directionally-selective rabbit ganglion cell[49] has failed to reveal any dendro-dendritic synapses, a possibility that must 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. For instance, the directionally-selective bipolar and amacrine cells recorded by DeVoe et al.[45] have a smaller velocity range than directionally-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.

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