Gap junctions with amacrine cells provide a feedback pathway for ganglion cells within the retina

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In primates, one type of retinal ganglion cell, the parasol cell, makes gap junctions with amacrine cells, the inhibitory, local circuit neurons. To study the effects of these gap junctions, we developed a linear, mathematical model of the retinal circuitry providing input to parasol cells. Electrophysiological studies have indicated that gap junctions do not enlarge the receptive field centres of parasol cells, but our results suggest that they make other contributions to their light responses. According to our model, the coupled amacrine cells enhance the responses of parasol cells to luminance contrast by disinhibition. We also show how a mixed chemical and electrical synapse between two sets of amacrine cells presynaptic to the parasol cells might make the responses of parasol cells more transient and, therefore, more sensitive to motion. Finally, we show how coupling via amacrine cells can synchronize the firing of parasol cells. An action potential in a model parasol cell can excite neighbouring parasol cells, but only when the coupled amacrine cells also fire action potentials. Passive conduction was ineffective due to low-pass temporal filtering. Inhibition from the axons of the coupled amacrine cells also produced oscillations that might synchronize the firing of more distant ganglion cells.

Keywords: primate; parasol cell; M cell; lateral inhibition; oscillation; synchrony

1. INTRODUCTION

In primates, the retinal ganglion cells that project to the magnocellular layers of the lateral geniculate nucleus ultimately contribute to many aspects of visual perception and, particularly, to the perception of motion (Merigan & Maunsell 1993). These magnocellular-projecting ganglion cells are more sensitive to luminance contrast than the cells that project to the parvocellular layers, and they also respond more transiently (Kaplan *et al.* 1990). Neurons with these responses have been identified morphologically as parasol ganglion cells by means of intracellular recording and dye injection (Dacey & Lee 1994). There is anatomical evidence that parasol cells make gap junctions with amacrine cells, the local circuit neurons that mediate lateral interactions in the retina. Small biotinylated tracers injected into parasol cells also label two types of amacrine cells, a large one and a smaller one (Dacey & Brace 1992; Ghosh *et al.* 1996), and this tracer-coupling is presumed to be mediated by the gap junctions seen in an electron microscopic study of parasol cells (Jacoby *et al.* 1996). Retinal ganglion cells have never been observed to make chemical synapses in mammalian retinas; therefore, the gap junctions provide their only pathway for output within the retina.

The larger type of tracer-coupled amacrine cell has an unusual morphology. It has dendrites approximately

200 μm long with very few branches and several axons that typically arise from the distal tips of the dendrites. Light responses have not been recorded from this type of amacrine cell in primates, but an ON amacrine cell that resembles the ones coupled to ON parasol cells has been studied in rabbits. This amacrine cell generates action potentials, and as the receptive field centre was the same size as the dendritic field, the axons appeared to be exclusively presynaptic (Taylor 1996). Two lines of evidence suggest that these amacrine cells are inhibitory. First, these amacrine cells have perikarya in the ganglion cell layer, where more than 90% of the amacrine cells contain GABA (Wassle *et al.* 1990; Koontz *et al.* 1993; Kalloniatis *et al.* 1996). Second, these cells contain immunoreactive cholecystokinin (CCK) precursor G6-gly (Jacoby *et al.* 1996), and CCK is inhibitory to brisk ganglion cells in the cat retina (Thier & Bolz 1985). The axons are likely to be presynaptic to the parasol cells because amacrine cells provided more than 80% of the input to parasol cells in the peripheral retina (Jacoby *et al.* 1996). G6-gly-IR amacrine cells form a dense plexus in the same two narrow strata of the inner plexiform layer (IPL) as the parasol ganglion cell dendrites, and they make more than 40% of their synapses onto ganglion cells (Marshak *et al.* 1990). Appositions between G6-gly-IR amacrine cells and parasol ganglion cells were seen in light microscopic double-labelling experiments, and statistical tests showed that there were more contacts than would be expected to occur by chance alone (Jacoby *et al.* 1996).

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Figure 1. Connectivity of simulated retinal neurons illustrated at three different spatial scales. The model retina was a torus consisting of a 64×64 array of identical circuits. The connectivity was shift invariant (lower right). Each local circuit contained bipolar cells (BP), large (LA) and small (SA) amacrine cells and parasol ganglion cells (GC). The large amacrine cells made inhibitory synapses (closed circles) onto the surrounding parasol cells, but not to the neighbouring parasol cells (upper right). Both ganglion cells and small amacrine cells received excitatory synaptic input from bipolar cells (open triangles), while all three cell types received inhibitory synaptic input from the small amacrine cells (left). The large amacrine cells made gap junctions (resistors) with ganglion cells and small amacrine cells, and with one another (not shown). Synaptic connections were weighted by Gaussian functions of the distance between the pre- and postsynaptic cells. For interconnections between the bipolar, small amacrine and ganglion cells, the distance over which the connection strengths were reduced by a factor of $1/e$ —the effective radius—was equal to half the distance between neighbouring parasol cells. The effective radius of the gap junction connections made by the large amacrine cells was twice as large. The effective Gaussian radius of the axon-mediated inhibition was six parasol cell radii.

The second type of amacrine cell is labelled more lightly by tracer injection into the parasol ganglion cell and has a smaller perikaryon (Dacey & Brace 1992). The dendrites of these small, tracer-coupled amacrine cells are too small in diameter to be the ones that make gap junctions with parasol ganglion cells (Jacoby *et al.* 1996). Therefore, we assumed that these small amacrine cells were lightly labelled because they are coupled indirectly, via the large amacrine cells, as they appear to be in rabbits (Xin & Bloomfield 1997). The synaptic connections of the small amacrine cells are unknown, but it is reasonable to assume that they make synapses onto the parasol cells, large amacrine cells and bipolar cells (the local circuit neurons that convey information from the photoreceptors to the IPL) because these synapses are common in the macaque retina (Koontz & Hendrickson 1987). It is likely that the small amacrine cells are inhibitory as the only amacrine cells known to use an excitatory neurotransmitter, the cholinergic cells, do not make gap junctions (Mariani & Hersh 1988).

We have developed a mathematical model of the primate inner plexiform layer with connectivity based on these anatomical data. The time constants of the model neurons and the strength of their interconnections were determined by comparing the responses of the model parasol cells to three different sets of electrophysiological data. The model was then used to predict the contributions of the electrically coupled amacrine cells to the luminance

contrast sensitivity of the parasol cells, to the time-course of their responses, and to the synchronization of their activity.

2. METHODS

(a) *Mathematical description*

We used a linear, mathematical model because electrophysiological studies have shown that the responses of parasol ganglion cells to stimuli of moderate contrast are linear (Kaplan & Shapley 1986; Lee *et al.* 1994). The model contained bipolar cells, parasol ganglion cells and two types of amacrine cells, which were connected as illustrated in figure 1. Each neuron was approximated as a simple RC (resistor-capacitor) circuit with an intrinsic time constant ranging from 30 to 75 ms. A formal expression describing the dynamics of the model neurons can be written as:

$$\frac{d}{dt} \vec{V}^{(i)} = -\frac{1}{\tau^{(i)}} \left[\vec{V}^{(i)} \left(1 + \sum_j \left(\vec{G}^{(ij)} \vec{1} \right) \right) - \sum_j \vec{T}^{(ij)} \vec{V}^{(j)} \vec{T}^{(ij)} - \sum_j \vec{G}^{(ij)} \vec{V}^{(j)} \vec{G}^{(ij)} - \vec{L}(t) \right]. \quad (1)$$

The superscript i denotes the neuron type: bipolar, large amacrine, small amacrine or parasol ganglion cell. The variable $\tau^{(i)}$ gives the membrane time constant. The term $\vec{V}^{(i)}$ is a 64×64 matrix of scalar activities, roughly corresponding to membrane

potential, for the cells of type i . Similarly, $\vec{T}^{(ij)}$ is a 64×64 Toeplitz matrix characterizing the synaptic connections from neurons of type j to neurons of type i . The connectivity of the large amacrine cell was represented by a sum of spatially separable Gaussian products. The terms involving $\vec{G}^{(ij)}$ similarly describe the gap junctions' connections. Finally, $\vec{L}^{(i)}$ is a matrix that characterizes the time-dependent input to the system. Equation (1) was augmented by an additional circuit element to approximate the delays due to the axons of the large amacrine cell.

Equation (1) was solved by first performing a two-dimensional Fourier transform to diagonalize the connectivity matrices $\vec{T}^{(ij)}$ and $\vec{G}^{(ij)}$. An additional diagonalization within the 4×4 space of interactions between the different cell types was then performed for each of the 64×64 Fourier components. The general initial value problem was solved exactly by expansion in terms of the eigenvectors of the linear system. These matrix operations were done using the Matlab programming environment (Mathworks).

(b) Light stimuli

To approximate the dynamics of photoreceptors, the light input to the model bipolar cells was low-pass filtered using a time constant of 30 ms. The bipolar cell responses to sinusoidally modulated gratings or to uniform bars of light were calculated by convolution with a two-dimensional Gaussian function. For spots of light, this convolution was done numerically. Analytical results were used for sinusoidal stimuli to account for spatial frequencies that exceeded the inherent resolution of the lattice. To reduce aliasing, the phase of the simulated grating was randomly shifted at each location by a normally distributed value representing random variations from perfect rectilinear spacing between cells (mean deviation was one-quarter of the average intercellular distance). Simulated responses to gratings represent the average and standard deviation of nine independent runs. To facilitate comparison with the results of the model, the radius of the receptive field centre of the parasol cell, determined in electrophysiological experiments, was set equal to one, and the surround was rescaled by the same factor. This scaling set the dendritic field diameter of the model parasol cell to the size of the receptive field centre measured experimentally but did not affect the shape of the spatial tuning curves. The amplitude of the response of the experimental parasol cell was also scaled to match the responses of the model parasol cell under uniform illumination.

(c) Standard model parameters

The time constants of the bipolar and parasol cells were set to 30 ms, which produced a good fit to the rising phase of the parasol cell flash response measured experimentally (Lee *et al.* 1994). The time constants of the large and small amacrine cells were set to 75 ms, in order to fit the peak and decay of the parasol cell flash response, respectively. To compensate for the absence of inhibitory inputs to the small amacrine cells in the model, the total integrated strength of their bipolar input was one-tenth of the corresponding value for ganglion cells. The total integrated strength of the inhibitory feedback onto bipolar cells was set to 1.5 times the forward gain in order to match the inhibition following the peak of the flash response. This value is consistent with the ratio of input to output synapses onto DB3 bipolar cells, which have been shown by electron micrograph double labelling experiments (Jacoby & Marshak 1997) and three-dimensional reconstruction of electron micrographs (Calkins *et al.* 1995) to contact OFF parasol cells. On DB3

bipolar cell axons there were 50% more inhibitory inputs from amacrine cells than output synapses (Jacoby & Marshak 1997). To produce a transient response to a maintained stimulus, the strength of the sustained, feedforward inhibition to the ganglion cells was assumed to equal the strength of their excitatory bipolar inputs. As 80% of the synapses onto parasol cells are from amacrine cells (Jacoby *et al.* 1996), and all but one type is inhibitory, this assumption is reasonable. The strength of the feedforward inhibition from the small to the large amacrine cells was similarly calibrated to cancel the depolarizing effect of the gap junctions between them. The ratio of bipolar input to gap junction strength was 10:8.5 for ganglion cells and 1:5 for small amacrine cells. These gap junctions' strengths mainly affected the relative amplitudes of the primary and secondary peaks in the flash response of the parasol cell. The ratio of the strength of the gap junctions between large amacrine cells to those with ganglion cells was 25:8.5, which produced the best fit to the spatial tuning curve (Croner & Kaplan 1995). The time constant of the axonal compartment of the wide-field amacrine cells was set to 5 ms, corresponding to a conduction velocity of 0.2 m s^{-1} .

3. RESULTS

In figure 2*a* the responses to brief, full-field light flashes of macaque parasol cells in the parafovea (Lee *et al.* 1994) are compared with the responses generated by the model. Inhibition from the small amacrine cells was responsible for the falling phase of this impulse response. The inhibition mediated by the large amacrine cells gave rise to the damped oscillations seen in both the simulated and the experimental data. The oscillations were more pronounced when the small amacrine cells were coupled directly to the parasol cells, a finding suggesting that the system is more stable when the coupling is indirect. In figure 2*b*, a simulated current pulse was injected simultaneously into all of the model parasol cells. This produced inhibition, mediated by synapses from the large amacrine cells, which had a similar time-course to the inhibition of light responses observed in phasic retinal ganglion cells of macaques after antidromic stimulation of the optic nerve (Gouras 1969).

Electrophysiological studies have shown that receptive field centres of parasol cells are the same size as their dendritic fields (Crook *et al.* 1988; Croner & Kaplan 1995). Therefore, it was important to show that the spatial tuning curve for parasol ganglion cells in macaque retina was also fit using the same parameters (figure 2*c*). The most important factors in determining the fit to the spatial tuning curve were the geometry of the axons of the large amacrine cells and the strength of their inhibitory synapses; the small amacrine cells made only a minor contribution. Despite the fact that the coupled amacrine cells had dendritic fields that were twice the diameter of those of the parasol cells, and that they responded to light with the same polarity, they did not enlarge the receptive field centres of the parasol cells.

Lateral inhibition mediated by the large, coupled amacrine cells greatly enhanced the responses of the parasol cells to luminance contrast (figure 3*a*). Because the parasol cells were coupled to neighbouring large amacrine cells, and these inhibited more distant parasol cells, the parasol cells essentially inhibited one another. Parasol cells on the unstimulated side of the edge were

Figure 2. Comparison of simulation results with published data. (a) Responses of a model parasol cell (dotted line) to 2 ms of uniform illumination. The simulated parasol cell response was scaled for comparison with experimental data (solid line, from Lee *et al.* (1994, fig. 1B)). (b) Direct simultaneous stimulation of all model parasol cells. The initial response is followed by a hyperpolarization that peaks near 11 ms. (c) Spatial tuning curves of model parasol cells (range indicated by dotted lines) compared with experimental results (circles, from Croner & Kaplan (1995, table 1), eccentricity 10–20°). Model parameters are the same for all panels.

inhibited, and this released parasol cells on the stimulated side of the edge from tonic inhibition. This effect was apparent even when the inputs and outputs were co-extensive, as they would be with conventional amacrine cells or horizontal cells, producing a 95% enhancement over baseline. However, this enhancement was 149% when the axons of the simulated large cells had an effective Gaussian diameter equal to the standard value. The model also suggests an explanation for the origin of these axons from the distal dendrites. The enhancement was only 129% when the axons of the large amacrine cells also inhibited nearby parasol cells, as they would with axons originating from the perikarya.

The major effect of the synaptic interactions between the large and the small amacrine cells was to shorten the time-course of the parasol cells' light response. Figure 3*b* shows the parasol cell response to a maintained spot of light filling the centre of the receptive field. This stimulus did not activate the surrounding large amacrine cells, and therefore there was very little inhibition from their axons.

Figure 3. Role of gap junctions in shaping parasol cell light responses. (a) Model parasol cell responses (lower trace) as a function of distance from the edge of a bar of light (upper trace). Using the same parameters as in figure 2, the response at the illuminated edge of the bar of light is enhanced by disinhibition by 149% over baseline (solid line). However, the response is enhanced by only 129% if the large cell also makes inhibitory synapses onto the neighbouring parasol cells (dotted line). This enhancement is further reduced to 95% when the axons of the large cells are coextensive with the dendritic field (dashed line). (b, c) The effects of synaptic interactions between large and small amacrine cells on the responses to steady light. (b) Parasol cell responses. The solid line shows the response predicted by the standard parameters. When both the gap junctions and the inhibitory synapses between the large and small amacrine cells were removed (dotted line), the responses became broader, even though the small amacrine cell time constants were reduced by eightfold so that their light responses were identical under both conditions (not illustrated). By increasing the strength of the inhibitory synapses onto bipolar cells by 60%, it was possible to match the time-course of the original response (circles). (c) Large amacrine cell responses. With the standard parameters (solid line), the step response of the large amacrine cell was more transient than without the synaptic interactions with the small amacrine cells (dotted line). Again, increasing the inhibitory feedback onto the bipolar cells by 60% restored the time-course of the original response (circles). The responses of the large amacrine cells without gap junctions and with enhanced inhibitory feedback of the bipolar cells were scaled to normalize the peaks of the three different responses.

Figure 4. Transmission of action potentials through gap junctions. (a) Action potentials with a peak amplitude of 100 mV were simulated by subtracting two impulse responses (each low-pass filtered with a time constant of 0.5 ms) with a delay of 0.5 ms between them. (b) The response of a coupled, large amacrine cell to a simulated action potential in the nearest neighbouring parasol cell is an excitatory postsynaptic potential of 1.7 mV (dotted line). (c) The response of a neighbouring parasol cell is negligible (0.15 mV) due to low-pass filtering (dotted line). If the spike in the original parasol cell is assumed to produce a synchronous action potential in the large amacrine cell, however, the depolarization produced in the neighbouring parasol cell is 1.75 mV (solid line). (d) Even when a line of 63 out of 64 parasol cells fire synchronously, the depolarization communicated to the remaining parasol cell via passive conduction through the gap junctions is only 0.5 mV (dotted line). In contrast, when a line of 64 large amacrine cells fires synchronously, the depolarization produced in the line of nearest neighbouring parasol cells is 7 mV (solid line).

When the small amacrine cells were electrically coupled to the large amacrine cells and also made inhibitory synapses onto them, the responses of both the parasol cells and the large amacrine cells decayed rapidly (figure 3c). This was due, in part, to the gap junctions made by the small amacrine cells, which reduced their effective time constants by lowering their input impedance. The synaptic interactions between the large and small amacrine cells were then omitted, and as a control, the time constants of the small amacrine cells were reduced so that their responses had the same amplitude and time-course as before. In this case, the large amacrine cells repolarized more slowly (figure 3c) and, because the large amacrine cells were electrically coupled to the parasol cells, this prolonged the light responses of the parasol cells as well (figure 3b). This result suggests that the mixed chemical and electrical synapse between the dendrites of the large and small amacrine cells makes the responses of the large amacrine cells more transient, and this contributes to the repolarization of the parasol cells via the gap junctions made by their dendrites. In the absence of interactions between the large and small amacrine cells, the strength of the inhibitory synapses onto the bipolar cells had to be increased by 60% in order to match the time-course of the original responses. Thus, our results suggest that electrical synapses allow the same results to be achieved with less inhibition and slower intrinsic time constants.

In the cat retina, ganglion cells fire action potentials synchronously under some conditions, and this has been attributed to their gap junctions (Mastrorade 1983; Neuenschwander & Singer 1996). To investigate whether

gap junctions via amacrine cells could promote synchronous firing of parasol cells, we simulated the effects of a single action potential in a parasol cell on the neighbouring large amacrine cells and parasol cells. A simulated action potential of 100 mV (figure 4a) produced a depolarization of 1.7 mV in each of the neighbouring large amacrine cells (figure 4b), but only 0.15 mV in the neighbouring parasol cells (figure 4c). These results suggest the gap junctions between parasol cells and amacrine cells do not provide a pathway for the passive spread of current between parasol cells. Even when 63 parasol cells in a line all spike synchronously, the remaining, unstimulated cell initially depolarizes by only 0.33 mV when the current is conducted through the amacrine cells passively (figure 4d). The gap junctions act as low-pass filters that attenuate brief membrane depolarizations such as action potentials, and therefore this pathway alone cannot account for synchronous firing of parasol cells. However, when the large amacrine cells also fire action potentials, an action potential in a parasol cell produces a depolarization of 1.75 mV in the neighbouring parasol cells (figure 4c). When 64 large amacrine cells in a line all fire action potentials, there is a brief depolarization of 7 mV in the neighbouring parasol cells (figure 4d). These findings suggest that the gap junctions with large amacrine cells could promote synchronous firing in the parasol cells, but only when the amacrine cells reach threshold. When the large amacrine cells fire action potentials they also produce hyperpolarizations in the parasol cells. The direct excitation through the gap junctions is followed by inhibition from both the large and the small amacrine

cells, producing a series of damped oscillations. When the amacrine cells do not fire action potentials this hyperpolarization is 0.67 mV, considerably larger than the depolarization mediated by the gap junctions. These findings suggest that the gap junctions between parasol cells and large amacrine cells have a net inhibitory effect on the neighbouring parasol cells unless the amacrine cells fire action potentials.

4. DISCUSSION

We found that three electrophysiological experiments with parasol cells could be reproduced using a single set of model parameters, indicating that the time constants of the model neurons and the strengths of the electrical and chemical synapses were not unrealistic. Amacrine cell inputs were particularly important to fit the time-course of the parasol cells' response to light stimulation. Although there have been a number of other studies in the past 25 years showing that amacrine cells make the light responses of ganglion cells more transient (reviewed by Nirenberg & Meister 1997), this appears to be the first to suggest a role for the gap junctions between amacrine cells and ganglion cells in this process. When parasol cells were stimulated, large amacrine cells were depolarized via the gap junctions made by their dendrites, and this feedback had both local and long-range effects on the parasol cells. First, after a short delay, the axons of the large amacrine cells inhibited parasol cells over a large area of the retina, although not the parasol cells nearby. Second, the small amacrine cells were depolarized via their gap junctions with the dendrites of the large amacrine cells. The small amacrine cells, in turn, inhibited the parasol cells directly and indirectly by inhibiting their bipolar cell input. The small amacrine cells also inhibited the large amacrine cells and, because the dendrites of the large amacrine cells were coupled to parasol cells, this provided a third pathway to repolarize the parasol cells.

Depolarizing all of the parasol cells simultaneously produced a hyperpolarization with a time-course similar to the inhibition of light responses seen after antidromic stimulation of the optic nerve (Gouras 1969). This inhibition was likely to be mediated by gap junctions with amacrine cells for several reasons. The inhibitory effect of antidromic stimulation was most pronounced in phasic cells, now known to correspond to parasol cells. Midget cells, the major type of tonic cells, do not make gap junctions (Dacey & Brace 1992). Ganglion cells with intraretinal collaterals have been described in primates, but they are unlikely to account for this effect as only one or two have been observed in each retina (Usai *et al.* 1991). Centrifugal axons would also have been stimulated in these experiments, but they are unlikely to produce responses with such a short latency since they contain the modulatory neurotransmitter histamine (Airaksinen & Panula 1988). Furthermore, there is no indication from their morphology that centrifugal axons contact parasol cells selectively (Usai *et al.* 1991).

The gap junctions made by horizontal cells and AII amacrine cells have been shown to increase the sizes of their receptive field centres (reviewed by Vaney 1994). This is not the function of the gap junctions between

parasol ganglion cells and amacrine cells (Crook *et al.* 1988; Croner & Kaplan 1995). According to our model, the inhibition from the axons of the large, coupled amacrine cells negates the excitatory effect of the current spreading through the gap junctions. It follows that blocking the postsynaptic actions of these amacrine cell axons with a cholecystokinin antagonist would enlarge the receptive field centres of parasol cells.

Inhibition from the axons of large amacrine cells also sharpened the responses of the model parasol cells to luminance contrast via disinhibition. The lateral inhibitory network formed by the parasol cells and the coupled amacrine cells functions in essentially the same way as eccentric cells in the *Limulus* lateral eye described by Hartline & Ratliff (1957), except that two electrically coupled cells are involved rather than one. Figure 3a shows that the amount of contrast enhancement produced by the large amacrine cells was greatest when they had long axons originating from their distal dendrites, as do the real tracer-coupled amacrine cells. These results suggest that the distinctive morphology of the large, tracer-coupled amacrine cells contributes significantly to their function.

Synchronous firing between parasol cells has been proposed to enable additional signals to be multiplexed in the optic nerve (Meister 1996). Our findings suggest at least two mechanisms that might promote synchronous firing in parasol cells responding to the same stimulus. The first pathway, via the dendrites of the large amacrine cells, would synchronize the activity of neighbouring parasol cells. According to our model, an action potential of 100 mV in a single parasol cell produces depolarizations of almost 2 mV in the neighbouring large amacrine cell. If this were sufficient to bring the amacrine cell to threshold, the resulting action potential would produce a depolarization of almost 2 mV in the neighbouring parasol cells. This hypothesis could be tested by studying a pair of parasol cells of the same subtype using intracellular electrodes. If transmission between parasol cells requires an action potential in the intervening amacrine cell, there would not be a simple, linear relationship between the voltage in the two parasol cells.

Meister *et al.* (1995) proposed a similar mechanism to account for the synchronous firing of neighbouring ganglion cells of the same type in the salamander retina. They found that the sensitivity profile for synchronous activation of two ganglion cells was smaller than the receptive field centres of the ganglion cells. These findings could be reconciled with ours if a single amacrine cell dendrite produced the excitatory input that synchronized the ganglion cells rather than the entire amacrine cell. It is likely that the action potentials in the large amacrine cells are generated at the beginning of the axons, which, in these cells, would be up to 200 μm from the soma at the distal tips of the dendrites. If the amacrine cells' dendritic membrane were not excitable, the action potential would be attenuated considerably as it was conducted toward the perikaryon (Rapp *et al.* 1996). This would also account for the small amplitude of the spikes recorded from the perikaryon of an amacrine cell like this in the rabbit retina (Taylor 1996). Further studies of the electrical properties of these dendrites, and more realistic, compartmental models of the neurons in the circuit will be needed to test this hypothesis.

Our model predicts that more distant parasol cells would be synchronized through a second pathway. According to our model, the axons of the large, coupled amacrine cells produce a transient hyperpolarization in parasol cells over a large area. Parasol cells should become more excitable following this inhibitory input, as Lipton & Tauck (1987) saw at least one action potential following a hyperpolarization in all the isolated rat retinal ganglion cells they studied. A similar mechanism has recently been proposed to mediate the synchronization of pyramidal neurons in the visual cortex (Bush & Sejnowski 1996). The axons of the large amacrine cells may also be the source of the synchronous oscillations in ganglion cells observed over long distances in the cat retina (Neuenschwander & Singer 1996).

In summary, our findings suggest that gap junctions with amacrine cells increase the sensitivity of parasol cells to luminance contrast, make their light responses more transient and promote synchronous firing between parasol cells responding to the same stimulus.

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