Synaptic Connections, Receptive Fields, and Patterns of Activity in the Tiger Salamander Retina

A Simulation of Patterns of Activity Formed at Each Cellular Level From Photoreceptors to Ganglion Cells

[The Friedenwald Lecture]

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The function of the retina is to transform the pattern of the visual world impinging on the photoreceptors into patterns of neural activity at the ganglion cells. These patterns are then further processed by higher centers for perception. The retinal transformations appear to take place in a series of stages: the initial neural pattern at the photoreceptors is transformed by interactions at the outer retina into patterns of activity at the bipolar cells. Bipolar patterns, in turn, are transformed by interactions at the inner retina into more complex patterns at the ganglion cells. These patterns of activity are dynamic: retinal cells are most sensitive to changes in space and time. Dynamic patterns have never been measured or, as far as I can tell, even suggested. Viewing the patterns can provide some valuable insights into retinal signal processing. This report is an attempt to predict and generate the dynamic patterns of cellular activity within each retinal cell mosaic.

Most physiologic studies record the electrical effects of convergent inputs to single retinal cells, a tradition established more than 5 decades ago by Hartline1 and further developed by Kuffler2 and Barlow3 in the cat and frog. They characterized the so-called “receptive fields” by measuring ganglion cell activity elicited by simple stimulus patterns. In an alternative single-cell approach, Maturana et al4 showed that retinal ganglion cells in the frog responded exclusively to a limited number of more complex stimulus patterns representing important (trigger) features of the frog’s visual environment. In an extension of the receptive-field tradition, Werblin and Dowling,5 Kaneko6,6a and many others characterized the receptive fields of retinal cells distal to the ganglion cells using simple stimulus patterns.

The description of patterns of activity within mosaics of retinal cells represents an alternative approach for integrating and understanding retinal function. The specific patterns formed at each retinal level are functions of both the stimulus configuration and the information processing properties of the retina. Unfortunately, there is currently no way to measure these directly within the mosaic of cells at each retinal level because we lack the capability of recording simultaneously from large numbers of neurons. (Methods are currently being developed to achieve this capability.) However patterns of activity can be predicted based on the known connections between retinal cells and the responses to each component of synaptic input. In this report, information about connectivity and cellular function was assembled using a real-time visual-image processing computer called PIPE. It then generated predicted patterns of cellular activity in both space and time at each retinal level. The procedures are described in more detail in Appendix I.

The predicted patterns of behavior across each cellular mosaic are based on information assembled from data derived from many recordings from a limited number of identified cell types. We assume here that each identified cell type represents a much larger population of identical units that exist in sufficient density to generate the complete and readable pattern of activity within each retinal cell mosaic.

It is important to point out here that the patterns of activity are related to, but necessarily coincident with or derivable from, the receptive field properties of the cells. For example, we will encounter a retinal cell

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The videotape from which the figures were taken is available from the author.

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that receives input over one spatial region and delivers its output at a different lateral site. So its receptive field will be spatially separate from the activity pattern it generates.

This study makes some specific dynamic graphic predictions, in space and time, of complex patterns of retinal activity; patterns that are not obvious from earlier studies of receptive-field properties. We hope that the visualization of cellular patterns derived here will enhance our understanding of retinal function by providing a different and valuable perspective from which to view retinal processing.

The Form of Presentation, Stimulus, and Display

To the extent it is known, the connectivity between cells and the conventional receptive-field properties for each cell type will first be summarized. Then the activity pattern generated within each mosaic of cell types will be displayed. A functional dynamic view is taken through the layers of each of the five major cell types, with one additional cut through the level of the synaptic terminals of the bipolar cells. (There is some evidence that bipolar terminal activity is different from, and not reflected in, the behavior of the cell body.) All pattern activity was initiated by the presentation of a flashing or moving stylized insect-like target, brighter than the background. The activity patterns in the retina are displayed in a plane parallel to the receptor mosaic, so the viewing screen will be filled with cells at a given retinal layer, and activity in these cells will be indicated by the “lighting up” of the representative responsive elements within the mosaic of cells. The shape and dimensions of the target, approximately 10° high and 15° wide, were chosen so that it would be large enough for the retina to resolve in some detail, but small enough that one could view the broader patterns of neural activity generated by its movement on a video monitor over larger retinal areas. The PIPE simulation system is described in detail in Appendix I.

Receptive Field Properties of the Rods

In the tiger salamander the photoreceptors are about 10 μm in diameter corresponding to a visual angle of the order of about 1°,7 a rather crude spacing by human standards. If rods and cones received no synaptic input their receptive field would be set by the spatial extent of their photosensitivity, about 1°, as shown sketched in Figure 1B. However rods are electrically coupled so that some fraction of the activity of each rod is generated by its neighbors.8-13 Cones are less strongly coupled to each other and to neighboring rods.14 We chose here to couple the rods so that the signal in each rod is fed to its neighbor’s

neighbor to illustrate the coupling phenomenon for rods.13 A sketch of the receptive field for rods, with coupling included, is shown in Figure 1D.

The rod receptive field is dynamic. Rod coupling carries the voltage and time-dependent signals from each rod through the network in such a way that the dimensions of the receptive field for the network varies in time.12,13,15 Initially, after presentation of the visual target, activity spreads broadly, but later it contracts.

Patterns of Activity in the Rod Mosaic

Figure 2A shows the pattern of activity generated in the uncoupled cone mosaic by the target. Except for the rather crude spacing between cones, the target is represented with good fidelity. The activity pattern in the coupled rods is shown in Figure 2B. Although the image is blurred by the coupling, the general characteristics of the target are still clearly discernible. Thus coupling has the disadvantage of blurring the target but the advantage of decreasing the noise in each rod because populations of rods now share random fluctuations; for targets larger than the effective coupling area, the signal-to-noise ratio for rods is enhanced.

Receptive Fields for Horizontal Cells

Horizontal cells in the salamander have been shown to be extensively electrically coupled so that the sensitivity to illumination extends beyond the physical dimension of a single horizontal cell.16-20 Estimates of the dimensions of the receptive field for horizontal cells are in the range of 100-200 μm. The coupling in horizontal cells is modulated by the transmitter dopamine; under conditions where dopamine release is high the horizontal cells become less coupled.21,22 For purposes of illustration we fixed the coupling between horizontal cells to generate the receptive field shown in Figure 1F.

Horizontal cells respond more slowly than photoreceptors or bipolar cells. This is thought to be due to γ-aminobutyric acid (GABA) autofeedback. Horizontal cells have been shown to release GABA,23-25a and they are also sensitive to GABA that appears to modulate chloride conductance.26 It has been suggested that the reversal potential for chloride in horizontal cells is more positive than the dark potential.27 If this is the case, GABA release can modulate chloride conductance in horizontal cells in a regenerative loop. Under the right conditions, this feedback loop may be able to control the slower kinetics of the horizontal cell response.27 This GABA release and sensitivity also serves to chemically couple horizontal cells. The GABA released by one horizontal cell will
Fig. 1. Sketches of connections and receptive fields for cells at the outer retina. In each profile on the right, elevation corresponds to the magnitude in arbitrary units of the response elicited by a spot presented at each point in the two-dimensional terrain. The field covers a region 350 × 350 µm, and each small square is 10 µm on a side. The receptive field is sketched for a cell at the center of the grid. Dimensions of the receptive fields are derived from various measurements using spots or lines and converted by the methods of Lamb (1976) or Hare and Owen (1990). A. Sketch of individual rod and cone, about 10 µm wide. B. Profile of the receptive field for either a rod or cone. The response is elicited over the 10-µm area spanned by the area of the rod or cone. C. Sketch of coupled rods. D. Receptive field for coupled rods. Rod signals spread to neighbors and next neighbors, so the receptive field spans an area with radius of approximately 30 µm. E. Sketch of coupled horizontal cells. F. Receptive field for the horizontal cells. The horizontal cells are so strongly coupled that signals initiated as far as 100 µm contribute to the response. G. Sketch of an array of (not coupled) cones that receive antagonistic input from an array of coupled horizontal cells. The dark cone at the center of the array is recorded. H. Receptive field of cone receiving antagonistic input from the horizontal cell network. This field has an active central region (upward deflection) surrounded by an antagonistic (downward) surrounding region mediated by the horizontal cells. I. Sketch of connections of bipolar cell. Here an array of five cones, antagonized by the horizontal cells, provides synaptic input to the bipolar cell. J. Bipolar cell receptive field consists of a central region of activation (upward deflection) formed by the breadth of the bipolar cell dendrites, but antagonized by the horizontal cell network over a broader dimension. Possible coupling between bipolar cells is ignored here (Borges and Wilson, 1984).

act to depolarize and increase release in its neighbors (Kamermans, personal communication).

Patterns of Activity in the Horizontal Cell Mosaic

The pattern of activity within the horizontal cell mosaic is shown in Figure 2C. Because these cells are much more strongly coupled than rods or cones, the image of the target is more blurred in space. The spread of signals due to horizontal cell coupling in the salamander covers about 200 µm. This is consistent with other reports in the salamander and turtle, and it illustrates the role of horizontal cells in forming spatially extended antagonistic signals.

The time constant for the horizontal cell response was chosen as 200 msec, a value similar to that found in other studies. This time constant is a function of the background level, but changes in this value will not affect substantively the general forms of
Fig. 2. Patterns of activity in the photoreceptor and horizontal cell matrices. A. Pattern in uncoupled photoreceptors. The photoreceptors activated by the visual target are brighter than those not affected. The target is a white paper cutout intended to resemble a stylized bug about 20° wide. The representation is crude, but the fidelity is good enough to resolve the fine features of the bug. B. Pattern in coupled photoreceptors. The photoreceptors in tiger salamander and many other animals are coupled such that a fraction of the activity in any one bleeds across to its neighbors. As a result, the image is more blurred, but the bug is still resolvable. C. Pattern of activity in the horizontal cell matrix. A. Pattern of activity for a stationary target. The horizontal cells are more strongly coupled than the photoreceptors, so the image of the bug at this level is much more blurred. Fine features of the bug are no longer resolvable. D. Pattern generated by a target moving from left to right. The horizontal cell responds sluggishly, so the image of the moving bug is greatly distorted. The leading edge of the bug is dim (unexcited) because the horizontal cells driven by the leading edge have not had time to respond. The trailing edge is more brightly represented, but the activity of the horizontal cells extends behind the bug because activity in these cells decays slowly. They continue to be active for a short time after the target has passed. Both photoreceptors and horizontal cells hyperpolarize when stimulated by a bright target. Hyperpolarization is conventionally thought of as a turning off of neural activity, but in this display it is shown as bright.

As a consequence of the slow response time for horizontal cells, a moving target generates an even more blurred pattern of activity in the horizontal cell mosaic. This is because horizontal cells representing the leading edge of the target have not been illuminated for long enough to become fully active as shown in Figure 2D. The trailing edge that extends beyond the target is fully active because the horizontal cells have had a longer time to respond to the presence of illumination. Because they turn off slowly, the representation of the target by horizontal cells extends well behind the moving target. In general, the rise time of the horizontal cell response is faster than the decay, so horizontal cell patterns persist long after the target is extinguished or has moved to a different retinal area.

Interactions Between Cones and Horizontal Cells: The Generation of Cone and Bipolar Cell Antagonistic Receptive Fields

It is thought that the horizontal cells exert an antagonistic influence on the signal generated by the photoreceptors. For the most part this antagonism seems to be mediated primarily by negative feedback to cones. It is still uncertain whether horizontal cells even feed back to rods or feed forward to bipolar cells. At present there is no clear evidence for feedback to
rods or for an antagonistic surround in the bipolar cells found in rod-dominated retinas. The mechanism for the computation of antagonism at the cones is shown in Figure 3. The feed back appears to be mediated at both GABA_A and GABA_B receptors at the cones. We do not fully understand the relationship between the magnitudes of patterns of activity in horizontal cells and cones, but we assume that at each point in the horizontal cell mosaic the antagonistic effect at the cones is a monotonic function of the level of activity as suggested by Wu.

The interactions between cones and horizontal cells lead to an important spatial relationship: the light response of each cone is antagonized by synaptic inputs elicited by light from regions surrounding the cone, in areas spanned by the more widely coupled horizontal cell network. The resulting receptive field for each cone is concentric: light at the center activates the recorded cone, but light falling in adjacent regions antagonizes the cone response by a sign-inverting synapse from horizontal cells as sketched in Figure 1H.

Horizontal cells feed back to cones. Therefore all cells postsynaptic to the cones will show evidence of an antagonistic surround including the horizontal cells themselves. We do not generally think of antagonistic surrounds in horizontal cells, but they have been shown to exist. An annular flash always exerts an antagonistic influence on horizontal cells, but when horizontal cells are strongly coupled, the antagonism is outweighed by the agonistic effect of coupling. In these cells the antagonism reduces, but does not reverse the agonistic influence of the surround.

An explicit antagonism can be measured in those horizontal cells with very narrow receptive fields. These narrow horizontal cell fields resemble those of bipolars; the agonistic influence of coupling is small and can be outweighed by surround antagonism leading to a reversed response.

The antagonistic receptive field of bipolar cells appears to be formed primarily at the cone terminals by horizontal cell antagonistic interactions with cones. Bipolar cells do not appear to participate in this antagonistic interaction: their dendrites simply reach up to the cone terminals to “read out” cone-horizontal cell interactions. Bipolar cell dendrites then integrate the antagonistic activity formed across the local population of cones in contact with their dendrites. This view is supported by the finding that under conditions where the antagonistic effect is lost in cones, it is also lost in horizontal cells. A map of the receptive field for the bipolar cell is sketched in Figure 1J.

The lateral antagonism mediated by horizontal cell feedback to cones is responsible for at least four functions: (1) within the spatial region of bipolar cell sensitivity, antagonism limits the magnitude of response of the bipolar cell; (2) because the spatial sensitivity of the horizontal cell extends beyond that of the bipolar cell, antagonism constrains bipolars to respond to the difference in illumination between center (local, near the dendrites) and surround (within the broader range of the horizontal cells), a process often associated with contrast detection; (3) surround illumination appears to set the “gain” of the center response to light, capable of decreasing sensitivity by more than 1 log unit as surround illumina-

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**Fig. 3.** Diagram of antagonistic pathway from horizontal cells to photoreceptors. The two patterns from the photoreceptors and horizontal cells combine antagonistically. Horizontal cell activity decreases the release of transmitter from the photoreceptors. Computation takes place via a feedback synapse from horizontal cell to cones at GABA_A and GABA_B receptors on the cones. Horizontal cells also feed back to themselves (autofeedback) and may, in this way, control their own kinetics, possibly explaining why their response is sluggish. The lower panel shows the general form of representation in the bipolar mosaic where the ON bipolars that represent the target are bright, surrounded by OFF bipolars driven by the antagonistic horizontal cell shadow.
tion is increased, and because horizontal cells respond more slowly than bipolar cells, bipolar activity is at first fully expressed (following a flash) and later reduced by (the slower) horizontal cell antagonism.

Patterns of Activity in the Bipolar Cell Mosaics: Integrating Cone and Horizontal Cell Patterns in Space and Time

The cone–horizontal cell interactions that form the bipolar cell receptive field transform the visual message in both space and time to generate the pattern of activity in the bipolar cell mosaic shown in Figure 4. The interaction is dynamic, but it is displayed here at three different times in freeze-frame after the onset of the target. Figure 4A shows the pattern 50 msec after the target is presented, representing the initially unantagonized pattern of cone-to-bipolar transmission, before the onset of horizontal cell activity. Figure 4B shows the pattern after 150 msec, in the presence of horizontal cell antagonism. Here the horizontal cells have reduced bipolar cell activity, particularly near the representation of the center of the target but not near the boundaries. The horizontal cells have also generated an antagonistic shadow (inactivated the bipolar cells) in regions surrounding the representation of the target. Figure 4C shows the pattern after termination of the stimulus. The cones have ceased to respond and no longer drive the bipolars, but the antagonistic effect of horizontal cells on the bipolar cell

Fig. 4. Response patterns to flashing target in bipolar cells; freeze frame of the receptor-horizontal cell antagonism. A. Pattern of bipolar responses to initial presentation of the target. B. Response pattern after 100 msec: the horizontal cells have decreased the activity of the photoreceptors and generated an inhibitory shadow in regions representing the center of the target and surrounding it. C. Pattern shortly after the target is turned off and the photoreceptors are silent. A residual activity remains in the horizontal cells, leaving a shadow of antagonism. D. Response patterns to movement in bipolar cells. Because the horizontal cells respond sluggishly, their activity will lag behind that of the photoreceptors when the target moves. This is an example of how movement paints time into space. Events that develop slowly in the retinal matrix will lag behind events that develop more quickly. The leading edge of the target is bright because it has not been overtaken by the horizontal cell antagonism. The trailing edge of the target is embedded in the antagonistic shadow of the horizontal cell. Consistent with the representation of photoreceptors and horizontal cells, this bipolar cell also hyperpolarizes with illumination. The hyperpolarization is shown as bright.
mosaic has not yet fully decayed and is shown as a residual shadow of inactivity in the bipolars throughout the region of the target and surrounding areas that then slowly decays in time.

The relative dimensions of bipolar and horizontal cell spatial regions of sensitivity are crucial for achieving the contrast-enhancing effect seen in Figure 4B. If the effective horizontal cell spatial spread is equal to or narrower than that of the bipolars, there can be no computation of spatial difference and therefore no contrast effect. If the horizontal cell sensitivity is very broad, then horizontal cells are unaffected by local changes near the bipolar cell field. In this case horizontal cell antagonism mediates a broad and general decrease in sensitivity, acting more like a camera diaphragm, and local contrast effects are also lost. The contrast effect exists only when the horizontal-cell spatial spread is larger, but of similar order of magnitude, to the bipolar spread.

Figure 4D shows the pattern elicited in the bipolar cell mosaic by a moving target. Here the components of the representation of the bipolar pattern are distributed in space. The bipolar cells representing the leading edge of the target are the most active (brightest) since they have escaped from the slower inhibitory shadow of the horizontal cells. The trailing edge of the bipolar representation of the target falls within the inhibitory shadow of the horizontal cells, and therefore the activity of the bipolar cells at the trailing edge is reduced. The bulk of the inhibitory shadow trails behind the target over a wide area because the sluggish response of the horizontal cells that mediate the shadow is spread out in space by movement. These patterns show clearly how target movement acts to separate fast and slow retinal processing activity in space, a function that is not obvious from the measurements of receptive fields shown in Figure 1J.

**ON and OFF Bipolar Cells Generate Complementary Activity Patterns**

The retina contains two types of bipolar cells with light-elicited activity that is, in a sense, complementary. The activity of the "ON" type is increased by illumination; the activity of the "OFF" type is decreased by illumination. Both bipolar cell types are thought to be driven by the same synaptic transmitter from the photoreceptors, but this transmitter impinges on a different type of postsynaptic receptor for each bipolar cell type.

Because the antagonism mediated by horizontal cells is fed back to cones, the bipolar cells receive input only from the cones, already containing "surround antagonism." This precludes the need for a separate sign of horizontal cell antagonism to fit each bipolar cell type.

The patterns of activity for populations of ON and OFF bipolar cells is shown in Figure 5. The pattern in the ON type (Fig. 5A) consists of a central active regions surrounded of an antagonistic shadow; the pattern in the OFF type (Fig. 5B) consists of a central inactive (darkened) region surrounded by an active halo of (lighter) activity. These two patterns of bipolar cell activity carry the complete input patterns projecting to the rest of the visual system.

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**Fig. 5.** Representation of activity in the mosaics of ON and OFF bipolar cells. The target is moving in the upward direction. A. The ON bipolar mosaic represents the bright target with bright activity, trailed by a shadow of antagonism mediated by input from the sluggish horizontal cell mosaic; the OFF bipolar mosaic represents the bright target with darkness trailed by a halo of bright activity mediated by horizontal cell antagonism.
Patterns of Activity in ON and OFF Bipolar Cells Do Not Overlap in Space

The signal levels in the patterns of activity in the ON and OFF bipolar cells are sketched, relative to the position of the target that drives them, in Figure 6. These levels of activity are derived, for example, from earlier direct measurements by Werblin\textsuperscript{47} of single bipolar cell responses to moving spots. They are also consistent with the receptive field representations for bipolar cells in Figure 1J. Activity in the ON bipolar occurs in regions representing the bright target, and these are shown by the filled area in the upper panel. However, the activity of the OFF bipolars is depressed in the region of the bright target (these cells are driven by target OFF), but it is expressed in regions surrounding the target as shown by the filled areas in the lower panel. The OFF bipolar cell activity surrounding the target is slower than ON activity because the active regions of the OFF bipolar cell representation are formed by the slower antagonistic feedback from the horizontal cells.

Responses of the ON and OFF bipolars to flashing spots have previously been thought of as mirror images,\textsuperscript{5,6} but the observation that the ON and OFF patterns of activity lie in different regions of space shows that populations of these two cell types generate complementary but not symmetric patterns of activity.

Figure 7 shows the concurrent patterns of activity in the ON and OFF bipolar cell mosaics at three separate freeze-frame times after the onset of the target. To separate them, ON bipolar activity is shown in red, and OFF bipolar activity is shown in blue. Figure 7A shows the patterns of activity in the two bipolar cell mosaics 50 msec after the target was presented, before the horizontal cells were active. The target is represented with good fidelity by the ON bipolar cells and is not yet antagonized. Activity (depolarization) in the OFF bipolars has not yet been initiated by the horizontal cells at this early time. Figure 7B shows activity in the two bipolar mosaics at 200 msec after the horizontal cells have become active; the horizontal cells have partially suppressed the activity of the ON bipolars in the region of the target. The activity of the OFF bipolars, mediated by the coupled sluggish input from horizontal cells, is now expressed with poorer fidelity in the regions surrounding the target. This is a good illustration of the separation in space and time of the ON and OFF bipolar cell patterns. The patterns in both cell types preserve with good fidelity the zero crossings representing the boundaries of the target.\textsuperscript{48}

Finally, Figure 7C shows the bipolar patterns 100 msec after the target has been extinguished. The ON bipolars rapidly become inactive (the red pattern disappears), and OFF bipolar activity is now initiated in the region of the (now OFF) target. At the same time the activity of the OFF bipolars, mediated by the sluggishly decreasing activity of the horizontal cells, persists in regions surrounding the target. Surprisingly, at this time OFF bipolars are active in both the region of the target and in regions surrounding the target.

The separation in space of the activity of the ON and OFF bipolar cells is displayed even more dramatically when the target is moving (Fig. 7D). The ON bipolars respond rapidly and represent with good fidelity the position of the moving target, but the OFF bipolar activity, mediated by the slower horizontal cell antagonism at the cones, lags behind the ON representation, creating a trailing plume of low-resolution OFF bipolar activity. We found few conditions under which both ON and OFF bipolar activity coexisted in space, although activity is high in both bipolar cell types near, but not at, the boundaries of the target.\textsuperscript{48,49}

High-Pass Filtering at the Bipolar Terminal Mediates Responses to Change Signaling Only the Arrival or Departure of the Target

Much of the inner retina is driven by signals derived from ON and OFF bipolar cell activity after being "high-pass filtered" at the bipolar terminals. That is, only the rapidly changing portions of the signal are transmitted to more proximal cells; the
sustained activity is lost. One circuit that appears to mediate this change-detecting operation is shown in Figure 8. In this scheme, when the target is presented and a sustained signal arrives at the two bipolar cells shown in the diagram, the cells are depolarized, and transmitter is released from both terminals. The terminal at the left drives a GABAergic amacrine cell that makes synaptic contact with the GABA$_B$ receptor in the right terminal. This receptor, acting through a G-protein decreases the conductance of L-type calcium channels at the terminal that are thought to mediate transmitter release. With less calcium available, release from the right terminal is truncated. We have not yet measured the kinetics of...
the second-messenger system, but it may account for the necessary delay of about 100 msec required to allow the initial signal through the terminal. This appears to be one of several ways sustained signals initiated at the outer plexiform layer are converted into transient or change-sensitive signals at the output of populations of bipolar cells. Bipolar cells receive other GABAergic inputs\textsuperscript{54,55} and contain voltage-gated currents\textsuperscript{56} that may also contribute to transient activity.

The pattern corresponding to the high-pass filter is best revealed in a dynamic display showing that sustained activity is lost. The activity pattern is only active when the target is either flashing or moving; the pattern for a stationary target of fixed intensity fades into the background. The effects of the high-pass filter can be seen to some extent by comparing the patterns of the trailing component generated by the moving target at the terminal with similar, but non-high-pass filtered patterns in Figure 7D at the cell body. The high-passed patterns at the terminal are more constricted in space because the filtering eliminates the more sluggish activity that is expressed as the extended leading and trailing edges of the patterns at the bipolar cell bodies in Figure 7D.

\textbf{Bipolar Cell Terminals Drive Three Major Pathways in the Rest of the Visual System}

Figure 9A shows the major pathways from bipolar to ganglion cells. It is generally thought that the ON ganglion cells are driven primarily by the ON bipolar cells and that the OFF ganglion cells are driven by the OFF bipolars.\textsuperscript{57-60} The ON-OFF ganglion cells are thought to be excited by transient inputs from both the ON and OFF bipolar cells. Each of these pathways is intersected by inhibitory inputs from various types of amacrine cells at the inner plexiform layer (IPL). There are two major types of amacrine cell: a wide-field glycinergic cell that receives a transient input and generates a transient spike-like response and a narrow-field GABAergic cell that receives and generates sustained activity. The wide-field amacrine cell is the counterpart of the horizontal cell in the IPL in that it seems to convey a lateral antagonistic signal. In all other physiologic characteristics, this amacrine cell is about as different as any cell can be from the horizontal cell. Table 1 outlines the differences between the amacrine and horizontal cells.

The transient and sustained amacrine cell types contribute to complex interactions that form receptive fields and patterns in the ganglion cells as described.

\textbf{Stratification in the IPL: ON-OFF, Transient-Sustained, and Rod-Cone Sublaminae}

Although the IPL at first appears to be an unintelligible tangle of processes from bipolar, amacrine, and ganglion cells, these processes are, in fact, very neatly organized. Famiglietti and colleagues\textsuperscript{61,62} showed that the outer half of the IPL was devoted to processing OFF signals and that the inner half processed ON activity. There are, in addition, other functional delineations to the IPL as shown in Figure 9B. The central area of the IPL processes signals that are rapidly decaying (transient), while the regions closer to the borders of the IPL process more sustained activi-
Fig. 9. General circuitry connecting bipolar cells to amacrine and ganglion cells. A. Sustained pathways: ON bipolar cells drive ON ganglion cells (left column). OFF bipolar cells drive OFF ganglion cells (next column). These bipolars also drive sustained ON and OFF amacrine cells (rectangular figures in right columns). Transient pathways: A separate class of ON and OFF bipolar cells, with processes terminating near the midline of the IPL (labeled ON OFF) appear to provide excitatory input to the ON-OFF amacrine and ganglion cells that also have dendrites near the IPL midline. The ON-OFF amacrine cells is shown by the inverted T-like figure spanning the diagram. These ON-OFF amacrine cells cast a broad inhibitory shadow across all classes of ganglion cells. B. Functional architecture for the IPL. By correlating the morphology of numerous Lucifer yellow-filled cells with their function, a picture of functional organization emerges: transient activity is mediated at regions near the midline of the IPL, sustained activity is carried at regions closer to the boundaries. Rod dominated activity is carried at regions near the boundaries, cone mediated activity falls closer to the midline.

ON-OFF Amacrine Cells Receive Inputs Locally and Deliver Outputs Globally

The class of amacrine cells that responds transiently at ON and OFF is thought to be excited by the ON and OFF bipolars. These amacrine cells have processes that extend widely across the IPL by up to 500 μm as shown in Figure 10. By probing along the processes in a retinal slice (Fig. 10D), we found that these cells are sensitive to the excitatory synaptic transmitter glutamate only over the central 200 μm of the processes.

By using postsynaptic cells as a bioassay for release, we discovered that these cells release glycine.
over the entire spread of their processes. So these amacrine cells have a functional field like that sketched in Figure 11, with a localized input region and an extended output region similar to other amacrine cells described by Dacey.69 There are, in addition, various sustained GABA pathways that feed forward to ganglion cells and back to bipolar cells.51,53 The GABA signals are generated by narrow-field amacrine cells with processes that extend laterally only by 200 μm. This GABA inhibition is therefore local rather than lateral.70,71 One component seems to be responsible for the truncation of activity at a class of bipolar terminals (Fig. 8).51,53 The patterns generated by GABA-releasing amacrine cells are not explicitly included in this analysis. Since they collect locally from a small population of bipolar cells, and since their response is confined to either ON or OFF phase, their receptive fields will resemble those of the bipolar cells. The remainder of this report focuses on the ON-OFF amacrine cell types contributing to complex interactions that form receptive fields and patterns in the ganglion cells as described below.

Table 1. Function differences between horizontal and amacrine cells

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<tr>
<th>Characteristics</th>
<th>Horizontal cells</th>
<th>Amacrine cells</th>
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<td>Inputs</td>
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<td>Glutamate transient</td>
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<td>Transmitter release</td>
<td>Ca** independent transport</td>
<td>Vesicles, Ca** dependent</td>
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<td>Passive, graded transport</td>
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<td>Synaptic output</td>
<td>Feeds back to cones</td>
<td>Feeds back and forward</td>
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The transient and sustained amacrine cell types contribute to complex interactions that form receptive fields and patterns in the ganglion cells as described below.

Patterns of Activity in the Amacrine Cell Mosaic

Wide-field amacrine cells typically generate a single, slowly decaying spike at light ON and OFF,5,65-67 but it is still not known whether these amacrine cells actively propagate this spike to the ends of their processes or if the spike is generated at the soma and spread electrotonically to the periphery. We assume here that wide-field amacrine cells radiate activity from the central core to a distance of about 250 μm within the first 200 msec after activation, and this activity pattern is shown in Figure 12B.

Amacrine cells of this type receive transient excitatory input from bipolar cells at both light ON and light OFF. Their activity is elicited at ON and OFF, but the patterns of response to a flashing target at ON or OFF are indistinguishable (and therefore not shown here). However, Figure 12B shows that when the target moves, two broad clusters of activity are generated: one follows the target closely, and the other lags behind. These two clusters are formed by the inputs from the patterns of activity in the ON and OFF bipolar cells in response to movement (Fig. 7D).

The ON-OFF amacrine cells represent the clearest example of a disparity between receptive-field properties and patterns of activity. Their receptive field, determined by the inputs, is narrow, in the range of 200 μm, resembling the bipolar cell receptive field; their patterns of activity, determined by the outputs, range as broadly as the processes covering more than 500 μm. These broad outputs form an antagonistic shadow, mediated by glycine, that envelops the response of the ON-OFF ganglion cells.

Receptive Fields for Amacrine Cells

For reasons that are not entirely clear, the receptive-field properties of retinal amacrine cells have not been characterized adequately. Our recent findings suggest that most amacrine cells have receptive fields that resemble those of the ON-OFF bipolar terminals: they receive excitatory input from these terminals over a limited extent of their processes (about 200 μm near the amacrine cell body). A sketch of the receptive field would resemble that of the bipolar cell shown in Figure 1J. This is surprising, since a major class of amacrine cells in the tiger salamander has processes that range broadly laterally throughout the IPL covering up to 500 μm. This disparity in function is not well documented, but there have been some hints consistent with the notion that amacrine and bipolar cells have similar receptive fields.73 There is also now anatomic evidence that amacrine cells in other animals have local dendritic and global axonal regions.69

Receptive Fields of Ganglion Cells: The Formation of a Second Change-Sensitive Antagonistic Surround

The class of ON-OFF ganglion cells is thought to receive excitatory input from the both ON and OFF bipolar cells. These ganglion cells retain some of the receptive-field properties of the bipolar cells, but the ganglion cell receptive field is much more complex because a second set of inhibitory inputs, generated at the IPL by different types of amacrine cells, contributes a significant inhibitory component to the ganglion cell response. All ganglion cell types receive...
Fig. 10. Photomicrographs of Lucifer yellow-stained cells (Stewart, 1978) in retinal slices. A. Photomicrograph of the retinal slice with patch pipette attached to a ganglion cell (lower pipette) and a puff pipette releasing glutamate at the bipolar cell dendrites (upper pipette). B. Lucifer yellow-stained horizontal cell. C. Lucifer yellow-stained bipolar cell. D. Lucifer yellow-stained wide-field amacrine cell. Cells have processes that extend up to 500 μm laterally across the inner plexiform layer. They receive input at a local region near the cell body, but appear to release the transmitter glycine over the full extent of their processes.
AMACRINE CELL FUNCTIONAL FIELD

Fig. 11. Functional field for the wide-field amacrine cell. Because these cells receive input centrally but release glycine over the extent of their processes, they are believed to have morphologic features outlined on the left: a narrow dendritic region near the cell body, but axonal processes emanating from this central region in all directions. The functional field is shown on the right: cells receive input at a central region that spans less than 200 μm, but deliver their output globally over the full extent of their processes.

transient inhibition from the ON-OFF amacrine cells.72,74,75 At least one glycinergic input arrives through a population of wide-field amacrine cells with processes that extend up to 500 μm across the IPL, forming a lateral inhibitory net. A static view of the receptive field of ganglion cells, antagonized by the wide-field glycinergic amacrine cells is sketched in Figure 13A. The primary receptive field center, shown in yellow (B), and its surround, shown in blue (H), is embedded in a wider inhibitory field set up by the wide-field amacrine cell net. The population of these amacrine cells has narrow centers distributed across the field, shown in orange, and together they set up an inhibitory net that encompasses the primary receptive field.

The dynamic characteristics of the amacrine cell inhibition is shown in Figure 13B. This is a simulation of the time sequence of the magnitude of the primary field after activation of the amacrine cell net. Amacrine cells feed forward and “shunt” the ganglion cell membrane by increasing conductance to chloride. This chloride conductance, following amacrine cell activity, increases rapidly after a flash, then decays more slowly. The main effect of the amacrine cell inhibition is not on the spatial characteristics of the receptive field but on the time course of the development of the primary field.

Few descriptions of the full receptive field for ON-OFF ganglion cells exist, but one of the most complete descriptions was presented by Hochstein and Shapley76,77 for cat Y cells. They showed a series of narrow-field nonlinear units superimposed on the conventional difference of gaussians, not unlike the sketch in Figure 13. Shapley and Victor78 also proposed a function for what appears to be the counterpart of change-elicited activation of inhibition in cat ganglion cells, referred to as contrast gain control. The role of the change-sensitive surround has been directly measured in the salamander42 and cat.79 A spinning windmill pattern in the receptive-field periphery activated the change-sensitive (probably amacrine cell-mediated) surround. This spin caused a steady decrement in response to illumination in the central receptive field. A flash in the surround caused a decrement with time course similar to that shown in Figure 13B.

Patterns of Excitation in the ON-OFF Ganglion Cell Mosaic

A class of ganglion cells also responds transiently at light ON and OFF.5,18,19,68 These cells probably receive excitatory input from both the ON and OFF bipolar cells after high-pass filtering of unknown mechanism at the bipolar cell terminals. We color code activity in this class of ganglion cells with red, and the pattern of activity generated by the moving target in the ON-OFF ganglion cells is shown in Figure 12C. As described for more distal cell types, the leading cluster in this pattern is formed by the excitatory input from the ON bipolar cells, and the trailing cluster is formed by excitatory input from the OFF bipolar cells. This pair of images generated by a single target in the ON-OFF ganglion cells leads to a form of monocular double vision, but the next level of interaction eliminates this problem. Under normal conditions the trailing excitatory patterns in the ON-OFF ganglion cells will be overshadowed by the inhibitory patterns generated by the ON-OFF amacrine cells shown in Figure 12B. The combined effect of these separate clusters of activity is described below.

Patterns of Excitation and Inhibition From Distal Cells Are Combined in the ON-OFF Ganglion Cells Activity Patterns

All ganglion cells appear to receive transient glycinergic inhibitory input at ON and OFF, presumably from the glycinergic amacrine cells.42,50,68,72,74,75,80,81 The ganglion cell patterns, in response to a flash, can be broken down into a series of four freeze-frame time segments as shown in Figure 14. Within 50 msec after the target appears, the ganglion cells representing its location are activated (Fig. 14A). At this time neither the amacrine or horizontal cells have initiated antagonism. About 100 msec later the amacrine cells become active, and the ganglion cells,
Fig. 12. Response patterns at the bipolar terminals, amacrine, and ganglion cell mosaics to a moving target. A, ON and OFF bipolar cell terminal responses to target moving to the left. These are much more abbreviated than the patterns in Figure 7D because of the high-pass filtering at the terminal. The extended wake of OFF bipolar activity has been severely truncated. B, ON–OFF amacrine cell pattern to movement downward to the right. The amacrine cell activity spreads laterally by up to 250 μm (in this simulation, the spread is square). Amacrine cell activity forms two clusters that represent the input from the ON and OFF bipolar cells. C, Ganglion cell pattern to movement of the target to the right. The pattern breaks into two components that represent input from the ON and OFF bipolar cells. These ON–OFF ganglion cells represent one population of cells and are represented by a single color (red).
Fig. 13. Sketch of the components of an ON-OFF ganglion cell receptive field. A. A topographic view of a field similar to that shown in Figure 1J. The central concentric circles represent the spatial extent of bipolar activation (B) antagonized by horizontal cells that form the antagonistic concentric surround (H). The additional matrix of fields throughout the figure (shown in orange) represents the excitatory receptive field centers of the amacrine cells that form a second antagonistic surround for the ganglion cells (A). Although each of these excitatory fields is relatively narrow, the output from each field, carried by the amacrine cell axons, can extend up to 500 μm. Amacrine cell inhibition can extend broadly across the figure and inhibit activity in the center region. B. Change in receptive field vs time. The second inhibitory surround mediated by the ON–OFF amacrine cells affects the time course of events in the receptive field center. This figure shows the time course of the change in center receptive field profile after a flash that activates the surrounding ON–OFF amacrine cells. Amacrine cell activity, transmitted by glycine, acts to shunt the ganglion cell membrane and decreases the response of all components of the receptive field carried from the OPL by the bipolar cells with a time course similar to that of the amacrine cell response. The spatial domain covers 350 μm; the time spans 1 sec after the flash.
still excited by the bipolars, are inhibited by the amacrine cell system (Fig. 14B). In the simulation, we represent the pattern of inhibited excitation in the ganglion cells in white, falling within the blue inhibitory shadow of the amacrine cells.

Figure 14C shows that, after another 50 msec, the amacrine cell activity has spread still further laterally. At the same time, the horizontal cells by antagonizing cone activity, mediate a suppression of activity in the bipolars, so the center of the bipolar pattern lost. Consequently the ganglion cell pattern is also suppressed near the center (Fig. 14C). Finally, Figure 14D shows that, after another 50 msec, the excitatory input to the ganglion cells is lost due to the high-pass filtering at the bipolar terminals. The receding residual inhibitory action of the amacrine cell pattern remains active even though ganglion cell activity has ceased.

The relationship between the pattern of activity of each retinal cell type, as represented in the ganglion cell pattern, is made more apparent when the target begins to move as shown in Figure 15. The patterns separate into two separate clusters: the leading cluster represents the ON bipolar-driven ganglion and amacrine cell patterns; the trailing cluster represents the time-delayed signals generated by the antagonistic
input to the OFF bipolar cells. The ON-OFF pairs of excitatory patterns appear here as the red and white areas. Inhibitory patterns are shown here in blue and overshadow all but the leading edge of the moving target. Because of the parameters we chose in this study, only populations of the ganglion cells at the leading edge of the target fire (red) when they can escape from the inhibitory shadow of the amacrine cells. If the amacrine cell activity spread more rapidly, even less of the ganglion cell pattern at the leading edge of the stimulus would remain active.

The presence of the pervasive amacrine cell inhibitory shadow helps to solve the problem of an ambiguous double image initiated at the bipolar cell level and shown in Figure 12C. There a bright moving target is represented by two components in tandem by the ON-OFF ganglion cells. Amacrine cell inhibition eliminates the activity in the trailing component of the response leaving an unambiguous representation of the moving target at the leading edge of the representation.

**Directionally Selective Movement Detection May Be Mediated by Asymmetric Amacrine Cell Connections: Activity Patterns**

In many retinas there are classes of ganglion cells that respond best to movement in one direction and weakly or not at all to movement in the opposite direction as shown by Barlow and Levick in the rabbit. Ganglion cells with similar properties have been found in salamanders. Currently, it is thought that this form of directionally selective movement detection is mediated by an asymmetry in either the activity, connectivity, or shape of some class of amacrine cell. In the rabbit the key inhibitory transmitter seems to be GABA rather than glycine, and there appears to be an excitatory cholinergic amacrine cell mediating directionality. Although we do not yet know clearly how this system operates, an amacrine cell population similar to the one described in Figures 11 and 12 could mediate such an asymmetric effect if cells in this population could extend their inhibitory shadow in one direction, corresponding to the darkened region in Figure 11. Activity patterns for a population of amacrine cells displaying these properties is shown in Figure 16. (In a variation of this scheme, Wyatt and Daw suggested a complementary mechanism: directionality was due, not to inhibition in the null direction, but to a lack of inhibition in the preferred direction.) The amacrine cells sketched in Figure 11 also could be configured to accomplish this function.

When the excitatory input to the ganglion cells is included in the complex of activity, it becomes clear that the inhibitory shadow that itself moves preferentially to the right, is much more effective in blocking movement-elicited activity when the target is moving.
Fig. 16. Directionally selective amacrine and ganglion cells. When amacrine cell inhibition is constrained to spread only to the left, ganglion cells will be most responsive to targets that move to the right. A. With leftward movement, ganglion cell activity is caught in the leftward-developing inhibitory shadow of the amacrine cells. B. With rightward movement, the ganglion cell activity escapes from the leftward-developing inhibitory shadow. The patterns of all distal ON-OFF cell types are represented in the two clusters of activity seen in these directionally selective ganglion cells.

to the right as in Figure 16B than when the target is moving to the left as shown in Figure 16A. The rates and specificity of the detection scheme depend on the specific parameters chosen for the simulation. We still need to learn how quickly, and by what mechanism, signals are propagated along the processes of these amacrine cells, and how segments of the amacrine cells outputs could connect to ganglion cells.

The Patterns of Activity for Distal Retinal Neurons Can Be Found in the Final Ganglion Cell Pattern

Figure 17 illustrates the sites of origin for the components of activity that can be read in the composite response of the ganglion cell. The leading edge of the ganglion and amacrine cell responses are generated
by signals transmitted along the direct fast pathway from photoreceptors to bipolar cells. The trailing components of the response are carried by the antagonistic signals to the OFF bipolar cells mediated by the slower horizontal cell pathway. Most of the gan

glion cell excitation is overshadowed by a (blue) veil of amacrine cell inhibition, so only the leading edge of the target that has escaped far enough from this shadow can be expressed in excitatory activity (red). The forms of activity shown in Figure 16 illustrate clearly that most patterns of activity formed at earlier, more distal stages of retinal processing are represented at the ganglion cell level.

But the Horizontal Cell Activity Pattern Is Lost at the Ganglion Cell Level

Most distally generated patterns are retained at the level of the ganglion cells with one notable exception. The pattern of horizontal cell activity, so important in forming the antagonistic surround of the ON bipolar and for generating activity in the OFF bipolar, is lost at the ganglion cell level. Horizontal cell activity is antagonistic, so its explicit representation may be suppressed after only one synaptic transfer. More important, much of the horizontal cell antagonism is slow and may be lost by the high-pass filtering at the bipolar terminal. Although there is no explicit representation of horizontal cell pattern, the important function of the horizontal cells in separating ON and OFF activity in both time and space continues to be clearly represented in the separate clusters of ON and OFF activity in the complete ganglion cell activity pattern.

Have Patterns Been Described Before?

There is very little discussion in the current literature about patterns of activity in sensory systems. This is probably largely due to our inability to measure the activity of many neurons simultaneously in a neural sheet such as the bipolar or ganglion cell mosaic. Although patterns cannot be measured with electrode arrays, in a few cases these patterns of activity have been inferred from other types of measurement in some systems. Phillips et al measured the patterns of activity in somatosensory cortical neurons by recording from a single unit and, in sequential trials, by positioning that unit at different locations with respect to the target. A similar approach was attempted by Creutzfeld and Northdurft in visual...
GENERATING RETINAL PATTERNS

Fig. 18. System for generating retinal patterns. The PIPE processor is a real-time image processing computer. The computational matrix embodied in the PIPE processor is programmed with the data taken from retinal recordings. Visual patterns are presented to the processor via a video camera. The processor displays the patterns of activity within each mosaic of retinal neurons, and these patterns of activity are viewed on a video monitor. In the figures, arrays of retinal neurons from different levels will fill the display, and those elements that are active will light up.

cortical cells. Therefore it should not be impossible to confirm or refine the predictions made in this report by recording from single bipolar or ganglion cells. These studies are currently under way.

Different Roles of ON and OFF Bipolar Cells Determined by Stimulus Contrast Retinal Patterns

For a bright target, such as the one used in this study, the activity of the ON bipolars tracks the target while the activity of the OFF bipolars lags behind. However, if the target were dimmer than the background we would predict that the OFF bipolars would respond more quickly and track the target while the ON bipolars, now driven by sluggish horizontal cell antagonism, would define its wake. We have not considered complex target with components that are both brighter and dimmer than the background. Clearly there could be a possible source of confusion between functions of the two bipolar types, and it would be interesting to determine which stimulus patterns can generate these ambiguous neural patterns that might lead to retinal illusions.

For targets of either contrast, the trailing representation is suppressed by the antagonistic action of the ON-OFF amacrine cells. Therefore the representations that appear to be ambiguous within the bipolar cell representation are, to some extent, sorted out at the ganglion cell level.

Many Complex Retinal Functions Are Not Represented Here

There are many retinal interactions that have not been included in this report, mainly because they are too complex, poorly understood, or do not significantly affect the form of the patterns shown here. For example, the wide-field amacrine cells inhibit ganglion cells according to the scheme in Figure 9, with the main form of inhibition is shown in Figure 14. However these amacrine cells also inhibit each other, and they may feedback to bipolar cells. Voltage-gated currents add a complexity to the response of almost all retinal cells but, in most cases including the currents, would not affect the visual display of patterns.

The transfer functions at most synapses are inherently nonlinear, and the problem of response magnitudes in postsynaptic cells versus presynaptic activation has been sidestepped here. Circuitry in many cases is recurrent, which may tend to linearize synaptic transfer. For example, horizontal cells appear to feedback to cones but perhaps not rods; thus there will be signals that are not antagonized by horizontal cells. Our representation of surround antagonism uses a simple subtraction of horizontal cell activity from photoreceptor response.

The sustained ON and OFF pathways continue from bipolar cells to the ON and OFF ganglion cells, and these contacts lie in regions displaced.
from the midline of the IPL as shown in the diagram in Figure 9B. The behavior of these ganglion cells resembles that of the bipolar cells, but we have not included them here. ON and OFF ganglion cell activity is made even more complex by inhibitory input from a variety of amacrine cell types to ganglion cells and bipolar cells, and by the fact that their activity is further modified by voltage-gated currents.

Interplexiform cells represent another component of retinal physiology not included here. These cells have only a brief electrophysiologic history but seem to respond with slowly decaying currents at both ON and OFF changes in the visual environment. The interplexiform cells will be activated by any richly textured visual scene. Their role in overall retinal performance is not yet well understood.

Future Studies Will Measure Patterns Directly

In the near future the use of multiple recording electrodes will make it possible to verify the predictions of activity patterns presented here and to determine the more subtle effects of specific second-order pathways on ganglion cell response patterns. To the extent that the measurements differ from these predictions, our understanding of retinal interactions will be enhanced.

Appendix I

Method of Simulating Images of Neural Activity at Each Retinal Level

Programming the computer. The data from single-unit studies was translated into pictures of the behavior of populations of neurons using a real-time image-processing computer, PIPE (Aspex, New York, NY). The PIPE connections resemble the architecture of a generalized retina so it can be programmed to conform with the measured spatial and temporal interactions of a specific retinal structure. In PIPE, each frame consists of 256 × 256 pixels and represents a cell layer. Each pixel or group of pixels represents the activity of a retinal cell. The value of each pixel (cell activity) is a function of the appropriate distal and lateral pixels (analogous to synaptic inputs from other retinal cells), accounting for feed forward, feedback, and lateral retinal connections. We used reasonable values of spatial and temporal interactions derived from our and other studies of the tiger salamander retina to constrain the PIPE processor to simulate activity in this retina.

The PIPE generates patterns of activity for each retinal level that are displayed in space and time on a video monitor. A video tape of this activity is available from the author; the figures in this paper were photographed from the tape and can only suggest the dynamic properties of the retinal patterns.

PIPE hardware. Patterns of activity at each retinal level were generated using a real-time image-processing computer as illustrated in Figure 18. A television camera provided input at the rate of 60 frames per second, of 256 × 256 pixels, at eight bits of gray level. Four internal processing units executed operations on entire frames at 60 per second. These included arithmetic and trigonometric functions, nonlinear operations such as thresholding, and 3 × 3 convolution with masks that simulate lateral interactions in space and time. Up to 64 frames of data could be stored for use in intermediate operations. Output from any computation could be routed to a video monitor for immediate display of patterns of activity at each retinal level.

Programming the PIPE. The algorithms for the retinal model are summarized for each cell type. Photoreceptors were simulated as direct copies of the visual image, but with two additional computations. The resolution of the image was reduced by a factor of two to approximate the course "grain" of the photoreceptor mosaic by averaging the input through convolution with a 3 × 3 mask, then selecting every other pixel in both the horizontal and vertical directions. Each pixel then subtended a visual angle of about 10°. Coupling at gap junctions was simulated by several convolution operations coupled with a low-pass filter difference equation.

The spread of activity in horizontal cells was implemented using a series of convolutions and low-pass filter difference equations similar to that used for the photoreceptors. Two states of convolutions and difference equations were used and the weight, w, for horizontal cells was set larger than that used for the photoreceptors to implement both larger lateral coupling and slower response.

Patterns at the bipolar cell bodies were formed as the difference between the photoreceptor and horizontal cell patterns. Bipolar cell terminal patterns were formed as the high-pass filter response to the threshold bipolar cell body signal.

This bipolar cell terminal signal provided the input to the amacrine and ganglion cells. Lateral spread of the amacrine cell signal was formed by repeatedly setting each bit of every element to the "or" of that bit and the corresponding bit of its neighboring elements. This results in a ring of activity spreading out from every element once it reaches threshold. The extent of lateral transmission is limited by shifting all bits right after every other "or" operation. This causes the signal to die out after a lateral spread of 16 elements. Asymmetric lateral transmission in the wide-field amacrine cells is modeled using an asymmetric "or" operation which causes each bit to be set only if it or its level side neighbors are set. The final wide-field amacrine response is computed by an additional amplification, spatial spreading by convolution, and temporal low-pass filter operation performed on the laterally transmitted signals.

The ON–OFF ganglion cell response is formed by subtracting the wide-field amacrine response from the amplified transient bipolar signals and limiting the result to be positive. The spread of activity of horizontal cells and amacrine cells were simulated as described, but the dendritic spreads of the bipolar and ganglion cells were not included in this simulation.
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