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SUSTAINED AND TRANSIENT AMACRINE CELL CIRCUITS UNDERLYING THE RECEPTIVE FIELDS OF GANGLION CELLS IN THE VERTEBRATE RETINA.

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1. Introduction

The responses of amacrine cells were first reported by Werblin and Dowling [1]. These are the first neurons in the visual system to respond to change because they respond at the onset and offset of a light step. They are important for the feature extracting properties of retinal ganglion cells. The transient amacrine cell appears important to movement detection and directional selectivity of ganglion cells, properties found in most retinas tested, from frogs to monkeys [2,3,4].

Sustained amacrine cells were not initially reported by Werblin and Dowling [1] in the mudpuppy, but were later discovered and shown to be a high percentage of the amacrine cell population in salamanders by Maguire et al [5]. That sustained amacrine cells exists has important implications for how we model the retina, including the modeling of the receptive field center-surround and of the trigger features, such as directional selectivity, of ganglion cells (GCs). Thus, even today, studies that "take apart" the retina, identifying its elements and the connectivity of the elements, are important for conceptualizing even the most basic functional properties of the retina [6]. Putting the retina back together into a biologically consistent computational model is dependent on knowing much more about

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the relatively poorly defined amacrine cell population. The studies described here are an attempt to better define the retinal amacrine cells in the tiger salamander retina, but we are now beginning to successfully record from amacrine cells in the primate retinal slice using patch clamp methods (Maguire, unpublished observations). These methods, along with those of patch recordings from GCs in the mammalian retinal whole mount [7] and patch recordings of GCs in the primate retinal slice [8], should provide precise descriptions of the synaptic interactions in the primate inner retina and lead to powerful structural and predictive models of primate visual processes at the level of the retina.

2. Sustained and Transient Amacrine Cells

The salamander retina is relatively simple compared to that of fish, cat, or primate for example. However, even in the salamander there are many types of bipolar and amacrine cells. Many of the amacrine cells can be classified into two groups: neurons that respond with sustained or transient classical spiking to a light step [5]. The transient amacrine

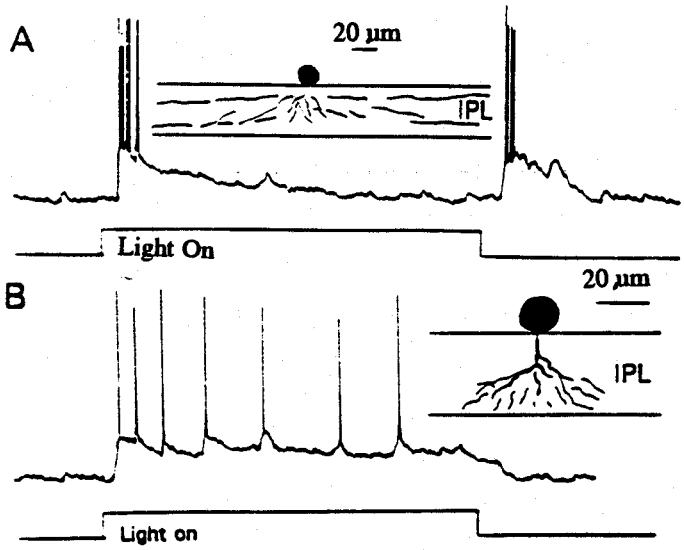

Fig. 1. A) Voltage response of a wide-field transient amacrine cell recorded using patch clamp methods in a retinal slice preparation. Stimulus: full field white light. Inset: Large lateral spread of processes in the inner plexiform layer (IPL). B) Voltage response of an ON type sustained amacrine cell. Continuous, regular spiking during the entire light step. Inset: Narrow spread of processes in the IPL.

cells usually respond to the onset and offset of a light step with a burst of spikes (Figure 1A), whereas the sustained cells respond with continuous spiking during the step (Figure 1B shows a sustained ON amacrine cell). Other studies have shown the transient amacrine cells to stain for glycine or GABA antibodies [9], while the sustained cells are often GABA positive [5].

3. Center-surround and receptive-field characteristics

Because the origins of the classical center-surround organization of the GC receptive field at the level of the bipolar/horizontal cell has been questioned [10, 11], another possible candidate, the GABAergic sustained amacrine cell can now be considered as a candidate for supplying the antagonistic surround. This is because GABA acting, either presynaptic at the bipolar cell terminal or postsynaptic at the GC dendrites, through a sign-inverting synapse, would oppose the sign-conserving (glutamatergic; see Massey and Maguire[12]) synaptic transmission from the bipolar cell terminal to the GC dendrites. Both glutamatergic and GABAergic synapses act in a sustained fashion and can be mutually antagonistic [13].

The light responses of the bipolar cells in the slice are sustained [14] and they presumably release glutamate onto the sustained amacrine cells in a tonic fashion. The glutamate receptors in the sustained cells have a large non-desensitizing component, and underlie the sustained EPSC [15]. In contrast, the transient amacrine cells respond to the sustained release of glutamate from the bipolar cells with a transient EPSC. Underlying this transient EPSC are glutamate receptors that rapidly desensitize in the presence of tonic glutamate release [15]. Control of the glutamate release from the bipolar cell terminals, and consequently control of the rate of desensitization of the glutamate receptors on the amacrine cells, can be achieved through activation of $GABA_B$ receptors in the bipolar axon terminal [16]. Further control of the amacrine cell's glutamate receptors may be achieved through postsynaptic $GABA_B$ receptors on the amacrine cells. These synaptic interactions are diagrammed in Fig. 2A.

The excitatory receptive field for the transient amacrine cells may be narrow. This is because only the processes close into the soma express glutamate receptors (Fig. 2B).

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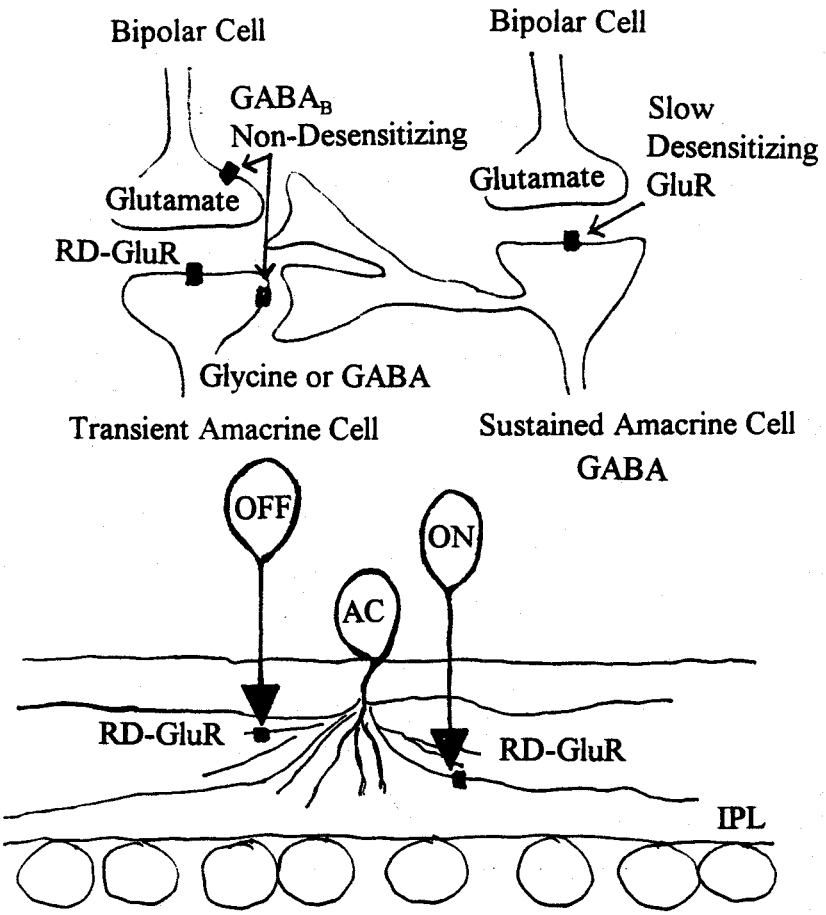

Fig.3. A) Synaptic interactions in the IPL responsible for sustained and transient EPSCs in amacrine cells. The transient EPSC in transient ON-OFF amacrine cells is at least partially mediated by rapidly desensitizing glutamate receptors, whereas the sustained amacrine cell's EPSC is mediated by slowly desensitizing glutamate receptors. GABA plays a role in regulating the amount of desensitization. B) The excitatory inputs to the transient amacrine cell are confined to processes near the soma. The peripheral processes are output sites only.

Peripheral portions of the processes do not express functional glutamate receptors. Thus, ON and OFF excitatory inputs are confined to a narrow lateral extent, even though the processes of the transient amacrine cell extend laterally much farther. These characteristics are similar to the non-linear subunits recorded in retinal ganglion cells [17], that have ON-OFF non-linear excitatory responses with small linear receptive fields thought to reflect linear bipolar cell inputs. Although these transient amacrine cells

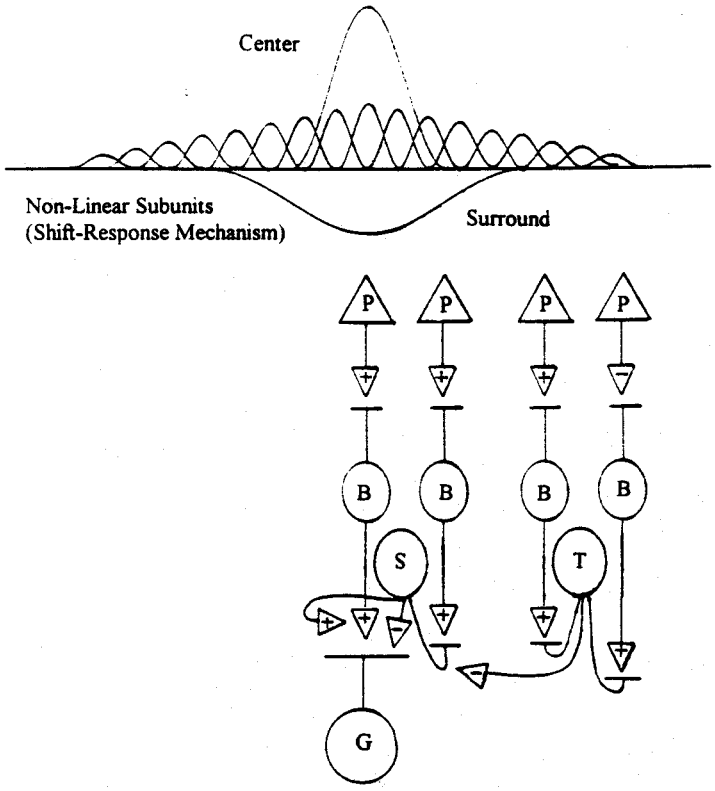

Fig. 3. Models of ganglion cell (GC) receptive field (RF). A) Model of GC RF center, surround, and non-linear subunits modified from Hochstein and Shapley. B) The liner center probably arises from bipolar cell inputs directly to the GC. The surround component may arise at the horizontal cell or amacrine cell (sustained type) level. The ON-OFF non-linear subunits reflect ON-OFF transient amacrine cell activity. The transient amacrines are inhibitory, and thus provide excitation to the GC through disinhibition of the sustained amacrine cells.

appear inhibitory [9], they are thought to provide excitation to the ganglion cells through disinhibition of other sustained, inhibitory amacrine cells [18]. Formalized computational models are now being developed to determine whether these amacrine cell interactions can account for the receptive field characteristics of the various ganglion cell types in the vertebrate retina.

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