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5. AUTHOR(S)

Dr Frank S. Werblin

6. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Dept of Molecular & Cell Biology  
University of California  
Berkeley, CA 94720

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11. ABSTRACT (Maximum 200 words)

A fully functional, real time dynamic model of retinal activity has been implemented on a high speed digital image processor. The model uses a complete set of physiological parameters derived from electrophysiological studies of synaptic transmission, cell coupling, voltage-gated currents and visual function in the retina of the tiger salamander. This model displays the patterns of activity generated at each sheet of retinal cells in real time, in response to any arbitrary stimulus pattern. Recent work measures both the patterns of activity and the activity of single units within the living retina itself at the level of the photoreceptors, horizontal and bipolar cells. These measurements are then correlated with the patterns generated by the model to verify the accuracy of the parameters and functions used to model the retina. For the most part, the correlations are quite close, suggesting that the parameters we have used and the functional relations between elements we have selected are adequate. A recording system using an array of electrodes to constructed and will be used during the next year to record patterns of activity. These patterns will then be compared with those generated by the model.

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# PROGRESS REPORT

## AFOSR -91-0196

January 27, 1994

### A PHYSIOLOGICALLY ACCURATE DYNAMIC MODEL OF RETINAL FUNCTION

Frank Werblin, PI

#### INTRODUCTION

This report covers the work performed during the last year. Each of the items reported represents the culmination of work proposed during the previous year's report. This work consists of two parts: 1) Development of a model of retina function based upon the full complement of physiological parameters derived from experimental data in the salamander, and 2) Verification of the model by comparing the patterns produced by the model retina with patterns measured in the living retina.

#### WORK DONE DURING THE CURRENT YEAR

##### Full retinal model:

The enclosed manuscript represents the culmination of 4 years of work defining the parameters of retinal function and incorporating these parameters into a fully functional model. The first part of the paper outlines the development of the retinal parameters used. These correspond to the synaptic functions that link the magnitudes of the synaptic gains for the different cell types throughout the retina and the space and time constants associated with these functions. Incorporating these functions into the model yielded a series of patterns that define the role of each layer in organizing the visual message. These patterns are displayed in the paper as wiremesh figures. As proposed last year, we also recorded from individual pixels in the model. These recordings correspond to what one would measure using conventional intracellular recording techniques in the living retina. This paper completes the first phase of the modeling of retinal function.

##### Comparing patterns in the model with those in the living retina:

During the current year we developed methods for measuring patterns of activity from all cell types in the living retina. The methods involved recording from a single representative cell, and in a sequence of experiments, moving the stimulus to all possible points with respect to that cell. This is equivalent to moving the cell to every possible position with respect to the stimulus. So the single cell then becomes the representative of all cells of that type, distributed in space with respect to the stimulus. These patterns are shown in Fig 1 where they are compared with the

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patterns generated by the model. In most cases the fit between the model and the physiology is quite good. There is a range of physiological outcomes that can be fit by adjusting the relative strength of center and surround in the model. This probably corresponds to normal differences in the strength of connections in the living retina. Since the time course of activity in the bipolar cells seems well fit by the model, there is probably no intervening process that we have not accounted for.

## **FUTURE DIRECTIONS FOR THIS WORK.**

### **Extending the result to encompass the full dynamic range of retinal function:**

The modeled patterns of activity and the single unit time courses in the outer retina fit the physiological patterns quite well. We have not yet tested the model to see if its dynamic range is similar to that of the elements in the living retina. Most of our synaptic transfer functions, based upon physiological recordings, define a very specific dynamic range for the networks involved, so it will be a good test of the model to measure this fit.

### **Recording multiple units with an electrode array:**

Most of our comparisons between model and physiology are based upon outer retina function. We now hope to extend these comparisons to regions at the inner retina. To accomplish this, we have assembled a system for measuring the activity of populations of ganglion cells using an array of electrodes and a multiplexing system for gathering the enormous amount of data that will be generated. This system is just about operational, and should provide the information we need for evaluating the functional relationship between all of the retinal components in our model.

With this system in place we will be able to look at the correlated activity across arrays of ganglion cells. Then we can assemble the activity of amacrine and bipolar cells according to the rules of retinal wiring to simulate these patterns. In this way we hope to be able to define network connections that cannot be measured by any kind of single cell analysis.

### **Generating a model of mammalian retinal function:**

All of the work described above applies to the retina of the tiger salamander, an example of lower vertebrate retinal function. During the upcoming year we will extend these results to encompass mammalian retinal function. Although less is known about the details of retinal physiology in mammals, we can borrow where necessary from the information we have available in the salamander where necessary. With these studies we will extend the applicability of the model to a broader range of problems. One possibility is that we will be able to perform a series of "what if" experiments, simulating both the pathology and the cure for a variety of retinal anomalies.

**Enclosures:**

1. Preprint of Paper #1 describing the retinal model.
2. Figures and captions for Paper #2 showing the comparison between physiologically measured and modeled patterns in the outer retina.

## ABSTRACT

A fully functional, real time dynamic model of retinal activity has been implemented on a high speed digital image processor. The model uses a complete set of physiological parameters derived from electrophysiological studies of synaptic transmission, cell coupling, voltage-gated currents and visual function in the retina of the tiger salamander. This model displays the patterns of activity generated at each sheet of retinal cells in real time, in response to any arbitrary stimulus pattern. Recent work measures both the patterns of activity and the activity of single units within the living retina itself at the level of the photoreceptors, horizontal and bipolar cells. These measurements are then correlated with the patterns generated by the model to verify the accuracy of the parameters and functions used to model the retina. For the most part, the correlations are quite close, suggesting that the parameters we have used and the functional relations between elements we have selected are adequate. A recording system using an array of electrodes to record simultaneously from populations of retinal output cells (the ganglion cells) has been constructed and will be used during the next year to record patterns of activity. These patterns will then be compared with those generated by the model.

# REPORT DOCUMENTATION PAGE

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## Figure Captions

Figure 1: Method of simulating the patterns of activity recorded in distal retinal cells. One cell was recorded, but the stimulus pattern, in this case a square, was moved, in a series of sequential experiments, to every possible position with respect to the cell's receptive field as shown in A. The data was then displayed simultaneously, with each response presented at a point in space that corresponded to the site at which it was recorded. The resulting pattern represents the behavior of a population of cells, each with properties identical to the recorded cell, but located at a variety of different locations with respect to the stimulus.

Figure 2: Overview of experimental procedure. a) A computer displays a repertoire of stimuli onto a display and simultaneously records the amplified intracellular neural responses. b) The recorded data for each cell is used to reconstruct the pattern of activity that would result if each cell in a layer responded as the recorded cell. This is done by first reconstructing an initial pattern which is used to determine the cell's receptive field center, then reflecting the data around the center to produce the final pattern.

Figure 3: Overview of model. a) The model consists of rods, cones, horizontal and OFF-bipolar cells. Each arrow represents interactions between cells included in the model. The labeled arrows designate non-linear synapses. b) The model for rods and horizontal cells was formed by incorporating experimental data directly into a lookup table. The Cone and bipolar cells were modeled as electrical circuits with light or transmitter controlled variable conductances. c) Exponential like functions based on experimental data was used to implement the non-linear synaptic functions. d) Spatial coupling between horizontal and bipolar cells was incorporated into the model, and adjusted to closely match experimental data. Details underlying the model outlined here are presented in (Teeters, Jacobs & Werblin, 1994).

Figure 4: Temporal response of model and data to a full field light step On at 200 ms and Off at 900 ms. There are large variations in the response between cells of the same type. (a) Receptors. Only rods were recorded. The model cone was formed from previously published data. The model rod was implemented to closely match the rod with the fastest Off-response. (b) Horizontal cell. The model cone and rod responses fell within the range observed. (c) Bipolars. Only Off-type Bipolars were recorded. The model cone driven bipolar response had a large depolarizing overshoot (only partially shown) which was not observed in the data. The model rod driven bipolar had an On response within the range observed, but an Off response close to the slowest observed. One bipolar had a bi-phasic response (Depolarization followed by hyperpolarization) with the peak of hyperpolarization about 1.2 seconds after the light Off.

Figure 5: Spatial response of data and model to stationary 300  $\mu\text{m}$  light bar. (a) Receptor responses (rods) were consistent with the midpoint of response closely matching location of the edges of the stimulus (dashed line). The model and stimulus are the same because rod coupling was not included in the model. (b) Horizontal cell responses were more varied. While the response of almost all cells leveled off to an asymptote with distance from the stimulus, in some cells the asymptotic level was hyperpolarized with respect to the resting level. This may be due to some global hyperpolarization caused by light scatter. The model response (Cones and rods were

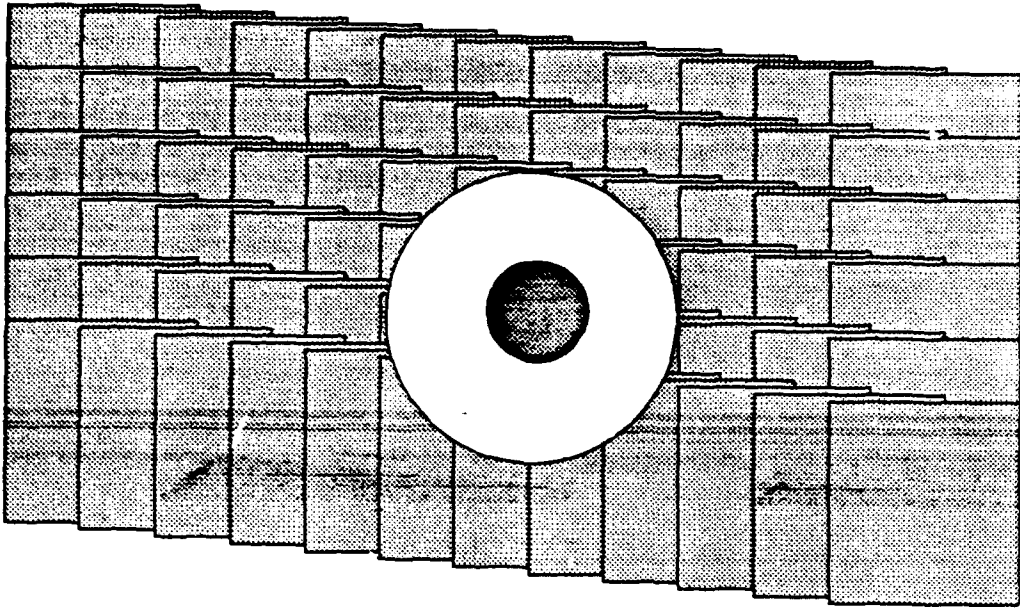
nearly identical) is close to the narrowest observed experimentally. (c) Most bipolar responses were close to the narrowest observed, as was the model. Two bipolar responses were much wider than the others. That could be due to different bipolar properties, or an improperly focused stimulus.

Figure 6: Rod pattern response to a moving and stationary 300  $\mu\text{m}$  square. Each mesh represents a square patch approximately 1000  $\mu\text{m}$  on an edge. The model response approximates the data in shape, but is narrower. The difference in width may be due to difficulties in focusing, or coupling between rods which were not incorporated into the model. <<Need to figure out why in spatial response to bar (previous figure) rod is narrower than stimulus, and here it is wider>>.

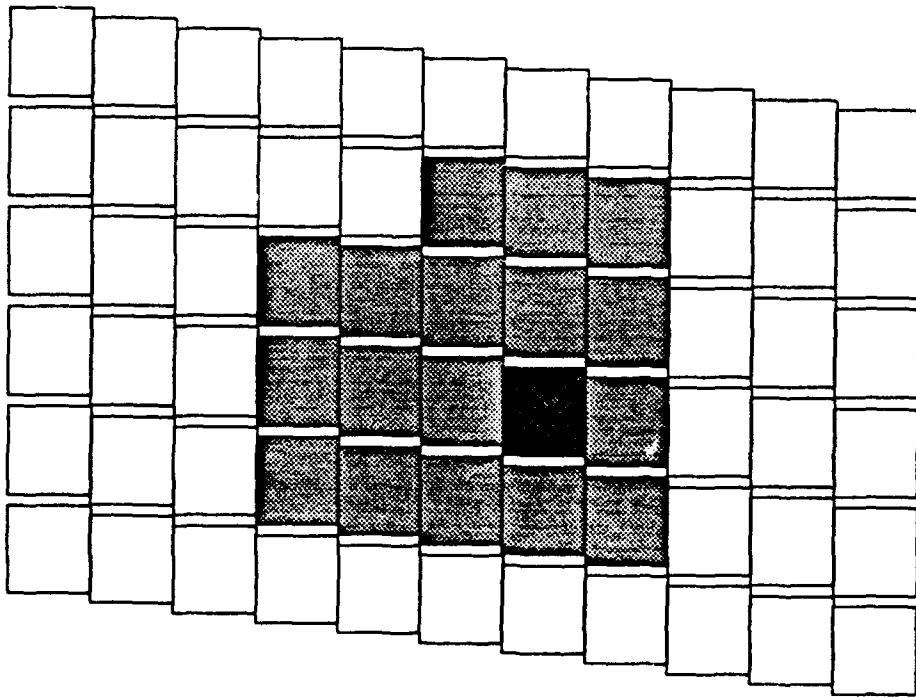
Figure 7: Horizontal cell pattern response to a moving and stationary square. Each mesh represents a 2000 x 2000  $\mu\text{m}$  patch. There is a good qualitative agreement between the model and data, although, the experimentally observed responses are somewhat wider.

Figure 8: Bipolar cell pattern response to a moving and stationary square. Each mesh represents a 2000 x 2000  $\mu\text{m}$  patch. There is good agreement between the model and rod-driven data, although the experimentally observed response is wider, and the Off response in the data is quicker than the model, and also has some hyperpolarizing side lobes that are not present in the model. The cone driven model response to the moving square has a fast Off response similar to that observed experimentally, but it also has a depolarizing overshoot which is not observed in the data. This suggests that a mix of cone and rod inputs to the bipolar would allow a better match between the model and data. However, the hyperpolarizing side lobes observed experimentally can not presently be accounted for by the model and represents an incompleteness in our understanding.

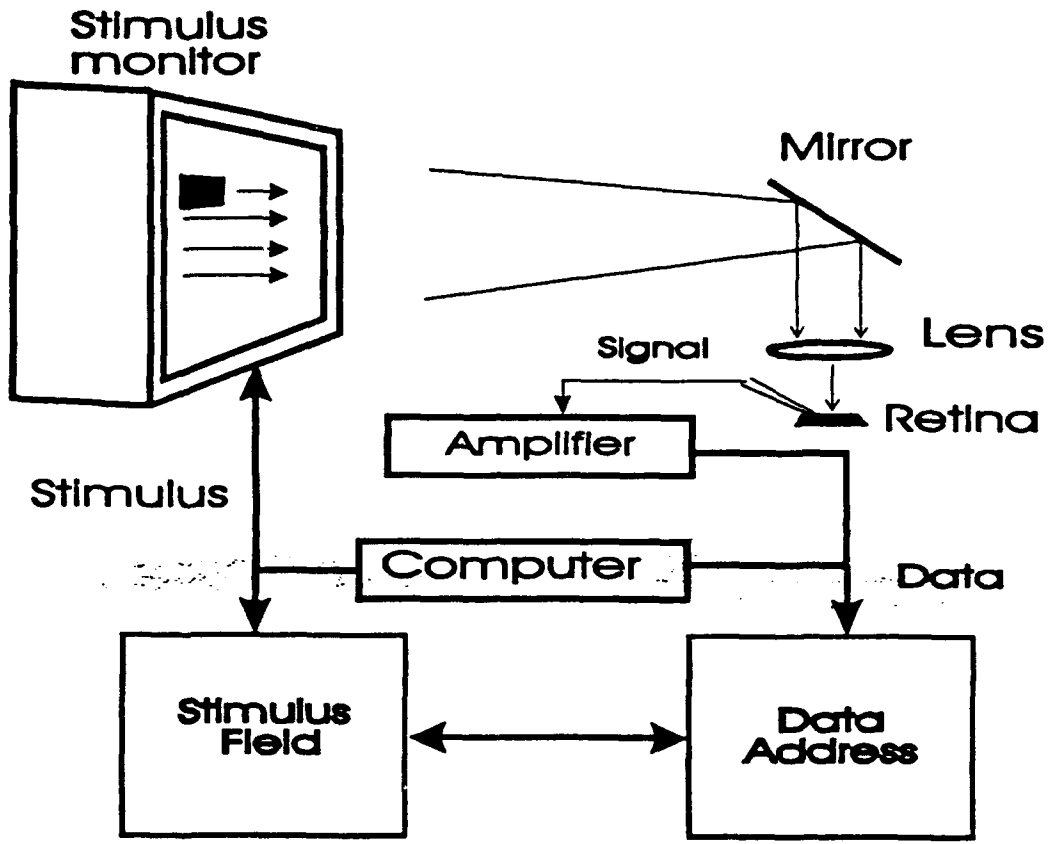
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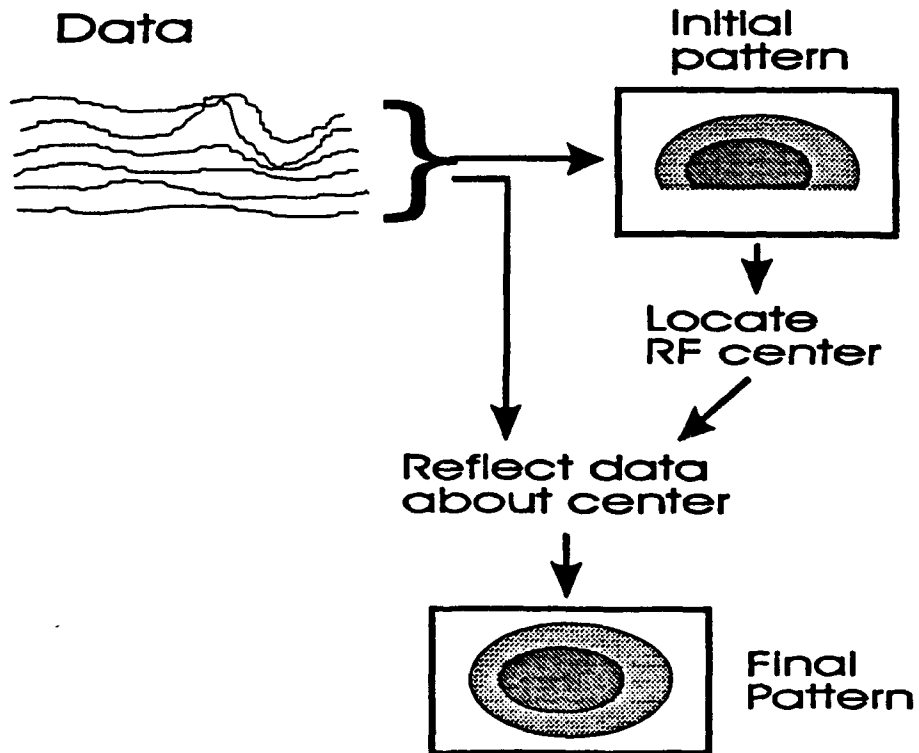
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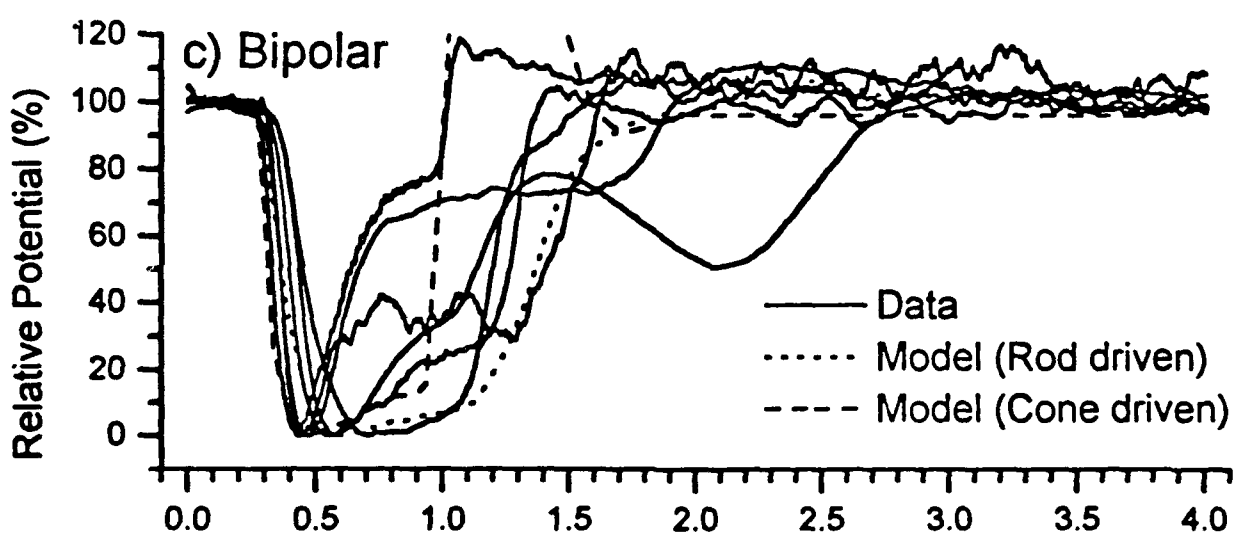
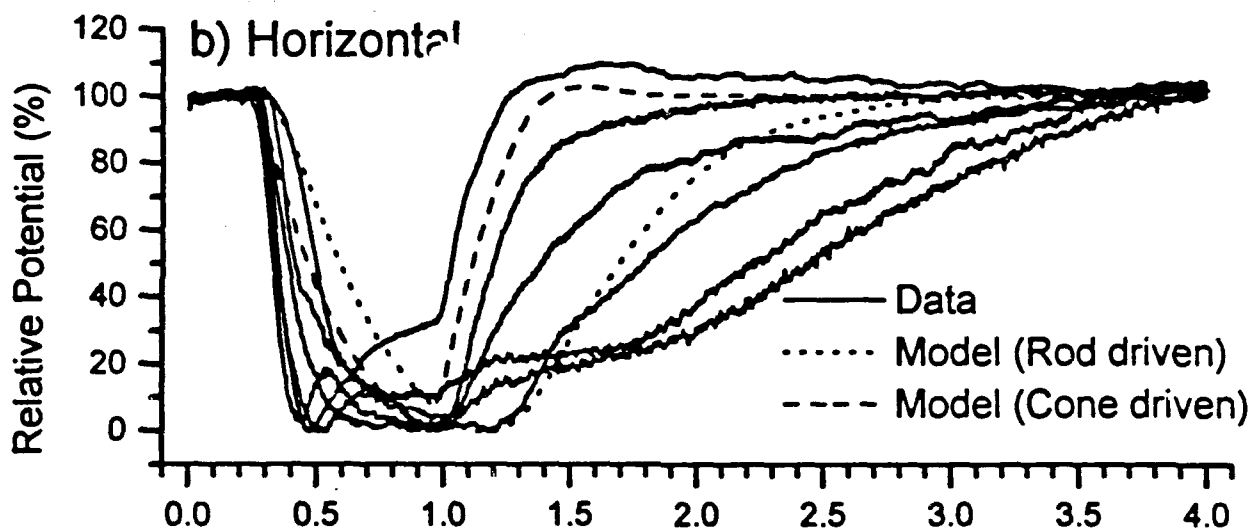
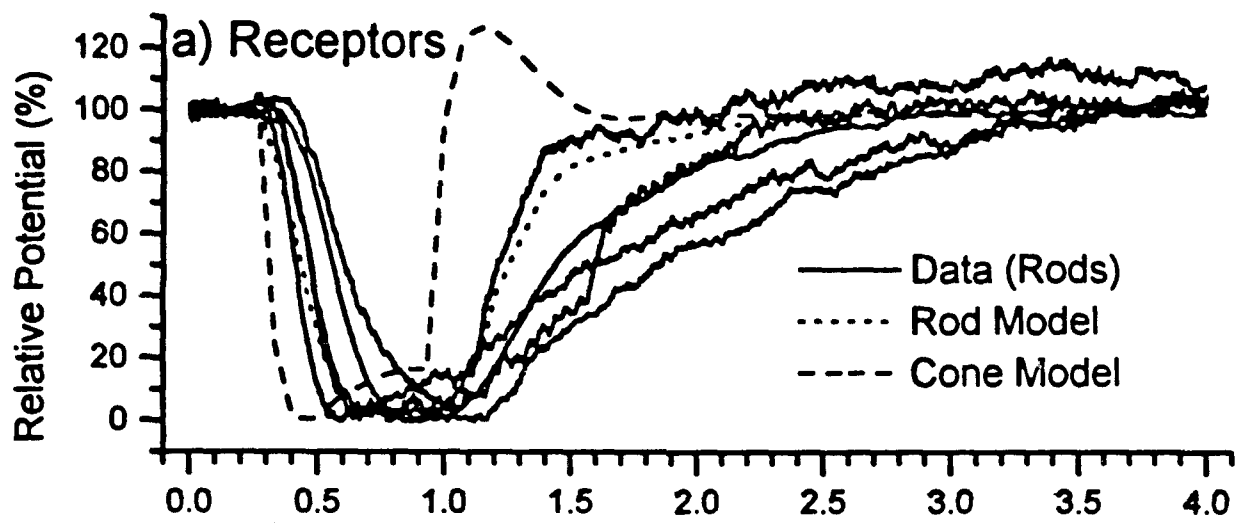
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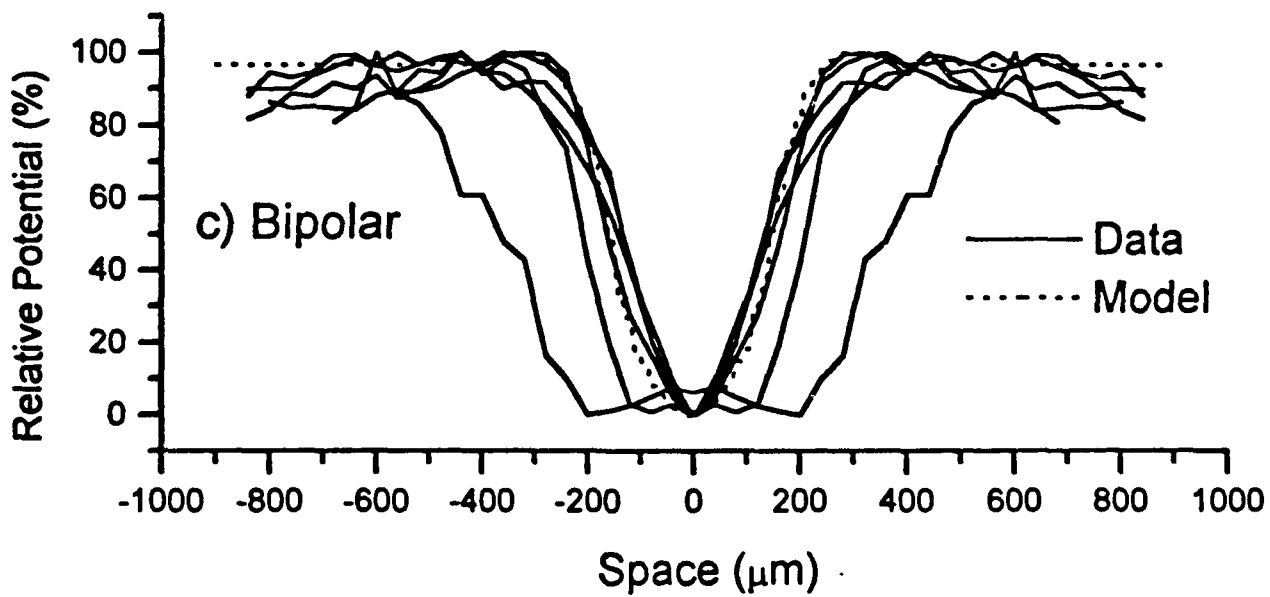
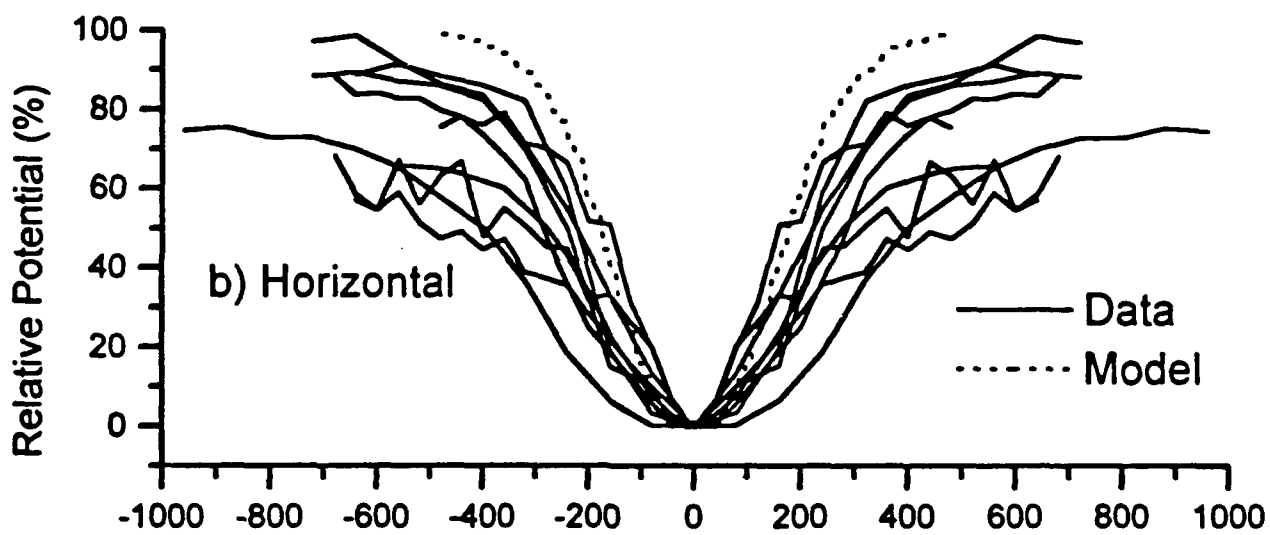
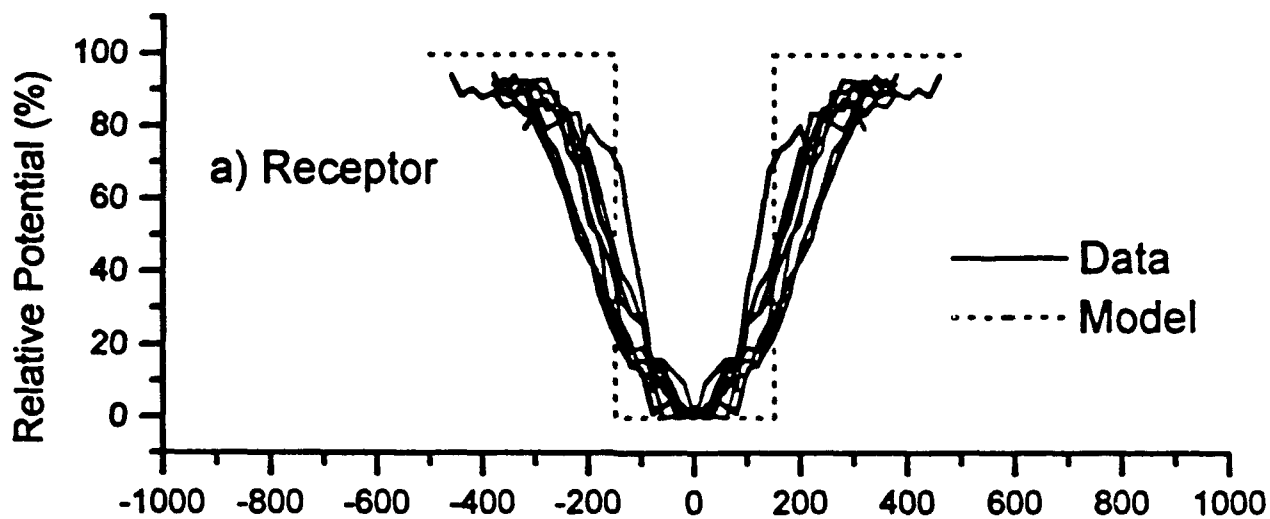


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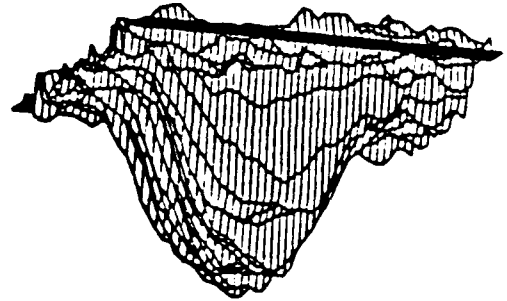
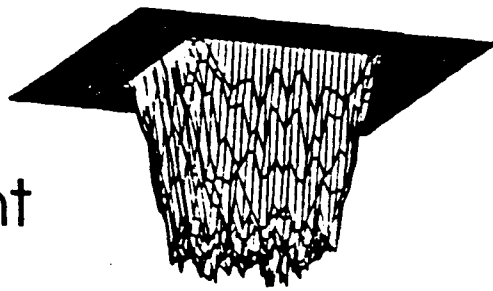




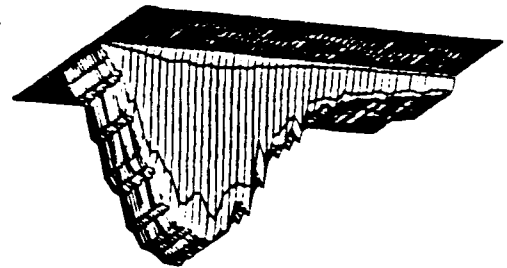
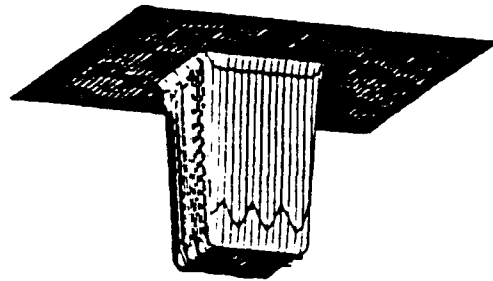
Stationary

Moving

Experiment



Model



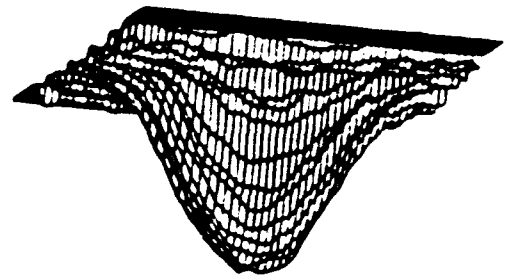
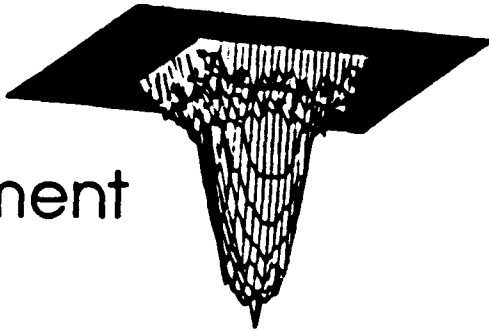
Rod response to moving and stationary square

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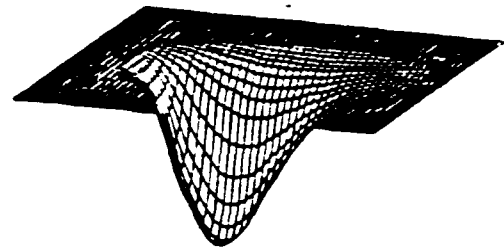
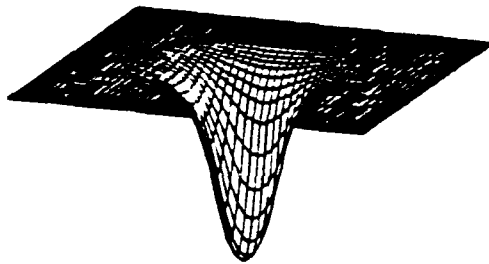
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Experiment



Model



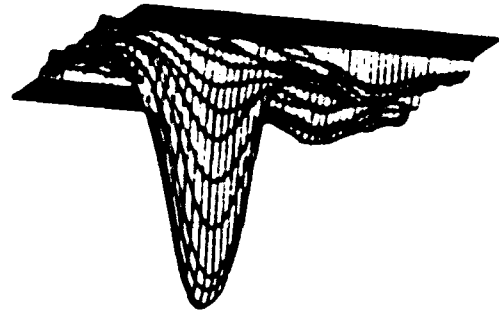
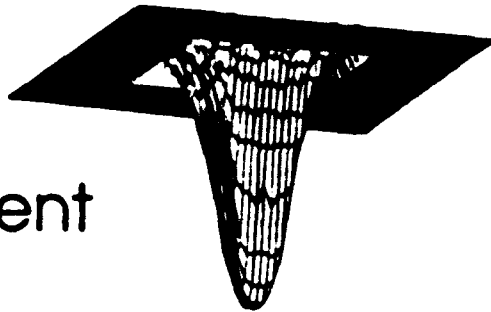
Horizontal cell response to moving  
and stationary square

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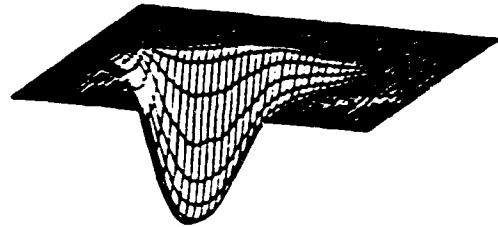
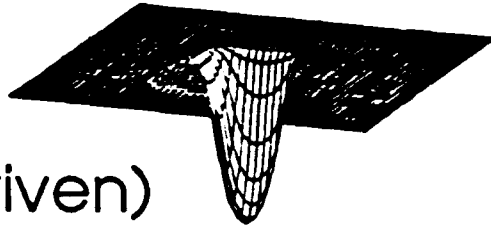
Stationary

Moving

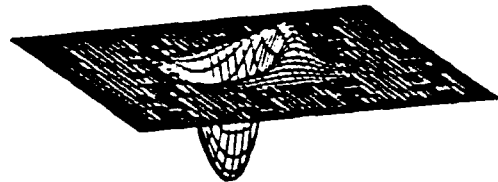
Experiment



Model  
(Rod Driven)



Model  
(Cone Driven)



Bipolar response to moving and stationary square

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