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Continuum Model of Light Response in the Retina

Shijie Yin, Nigel H. Lovell, *Fellow*, *IEEE*, Gregg J. Suaning, *Member*, *IEEE*, and Socrates Dokos, *Member*, *IEEE*

***Abstract*— A continuum model is presented of the retinal ON cone pathway to simulate the effects of light stimulation, motivated to provide validation of retinal response to electrical stimulation from vision implants. The model embodies four cell types involved in the direct pathway of light from cones to retinal ganglion cells. Center and surround mechanisms were incorporated through lateral inhibition via horizontal cells and convergence of inputs at the level of bipolar cells. Simulations were performed to investigate the network response to large and small spots of light. The results indicate the presence of surround suppression is correlated to spot size, consistent with experimental findings.**

I. Introduction

In the field of visual neuroscience the concept of receptive fields and spatial opponency in the retina has been around for over half a century [1], [2]. When the retina is stimulated with a spot of light, ON-pathway retinal ganglion cells (RGCs) at the center of the light spot are activated, whilst those at the periphery are suppressed. The formation of these center and surround patterns of activation and suppression are thought to arise due to several mechanisms. Visual information passes down from millions of photoreceptors to the RGCs, creating the center response. These photoreceptors however receive negative feedback from neighboring horizontal cells (lateral inhibition), leading to suppression of activation in the surround [3]. A consequence of this is that under identical lighting conditions cones at the center and periphery exert opposing influences on the bipolar cells (BCs). As such it is widely accepted that this center-surround mechanism is first observed at the level of the BCs, and the quantification of the response amplitude may be mathematically expressed as a sum of two Gaussians [3], [4].

Modeling the role of the retinal network in visual light perception is important in understanding how retinal prosthetic devices are able to restore vision to blind patients suffering from degenerative illnesses such as retinitis pigmentosa (RP). The ability of these implant devices to facilitate useful vision through electrical stimulation by taking advantage of the remaining intact retinal circuitry has been validated in several clinical studies where patients have reported light perception [5], [6].

It has been shown in RP patients that pockets of healthy retinal tissue still exist dependent on the progression of the disease [7]. This is of particular interest as the implant device covers a large area of the retina and is likely to stimulate both healthy and degenerate tissue. From a modeling perspective, lack of experimental data on paired recordings of pre and postsynaptic cells due to electrical stimulation insists upon examination of the retinal response due to light stimulation for model validation. A requirement of this is modeling the micro-circuitry, in particular the generation of center and surround which is still not well understood [8], [9].

A continuum model is presented to examine the effects of light stimulation in the ON cone pathway; this novel approach provides a cohesive means for model comparison and validation of previous studies of retinal response to electrical stimulation [10]. Center surround architecture is approximated through convergence of inputs at the BC layer, and lateral inhibition is captured through horizontal cells.

II. Methods

A. Retinal Micro-circuitry

Light is modeled as a current source hyperpolarizing the cone photoreceptor membrane potential [3]. Convergence of input then occurs at the level of cone BCs and relayed to RGCs: this is well documented in studies of the cat retina [11]. Micro-circuitry of the ON cone pathway was modeled with four cell types (Fig. 1): amacrine cell contribution to surround suppression was not implemented for this study. Consideration of specific cell types was made based on prevalence over the entire cell population. Beta RGCs are known to account for 50% of the population in the cat retina, with cone BCs making up 38% of the inputs [12]. In the primate, these RGCs are responsible for spatial acuity and make up 70% of the population [13].

B. Model Formulation

A 3D finite element model was developed to investigate retinal tissue activation (Fig. 2). The vitreous fluid and all relevant layers of the neural retina are modeled with constant conductivities and realistic thicknesses based on experimental measurements. Detailed description of the model formulation has been addressed in a prior publication [10]; a brief outline of all relevant aspects will be presented here.

An equivalent circuit diagram is presented in Fig. 3 representative of the cellular models: RGCs are modeled with an active implementation and the remaining cell types with a passive implementation. Detailed ionic mechanisms of the cones, horizontal and BCs were sacrificed for computational efficiency, as interest lies predominantly in the gross network behavior, particularly at the ganglion cell level. Previous computational models for these cells have been shown to be unnecessarily complex [14] as electrophysiological studies suggest that these membrane potentials behave passively [3].

S. Yin, S. Dokos, N.H. Lovell and G.J. Suaning are with Graduate School of Biomedical Engineering, University of New South Wales, Sydney, NSW 2052, Australia. n.lovell@unsw.edu.au.

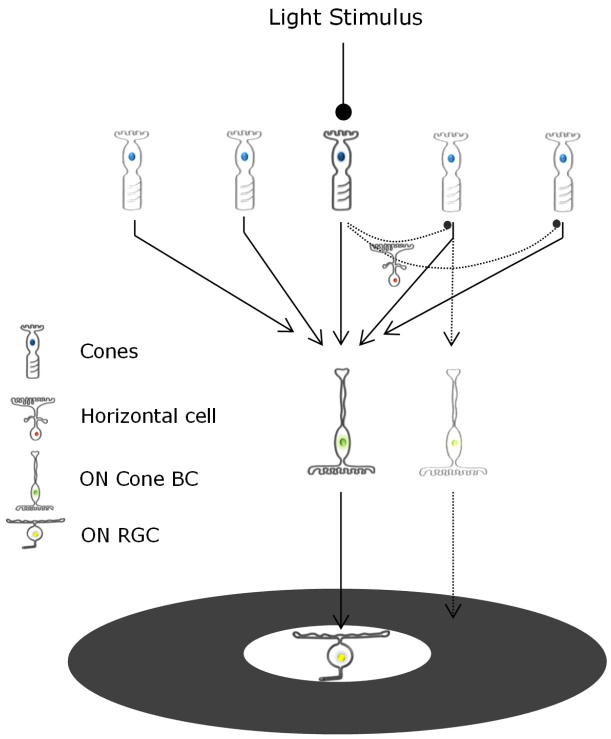

Fig. 1. Schematic diagram of retinal micro-circuitry, arrowheads represent excitatory presynaptic input, circles represent inhibitory presynaptic input. The direct pathway arising from light stimulation is shown by solid lines leading to an ON center response. Negative feedback via horizontal cells to neighboring cones and subsequent suppression of the surround is shown by dotted lines.

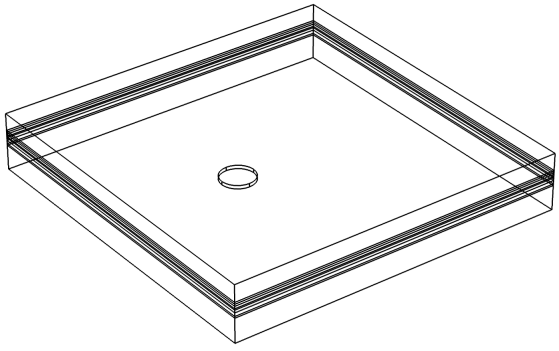

Fig. 2. Schematic diagram of the retinal model with a cylindrical domain located in the sub-retinal space with a radius of 0.2 mm. The dimension of the rectangular domain is 4 x 4 x 0.666 mm. Specific layer thicknesses are described in [10].

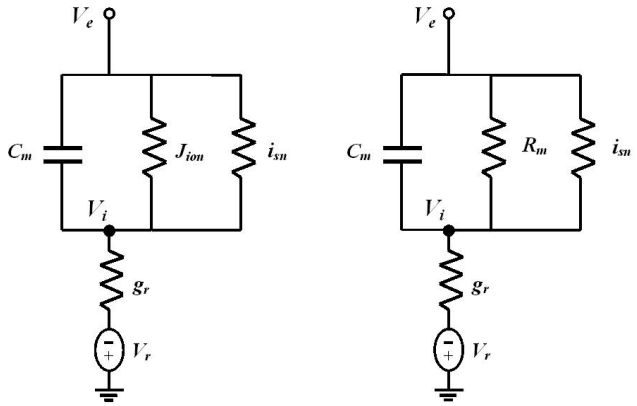

Fig. 3. Equivalent circuit of the active (left) and passive (right) membrane potential implementations. C_m represents the membrane capacitance, R_m is the specific membrane resistance, J_{ion} is the ionic current per unit area through gated channels in the cell's soma, i_{sn} represents presynaptic currents and g_r is the resistive tie connecting the intracellular potential V_i to a remote resting potential V_r.

Light stimulation was modeled by application of a synaptic current directly to the cones inside a cylindrical sub domain (Fig. 2). It is implicitly assumed that illumination is uniform throughout this sub domain. Stimulus onset occurred at 1 ms with a duration of 20 ms. Either a large (300 μm radii) or small (50 μm radii) spot of light was used. Convergence of inputs was estimated by assuming circular receptive fields, consistent with other studies [15]. Intrinsic membrane properties for cones, horizontal cells and BCs were obtained from [3], synaptic conductances and time constants were adapted from [16], and receptive field data was obtained from [9], [17]. Parameters were tuned to reflect the physiological behavior of each individual cell type, in particular the temporal and spatial characteristics to light stimulation such as an optimal response to a specific sized spot of light. A more detailed analysis is presented in the discussion section.

III. Results

Simulation results of the two light spot sizes are presented in Fig. 4. The spatial plots in Fig. 4A & 4B illustrate the activation of the cone, bipolar and horizontal cells at specified times of 5, 10, or 20 ms following light onset. Spatial suppression was observed in cones and BCs for the large spot size. The horizontal cell response however, was largely uniform showing a slight increase from 5 to 10 ms. Comparison of the cone response at 5 and 20 ms indicates a decline in the central region: this is also seen to a lesser extent in the BCs (Fig. 4C). The more interesting observation was the increase in suppression in the BC annulus. These spatial patterns were unique to the large spot of light, as uniform activation was seen in all the cell types for the small spot size (Fig. 4B & 4D). It may be noted that the spatial activation of the BC and RGC responses are not perfectly circular for the small spot size, due to the mathematical implementation of discretely pooling presynaptic inputs.

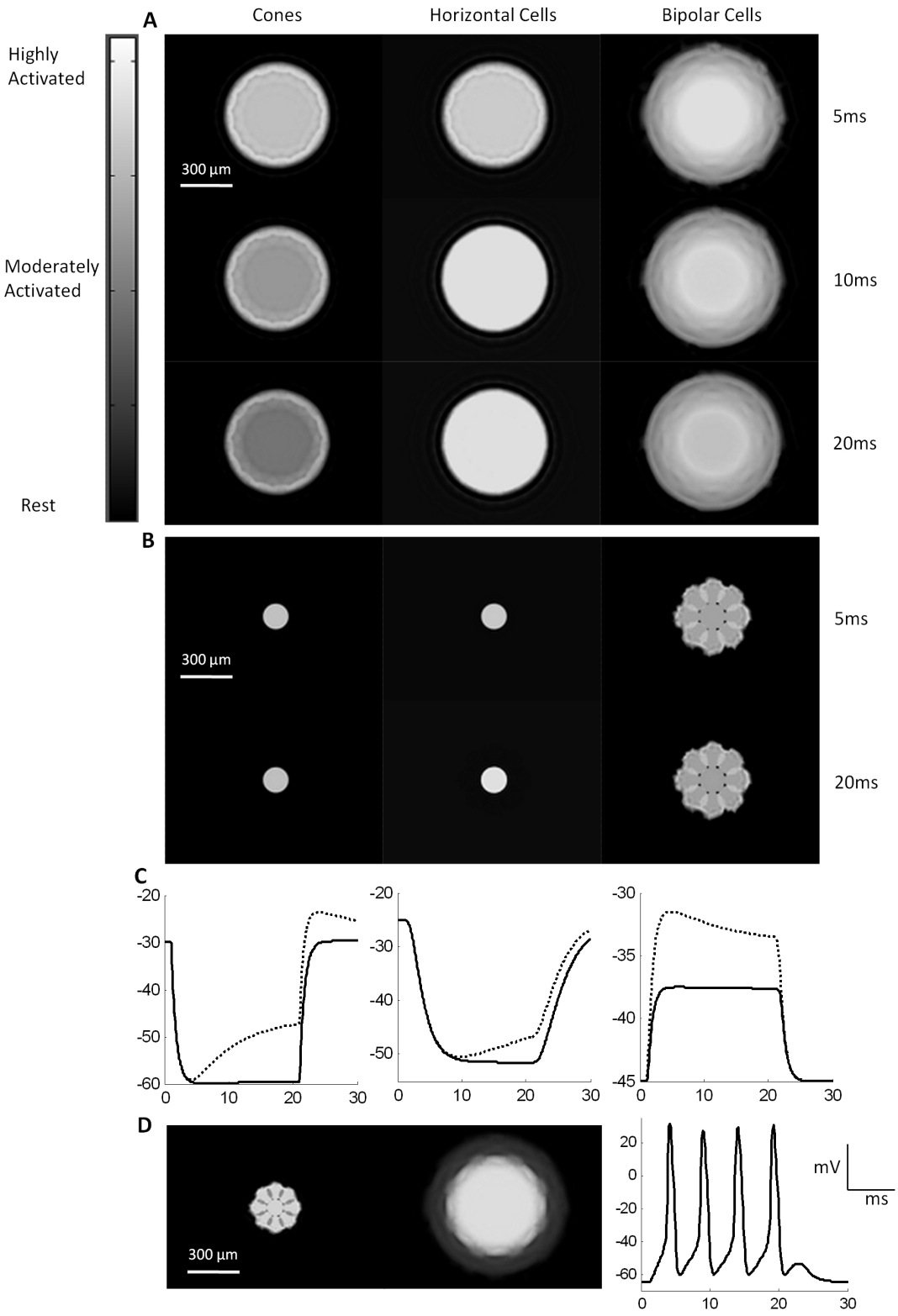

Fig. 4. Retinal response to light stimulation with 300 μm radius (A) and 50 μm radius (B) spots of light: light onset at 1 ms with a duration of 20 ms. Same activation legend was used for A, B and D. Cone, horizontal and bipolar cell spatial activation plots are shown at time stamps of 5, 10 and 20 ms for 300 μm spot size: 5 and 20 ms for the 50 μm spot. C. Membrane potential plots for cone, horizontal and bipolar cells (left to right) for both 50 μm (solid) and 300 μm light spots (dashed). D. Ganglion cell spatial response at the first action potential peak for 50 μm (left) and 300 μm (middle) spot sizes along with membrane potential response (right).

Temporal comparison of the two spot cases reaffirms this dependency of response based on size of the illuminated area (Fig. 4C), as an absence of suppression is observed for the small spot size. This suppression appears to be mediated with a delay through the negative feedback from horizontal cells, resulting in subsequent suppression of cone to BC activity and RGC activation. The RGC response (Fig. 4D) is also characteristic of the ON type, where an increase in spiking activity is seen at light onset and is maintained until light offset.

IV. Discussion

A continuum model has been described to examine the behavior of the retina in response to light. This may appear counter-intuitive to the generally accepted practice of summing two Gaussians to quantify the RGC response to visual stimuli [4], [18]. However, an accurate model of the retina to light stimulation is important in modeling the retinal response to electrical stimulation by a visual prosthesis. This preliminary study with further refinement provides a means of model validation for technically-difficult experiments where data is absent.

The exclusion of amacrine cells was made for the purpose of model simplification, as some studies have suggested only minor surround contributions in the primate retina [18], with a largely transient role in inhibition [3]. Other studies indicate that amacrine cells are responsible, if only in part, for the generation of surrounds [19], [20]. Regardless, the amacrine-RGC interaction presents a challenging problem, not only due to the sheer number of different cell types [13], but also the nonlinear response patterns. Therefore, amacrine cells may be excluded when considering the most direct pathway of light.

Early studies have outlined the concept of receptive fields in non-mammalian vertebrates: this has also been presented recently in studies of the primate retina [17]. Our simulations strongly indicate the presence of this antagonistic surround at both the BC and RGC levels, in agreement with experimental observations [17], [21]. This is directly linked to feedback of horizontal cells, which was modeled as an inhibitory input to neighboring cones. This center surround organization is then relayed to the RGCs through the BCs.

Experiments conducted with increasing spot sizes indicate an optimal size, where response amplitude increases until a peak is reached, after which a reduction in response is observed [17]. We were able to reproduce this to some extent, through the implementation of horizontal and bipolar cell receptive fields.

Horizontal cell responses have also been noted to be slower than both cones and bipolar cells, which give rise to a delayed suppression [3], [22]. This allows initial BC activation before the slow onset of the antagonistic surround: comparison of the first snap shots between the two simulations (Fig. 4A, 4C) highlights this observation.

V. Conclusion

This modeling study of retinal responses to light stimulation was undertaken to provide a basis for future validation of model parameters in order to investigate the response to electrical stimulation. The model was able to simulate the known response of RGCs to both small and large spots of light, and will serve as a useful basis for future models simulating the response of the retina to electrical stimulation by a visual prosthesis.

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