Influence of cell morphology in computational models of on and off retinal ganglion cells

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ON and OFF retinal ganglion cells (RGCs) demonstrate significantly different mechanisms in terms of activation and neural encoding. Recent experimental and modelling studies suggest that inherent biophysical properties play an important role in these differences. However, the contribution of their cell-specific morphologies is still unclear. Towards this aim, we have developed anatomically and biophysically detailed RGC models to understand the contribution of cell morphology to RGC responses.

In this study, ON (196 μm average dendritic diameter and stratified at a depth of 40% in the inner plexiform layer) and OFF (191 μm average dendritic diameter, at a depth of 70% in the inner plexiform layer) RGC morphologies were traced from mice retinas. Morphological data were digitized and subsequently imported into NEURON. In all simulations, an extension of an ionic RGC model (Fohlmeister & Miller, 1997) was optimized to reproduce ON and OFF RGC responses using a custom curvilinear gradient-based optimization method (Dokos & Lovell, 2004). Specifically, a hyperpolarizing activation current and a low-voltage Ca^{2+} current were added to the existing ionic model. These two currents are responsible for initiating rebound action potentials following hyperpolarization of the RGCs. We included in the model representations of soma, axon initial segment (AIS), axon hillock, axon and dendrites. The ionic channel distributions were set neuronal compartment-specific to reflect the proportion of ion channels in specific regions of the RGC.

In order to isolate the contribution of morphology to cellular responses, the ON and OFF cell models shared the same optimized biophysical parameters. Our model can reproduce experimental cell-specific responses in the two RGCs. Typically, OFF cells demonstrated significant rebound excitation while ON cells did not. In addition, these two cell types exhibited significantly different spiking frequency, response latency and Ca^{2+} dynamics. All of these responses closely match experimental observations (Margolis *et al.*, 2010). These results suggested that in addition to their inherent biophysical properties, RGC morphology can also significantly influence the responses elicited. Since all biophysics-defining model parameters were constrained to share the same values, the individual response of ON and OFF cells was solely dependent on cell morphology.

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