A Computational Network Model of Healthy Mammalian Retina Connectome

Ege Iseri*[(1)], Javad Paknahad[(1)], Guanbo Chen[(1)],Pragya Kosta[(2)], Kyle Loizos[(2)] and Gianluca Lazzi[(1)]
(1) Department of Electrical Engineering, University of Southern California, Los Angeles, CA 90007
(2) Department of Electrical and Computer Engineering, University of Utah Salt Lake City, UT 84112

Mammalian retinal degeneration can present itself in different ways including impaired vision, night blindness, elevated sensitivity and loss of peripheral vision. Degeneration typically progresses through three phases with increasing degrees of cell loss and a remodeling response by the retina to rewire lost or damaged retinal circuits. It is predicted that retinal remodeling induced by retinal degeneration starts before the symptoms manifest and is progressive over the course of three phases [Robert E. Marc *et al.*, Prog. Retin. Eye Res., 22(5), 607-655, 2003]. The remodeling process and how it alters the retinal network should be well established to classify degeneration mechanisms and the changes it causes in neural synapses.

To understand the degeneration mechanisms at the cell network level, it is important to have a reference point from the healthy retina connectome. Once the healthy connectome model is realized, we will have the capability to manipulate the network of cells with high precision, in a step-by-step manner. Some key features of retinal degeneration during the initial phases include abnormal sprouting of cell parts (axon, dendrites) that reach beyond their home plexiform layer and connections between cone bipolar and rod bipolar cells due to rewiring [Pang, J.J. *et al*., Proc. Natl. Acad. Sci. USA, 107(1), 395-400, 2010]. Isolating and successfully stimulating such changes in the network will be useful in identifying key components responsible for degeneration, with high specificity. Thus, our focus is to create a network model of healthy retina connectome using realistic morphologies of retinal cells.

In this work we implement a complete signal pathway for the healthy retina, comprising of the signal transduction from the photoreceptors to ganglion cells using NEURON simulation environment. The network is based on connectome datasets and TEM images of healthy rabbit retina. The cells are represented with passive membrane and active ionic currents that are implemented using conductance-based models. Manipulating biophysical parameters and cell topologies that govern the current flow along retinal cells to match the circuitry of degenerated states will lead to a better understanding of the signal transduction in the visual pathway. This knowledge will aid in development of optimized neural prosthetics that can better mimic retinal functionality for treatment therapies.