Biophysical vs reduced rate models for predicting retinal ganglion cell spike trains

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Abstract

Retinal ganglion cells (RGCs) respond to spatiotemporal patterns falling on photoreceptors by firing spike trains with an exquisitely precise temporal structure. Existing models of RGCs are reduced input-output models of light intensity or other features (eg contrast), but contain no biophysical parameters for a single RGC. These models, such as the stochastic integrate and fire (IF) and linear-nonlinear (LN) Poisson models are unable to account for the spike trains that are observed in actual data. The generalized linear model (GLM) is the most promising for reproducing the temporal structure of spike trains, even though it is not biophysically constrained. It would be an important result to generate a biophysical model of RGC spiking, and compare that model to one fit to the GLM to determine whether reduced models of that type are capable of capturing some spiking characteristics that full biophysical models contain. This paper analyzes some possible methods of comparison between these two types of models. It found that certain relations between elements of the two models reproduce actual retina data more faithfully.

1 Introduction

The retina, which lines the back of the eye, is the sensory organ that transduces light into electrical signals in many types of animals. It is responsible for coding visual information into electrical spike trains that are transmitted to the brain. The structure of spike trains contains the relevant information about a visual stimulus. Understanding the relationship between spike trains and information is important in understanding visual processing. The retinal is a particularly good neural circuit for examining this problem, because the full input-output relationship for a population of cells can be examined. The focus on pure information processing in the retinal literature has led to the development of many reduced rate models that describe the conversion of light into spikes in retinal ganglion cells (RGCs) the final common output cell of the retina. However, these models contain no biophysical information about neurons, and thus are missing an important amount of knowledge that has been discovered about how individual neurons generate spike trains. Comparing a true biophysical model to existing rate models makes it possible to investigate more thoroughly the failings of both types of models in producing characteristic activity in the retina, such as the highly temporally precise nature of spike trains.

To begin to compare these two types of models, it is necessary to understand the retinal circuit and how each model is built.

1.1 The retinal circuit

The retina is composed of multiple layers of distinct cells that each play a role in the initial stages of visual processing and signal transduction (figure 1). Light signals are not merely passed from one layer to the next; they are actively modified and decoded at each step [1]. The final output pathway of the retina is via RGC axons, which project from individual cells and come together to form the optic nerve, which travels to higher cortical centers.

The first layer of the retina is the photoreceptor layer. Photoreceptors contain pigments that are photoconvertible by different wavelength of light. This conversion leads to the spiking activity that is the first event in retinal processing. The second layer of the retina is formed generally from bipolar, horizontal, and amacrine cells, which are highly heterogeneous types of cells that form characteristic synaptic connections between other levels and cell types. The third and final layer is the ganglion cell layer, which contains both RGC somas as well as the nerve fiber layer, which is composed of axons projected from surrounding RGCs.

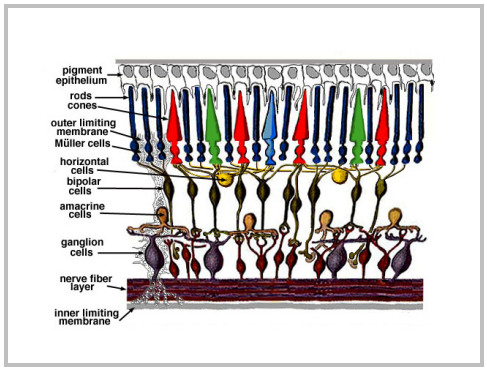

Figure 1: Diagram of signal transduction in the retina. Light excites photoreceptors, which pass the signal on to horizontal and bipolar cells, where processing occurs. Bipolar cells and amacrine cells converge onto RGCs.

1.2 Current state of retinal models

One of the central goals of retinal physiologists is to generate a full input-output diagram of retina activity. Meaning that, given an input (particular pattern of light or a visual scene) that falls on the retina, what will the spikes produced by RGCs look like? This is accomplished by building rate models, which take a visual stimulus, put it through one or more filters or nonlinearities that are supposed to represent visual processing in the retina, and output the activity of ganglion cells in terms of a spike rate. This is very different from biophysical modeling, because it captures none of the activity of a spiking RGC – no voltage changes, no channel gating variables, nothing. It derives from an electrical engineering perspective that is dominant in the field. However, because it does not incorporate information about cells, it fails to precisely reproduce the spike trains observed when an actual population of retinal cells is shown a visual stimulus.

Models like these take many forms, most of which are rearrangements of filters or terms, addition of nonlinearities, and variable numbers and types of parameter fits. The dominant rate models that describe retinal activity are the integrate and fire model (IF), linear-nonlinear Poisson (LNP), and a generalized linear model (GLM) (figure 2) [2,3]. The GLM is the most efficient model at reproducing the highly precise temporal structure of retinal spike trains, but it even fails under many situations and under a variety of parameterization strategies.

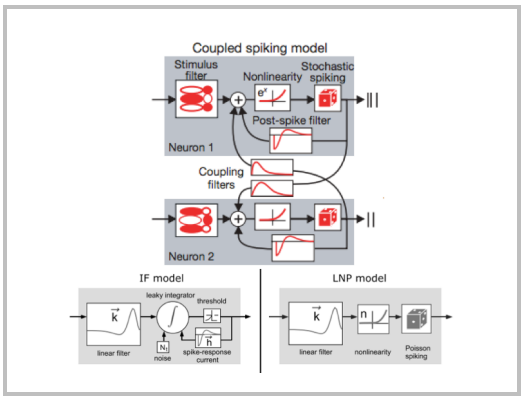

Figure 2: Diagram of three rate models used in the retina. Above is the GLM, in which a post-spike filter is applied before a nonlinearity and stochastic spiking. Bottom left is an integrate and fire (IF) model and bottom right is a linear-nonlinear Poisson model (LNP).

1.3 Objectives

In this paper, a basic biophysical neuronal model is compared to the fitted GLM in reproducing RGC spike trains. In particular, the GLM is simplified to eliminate its post-spike filter – primarily designed to capture biophysical constraints – and the upstream retinal circuitry is used to generate an input current into a Hodgkin Huxley neuron. The resulting spike trains are compared with the spike trains produced by the same visual stimulus by computing the Victor-Purpura distance [4,5].

2 Methods

2.1 A biophysical RGC model

There are several well-known biophysical models of general neurons. However, RGCs are very infrequently modeled in this way, therefore few examples existed which could be built upon. In light of this, it was chosen to model the RGC with a classical Hodgkin-Huxley (HH) model. This is because the HH neuron is very well characterized and its parameters can be fit to RGC spiking data with relative ease. This HH neuron was implemented in MATLAB as a single compartment model with the parameters listed (table 1).

Table 1: Hodgkin-Huxley Neuron

Parameter	Value
C_m	1.0 uF/cm^2
g_Na	120 mS/cm^2
g_K	36
g_L	0.3
E_Na	45 mV
E_K	-82
E_L	-59.387
alpha_m	0.1.*(V+45.0)./(1.0- exp(-(V+45.0) ./ 10.0))
beta_m	4.0.*exp(-(V+70.0) ./ 18.0)
alpha_h	0.07.*exp(-(V+70.0) ./ 20.0)
beta_h	1.0./(1.0 + exp(-(V+40.0) ./ 10.0))
alpha_n	0.01.*(V+60.0)./(1.0-exp(-(V+60.0)./ 10.0))
beta_n	0.125.*exp(-(V+70) ./ 80.0)

I_Na	g_Na .* m.^3 .* h .* (V - E_Na)
I_K	g_K .* n.^4 .* (V - E_K)
I_L	g_L .* (V - E_L)

2.2 Conversion of input current from rate model

The main variable examined in this model was the external injected current. Since the GLM models all the steps of light processing upstream from RGCs, to compare its output to that of a model with only RGCs, as above, there must be a common input. This was done by removing the post-spike filter and coupling filters from the model (figure 3). The model was then fit to data from a complete RGC population recorded on a 512 electrode multielectrode array. Briefly, a piece of primate retina was placed ganglion cell side down on a multielectrode array and superfused with oxygenated Ames solution. A white noise visual stimulus was projected onto the photoreceptor layer while electrical activity was being recorded on all channels. Spike sorting and cell classification was done according to previously described methods [6]. 800 parameters in the stimulus filter were fit with simple white noise data runs. The output of the modified GLM (mGLM) is a binned conditional intensity function that codes an instantaneous spike rate. After epoching the data based on bin size, the output was scaled to the largest bin and then mapped either linearly or exponentially onto an injected current that varied between 0 and 160 uA/cm^2 (figure 3).

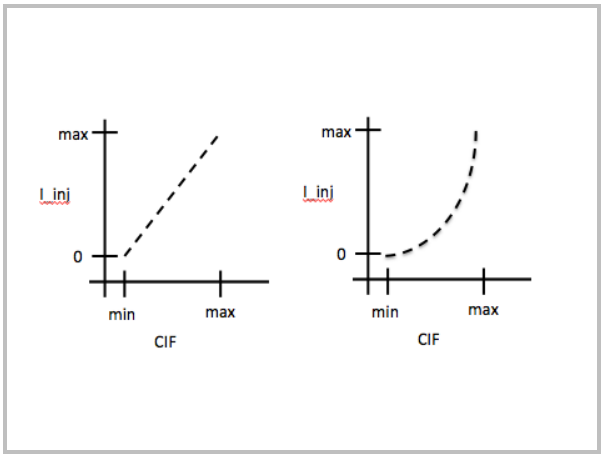

Figure 3: Linear (left) and exponential (right) conversion regimes from CIF to injected current.

2.3 Spike train analysis

Spike trains were analyzed in two different ways. First, because epoching binned data is imprecise, and an arbitrary threshold had to be set for determining the instantaneous time of a HH neuron spike, spike trains were optimally aligned via cross correlation prior to comparison. Second, the Victor-Purpura distance, which computes the distance between two spike trains by determining the cost of converting one into another using three basic operations, was used to compare spike trains to determine the optimal conversion of CIF to injected current for reproducing spike trains.

3 Results

A large number of current conversion regimes were attempted to determine the most efficient at reproducing RGC spikes. Spike trains generated from the HH neuron were compared to spike trains from real retinal data as described above. An example is shown (figure 4) in which multiple linear scalings of injected current from 4 to 44 uA/cm^2 were

tried and plotted against rasters (each representing a trial of the same visual stimulus) of retinal activity.

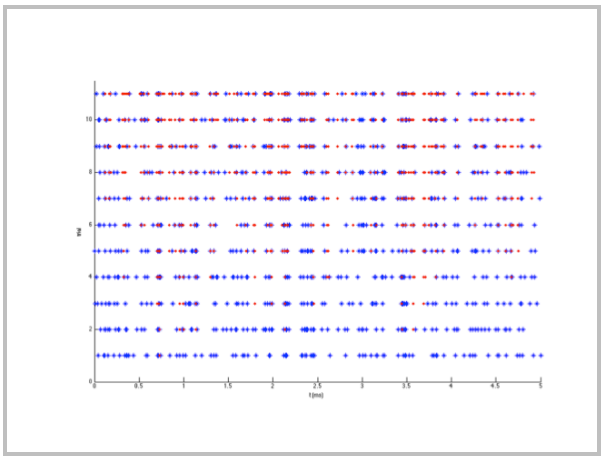

Figure 4: Linear current scalings from 4 to 44 uA/cm^2 (red dots) overlaid on trials of retinal data (blue dots) over 5s of visual scenes.

Victor distance calculations suggested that the optimal current conversion of all tested regimes was a scaling from 0 to 28 uA/cm^2, although even this produced fairly large deviations from observed spiking data (figure 5). Exponential current conversion was highly inefficient at producing spikes, even when the scaling was done on a scale of 0 to 160 uA/cm^2 (the largest injected current that results in HH neuron spiking). The injected current was not responsive enough to changes in the CIF under this conversion. Often times there were observed spikes when the model did not produce a spike.

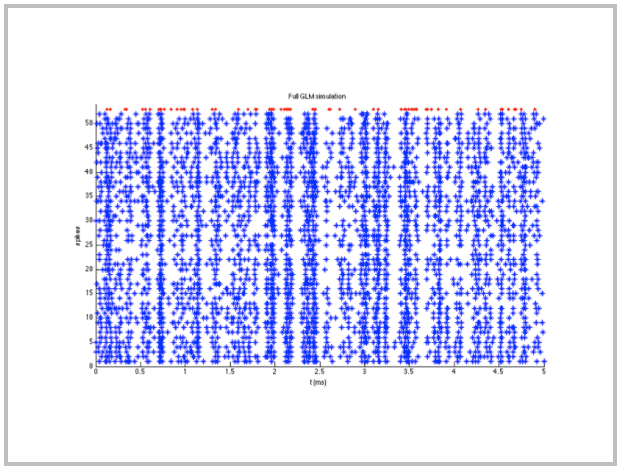

Figure 4: The optimal current conversion of 0 to 28 uA/cm^2 as determined by cross-correlation alignment of spike trains and Victor distance calculations shown in red dots vs retinal spiking data (blue dots).

4 Conclusions and Future Directions

The HH neuron with current conversion here showed some ability to replicate natural RGC spiking. Although the spike trains are obviously similar, the distance between predicted and observed spike trains is still quite large. The absence of predicted spikes suggests that this model is missing one of two critical elements. Stochastic spiking would produce spikes in

areas where injected current is low (occasionally) and likely increase the effectiveness of the model. Further, with the coupling filter missing there is no concept of correlated firing among the population, and this clearly contributes to retinal activity *in vitro*. This can be corrected by adding synaptic coupling between several RGCs. Additionally, since a generic HH model was used here, another biophysical model fit with parameters from RGC data should be generated and used to run these simulations.

5 References

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