

A Dynamical Model of Fast Intrinsic Optical Signal of Neural Burstings

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Abstract. Recent advances in optical imaging techniques allow us to acquire the structure of living nerve cells and their changes. While the commonly used dye-stained extrinsic optical signal mimics the intracellular voltage or the ion currents of the membrane directly, the fast intrinsic optical signal measures longer term physiological changes such as cell structure and sub-cellular level properties after a sustained intracellular spike under the electric and other stimulations. We build a 2-D computational model to simulate the dynamic behavior from neurons' activity leading to optical functional imaging. Such a simulation model requires structural information (cellular volume) at the neuronal level to quantify optical scattering coefficients and a realistic Hodgkin-Huxley model of the neuron to be constructed. Initial computational results show the model as a good indication of the fast intrinsic optical signal.

Keywords: Mathematical Model, Intrinsic Optical Imaging, Bursting Neurons

1 Introduction

Two major neuronal monitoring methods are intrinsic optical imaging (Shtoyerman et al [1], 2000 and others) or extrinsic optical imaging with voltage (or calcium)-sensitive dye. While the dye-stained optical signal mimics the intracellular voltage or Ion current of the membrane directly (< 1 millisecond), the considered fast intrinsic optical signal measures optical properties with a longer term (signals started after 10-100 millisecond and lasted several seconds) physiological consequence in functional imaging (Salzberg et al [2] 1983 and its references). Yet, this is different from slow optical signals (in 1-10 second to minutes range) caused by hemodynamic changes that have used in the standard modality for optical imaging. The fast intrinsic optical signal/imaging offers a window for studying the links between electrophysiological activities and functional behavior. However, the fundamental mechanism as how neuronal activities at cellular- or subcellular-scale lead to observable changes in optical imaging is not well understood. It calls for a mathematical modeling study and improved method for processing the measurement data.

We construct a 2-D computational model to simulate the dynamic behavior from a single neuron's activity to optical functional imaging, a process crossing

multiple orders of temporal as well as spatial scales. Such a simulation model requires structural information (cellular volume) at the neuronal level, and a realistic Hodgkin-Huxley model of the neuron to be constructed. Later on, we can further perform calculation of light intensity distribution of optical imaging in continuous wave or time domain based on these biophysical changes.

2 Background In Fast Optical Imaging For Neural Activities

The main hypothesis for the fast optical signal is based upon cell (fiber) volume changes during the action potential change within the 10 millisecond to several seconds range after stimulations. This mechanism is well documented by Cohen [4] for giant axons of squid and many others, and it is considered the dominant signal in the NIR spectrum region. The cause of change in cell volume and the extra-cellular space is attributed to the change in osmotic pressure due to ion concentration and water movement.

3 Neural Models for Fast Optical Signals

To understand the connection between electrophysiological activities of neurons and light scattering signals observed from experiments, we start with a modified Hodgkin-Huxley (HH) model to describe the intracellular electrophysiological activities of sensory neuron, and the neuron is assumed (for now) to be a long 1-dimensional nerve fiber. The function $V(x, t)$ represents the trans-membrane potential, and $(m, n, h)(x, t)$ represents the variables involved in potassium and sodium currents. To model a specific area of the spinal cord [5], our neural model takes classical HH parameter values except $\bar{g}_{na} = 50$, $g_i = 0.7$, $V_i = -77.5$, $\bar{g}_k = 2.6$;

$$\begin{aligned} \frac{\partial V}{\partial t} &= \frac{1}{CM} (D\Delta V - (\bar{g}_{na} m^3 h (V - V_{na}) + \bar{g}_k n^4 (V - V_k) + g_i (V - V_i)) + I_{app}) ; \\ \frac{\partial h}{\partial t} &= (h_{inf}(V) - h) / \tau_h(V) ; \frac{\partial n}{\partial t} = (n_{inf}(V) - n) / \tau_n(V) ; \frac{\partial m}{\partial t} = (m_{inf}(V) - m) / \tau_m(V) . \end{aligned} \quad (1)$$

We denote the difference of ion concentration across the cell membrane as $C(x, t)$, and cellular water volume as $R(x, t)$, and the diameter of the fiber as $D(x, t)$. Then it holds

$$\frac{\partial C}{\partial t} = \kappa \Delta C - (\bar{g}_{na} m^3 h (V - V_{na}) + \bar{g}_k n^4 (V - V_k) + g_i (V - V_i)) - \gamma g(C, V) ; \quad (2a)$$

$$\frac{\partial R}{\partial t} = \mu C \quad (2b)$$

where eq. 2a describes the concentration change due to intracellular ion flows as well as leaking and pumping effects, and eq. 2b reflects the water flow rate to be proportional to osmotic pressure generated by concentration difference. The diameter

of the nerve fiber, D , is related to volume, R , in $R = MD^2$, and the scattering coefficient of optical signals is given by $D' = KR^{-n}$ based on Mie theory [6] (reciprocal of a power of cross-sectional area). The correlation between one spike and the change in fiber radius is shown in Figure 1(a).

When the effect of Calcium flux was included in consideration, experimental evidence [7] indicated the calcium-dependence of K-channel:

$$\bar{g}_k = \bar{g}_{k,0} + Ca, \quad \frac{\partial Ca}{\partial t} = \mathcal{E}f(V + V_{Ca}, Ca, m, n, h), \quad (3)$$

where we take $V_{Ca} = -55\text{mV}$ as the threshold for Ca^{2+} flow, and Ca^{2+} is taken as a simplified model (one threshold). Then bursting is presented in Figure 1(b). Superimposed is the corresponding changes in radius during the bursting.

4 Simulated optical signals of neuron activities

The preliminary model study for optical signals of neuron activities was simulated for a 50- μm -diameter iso-potential cell, using XPPAUT software [8]. The effect of soma, myelination was not included in the model. Specific membrane capacitance was $1 \mu\text{F}/\text{cm}^2$, specific longitudinal resistance was $110 \Omega\text{-cm}$, and temperature was 20°C . The cell was divided into 99 segments. XPPAUT used the Runge-Kutta method for integration ($dt = 0.01 \text{ msec}$). The calculation was performed on SGI Origin 2000 by Unix version of XPPAUT.

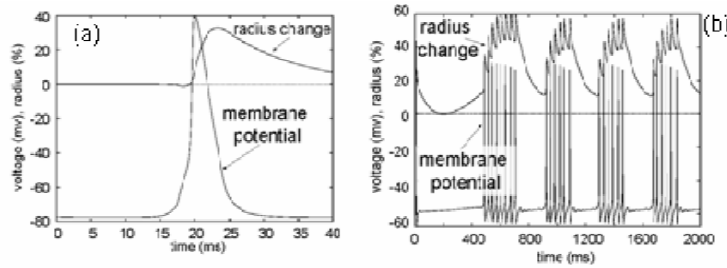


Figure 1. The trans-membrane potential and the cell radius varying with time in a single potential spike (a) and a bursting scenario (b).

We set the applied current, I_{app} , at zero in our first case. The procedure of numerical simulation was as follows. We raised the membrane potential of the first segment $V_1 = -45.0 \text{ mV}$ from equilibrium (-77.5mV) while ion currents remain at equilibrium. All other segments were left unchanged at equilibrium. An action potential spike was generated in segment 1 first, and then propagated along the fiber. We detected the action potential changes in segment 10, immediately followed by cell radius changes as shown in Figure 1(a). This figure demonstrates that the trans-membrane potential and the cell radius at segment 10 vary with time t . Within 1 ms of

the voltage spike, the cell radius increases 30% and then retreats slowly to a normal level.

In our second simulation, we raised I_{app} to 12 μA at a constant value, where as the neuron was in hyperexcitability state, but otherwise performed the same simulation. The initial stimulation led to a neuron bursting (a sustained period of intensive spikes before a large influx of Ca Ions terminated active phase). As shown in Fig. 1(b), the radius of the cell is also changed after each spike and accumulated to a greater level after the active phase before retreating. The two superimposed curves show that the intensity of the spike forces the continued increase of cell radius. The time interval between spikes is not long enough to allow retreating to balance. The increase in radius can be as large as 60% and can provide a much stronger optical signal for the bursting.

Unlike the single spike case, even in the quiescent phase of bursting, the radius remains at 16% increase at its low. This is consistent with 20% radius change observed in experiments [9].

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