Simpli5ed Dynamics of Human and Mammalian Neocortical Neurons

HUGH R. WILSON

Question 1: What is the statement of the problem?

The paper aims to develop a simple system to approximate the complex dynamics of the neocortical neurons in Humans and Mammals, consistent with the observed diversity of dynamic behaviour. The simplified model is aimed at capturing the 4 distinct patterns of spiking - RS (regular spiking), FS (fast spiking), CB (continuously bursting), IB (intrinsic bursting). Further, the authors wish to address 2 questions including the dynamical basis for this diversity and whether the firing patterns form a continuum or do they fall into discrete categories.

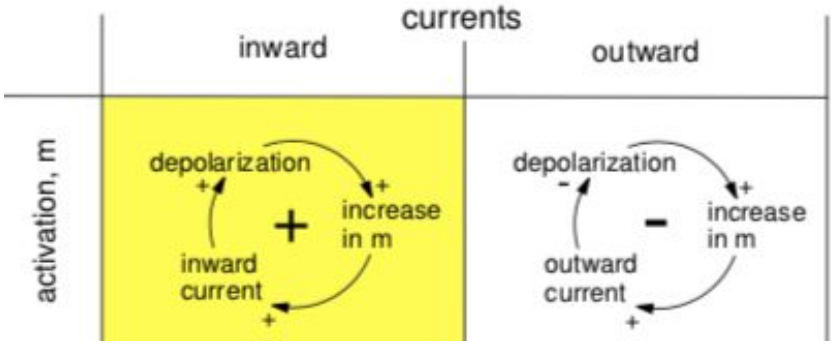
Question 2: Why this model is constructed and what are the terms taken?

The system uses the interplay of 4 simulated ion currents namely I_{Na} (Na^+ current), I_K (K^+ current), I_T (Ca^{2+} current), I_{AHP} (Ca^{2+} mediated K^+ hyperpolarizing current). The system is constructed ensuring it obeys Ohm's law and the dynamics are restricted to cubic nonlinearities. The I_{Na}, I_K, are faster currents while I_T, I_{AHP} are slower currents. The parameters of the model are g_T, g_H, I and tau_R. The system of equations is as given below:

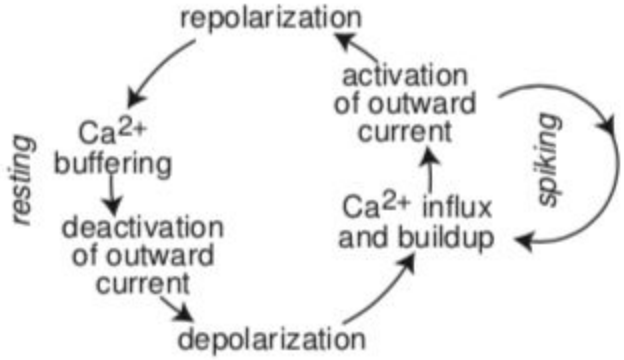
$$
\begin{aligned}
C\frac{dV}{dt} &= -m_\infty(V-0.5) - 26R(V+0.95) \\
&\quad - g_T T(V-1.2) - g_H H(V+0.95) + I, \\
\frac{dR}{dt} &= \frac{1}{\tau_R}(-R + R_\infty(V)), \\
\frac{dT}{dt} &= \frac{1}{14}(-T + T_\infty(V)), \\
\frac{dH}{dt} &= \frac{1}{45}(-H + 3T),
\end{aligned}
\tag{5}
$$

Question 3: What are the positive and negative feedback loops in this model? Put it in a tabular form.

The model began by consisting of a 2D system consisting of the Na^+ activation and the K^+ activation having positive and negative feedback respectively. These 2 together lead to limit cycle oscillations. However, to model bursting, 2 slower currents are added to the system, I_T and I_{AHP}.



Mechanism of Ca^{2+} gated I_{AHP} activation:



Question 4: What is the mechanism? Give the mechanism of hyper and depolarization as given in chapter 5 of EI's book.

For the Na^+ activation current, an increase of m results in an increase of the inward current; hence more depolarization and further increase of m until

the excited state is achieved. The Na^+-K^+ system is able to produce limit-cycle oscillations. Each spike in the initial bursts activates a slow voltage- or Ca^{2+}-dependent outward K+ current, which eventually stops the burst and hyperpolarizes the membrane potential. During the AHP period, the slow outward current deactivates, and the neuron can fire again. Of the four currents, the two faster ones are responsible for spike generation via saddle-node bifurcation to a limit cycle, while the slower two modulate to produce spike frequency adaptation and bursting.

Question 5: How is this model different from the conductance model of HH?

The Hodgkin Huxley, a 4d model, involves the interplay of membrane potential V, Na^+ activation m, Na^+ inactivation h, and K^+ activation n. This model does not consider the Na^+ inactivation, instead deals with the Ca^{2+} current and the afterhyperpolarizing current I_{AHP}. In addition, the HH system has the leakage current, which is not explicit in this system. Also, $m_{inf}(V)$, $R_{inf}(V)$, $T_{inf}(V)$ are set to be polynomial functions, whereas in the HH system, $m_{inf}(V)$, $n_{inf}(V)$, $h_{inf}(V)$ are set to be sigmoidal in nature.

Question 6: Can a 2D system explain all the dynamics like bursting etc?

A 2D system cannot explain all dynamics as bursting is a result of interaction of oscillations with two time scales: a fast spiking oscillation within a single burst and one modulated by a slow oscillation between the bursts, which could typically be the interaction a slow and a fast current. Further, to incorporate all the bursting phenomenon, RS, FS, CB, IB, we need to alter the parameters g_H and g_T, governing 2 different currents, which along with the membrane voltage, yields a 3D system.

Question 7: What is a synaptic connection and how this is modeled in this paper?

A synaptic connection is used to model the relationship across neurons, or perform coupling of neurons and perform network simulations. The authors have added 2 equations to the system to model coupling:

$$\frac{df}{dt} = \frac{1}{\tau_{syn}}(-f + Hvs(V_{pre} - \Omega))$$

$$\frac{dS}{dt} = \frac{1}{\tau_{syn}}(-S + f),$$

Where S is the synaptic current.

Question 8: What is an alpha function?

The alpha function, or the Rall's alpha function is a waveform commonly used to model the time course of synaptic conductance, and which can provide realistic representations of the conductance change at a typical synapse. The authors have used this function to formulate synaptic connections.

$$g_{syn}(t) = \overline{g}_{syn} \frac{t - t_s}{\tau} \exp\left(-\frac{t - t_s}{\tau}\right)$$

Question 9: What is the summary and conclusion of this paper?

In summary, the 4 currents together, where the faster currents are responsible for spike generation while the slower currents produce spike frequency adaptation and bursting. Also, the equations describe an isopotential model, indicating that 2 different compartments/separation of slow and fast currents is not necessary. Further, 4 types of dynamics are

observed simply by varying a few parameters - RS, with $g_T = 0.1$, $g_H > 0$, FS with $g_T >= 0$ and $g_H = 0$, CB, with $g_T > 2.2$ and $g_H > 8$ and IB, with $1.4 > g_T > 0.7$ and $5 > g_H > 3$.

Compared with other models, the FitzHugh Nagumo Model and Hindmarsh Rose Model are unable to accurately represent spiking shapes or firing rates and the Integrate-and-Fire models do not describe action potential shapes and are unable to simulate neocortical bursting.

In conclusion, the model described in the paper is able to effectively simulate neocortical dynamics including bursting and synaptical connections.

Question 10: Simulate all the figures including the linear stability analysis provided in the appendix in Jupyter notebook and BRIAN software if necessary.

Attached .ipynb file