

The Wilson Model of Cortical Neurons

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I. Refinements on the Hodgkin-Huxley Model

The years since Hodgkin's and Huxley's pioneering work have produced a number of derivative Hodgkin-Huxley-like models. Recall that Hodgkin and Huxley developed their model from data measured in the giant axon of the squid. Therefore the original model only had voltage-dependent channel models for a Na^+ channel and a K^+ channel. There are in addition to these types of channels found in axons a great many other species of voltage-gated channels (VGCs), both of the Na^+ and K^+ types as well as VGCs that conduct Ca^{2+} currents. These channels are characterized by different rate constants controlling their channel gating as well as different values of maximum channel conductance.

Different researchers have employed different approaches to modeling the Hodgkin-Huxley channel dynamics. Some researchers stick very close to the biophysical "picture" presented in Hodgkin's and Huxley's work. Their expressions for the voltage dependence of the rate constants tend to look very much like those of Hodgkin-Huxley, and their circuit models tend to look very

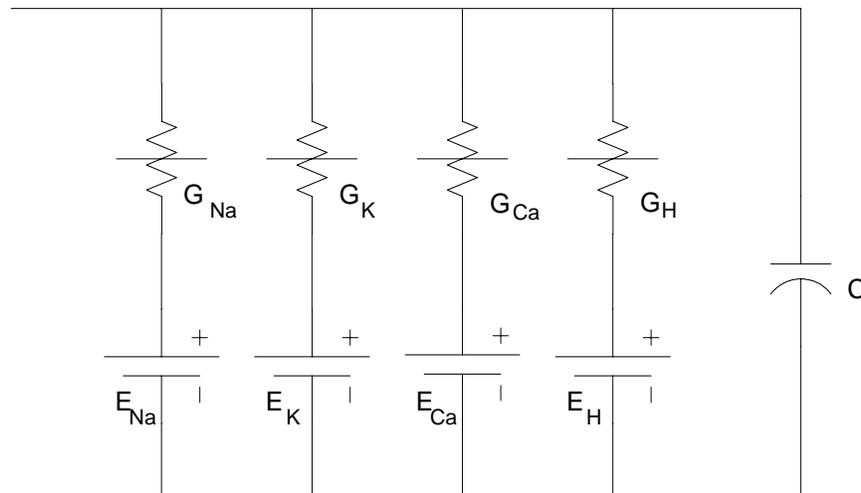


Figure 1: Basic Wilson model of cortical neurons. It is a single-compartment model. Ionotropic synapses (or test current sources) are connected at the terminals on the left. The model combines the Na^+ voltage-gated channel and the leakage channel together in one element, modeled as a fictitious persistent Na^+ channel. It adds a voltage-dependent Ca^{2+} channel, commonly called a "T" channel, and a Ca^{2+} -dependent K^+ channel (the "H" channel) to the basic Hodgkin-Huxley channels. The batteries representing the Nernst potentials are all placed with the "+" terminal facing the cytoplasmic side of the membrane, and the numerical values for the various "E" terms above carry the sign of the Nernst potential. Thus E_K would be a negative number in this circuit model, while E_{Na} would be a positive number. This is indeed the preferred circuit convention for numerical modeling because it simplifies the computer code used.

similar except for the addition of more conductance & battery segments modeling the additional VGCs. Most incorporate the usual leakage-current element and treat the various channels separately from one another. These researchers produce models that keep as close a connection as possible to identifiable biological entities and which match more or less one-for-one with the qualitative “picture” of the neuron produced through laboratory neurobiology research.

Other researchers take a different approach. While their circuit and gating-dynamics models are designed to produce the same voltage- and current- waveforms measured by physiologists, their models are less concerned with retaining a one-for-one match with the qualitative biological model than they are with obtaining more efficient numerical algorithms for calculating the voltage and current waveforms. The Wilson model, named after its modeler, Hugh R. Wilson, is one example of such a modeling approach.

The basic Wilson circuit model for cortical neurons is shown in figure 1. In appearance this circuit model is no different from those typically produced by the researchers adhering to a close correspondence with neurobiological qualitative models. What is different about the Wilson model can only be seen when we look at the specific mathematical expressions he uses to model voltage and current waveforms.

II. The Wilson Model

Wilson’s model differs from the Hodgkin-Huxley model in several ways. First, recall from the Hodgkin-Huxley model that the transient Na^+ channel responsible for action potential (AP) generation has much faster dynamics than those of the persistent K^+ channel. The activation time constant, τ_m , is smaller by approximately an order of magnitude than the inactivation time constant, τ_h , or the activation time constant for the K^+ channel, τ_n . This means that the activation of the Na^+ channel comes very close to reaching its steady-state value during the AP generation. Wilson takes advantage of this by approximating the Na^+ channel as if its time constant were zero in the differential equation for activation variable m . He then combines the Na^+ channel with the leakage channel (which has a zero-value for its time constant) and models both types of channels with a single conductance in series with a battery.

He also takes another step, for purposes of reducing computation time, and this step departs from physiological “reality” in the neuron model. It must be viewed as a straight-up numerical approximation and not as representative of the biophysics of Na^+ channel conductance: He ignores the inactivation gate of the Na^+ channel. The argument mounted in justification of this seemingly radical step is based on another numerical approximation. Recall from the Hodgkin-

Huxley model that the time constant for Na^+ inactivation, τ_h , is roughly of the same numerical value as that for the K^+ channel, τ_n . Wilson argues that this means replacing h by $(1 - n)$ in the Hodgkin-Huxley expression for G_{Na} approximates the effects of the inactivation gate with reasonable accuracy.

He then mounts an additional argument, applicable to cortical neurons (neurons in the neocortex of the brain), that justifies an additional approximation. Many of the neurons found in the neocortex have, in addition to the transient Na^+ VGC, a number of persistent Na^+ VGCs. For a persistent Na^+ channel, the conductance G_{Na} has the form

$$G_{Na} = \bar{g}_{Na} \cdot m^r$$

where \bar{g}_{Na} is the maximum channel conductance and r is an experimentally-determined integer. Wilson argues that the ion current through these persistent Na^+ channels is much larger than the current conducted through the transient Na^+ conductance, and therefore to a reasonable approximation the transient channel can be ignored in modeling voltage and current waveforms in the cortical neuron. Note that by taking this step the Wilson model completely gives up the ability to model the transient Na^+ current; but since his model is intended to achieve sufficient simplification of the numerical calculations to permit its use in modeling small cortical neural networks, he regards giving up the ability to model the transient current as an acceptable modeling tradeoff.

With these approximations, the circuit of figure 1 is analyzed using Kirchoff's current law to obtain the differential equation

$$C \frac{dV_m}{dt} = -G_{Na}(V_m - E_{Na}) - G_K(V_m - E_K) - G_{Ca}(V_m - E_{Ca}) - G_H(V_m - E_H) + I_{in}(t) \quad (1)$$

where I_{in} is an input current (from synaptic ionotropic channel circuits or from a test current source), V_m is the membrane voltage (the voltage at the top of figure 1), and the other symbols are defined in figure 1 and its caption. There are two new VGC channels in the Wilson model. The first, labeled "T", is a channel that conducts Ca^{2+} ions. It is widely known in the literature as "the T channel." The second is a K^+ channel that has the property that its conductance depends on intracellular Ca^{2+} levels (and therefore is tied to the actions of the T channel). This conductance produces a very pronounced hyperpolarization of the membrane potential and is therefore known as an "AHP" channel ("after-hyperpolarization"). With the batteries drawn in the directions

shown in figure 1, the battery voltages, E_{Na} & etc., are numbers that include the sign of the Nernst potential. Thus, E_K is a negative number, E_{Na} is a positive number, etc.

The voltage dependence of the conductances must also be modeled, and here, too, the Wilson model departs from the Hodgkin-Huxley method. Recall that the equations for the rate constants' voltage dependence in Hodgkin-Huxley involved the calculation of exponentials. This type of calculation is computationally expensive (i.e. it takes longer to compute $e(x)$ terms). Wilson replaces these exponential functions with second-order polynomial curve fit approximations, and combines the calculation of the voltage-dependent rate "constants" with the calculation of the differential equations for the activation variables. He does this by expressing the channel conductances as

$$\begin{aligned}
 G_K &= g_K \cdot R \\
 G_{Na} &= 17.8 + 0.476 \cdot V_m + 33.8 \cdot 10^{-4} \cdot V_m^2 \\
 G_{Ca} &= g_T \cdot T \\
 G_H &= g_H \cdot H
 \end{aligned} \tag{2}$$

where V_m is in mV, R , T , and H are Wilson's activation variables, and g_K , g_T , and g_H are conductance parameters in micro-Siemens (μS). Note that G_{Na} is modeled simply as a nonlinear voltage-dependent conductance. The activation variables, which are dimensionless, are calculated from the set of differential equations

$$\begin{aligned}
 \tau_R \frac{dR}{dt} &= -(R - R_0), \quad R_0 = 1.24 + 0.037 \cdot V_m + 3.20 \cdot 10^{-4} \cdot V_m^2 \\
 \tau_T \frac{dT}{dt} &= -(T - T_0), \quad T_0 = 4.205 + 0.116 \cdot V_m + 8.0 \cdot 10^{-4} \cdot V_m^2 \\
 \tau_H \frac{dH}{dt} &= -(H - 3 \cdot T)
 \end{aligned} \tag{3}$$

where the three τ terms are time constants in msec and V_m is again in mV.

With the variable dimensions as described above, the ion currents are in nanoamperes (nA) and the capacitance C is in nanoFarads (nF). This is a "whole neuron" model, by which I mean that the quantities above are not expressed in terms of "per unit area."

At this point there are a couple of things that need to be pointed out. First, although the g and C terms above seem very "biological" in actual fact they are based on curve fits to empirical data and are not necessarily representative of actual biological values. Wilson obtained g values for

four different classes of cortical neurons (one excitatory neuron class, one inhibitory neuron class, and two bursting neuron classes). He chose his time constants in (3) to force agreement with observed firing rates. Interestingly, for C he used a value of $1 \mu\text{F}/\text{cm}^2$ in his numerical work.¹ This is peculiar and, I would have to say, erroneous because such a choice is dimensionally incompatible with his other quantities. Presumably he didn't notice this because the "1" entered into his computer equations as a "1". With three adjustable " τ terms" in the model it would not be particularly difficult to obtain a curve fit even with the erroneous capacitance value. This is an example carelessness in quantitative modeling work, and unfortunately this is not uncommon in the literature. However, the fact that it is common does not make it acceptable. We can note that even a value of $C = 1 \text{ nF}$ implies a surface area for the neuron on the order of about 0.1 mm^2 , which is an absurdly large value since it implies a neuron with a diameter on the order of about 150 to 200 μm . Real neurons in the neocortex are only about one tenth this size. Trappenberg in his textbook unconcernedly duplicated Wilson's values in chapter 2 and in the MATLAB scripts.

This brings me to the second point. *All* of the quantities in the Wilson model have to be regarded as non-physiological quantities. The model is a straight curve fit aimed to reproduce specific neuronal action potentials. The parameters of the model cannot be trusted to be exact biological quantities, and cannot be used to explore the physiology of specific cortical neurons. What we can do with the Wilson model is build a circuit that bio-mimics signal processing in small neural networks without the pretense that the model itself tells us anything about the quantitative physiology of the neocortex. Wilson points this out in his paper.

Because Wilson's purpose in developing this model was to permit simulation of small neural networks, he also needed to develop a way for action potentials from one neuron to stimulate the opening of synaptic channels in another. To do this he added two more differential equations. Each neuron is given a "firing variable" that is an abstract index of the amount of neurotransmitter it is currently releasing from its presynaptic terminals. Let each neuron be identified with an integer label. For neuron j its firing variable is described by the equation

$$\frac{df_j}{dt} = \frac{1}{\tau_{syn}} \left(-f_j + U[V_{mj} - \Omega] \right) \quad (4)$$

where τ_{syn} is a synaptic time constant, Ω is a threshold (in mV), and the function U is called the Heaviside step function², defined as

¹ H.R. Wilson (1999), "Simplified dynamics of human and mammalian neocortical neurons," *J. Theor. Biol.* **200**, 375-388.

² Named after Oliver Heaviside (1850-1925), a prominent 19th century physicist.

$$U(x) = \begin{cases} 1, & x > 0 \\ 0, & x \leq 0 \end{cases} . \quad (5)$$

If neuron j makes a synaptic connection to postsynaptic neuron i , neuron i is linked to the firing variable of neuron j by a “synapse activation” variable $S_{i,j}$. The equation describing this variable is

$$\frac{dS_{i,j}}{dt} = \frac{1}{\tau_{syn}} (-S_{i,j} + f_j) . \quad (6)$$

The synapse activation variable determines the conductance of the synaptic channel of neuron i through a synaptic conductance / synaptic battery circuit such as we used earlier to model synapses in the Hodgkin-Huxley circuit. The synaptic current in neuron i is given by

$$I_{syn_i}(t) = g_{syn} \cdot S_{i,j} \cdot (E_{syn} - V_m) \quad (7)$$

where g_{syn} is the peak synaptic conductance, E_{syn} is the synaptic battery potential, and V_m is the membrane voltage of neuron i .

III. Scaling.

A casual examination of equations (2) and equations (3) shows that the numerical constants used in Wilson’s equations span a range of about 4 orders of magnitude. This can often be a serious issue affecting the accuracy of a computational model. Every arithmetic operation a computer performs introduces small round-off errors, and over time these errors can build up to the point where they lead to serious inaccuracies. This is especially the case when there is a very large spread in the numbers, as is the case in Wilson’s model.

Fortunately, there is usually a very simple way to avoid this problem, and this trick is called “scaling”. As an example of how scaling works, let’s re-write the expression for R_0 in equation (3):

$$R_0 = 1.24 + 0.037 \cdot V_m + 3.20 \cdot 10^{-4} \cdot V_m^2 = 1.24 + 3.7 \left(\frac{V_m}{100} \right) + 3.20 \left(\frac{V_m}{100} \right)^2 .$$

The coefficients are now all of the same order of magnitude but V_m is replaced in the expression by the scaled value $v = V_m/100$. This is a simple trick that yields identical results except for the fact that the computer will now calculate v instead of V_m . But since we know the relationship between the two, we can easily get the membrane potential from the scaled variable after the calculations have completed.

In order for scaling to work we must apply it consistently over all the equations. Thus (1) – (3) become

$$100 \cdot C \frac{dv}{dt} = -G_{Na} \cdot \left(v - \frac{E_{Na}}{100} \right) - G_K \cdot \left(v - \frac{E_K}{100} \right) - G_{Ca} \cdot \left(v - \frac{E_{Ca}}{100} \right) - G_H \cdot \left(v - \frac{E_H}{100} \right) + I_{in}(t) \quad (1s)$$

$$\begin{aligned} G_K &= g_K \cdot R \cdot 100 \\ G_{Na} &= 17.8 + 47.6 \cdot v + 33.8 \cdot v^2 \\ G_{Ca} &= g_T \cdot T \cdot 100 \\ G_H &= g_H \cdot H \cdot 100 \end{aligned} \quad (2s)$$

$$\begin{aligned} \tau_R \frac{dR}{dt} &= -(R - R_0), \quad R_0 = 1.24 + 3.7 \cdot v + 3.20 \cdot v^2 \\ \tau_T \frac{dT}{dt} &= -(T - T_0), \quad T_0 = 4.205 + 11.6 \cdot v + 8.0 \cdot v^2 \\ \tau_H \frac{dH}{dt} &= -(H - 3 \cdot T) \end{aligned} \quad (3s)$$

We simply multiply the conductances and the capacitor by 100, rescale the Nernst potentials by dividing them by 100, and adjust the constants in (2) and (3) to make them consistent with the scaled membrane voltage v . This is what Wilson does in his computer program, and Trappenberg did the same scaling trick in his MATLAB script.

In the computer simulation program the scaling factor can be directly incorporated into the parameters of the model, and this, too, is what Wilson and Trappenberg have done. The battery potentials in the model are $E_{Na} = 50 \text{ mV} \rightarrow 0.50$, $E_K = -95 \text{ mV} \rightarrow -0.95$, $E_{Ca} = 120 \text{ mV} \rightarrow 1.20$, and $E_H = -95 \text{ mV} \rightarrow -0.95$. Note that $E_K = E_H$ because these are both K^+ channels. Wilson modeled four classes of cortical neurons, and the maximum conductance values for each type are as follows. For all four types, $g_K = 0.26 \mu\text{S} \rightarrow 26$ (scaled units), $\tau_T = 14 \text{ msec}$, and $\tau_H = 45 \text{ msec}$.

For the excitatory “regular spiking” (“RS”) neuron,

$$g_T = 0.001 \mu\text{S} \rightarrow 0.1 \text{ scaled units,}$$

$$g_H = 0.05 \mu\text{S} \rightarrow 5.0 \text{ scaled units,}$$

$$\tau_R = 4.2 \text{ msec (4.2 in computer units).}$$

For the inhibitory “fast spiking” (FS) neuron,

$$g_T = 0.0025 \mu\text{S} \rightarrow 0.25 \text{ scaled units,}$$

$$g_H = 0 \text{ (no AHP channel),}$$

$$\tau_R = 1.5 \text{ msec (1.5 in computer units).}$$

For the “continuous bursting” (CB) neuron,

$$g_T = 0.0225 \mu\text{S} \rightarrow 2.25 \text{ scaled units,}$$

$$g_H = 0.095 \mu\text{S} \rightarrow 9.5 \text{ scaled units,}$$

$$\tau_R = 4.2 \text{ msec (4.2 in computer units).}$$

Finally, for the “intrinsic bursting” or IB neuron, Wilson reported two subtypes characterized as shown in the following table.

first subtype	second subtype
$g_T = 0.008 \mu\text{S} \rightarrow 0.80$	$g_T = 0.012 \mu\text{S} \rightarrow 1.20$
$g_H = 0.04 \mu\text{S} \rightarrow 4.0$	$g_H = 0.034 \mu\text{S} \rightarrow 3.4$
$\tau_R = 4.2 \text{ msec}$	$\tau_R = 4.2 \text{ msec}$

Despite the ambiguity in Wilson’s value for the circuit capacitance, we can determine its value from an examination of Trappenberg’s MATLAB script. Here we see that C enters into the calculations as unity, which implies $100C = 1$ or $C = 0.01 \text{ nF}$, corresponding to a neuron diameter of about $18 \mu\text{m}$ (a biologically realistic value).

Finally, it is important to note that the same scaling factor must be applied to Ω , g_{syn} and E_{syn} when synaptic inputs are incorporated into the model. Representative scaled values are given in Wilson’s paper.