## I. Leaky integrate-and-fire (LIF) model

*Reference:* Lapicque L (1907) Recherches quantitatives sur l'excitation électrique des nerfs traitée comme une polarization. *J. Physiol. Pathol. Gen.* **9**, 620-635.

$$C_m \frac{dV}{dt} = -g_L(V - E_L) + I_{app} \tag{1}$$

if $V(t = t_{spike}) = V_{th}$, a spike is discharged and $V$ is reset to $V_{reset}$. $C_m$ is the capacitance, $I_{app}$ is the input current, $g_L$ is the leak conductance, and $E_L$ is the leak reversal potential. When $I_{app} = 0$, the membrane potential is in the resting state of $V = E_L$.

The firing rate $f$ as a function of the current $I_{app}$ is given by

$$f = \frac{g_L/C_m}{\ln\left[1 + g_L\theta/(I_{app} - g_L(V_{th} - E_L))\right]} \quad \text{if } I_{app} > g_L(V_{th} - E_L); \qquad 0 \quad \text{otherwise.} \tag{2}$$

where $\theta = V_{th} - V_{reset}$.

## II. LIF Model with spike-frequency adaptation

*Reference:* Liu YH and Wang X-J (2001) Spike-frequency adaptation of a generalized integrate-and-fire model neuron. *J. Comput. Neurosci.* **10**, 25-45. (download at http://www.wanglab.brandeis.edu)

Spike-frequency adaptation is assumed to be produced by a $Ca^{2+}$ -gated $K^+$ current $I_{KCa}$. Experiments suggest that the intrinsic gating of $I_{KCa}$ is fast, thus its slow activation is due to the kinetics of the cytoplasmic $Ca^{2+}$ concentration. Let $I_{KCa} = g_{KCa}\left[Ca^{2+}\right](V - E_K)$. Each action potential generates a small amount $\alpha$ of calcium influx, hence $I_{KCa}$ is incremented accordingly. Note that $g_{KCa}\left[Ca^{2+}\right]$ is the effective $K^+$ conductance, and the product $\alpha g_{KCa}$ is the amount of $KCa$-conductance increase by a single spike. The modified integrate-and-fire model with adaptation is given by:

$$C_m \frac{dV}{dt} = -g_L(V - E_L) - g_{KCa}\left[Ca^{2+}\right](V - E_K) + I_{app} \tag{3}$$

$$\frac{d\left[Ca^{2+}\right]}{dt} = -\frac{\left[Ca^{2+}\right]}{\tau_{Ca}} \tag{4}$$

$$if\ V(t) = V_{th},\ then\ \begin{cases} V \rightarrow V_{reset} \\ [Ca^{2+}] \rightarrow [Ca^{2+}] + \alpha \end{cases} \tag{5}$$

where the $[Ca^{2+}]$ dynamics is modeled as a leaky integrator with a decay time constant $\tau_{Ca}$. $[Ca^{2+}]$ is initially set to be 0 $\mu$M (its resting baseline is neglected).

For a given neuron type, each of the model parameters can be estimated experimentally. In the case of cortical pyramidal neurons: (a) $C_m = 0.5$ nF, $g_L = 0.025$ $\mu$S (the input resistance $R_{in} = 1/g_L = 40M\ \Omega$) so that the time constant $\tau_m = C_m/g_L = 20$ ms, and the resting membrane potential $E_L = -70$ mV. (b) The firing threshold $V_{th} = -54$ mV. (c) The slope of the $f$-$I$ curve (at large $I$ and with $g_{KCa} = 0$) is given by $1/(C_m\theta)$, where $\theta = V_{th} - V_{reset}$. We choose $V_{reset} = -60$ mV ($\theta = 6$ mV) so that the slope is about 330 Hz/nA, comparable with the $f$-$I$ data measured before adaptation onset. (d) the $[Ca^{2+}]$ influx per spike $\alpha = 0.2$ $\mu$M, and $\tau_{Ca} = 50 - 600$ ms. The adaptation conductance $g_{KCa} = 0.015\,mS/cm^2$ (with $E_K = -80\,mV$) so that the degree of adaptation is comparable to data from cortical pyramidal cells.

## III. Hodgkin-Huxley (Type 2) Model

*Reference:* Hodgkin AL, Huxley AF (1952) A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol. (London)* **117**, 500-544.

$$C_m \frac{dV}{dt} = -I_{Na} - I_K - I_L + I_{app} \tag{6}$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m = \frac{(m_\infty(V) - m)}{\tau_m(V)} \tag{7}$$

$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h = \frac{(h_\infty(V) - h)}{\tau_h(V)} \tag{8}$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n = \frac{(n_\infty(V) - n)}{\tau_n(V)} \tag{9}$$

$$\tag{10}$$

where $I_{Na} = g_{Na}m^3h(V - E_{Na})$, $I_K = g_K n^4(V - E_K)$, $I_L = g_L(V - E_L)$. The kinetic rates are

$$\alpha_m(V) = -0.1(V+40)/(\exp(-0.1(V+40)) - 1);\ \beta_m(V) = 4\exp(-(V+65)/18) \tag{11}$$

$$\alpha_h(V) = 0.07\exp(-0.05(V+65));\ \beta_h(V) = 1/(1+\exp(-0.1(V+35))) \tag{12}$$

$$\alpha_n(V) = -0.01(V+55)/(\exp(-0.1(V+55)) - 1);\ \beta_n(V) = 0.125\exp(-(V+65)/80) \tag{13}$$

The parameter values are: $C_m = 1$ $\mu$F/cm$^2$, and $I_{app}$ is the injected current (in $\mu$A/cm$^2$). The maximum conductances $g_{Na} = 120$, $g_K = 36$, $g_L = 0.3$ (in mS/cm$^2$); the reversal potentials $E_{Na} = +50$, $E_K = -77$, $E_L = -54.4$ (in mV). The passive time constant $\tau_m = C_m/g_L \simeq 3.3$ ms.

**Note:** reduced two-variable HH model: (a) The activation variable $m$ is fast ($\tau_m$ is less than 0.5 msec), hence is substituted by its steady-state function $m_\infty = \alpha_m/(\alpha_m + \beta_m)$. (b) $n + h \simeq 0.85$.

### IV. Modified (Type 1) HH model

*Reference:* Wang X-J and Buzsáki G (1996) Gamma oscillations by synaptic inhibition in a hippocampal interneuronal network. *J. Neurosci.* **16**, 6402-6413.

Same notations as before. The activation variable $m$ is substituted by its steady-state $m_\infty = \alpha_m/(\alpha_m + \beta_m)$; $\alpha_m(V) = -0.1(V + 35)/(\exp(-0.1(V + 35)) - 1)$, $\beta_m(V) = 4\exp(-(V + 60)/18)$. The inactivation variable $h$ obeys a first-order kinetics,

$$\frac{dh}{dt} = \phi(\alpha_h(1 - h) - \beta_h h) \tag{14}$$

where $\alpha_h(V) = 0.07\exp(-(V+58)/20)$, and $\beta_h(V) = 1/(\exp(-0.1(V+28))+1)$. $g_{Na} = 35$ mS/cm$^2$, $E_{Na} = 55$ mV, $\phi = 5$.

The delayed rectifier $I_K = g_K n^4(V - E_K)$, where the activation variable $n$ obeys the following equation:

$$\frac{dn}{dt} = \phi(\alpha_n(1 - n) - \beta_n n) \tag{15}$$

with $\alpha_n(V) = -0.01(V + 34)/(\exp(-0.1(V + 34)) - 1)$, and $\beta_n(V) = 0.125\exp(-(V + 44)/80)$; $g_K = 9$ mS/cm$^2$, $E_K = -90$ mV. Other parameter values: $C_m = 1$ $\mu$F/cm$^2$, $g_L = 0.1$ mS/cm$^2$, and $E_L = -65$ mV.

### V. Two-compartment model with spike-frequency adaptation

*Reference:* Wang X-J (1998) Calcium coding and adaptive temporal computation in cortical pyramidal neurons. *J. Neurophysiol.* **79**, 1549-1566.

The neuron model has two-compartments, representing the dendrite and the soma plus axonal initial segment, respectively. The somatic and dendritic membrane potentials $V_s$ and $V_d$ obey the following current-balance equations:

$$C_m\frac{dV_s}{dt} = -I_L - I_{Na} - I_K - \frac{g_c}{p}(V_s - V_d) + I_s; \tag{16}$$

$$C_m\frac{dV_d}{dt} = -I_L - I_{Ca} - I_{KCa} - \frac{g_c}{(1-p)}(V_d - V_s) + I_d \tag{17}$$

where $C_m = 1$ $\mu$F/cm$^2$, and $I_L = g_L(V - E_L)$ is the leak current. We express the current flows between the soma and dendrite (proportional to $(V_s - V_d)$) in $\mu$A/cm$^2$, with the coupling conductance

$g_c = 2$ mS/cm$^2$; and the parameter $p$=somatic area/total area=0.5. Other, voltage-gated currents are described below. The cell is excited by an injected current (in $\mu$A/cm$^2$) to the soma or dendrite ($I_s$ or $I_d$ respectively).

Same notations as before for the spike-generating currents. The sodium current $I_{Na} = g_{Na} m_\infty^3(V) h (V - E_{Na})$, where the fast activation variable is replaced by its steady-state, $m_\infty = \alpha_m/(\alpha_m + \beta_m)$, $\alpha_m = -0.1(V+33)/(\exp(-0.1(V+33))-1)$, $\beta_m = 4\exp(-(V+58)/12)$; $\alpha_h = 0.07\exp(-(V+50)/10)$, and $\beta_h = 1/(\exp(-0.1(V+20))+1)$. The delayed rectifier $I_K = g_K n^4 (V - E_K)$, where $\alpha_n = -0.01(V+34)/(\exp(-0.1(V+34))-1)$, and $\beta_n = 0.125\exp(-(V+44)/25)$. The temperature factor $\phi_h = \phi_n = 4$.

The high-threshold calcium current $I_{Ca} = g_{\rm Ca} m_\infty^2(V)(V - E_{Ca})$, where $m$ is replaced by its steady-state $m_\infty(V) = 1/(1+\exp(-(V+20)/9))$. The voltage-independent, calcium-activated potassium current $I_{KCa} = g_{KCa}([Ca^{2+}]/([Ca^{2+}]+K_D))(V - E_K)$, with $K_D = 30\mu$M. The intracellular calcium concentration $[Ca^{2+}]$ is assumed to be governed by a leaky-integrator:

$$\frac{d\left[Ca^{2+}\right]}{dt} = -\alpha I_{Ca} - \left[Ca^{2+}\right]/\tau_{Ca}. \tag{18}$$

where $\alpha$ is proportional to $S/V$ with $S$ being the membrane area and $V$ the volume immediately beneath the membrane. We used $\alpha = 0.002$ (in $\mu$M/(ms$\mu$A/cm$^2$)) so that the $[Ca^{2+}]$ influx per spike is $\sim 0.2$ $\mu$M. The various extrusion and buffering mechanisms are collectively described by a first-order decay process with a time constant $\tau_{Ca} = 80$ ms.

The parameter values were chosen so that the model displays the initial as well as the adapted $f$-$I$ curves similar to data from cortical pyramidal cells: $g_L = 0.1$, $g_{Na} = 45$, $g_K = 18$, $g_{Ca} = 1$ and $g_{KCa} = 5$ (in mS/cm$^2$); $E_L = -65$, $E_{Na} = +55$, $E_K = -80$, $E_{Ca} = +120$ (in mV). The resting state (with $I_s = I_d = 0$) is at $V_s = -64.8$ and $V_d = -64$ mV.

**Question:** can you obtain burst discharges by using a different parameter set? Try smaller $p$ (higher dendrite/soma membrane ratio), smaller $g_c$ (weaker coupling between the soma and dendrite), larger $g_{Ca}$ (stronger voltage-activated inward current in the dendrite).