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Box 10.4. Model leech heart interneuron: Equations and parameters

An oscillator heart interneuron is modeled as a single isopotential compartment with membrane conductances represented by the Hodgkin and Huxley formalism (Hodgkin and Huxley, 1952). The simulations were done with GENESIS software (Bower and Beeman, 1998). The differential equations were integrated with the exponential Euler method with a time step of 10^{-4} seconds. All values are provided in SI (MKS) units.

The dynamics of membrane potential (*V*) of each neuron obey

$$C\frac{dV}{dt} = -(I_{Na} + I_P + I_{CaF} + I_{CaS} + I_h + I_{K1} + I_{K2} + I_A + I_L + I_{SynG} + I_{SynS} - I_{inject}) \quad (1)$$

(From Equation 12)

where C is total membrane capacitance (5×10^{-10} F), I_{ion} is an intrinsic voltage−gated current, I_L is the leak current, I_{SynG} is the graded synaptic current from all presynaptic sources, I_{SynS} is the spike−mediated synaptic current from all presynaptic sources, and I_{inject} is the injected current. Flux of cations into a neuron through voltage−gated and ligand−gated channels is represented by negative current and injected current has the opposite sign convention. Voltage−gated currents are represented by

$$I_{Na} = \bar{g}_{Na} m_{Na}^3 h_{Na} (V - E_{Na}) \quad (2a)$$

$$I_P = \bar{g}_P m_P (V - E_{Na}) \quad (2b)$$

$$I_{CaF} = \bar{g}_{CaF} m_{CaF}^2 h_{CaF} (V - E_{Ca}) \qquad (2c)$$

$$I_{CaS} = \bar{g}_{CaS} m_{CaS}^2 h_{CaS} (V - E_{Ca}) \qquad (2d)$$

$$I_{K1} = \bar{g}_{K1} m_{K1}^2 h_{K1} (V - E_K) \qquad (2e)$$

$$I_{K2} = \bar{g}_{K2} m_{K2}^2 (V - E_K) \qquad (2f)$$

$$I_{KA} = \bar{g}_{KA} m_{KA}^2 h_{KA} (V - E_K) \qquad (2g)$$

$$I_{KF} = \bar{g}_{KF} m_{KF} (V - E_K) \qquad (2h)$$

$$I_h = \bar{g}_h m_h^2 (V - E_h) \qquad (2i)$$

$$I_l = \bar{g}_l (V - E_l) \qquad (2j)$$

where $\bar{g}_{ion}$ is the maximal conductance, E_{ion} is the reversal potential, and m and h are the activation and inactivation variables respectively. These variables are governed by

$$\frac{dm_{k2}}{dt} = \frac{f_\infty(-83, 0.02, V) - m_{K2}}{\tau(200, 0.035, 0.057, 0.043, V)} \qquad (3a)$$

$$\frac{dm_P}{dt} = \frac{f_\infty(-120, 0.039, V) - m_P}{\tau(400, 0.057, 0.01, 0.2, V)} \qquad (3b)$$

$$\frac{dm_{Na}}{dt} = \frac{f_\infty(-150, 0.029, V) - m_{Na}}{0.0001} \qquad (3c)$$

$$\frac{dh_{Na}}{dt} = \frac{f_\infty(500, 0.030, V) - h_{Na}}{\tau_{hNa}(V)} \qquad (3d)$$

$$\frac{dm_{CaF}}{dt} = \frac{f_\infty(-600, 0.0467, V) - m_{CaF}}{\tau_{mCaF}(V)} \qquad (3e)$$

$$\frac{dh_{CaF}}{dt} = \frac{f_\infty(350, 0.0555, V) - h_{CaF}}{\tau(270, 0.055, 0.06, 0.31, V)} \qquad (3f)$$

$$\frac{dm_{CaS}}{dt} = \frac{f_\infty(-420, 0.0472, V) - m_{CaS}}{\tau(-400, 0.0487, 0.005, 0.134, V)} \quad (3g)$$

$$\frac{dh_{CaS}}{dt} = \frac{f_\infty(360, 0.055, V) - h_{CaF}}{\tau(-250, 0.043, 0.2, 5.25, V)} \quad (3h)$$

$$\frac{dm_{K1}}{dt} = \frac{f_\infty(-143, 0.021, V) - m_{K1}}{\tau(150, 0.016, 0.001, 0.011, V)} \quad (3i)$$

$$\frac{dh_{K1}}{dt} = \frac{f_\infty(111, 0.028, V) - h_{K1}}{\tau(-143, 0.013, 0.5, 0.2, V)} \quad (3j)$$

$$\frac{dm_{KA}}{dt} = \frac{f_\infty(-130, 0.044, V) - m_{KA}}{\tau(200, 0.03, 0.005, 0.011, V)} \quad (3k)$$

$$\frac{dh_{KA}}{dt} = \frac{f_\infty(160, 0.063, V) - h_{KA}}{\tau(-300, 0.055, 0.026, 0.0085, V)} \quad (3l)$$

$$\frac{dm_{KF}}{dt} = \frac{f_\infty(-100, 0.022, V) - m_{KF}}{\tau_{mKF}(V)} \quad (3m)$$

$$\frac{dm_h}{dt} = \frac{f_{h\infty}(V) - m_h}{\tau(-100, 0.073, 0.7, 1.7, V)} \quad (3n)$$

where the steady−state activation and inactivation functions are given by a sigmoidal function

$$f_\infty(a, b, V) = \frac{1}{1 + e^{a(V+b)}} \quad (4a)$$

except for the steady−state activation of I_h which is given by

$$f_{h\infty}(V) = \frac{1}{1 + 2e^{180(V+0.047)} + e^{500(V+0.047)}} \quad (4b)$$

The time constants are also sigmoidal except for the inactivation time constant of I_{Na}, the activation time constant of I_{KF}, and the activation time constant of I_{CaF}

$$\tau(a,b,c,d,V) = c + \frac{d}{1+e^{a(V+b)}} \quad (5a)$$

$$\tau_{hNa}(V) = 0.004 + \frac{0.006}{1+e^{500(V+0.028)}} + \frac{0.01}{\cosh(300(V+0.027))} \quad (5a)$$

$$\tau_{mKF}(V) = 1.5 + \frac{8.0}{1+e^{-100(V+0.022)}} + \frac{-2.2}{\cosh(100(V+0.04))} \quad (5a)$$

$$\tau_{mCaF}(V) = 0.011 + \frac{0.024}{\cosh(-330(V+0.0467))} \quad (5a)$$

The graded synaptic current from each graded synaptic input is given by

$$I_{SynG} = \overline{g}_{SynG} \frac{P^3}{C+P^3}(V - E_{Syn}) \quad \text{(6a) (From Equation 7a)}$$

where C is a constant (C=10^{-32} Coulombs^3) and P (Coulombs) is governed by the presynaptic Ca^{2+} currents and a voltage−dependent variable (A) such that

$$\frac{dP}{dt} = I_{Ca} - BP \quad \text{(6b) (From Equation 7b)}$$

where B is a buffering rate constant (B=10 s^{-1}) and

$$I_{Ca} = \max(0, -I_{CaF} - I_{CaS} - A) \quad \text{(6c) (From Equation 7c)}$$

A is given by

$$\frac{dA}{dt} = \frac{A_\infty(V_{pre}) - A}{0.2}$$ (6d) (From Equation 7d)

$$A_\infty(V_{pre}) = \frac{10^{-10}}{1 + e^{-100(V+0.02)}}$$ (6e) (From Equation 7e)

where V_{pre} is the presynaptic membrane potential.

The total spike−mediated synaptic current in each postsynaptic neuron from each spike−mediated synaptic input consists of the sum of the currents of synapses indexed i =1 to N (N is provided in Table 1). The index i is defined for each postsynaptic neuron and enumerates the synapses coming from different presynaptic neurons. For an individual synapse the synaptic conductance is presented as the sum of the conductance changes resulting from the activation by a number of presynaptic spike events (s is the spike index). The latest spike is assigned s=1, and s of all previous spike events is incremented by one. Spike events are detected when the presynaptic voltage (V_{pre}) crosses over a threshold (−0.10 mV) for the first time after a refractory period (0.010 sec) from the latest spike event. The time of a spike event is assigned a time of occurrence (t_{spike}). The synaptic current is

$$I_{SynS}(t,V) = \left(V(t) - E_{Syn}\right) \sum_{i=1}^{N} \sum_{s=1}^{\infty} M_i \bar{g}_{SynS\,i} f_{SynS_i}\left(t - t_{spike}\right)$$ (7) (From Equation 2).

where $\bar{g}_{SynS}$ is the maximal synaptic conductance and M is a modulation variable and

$$f_{SynS}(t) = a\left(e^{-t/\tau_1} - e^{-t/\tau_2}\right)$$ (8a) (From Equation 4)

where a is a normalization constant chosen so that f_{SynS} reaches a maximal value of 1. Thus,

$$a = \frac{1}{e^{-t_{peak}/\tau_1} - e^{-t_{peak}/\tau_2}}$$ (8b) (From Equation 4)

where t_{peak} is the time to peak of the postsynaptic conductance and

$$t_{peak} = \frac{\tau_1 \tau_2 \ln\left(\frac{\tau_1}{\tau_2}\right)}{\tau_1 - \tau_2}$$ (8c) (From Equation 4)

where τ_1 and τ_2 are time constants that determine, respectively, the decay and rise times of the synaptic conductance ($\tau_1 > \tau_2$). For spike−mediated synapses between elemental oscillator neurons (e.g. HN(L,3) to HN(R,3)). M is determined by

$$\frac{dM}{dt} = \frac{M_\infty(V_{pre}) - M}{0.2}$$ (9a) (From Equation 10a)

$$M_\infty = 0.1 + \frac{0.9}{1 + e^{-1000(V_{pre}+0.04)}}$$ (9b) (From Equation 10b)

where V_{pre} is the presynaptic membrane potential. For all other spike−mediated synapses M=1.

Canonical synaptic parameter values:

Table 1. Parameters of spike−mediated synapses. Each postsynaptic neuron receives synapses indexed by a number (*i*). For example, *i*=1 for the synapse that HN(L,1) receives from HN(L,3). Each synapse is described by 3 parameters that are ordered as follows, $\bar{g}_{SynS}$ (S), τ_1 (sec), τ_2 (sec). The parameters of the synaptic connections for HN(2) are identical to those for HN(1).

Postsynaptic neuron	*i*=1	*i*=2	*i*=3
HN(L,1) HN(L,2)	HN(L,3) 6×10^{-9}, 0.055, 0.01	HN(L,4) 6×10^{-9}, 0.055, 0.01	not applicable
HN(R,1) HN(R,2)	HN(R,3) 6×10^{-9}, 0.055, 0.01	HN(R,4) 6×10^{-9}, 0.055, 0.01	not applicable
HN(L,3)	HN(L,1) 8×10^{-9}, 0.011, 0.002	HN(L,2) 8×10^{-9}, 0.011, 0.002	HN(R,3) 60×10^{-9}, 0.011, 0.002
HN(R,3)	HN(R,1) 8×10^{-9}, 0.011, 0.002	HN(R,2) 8×10^{-9}, 0.011, 0.002	HN(L,3) 60×10^{-9}, 0.011, 0.002
HN(L,4)	HN(L,1) 8×10^{-9}, 0.011, 0.002	HN(L,2) 8×10^{-9}, 0.011, 0.002	HN(R,4) 60×10^{-9}, 0.011, 0.002
HN(R,4)	HN(R,1) 8×10^{-9}, 0.011, 0.002	HN(R,2) 8×10^{-9}, 0.011, 0.002	HN(L,4) 60×10^{-9}, 0.011, 0.002

Table 2. Parameters of graded synapses. Each postsynaptic neuron receives 1 synapse that is determined by the parameter $\bar{g}_{SynG}$ (S).

Postsynaptic neuron	
HN(L,3)	HN(R,3): 30×10^{-9}
HN(R,3)	HN(L,3): 30×10^{-9}
HN(L,4)	HN(R,4): 30×10^{-9}
HN(R,4)	HN(L,4): 30×10^{-9}

Canonical parameter values:

Reversal potentials are $E_{Na} = 0.045$ V, $E_{Ca} = 0.135$ V, $E_k = -0.07$ V, $E_h = -0.021$

V, $E_{Syn} = -0.0625$ V, for {HN(L,1), HN(R,1), HN(L,2), HN(R,2)} $E_L = 0.04$ V, for {HN(L,3), HN(R,3), HN(L,4), HN(R,4)} $E_L = -0.06$ V.

Maximal conductances for the elemental oscillator neurons {HN(L,3), HN(R,3), HN(L,4), and HN(R,4)} are $\bar{g}_{Na} = 200\times10^{-9}$ S, $\bar{g}_P = 7\times10^{-9}$ S, $\bar{g}_{CaF} = 5\times10^{-9}$ S, $\bar{g}_{CaS} = 3.2\times10^{-9}$ S, $\bar{g}_{K1} = 100\times10^{-9}$ S, $\bar{g}_{K2} = 80\times10^{-9}$ S, $\bar{g}_{KA} = 80\times10^{-9}$ S, $\bar{g}_{KF} = 0$ S, $\bar{g}_h = 4\times10^{-9}$ S, $\bar{g}_l = 8\times10^{-9}$ S.

Maximal conductances for coordinating neurons {HN(L,1), HN(R,1), HN(L,2), HN(R,2)} are $\bar{g}_{K1} = 150\times10^{-9}$ S, $\bar{g}_{K2} = 75\times10^{-9}$ S, $\bar{g}_l = 10\times10^{-9}$ S. For HN(L,1) and HN(R,1) $\bar{g}_{Na} = 255\times10^{-9}$ S, and for HN(L,2) and HN(R,2) $\bar{g}_{Na} = 250\times10^{-9}$ S.

This entire model is provided here as part of a GENESIS tutorial (accompanying CD). All free parameters are accessible for manipulation by the user, and the reader is encouraged to explore model behavior and the effects of parameter changes, and to perform the suggested exercises. Model GENESIS scripts can be examined with any conventional text editor such as VI or emacs. We have recently used the current network model as a GENESIS tutorial in an undergraduate/graduate level course in computational neuroscience at Emory University.
