UNIVERSITY OF RHODE ISLAND
Department of Electrical, Computer and Biomedical Engineering

BME 307 Bioelectricity Fall 2015

Purkinje Fiber Action Potential Model (Noble 1962)

Simulation Project

Report due on Wednesday, December 23, 2015, by 2:30 pm
Late reports: 20% will be deducted for each hour after the deadline.

The MATLAB scripts and functions you wrote as part of Homework Assignments 8, 9, and 10 are the starting point. You will modify your scripts and/or functions, and possibly create new ones, to conduct this experiment and analyze the results.

Report: Your report should be targeted to an audience that understands the Hodgkin-Huxley model, but not your topic of study. The report must include a statement of the problem (or the question being studied), the methods used to solve the problem (including equations and numerical algorithms), and the results of your investigation. Figures or graphics may be integrated with the text or arranged sequentially immediately after the references. The report must close with a discussion section, where the results and their implications are described. Plots must show appropriately labeled axes, including units. Appendices will contain your scripts and any lengthy derivations. Full citations to any reference materials used in your study must be included.

Score: The projects will be graded 15% for your analysis (the content of the report) and 5% for the style of the report. Superior reports will include analysis beyond what is required.

The first mathematical description of the cardiac action potential was developed in 1962. The Noble model [1] was the basis for more recent models of the electrical conduction system in the heart [2, 3]. The model was formulated directly from the Hodgkin-Huxley model: nonlinear membrane conductances are modeled using a saturation value and activation and inactivation gates, with voltage-dependent opening and closing rates. This model is more complex, however, because it reproduces the natural rhythmic depolarizations of the Purkinje fiber. In addition, the model includes a chloride current in place of the Hodgkin-Huxley leak current.

The purpose of this study is to implement the Noble model and compare the Purkinje action potential to the action potential in the squid giant axon.

The Noble model uses four state variables:

1. V_{m}, membrane potential
2. n, slow potassium activation gate
3. m, sodium activation gate
4. h, sodium inactivation gate

These state variables are handled same way as those in the Hodgkin-Huxley model. The complete Noble model is listed below. The simulation will generate a membrane action potential (a non-propagating action potential at a point).

Modify the Hodgkin-Huxley scripts to implement the Noble Purkinje fiber model. The simulation should cover 2 seconds using a time step Δt = 0.10 milliseconds.

Show the equivalent circuit model of Noble's purkinje membrane model. Generate plots of the membrane potential, currents, and gates. Plot the gate time constants versus V_{m}. Compute the action potential amplitude, the duration at 90% repolarization (APD_{90}) and the maximum upstroke velocity, $dV/dt_{\max}$. What is the intrinsic period of the action potentials? Vary the chloride conductance from zero to 0.14 mS/cm^2. How does the action potential change? Does the amplitude, APD_{90}, $dV/dt_{\max}$, and/or the period change? You should read the original article [1] for more information.

Purkinje Fiber Action Potential Model (Noble 1962)

Currents are given in μA/cm^2, conductances in mS/cm^2, and potentials in mV. Note that l'Hôpital's rule must be applied to some of the opening and closing rates.

$$J_{\text{ion}} = J_{\text{Na}} + J_{\text{K}} + J_{\text{Cl,b}} + J_{\text{Na,b}} \qquad \text{ion current}$$

$$J_{\text{Na}} = \overline{g}_{\text{Na}} \cdot m^3 \cdot h \cdot (V_{\text{m}} - E_{\text{Na}}) \qquad \text{fast Na}^+ \text{ current}$$

$$J_{\text{K}} = (g_{K1} + g_{K2}) \cdot (V_{\text{m}} - E_{\text{K}})$$

$$g_{K1} = \overline{g}_{\text{K}} \exp\left[-\left(V_{\text{m}} + 90\right)/50\right] + 0.015 \exp\left[\left(V_{\text{m}} + 90)\right)/60\right]$$

$$\text{pacemaker K}^+ \text{ conductance}$$

$$g_{K2} = \overline{g}_{\text{K}} \cdot n^4 \qquad \text{outwardward rectifying K}^+ \text{ conductance}$$

$$J_{\text{Na,b}} = g_{\text{Na,b}} \left(V_{\text{m}} - E_{\text{Na}}\right) \qquad \text{background Na}^+ \text{ current}$$

$$J_{\text{Cl,b}} = g_{\text{Cl,b}} \left(V_{\text{m}} - E_{\text{Cl}}\right) \qquad \text{background Cl}^- \text{ current}$$

Nernst potentials, conductances, and membrane capacitance:

$$E_{\text{Na}} = 40 \qquad \overline{g}_{\text{Na}} = 400$$
$$E_{\text{K}} = -100 \qquad \overline{g}_{\text{K}} = 1.2$$
$$E_{\text{Cl}} = -60 \qquad g_{\text{Na,b}} = 0.14$$
$$C_{\text{m}} = 12\ \mu\text{F/cm}^2 \qquad g_{\text{Cl,b}} = 0.075$$

The initial values of the state variables are:

$$V_{\text{m}} = -81.6 \text{ mV} \qquad m = 0.04338$$
$$n = 0.60888 \qquad h = 0.85218$$

The three gates are governed by the opening and closing rates (in msec^{-1}):

$$\alpha_m = \frac{0.1\left(V_{\text{m}} + 48\right)}{1 - \exp\left[-(V_{\text{m}} + 48)/15\right]} \qquad \beta_m = \frac{0.12\left(V_{\text{m}} + 8\right)}{\exp\left[(V_{\text{m}} + 8)/5\right] - 1}$$

$$\alpha_h = 0.17 \exp\left[-(V_{\text{m}} + 90)/20\right] \qquad \beta_h = \frac{1}{1 + \exp\left[-(V_{\text{m}} + 42)/10\right]}$$

$$\alpha_n = \frac{0.0001\left(V_{\text{m}} + 50\right)}{1 - \exp\left[-(V_{\text{m}} + 50)/10\right]} \qquad \beta_n = 0.002 \exp\left[-(V_{\text{m}} + 90)/80\right]$$

[1] Denis Noble. A modification of the Hodgkin-Huxley equations applicable to Purkinje fibre action and pace-maker potentials. *Journal of Physiology*, 160:317–352, February 1962.

[2] R. E. McAllister, D. Noble, and R. W. Tsien. Reconstruction of the electrical activity of cardiac Purkinje fibres. *Journal of Physiology*, 251(1):1–59, September 1975.

[3] D. DiFrancesco and Denis Noble. A model of cardiac electrical activity incorporating ionic pumps and concentration changes. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, 307(1133):353–398, January 10 1985.