

# Neurodynamics - Fall 2017

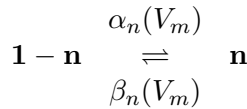
## BENG 260 / BGGN 260 / PHYS 279

### Homework 2: Due October 20

#### Computational Lab

##### 1. Two State Markov Model [30 points].

Assume we have a simple two state Markov model where  $n$  denotes the fraction of gates open, and  $1 - n$  denotes the fraction of gates closed. The opening rate is  $\alpha_n(V_m) = \alpha_0 e^{\lambda V_m}$  and the closing rate is  $\beta_n(V_m) = \beta_0 e^{-\mu V_m}$ . Let  $\alpha_0 = \frac{0.7}{s}$ ,  $\beta_0 = \frac{0.9}{s}$ ,  $\lambda = \mu = \frac{0.01}{mV}$ . The Markov diagram is as follows:



The rate equation for the mean field for this Markov process is

$$\frac{dn}{dt} = \alpha_n(V_m)(1 - n) - \beta_n(V_m)n$$

We apply an input voltage  $V_m(t) = 30 * H(t - t_{input})$  where  $H(t)$  is the Heaviside step function and  $t_{input} = 8$  s. Assume all gates begin in the closed state.

- Solve for  $n(t)$  analytically.
- Plot the time constant,  $\tau_n$  from -100:100. *Hint:*  $V_m$  is a step function, so  $\tau_n$  should also be a step function.
- Solve for  $n(t)$  computationally using an ode solver.
- Simulate this Markov process stochastically to find the fraction of gates open,  $n(t)$ , for different number of channels  $N = 1, 400, 1000$ . Compare your three solutions by plotting  $n(t)$  for  $t$  from 0 to 16 s.

##### 2. Simulating Hodgkin-Huxley neurons [30 points].

We will simulate the Hodgkin-Huxley (HH) model of action potential generation in the squid giant axon. You will program these equations so you can use them on the homework. The template code provides a coded example of the Morris-Lecar equations which you can use for reference.

The equations describing the HH dynamics are replicated here for convenience:

$$\frac{dV}{dt} = \frac{1}{C} (-I_{Na} - I_K - I_L + I_{ext}) \quad (1)$$

$$I_{Na} = g_{Na} m^3 h (V - E_{Na}) \quad (2)$$

$$I_K = g_K n^4 (V - E_K) \quad (3)$$

$$I_L = g_L (V - E_L) \quad (4)$$

with parameters:

$$\begin{aligned}
C &= 1 \mu F/cm^2 \\
E_{Na} &= 115 mV; & g_{Na} &= 120 mS/cm^2 \\
E_K &= -12 mV; & g_K &= 36 mS/cm^2 \\
E_L &= 10.613 mV; & g_L &= 0.3 mS/cm^2
\end{aligned} \tag{5}$$

where the dynamics of gating variables:

$$\frac{dm}{dt} = \alpha_m(V) (1 - m) - \beta_m(V) m \tag{6}$$

$$\frac{dh}{dt} = \alpha_h(V) (1 - h) - \beta_h(V) h \tag{7}$$

$$\frac{dn}{dt} = \alpha_n(V) (1 - n) - \beta_n(V) n \tag{8}$$

is determined by rate functions:

$$\alpha_m(V) = (25 - V)/(10 * (\exp((25 - V)/10) - 1)) \tag{9}$$

$$\beta_m(V) = 4 \exp(-V/18) \tag{10}$$

$$\alpha_h(V) = 0.07 \exp(-V/20) \tag{11}$$

$$\beta_h(V) = 1/(\exp((30 - V)/10) + 1) \tag{12}$$

$$\alpha_n(V) = (10 - V)/(100 * (\exp((10 - V)/10) - 1)) \tag{13}$$

$$\beta_n(V) = 0.125 \exp(-V/80) \tag{14}$$

- A. Plot the rates  $\alpha_m$ ,  $\beta_m$ ,  $\alpha_h$ ,  $\beta_h$ ,  $\alpha_n$ , and  $\beta_n$  as functions of membrane voltage  $V$ , for range -20 to +120 mV.
- B. Starting with just  $I_L$ , the leak current, leaving out  $I_{Na}$  and  $I_K$ :

$$\frac{dV}{dt} = \frac{1}{C} (-I_L + I_{ext}) \tag{15}$$

$$I_L = g_L (V - E_L) \tag{16}$$

$$C = 1 \mu F/cm^2; \quad E_L = 10.613 mV; \quad g_L = 0.3 mS/cm^2 \tag{17}$$

We have an RC circuit representing a passive membrane. Plot  $V$  as a function of time  $t$ . Try different values for the injected current  $I_{ext}$ , starting with a value  $I_{ext} = 10 \mu A/cm^2$ .

- C. Now add  $I_{Na}$ ,  $I_K$ , and their gating variables  $n$ ,  $m$ , and  $h$  to observe spiking. Plot the membrane voltage  $V$  and the gating variables  $n$ ,  $m$ , and  $h$  as a function of time  $t$ , for different values of injected current  $I_{ext}$  as in (B).
- D. These parameter settings in the HH equations set the resting potential at zero. How would you modify the parameters to set the resting potential at -70 mV? How would you modify the parameters to increase the threshold of injected current  $I_{ext}$  for spiking?

## Homework Problems

### 3. Reduction of HH to two-dimensional dynamics [40 points].

The HH equations that you just simulated involve 4 dynamic variables,  $V$ ,  $n$ ,  $m$ , and  $h$ . Now we will try to simplify the dynamics to the smallest possible number of dynamic variables capable of generating spiking dynamics. In this case it will be 2 dynamic variables - systems with fewer than 2 variables can generate limit cycles.

- A. We will first try to collapse  $h$  and  $n$  into a single dynamical variable,  $n$ . For the full HH data that you generated in (2C), show a scatter-plot of  $h$  as a function of  $n$ . How strong is the relationship? Try a linear regression of  $h$  in terms of  $n$ :

$$h = \lambda - \mu n. \quad (18)$$

- B. Next, we will approximate the dynamics of the fast Na activation variable  $m(t, V)$  with its instantaneous (equilibrium) value

$$m_{\infty}(V) = \alpha_m(V)/(\alpha_m(V) + \beta_m(V)). \quad (19)$$

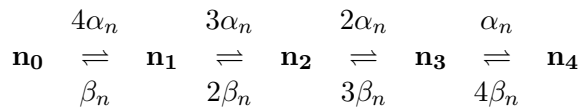
For the full HH data that you generated in (2C), show a scatter-plot of  $m_{\infty}(V(t))$  as a function of  $m(t)$ . How strong is the relationship?

- C. Now rerun the HH simulations of (2C) in reduced form, replacing  $h$  with its linear regression from (A), replacing  $m$  with  $m_{\infty}(V)$ . Compare the reduced HH output with the full HH output of (2C).

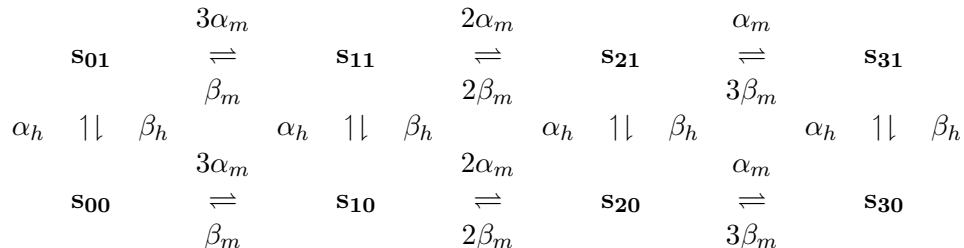
*Note:* The reduced HH model that you just simulated is similar to the FitzHugh-Nagumo, and Morris-Lecar simplified spiking models in two reduced variables ( $V$  and  $W$  for FitzHugh-Nagumo, and  $V_m$  and  $w$  for Morris-Lecar, as in the Week 2 lecture notes.) Two-dimensional models are useful for stability analysis using null-clines as we will see in Week 3.

### 4. Hodgkin-Huxley Model With Expanded Channel Gating Dynamics [Bonus Problem: 20 points].

- (a)  $K^+$  Channel Gating Dynamics: Show that  $n_4 = n^4$  where  $n_4$  is the only state of the Potassium channel Markov model that corresponds to an active channel, and  $n^4$  denotes the solution of a two state Markov model (using opening and closing rates corresponding to the Potassium channel) raised to the fourth power. The full Potassium channel Markov model is as follows:



- (b)  $Na^+$  Channel Gating Dynamics: Show that  $s_{31} = m^3 h$ .  $s_{31}$  is the only state of the sodium channel Markov model that corresponds to an active channel;  $m^3$  denotes the time course probability of the sodium activation gate being in the open state, raised to the third power;  $h$  denotes the time course probability of the sodium inactivation gate being in the open state. The full sodium channel Markov model is as follows:



- (c) Now simulate the entire Hodgkin-Huxley model stochastically and compare with your simulation from Problem 2. Vary your differential equation for  $V_m$  by using different combinations of currents. Adjust your external current so that you are slightly below threshold, then increase your current so you are slightly above threshold, and compare.

### **Submission Guidelines**

Solutions without work or explanations where applicable will receive no credit. Submit a single .zip file containing solutions, plots, and Matlab/Python code to both computational lab and homework problems by 3:00pm of due date on TritonEd.

The submission file should follow the naming scheme `LastFirst_A12345678_HW2.zip`.