# Winter 2019 PHYS 178/278, Homework 1
# Due 11:59 PM, January $27^{th}$

Please submit your assignment either as a printed hard copy or as *.pdf file via email (whsu@physics.ucsd.edu). The supplemental codes of Prob. 2 are written in MATLAB, but you are welcome to use any software or programming language you are familiar.

## 1 Poisson statistics

**1.1** Compute the first and second moments ($\langle n \rangle, \langle n^2 \rangle$) of the Poisson distribution:

$$P(n) = \frac{\lambda^n}{n!} e^{-\lambda} \tag{1}$$

$$\langle n \rangle = \sum_{n=0}^{\infty} n P(n) \tag{2}$$

$$\langle n^2 \rangle = \sum_{n=0}^{\infty} n^2 P(n) \tag{3}$$

**Hint**: First show that $P(n)$ is normalized ($\sum_{n=0}^{\infty} P(n) = 1$) by using the Taylor series expansion of $e^{\lambda}$.

**1.2** Discuss how having measured a spike train with Poisson or non Poisson firing statistics may inform you on the type of code a certain neuron is using (rate/temporal code).

**1.3** Why can't a neuron with an absolute refractory period or a tendency to burst be properly modeled by a Poisson process with a time independent firing rate?

**1.4** Why can't a neuron with nonlinear dendritic integration be properly modeled by a Poisson process?

## 2 Conductance models and ion channels

**2.1** The attached `MATLAB` file, `HHModel.m`, includes the original equations written by Hodgkin and Huxley:[1]

$$C\frac{dV}{dt} = -\overline{g}_L (V - V_L) - \overline{g}_{Na} m^3 h (V - V_{Na}) - \overline{g}_K n^4 (V - V_k) + I(t), \tag{4}$$

$$\frac{dn}{dt} = (1-n)\alpha_n - n\beta_n, \tag{5}$$

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

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

[1] The only difference from the original paper is that we use the modern sign convention for the voltage. Notice that this original formulation is in terms of a "maximal conductance" for each type of "current," while in modern language we could talk about the number of each type of channel. In fact, the more phenomenological description persists, because it corresponds more directly to what is measured, but this allows us to forget that parameters such as $\overline{g}_K$ actually measure the number of copies of a protein that have been inserted into the membrane.

A. L. Hodgkin & A. F. Huxley, "A quantitative description of membrane current and its application to conduction and excitation in nerve." The Journal of Physiology 117 (4): 500–544 (1952).

and all the $\alpha$ and $\beta$ are given by,

$$\begin{aligned}
\alpha_n(V) &= \frac{0.01(-V+10)}{e^{\left(\frac{-V+10}{10}\right)}-1}, \quad \beta_n(V) = 0.125\exp\left(\frac{-V}{80}\right); \\
\alpha_m(V) &= \frac{0.1(-V+25)}{e^{\left(\frac{-V+25}{10}\right)}-1}, \quad \beta_m(V) = 4\exp\left(\frac{-V}{18}\right); \\
\alpha_h(V) &= 0.07\exp\left(\frac{-V}{20}\right), \quad \beta_h(V) = \frac{1}{e^{\left(\frac{-V+30}{10}\right)}+1},
\end{aligned}$$

where $Na$ and $K$ refer to sodium and potassium channels, respectively; time is measured in milliseconds and voltage $V$ is measured in milliVolts (mV). These equations are intended to describe a small patch of the membrane, and so many parameters are given per unit area: $c_m = 1\mu\text{F/cm}^2$, $\bar{g}_L = 0.3$ mS/cm$^2$, $\bar{g}_{Na} = 120$ mS/cm$^2$, $\bar{g}_K = 36$ mS/cm$^2$[2]; the reversal potentials are $V_L = 10.613$ mV, $V_{Na} = 115$ mV, $V_K = -12$ mV.

**Rewrite Eqn. (5), (6) and (7) in terms of equilibrium values and relaxation times for the gating variables, e.g.,**

$$\frac{dm}{dt} = -\frac{1}{\tau_m(V)}\left[m - m_{eq}(V)\right],$$

**where $m_{eq}(V)$ is the solution when system reaches dynamical equilibrium, and $\tau_m(V)$ is the relaxation time. Both $m_{eq}(V)$ and $\tau_m(V)$ can be expressed in terms of $\alpha_m(V)$ and $\beta_m(V)$. Plot these quantities: $m_{eq}(V)$, $n_{eq}(V)$, $h_{eq}(V)$, and $\tau_m(V)$, $\tau_n(V)$, $\tau_h(V)$, as a function of voltage $V$. Can you explain, intuitively, the form of the curves?**

**2.2** Use the `MATLAB` files, `HHModel.m` and `plotHH.m`, **to simulate a Hodgkin-Huxley neuron in response to different constant current inputs. What is the minimal input (threshold current) required for spike generation?**

**2.3** Explore the frequency of the pulses as a function of current. Count the number of spikes in a window of fixed size (say, 1000 ms) for different values of the driving current and **plot the "F-I curve" (the frequency as a function of the driving current). Can the cell be driven to fire at an arbitrarily high frequency?**

**Hint:** `MATLAB` function `findpeaks`(...) could be helpful for counting the number of spikes. You may need to write a short `MATLAB` code to finish this plot.

**2.4** Spike triggered average (STA). **Firstly, simulate and plot a Hodgkin-Huxley neuron in response to white Gaussian noise input currents $\mathtt{I_{in}(t)}$** at a short time window (ex, $\mathtt{t} = 0$ to 2000 msec). The values of $\mathtt{I_{in}(t)}$ are sampled at the time step between $0.05 \sim 1$ mesc. You may have to adjust the power of noise samples such that the $\mathtt{I_{in}(t)}$ induces many *isolated* spikes (not bursting).

From the sequence of spiking events, **calculate and plot the spike-triggered average** over the range of 30 msec before and after the spike (i.e., show STA between -30 to 30 msec relative to a spike). The time of a spike is defined as the moment of reaching the maximal peak voltage.[3]

Next, **try to increase the simulation time** (ex, 20000 msec or more) **to get a smother STA curve. Is there anything special about the STA trajectory? Briefly describe your results.**

**Hint:** `MATLAB` function `wgn`(...) returns white gaussian noise values. Use the additional file `runHHModel.m` to simulate a H-H neuron that receives the time-dependent currents.

[2]The symbol **S** (siemens) is the unit of electric conductance in SI unit; **S**(siemens) = $1/\Omega$(Ohm).
[3]Arcas, B. A. Y., Fairhall, A. L., & Bialek, W. (2003). Neural Comp., 15(8), 1715-1749.

**2.5** The leaky integrate-and-fire neuron is a simplified of spiking neuron model. The equation for a dimensionless leaky integrate-and-fire neuron is:

$$\begin{cases} \dot{v} = -v + I & \text{if } v < v_{th} \\ \text{reset } v \text{ to } 0 & \text{if } v \geq v_{th},\ v_{th} = 1 \end{cases} \tag{8}$$

Here is how it works: if a large enough input current is applied, the membrane voltage increases with time until it reaches a constant threshold $v_{th}$, at which a spike occurs by stipulation and the voltage is reset to its resting potential, after which the model continues to run. **Find the F-I curve without simulating the neuron model and plot it alongside the F-I curve you found in 2.3. Are they qualitatively the same? Why or why not?**

**Hint:** To find the F-I curve solve the differential equation assuming there is no reset condition.
Then set the initial condition to $v(t = 0) = 0$.
Find the time it takes the neuron to spike from that initial condition, as a function of $I$.

**2.6** From dimensional analysis and using the electrophysiological properties of "typical cells" as shown in the lecture notes, **estimate the number of ions that cross the membrane during a single action potential**.

**Hint:** you may treat the cell as a capacitor obeying the equation $Q = CV$, and its size is approximated as a sphere of radius $a \approx 20\mu m$.