Problem Set #2: biophysical models

For this problem set, you will need several more MATLAB functions, downloadable from the ELMs site. Most are for the Hodgkin-Huxley model described in lecture, and also described in detail in Dayan & Abbott Section 5.6.

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1. INTEGRATE-AND-FIRE NEURON. Simulate an integrate-and-fire neuron responding to a current step, following the instructions below. This neuron works as described in lecture: its voltage at rest is zero, and is governed by the following dynamical equation:

$$\tau \frac{dV}{dt} = -V + R_m I_{ext}(t)$$

This means that, to calculate the voltage at time step $t+\Delta t$, you use the following equation:

$$V(t+\Delta t) = V(t) + \frac{\Delta t}{\tau}\left[-V(t) + R_m I_{ext}(t)\right]$$

For this problem, set τ = 10 ms (1e-2 sec) and R_m = 2.5 MΩ (2.5e6 Ω). Note that using the units in parentheses will make everything scaled appropriately, with the resulting voltage in units of volts (V) -- i.e., multiply by 1000 to give it units of mV. Because we are using V = 0 as rest, assume that the threshold is at +15 mV (remember to use units of Volts) and the V_{reset} = -5 mV;

A. Define the experiment: Make a time variable **`ts`** that extends with resolution with resolution **`dt`** = 0.01 ms (1e-5 sec) for the duration of the experiment (500 ms). Define a second array **`I0template`**, which will be a template for the current step. It should be set to zero for the first 100 ms, then set to 1.0 for then next 300 ms, and then back to 0 for the last 100 ms. Note that this template can then be multiplied by any constant value to set the current step to a variety of currents, i.e., **`1e-9*I0template`** would produce a 1 nA current step. Using this template, make and plot **`I0`** corresponding to a 7 nA current step versus time.

B. Simulate the I&F neuron to 7 nA current pulse: Simulate the response of the integrate-and-fire neuron described above to the 7 nA current **`I0`** defined in part A. In addition to following the differential equation shown above, when the neuron hits threshold, make the neuron "spike" by setting the voltage to 60 mV above threshold for one time step, and in the next time step set it to V_{reset}. Plot the resulting voltage as a function of time for the duration of the experiment. How many spikes does it fire? (please determine this answer by visual inspection)

C. Generate the I-F (current versus firing rate) curve for the I&F neuron: Calculate the voltage response to current steps from 0 nA up through 20 nA at 0.5 nA resolution. In each case, count the number of spikes using the function (on the ELMs site) **`simple_spike_count.m`**, e.g.,

```
>> Nspks = simple_spike_count( Vt, 0.04 );
```

Note that the second parameter for this function is the voltage threshold -- above which a spike is defined. [Feel free to look at the code for this, although its function may be more interesting in Problem #2.] Definitely verify that it returns the answer you get from visually counting spikes.

Plot the firing rate versus the size of the current step. Does this look like you would expect? Why or why not?

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2. HODGKIN-HUXLEY NEURONS. Rather than ask you to implement the equations of the Hodgkin-Huxley neuron from scratch, I have provided the relevant MATLAB functions on the ELMs site. The only one you will need to call is **`HHmodel.m`**, whose function can be seen by typing **`help HHmodel`**. It uses the other function on the ELMs site, so make sure that they are in the same directory. Please feel free to play around with this code, and see how it is written: it is very straightforward.

   IMPORTANT: In this case, the response of the H-H model code takes the current in units of nA, so the current step fed in should be of magnitude 7, not 7e-9 as in the first problem.

   A. Using the same current step and time variables defined in Problem #1, use **`HHmodel`** to simulate the response of a Hodgkin-Huxley neuron to the current step of magnitude 7 nA without the noise. Plot the resulting voltage versus time.

   B. Find a time window from the beginning of the current step (100 ms) up to the beginning of the third spike, and replot the voltage within this range. On a separate plot (or subplot), plot the variables m, n, and h. Explain why each of these curves increases and decreases (not necessarily in this order) over the course of the first spike.

   C. Calculate the F-I curve for the Hodgkin-Huxley model, as described above in Problem 1C. Plot the firing rate as a function of the size of the current step from 1 nA up to 20 nA. Describe how this F-I curve looks different than that of problem 1, and describe one reason.

3. NOISE IN HODGKIN-HUXLEY NEURONS. Biophysical modeling of neurons is generally deterministic, meaning injecting the same current will result in the exact same response. Neurons in most experimental contexts are not like this, however. There are many sources of neuronal variability, and in realistic contexts, one of the largest contributors to variability is inputs from other neurons. Neurons are generally embedded in a large network with many excitatory and inhibitory inputs at any given time, which often cannot be experimentally determined, and thus can be thought of as "noise".

   One of the easiest ways to realistically introduce noise is to treat it as an additional current input that varies from trial to trial. Membrane noise and noise from unknown synaptic inputs can be modeled as "correlated noise". It is correlated because it does not instantaneously vary over time, but rather has a particular context. You will use **`lowpass_gwn.m`** to generate this noise, which takes Gaussian white noise and filters out the highest frequency components, resulting a current that changes randomly in a correlated way (meaning it smoothly varies at small time scales). We will use noise with a 1 ms time scale (1000 Hz cutoff). With **`dt = 1e-5`** (0.01 ms), and a 500 ms-long experiment, to create an instance of noise:

   ```
   >> Inoise = lowpass_gwn( 1000, 0.5, 1e-5 );
   ```

   You can play around with the frequency cutoff to see how it affects the noise. Use the current step generated in Problem 2, with a magnitude of 7 nA.

   A. Generate one instance of noise as described above. Multiply the noise such that it has a standard deviation of 3 nA, and add it to the current. Simulate the H-H neuron in response to this current step with and without noise, and plot each voltage versus time on the same plot.

   B. Perform 32 repetitions of the experiment with noise, each with a different instance of noise (simply run **`lowpass_gwn`** to generate a new instance). In each instance, count the number of spikes during the current step (using simple_spike_count), and plot the number of spikes versus trial number.

   C. Calculate the mean firing rate during the current step, and the Fano factor for this neuron. Does this neuron appear to be Poisson? Why or why not?