BME 665/ 565 Exam 2 Solutions

1. **Spiking neuron models**

   A. The conductance introduced in this question is similar to the I_{AHP} calcium-dependent potassium conductance. Spike rate adaptation is caused by the opposition of the input current and the adaptation current *g*; the spike rate reaches a maximum level dependent on the interaction of these two factors. The magnitude of the effect is determined by the resistance r_m and the time constant τ_{rsa}, as some folks saw by varying these parameters during their simulation. In addition, the relationship between τ_{rsa} and τ_m can determine whether or not this conductance leads to a refractory period without resetting *g* after each spike. Greater r_m means there is a greater effect of the adaptation current – it leads to a lower spike rate (and faster adaptation); greater τ_{rsa} (slower time constant for the conductance) leads to a larger adaptation. When τ_{rsa} is very short (close to the inter-spike interval), then a refractory period is observed.

   For adaptation to occur, the current must change over time (which happens because g_{rsa} decreases in time). The new conductance creates a driving force towards E_K. Whether or not the neuron spike rate adapts to a *higher* or *lower* rate depends on whether or not the driving force towards E_K is increasing or decreasing. If the new conductance causes a negative current that drives the cell away from the firing threshold, then the spike rate will be lower because the neuron will take longer to reach threshold. The converse is also true. It was possible to see either an increase or a decrease in the firing rate using just the conductance as defined by the problem.

   However, resetting (increasing) *g* after each spike, as happens with IAHP, results in a firing-rate adaptation where the firing rate decreased over time.

   B. Resetting *g* after each spike allows us to model the refractory period. It is important in this case that the larger *g* inhibit a spike. For this to be true, the current must be negative – that is, we need to have $V<E_K$. Physiologically, this could represent a voltage-dependent conductance that increases in response to a spike, then decreases exponentially over time. Considering the case where we have ($V < E_K$), the increase in conductance after a spike would result in an increasing negative current immediately following the spike, slowing the movement of the membrane potential to threshold – i.e. causing a refractory period. Bottom line: large g_{rsa}, fast (small) τ_{rsa} is needed.

2. **Population decoding**

   A. Most people correctly noted that without noise, this system can accurately encode any wind direction. However, neural systems are not without noise, and hence the noise is an important component to model. Most people pointed out the variability in the noise with the true wind direction, and proposed a reasonable interpretation for why it occurred. For example, since each neuron contributing to the response is noisy, the noise is least where

the fewest neurons are contributing – i.e. in the preferred direction of any particular neuron.

B. The source of the error is, of course, the noise, and so the solution is to modify the model to reduce the effect of the noise. Most people chose to add neurons with additional optimal tuning directions, but other solutions were proposed, including changing the tuning curve. Some people suggested just removing the noise – while obviously this reduces the noise, it's a trivial result and I was looking for more than this. I was also looking for some evidence that your solution worked (such as a simulation of the results).

3. **Phase Plane analysis**

A. At I=1.0, the equilibrium point is a complex conjugate pair with negative real parts, indicating that it is a stable spiral. Consequently, you would expect the voltage to spike, and then exhibit damped oscillations to a steady state value. At I=1.1, the equilibrium point is a complex conjugate pair with positive real parts, indicating an unstable spiral. However, because of the cubic nonlinearity in dV/dt, we can predict that there exists a limit cycle which will result in repetitive firing of the neuron. Experimenting with FH_run.m confirms this analysis.

B. Experimentally, it can be determined that the input threshold for firing a single action potential in this simplified neuron is 0.7mA. At this point the equilibrium point is sufficiently far from the initial membrane potential that the membrane potential achieves a spike before reaching to the resting voltage. The equilibrium point at this current is an asymptotically stable node. The "spike" can be seen by plotting the voltage response for different inputs.

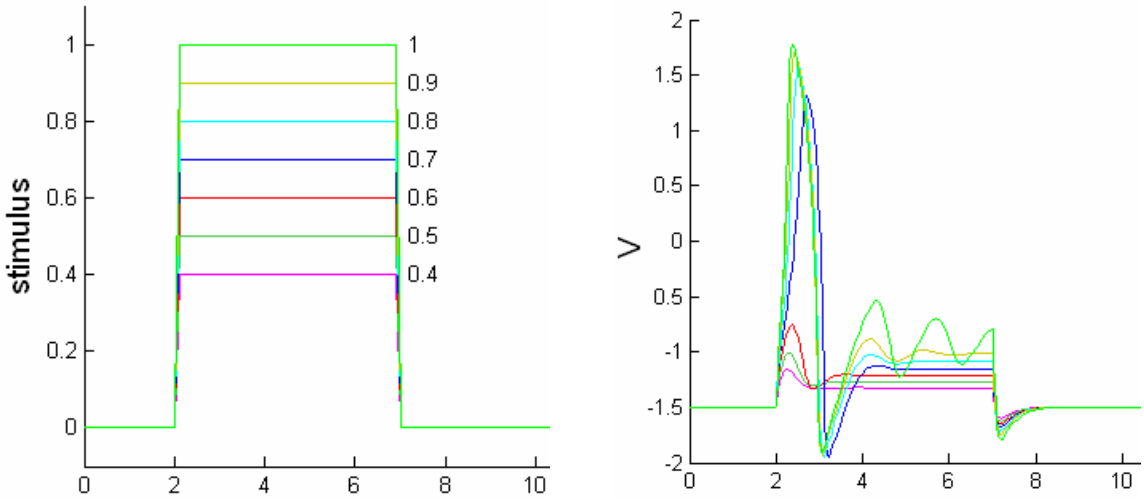

Figure 1. Voltage response to different stimuli values

Several people noted that the equilibrium point for R changed sign between I=0.6 and 0.7 (one can calculate this point precisely, it is I=0.624); however, this is just coincidental, since the change in driving force is controlled by the direction of the phase plane response at the point at which V begins to increase. The "jump" actually occurs somewhere between I=0.66 and I=0.67.

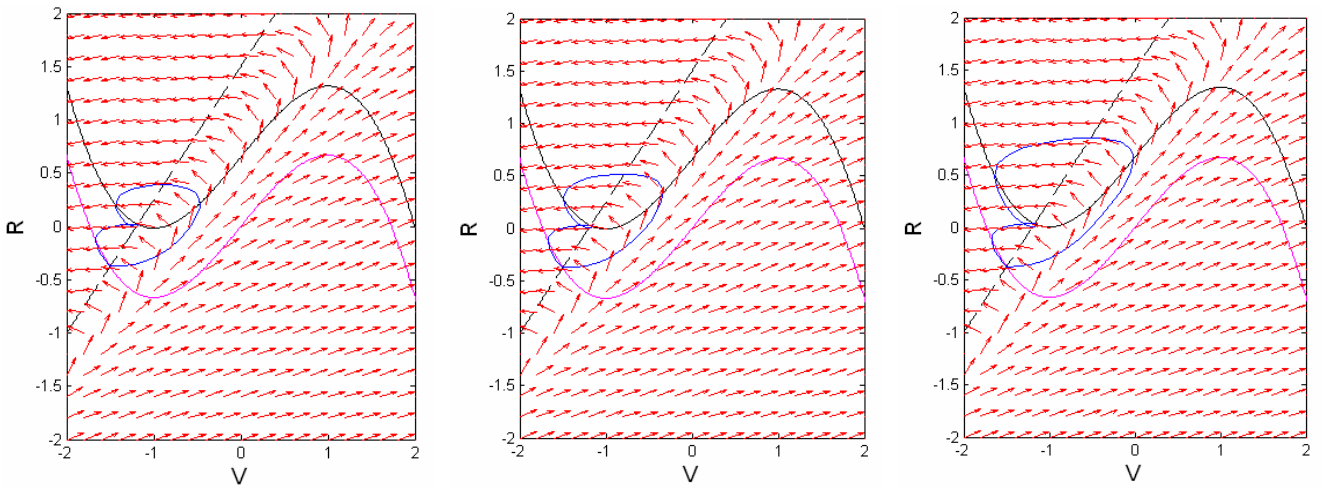

Figure 2. Phase plane response for I=0.65 (left), I=0.66 (middle), I=0.67 (right)

4. **Course review**

   A. Location of calcium channels. T-type low-threshold calcium currents are involved intimately in the process of postinhibitory rebound; as such, it makes sense for these channels to be located at the distal dendrites where action potentials are initiated; at this location, they can function in the initiation of a postinhibitory spike. Furthermore, their low threshold make them sensitive to relatively small changes, which are typical in distal dendrites were only a few EPSPs occur at once. In contrast, the high-threshold L channels open only in the presence of a relatively depolarized membrane. The L-type channels play a role in activating certain potassium channels that can accelerate repolarization of the membrane after an action potential; with this in mind, the placement of the L-type channel near the soma makes sense as an adaptation to reduce the refractory period of a neuron. In addition, inhibitory currents operate most efficiently in proximity to the soma, so from this perspective it makes sense for these channels and their activators to cluster in proximal dendrites and in the soma.

   B. Phase locking. Mutually inhibitory neurons exhibit phase locking due to the property of post-inhibitory rebound. Using GABAnergic neurons as an example, one neuron inhibits the other, causing the inhibited neuron to hyperpolarize due to influx of Cl- ions. If the inhibited neuron has T-type calcium channels in its membrane, this hyperpolarization will be sufficient to deinactivate some of these channels. Termination of inhibition will cause the membrane to repolarize towards the resting potential, at which point the T-type channels will undergo transient opening and admit calcium to the cell, depolarizing it and triggering a sodium-mediated action potential due to activation of the voltage-gated sodium channels. This rebound spike causes release of GABA at the synapses to the first neuron, hyperpolarizing the first neuron and reinitating the cycle. These neurons are thus phase-locked; at a given time, one is firing and inhibiting the other, which sets up the conditions for the other to fire and inhibit the first neuron during the next phase of the cycle.

   C. Inhibitory synapses. Inhibitory synapses with reversal potentials close to the resting potential of the neuron (i.e, most Cl-/$GABA_A$ synapses) take part in "silent inhibition."

When the neuron is not being stimulated, the opening of these channels creates a relatively modest drop in the neuron's voltage, as they are close to their resting potential and cannot drop the potential very far without reversing. However, if the neuron is stimulated while these synapses are active, the influx of negative ions acts to cancel the influx of sodium/calcium ions and thus reduces the voltage of the cell and may prevent action potential propagation. Such a synapse is at its most effective close to the interface of the dendritic tree with the cell soma; at this point, the action potential in the dendrites will have attenuated due to passive effects and, potentially, the action of other inhibitory synapses. The current shunting required to stop the action potential is hence much lower than if the synapse were attempting to stop the action potential at the point of generation.

D. Stochastic firing. There are many possible explanations for the stochastic nature of neuronal firing, relating to the sources of noise in the system. The combination of many sources of noise makes the Poisson model a reasonable model of neuronal firing for some neurons. Examples: The metabolic processes for a cell are stochastic, which introduces noise. The input for any particular neuron consists of spike trains that are themselves probabilistic in nature. The binding and unbinding of ligands on ligand-gated channels is stochastic so this introduces noise. Dendritic spines are formed and lost, which can cause the neuron to receive completely uncorrelated signals which is more noise. The diffusion of ions, chemical transmitters and other important molecules is very stochastic, introducing more noise. However, the Poisson firing distributions assumes that each firing of the neuron is independent (which is usually not the case), and not all neurons have an innate Poisson firing distribution. In addition, the Poisson model cannot account for the refractory period in neuronal firing (unless it is explicitly added to the model).