**Simulation Exercises and Homework Assignment – Ion channels Part 2**

**The simulation exercises that follow will allow you to complete this homework assignment:**

**Homework Assignment #4 - Advanced ion channels**
Answer the following three questions and submit them to the appropriate dropbox folder by the assigned due date. For this assignment, *submit just one document for each team.* Each submitted assignment should include a brief statement of the contributions that each member made to the assignment. The grade assigned to the team's homework will apply to all members of the team.

1. (12 points total) Based on the results of your simulations and the table of properties that you created, write a description of the key functional properties for these ion currents. Be sure to use your simulation data to support your answers!
   a) Delayed rectifier $K^+$ current (IK in the simulations)
   b) The A-type $K^+$ current (IA in the simulations)
   c) The M-type $K^+$ current (IM in the simulations)
   d) The T-type calcium current (IT in the simulations)
   e) The L-type calcium current (IL in the simulations)
   f) The BK $K^+$ current (IC in the simulations)

2. (3 points) What are your hypotheses about how these channels might affect neuronal firing rate, and spike frequency adaptation? No right or wrong answers here, but your answers must address a) the predicted effect on neuronal function and b) the reason for the effect you predict.
   a) The A-type $K^+$ current (IA in the simulations)
   b) The M-type $K^+$ current (IM in the simulations)
   c) The T-type calcium current (IT in the simulations)
   d) The L-type calcium current (IL in the simulations)
   e) The BK $K^+$ current (IC in the simulations)

**Experimental Instructions**

Begin by running the SimVC program. This simulates patch-clamp experiments in the "voltage-clamp" mode, which is to say that the experimental configuration allows you to control the membrane voltage while measuring membrane current..

In these simulations you will characterize key features of the voltage-dependence and kinetics for the $Ca^{2+}$ and $K^+$ channels that we will use to understand complex firing patterns in neurons. As you complete the five simulation experiments below, use your results to fill in the table at the end of this assignment.

<u>Simulation 1: Activation/Deactivation properties of voltage-gated $K^+$ currents</u>

Begin by comparing the three different voltage-gated $K^+$ currents. Open the file CompareIK.VC5. Use this protocol to characterize the activation and deactivation properties for each current as follows.

Navigate to Parameters | Conductances and isolate only IK ($I_{KDR}$) by setting gK to 1 and all other conductances to 0. Run the protocol. At the top of the screen are the voltage steps. In the center are the current traces for each step. At the bottom of the screen is the current-voltage plot for this current. Repeat this process again, isolating only IA, then IM.

<u>Simulation 2: Inactivation properties of voltage-gated $K^+$ currents</u>

Open the file CompareIKinact.VC5 and run this protocol as in the first simulation, sequentially isolating IA, then IK, then IM. Use the information you get from these protocols to characterize the inactivation properties of each current (or lack of inactivation). Remember that the traces are color-coded. The color of each voltage trace corresponds to the color of the corresponding current trace.

Simulation 3: Activation/Deactivation properties of T- and L-type voltage-gated $Ca^{2+}$ currents.

Open the file CompareT_L.VC5 and isolate T-type calcium currents by setting pT to 10 and all other conductances to 0. Run the protocol, then repeat after isolating only the L-type $Ca^{2+}$ current by setting pL to 10 and all other conductances to 0.

Simulation 4: Inactivation properties of T- and L-type voltage-gated $Ca^{2+}$ currents.

Open the file CompareT_L_inact.VC5 and run this protocol as in the previous simulation, sequentially isolating T-type then L-type $Ca^{2+}$ currents. Use this protocol to characterize the inactivation properties of this current.

Simulation 5: Activation/Deactivation properties of BK channels.

Open the file CompareBK.VC5. This protocol isolates only currents through BK potassium channels (the conductance is referred to as IC in the simulation software). Run the protocol at three different intracellular calcium concentrations, 20 nM, 100 nM, and 500 nM. Change the intracellular calcium concentration by navigating to Parameters | Ions and changing the values for $[Ca]_{internal}$ A concentration of 20 nM represents a typical intracellular calcium concentration at rest, 100nM is a concentration that would result from a small calcium current, and 500 nM is a concentration that would occur during very large, sustained calcium current. Compare the properties of the BK current at these three concentrations and use this information to fill in the remainder of the table.

Table is on the next page

| | **Current** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | **BK (IC)** | | |
| | **$IK_{DR}$ (IK)** | **$I_{KA}$ (IA)** | **$I_{KM}$ (IM)** | **$Ca^{2+}$-T (pT)** | **$Ca^{2+}$-L (pL)** | **(20nM $Ca^{2+}$)** | **(100nM $Ca^{2+}$)** | **(500nM $Ca^{2+}$)** |
| Approximate voltage of activation | | | | | | | | |
| At +20 mV how long to reach max current? | | | | | | | | |
| Approximate time required for deactivation? | | | | | | | | |
| Approximately how long to inactivate at +20 mV (only if current inactivates)? | | | | | | | | |
| Approximate voltage of 50% inactivation (only if current inactivates)? | | | | | | | | |