Exercise 2 (18 pts in total)

HH_single.py/m implements a single compartment Hodgkin-Huxley model. A current clamp, i.e., an injection of current into the compartment, stimulates the neuron. For the stepwise integration, the forward and backward Euler methods are implemented (variable *solver*).

1. Vary the amplitude of the applied stimulus *I* to find the spiking threshold, i.e., the minimum stimulus amplitude that results in an action potential, for a 0.5 ms long pulse (*tDur* = 0.5). Compare elicited action potentials for threshold amplitude as well as 2x threshold amplitude. What are the differences? (**1 pt**)

2. What happens if you set the time step *tDt* = 0.1 and *I* = 20 µA/cm². Compare both, forward and backward Euler method. Why is there such a difference in the plots? (**1 pt**)

3. An action potential is driven by ionic currents crossing the cell membrane through ion channels. For a stimulus amplitude which causes an action potential for a 0.5 ms long pulse: Provide a plot which contains (a) the membrane voltage and (b) the sodium and potassium current densities (iNa, iK) over time (Hint: All state variables *m, h & n* are returned by the function so use them) (**1 pt**). By the help of the plot describe why the membrane voltage rises for an action potential, and what causes the drop back to the resting voltage after a while (**1 pt**). (Hints: set *tDt* back to 0.025 ms or smaller. The plot requires two y-axes)

4. Temperature influences action potential generation. The classical Hodgkin and Huxley model was developed at 6.3°C. For higher temperatures, the temperature coefficient *kT*(emp) has the form of:

   $kT = 3^{((T-6.3)/10)}$ with T … temperature in °C

   Describe the influence of temperature on the generated action potentials (action potential width & height) (**1 pt**). What happens at temperature 37°C, is the model valid for humans? (**1 pt**)

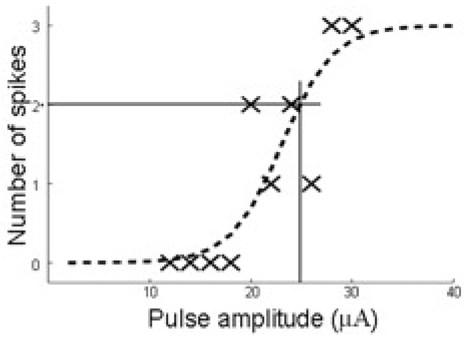
5. The sodium current (density) *iNa* is given by:

   $iNa = gNa*m^3h*(v-eNa)$

   iNa normally has a depolarizing effect on the cell as it is inward directed (negative sign). At which condition the sodium flux reverts its direction and therefore has a repolarizing effect on the cell? (**1 pt**) How do the gating variables *m* (activation) and *h* (inactivation). respond to an increase in the membrane voltage? (**1 pt**)

6. A common way to characterize neurons is to compute a so-called Strength-Duration (SD) curve - it plots threshold versus pulse duration. Write a script that computes the SD curve for the single compartment Hodgkin Huxley model; you should use HH_single.py/m as a template. Compute thresholds for pulse durations of 0.01 to 100 ms in 20 logarithmic steps (Hint: Use *logspace* in Matlab and *numpy.logspace* in Python). Thresholds can be found efficiently by a binary search algorithm (https://en.wikipedia.org/wiki/Binary_search_algorithm). (**4 pts**) An SD curve is characterized by two parameters: 1) the rheobase (https://en.wikipedia.org/wiki/Rheobase) which is the threshold for an infinitely long (in our case 100 ms) pulse and 2) the chronaxie (https://en.wikipedia.org/wiki/Chronaxie) which is the minimum time required for a pulse amplitude double the strength of the rheobase to activate a neuron. Extract the rheobase and chronaxie from the Hodgkin Huxley SD curve. (**2 pts**)

7. Threshold in real experiments is not at a fixed level but a spiking probability increases monotonically with increasing stimulus amplitude. The recorded data ('x') can be best fitted with a logistic curve (dashed):



In order to also incorporate randomness in the model (*tDur* = 0.5 ms, *temp* = 6.7 degrees Celsius) a simple noise term (Hint: This is a current density so it must be added to other current densities)

iNoise = 20*randn … with randn being a normally distributed random number

should be added. Now compute the spiking probability in % for amplitudes between 0-30µA/cm² in 1µA/cm^2 steps. At each amplitude run the simulation 50 times and fit a logistic curve to your simulated data. (**4 pts**)

Short meaningful answers underlined with screenshots of the results are appreciated. For programming tasks, also provide the source code.

After completion of all four exercises, send your reports including your name and student ID to paul.werginz@tuwien.ac.at.