4G7 CODING ASSIGNMENT 2

DUE: DECEMBER 4, 2024 AT 4PM (VIA MOODLE)

Do neurons have a well-defined firing threshold?

The following ordinary differential equations describe the classic Hodgkin Huxley model of the action potential, as first proposed in their 1952 paper:

$$\dot{v} = -g_{Na}m^3h(v - e_{Na}) - g_K n^4(v - e_K) - g_L(v - e_L) + I_{ext} \tag{1}$$

$$\dot{m} = \alpha_m(v)(1 - m) - \beta_m(v)m \tag{2}$$

$$\dot{h} = \alpha_h(v)(1 - h) - \beta_h(v)h \tag{3}$$

$$\dot{n} = \alpha_n(v)(1 - n) - \beta_n(v)n \tag{4}$$

v denotes membrane potential (in mV) and n, m and h are state variables for the membrane currents. The α and β functions describe the rates of ion channel gating as a function of voltage (provided as an appendix) and the g_x, e_x are conductance densities (normalised to membrane capacitance) and reversal potentials (in mV) of the different ionic currents, Na (sodium), K (potassium) and L (leak). I_{ext} is externally applied current (in mA/nF). Time is in units of milliseconds.

The goal of this assignment is to understand how this physiologically realistic model responds to external input and how this differs from simplified models. You will need to numerically integrate this equation using MATLAB or Python. For all simulations directly implement (forward) Euler integration with a fixed timestep of 0.001 ms. The values of the parameters (in appropriate units) are provided in Table 1 below:

	[μS/nF]		[mV]
g_{Na}	120	e_{Na}	115
g_K	36	e_K	-12
g_L	0.3	e_L	10.6

Table 1. Parameter values

Exercises

Q1 Using an appropriate initialisation, simulate the response of system (1-4) to 200 ms-long pulses of applied current (I_{ext}) with amplitudes in the range 0.1 - 5 mA/nF.

Generate example plots showing the membrane potential as a function of time. Plot action potential frequency as a function of input amplitude. Comment on the shape of the plot. What is the input threshold for inducing firing?

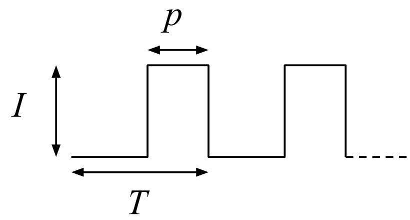

FIGURE 1. current input waveform

Q2 Write code to generate periodic square pulse input with variable period (T), pulse width (p) and amplitude (I) as shown in Figure 1. Systematically explore the effect of driving the model with such an input. To begin with, include the following input parameters in your exploration:

$$T = 10, 11, 12, ..., 20 \text{ ms with } p = 5 \text{ ms, and } I = 2.3 \text{ mA/nF}$$

Summarise your data graphically, giving example membrane potential plots of any relevant or noteworthy phenomena. Comment on the biological relevance of your findings and provide a qualitative explanation for the phenomena you observe. How do your findings relate to your answer to question 1? Is it possible to elicit a spike with a negative current pulse?

Do your findings pose a problem for commonly used simplifications of neurons such as firing rate models and leaky integrate-and-fire models?

APPENDIX: RATE FUNCTIONS

The rate functions α_x, β_x in the model (1-4) are defined as follows:

$$\begin{aligned}
\alpha_m(V) &= \frac{(2.5 - 0.1V)}{(\exp(2.5 - 0.1V) - 1)};\\
\beta_m(V) &= 4\exp(-V/18);\\
\alpha_h(V) &= 0.07\exp(-V/20);\\
\beta_h(V) &= \frac{1}{(\exp(3.0 - 0.1V) + 1)};\\
\alpha_n(V) &= \frac{(0.1 - 0.01V)}{(\exp(1 - 0.1 * V) - 1)};\\
\beta_n(V) &= 0.125\exp(-V/80);
\end{aligned}$$