Hand-in 2

THE BACKBONE OF THE BACKBONE OF YOURSELF

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BIOPHYSICS 2 | ENGINEERING PHYSICS

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Theory on subunit structures

A description of around 250-500 words of what an alpha subunit is and how is it related with a sodium channel and its basic structure. Define briefly the different subunit structures present in the channels of neurons. Also discuss where calcium channels are more relevant.

Some cells such as neurons communicate via action potentials and voltage-gated ion channels play an essential role in the process.

Ion channels are proteins that allow ions to cross the cell membrane; they can be in an open, closed or inactivated state with a probability of transition.

In concrete, sodium channels are ion channels that regulate the flow of sodium. These channels are very important in the functioning of neurons and have a particular structure with different subunits. The most important one is the alpha subunit that is the nucleus of the channel. These subunits associate with other proteins such as beta subunits that modulate multiple aspects of the channel behavior.

An alpha subunit is a polypeptide chain that contains ion-selective components. This chain has four repeated domains and each domain is formed by six segments (S1-S6). The pore is found between the S5 and S6 segments and its extracellular part is the one responsible of the ion selectivity. The S4 segment is the acts like the channel voltage sensor due to the fact that is formed by positive charged amino acids. When this segment is stimulated it move to the extracellular part to allow the flow of ions into the cell.

There are nine different types of alpha subunits in sodium channels; some of them are present in neurons, specifically the types 1, 2, 3, 5, 6 and 7. All of them are included in central neurons except the type number 7 and type number 1, 2, 3, 6 and 7 are also included in peripheral neurons.

There exist also another type of channels that are calcium channels. Calcium channels are relevant in linking muscle excitation and also play a very important role in the well-functioning of neurons present in the brain. Its malfunction can cause neurological disorders such as pain, migraine or epilepsy.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4313373/

https://en.wikipedia.org/wiki/Sodium_channel#Alpha_subunits

Brett A. Simms, Gerald W. Zampon. "Neuronal Voltage-Gated Calcium Channels: Structure, Function, and Dysfunction". Neuron Volume 82 Issue 1, 2 April 2014, Pages 24-45.

Theory on gated variables

An explanation of around 250-500 words of what a gated variable is. Among other things, comment how they are used to model currents across the membrane and how they are related with the alpha and beta subunits.

The model we will be working on is the Hodgkin-Huxley model that represents, in a set of non-linear differential equations, how action potentials in neurons are initiated and propagated in three types of transmembrane channels: voltage-gated sodium and potassium channels and a leak current channel represented by the leak of chlorine ions. Alan Lloyd Hodgkin and Andrew Huxley along with John Eccles won the Nobel Prize in Physiology or Medicine in 1963 for "for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane".

To represent the state of this channels gated variable are used. In our case we will call them as proposed: n, h and m. Those variables, that have associated a differential equation, represent the probability that a gate its open and their values rate from 0 to 1. Specifically the m and h variable control the behavior of sodium channels and the n variable control the behavior of potassium channels. They follow first order kinetics with voltage-dependent rate constants α (V) and β (V) and they allow us to relate the electrical properties of neurons that can depend on impulses arriving from all over the body with the flow of ions and see how a neuron works under different conditions.

The relationship of this variables with the alpha and beta subunits is that we mentioned before that the sodium channels contained alpha subunits with different segments and those segment where the ones regulating the flow of ions crossing the membrane. Specifically there was the segment four (S4) that when it was stimulated it moved to the extracellular part of the membrane and allowed the pass of sodium ions. The gated variables are the ones in charge to model this behavior of the segment that moves to the extracellular part to open the gate or remains inside the cell when it is not stimulated.

http://icwww.epfl.ch/~gerstner/SPNM/node14.html

First MATLAB code

Give the fixed points of the HH system (solution of question a), the graph requested in section b) above and the current threshold I_t which leads to periodic pulses (solution of question c).

Fixed points of the HH system

$$\boxed{V_f = -63.6627320430208\, mV}$$

$$\boxed{m_f = 0.0661667790568666}$$

$$\boxed{n_f = 0.338336403155621}$$

$$\boxed{h_f = 0.548759257364258}$$

Graph requested in section b)

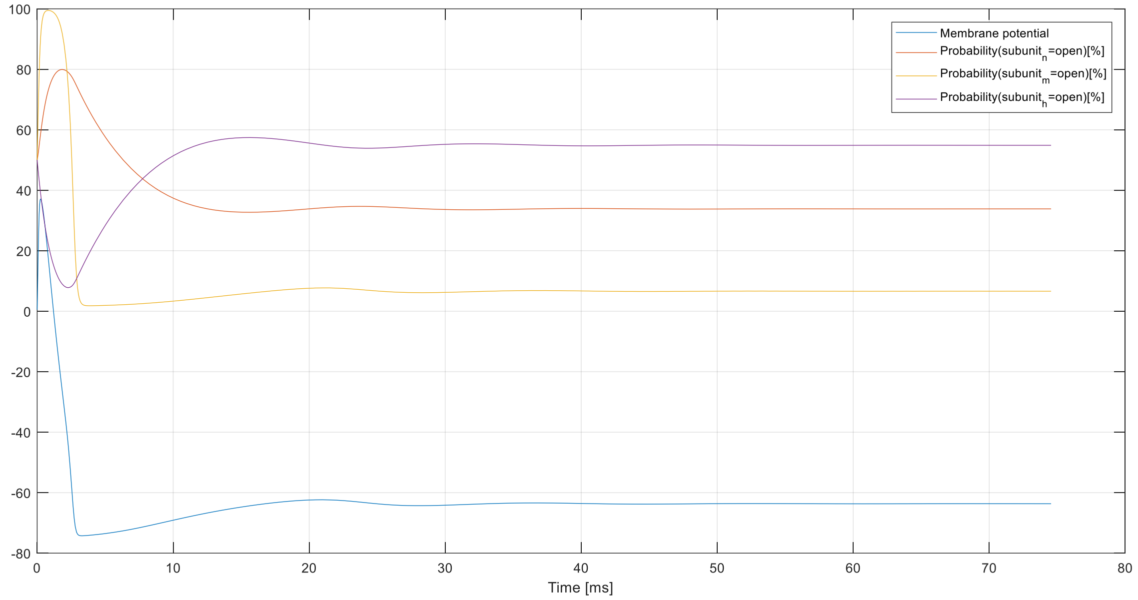

Figure 1: The evolution of voltage (blue) and the dynamics for gate m (yellow), gate n (orange) and gate h (purple).

Current threshold

$$\boxed{I_t = 1.05418\, V/s}$$

Second MATLAB code

A graph showing the input current constructed in section d) for the four cases identified with your DNI. Also a graph with the resulting response of the neurons indicating the times where the neuron fired in the different runs.

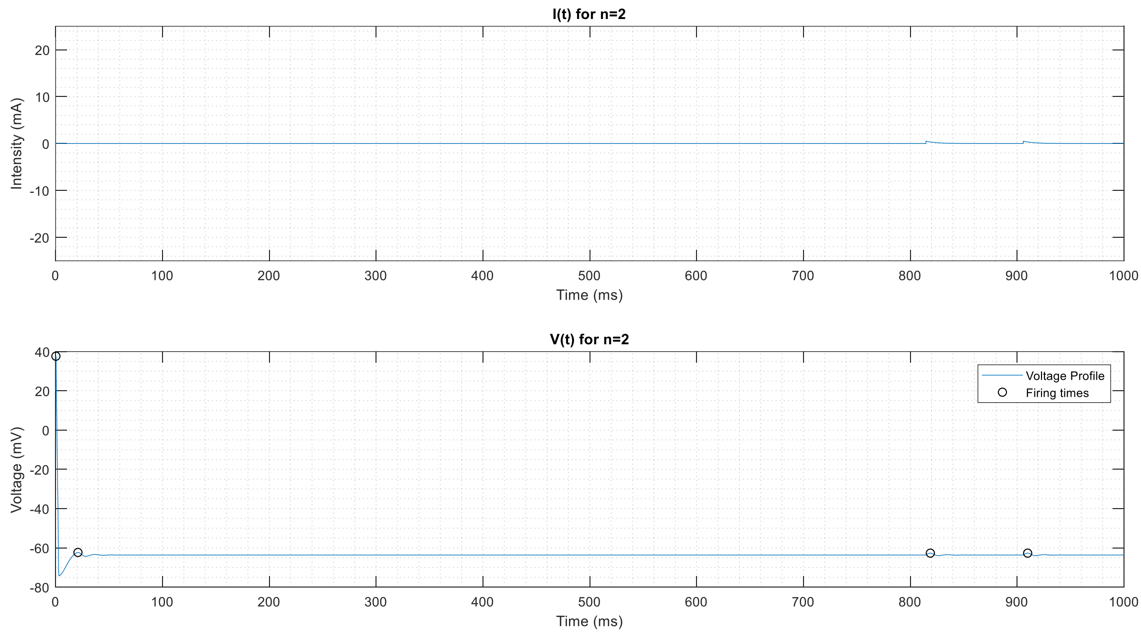

Figure 2: Input current and resulting response of the neurons when setting 2 pulses per second.

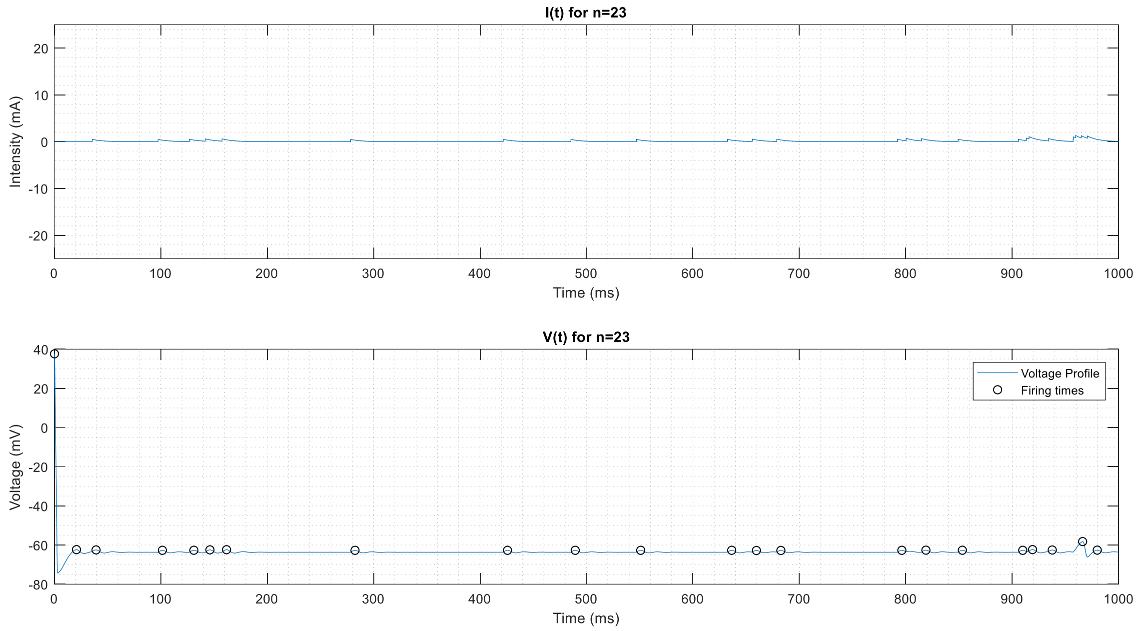

Figure 3: Input current and resulting response of the neurons when setting 23 pulses per second.

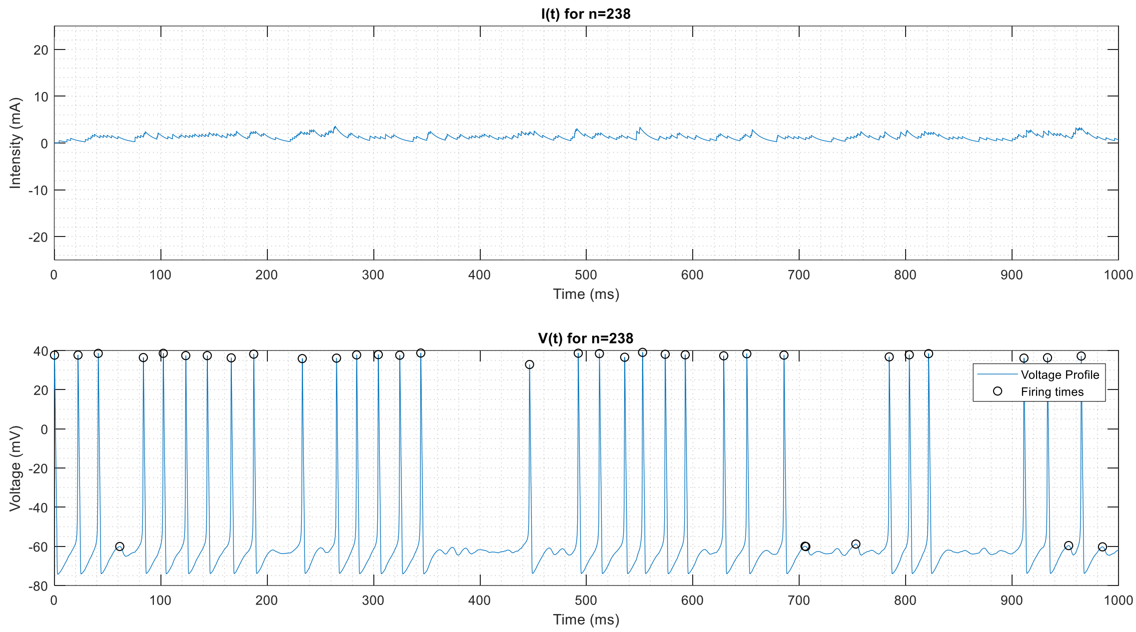

Figure 4: Input current and resulting response of the neurons when setting 238 pulses per second.

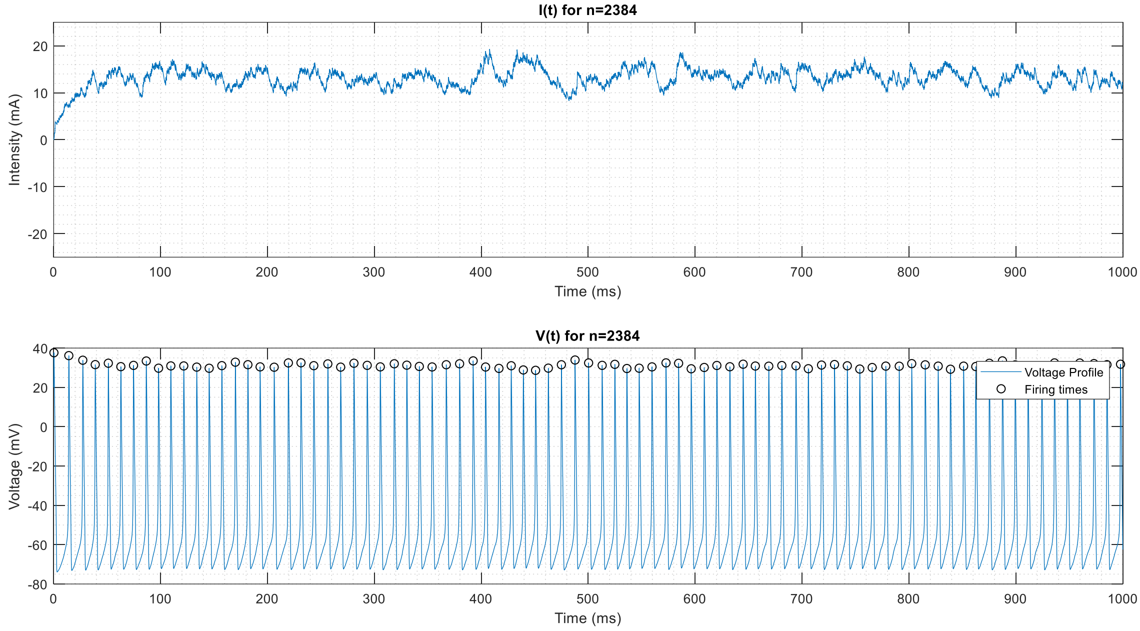

Figure 5: Input current and resulting response of the neurons when setting 2384 pulses per second.

Third MATLAB code

A graph indicating the average of the number of spikes per second of your neuron as a function of I_c and its error bar as a solution of section e.

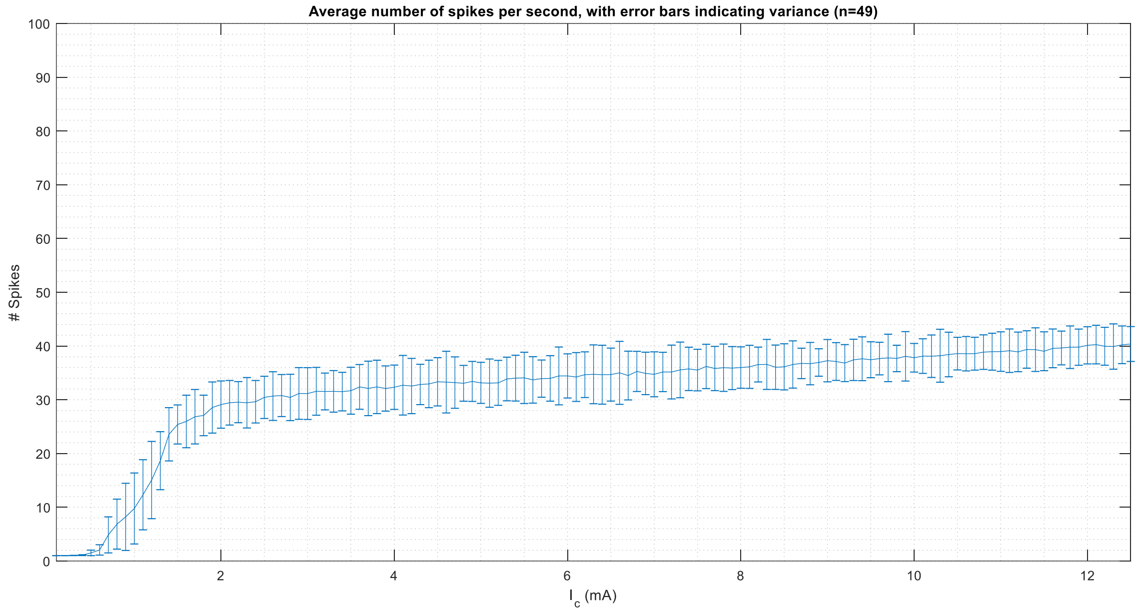

Figure 6: Average number of spikes after 100 realizations. The error bar shows the variance. At $I_c = 12.5\ V/s$, the average number is just above 40 spikes per second.

How to code ID card number

LTP is an enhancement of synapses between neurons as a consequence of using that connection frequently. Memories are associated with changes in the synaptic strength between neurons and thus LTP is considered one of the mechanisms underlying learning and memory. When a signal arrives to a neuron (current from a neighbor neuron) creates an action potential releasing glutamate neurotransmitters. The frequency of the currents arriving from other neurons will determine the frequency of the action potential which will determine the amount of glutamate released. The receptors on the postsynaptic neuron are the AMPA (permeable to Sodium ions) and NMDA (high permeability also to Ca ions) which is initially blocked by Magnesium. When a low frequency action potential is triggered the NMDA receptor remains closed. But when a high frequency action potential is induced the NMDA is opened and Ca ions enter the postsynaptic cell and as a consequence new AMPA receptors are added to the membrane of the postsynaptic cells, strengthening in this way the connection between both neurons. In our model we can also find this behavior when for a few current pulses we obtain a low frequency voltage and for an increasing number of pulses a higher frequency voltage is obtained.