BE-M260/EE-M255/NS-M206
Homework-3: Stimulation
(This homework consists of two parts – Electrode and Nerve Stimulations)

Part 1: Electrode Stimulation
Assigned: Nov. 7, 2023
Due: Nov. 21, 2023

Problem 1.1: Voltage and Current Mode Stimulation
Given the specification of the electrode as R_S = 2KΩ, R_{CT} (R_P) = 15KΩ, and C_{dl} = 220nF, answer the following questions:

a) You are asking for designing a stimulation experiment and you find out the published paper shows the monophasic (anodic) voltage protocol of 8 volts with a pulse width of 1ms at a refresh rate of 10 Hz works effectively for the intended experiment. Draw the stimulation current waveform for at least two anodic stimulation pulses? (hint: use the formula presented in the course note).

b) However, your lab only has current mode stimulator and thus you have to perform a conversion of the protocol in order to carry out the experiment. The new protocol is monophasic anodic current of X mA at 1ms at 10Hz. Assume that the effective threshold current is 0uA and both protocols (current and voltage) carry the same amount of charge. What is X? Justify your derivation.

Problem 1.2: Estimation using Cyclic Voltammetry (CV)

You are asked to evaluate the electrode of the material X. A cyclic voltammagram for this material is in the CV worksheet in the data file (***homework-3-2023-fall-cv.xls***) provided with this homework. This was acquired at a scan rate of 100 mV/sec. The CV testing has determined that safe electrochemical limits of material X are -0.7 and 0.8 Volts. The pulse data (also in the ***homework-3-2023-fall-cv.xls***) is the voltage generated when a biphasic pulse of 0.5 ms and 50 uA at each phase is applied to the electrode. The biphasic pulse starts at t = 1msec and ends at t = 2msec. The voltage is measured between the electrode of material X and a large, distant return electrode.

a) Estimate the values for the spread resistance, R_s, the double layer capacitance, C_{dl}, and the charge transfer resistance, R_{CT}
b) What percentage of the charge storage capacity of material X can be used with a pulse of 0.5 ms?
c) If the testing was done in physiological saline (0.9 % sodium chloride), then estimate the diameter of the electrode at 37ºC and 20ºC. (Note - The resistivity of the saline is temperature dependent. At 37ºC, the resistivity is 0.502 Ω-m, while it is 0.7 Ω-m at temperature of 20ºC).

Problem 1.3: Residual Charge after Stimulation

Use the Randles cell model to answer the following questions:

a) Show that no residual charge exists after a biphasic constant current stimulation (anodic first) for non-Faradaic electrode.

b) Show that residual charge exists after a biphasic constant current (anodic first) stimulation for Faradaic electrode?
c) Do you know any mechanism to cancel the residual charge? Briefly explain?
d) **(*Optional but with extra credit as a research problem*)** Will the accumulated residual charge reach a steady state if an infinite pulse train of biphasic constant current stimulation is applied? Justify your answer with the necessary mathematical derivation.

Problem 1.4: Correlation of Water Window (CV) and EIS Model

Given the specification of the electrode as $R_S = 2K\Omega$, R_{CT} (R_P) = $15K\Omega$, and $C_{dl} = 220nF$. CV shows the water window of [-0.8V, 08V]. Answer the following questions:

a) Is it safe (meet with the electrochemical safety limit) if a constant current pulse stimulation protocol at 0.2mA, and 1ms is applied?

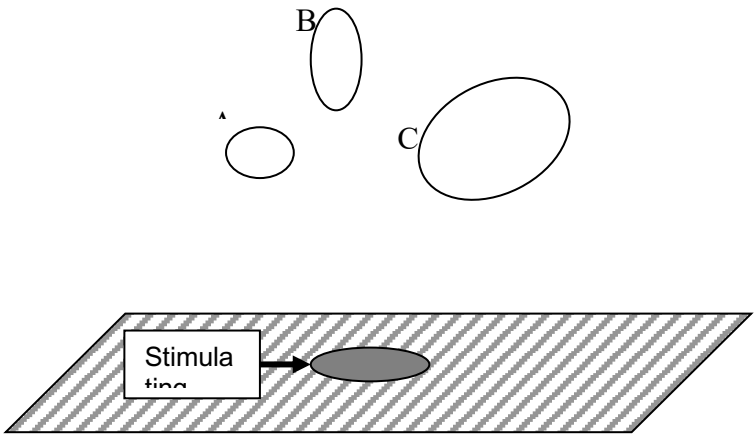
b) What happens if the protocol of 2mA and 1ms is applied?

Part 2: Nerve Stimulation
Assigned: Nov. 7, 2023
Due: Nov. 30, 2023

Problem 2.1: Strength Duration Curve (SDC)

Refer to the following drawing for this problem. Three cells (only show the cell soma) labeled A, B, C are positioned near a stimulating electrode as shown in the figure. Cells A and B and C are different cell types. The cells are all far enough away from the stimulating electrode that any non-uniformity of the current distribution does not affect their response to stimuli. Assume *the soma of all three cells are the most sensitive and the larger one is more excitable* for stimulation, so an action potential results when the soma is depolarized to a certain level by a current stimulus delivering via an electrode. You can record action potentials from the three cells and gather strength duration data which is listed in the table under data columns 2, 3, 4.

1.1) Use the data to construct 3 strength duration curves. Determine the rheobase and chronaxie for each curve and label them on the curve.
1.2) Assign strength duration curve belongs to the cells and justify your assignment?
1.3) Is it possible to selectively stimulate Cell A? How would you do this?



Pulse Duration (ms)	Threshold current-1 (mA)	Threshold current-2 (mA)	Threshold current-3 (mA)
0.1	6	8	4
0.2	3	5	2
0.5	2	2	1
1	1.7	1.5	0.6
2	1.5	1.0	0.4
4	1.4	0.7	0.3
8	1.4	0.6	0.3
16	1.4	0.6	0.3

Problem 2.2: Stimulation Safety Limits

Consider a neural prosthetic device using a microelectrode array of the circular electrode with a radius of 30um. In the design, the stimulation safety is studied according to the criterions of electrode charge density limit (electrochemical safety), water window limit, and neural damage limit. Assume the following parameters:

$\rho = 560\Omega - cm -$ retina tissue resitivity

$C_0 = 54.5uF / cm^2 -$ double layer capacitance (unroughened)

$R_{CT}(platinum - black) = 5.1 \times 10^4 - cm^2$

Electrochemical safe charge density for the platinum = $0.35mC/cm^2$

Electrochemical safe charge density for the IrOx = $4mC/cm^2$

a) If I = 80uA is applied to the electrode for 1ms, what is the charge density at the electrode?
b) What is the charge density at the electrode?
c) Is it an electrochemical safe stimulation?
d) In case to the limit of the charge density for safe electrochemical stimulation is not met, the following two approaches are used:
   a. What is the maximally allowed simulation pulse width if 80uA is used?
   b. What is the roughness factor should be applied if 1ms of pulse width is used?

e) Extract the Randles cell model for the given microelectrode (without roughing) by calculating
   1) Tissue spread impedance, R_s?
   2) Double layer capacitance C_{dl}?
   3) The Faraday charge transfer impedance, R_{CT}?
   4) Sketch the Bode plots (gain and phase) of this electrode. What is the electrode impedance at DC? What is the electrode impedance at high frequency (say 1 MHz)?

f) Assume that the water window of the platinum is the range of [-0.9V, 0.9V]
   1) Would the stimulation result in water electrolysis? Justify your answer by calculating the voltage drop across the electrode-electrolyte interface using Randles cell model instead of using CV. *For simplicity, ignore the R_{CT} for the calculation.* Note the voltage across the electrode-electrolyte interface is different from the one across working and counter electrode terminals.
   2) With the stimulation pulse width, what will be the limit of the pulse current amplitude such that the stimulation will not result in electrolysis?
   3) Assume the electrode is a non-Faradaic electrode, what will be the major different in CVs between roughness (10X) and non-rough electrodes.

g) Shannon's neural damage model is expressed as log (D) = 1.5 - log (Q), where D is charge density (uC/cm^2) and Q is the charge/phase (uC).
   1) What is the neural damage limit (D) in terms of charge density for this design?
   2) In the current stimulation experiment, which limit is lower, the neural damage limit or electrochemical safety limit?

3) If you are asking to design the stimulation parameters based on the given size of platinum electrode, what is the range of the stimulation current at a stimulation pulse width = 1ms such that it meets both requirements of safe electrochemical stimulation limit as well as the neural damage limit?
4) Answer g)-3 if the IrOx is used?