EN580.435 APPLIED BIOELECTRICAL ENGINEERING Feb. 14, 2019
The Johns Hopkins University

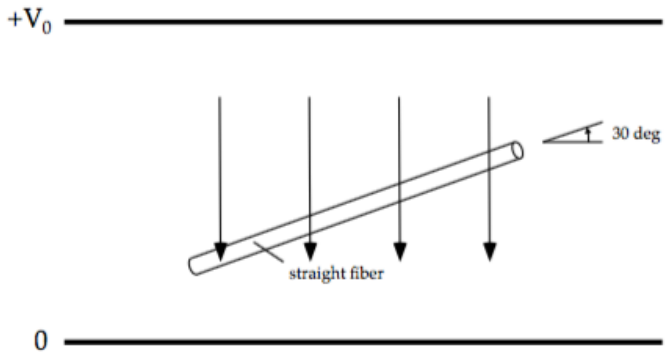
The homework policy for this course is that you are expected to work on the problems on your own. You may collaborate on homework assignments only insofar as group discussion and peer learning. Assignments must be written up individually in each individual's words and NOT COPIED. It is highly recommended that the actual solution of the problem be done by yourself, much like you would do on an exam since the exam will be modelled after the homework questions. If you need further help to understand the problem, you should contact or meet with either Dr. Hunter or Dr. Tung. Homework turned in after the start of class on the due date will receive only 50% credit until noon the next day and only if it is not discussed in class, and 0% after that.

Furthermore, some homework questions given throughout the course may require that you do some research or make some assumptions regarding relevant parameters or other information. Conversely, extra information will sometimes be given that is not needed to solve the problem. You will need to recognize these situations when they come up.

Homework #2 (due beginning of class on Feb. 21)

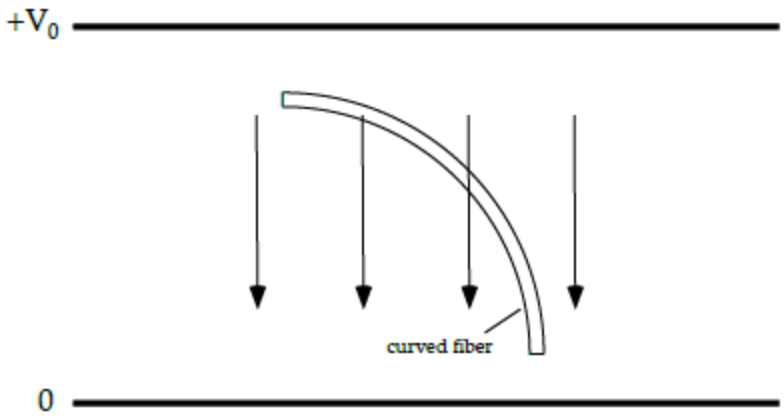
Problem 1 (20 pts)

(a) An excitable nerve fiber is placed in a bath at a 30 degree angle between two electrodes generating a constant electric field, as shown below.

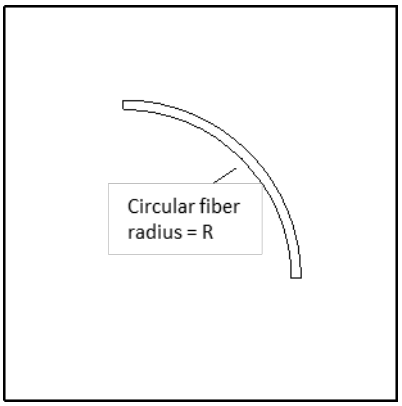


Determine the activating function at the fiber surface, assuming a conductivity in the solution of 0.02 S/cm. Please show your derivation.

(b) The straight nerve fiber is now replaced by a circularly-shaped fiber (quarter circle) with radius 2 cm as shown below. Will a linear field be able to stimulate this fiber? Explain your reasoning. Determine the activating function along the surface of the fiber. Please show your derivation.



(c) In a future SBE lab, you are asked to use optical mapping to measure V_m along the length of a circularly shaped nerve fiber (with radius R) sitting in a saline bath, as shown below. The fiber itself is circular in cross-section with a much smaller radius a. The chamber dimension can be assumed to be very large (much much larger than R).



You start without your lab partner. You pick a spot to place a stimulus electrode in the bath, and place the return electrode in a distant corner. As expected, you are able to measure a steady-state voltage response along the fiber for a constant current input. However, when your lab partner takes his turn, picks a spot spot in the vicinity of the fiber to place the stimulus electrode in the bath and repeats the experiment, he fails to measure any response of the fiber at all even with the current turned all the way up (so it isn't a matter of the electrode being too far away). You ask your TA for help, and he verifies that the electronics and instrumentation are all working properly, and that the nerve fiber is still alive and functional.

Explain where you lab partner placed the stimulus and why he didn't see any voltage response on the fiber, and how you would correct that problem.

Problem 2 (15 pts)

(a) Using the RC model derived in class for the strength-duration relationship (with square pulses of current) it can be shown that:

$$e^{d/\tau} = \frac{1}{1 - {}^{v_{th}}/_{IR}}$$

where d is the pulse width and I is the pulse amplitude. Suppose a colleague of yours applied pulses of two different durations and found the corresponding pulse amplitudes that bring the membrane voltage up to threshold. You are interested in the same cell type and need to know the membrane time constant. From the four values he obtained (I_1, d_1, and I_2, d_2) is it possible to determine τ? If so then write an expression for τ in terms of the measured parameters. If not then explain what additional measurements you would need for the calculation and provide an expression for τ.

(b) Given your expression for τ what are the likely sources of error (other than simply measurement error)? Hint: Please address specifically how the measured parameters should be chosen to ensure that the core assumptions of the RC model are satisfied.

Problem 3 (25 pts)

The goal of this problem is to determine the time course of development of transmembrane voltage V_m of a spherical cell when an electric field is turned on.

Assume the following:

1) The electric field **E** (bold indicates vector) with intensity E_0 is turned on at time $t = 0$, and is uniform in space and aligned along the $+x$-axis.

$$\mathbf{E} = [E_0 u(t)]\hat{\mathbf{x}} \qquad (1)$$

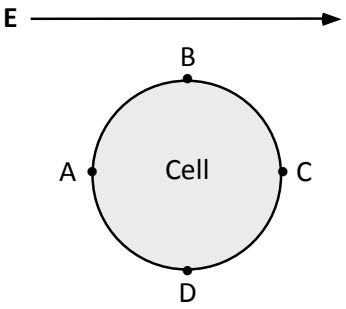
$u(t)$ is the unit step function, and $\hat{\mathbf{x}}$ is the unit vector in the x-direction.

2) The spherical cell has a diameter of 10 μm.
3) Resistivities of bath solution and cytoplasm are 50 Ω-cm and 50 Ω-cm.
4) Area-specific resistivity and capacitance of cell membrane are 5 kΩ-cm^2 (membrane thickness has been taken into account in this parameter, which is why the units differ from those of the usual resistivity parameter) and 1 μF/cm^2, respectively.

You should be able to solve this problem from material covered in the handouts and lectures.

(a) Using a plotting program, plot the time course of development of transmembrane voltage at the 4 points lying in a plane cutting through the center of the cell, as shown below.

Figure 1



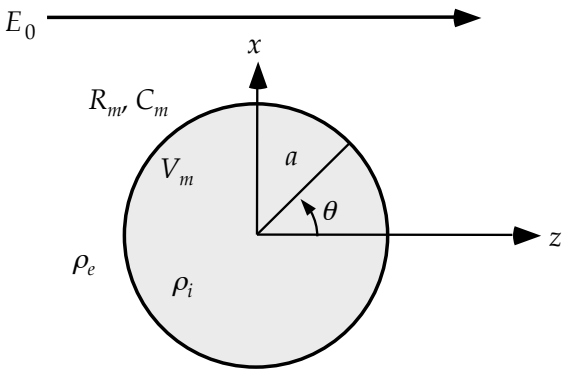
(b) The equation for transmembrane potential for a spherical cell in a uniform electric field can actually derived by determining the extracellular surface potential on the sphere when the sphere is a non-conductor. The interior of the cell will be isopotential and is usually assumed to be zero. Thus, working backwards, you should be able to determine the surface (i.e. extracellular) potential of the cell membrane in an applied electric field, and from that, determine the magnitude of the electric field that is *parallel to the surface* (i.e., the *tangential* electric field).

For the same 4 positions as in part a, plot the time course of the magnitude of the tangential electric field in response to the applied electric field of Equation 1.

(c) Suppose the spherical cell of part b is treated with chemicals that effectively "skin" the membrane, leaving it so leaky it has a resistivity similar to that of the surrounding media. As you did in part b, plot the time courses of the magnitudes of the tangential electric field parallel to the cell surface at the 4 positions in Figure 1.

Problem 4 (20 pts)

An excitable, spherical cell with radius a and surface area $4\pi a^2$ is placed in a chamber filled with electrolyte and stimulated with a DC electric field pulse. Assume that near its resting potential of –70 mV, the cell has a membrane resistance of 5 kΩ-cm^2 and capacitance of 1 μF/cm^2, and excites *when a liminal membrane area of πa^2 depolarizes by 20 mV and reaches a transmembrane potential of –50 mV.* Finally, assume that a = 20 μm, ρ_e (electrolyte resistivity) = 1 kΩ-cm, and ρ_i (cellular resistivity) = 2 kΩ-cm.

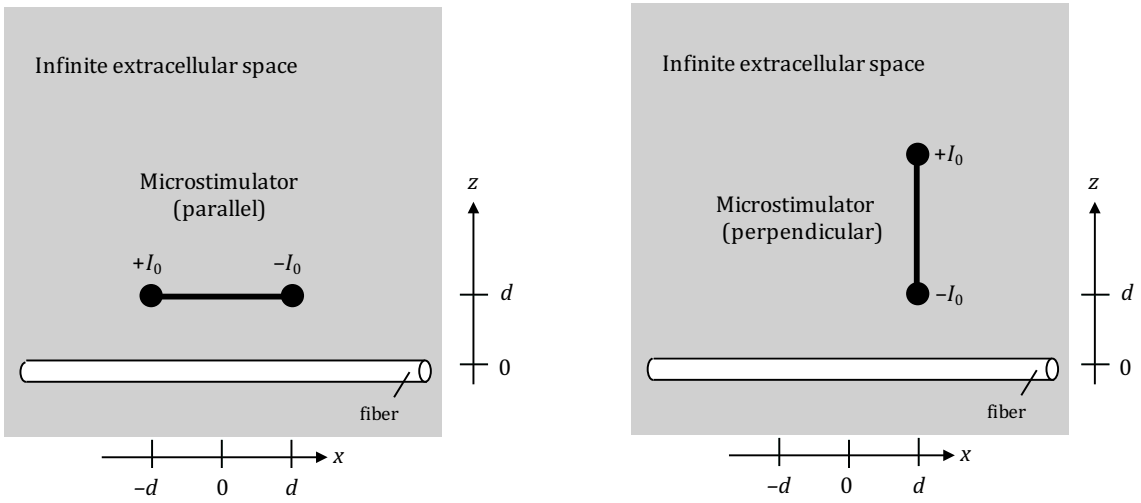


(a) In the diagram above drawn in the *x*-z plane, color in by pen or pencil where the liminal area would be located and indicate the angles at which it starts and ends.

(b) Using your answer in (a), and knowing the spatial distibution of V_m around the perimeter of the cell, determine the minimum field intensity (rheobase) required for E_0 to excite the cell.

Problem 5 (20 pts) extra credit for 580.435; required for 580.635

A miniaturized electrical stimulator is surgically implanted into skeletal muscle, and the goal of this problem is to examine the effect of the stimulator axis with respect to fiber response. Assume the following simplified scenario. A linear, infinitely long muscle fiber is lying in an infinite volume conductor, and the stimulator (a device of length d = 1.5cm with a cathode at one end and an anode at the other) is situated near the fiber in one of two ways: (a) the device is parallel to the fiber at a constant distance d from the fiber, or (b) the device is perpendicular to the fiber with the cathode a distance d from the fiber. See the diagram below.



(a) *Derive* the activating function A along the surface of the fiber starting with Eq. 16 of Handout #4, for both the parallel and perpendicular configurations, and plot both out as a function of x ($-5d < x < 5d$). Hint: superimpose the functions for a positive and negative monopole current source.

(b) To derive the transmembrane potential, it would be necessary to convolve A with the impulse response of the system for a point source. That is beyond the scope of the course this year, However, if one assumes that the fiber behaves like a linear system, it is possible to estimate the ratio in thresholds for stimulation for the parallel vs. perpendicular configurations based on your answer in (a). Provide such an estimate, and explain how you arrived at that number.