Note: Revision 1 (EFL, 12/15/99). This material now covers Weiss II, Chapters 2 and 3 and 4 as well as what you are responsible for from the flow lectures. Corrections, if needed, and some solution material will follow.

BMEN E3500, Fall, 1999

Practice Problems: (1) Ionic Transport across Cell Membranes. (Chs. 2-4, Weiss, T. F., Cellular Biophysics, V. 2 (Electrical Properties) M.I.T. Press, Cambridge, 1996). (2) Laminar flow in straight conduits.

1. Define *electrically small* cells and *electrically large* cells.

2. Give a physical explanation of why the conduction velocity is larger in fibers of larger diameter if all other factors are the same.

3. Give a physical explanation of the meaning of Equation 2.18,

$$\frac{\partial I_i(z,t)}{\partial z} = -K_m(z,t)$$

without the use of equations.

4. Consider the measurements of the action potential shown in the figure below, in both oil and seawater.

a. Find the conduction velocity of the action potential in oil.
b. Find the conduction velocity of the action potential in seawater.
c. Sketch the action potential as a function of distance along the axon in both oil and seawater.

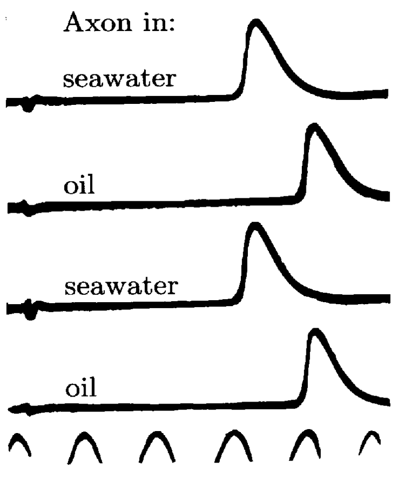


Figure: The effect of increasing the resistance of the extracellular solution on the conduction velocity of the action potential of an unmyelinated axon (adapted from Hodgkin, 1939, Figure 2). A crab (Carcinus maenas) axon of 30 um diameter was immersed alternately in seawater and in oil and the action potential recorded 13 mm from the site of stimulation. The time scale is given by a simultaneously recorded sine wave of period 1 ms (lowest panel).

5. Equations 2.35 $(2p\,a(r_o + r_i)n^2 = K_m)$ and 2.38 $(n = \sqrt{\frac{K_m a}{2 r_i}})$ appear to imply different dependences of conduction velocity on axon radius. Equation 2.35 appears to imply that $n \propto 1/\sqrt{a}$, whereas Equation 2.38 appears to imply that $n \propto \sqrt{a}$. Resolve this dilemma, and determine which result is correct.

6. The function f(z, t) is the solution to a wave equation. The solution is shown in the figure below as a function of time t at the position z = 0.

a. Suppose that f(z, t) is propagating in the positive z-direction at a propagation velocity of 100 mm/ms. Plot f(z, t) versus z at time t = 2 ins.

b. Suppose that f(z, t) is propagating in the negative z-direction at a propagation velocity of 100 mm/ms. Plot f(z, t) versus z at time t = 2 ins.

7. An electrically large cylindrical cell of 100 um radius has an internal longitudinal current that is constant in time with a spatial dependence of $I_i(z) = -\exp(5z)$ for $z < 0$, where $I_i(z)$ has units of uA and z has units of cm. There are no external currents for z <0.

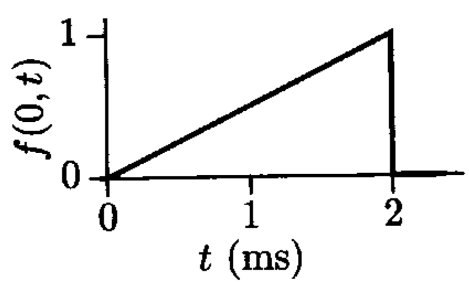


Figure. Solution of the wave equation as a function of time at one position (z = 0) (Exercises 2.10 and 2.11). The time function is nonzero for 0 < t <2 ins.

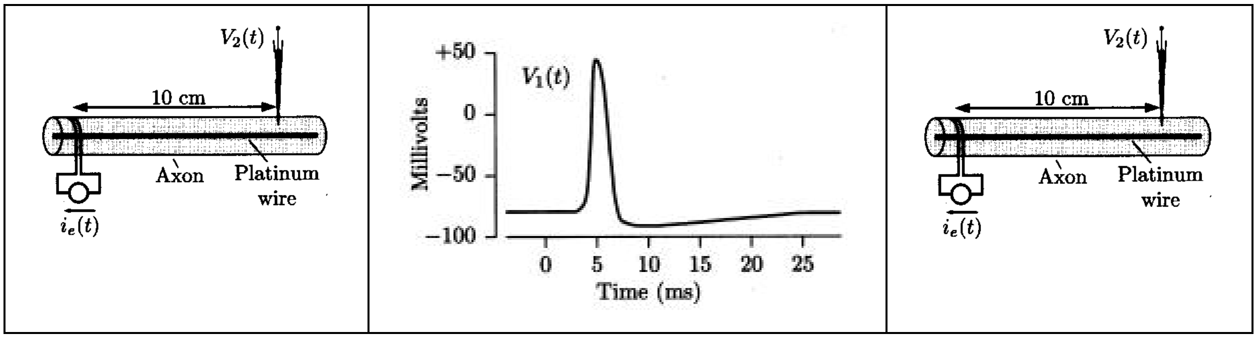
a. Determine the longitudinal current density in the cytoplasm, $J_i(z)$.
b. Determine the current per unit length through the membrane, $K_m(Z)$.
c. Determine the current density through the membrane, $J_m(z)$.
d. Determine the total current flowing through the membrane, I_m, in the segment -1 <z <0.

8. A squid axon (500 um in diameter) is placed in seawater and stimulated electrically at t = 0 (Figure below) to produce an action potential, V_1 (t), that is recorded at a site 10 cm from the point of stimulation, as also shown below. The resistivity of the axoplasm of this axon is (remarkably enough) $10p\ \Omega - \text{cm}$. The resistance of the external solution can be assumed to be negligibly small. A fine platinum wire with a resistance per unit length of 160 Ω/cm is inserted down the entire length of the axon, third figure below.. The wire takes up negligible space. The axon is stimulated electrically in an identical manner to produce an action potential, V_2 (t).

a. Find the conduction velocity, v_1, of the peak of the action potential under the conditions shown in the left figure.

b. Find the conduction velocity, v_2, of the peak of the action potential under the conditions shown in the right figure.

c. Sketch $V_2(t)$ on the same time axis as $V_1(t)$.
d. Write an expression for $V_2(t)$ in terms of $V_1(t)$.



The following are "Exercises" from Weiss, Ch. 3:

3.1 Define both the space constant and the time constant.

3.2 Does the time constant of a cylindrical cell depend on its dimensions? Does the space constant of a cylindrical cell depend on its dimensions?

3.3 The space constant decreases as the specific membrane conductance is increased. Give a physical explanation of this result.

3.4 Give a quantitative explanation of what is meant by an *infinitesimal electrode.*

3.5 For each of the following statements, assume that the electrical properties of a patch of the membrane of the cell can be represented as a parallel resistance and capacitance. Assume that the cell has a cylindrical shape, with a radius that is small compared to the length of the cell. Determine if each assertion is true or false, and give a reason for your choice.

a. For an electrically small cell, the membrane potential in response to a step of current through the membrane is an exponential function of time.

b. For an electrically small cell, the steady-state value of the membrane potential in response to a step of current applied through the membrane at one position along the cell is a constant that is independent of position along the cell.

c. For an electrically large cell, the membrane potential in response to a step of current applied through the membrane at one position along the cell is an exponential function of time.

d. For an electrically large cell, the steady-state value of the membrane potential in response to a step of current applied through the membrane at one position along the cell is an exponential function of longitudinal position along the cell.

e. For an electrically large cell, the steady-state value of the membrane potential in response to a step of current applied through the membrane at one position along the cell is a Gaussian function of position along the cell.

3.6 (modified) Know the difference among the conductance variables: G_m,(specific conductance, S/m^2), $\grave{I}_m$ (conductance, S, shown in the text as a script italic capital G) and g_m, (conductance per unit length, S/m) *?*

3.7 Physically, what does the characteristic conductance of an infinite cable represent?

3.8 Explain why a cell is an electrically small cell if its dimensions are small compared to the space constant.

Exercises omitted here make extensive reference to figures in the text. They aren't -in general- irrelevant; they are just too difficult to reproduce here.

3.1 A squid axon is placed in a large volume of seawater so that you may assume that $r_o \ll r_i$. The following data are given: resistivity (specific resistance) of squid axoplasm, $\rho_i = 30\Omega\cdot$cm; diameter of axon, 500 µm; space constant, λ_c = 6 mm; thickness of membrane, d = 50 Å; capacitance per unit area of membrane, C_m = 1 µF/cm^2

a. Find the conductance of the axon per unit length, g_m.

b. Find the conductance of the axon per unit area, G_m.

c. Find λ_c for unmyelinated axons whose membranes have specific properties (i.e., G_m and , ρ_i) that are identical to those of the squid axon, but whose diameters are 1 mm, 0.1 mm, 0.01 mm, and 0.00 1 mm.

d. Find t_m for the squid axon and for the same axons considered in part c.

Problems, Chapter 4. (Exercises have not been included here but several of them would be a good basis for exam questions.)

4.11 The figure below shows the relation between the membrane potential and the membrane current density during a propagated action potential as computed from the Hodgkin-Huxley model. The membrane current density consists of an initial outward current followed by an early inward current whose peak occurs before the peak in the action potential.

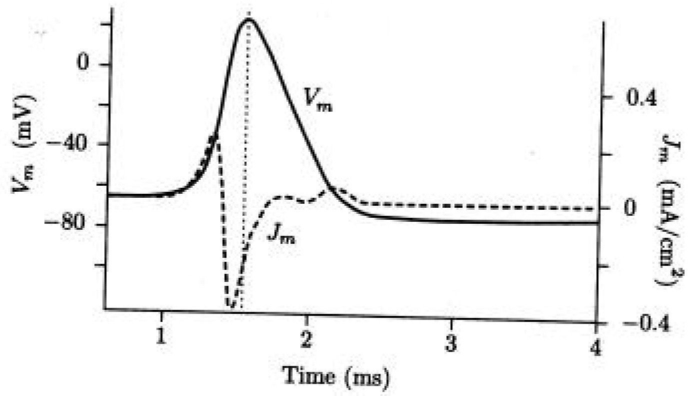
a. The initial outward current is due primarily to (choose one of the following)

i. an ionic current carried by sodium ions.
ii. an ionic current carried by potassium ions.
iii. an ionic current carried by chloride ions.
iv. an ionic current carried by calcium ions.
v. a capacitance current.

b. The early inward current is due primarily to (choose one of the following)

i. an ionic current carried by sodium ions.
ii. an ionic current carried by potassium ions.
iii. an ionic current carried by chloride ions.
iv. an ionic current carried by calcium ions.
v. a capacitance current.

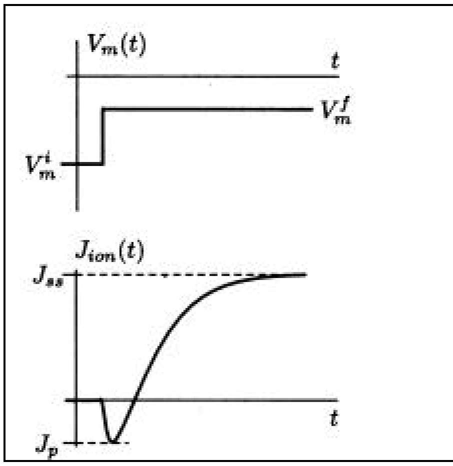
c. Before the peak of the action potential, the membrane potential increases from its resting value, whereas the membrane current density is first outward (increasing and then decreasing) and then reverses polarity to become inward (decreasing and then increasing again). Discuss this complex relation between membrane potential and current. In particular, explain how the Hodgkin-Huxley model accounts for the fact that the current can be both inward and outward during an interval of time when the membrane potential is depolarizing.



Relation of membrane potential and membrane current density during a propagated action potential (Exercise 4.11). The calculation is the same as in Figure 432. The dotted vertical line marks the time of occurrence of the peak of the action potential.

4.12 The membrane ionic current density is computed for the Hodgkin-Huxley model of a voltage-clamped squid giant axon. All parameters of the model are at their standard values. The initial voltage V^i_m is set equal to -80 mV, the final voltage V^f_m is -40 mV, and the resulting waveforms are shown in the figure below. In each part of this problem, determine the effect of changing a single parameter of the model on the peak inward current density J_p and on the steady-state outward current density J_{ss}. Indicate whether the change causes the current component to become more positive or more negative or to change only a small amount (less than 10%). For all parts, explain your reasoning.

a. The external concentration of sodium is doubled.
b. The external concentration of potassium is doubled.
c. V^f_m is changed from -40 mV to -30 mV.
d. V^i_m is changed from -80 mV to -70 mV.



Definition of the peak inward current density (J_p) and the steady-state outward current density (J_{ss}) (Exercise 4.12).

The following material is excerpted from Chapter 2, pp.35-41 of Bird, R. B. *et al.*, "Transport Phenomena", Wiley, New York, 1960. It deals with the flow of a falling film of liquid and is a parallel example to the development of the Poiseuille equation developed in class.
The problems we have considered are approached by setting up momentum balances over a thin “shell” of fluid. For *steady-state* flow, the momentum balance is

rate of momentum in $-$ rate of momentum out $+$ sum of forces acting on system = 0

Momentum may enter the system by momentum transfer according to the Newtonian (or non-Newtonian) expression for the momentum flux. Momentum may also enter by virtue of the over-all fluid motion. The forces we are concerned with are pressure forces (acting on *surfaces)* and gravity forces (acting on the *volume* as a whole).

This momentum balance is easy to apply *only when the streamlines of the system are straight lines* (i.e., in rectilinear flow).

Generally, the procedure for setting up and solving viscous flow problems is as follows: first we write a momentum balance of the form given above for a shell of finite thickness; then we let this thickness approach zero and make use of the mathematical definition of the first derivative to obtain the corresponding differential equation describing the momentum flux distribution. Now one may insert the appropriate Newtonian or non-Newtonian expression for the momentum flux to obtain a differential equation for the velocity distribution. The integration of these two differential equations yields, respectively, the momentum flux and velocity distributions for the system. This information can then be used to calculate various other quantities, such as average velocity, maximum velocity, volume rate of flow, pressure drop, and forces on boundaries.

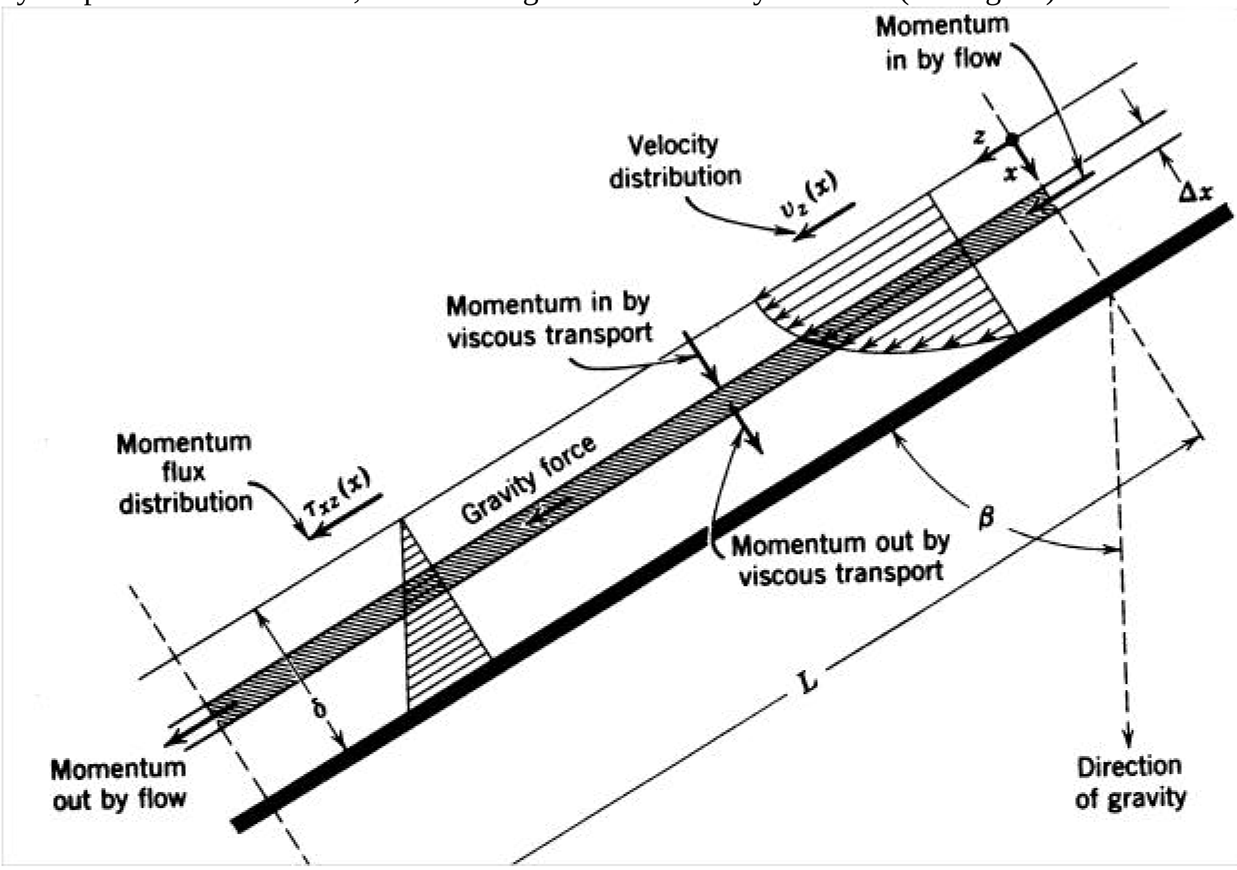
In the integrations mentioned above, several constants of integration appear, which are evaluated by the use of “boundary conditions,” that is, statements of physical facts at specified values of the independent variable. The following are the most used boundary conditions:

a. At solid-fluid interfaces the fluid velocity equals the velocity with which the surface itself is moving; that is, the fluid is assumed to cling to any solid surfaces with which it is in contact.
b. At liquid-gas interfaces the momentum flux (hence the velocity gradient) in the liquid phase is very nearly zero and can be assumed to be zero in most calculations.
c. At liquid-liquid interfaces the momentum flux perpendicular to the interface, and the velocity, are continuous across the interface.

FLOW OF A FALLING FILM

We consider the flow of a fluid along an inclined flat surface, as shown below. Such films have been studied in connection with many artificial organs and in the analysis of various natural flows in organs and organisms. We consider the viscosity and density of the fluid to be constant. We focus our attention on a region of length *L*, sufficiently far from the ends of the wall that the entrance and exit disturbances are not included in *L*, that is, in this region the velocity component v_z does not depend on *z*. This is the condition of *fully developed* flow mentioned in class.

We begin by setting up a z-momentum balance over a system of thickness Δx, bounded by the planes $z = 0$ and $z = L$, and extending a distance in the y-direction. (See Figure.)



The various components of the momentum balance are then:

rate of *z* momentum in across surface at x $\qquad (LW)(t_{xz})\big|_x$

rate of *z*-momentum out across surface at x + Ax $\qquad (LW)(t_{xz})\big|_{x+\Delta x}$

rate of *z*-momentum in across surface $\qquad (W\Delta x v_z\,(r v_z)\big|_{z=0}$

at z = 0

rate of z-
momentum out $(W \Delta x v_z\ (r v_z)|_{z=L}$
across surface
at $z = L$

gravity force
acting on fluid $(LW\Delta x)(r g \cos b)$

Note that we always take the “in” and “out” directions in the direction of the positive x- and z-axes (in this problem these happen to coincide with the direction of momentum transport). The notation x+Δx means “evaluated at x + Δx.”
When these terms are substituted into the momentum balance of Eq. 2. 1—1, we get

$$LWt_{xz}\Big|_x - LWt_{xz}\Big|_{x+\Delta x} + W\Delta x\, r v_z^2\Big|_{z=0} - W\Delta x\, r v_z^2\Big|_{z=L} + LW\Delta x\, r g \cos b = 0$$

Because v_z is the same at z = 0 as it is at $z = L$ for each value of x, the third and fourth terms just cancel one another. We now divide this equation by LW Δx and take the limit as Δx approaches zero:

$$\lim_{\Delta x \to 0}\left(\frac{t_{xz}\big|_{x+\Delta x} - t_{xz}\big|_x}{\Delta x}\right) = r g \cos b$$

The quantity on the left side may be recognized as the definition of the first derivative of t_{xz} with respect to x. Therefore, the equation may be rewritten as

$$\frac{d}{dx} t_{xz} = r g \cos b$$

This is the differential equation for the momentum flux t_{xz}. It may be integrated to give

$$t_{xz} = r g \cos b + C_1$$

The constant of integration may be evaluated by making use of the boundary condition at the liquid-gas interface, as discussed above.

B.C. 1: at x=0, t_{xz} =0

Thus C_1 = 0. Hence the momentum-flux distribution is

$$t_{xz} = r g \cos b$$

as shown in the figure above.

If the fluid is Newtonian, then we know that the momentum flux is related to the velocity gradient according to Newton's (phenomenological) 'law' of viscosity:

$$t_{xz} = -m\frac{dv_z}{dx} \text{ (for this geometry)}$$

Substitution of this expression for t_{xz} into the momentum-flux distribution gives the following differential equation for the velocity distribution:

$$\frac{dv_z}{dx} = -\left(\frac{r\,g\cos b}{m}\right)x$$

This equation is easily integrated to give

$$v_z = -\left(\frac{r\,g\cos b}{m}\right)x^2 + C_2$$

The constant of integration is evaluated by using the boundary condition

B.C. 2: at x = δ, $v_z = 0$

Substitution of this boundary condition into the velocity distribution shows that

$$C_2 = \left(\frac{r\,g\cos b}{2m}\right)d^2$$

Therefore, the velocity distribution is

$$v_z = \left(\frac{r\,gd^2\cos b}{2m}\right)\left[1-\left(\frac{x}{d}\right)^2\right]$$

Hence the velocity profile is parabolic. (See the figure.)

Once the velocity profile has been found, a number of quantities may be calculated:

(i) The *maximum velocity* is clearly the velocity at x = 0; that is

$$v_z\big|_{\max} = \left(\frac{r\,gd^2\cos b}{2m}\right)$$

(ii) The *average velocity* $\langle v_z \rangle$ over a cross section of the film is obtained by the following calculation:

$$\langle v_z \rangle = \frac{\int_0^W\int_0^d v_z\,dxdy}{\int_0^W\int_0^d dxdy} = \frac{1}{d}\int_0^d v_z\,dx = \frac{r\,gd^2\cos b}{2m}\int_0^1\left[1-\left(\frac{x}{d}\right)^2\right]d\left(\frac{x}{d}\right)$$

$$= \frac{r\,gd^2\cos b}{3m}$$

(iii) The *volume rate of flow Q* is obtained from the average velocity or by integration of the velocity distribution:

$$Q = \int_0^W \int_0^d v_z dxdy = Wd \left\langle v_z \right\rangle = \frac{r g W d^3 \cos b}{3m}$$

(iv) The *film thickness d* may be given in terms of the average velocity, or the volume rate of flow**:**

$$d = \sqrt[3]{\frac{3m \left\langle v_z \right\rangle}{r g \cos b}} = \sqrt[3]{\frac{3mQ}{r g W \cos b}}$$

(v) The z-component of the *force F of the fluid on the surface* is given by integrating the momentum flux over the fluid-solid interface:

$$\begin{aligned} F_z &= \int_0^L \int_0^W t_{xz}\Big|_{x=d} dydz \\ &= \int_0^L \int_0^W -m \frac{dv_z}{dx}\Big|_{x=d} dydz \\ &= (LW)(-m)\left(\frac{-r g d \cos b}{m} \right) \\ &= r g d L W \cos b \end{aligned}$$

This is clearly just the z-component of the weight of the entire fluid in the film. The foregoing analytical results are valid only when the film is falling in laminar flow with straight streamlines. For the slow flow of thin viscous films, these conditions are satisfied. It has been found experimentally that as the film velocity <vz) increases, as the thickness of the film d increases, and the kinematic viscosity $v = m/r$ decreases, the nature of the flow gradually changes; in this gradual change three more or less distinct stable types of flow can be observed: (a) laminar flow with straight streamlines, (b) laminar flow with rippling, and (c) turbulent flow.