JOURNAL OF OPINIONS, IDEAS, & ESSAYS

New Topics for the Pre-med Physics Course

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Article Number: 4

Date of publication: August 15, 2013

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Abstract: This article describes some topics that the author suggests be included in the pre-med physics course, based on his experience auditing the first two years of medical school in the early 1970s. They are: exponential growth and decay, fitting exponentials and power laws to data, diffusion and solute transport, Intracellular potentials, the cable model for nerve conduction, and the electrocardiogram. The paper is aimed at physics instructors. It explains why the topics are important and suggests how they might e made accessible to the students.

Background

In the early 1970s I was interested in finding clinical examples to "jazz up" the pre-med physics course. On the advice of Medical School Associate Dean W. Albert Sullivan, I audited the lectures in the first two years of medical school from 1971 through 1973. I was amazed at the amount of physics I found in these courses—and how little of it we discuss in the general physics course. I also found a great discrepancy between the physics in papers in the biological research literature and what I knew to be the level of understanding of most biology majors or premed students who have taken one year of physics.

This experience led to two developments:

- A series of articles about physics for premedical students that appeared in the American Journal of Physics.[1 2 3 4 5]
- A new senior-graduate level course and an advanced text, *Intermediate Physics for Medicine and Biology*,[6] now in its 4th edition.[7]

During the early 1970s I gave a number of talks at meetings and in physics departments, all with the goal of fostering changes in the introductory course. But these ideas did not gain much traction.

A recent report by the National Academy of Sciences (BIO 2010[8]) describes the ideal curriculum for students going into research in the biological sciences. Another report by the Association of American Medical Colleges and the Howard Hughes Medical Institute[9] discusses the preparation of pre-med students. Both reports recommend topics in the introductory physics course which are not usually taught. Because of these reports, there is renewed interest in modifying the introductory course. The American Association of Physics Teachers has sponsored invited sessions at four consecutive national meetings. I was asked to present a paper at the third of these sessions, at the summer 2010 meeting in Portland, OR. My travel was supported by a University of Minnesota Professional Development Grant for Retirees. This paper is based on that talk.

It seems that this time there may be enough interest so that the introductory physics course can actually be changed to be of greater interest to life science and premed students. The National Academy's BIO 2010 report proposes not two, but three semesters of physics, with topics of direct relevance to life science students. I identified many of these topics in references 1–5; others are in areas of molecular biology that I did not touch on, and still others (such as non-linear dynamical systems, which cause a number of cardiac arrhythmias) were not even on the horizon at that time. BIO 2010 also suggests including some topics that are usually called engineering

rather than physics (for which physics departments, seeking increased course enrollments, should be happy to take ownership). The AAMC-Howard Hughes report also recommends topics that are not usually included.

Physics in Medicine

There are many physics topics that are important in medicine. Some physics teachers have asked medical colleagues to indicate which topics in an existing introductory physics text they deem important. But this approach will not reveal topics which are relevant but not in the book. I hope that this paper will show a way to identify such topics. Some fall in an area called medical physics; others are basic in physiology; still others might be called biomedical engineering or medical physics. In the United States, medical physics is the physics used to diagnose and treat disease: ultrasound, x rays, nuclear medicine, magnetic resonance imaging. Two resource letters survey Medical Physics[10] and the subspecialty Radiation Therapy.[11]

Just one example of what ought to be in the introductory course: It became clear to me when I was auditing medical school courses that the only exposure a medical student has to x-rays, their interaction with matter, and their possible effect on people is what they receive in the premed physics course—unless, of course, they become radiologists. But we rarely discuss this in the introductory course. These are important topics. There is growing concern about the rise in CT examinations and the resulting population dose,[12] and "82% of the total effective dose is administered to outpatients, mostly in physicians' offices."[13] We physicists can—if we will—provide the background to understand issues like this, for both pre-medical students and future patients who are in our classes.

This paper identifies six topics that I feel should be covered in the introductory course and which are interesting physics in their own right:

1. Exponential growth and decay
2. Fitting exponentials and power laws to data
3. Diffusion and solute transport
4. Intracellular potentials
5. The cable model for nerve conduction
6. The electrocardiogram

They are not presented as complete discussions, nor at a level appropriate for the pre-med student, but as summaries addressed to the physics instructor.

Exponential growth and decay

Many times the rate of increase or decrease of some quantity is proportional to the present amount of that quantity. In traditional physics these include attenuation or absorption of photons, radioactive decay, and the explosive growth of a chain reaction. In medicine it is seen in physiology, drug delivery, and some stages of bacterial growth. We need to introduce the equations

$$\frac{dy}{dt} = by \qquad \frac{dy}{dt} = -by$$

Students can learn what these equations mean and recognize them and their solutions:

$$y = y_0 e^{bt} \qquad y = y_0 e^{-bt}$$

The introductory course may not have a calculus prerequisite, but we are familiar with introducing similar differential equations in one-dimensional kinematics. Interest accrued in a savings account is a good way to introduce this topic.

A related concept important in physiology is *clearance*. There are a number of definitions of clearance in the physiology literature. While all are correct, some seem rather confusing to me. Here is the approach I like.

Imagine a compartment in the body that carries fluid of total volume *V*. (A compartment is a volume that we want to single out for study. It might be an organ, the blood in the body, all the extracellular fluid, or even the entire body.) The total amount of some substance in the compartment is *y*. The substance is uniformly distributed throughout the volume; its concentration is $C = y/V$. Some process removes the substance at a rate proportional to the concentration. The process might occur in the lungs, the liver, or the kidney. This is shown schematically in Figure 1.

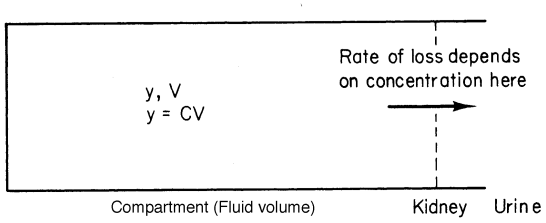

Figure 1.

The rate of change of *y* is

$$\frac{dy}{dt} = -bC = -\frac{b}{V}y = -Ky$$

$K = b/V$ is the clearance

Fitting exponential and power law data.

This topic is not strictly for pre-med students, but it is important. While it is known to professional statisticians, there is much abuse in the research literature. I became aware of it through discussions with my daughter, who is an ecology professor. I have never seen it discussed in a physics course. I hope that some reader will see a way to incorporate it in a lab experiment.

Consider how error bars behave on linear and log scales. Never mind the source of these error bars for now. Assume a simple exponential decay with constant error bars where *y* is the fraction of the initial amount that remains:

$$y = e^{-0.5t} \pm 0.09$$

Figure 2 shows the data and error bars in both a linear and a semi-log scale. Note that *t* = 0 is not a datum, since everything is normalized to this value.

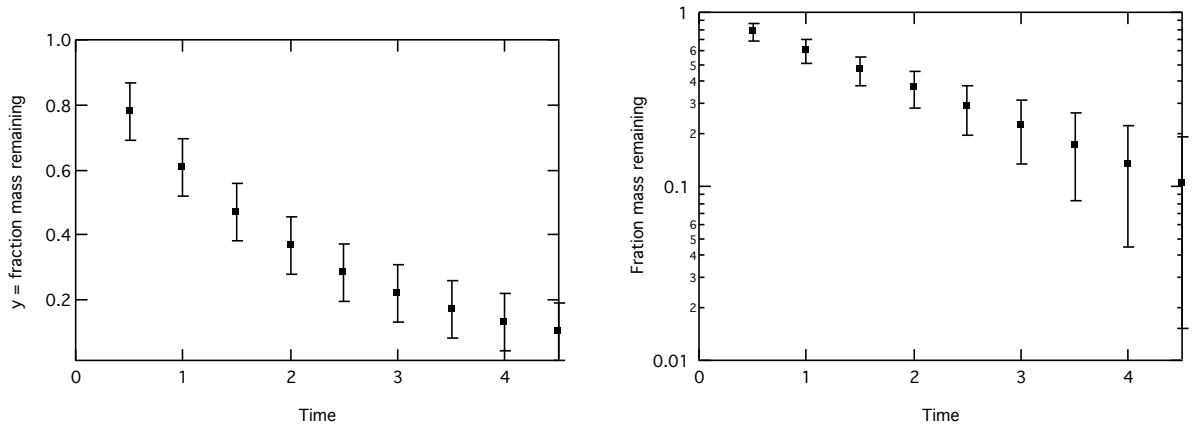

Figure 2

The other case is a constant percent error

$$y = e^{-0.5t} \pm 9\% \text{ of } y$$

which is plotted in Figure 3.

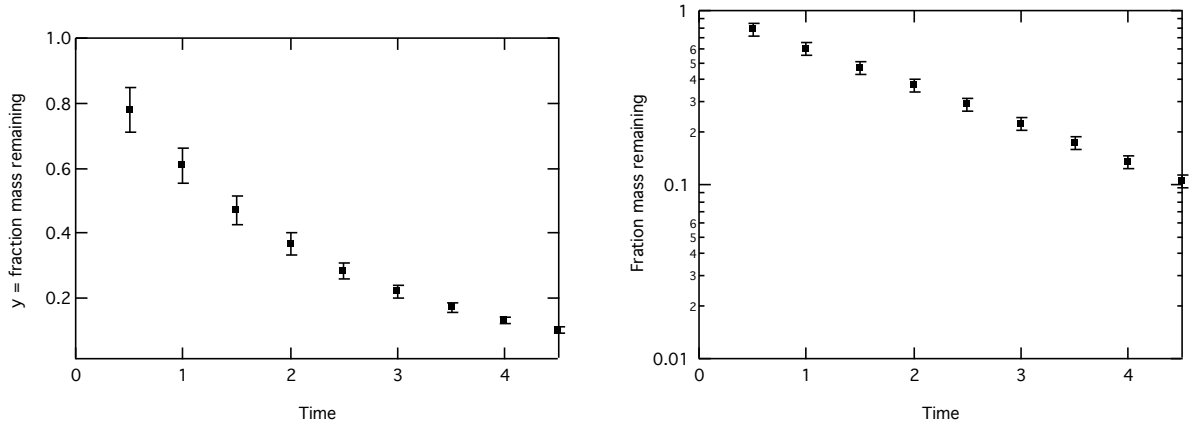

Figure 3

Least squares fitting involves adjusting the parameters *A* and *k* in $y_{calc} = Ae^{-kt}$ to minimize the quantity

$$Q = \sum \left(y_i - y_{calc}(t_i) \right)^2$$

In our case A is 1. Determining k requires the method of non-linear least squares.

On the other hand if we take the logarithm of *y*

$$u = \ln y = \ln A - kt = a - kt$$

then minimizing

$$Q' = \sum \left(u_i - u_{calc}(t_i) \right)^2$$

is a linear least squares problem. Each data point has the same weight. This implies the same error for each data point when minimizing *Q* and the same percentage error when minimizing *Q'*.

Figure 4 shows some artificial data: an exponential decay $y = e^{-0.5t}$ with noise added to each data point. The noise is Gaussian distributed with standard deviation 0.05. The black line is $y = e^{-0.5t}$. The blue line shows the linear least squares fit to the log-transformed data. The estimated value for *k* is 0.34 with $Q' = 0.013$. The red line shows

the nonlinear least squares fit to the untransformed data which gives k = 0.47 and $Q = 0.008$. The non-linear fit is clearly better. A number of statistical packages can do nonlinear least squares fitting; some, such as R, are free.

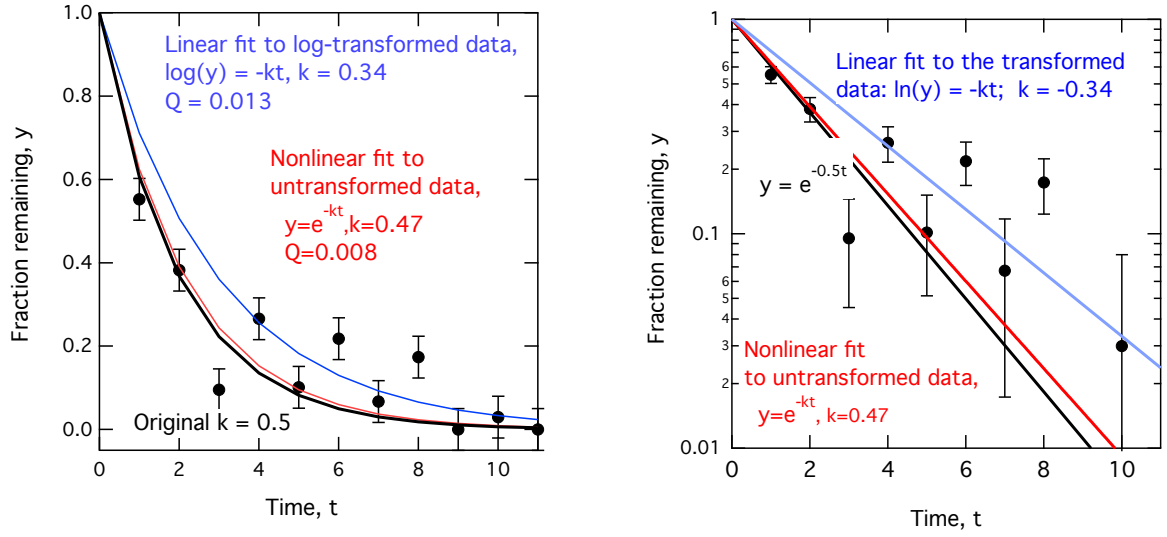

Figure 4

Why does it matter? Adair *et al.*[14] examined 498 papers on the decomposition of litter on the forest floor. In these studies litter is placed in mesh bags that are distributed in the forest and weighed annually. The studies fit the remaining fraction data using least squares. Of the 498 papers, only 15% explicitly used NLLSQ; at least 50% used a linear fit to log-transformed data. In the remaining papers the method could not be ascertained. Moreover, 60% of the papers made A an adjustable parameter when it was defined to be 1.00.

We should develop a lab experiment that analyzes both the raw data and the log-transformed data. For exponential decay with roughly constant error bars it is best to minimize Q. The problem also occurs in allometric and physiologic scaling studies when using log-log plots.[15] One must think carefully. When measuring the mass of a mouse or an elephant, the errors are much more likely to be percent errors rather than absolute errors, and minimizing Q' may be more appropriate.

Diffusion and solute transport

The movement of solute molecules from place to place in the body is essential for the physiologic processes that support life. The buildup or removal of solute particles from some region is given in one dimension by the continuity equation. Students will see it in this one-dimensional form in physiology.

$$\frac{\partial C}{\partial t} = -\frac{\partial j}{\partial x}$$

where C is the solute concentration (m^{-3}) and j is the solute fluence rate ($m^{-2}\ s^{-1}$). We can derive this, even for students who have not taken calculus, with reasoning similar to that used to obtain the differential equation for exponential growth and decay.

Consider the situation shown in Figure 5. Solvent (water) molecules are open circles and solute molecules are closed circles. The narrow region in the middle represents a channel through which the molecules can move.

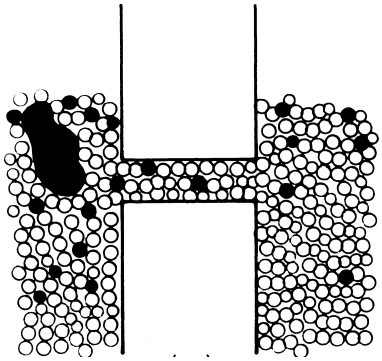

Figure 5

The solute molecules are in contact with water molecules, but they are rarely in contact with one another. Two important mechanisms of solute transport are *solvent drag* and *diffusion*. Both can take place at the same time.

In solvent drag, the solute particles are carried along with the flowing liquid. The fluence rate of solute particles is the concentration times the volume flow (velocity) of the solution:

$$j = Cv$$

where j is in $m^{-2}\ s^{-1}$, C is in m^{-3} and v is in $m\ s^{-1}$.

Diffusion is the transport of solute from a region of higher to lower concentration because of the **independent random walking** of the solute molecules. This is described by Fick's first law:

$$j = -D\frac{\partial C}{\partial x} \ .$$

D has the units $m^2\ s^{-1}$. Combining the First Law with the continuity equation gives Fick's second law:

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} \ .$$

One solution of Fick's second law is a Gaussian-distributed concentration that spreads with time:

$$C(x,t) = \frac{N}{\sqrt{2\pi}\sigma(t)} e^{-x^2/(2\sigma^2)}$$

$$\sigma^2(t) = \sigma^2(0) + 2Dt$$

This is plotted in Figure 6. It is hugely important: the distance diffused is proportional to the square root of the time. For a solute particle to go 100 times as far takes 10000 times longer. D for oxygen in water at 20°C is 1 micrometer^2 per millisecond. An oxygen molecule diffuses 1 μm in 1 msec. To diffuse 100 μm would require 10 sec. This is why we have a circulatory system. The oxygen molecule can rapidly travel large distances by solvent drag.

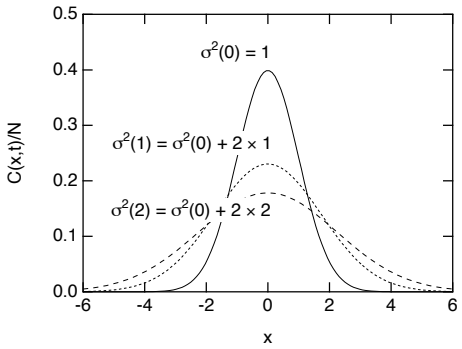

Figure 6

Another interesting result is time-independent diffusion from a spherical cell of radius *R* to infinity when the concentration at the cell surface is C_0. The steady-state solution is

$$C(r) = C_0 DR / r$$
$$j_r = C_0 DR / r^2$$
$$i = 4\pi DC_0 R$$

where i is the total particle flow (current) away from the cell. The total diffusive current away from the cell is proportional to the cell radius *R*, not to the cell surface area.

Related to this is osmotic pressure and solvent flow. Referring back to Figure 5, there is a large particle on the left. It cannot pass through the channel in the membrane, and it creates an osmotic pressure difference that (if the total pressure is the same on both sides of the membrane) gives rise to flow of both water and permeant solute molecules from right to left. We should emphasize this point. Osmotic flow is *not* simply "diffusion of water." This is discussed in detail in Reference 7, where it is shown that the volume flux (water plus permeant solute) through a membrane is $J_v = L_p\left(\Delta p - k_B T \Delta C\right)$. The expression in parentheses is the "entropic" contribution to the chemical potential of the water and depends only on the properties of the solution. The hydraulic permeability L_p depends on the transport process through the membrane and is very different for different processes, such as diffusion of independent water molecules vs. bulk flow.

Intracellular potential

Cells are surrounded by a bilayer lipid membrane called the plasma membrane. There is a difference in electrical potential between the outside of the cell and the inside. It is called the resting potential, typically -50 to -200 mV. Ion concentrations are also different, as shown in Figure 7.

The potential can change because of ion flow through the membrane. This gives rise to the propagating action potential in a nerve or muscle cell.

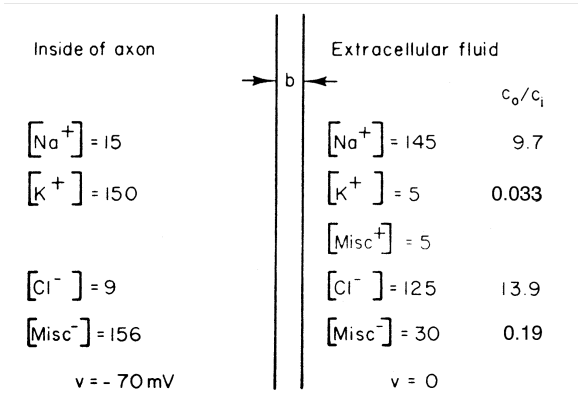

Figure 7

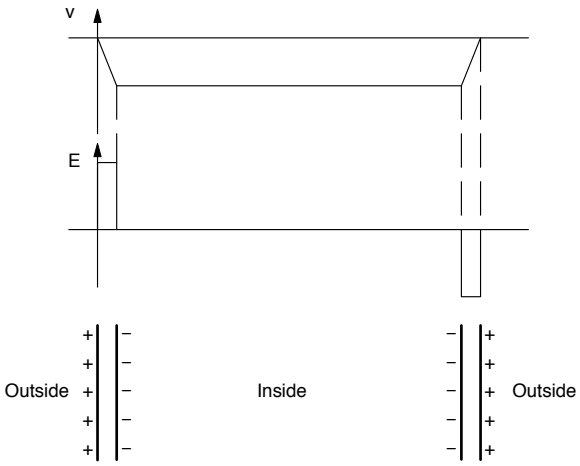

Figure 8

Figure 8 shows how the electric field and potential vary along a line coming in one side of the cell and out the other. The potential decreases as one enters through the membrane and rises again when one passes out through the other side of the cell. There is no electric field in the resting state inside the cell because the intracellular fluid is a conducting medium. The electric field within the membrane is quite large, typically 10^7 V m^{-1}. The electric field within the membrane is caused by a layer of unneutralized ions at the surface of the membrane. Typically, only one in every 100,000 atoms in contact with the cell membrane carries an unneutralized charge.

Suppose that a particular ion species can pass through the cell membrane. It will be in equilibrium when the concentration ratio is related to the transmembrane potential by a Boltzmann factor:

$$\frac{C_{in}}{C_{out}} = e^{-ze(v_{in}-v_{out})/k_BT}$$

The Boltzmann factor tells us what the equilibrium concentration ratio is for a given transmembrane potential. At the equilibrium ratio, the concentration of that species will not change, even if the membrane is quite permeable to those ions. Physiologists invert the Boltzmann factor and call it the Nernst Equation:

$$v_{Nernst} = v_{in} - v_{out} = \frac{k_BT}{ze}\ln\left(\frac{C_{out}}{C_{in}}\right)$$

Some authors say that the Nernst equation shows how the concentration ratio gives rise to the potential difference. This is not true: the thin layer of charge at the membrane surface gives rise to the potential difference and does not change the concentration measured in the intracellular volume.

The cable model for action potentials

Action potentials are electrochemical waves that propagate in both nerve and muscle cells. The intracellular potential rises from its resting state (depolarization) and then returns to the resting state in about as millisecond as shown in Figure 9. The action potential in a myocardial (heart muscle) cell lasts about 100 milliseconds (Figure 10).

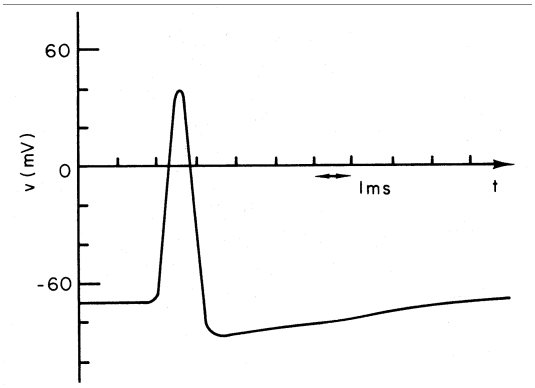

Figure 9

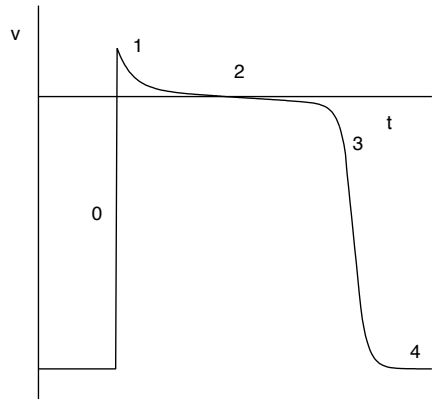

Figure 10

The first day of the neurophysiology class I audited, the lecturer wrote on the blackboard the telegrapher's equation with no inductance:

$$c_m \frac{\partial v}{\partial t} + j_m = \frac{1}{2\pi a r_i} \frac{\partial^2 v}{\partial x^2}$$

He said the students would remember it from their physics course. Of course they didn't. We never taught it. But it would not be hard for us to derive it in the introductory course. We don't need to ask the students to solve it!

Consider a 1-dimensional case: a cylindrically shaped nerve axon or myocardial cell stretched along the *x* axis. Divide the universe into three regions as in Figure 11:

- The interior of the axon or muscle cell
- The cell membrane
- Everything outside

The cell membrane acts as the dielectric in a capacitor whose plates are the conducting intra- and extra-cellular fluid.

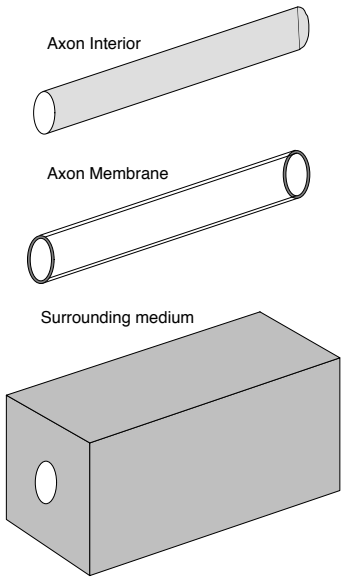

Figure 11

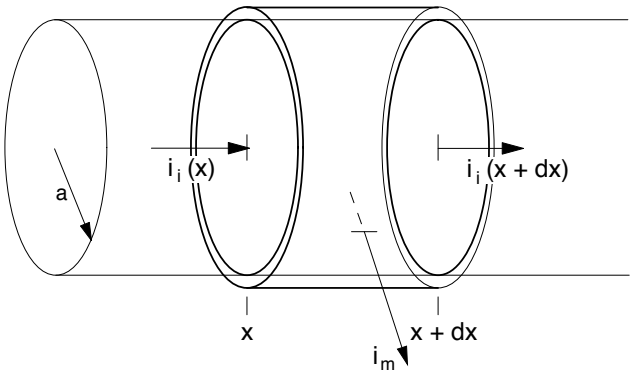

Figure 12

The interior is shown in Figure 12. By conservation of charge, if i_i changes between x and $x+dx$, the difference is i_m, part of which flows through the cell membrane, and the rest of which changes the charge and hence the transmembrane potential on the cell membrane

$$i_{cap} = C\frac{\partial v}{\partial t}.$$

The capacitance of that segment is $C = 2\pi a c_m dx$, where a is the cell radius and c_m is the membrane capacity per unit area. Similarly, the current out through the membrane is $2\pi a j_m dx$.

Thus, conservation of charge gives

$$c_m \frac{\partial v}{\partial t} + j_m = \frac{1}{2\pi a r_i} \frac{\partial i}{\partial x}.$$

The intracellular solution obeys Ohm's law, which in this case can be written as

$$i_i(x) = -\frac{1}{r_i} \frac{\partial v_i}{\partial x}$$

where i_i is the current along the cell and r_i is the resistance per unit length. Combining these we have the telegrapher's equation:

$$\underbrace{c_m \frac{\partial v}{\partial t}}_{\substack{\text{changes} \\ \text{membrane} \\ \text{charge}}} + \underbrace{j_m}_{\substack{\text{current} \\ \text{through} \\ \text{membrane}}} = \underbrace{\frac{1}{2\pi a r_i} \frac{\partial i_i}{\partial x} = \frac{1}{2\pi a r_i} \frac{\partial^2 v}{\partial x^2}}_{\text{change in current along axis}}$$

This is an important equation in neurophysiology. The action (pun intended) is all in the membrane current density j_m. If j_m follows Ohm's law, the phenomenon is electrotonus. Non-linear behaviors are used to model nerve conduction, depolarization of muscle, and electrical behavior of the heart.

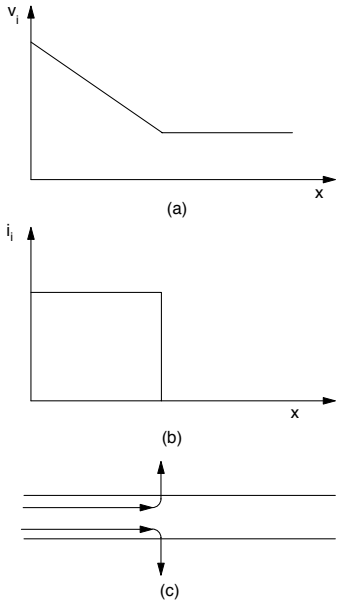

Figure 13

The Electrocardiogram

Now we turn our attention to what happens outside the cell during the depolarization phase of a wave traveling along the cell. Figure 13a is a snapshot of a depolarization wave propagating to the right. Furthest to the right the cell is at the resting potential. The potential rises linearly in the depolarizing region. Figure 13b shows the constant current associated with the rise in potential. Where the current i_i suddenly falls to zero, it must flow out through the membrane into the extracellular region as in Figure 13c.

Suppose a wave of depolarization extends from the origin to $x = x_2$ as in Figure 14. The interior potential is constant to the left of $x = 0$. Inside the cell there is a constant current i_i from $x = 0$ to $x = x_2$

$$i_i = \frac{\Delta v_i}{r_i x_2} = \frac{\Delta v_i \sigma_i \pi a^2}{x_2}$$

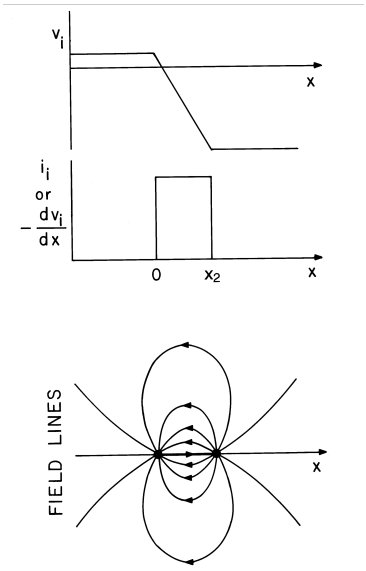

Figure 14

where *a* is the cell radius, r_i is the resistance per unit length along the axointeror, and σ_i is the electrical conductivity of the intracellular substance. Imagine that the cell radius *a* is very small and that the surrounding medium goes on forever. The cell does not distort the current flow in the surrounding medium significantly. If current i_i is injected into the surrounding medium at the origin, then the current density, electric field and potential in the surrounding medium are given by

$$j = \frac{i_i}{4\pi r^2}$$

$$E = \frac{j}{\sigma_{out}} = \frac{i_i}{4\pi\sigma_{out} r^2}$$

$$v = \frac{i_i}{4\pi\sigma_{out} r}$$

where *r* is the distance from the injection point to the observation point.

In terms of Figure 14, current i_i flows out of the cell at x_2 and current $-i_i$ flows in at the origin This constitutes a current dipole **p**, a source and sink injecting current into the surrounding tissue. **p** points along the cell and has units A-m:

$$p = |\mathbf{p}| = x_2 i_i = \pi a^2 \sigma_i \Delta v_i$$

If there is an advancing wave front of depolarization encompassing many cylindrical cells packed side-by-side, then *a* is the radius of the wave front. The current dipole **p** has many names, often confusing, such as electric force

vector. This name confused me greatly when I was first trying to understand the electrocardiogram. I prefer electrical activity vector.

To understand the electrocardiogram, assume the exterior medium–the body–is an infinite homogeneous conductor. Then at a distant point *r* from the current dipole and at angle θ with the axis of the cell,

$$v = \frac{\Delta v_{in}\sigma_{in}\cos\theta}{4\pi\sigma_{out}r^2} = \frac{\mathbf{p}\bullet\mathbf{r}}{4\pi\sigma_{out}r^3}$$

One can show that in an infinite conducting medium the voltage difference between two electrodes separated by **R** arising from a source **p** in the heart a distance *r* from each electrode is

$$v = \frac{\mathbf{p}\bullet\mathbf{R}}{4\pi\sigma_{out}r^3}$$

Three of the electrocardiogram electrodes are placed on the body at positions A, B and C in Figure 15, giving three values of **R**: R_I, R_{II} and R_{III}. Other electrodes are placed on the chest.

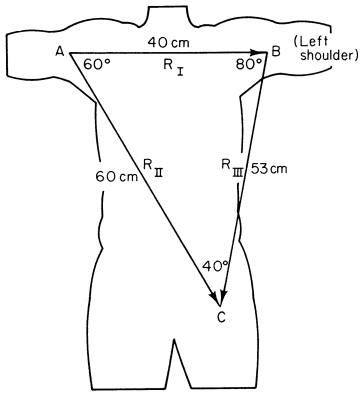

Figure 15

This model can explain quantitatively the size of the QRS wave in an electrocardiogram.[7] A number of electrocardiogram labs have been described over the years.[16]

Conclusion

I hope that these examples convince you that there is some topics, of interest to both physics instructors and pre-med and biology students, that can replace some of the topics now covered in the introductory course.

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[1] R. K. Hobbie. Teaching exponential growth and decay: examples from medicine, *Amer. J. Phys.* **41:**389 (1973).
[2] R. K. Hobbie. The electrocardiogram as an example of electrostatics, *Amer. J. Phys.* **41**: 824 (1973).
[3] R. K. Hobbie. Nerve conduction in the pre-medical physics course, *Amer. J. Phys.* **41**: 1176 (1973).

[4] R. K. Hobbie. Osmotic pressure in the physics course for students of the life sciences, *Amer. J. Phys.* **42**:188 (1974).
[5] R. K. Hobbie, Physics useful to a medical student. *Am. J. Phys.* **43**(2): 121-132 (1975); Erratum. *Amer. J. Phys.* **45**(3): 320 (1977)

[6] Russell K. Hobbie. *Intermediate Physics for Medicine and Biology*, 1st ed. New York, Wiley, 1978.

[7] Russell K. Hobbie and Bradley J. Roth. *Intermediate Physics for Medicine and Biology*, 4th ed. New York, Springer, 2007.
[8] *BIO 2010: Transforming undergraduate education for future research biologists.* National Research Council. National Academies Press, 2003. Available at http://www.nap.edu/openbook.php?isbn=0309085357
[9] *Scientific Foundations for Future Physicians.* AMC-HHMI. Available at https://members.aamc.org/eweb/upload/Scientific Foundations for Future Physicians Report2 2009.pdf
[10] R. K. Hobbie and B. J. Roth. Resource Letter MP-2: Medical Physics. *Amer. J. Phys.* **77**(11): 967-978 (2009).
[11] S. T. Ratliff. Resource Letter MPRT-1: Medical Physics in Radiation Therapy. *Amer. J. Phys.* **77**(9): 773–864 (2009).

[12] R. Fazel, H. M. Krumholz, Y. Wang *et al*. Exposure to low-dose ionizing radiation from medical imaging procedures. *N Engl J Med* **361**: 849–857 (2009).
[13] G. J. Becker, J. Bosma and W. R. Hendee. Radiation exposure from medical imaging procedures (letter). *N Engl J Med* **361**: 2289–2290 (2009).
[14] E. C. Adair, S. E. Hobbie, and R. K. Hobbie. Single-pool exponential decomposition models: potential pitfalls in their use in ecological studies. *Ecology* **91**(4): 1225- 1236 (2010).
[15] G. C.Packard. On the use of logarithmic transformations in allometric analyses. *Journal of Theoretical Biology* **257**: 515–518 (2009).

[16] See http://www.phys.gwu.edu/iplswiki/index.php/Laboratories