

Physics useful to a medical student

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The author recently audited all of the courses taken by first and second year medical students at the University of Minnesota. On the basis of that experience, he recommends physics topics which those students will find useful, such as the Boltzmann factor, diffusion and osmosis, Thevenin's theorem, nerve conduction, a detailed discussion of the electrocardiogram, relaxation oscillators, feedback, Fourier series, correlation functions, and power spectra. In addition, examples are given of applications of physical principles from each of the major areas of physics.

INTRODUCTION

From November, 1971 through August, 1973, I had occasion to audit all of the non-clinical courses taken by first- and second-year medical students at the University of Minnesota. This came about because I had chanced upon an article¹ pointing out that the number of survivors in certain chronic diseases decays exponentially. This example increased student interest when exponential decay was discussed in our general physics course,² so I approached Assistant Dean W. A. Sullivan, M.D. about the possibility of my searching for other examples which we might use in our course. He wisely said, "Go to class." This turned out to be a much better way to learn what physics is important than the casual visits I had originally planned.

Several articles have appeared recently in this Journal describing introductory physics courses with biomedical examples^{3,4} and more advanced courses in biophysics.⁵⁻⁸ These courses have largely emphasized biomechanics, thermodynamics, nerve conduction, molecular biology, or applications of atomic or nuclear physics.

Textbooks with a biological or medical slant are beginning to appear.⁹⁻¹³ In some, the biomedical examples are of the "gee whiz" variety and do not involve physical principles at any great depth. Although it is difficult, Benedek and Villars⁹ is the only one which I feel has sufficient depth: According to the Table of Contents, the three volumes, when they are all out, will cover all of the essential topics.

The purpose of this paper is to report what I learned about medical students and their courses, to propose some new topics which we might include in our courses, and to list topics and examples for as many of the major areas of physics as possible.

STUDENTS

The premedical physics course contains two populations of students. One is future biomedical research workers; the other is future clinicians. While the needs of both groups have much in common, there are some differences. While it is not feasible to teach general physics separately to these groups (both because of the class size and because the student's ultimate career is not known when he takes physics), we can design appropriate second courses in physics for the researchers.

The researchers need to be more competent in the use of physical and mathematical reasoning than many now are: we need to teach them to solve problems. The trouble is that most of the problems we assign are those that seem interesting to physicists. Our graduates fail to recognize the utility of physics later on when the problems we gave them concerned only automobiles, projectiles thrown out windows, and the like. A book by Riggs¹⁴ shows the kind of mathematical reasoning which these students need to learn. It includes material on quantifying problems, using graphs, feedback, exponential growth and decay, diffusion and chemical kinetics. In many cases we can give examples from physics to help the student master these techniques, but we also need to include some biological examples to show them that the techniques are worth mastering.

The second group of students is those who will become clinicians. They tend to memorize a lot and to deemphasize the kind of reasoning from basic principles which we physicists love so well. (In their defense it should be said that such reasoning does not work for every problem they encounter; furthermore, a patient under our care would probably expire while we stood there reasoning from first principles.) I cannot claim that an understanding of the basic principles we teach will help them to cure any patients (though it might); I can say with confidence that what we teach may save them a few hours sleep while they are in medical school, and that it will probably reduce slightly the clutter in their minds. Because these benefits are most obvious while they are in medical school, their acceptance of physics depends on the stage of their education. When we present material on the electrocardiogram in our physics course it is eagerly accepted by the premedical student as a clinical example. A second year medical student won't regard the material as clinical, but he will acknowledge that it is helpful. The fourth year student or intern no longer has the time for it.

NEW MAJOR TOPICS

Several of the topics below are not usually taught in a general physics course. They are enumerated here to em-

phasize that they are topics to which considerable time should be devoted. They are diffusion and osmosis, free energy, Thevenin's theorem, nerve conduction, operational amplifiers, digital logic, feedback systems, relaxation oscillators, Fourier transforms, correlation functions and power spectra. Several of these are topics usually found in electrical engineering. Physics is the basic science underlying electrical engineering. As that technology becomes more important in medicine, our course should reflect the fact.

TOPICS AND EXAMPLES

This section presents a summary of the biomedical applications which I have found for each of the traditional areas of general physics. In some cases the material presented is the nucleus for an extensive discussion; in other cases it is simply an example which can be mentioned in passing. If material about the topic is readily accessible in the physics literature, few details are given. When you must go to the medical literature, somewhat more detail is presented, so that you can decide whether or not you want to track down the reference. The list of examples is not exhaustive; it represents only those topics which I have come across in the last three years. Even though I have been looking for these topics, finding them still owes much to chance.

I. Mathematical Tools.

We should introduce our students to graphical techniques including the use of both semi-log and log-log paper. The use of semi-log paper should include the analysis of both single exponentials² and multiple half-lives.¹⁴ Radioactive series decay is analogous to some of the simpler situations in which a substance flows from one compartment of the body to another in only one direction. (For example, if a drug is absorbed from an intramuscular injection site at a certain rate and is irreversibly destroyed by the liver at another rate, what is the concentration in the blood?) Compartment theory is a complex subject to which entire courses are devoted, but the medical student usually does not take them. Instead, the results are mentioned in passing and the lecturer hopes that the student knows what it is all about. The use of log-log paper to analyze data obeying a power law is related to scaling, which has become a popular subject in physics courses in recent years.^{10,15,16}

Error analysis is not very fashionable these days, probably because the calculations are so tedious to perform by hand. Perhaps with the increasing availability of small computers and sophisticated calculators, we can consider treating this topic again. It is important: I have seen laboratory tests reported with an absurd number of "significant" figures, and I have seen clinicians become upset when an analog and a digital presentation of the same test value differed by a percent or two, well within the accuracy of the measurement.

A good grounding in probability and statistics is useful for discussing both experimental errors and statistical physics. The medical students I met had very weak backgrounds in statistics: for most, their only experience was

a two week course in medical school which went so fast that they did not understand the basic principles. One of the results of such a weak background is that, at least until recently, there was considerable confusion among physicians about whether or not all laboratory test results have a Gaussian distribution. Statisticians periodically have to point out that they do not.¹⁷ The confusion stems partly from a misunderstanding of the central limit theorem of statistics (that the distribution of the *means* of samples of size n approaches a normal distribution as n becomes large), and partly because of the word *normal*, which is assumed by some to signify the state of health of a patient. We are in a good position to help prevent this misunderstanding because we deal with distributions, such as molecular speeds and mean free paths, which are not Gaussian.

LaFleur and her colleagues¹⁸ have suggested some interesting laboratory experiments in which students verify whether or not certain variables (such as the number of cups of coffee consumed per person per day or the variation of SO₂ content of Montreal air) are Poisson distributed. Another interesting example is the release of acetylcholine at a neuromuscular junction, which is described in detail by Katz.¹⁹ In response to the excitation of a motor nerve, small, quantized amounts of acetylcholine are liberated and diffuse from the nerve to the muscle. The number of quanta liberated can be measured by the electrical response of the muscle cell if it is poisoned so that a full-fledged electrochemical discharge does not take place. The number liberated in each excitation of the nerve is found to be Poisson distributed. Another example is that the number of bacteria in small volumes of a very dilute bacterial solution obeys the Poisson distribution.

II. Mechanics.

Vectors and their projections are needed to discuss the electrocardiogram, as well as for mechanics. Statics problems involving forces in bones and joints are covered well in existing textbooks.^{20,21}

Benedek and Villars have given some interesting material on free fall terminal velocities.²² Viscous forces are also necessary to treat ion mobility and diffusion. Circular motion, viscosity and buoyancy must all be used to understand the ultracentrifuge: Argos gives an extensive set of references.⁴ Several different methods of separating cells are reviewed by Shortman.²³ These include sedimentation rate (centrifuge), differences in buoyancy (layers of liquid of different density or liquids with uniform density gradients) and electrophoresis.

When we discuss work and energy, we should spend some time talking about muscles and their energy consumption.⁴ I find it helpful to introduce the first law of thermodynamics as soon as I begin to talk about work. We tend to sound a bit silly when we talk about work without carefully specifying that we mean work done *by* a particular force *on* some object. When we hold up a heavy object we are doing no work on it (its energy is not changing); yet we are obviously getting tired and consuming energy to maintain the force. This distinction is blurred when we delete the words "on the body" and just say "we are doing no work." The reaction of

physiologists to our incomplete discussion is predictable:

Some confusion exists on the meaning of the term "work" when applied to muscle contraction, to exercise, etc. For example, if a subject holds a 10 kg (22 pound) weight horizontally at arm's length, the physicist would correctly claim that the subject is doing no physical work, since the weight is stationary. (However, no evidence can be found that a physicist has ever attempted this experiment.) But the physiologist would claim, also correctly, that physiologic work has increased significantly, since this task has increased the subject's oxygen consumption, heat production, metabolic rate, etc. Thus, in discussions of "work," the external, physical, force-times-distance work must be carefully distinguished from the internal rate of free energy expenditure.²⁴

To explain the energy consumption of muscle under constant tension, note that each time a fiber of skeletal muscle is activated by a nerve impulse its tension rises and then falls again in several milliseconds. The force exerted by a muscle is the average of a lot of pulses like this, the average repetition rate determining the magnitude of the force. A. V. Hill²⁵ has identified three components of the energy required for the contraction of skeletal muscle: (1) a fixed amount of energy is dissipated each time a muscle fiber "fires"; (2) additional heat is generated which is proportional to the change of length of the muscle; and (3) energy is used which is equal to the mechanical work done. In his article, Hill claims that the third component may be either positive or negative, depending upon the sign of the mechanical work done by the muscle. In spite of the fact that this paper is over ten years old, I have not been able to find any other discussions of it. Whether or not the third component is actually reversible, it is certainly easier to walk down stairs than to climb them. Hill describes a spectacular demonstration using two stationary bicycles with their sprockets chained together. Rider A, exerting a forward force on the pedals while they turn backwards, can quickly and effortlessly exhaust rider B, who pedals normally. We have modified this demonstration to use hand cranks, and we record the pulse rates of the students who try it during lecture.

The ballistocardiograph, although not widely used, is an interesting example of the conservation of momentum. A patient is placed on a frictionless platform to measure the momentum of the blood as it leaves the ventricle and is deflected downward by the aorta. The theory and examples are found in Benedek and Villars.²⁶

Trauma in collisions of people with various surfaces provides another example of momentum. There is a discussion in Benedek and Villars,²⁶ and there is an extensive literature.²⁷⁻²⁹

Although we usually do not mention the term compliance in an introductory course, students will encounter the term in pulmonary physiology where it will mean $c = dV/dp$. The lungs consist of a branching network of finer and finer bronchi terminating in small sacs called alveoli. The stiffness of the lungs to changes of volume is due to two effects: elasticity of the alveolar walls and surface tension of the fluid lining the alveoli.³⁰ A crude

model for the behavior of alveoli can be constructed by noting that they are all small sacs connected to a common airway. In that sense they are analogous to two soap bubbles connected to each end of a pipe. We often derive the formula relating the pressure, p , in a soap bubble to the surface tension, γ , and radius, r : $p = 4\gamma/r$. This equation is quoted without proof in medical literature as the "Law of Laplace." Since p is inversely proportional to r , when two soap bubbles are connected in this manner, the smaller one will grow still smaller, while the large one expands. We often demonstrate this in class. Why do all of the alveoli remain inflated? The answer is that the stiffness of the alveolar walls prevents one alveolus from expanding at the expense of another. The stiffness would not be sufficient to overcome surface tension if the alveoli were lined with pure water; however, the water contains lecithin, a surfactant which reduces the surface tension. This surfactant is not present in the lungs of infants until they are near term.^{31,32} Premature infants often have trouble breathing because of the high surface tension, leading to what is called hyaline membrane disease. Cromer³³ has a brief quantitative discussion of surfactants.

III. Fluids.

Whole body measurements of specific gravity are used sometimes to estimate the fraction of body fat. Floating feces used to be attributed to the presence of fat, which indicates intestinal malabsorption. However, it was recognized only recently³⁴ that the presence of gas can cause the same effect.

We need to discuss viscosity and the dependence of viscous laminar flow on the fourth power of the vessel radius.^{35,36} (The fact that the vessels are elastic is also important in a more detailed analysis of blood flow.)³⁷⁻³⁹ The large changes in flow resistance which accompany small changes in vessel radius are the reasons that vasodilators such as nitroglycerin are effective in relieving the pain of angina pectoris. The drug relaxes the smooth muscle in the walls of the blood vessels. Incidentally, it is not the increased flow to the coronary vessels which gives relief, but the decreased demand of the heart for oxygen, because the load on the heart has decreased with the lowered systemic resistance.⁴⁰

Blood flow becomes turbulent if a constriction makes the blood velocity high enough. This turbulence is responsible for some of the sounds which the doctor listens for when he auscultates (listens to) the heart or a major blood vessel such as the carotid artery. (Noises due to turbulence in an artery are called *bruits*.) Very few medical students to whom I have talked understand the physics of measuring blood pressure. When the brachial artery in the upper arm is pressed partially shut by the blood pressure cuff, the increase in blood velocity causes the flow to become turbulent. The resulting noise can be heard in the artery at the elbow. If the artery is clamped shut during the entire pulse, no sound is heard. As the pressure of the cuff is lowered, the artery is open for an instant at the peak (systolic) pressure and the turbulent noise is heard as a tapping sound. As the the pressure in the cuff falls further, the sound changes character as the

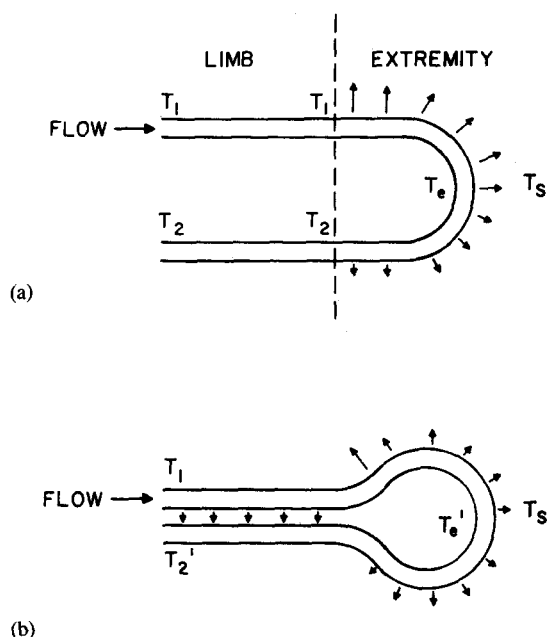


Fig. 1. Illustration of the principle of counter current heat transfer. When heat can flow from the blood in the outgoing vessel to the blood in the return vessel, as in the bottom figure, the temperature of the extremity is lower and there is less heat loss for a fixed temperature of the surroundings, T_s . The temperature of the return blood, T_2' is greater than T_2 .

length of time during which turbulence occurs increases. There is some disagreement as to just when the minimum (diastolic) pressure should be read.⁴¹ The answer, which would appear obvious to a physicist, is really not so simple, since a change to the more logically correct point would require a redetermination of what constitute normal values of diastolic pressure.

IV. Heat and Kinetic Theory.

Our discussion of the First Law should include energy unit conversions. It is still necessary occasionally to point out the difference between the calorie and the Calorie,⁴² although it is an academic point since most physicians work only with the kilocalorie.

A microscopic treatment of the Second Law, simplified from the discussions by Reif⁴³ or Kittel,⁴⁴ has several advantages. It provides an intuitive picture of entropy and temperature. If the two systems used in the derivation are allowed to exchange particles as well as energy, one also obtains the chemical potential. The Boltzmann factor drops out as a bonus, representing the temperature dependence of the number of accessible states in the reservoir. The examples of entropy given by Zinman⁴⁵ are helpful. A discussion of the Overhauser effect^{46,47} allows one to understand coupled chemical reactions, one of which appears to violate the Second Law.

The Boltzmann factor, which can be obtained easily from the treatment described above, is not often discussed in elementary courses. Yet it is essential to understand many processes in living things, such as nerve conduction, muscle contraction, glandular secretion, and the need for active transport. A failure to understand it can lead one to some remarkably confused thinking. For example,⁴⁸ the Nernst equation relates the concentration, C , of a species on each side of a permeable membrane to

the potential difference across the membrane:

$$V_2 - V_1 = (RT/Fz) \log(C_1/C_2).$$

(Here R is the gas constant, z the ionic charge, F the Faraday and T the absolute temperature.) Solving this for the concentration ratio, C_1/C_2 , shows that it is just an expression for the Boltzmann factor, for ions whose potential energy differs on either side of the membrane. (If we are not prepared to derive the Boltzmann factor, we can at least relate the Nernst equation to an exponential atmosphere.) I have found many students who do not recognize this connection between the Nernst equation and the Boltzmann factor. Some are confused enough to think that the order in which the Nernst equation is written implies that the concentration ratio causes the potential difference. In fact, most students are surprised to be told that the bulk of intracellular or extracellular fluid is electrically neutral, and that the potential difference between the inside and outside of the cell is caused by a double layer of charge on the cell membrane.

Diffusion is used extensively in physiology courses. The diffusion equations are quoted as "Fick's Laws of Diffusion" with no discussion of their origin. We can discuss the continuity equation (at least in one dimension)

$$\partial n / \partial t = - \partial J / \partial x$$

(where n is the concentration of particles and J their flux). Then we should discuss the linear approximation which is inherent in the equation

$$J_x = - D \partial n / \partial x,$$

and how these two equations can be combined to give

$$\partial n / \partial t = D \partial^2 n / \partial x^2.$$

You may raise your eyebrows at the use of partial derivatives in the general physics course, but our students will see these equations in this form later, with no discussion of their physical meaning.

Osmotic pressure and flow are two very important topics. Their treatment, along with clinical examples, has been discussed in this Journal.⁴⁸ Osmotic flow is sometimes thought of, erroneously, as a form of diffusion. Most clinical measurements of serum osmolality are made by measuring freezing point depression. A simple derivation of this relationship can be made.⁴⁹

The body cools by convection, evaporation and radiation.⁴ Ruch and Patton⁵⁰ give quantitative data. Radiation is surprisingly important: the emissivity of human skin is close to one.⁵¹ A premature infant in an incubator can be dangerously cooled by radiation to a wall of the incubator which happens to be cold (perhaps because of radiation to a nearby window), even when the air temperature in the incubator is warm. In newer incubators, the temperature of the air is controlled by measuring the baby's skin temperature.

Thermography measures the temperature of skin by its infrared radiation. It is particularly useful for measuring some circulatory abnormalities. It received wide publicity

about ten years ago for the detection of breast cancer. Its usefulness for that may not be as great⁵² as was once thought; however, it appears to have some utility for screening.⁵³ (Incidentally, it has been suggested that the merit of a medical discovery is inversely proportional to the publicity it receives in the lay press.⁵⁴ We should be careful when we use examples learned from that source.)

Counter-current heat transfer reduces the heat loss from an extremity by maintaining the extremity at a lower temperature. To see how this works, refer to Fig. 1. In (a), blood at temperature T_1 flows to the extremity which is at an average temperature T_e . Heat is lost to the surroundings by the extremity at a rate proportional to $(T_e - T_1)$. The blood then returns to the body through a vein at constant temperature T_2 . In configuration (b), the returning vein is close to the artery, and heat flows from artery to vein, warming up the venous blood and cooling off the arterial blood. As a result, the blood which reaches the extremity has a temperature lower than T_1 , so that T_e' is less than T_e , and the heat loss is reduced. An analogous process is important for the transport of solutes in the kidneys.⁵⁵ Quantitative arguments based on this model are found in chemical engineering and occasionally in the physics literature.⁵⁶ The body regulates heat loss by switching between deep and superficial veins in the limbs.⁵⁷

Patients with chronic obstructive lung disease have progressively greater difficulty breathing. Eventually they need continuous oxygen therapy. The "Linde Walker"⁵⁸ is a portable oxygen supply derived from liquid oxygen which is evaporated at a constant rate. An interesting homework problem is to compare the amount of oxygen which can be carried for a given weight of equipment, when it is carried as a liquid and when it is carried as a high pressure gas.

V. Feedback, Oscillations and Signal Analysis.

Feedback, oscillations and signal analysis are topics which we do not usually cover. The mathematics which goes with them is regarded as being too complex. Yet the ideas are far-reaching, and the essential ideas can be discussed without using advanced mathematics. Both linear and non-linear analysis find application in biological systems. A number of books on systems analysis for biologists have appeared,^{59,60} and Benedek and Villars⁹ devote a chapter to this topic.

The first step is to show how to find the equilibrium operating point of a feedback system. If this is done graphically, the technique can be used for both linear and non-linear systems. The example which is familiar to most physicists and which strikes a responsive chord among the audiophiles in our classes, is the feed-back audio amplifier. There are two equations whose simultaneous solution determines the operating point, as shown in Fig. 2(a). The gain v_o/v_{in} is nearly $1/\beta$, and one can see from the graph that for large A the gain is nearly independent of A . Compare this to the biological example of Fig. 2(b), which shows the interrelationship of the rate of alveolar ventilation, \dot{V} and the pressure of carbon dioxide in the blood, P_{CO_2} . For a given metabolic rate, an increase in \dot{V} will cause P_{CO_2} to fall, as indicated schematically in Fig. 2(b), curve 1. Sensors detect the level of P_{CO_2} , and as it rises the ventilation rate \dot{V} is increased (curve 2). The

equilibrium point, X , corresponds to P_{CO_2} value x . If the body exercises and needs more oxygen and gives off more CO_2 , a different curve, $1'$, relates P_{CO_2} and \dot{V} . A new equilibrium point, Y , corresponds to value y for P_{CO_2} . Without the sensors to change ventilation rate, \dot{V} would have stayed constant and P_{CO_2} would have risen to a much larger value, z . The feedback minimizes the change of P_{CO_2} , just as the feedback in the audio amplifier minimized the change of v_1 . Several other feedback systems are analyzed by Riggs⁵⁹ and by Benedek and Villars.⁹ The endocrine system is a whole series of feedback loops, in which the concentrations of various hormones are the variables.

When a feedback loop is broken in certain places, the variable just before the break may assume an extreme value. This is easily demonstrated by breaking the loop in an x - y plotter and watching the pen go off scale. This effect is also seen in the body's feedback loops. The thyroid gland normally makes thyroid hormone in response to thyroid stimulating hormone (TSH) from the pituitary. The thyroid hormone in turn inhibits (via the hypothalamus) the pituitary's production of TSH. Certain areas of the country used to lack dietary iodine. Since thyroid hormone contains iodine, the gland could not produce it. In response to the continual high levels of

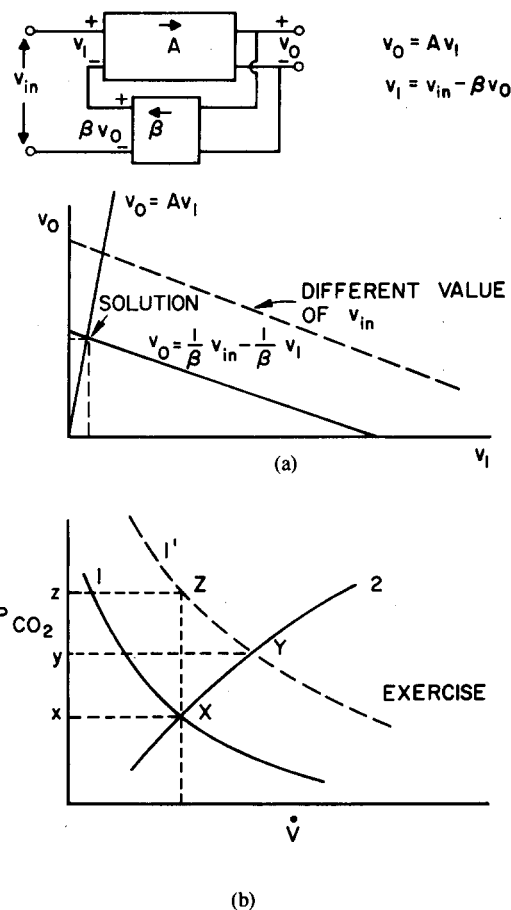


Fig. 2(a). Amplifier with feedback and the graphical method of determining the closed loop gain. The curve $v_o = A v_1$ describes the amplifier without feedback; the curve $v_o = v_{in}/\beta - v_1/\beta$ describes the feedback circuit. The intersection of these curves gives the output voltage for that value of v_{in} . (b) Hypothetical curves of carbon dioxide concentration in the blood (P_{CO_2}) vs rate of pulmonary air exchange, \dot{V} . The curves are explained in the text.

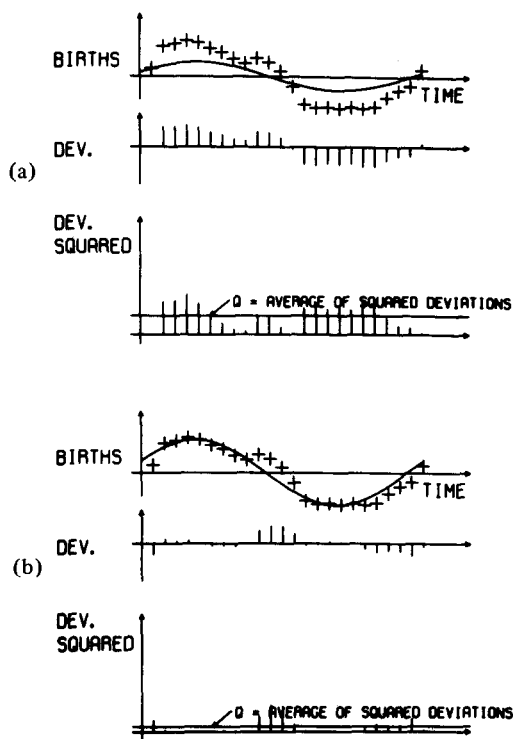


Fig. 3. Two stills from the film "Rhythmometry in Biology and Medicine," (Ref. 21), illustrating how the principle of least squares can be explained without using mathematics. (a) For a particular amplitude of the sine wave used to fit the data, the deviations of each data point their squares and the average of the squared deviation are shown. (b) The amplitude of the sine curve has been increased. This is the value for which Q , the mean square error, has the smallest value.

TSH, the gland grew larger and larger—an iodine deficiency goiter.⁶¹ Another example is found in post-menopausal women. Their levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are high because their ovaries no longer produce estrogen, which inhibits the production of these hormones by the pituitary.^{62,63}

When a feedback system is not in equilibrium, the equations relating the variables have additional terms, involving either time derivatives or the values of the variables at earlier times.^{9,59} This can lead to oscillations, which we can discuss in terms of the mass on a spring or the series RLC circuit. One biological example is Cheyne–Stokes respirations, which involve oscillations of the CO_2 -regulating mechanism discussed above. The patient goes from almost not breathing to hyperventilating and back again in the course of several minutes.^{64,65} Another example is the oscillations which occur in the concentrations of some chemicals involved in coupled reactions in the metabolism of yeast cells. To a step change in oxygen concentration there is both a transient and a steady state response.^{66,67}

It is the exception to find linear relationships between variables. A very nice non-linear model of the human menstrual cycle has been constructed by a group at the Columbia College of Physicians and Surgeons.⁶⁸ Based upon the observed interrelationships among hormone levels, it reproduces the very rapid changes in level of FSH and LH which accompany ovulation.

One form of non-linear oscillator is the relaxation oscillator, such as a multivibrator or the escapement and bal-

ance wheel in a watch. An article about relaxation oscillators appeared in this Journal in 1940.⁶⁹ The central point of it was that the relaxation oscillator can take some of the energy which is flowing from one part of a system to another, and use it to replace energy which has been dissipated by a periodic oscillator. The harmonic oscillator alone cannot perform this vital task. An example of a relaxation oscillator in the body is the S–A node which triggers the beating of the heart.⁷⁰ It is completely analogous to an astable multivibrator. Nerve conduction is analogous to a monostable multivibrator.

When we talk about vibrating strings and organ pipes, we can introduce Fourier series. It is possible to make a graphical argument⁷¹ to show that the Fourier series is a least-squares approximation to a periodic function. The same graphical argument can be used to explain least-squares fits to experimental data,⁷² as shown in Fig. 3. When we discuss fitting periodic functions to experimental data, we should mention aliasing. This is a natural topic to consider when we talk about beats. If there exists in the process being measured a frequency which is so high that we do not sample at least twice during its period, there will appear in our recording a spurious frequency which is the difference beat between our sampling frequency and the frequency which is present in the data. It has been necessary on at least one occasion to remind biological research workers of the importance of this effect.⁷³

We can talk about the average of a periodic signal. Without indulging in a lot of detailed mathematics, we can extend this to the average of the signal multiplied by itself, or multiplied by a time-shifted replica of itself, which is the autocorrelation function. The power spectrum tells us what frequencies are present in the signal. It can be calculated either from the Fourier expansion coefficients of the signal (if they exist) or from a Fourier analysis of the autocorrelation function. The power spectrum of an electroencephalogram can be used, for example, to monitor the stage of a patient's anesthesia.⁷⁴ Such monitoring is not at all easy when the patient is very sick and when he has been given muscle relaxant. A non-mathematically oriented neurologist with whom I have discussed this believes that in 20 years the use of signal analysis techniques^{75–77} to analyze electroencephalograms will be universal.

Having gone this far, it would be easy for us to discuss spatial filtering when we talk about optics. It is being used, for example, for pattern recognition and for image enhancement of x-rays.⁷⁸

Another example of Fourier analysis is the decomposition of arterial pressure into frequency components to study blood flow.⁷⁹ The vascular system can be characterized by a complex, frequency-dependent impedance.

Arbitrary travelling waves, $f(x-vt)$, are used to discuss sound and light, and also nerve conduction.⁸⁰

Physicians measure hearing loss in decibels from a standard level which depends on frequency and which represents the threshold of hearing for an average young subject. There is a lot of interesting physics connected with the physiology of hearing. It has been summarized by Argos⁴; e.g., the eardrum and the small bones (ossicles) of the middle ear serve as an impedance matching device between the low impedance air and the higher impedance fluid of the inner ear.

Ultrasound is used extensively for diagnosis and has

seen limited therapeutic use. For diagnosis, it is reflected from the surface of various structures within the body.⁸¹ Therapeutic efforts have centered on focusing the ultrasound to produce localized regions of tissue destruction (deep within the brain, for example) with minimal damage to intervening tissues.^{4,82}

When ultrasound is reflected from an underlying structure which moves, the frequency of the reflected wave is shifted by the Doppler effect.⁸³ This has been used for such diverse measurements as blood flow (reflection from red cells), blood pressure⁸⁴ (by detecting arterial motion downstream from the blood pressure cuff), fetal heartbeat monitoring, and detecting movement of the fetal chest as the fetus breathes in utero.⁸⁵

VI. Electricity and Magnetism.

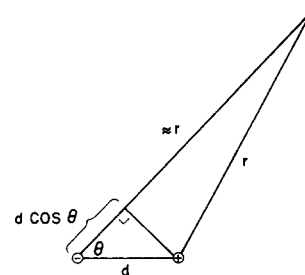
One needs to know the field and potential of a sheet of charge in order to discuss potential changes across a cell membrane. The fact that the intracellular and extracellular fluid are electrically neutral, except for a double layer at the cell membrane, comes as a surprise to many students. The most important application of electrostatics is the dipole model of the electrocardiogram. The model is useful in clinical interpretation of EKG data. We need to work to present this material in depth, but at an elementary level. A book which discusses voltage and then says "the electrocardiogram measures voltages on the surface of the body," perhaps with an unreasonable facsimile of an EKG tracing, is absolutely worthless. A student will grant that this is a true statement, but will wonder how physics could possibly be useful in understanding it. For the elementary student, my recent article⁷⁰ is almost as bad. I have recently spent several months working with two cardiologists trying to discover how best to teach this material. They have forced me to simplify the treatment so that it can be taught in one lecture in a noncalculus course; yet it is still correct within the framework of the model. Two major simplifications arose from his work. First, it is possible to derive the potential of the dipole without using calculus or a Taylor's series expansion, if we use the same geometrical trick that we do when discussing two-slit interference. This is shown in Fig. 4. Secondly, the physicians had a great deal of difficulty understanding the fictitious end cap in Fig. 4 of Ref. 70. However, this argument, though pleasing to a physicist because of its elegance, is not really necessary. Since one is dealing with charge layers on a cell membrane and the observer is a large distance away compared to the cell size, one can simply make a vector sum of the dipole moments due to each pair of charges in Fig. 4(a) of Ref. 70, to arrive at the same result.

Capacitance is necessary to understand leakage current in equipment. If the level of the course does not permit a treatment in depth, one can argue that charges moving in one conductor (for example, the primary of a transformer or the winding of the motor of an electric drill) will induce motion of charges in other nearby conductors (such as the core of the transformer or the case of the electric drill). Capacitance is also necessary to understand the integrating circuits which are used in some medical equipment.

The dielectric constant of a cell membrane is about

Fig. 4. Construction for a simple derivation of the potential of a dipole. The potential is given by

$$V = q/r - q/(r + d \cos \theta) \\ \approx qd \cos \theta / r^2.$$



eight. Thus, an understanding of polarization and dielectrics is necessary to relate the charge density on the membrane to the potential across it.

Piezoelectricity can be mentioned with transducers as an example. There is some evidence that electric currents stimulate bone growth.^{86,87} The drift of charged particles in an electric field is an example of terminal velocity. It is useful not only for the cell separations mentioned above, but for the electrophoretic separation of amino acids.⁸⁸

The Hall-effect blood-flow meter measures blood velocity by measuring the Lorentz force on a moving charged particle.⁸⁹ A laboratory experiment demonstrating the Hall effect has been described.⁹⁰ Some preliminary experiments are being done to detect the magnetic fields generated by currents within the body.⁹¹

Radio waves have been used for a long time for local heating of tissues (diathermy). The harmful effects of microwave radiation have attracted a lot of student interest recently. A comprehensive review of the physiological effects of microwave radiation is available.⁹²

VII. Circuits.

The exponential decay of voltage along a cable having both series and leakage resistance is central to the study of nerve conduction. Physiologists call this decay electrotonus. The decay can be derived by regarding the cable (nerve) as a resistance ladder,⁸⁰ the solution of which provides an exercise in simple circuit theory.

Possible hazards^{93,94} when patients are connected simultaneously to several electrical devices stimulate student interest, particularly since this problem has received some publicity in the lay press. It should be pointed out that accidents of this type have not been as frequent^{95,96} as was originally feared.

We should discuss the linear current-voltage characteristics of an ideal battery in series with a resistor. It is not hard to make a qualitative argument that the current-voltage relationship between any two terminals of a linear network will be linear. The network can therefore be replaced by the Thevenin equivalent, an ideal battery in series with a resistor. Thevenin's theorem is useful for discussing implanted biogalvanic cells⁹⁷ (the resistance of which varies with the nutritional state of the subject), voltage clamp experiments in neurophysiology (in which current is provided as necessary to keep the transmembrane potential at a constant value),⁹⁸ and sodium transport through a membrane.⁹⁹ The use of Thevenin's theorem also simplifies the discussion of electrical circuit hazards, and it makes it possible to discuss the input impedance and output impedance of amplifiers.

Joule heating is an important cause of tissue damage in low frequency electrical burns.¹⁰⁰ Because the current flows throughout a volume conductor, the destruction in burns due to kilovolt sources is very widespread and much deeper than from a thermal burn; in fact, the production of steam in deep tissues can mimic gas gangrene on an x-ray.

Students will almost certainly encounter various instruments containing operational amplifiers (although they will usually have no idea what is inside). They will be used not only for amplification, but for integration and differentiation. We can discuss how a feedback loop determines both the gain and frequency response of an amplifier, and how a balanced input reduces the sensitivity to common mode noise. Both digital and servomechanism techniques are used in a wide variety of instruments—not always with ideal results.¹⁰¹ In many cases, our general physics course will provide most of a physician's armament for dealing with instrument salesmen.

VIII. Optics.

Many physics texts discuss refractive errors and combining thin lenses. The ophthalmoscope provides an interesting example of combining lenses. It allows the physician to inspect the patient's retina by illuminating it using a half-silvered mirror. If the patient's eye is focused on infinity, then an examiner focusing his own eye on infinity while looking at the light emerging from the patient's eye will see an image of the patient's retina. If the patient is nearsighted, however, the rays leaving his eye will be converging, and the examiner will have to place a diverging lens in the path in order to focus on the patient's retina.

Although we often discuss the magnification of a microscope and write it as the product of the magnifications of the objective and ocular, we usually do not discuss numerical aperture (NA). Yet the NA is engraved on most microscope lenses these days. Sears¹⁰² derives the relationship of diffraction-limited resolution to numerical aperture and summarizes the rules for using a microscope with maximum efficiency. His discussion also shows why oil immersion lenses are used to obtain the highest resolution. Phase contrast microscopy is used where staining is not practical to create contrast; most of its users have only a vague idea of how it works. Argos gives a list of references.⁴

It is interesting to point out that the resolution of the eye is not limited solely by diffraction effects, but that it is determined by several factors which have roughly equal magnitudes:¹⁰³ the diffraction limit ($5\text{--}8\ \mu$), spacing of the receptors in the eye ($3\ \mu$), noise in the aim of the eyeball (a few microns), and chromatic and spherical aberration ($10\text{--}20\ \mu$).

[*Note added 8 August 1974.* I have recently learned that the definitive calculation of corneal opacity due to the scattering of light by randomly spaced collagen fibers was done by G. Benedek, *Appl. Op.* **10**, 459 (1971). He also calculated the opacity of a cataractous lens.]

The rotation of polarized light by an optically active substance is an important tool in biological investigation. Optical rotatory power is used to measure the conformation (three-dimensional shape) of proteins.^{4, 104–106}

This structure changes, sometimes reversibly, depending on the temperature and pH of the solution the protein is in. In clinical medicine birefringence is measured to tell whether crystals in the synovial fluid from arthritic joints are composed of monosodium urate (gout) or calcium pyrophosphate (pseudogout),¹⁰⁷ and to detect silicate particles in biopsies from the lungs and lymph nodes of patients suspected of having silicosis.¹⁰⁸ The identification of different crystals in patients with gout is accomplished by placing polarizing filters in the microscope above and below the specimen. Because the unknown crystals are very thin, the rotation of the plane of polarization is too small to be measured directly. To increase the sensitivity, a retarder plate (called a "first order red filter" in the medical literature) is placed in the path with the specimen with its optic axis at 45° to the axes of the crossed polarizers. The half-wave plate rotates the plane of polarization so that everything but green light gets through the microscope. The entire field appears reddish purple. The unknown crystals in the specimen are now aligned (by rotating the microscope slide) so that their long axis (which is their optic axis) coincides with the optic axis of the half-wave plate. If the unknown crystal is monosodium urate, which has a negative birefringence (that is, the index of refraction for a wave polarized along the crystal axis is less than the index of refraction for a wave polarized at right angles to that direction), the crystal appears yellow, which means that blue is the color that is not getting through the system. This is the same color one would see if the half-wave plate were thinner. If the unknown is calcium pyrophosphate, which has positive birefringence, the color of the crystal is blue, meaning that red is not getting through. This is the same color that would appear if the half-wave plate were thicker. We seldom discuss birefringence at an elementary level, except possibly to show the formation of double images by a piece of calcite. A discussion in which the polarization is either parallel or perpendicular to the optic axis, as in the case above, is considerably simpler. Cloud¹⁰⁹ has pointed out that we can make our treatment of birefringence more understandable and has proposed some interesting laboratory experiments. Cellophane tape can also be used as an inexpensive half-wave plate.^{110, 111}

The physiology of vision provides many examples of physics.¹¹² Photographs of a girl taken with different numbers of photons entering the camera are becoming some of the classic pictures in physics. Rose, who took them, has written a fascinating review of quantum effects in human vision.¹¹³ He argues that n , the number of photons striking the receptors in the eye at high brightness levels, is just large enough so that fractional statistical fluctuations ($n^{-1/2}$) are small enough to allow an excellent picture. He also calculates that the effective quantum efficiency¹¹⁴ of the eye for a bright scene is about 1% (6% for light at the retina) and that in very dim light the efficiency increases only by a factor of 3 or 4. On the other hand, the sensitivity of the eye changes by a factor of 1000 with this change in illumination. Therefore, the sensitivity change of the eye must involve something other than the quantum efficiency of the photoreceptors. (At one time it had been proposed that the decrease in sensitivity at high light levels was due to bleaching of the visual pigment.) This conclusion is now well established. However, more recent studies of the ability of the eye to

detect patches of differing brightness indicate that simple statistics based on quantum efficiency are not adequate to explain all of the effects observed.¹¹⁵ The quantum effect in the photoreceptors involves a change in the isomeric state of the visual pigment on absorption of a photon. The details of the transduction process are the subject of extensive current research.^{116,117} Incidentally, the response of the visual receptors is not logarithmic,¹¹⁷ although it is sometimes said to be.

Fiber optic light pipes are used extensively to examine body cavities with openings to the outside. They are even threaded into veins to measure the oxygen concentration in the blood by colorimetric absorption.

A discussion of biomedical applications of holography appeared in *Physics Today*.¹¹⁸ Quasi-elastic scattering of laser light is used as a research tool to study molecular structure.¹¹⁹

IX. Atomic Physics.

There are many examples of energy levels in atoms and molecules and of the emission and absorption of light. Absorption spectroscopy and flame spectroscopy are used to determine concentrations of many chemicals in solution. As another example of absorption, consider the treatment of neonatal jaundice.¹²⁰ Bilirubin is a waste product formed when red cells die. In newborns whose livers do not yet have the ability to convert bilirubin into a water soluble substance so it can be excreted, the level of bilirubin in the blood can rise to toxic values. If these patients are irradiated with blue light, the photons are sufficiently energetic to dissociate bilirubin molecules in capillaries just under the skin. The dissociation products are water soluble. As still another example, it is sometimes desirable to make scars on the retina of the eye (to reattach a detached retina, for example). To do this, one can use a xenon arc (white light) or an argon laser (green light). However, light from a ruby laser (red) will not be absorbed by the red retina.

Fluorescence is used in several ways.¹²¹ Antibodies are Y-shaped molecules, two arms of which are identical and have the ability to bind to selected antigens (proteins) by van der Waals forces.¹²² Because these forces are very short range, a strong bond requires a very close fit between all the atoms of the arm of the antibody and the antigen. Thus the bonding is very specific. An inactive part of the antibody molecule can be tagged with fluorescein isothiocyanate. The antigens to which these tagged antibodies have attached themselves can then be identified by their green fluorescence. Even without this special tag, antibodies fluoresce in the near ultraviolet when excited by photons in the far ultraviolet. This fluorescence is quenched if the antibody is bound to an antigen, so the quenching can be used to detect binding. Still another application uses exciting light which is polarized. The polarization of the fluorescence radiation can be measured to learn how much the antibody molecule had rotated before it decayed (in the absence of its antigen). The amount of rotation is related to the size of the molecule.^{121,123}

A simple chest x-ray shows the dependence of x-ray absorption on atomic number (since the absorption is greater in bone than in tissue) and the exponential decay of the photons going through matter (because one can see

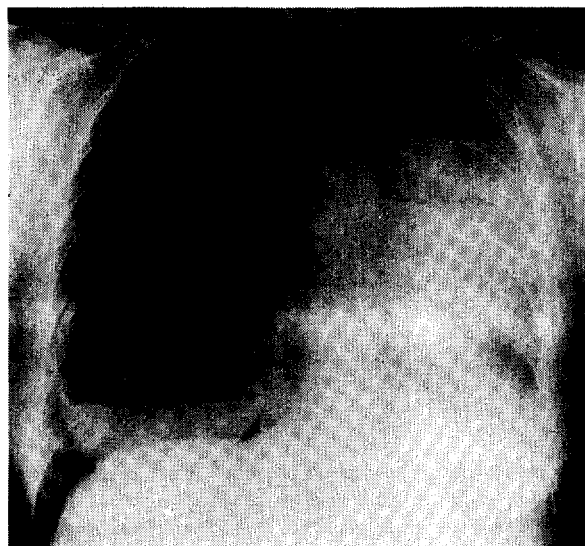


Fig. 5. Chest x ray showing cavities in the lung with air-fluid levels. It was not known at the time of this x ray whether the patient had a pulmonary infection or multiple metastases from carcinoma of the cervix. (X-ray courtesy of Douglas Ketcham, M.D.)

shadow upon shadow). Figure 5 shows an x-ray of a lung with several abscesses in it. The patient's right lung (except for the large cavity) is more or less normal. It is black because it is filled with air and has little attenuation. The left lung, on the other hand, is quite opaque, almost obliterating the shadow of the heart, because it is filled with fluid of higher density. An air-fluid interface can be seen in the right lung and another can be seen near the apex. You can find many more examples in textbooks;¹²⁴ however, since a lot of detail is lost in copying an x ray, you might ask your personal physician to obtain an unneeded plate for you.

The dependence of absorption on atomic number is greater in the low energy region, where the photoelectric effect is important, than it is in a higher energy region. This means that the contrast between bone and other tissue is enhanced by using low energy photons. A comparison of plates made with low energy and high energy x-rays of the same subject is quite striking.¹²⁵

X-ray emulsions are relatively thin (a typical surface density of silver halide being 2-7 mg/cm²), and their sensitivity to x-rays is low. Radiation exposures to patients are reduced by using fluorescent screens, such as Ca₂WO₄ (with a surface density of 50-100 mg/cm²) next to the film. Each x-ray photon in the beam is converted on the average into 100 or more visible photons.¹²⁶ The result is an intensification of the image by a factor of 50 or more. More recently, screens have been developed using a rare earth phosphor which provide additional sensitivity increase by a factor of 10 or so.¹²⁷

X-ray diffraction is used to study crystal structure.^{4,128} The famous examples are the structure of myoglobin, hemoglobin, and DNA.¹²⁹ Even though Fourier series have been mentioned, it is unrealistic in an elementary course to try to relate the diffraction pattern to the Fourier transform of the electron density. However, various diffraction patterns can be demonstrated qualitatively using a laser and the optical crystals described by Bergsten.¹³⁰

Both the regular and scanning electron microscope are

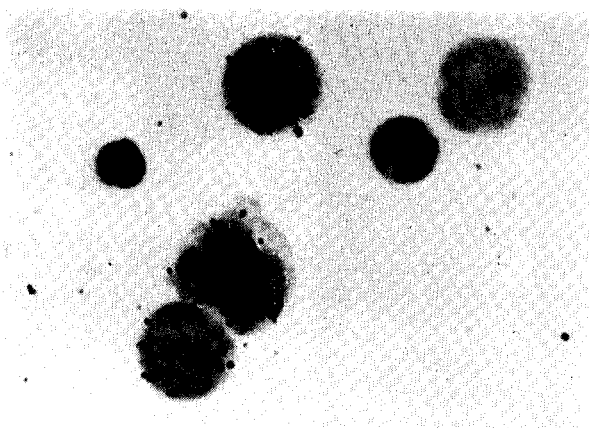


Fig. 6. Radioautograph of human lymphoblasts from a leukemic patient. The cells were incubated with tritiated thymidine for one hour. Cells in the process of division incorporated the thymidine. The cells were then smeared on a microscope slide. A silver halide solution was layered on top of the slide. After 10 days the halide was developed and the cells were stained with Wright's stain. (Slide courtesy of Mark Nesbit, M.D.)

used extensively. In addition to the references described by Argos,⁴ see *The Scanning Electron Microscope*,¹³¹ which describes in detail the technique for scanning electron microscopy and contains some beautiful photographs of many different applications.

IX. Nuclear Physics.

This paper intentionally says very little about nuclear physics and x rays, since these are the two most obvious examples of medical applications. Indeed, for many people medical physics is synonymous with radiology and nuclear medicine. Applications have been covered in recent articles in *Physics Today*.¹³²⁻¹³⁴

We should certainly discuss the difference between exponential absorption of photons in matter and the finite range of charged particles. This discussion should include the basic principles of dosimetry. There have been experiments using the Bragg peak of protons for the destruction of deep-seated lesions.^{135,136} Because negative pions which come to rest in matter interact strongly with nuclei to produce heavily ionizing stars,¹³⁷ similar work is going on with meson beams.

The mass spectrometer, in conjunction with the gas chromatograph, provides a rapid way to identify drugs in the blood. Many drugs have similar properties when measured by the chromatograph, but they can be distinguished by their molecular weights.¹³⁸ Nuclear magnetic resonance¹³⁹ is used to study molecular structure and rates of reaction.

Neutron activation analysis can identify chemicals¹⁴⁰ and locate tumor sites which selectively take up certain elements. Neutron scattering is being used to study molecular structure in a manner analogous to x-ray diffraction. Its advantage is the higher sensitivity to hydrogen than one has with x-rays.¹⁴¹

Radioautographs¹⁴² involve the uptake of radioactive substances by cells. The cells are then placed on a slide and coated with liquid photographic emulsion. The cells which have taken up the radioactive substance leave a dis-

tinct signature (Fig. 6). An excellent textbook on nuclear medicine is by Wagner.¹⁴³

CONCLUSION

This paper has attempted to show that many topics in physics are useful to medical students, physicians and biomedical research workers. Some major topics, such as the Boltzmann factor, osmotic pressure, the physics of nerve conduction, and signal analysis have been presented, along with examples for other areas in physics.

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¹B. Zumoff, H. Hart and L. Hellman, *Ann. Intern. Med.* **64**, 595 (1966).

²R. K. Hobbie, *Am. J. Phys.* **41**, 389 (1973).

³M. H. Shapiro, *Am. J. Phys.* **41**, 919 (1973).

⁴P. Argos, *Am. J. Phys.* **41**, 1224 (1973).

⁵D. C. Giancoli, *Am. J. Phys.* **39**, 739 (1971).

⁶L. Finegold, *Am. J. Phys.* **39**, 742 (1971).

⁷J. Glas and G. Graf, *Am. J. Phys.* **40**, 471 (1972).

⁸L. D. Roper, *Am. J. Phys.* **42**, 27 (1974).

⁹G. B. Benedek and F.M.H. Villars, *Physics with Illustrative Examples from Medicine and Biology, Volume 1: Mechanics* (Addison-Wesley, Reading, MA, 1973), Chap. 6.

¹⁰A. H. Cromer, *Physics for the Life Sciences* (McGraw-Hill, New York, 1974).

¹¹D. E. Tilley and W. Thumm, *Physics for College Students* (Cumplings, Menlo Park, CA, 1974).

¹²D. M. Burns and S. G. G. MacDonald, *Physics for Biology and Pre-Medical Students* (Addison-Wesley, Reading, MA, 1970).

¹³I. W. Richardson and E. B. Neergaard, *Physics for Biology and Medicine* (Wiley-Interscience, New York, 1972).

¹⁴D. S. Riggs, *The Mathematical Approach to Physiological Problems* (M.I.T., Cambridge, MA, 1970).

¹⁵See Ref. 9, Chap. 5.

¹⁶E. D. Yorke, *Am. J. Phys.* **41**, 1286 (1973).

¹⁷D. Mainland, *Clin. Chem.* **17**, 267 (1971).

¹⁸M. S. Laffleur, P. F. Hinrichsen, P. C. Landry and R. B. Moore, *Phys. Teach.* **10**, 314 (1972).

¹⁹B. Katz, *Nerve, Muscle and Synapse* (McGraw-Hill, New York, 1966), Chap. 9.

²⁰See Ref. 9, Chap. 3.

²¹See Ref. 10, Chaps. 2, 3.

²²See Ref. 9, Chap. 2.

²³K. Shortman, *Ann. Rev. Biophys. Bioeng.* **1**, 93 (1972).

²⁴T. C. Ruch and H. D. Patton, *Physiology and Biophysics* (Saunders, Philadelphia, 1965), 19th ed., p.1033.

²⁵A. V. Hill, *Sci.* **131**, 897 (1960).

²⁶See Ref. 9, Chap. 4.

²⁷R. G. Snyder, "Impact," in *Bioastronautics Data Book*, edited by J. F. Parker, Jr. and V. R. West (NASA, Washington, DC, 1973), 2nd ed., Chap. 6.

- ²⁸N. Perrone, "Biomechanical Problems Related to Vehicle Impact" in *Biomechanics, Its Foundations and Objectives*, edited by Y. C. Fung, N. Perrone and M. Anliker (Prentice Hall, Englewood Cliffs, NJ, 1972) p. 567.
- ²⁹W. Goldsmith, "Biomechanics of Head Injury" in Ref. 28, p. 585.
- ³⁰G. C. Lee and F. G. Hoppin, Jr., "Lung Elasticity" in Ref. 28, p. 317.
- ³¹V. Chernick, *New Eng. J. Med.* **289**, 302 (1973).
- ³²M. E. Avery, N-S. Wang and N. W. Taesch, Jr., *Sci. Am.* **228**, No. 4, 75 (April, 1973).
- ³³See Ref. 10, p. 184.
- ³⁴M. D. Levitt and W. C. Duane, *New Eng. J. Med.* **286**, 973 (1972).
- ³⁵J. F. Herrick, *Am. J. Phys.* **10**, 33 (1942).
- ³⁶See Ref. 10, Chap. 7.
- ³⁷*Pulsatile Blood Flow*, edited by E. O. Attinger (McGraw-Hill, New York, 1964).
- ³⁸A. L. King, *Am. J. Phys.* **15**, 240 (1947).
- ³⁹W. Klip, *Theoretical Foundations of Medical Physics* (University of Alabama, University, AL, 1969).
- ⁴⁰M. M. Wintrobe, et al., *Harrisons' Principles of Internal Medicine* (McGraw-Hill, New York, 1970), 6th ed., p. 1161.
- ⁴¹See Ref. 24, p. 534.
- ⁴²R. K. Hobbie, *New Eng. J. Med.* **290**, 864 (1974).
- ⁴³F. Reif, *Statistical Physics* (McGraw-Hill, New York, 1965), Berkeley Physics Course, Vol. 5.
- ⁴⁴C. Kittel, *Thermal Physics* (Wiley, New York, 1969).
- ⁴⁵W. G. Zinman, *Am. J. Phys.* **41**, 1284 (1973).
- ⁴⁶S. P. Heims, *Am. J. Phys.* **38**, 1128 (1970).
- ⁴⁷C. Kittel, *Am. J. Phys.* **40**, 60 (1972).
- ⁴⁸R. K. Hobbie, *Am. J. Phys.* **42**, 188 (1974).
- ⁴⁹E. Fermi, *Thermodynamics* (Dover, New York, 1956), pp. 130 ff.
- ⁵⁰See Ref. 24, Chap. 54.
- ⁵¹J. Steketee, *Phys. Med. Biol.* **18**, 686 (1973).
- ⁵²I. M. Freundlich, *New Eng. J. Med.* **287**, 880 (1972).
- ⁵³H. J. Isard et al., *Am. J. Roentg.* **115**, 811 (1972); A. M. Lillienfeld et al., *Cancer* **24**, 1206 (1969).
- ⁵⁴K. Reemstma and J. V. Maloney, Jr., *New Eng. J. Med.* **290**, 439 (1974).
- ⁵⁵R. F. Pitts, *Physiology of the Kidney and Body Fluids* (Yearbook Medical, Chicago, 1968), 2nd ed., p. 121.
- ⁵⁶J. L. Stephenson and R. Mejia, *Bull. Amer. Phys. Soc.*, Ser. 11, **19**, 604 (1974).
- ⁵⁷See Ref. 24, p. 1057.
- ⁵⁸Linde Division, Union Carbide Corp., 270 Park Ave., New York, NY 10017.
- ⁵⁹D. S. Riggs, *Control Theory and Physiological Feedback Mechanisms* (Williams and Wilkins, Baltimore, MD, 1970).
- ⁶⁰T. Pavlidis, *Biological Oscillators: Their Mathematical Analysis* (Academic, New York, 1973).
- ⁶¹J. M. Hershman and J. A. Pittman, *New Eng. J. Med.* **285**, 997 (1971).
- ⁶²*Textbook of Endocrinology*, edited by R. H. Williams (Saunders, Philadelphia, PA, 1968), 4th ed., p. 513.
- ⁶³D. S. Schalch et al., *J. Clin. Invest.* **47**, 665 (1968).
- ⁶⁴See Ref. 59, p. 417.
- ⁶⁵N. S. Cherniack and G. S. Longobardo, *New Eng. J. Med.* **288**, 952 (1973).
- ⁶⁶A. T. Winfree, "Time and Timelessness in Biological Clocks" in *Temporal Aspects of Therapeutics*, edited by J. Urquhart and F. E. Yates (Plenum, New York, 1973).
- ⁶⁷J. M. Smith, *Mathematical Ideas in Biology* (Cambridge University, U.K., 1968) p. 105.
- ⁶⁸R. J. Bogumil et al., *J. Clin. Endocrin. Metab.* **35**, 126 (1972); **35**, 144 (1972).
- ⁶⁹G. F. Herrenden-Harker, *Am. J. Phys.* **8**, 1 (1940).
- ⁷⁰R. K. Hobbie, *Am. J. Phys.* **41**, 824 (1973).
- ⁷¹R. K. Hobbie, *Fourier Series*, Super-8 mm film loop (Wiley, New York, 1970).
- ⁷²R. K. Hobbie and F. Halberg, "Rhythmetry Made Easy" in *Biorhythms and Human Reproduction*, edited by M. Ferin et al. (Wiley, New York, 1974), p. 37.
- ⁷³W. Z. Maughan et al., *Blood* **41**, 85 (1973).
- ⁷⁴J. Stockard et al., *Proc. San Diego Biomed. Symp.* **11**, 277 (1972).
- ⁷⁵N. Wiener, *Cybernetics* (Wiley, New York, 1961), p. 181.
- ⁷⁶*Processing Neuroelectric Data*, edited by W. A. Rosenblith (M.I.T., Cambridge, MA, 1959).
- ⁷⁷J. Vidal, *Ann. Revs. Biophys. Bioeng.* **2**, 157 (1973).
- ⁷⁸D. G. Cain and P. R. Metz, *Proc. San Diego Biomed. Symp.* **10**, 245 (1971).
- ⁷⁹W. R. Milnor, *New Eng. J. Med.* **287**, 27 (1972).
- ⁸⁰R. K. Hobbie, *Am. J. Phys.* **41**, 1176 (1973).
- ⁸¹P. P. Lele, *N. Eng. J. Med.* **286**, 1317 (1972); P. N. T. Wells, *Physical Principles of Ultrasonic Diagnosis* (Academic, New York, 1969).
- ⁸²P. P. Lele, "Ultrasound in Biology and Medicine" in *Biomedical Physics and Biomaterials Science*, edited by H. E. Stanley (M.I.T., Cambridge, MA, 1972), p. 257.
- ⁸³See Ref. 11, p. 288.
- ⁸⁴I. F. S. Black et al., *J. Pediatr.* **81**, 932 (1972).
- ⁸⁵G. S. Dawes, *New Eng. J. Med.* **290**, 557 (1974).
- ⁸⁶R. O. Becker, *Nature* **235**, 109 (1972).
- ⁸⁷R. O. Becker, *Technol. Rev.* **75**, No. 2, 32 (Dec. 1972).
- ⁸⁸A. L. Lehninger, *Biochemistry* (Worth, New York, 1970), p. 131.
- ⁸⁹E. R. Raman et al., *Phys. Med. Biol.* **18**, 704 (1973).
- ⁹⁰J. Wright and S. Van der Beken, *Am. J. Phys.* **40**, 245 (1972).
- ⁹¹D. B. Geselowitz, *Ann. Rev. Biophys. Bioeng.* **2**, 37 (1973).
- ⁹²B. D. McLees and E. D. Finch, "Analysis of Reported Physiologic Effects of Microwave Radiation," in *Advances in Biological and Medical Physics*, edited by J. H. Lawrence and J. W. Goffman (Academic, New York, 1973), Vol. 14, p. 163.
- ⁹³J. M. R. Brunner, *Anesthesiology* **28**, 396 (1967).
- ⁹⁴W. F. Craven, *Hewlett-Packard J.* **21**, No. 7, 11 (March 1970).
- ⁹⁵J. M. Bruner et al., *J. Assoc. Adv. Med. Instr.* **6**, 222 (1972).
- ⁹⁶H. Salomon, *N. Eng. J. Med.* **287**, 146 (1972).
- ⁹⁷J. K. Cywinski, A. W. Hahn and J. B. Cooper, *Proc. San Diego Biomed. Symp.* **11**, 113 (1972).
- ⁹⁸See Ref. 19, Chap. 5.
- ⁹⁹A. Essig, "Salt and Water Transport in Biological Systems" in *Biomedical Physics and Biomaterials Science*, edited by H. E. Stanley (M.I.T., Cambridge, MA, 1972), p. 25.
- ¹⁰⁰H. S. Sturim, *Med. Times* **96**, 1051 (1968).
- ¹⁰¹M. X. Fitzgerald, A. A. Smith and E. A. Gaensler, *N. Eng. J. Med.* **289**, 1283 (1973).
- ¹⁰²F. W. Sears, *Optics* (Addison-Wesley, Reading, MA, 1949), p. 260.
- ¹⁰³L. Stark and G. C. Theodoris, "Information Theory in Physiology" in *Engineering Principles in Physiology*, edited by J. H. V. Brown and D. S. Gann (Academic, New York, 1973), Vol. I, p. 13.
- ¹⁰⁴J. W. Teipel and D. E. Koshland, Jr., *Biochem.* **10**, 792 (1971).
- ¹⁰⁵D. Ridgeway, "Polarimetric Analysis of Protein Structure," in *Advances in Biological and Medical Physics*, edited by J. H. Lawrence and J. W. Goffman (Academic, New York, 1963), Vol. 9, p. 271.
- ¹⁰⁶A. R. Martin, "Spectroscopic Methods in Biology With Application to Neurophysiology" in *Advances in Biological and Medical Physics*, edited by J. H. Lawrence and J. W. Goffman (Academic, New York, 1973), Vol. 14, p. 225.
- ¹⁰⁷P. Phelps, A. D. Steele and D. J. McCarty, Jr., "Compensated Polarized Light Microscopy," *J. Am. Med. Assoc.* **203**, 508 (1968).
- ¹⁰⁸S. L. Robbins, *Pathology* (Saunders, Philadelphia, 1967), 3rd ed., p. 748.
- ¹⁰⁹S. D. Cloud, *Am. J. Phys.* **41**, 1184 (1973).
- ¹¹⁰D. S. Owen, Jr., *N. Eng. J. Med.* **285**, 1152 (1971).
- ¹¹¹F. S. Crawford, *Waves* (McGraw-Hill, New York, 1965), Berkeley Physics Course, Vol. 3, Chap. 8.
- ¹¹²*The Eye* edited by H. Davson (Academic, New York, 1962), Vol. 2.
- ¹¹³A. Rose, "Quantum Effects in Human Vision," in *Advances in Biological and Medical Physics*, edited by C. A. Tobias and J. H. Lawrence (Academic, New York, 1957), Vol. 5, p. 211.
- ¹¹⁴By effective quantum efficiency, he means 100 times the number of photoelectrons liberated per photon, in an ideal fluctuation-limited device with the same ability to detect contrast changes as exhibited by the eye.

- ¹¹⁵M. H. Pirenne, "Liminal Brightness Increments," in Ref. 112, p. 159.
- ¹¹⁶W. A. Hagins, *Ann. Rev. Biophys. Bioeng.* **1**, 131 (1972).
- ¹¹⁷R. W. Rodieck, *Ann. Rev. Physiol.* **33**, 257 (1973).
- ¹¹⁸E. J. Feleppa, *Phys. Today* **22**, No. 7, 25 (July, 1969).
- ¹¹⁹R. Pecora, "Quasi Elastic Light Scattering from Molecules," *Ann. Rev. Biophys. Bioengin.* **1**, 257 (1972).
- ¹²⁰C. H. Kempe, H. K. Silver and B. O'Brien, *Current Pediatric Diagnosis and Treatment* (Lange Medical, Los Altos, CA, 1972) p. 70.
- ¹²¹B. Davis *et al.*, *Microbiology* (Harper and Row, New York, 1969), p. 407.
- ¹²²J. D. Watson, *The Molecular Biology of the Gene* (Benjamin, Menlo Park, CA, 1970), 2nd ed., p. 114.
- ¹²³G. Weber, *Ann. Rev. Biophys. Bioengin.* **1**, 553 (1972).
- ¹²⁴L. F. Squire, *Fundamentals of Roentgenology* (Harvard University, Cambridge, MA, 1964).
- ¹²⁵M. M. Ter-Pogossian, *The Physical Aspects of Diagnostic Radiology* (Harper and Row, New York, 1967), p. 176.
- ¹²⁶See Ref. 125, p. 202.
- ¹²⁷R. A. Buchanan, S. I. Finkelstein and K. A. Wickersheim, *Radiology* **105**, 185 (1972).
- ¹²⁸D. Harker, "X-Ray Diffraction Applied to Crystalline Proteins," in *Advances in Biological and Medical Physics*, edited by J. H. Lawrence and C. A. Tobias (Academic, New York, 1956), Vol. 4, p. 1.
- ¹²⁹J. C. Kendrew, *The Thread of Life* (Harvard University, Cambridge, MA, 1966).
- ¹³⁰R. Bergsten, *Am. J. Phys.* **42**, 91 (1974).
- ¹³¹J. W. S. Hearle, J. T. Sparrow and P. M. Cross, *The Use of the Scanning Electron Microscope* (Pergamon, Elmsford, NY, 1972).
- ¹³²C. J. Karzmark and R. F. O'Foghluha, *Phys. Today* **26**, No. 11, 38 (Nov. 1973).
- ¹³³K. G. McNeill, *Phys. Today* **27**, No. 4, 75 (April, 1974).
- ¹³⁴G. L. Brownell and R. J. Shalek, *Phys. Today* **23**, No. 8, 32 (Aug. 1970).
- ¹³⁵R. N. Kjellberg *et al.*, *N. Eng. J. Med.* **278**, 689 (1968).
- ¹³⁶J. H. Lawrence *et al.*, *N. Eng. J. Med.* **285**, 1263 (1971).
- ¹³⁷T. W. Armstrong, R. G. Alsmiller, Jr. and K. C. Chandler, *Phys. Med. Biol.* **18**, 830 (1973).
- ¹³⁸R. F. Skinner *et al.*, *J. Forensic Sci.* **17**, 189 (1972).
- ¹³⁹B. D. Sykes and M. D. Scott, "Nuclear Magnetic Resonance Studies of the Dynamic Aspects of Molecular Structure and Interaction in Biological Systems," *Ann. Rev. Biophys. Bioeng.* **1**, 27 (1972).
- ¹⁴⁰G. R. D. Catto *et al.*, *Phys. Med Biol.* **18**, 508 (1973).
- ¹⁴¹B. P. Schoenborn and A. C. Nunes, *Ann. Rev. Biophys. Bioeng.* **1**, 529 (1972).
- ¹⁴²J. H. Taylor, "Autoradiography With Tritium—Labelled Substances," in *Advances in Biological and Medical Physics*, edited by C. A. Tobias and J. H. Lawrence (Academic, New York, 1960), Vol. 7, p. 107.
- ¹⁴³*Principles of Nuclear Medicine*, edited by H. N. Wagner (Saunders, Philadelphia, 1968).

EMERGENCY ASCENT

Suppose that while scuba-diving at some great depth, say 100 feet, you had to make an emergency ascent without additional air. One lungful has to be enough for you to reach the surface, or you'll die. How would you do it? (This is not really just an academic question, for submarine crews are trained to make such emergency escapes.) Would you continuously release air as you ascend, or keep it all in? Well, though it may seem unreasonable, you had better release air or you won't make it. In fact, novice scuba divers practicing in swimming pools are occasionally killed because they neglect to exhale when practicing emergency ascents. Why?

It is said that the urge to take another breath stems from the partial pressure of the CO_2 . Researchers conclude from this that the most dangerous and crucial point in your ascent will be at some intermediate point and not near the surface. Once you pass the crucial point, the urge to take another breath will relax considerably. Why is this? What is the crucial depth? How fast should you swim to the surface? Can you swim too fast? If you can, then what's a reasonable rate? [From *The Flying Circus of Physics* by Jearl Walker. Copyright © 1975 by John Wiley & Sons, Inc.]