A Survey Course in

BIOLOGICAL TRANSPORT PHENOMENA AND BIOMEDICAL ENGINEERING

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A one-semester (14 week) course dealing with biological transport phenomena and biomedical engineering has been developed at Clarkson by the author and taught to seniors and graduate students. Prerequisites for the course consist of previous acquaintance with fluid mechanics, heat transfer, and mass transfer. No background in life sciences is required or assumed.

As the course title suggests, one part of the material covered deals with momentum, heat and mass transport phenomena in living systems, without reference to engineering applications. Another major part of the course, as implied by the second half of the course title, deals with engineering as related to living systems (more specifically, medical engineering concerned with humans). Topics like blood rheology, heat transfer in the body, and mass transfer across cell membranes are typical of those in the biological transport category. Modeling of the body, artificial kidney devices, and artificial heart valves are subjects which fall into the biomedical engineering category.

Besides these two general areas, the course contains a small amount of anatomy and a considerable content of physiology, e.g., circulatory system, kidney, and lung physiology. As can be seen from the course outline, Table I, the course stresses biological transport phenomena in the first half and biomedical engineering in the second half, with physiology interspersed throughout. This sequencing is logical in the sense that a proper consideration of the engineering applications (artificial kidney, etc.) relies on a firm knowledge of the physiological and physical chemical workings of the human body.

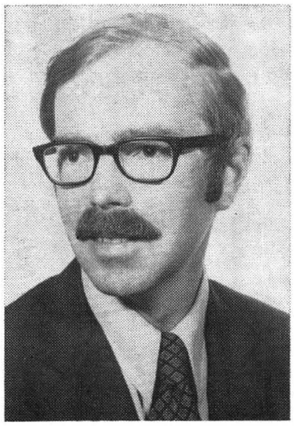
One can see from the course outline that a number of topics that could have been included do not appear, for example, nerve impulse transmission, physiological control systems, etc. For lack of time, it was decided to omit those topics, and areas such as bioelectronics (instrumentation), biomechanical devices (artificial limbs), and systems analysis. Many of these subjects seemed to be of questionable value and appropriateness for chemical engineers. It should be mentioned that an advanced follow-up course has also been offered. While this course mainly goes into greater depth on subjects found in the introductory course, some added items (e.g., on nerve impulse transmission) do appear. In general, both courses accent areas where chemical engineers have made their greatest contributions.

TABLE 1.—COURSE OUTLINE—BIOLOGICAL TRANSPORT PHENOMENA AND BIOMEDICAL ENGINEERING

		References*	Films
I.	Introduction and Brief Survey of History of Biomedicine (1)	1	F1
II.	The Human Body: Basic Description in Qualitative and Quantitative Terms (2)	1,11,12	
III.	The Human Thermal System (6)	1,3,10,12	F2
IV.	Modeling the Body as Compartments, Production Sources, and Fluid Streams (3)	4	
V.	The Properties and Rheology of Blood (3)	7,11	F3
VI.	Dynamics of the Circulatory System (5)	1,6,11	F4
VII.	Artificial Hearts and Heart Valves (2)	9	F5
VIII.	Cell Membrane Transport (5)	1,11	
IX.	Physiology of the Human Kidneys (2)	1	F6
X.	Artificial Kidney Devices (5)	5,9	F7
XI.	Physiology of the Human Respiratory System (2)	1	F8
XII.	Heart-Lung Machines [Oxygenators] (5)	8	
XIII.	Review and Summary (1)		

Note: numbers in parentheses denote the number of class periods devoted to each topic.
*Selected references only. A large number and variety of sources were actually employed.

There exists no suitable text for the course, and this has been a problem. Most biomedical engineering books in print consist of collections



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of research or review type articles of a wide variety. It is not uncommon that in any single book only one or two of the topics in the course outline appear. Even then, coverages of those topics are usually unsuitable. Moreover, as mentioned, the course includes a substantial amount of standard physiology, which is usually missing from the more engineering oriented texts (a book just published which appears to be quite suitable for parts of the course is that by Stanley Middleman[13]). As the basic text for the course it was therefore decided to use Guyton's *Textbook of Medical Physiology*,[1] a large standard work, as the primary source of material on heart, lung, and kidney physiology, and on several aspects of biological transport, e.g. the elements of blood rheology and membrane transport, and the basics of circulatory system dynamics. For the other topics (or to supplement those in Guyton's book), handouts consisting of a wide variety of materials are employed. This approach works well enough, but the students would prefer having one large or two small appropriate textbooks.

In preparing lectures the author found the sets of notes by Lightfoot[11] and by Keller and Leonard[12] to be of great assistance. Parts of Lightfoot's notes seemed a little too advanced, for the seniors especially, and both references lacked material on certain subjects. However, both works are oriented toward engineers, particularly chemical engineers, and would, if developed further, constitute excellent texts for this type of course.

Each week a 20 minute quiz is given on the previous week's material. Hour examinations are omitted. Students have the option of taking a conventional three-hour final examination or of submitting a term paper or term project report. This option introduces the opportunity for each student to pursue specific topics of interest in detail without jeopardizing his course grade.

INTRODUCTORY MATERIAL

To convey to the student a feeling for the context of present-day advances, and especially the idea that biomedical engineering is not totally new, but an ongoing activity of ancient origin, a brief historical background is given. Mention is made of da Vinci, Vesalius, Sanctorius (inventor of the first fever thermometer), Harvey, Descartes, Hales, Laënnec (inventor of the stethoscope), and later pioneers. From here the course moves to a very general introduction to human anatomy, illustrated by charts. The sizes, locations, and functions of the major organs and other body components are reviewed. Quantitative steady-state "operating data" and time-averaged mass balances for a typical person at rest are quoted. Data include organ sizes, organ weights, volumes of body fluids, respiratory and cardiac frequencies and flow rates, O_2 consumption, CO_2 production, daily water balances, etc.

Students are assigned the reading of K. B. Bischoff's paper[2] "A Chemical Engineering View of Bioengineering," which helps them to see what chemical engineers have done, are doing, and can do in the bio-transport and biomedical engineering areas. Along with this the students are asked to construct a plastic model "Human Anatomy Kit" (Renwall Products, Inc., Mineola, N.Y., $1.69) — a detailed scale model kit containing roughly thirty pieces. After assembling all major organs and fitting them into the proper body cavity locations, the students find that they have learned a great deal about human anatomy.

During the first week, a film, "Man-Made Man," originally produced for the CBS Twenty-First Century Series, is shown. The film contains footage on artificial organs, organ transplants, and other advances related to the repair or replacement of body parts. This, and seven other films shown during the course (see listing below), greatly stimulates student interest. While most of the films are of college level, a couple are perhaps too elementary. Although these could be deleted they are kept in the course for their value in creating variety. They are:

F1 "Man-Made Man" (produced by CBS for "21st Century" Series), McGraw-Hill Films, New York.
F2 "Control of Body Temperature," Encyclopedia Brittanica Educational Corp. (EBEC), Chicago.
F3 "The Blood," EBEC, Chicago.
F4 "Circulation of the Blood," produced for American Heart Assn., obtainable from National Medical Audiovisual Center, Atlanta.
F5 "The Human Heart" (produced by CBS for "21st Century" Series), McGraw-Hill Films, New York.
F6 "Work of the Kidneys," EBEC, Chicago.
F7 "Gift of Life" (describes daily life of an artificial kidney patient), obtainable from National Medical Audiovisual Center, Atlanta.
F8 "Respiration in Man," EBEC, Chicago.

THE HUMAN THERMAL SYSTEM

This topic is considered next because it allows the student to get back to familiar ground (heat transfer) and enables him to relate his engineering knowledge to a living system. Also, this topic is more "compact" and less complex than, say, mass transport in living systems.

We first quickly review the basic processes of digestion and the conversion of food into metabolic energy. Chemical reaction (stoichiometric) equations and overall energy balances are written. Having learned about heat production, we then consider the quantitative description of heat dissipation from the body's surfaces via radiation, evaporation, convection, and conduction. A few interesting homework problems in thermal phenomena are listed in Table II. The class reads Eugene Wissler's paper[3] "A Mathematical Model of the Human Thermal System" to learn how standard analytical modeling techniques can be used in this area. Finally, we consider heat transfer *within* the body, such as between arteries and veins via tissue conduction and perfusion through connecting capillaries. The development of models for such processes and the setting up of appropriate equations are demonstrated. However, details of their solution are not presented (the advanced follow-up course pursues these aspects). Thermo-regulation mechanisms (e.g., vasoconstriction) are mentioned only briefly.

MODELING THE BODY

The paper by Wissler introduces them to the idea of modeling. This is continued by having the class read Bischoff and Brown's "Drug Distribution in Mammals."[4] In lectures we also consider a variety of additional body models which have appeared in the literature. The notions of splitting the body into appropriate compartments, production sources (or sinks for elimination), and fluid streams are taught. Problems of obtaining accurate and meaningful parameter values are discussed. In addition, the general solution schemes for the sets of linear equations which usually result from compartmental analyses are reviewed. The experience in modeling that the student gains here is useful in a large part of the remainder of the course

. . . the course deals with momentum, heat, and mass transport phenomena in living systems and medical engineering concerned with humans.

TABLE 2.—SELECTED EXAMPLES OF HOMEWORK PROBLEMS USED IN THE COURSE

Heat Transfer
1. Effect of Zero Heat Loss on Body Temperature Rise
2. Sensible Heat Loss Associated with Respiration
3. Effect of Wind Velocity on Convective Heat Loss from the Body
4. Importance of Countercurrent Arterial-Venous Heat Transfer in Maintaining Body Core Temperature
5. Heat Transfer Under Extreme Environmental Conditions

Circulatory System Dynamics
1. Blood Velocities and Residence Times in Capillaries
2. Calculation of Theoretical Horsepower of the Heart
3. Interconversion of Kinetic Energy and Pressure Throughout the Circulatory System
4. Hydrostatic Contributions to Pressure Distribution in the Circulatory System

Artificial Kidney Systems
1. Membrane Area Needed to Produce a Given Mass Transfer Rate
2. Treatment Time for Patient Connected to a Flat Plate Dialyzer (Body Modeled as a Single Stirred-Tank)

FLUID MECHANICAL PHENOMENA

An understanding of blood rheology and of the dynamics of the human circulation is essential to a very wide variety of biomedical problems, including extracorporeal blood flow in artificial organs, studies of capillary-tissue mass transfer, analyses of atherosclerosis, etc. This important area is introduced by a discussion of the composition, properties, and rheological characteristics of plasma and whole blood. The non-Newtonian behavior of blood, effects of rouleaux formation at low shear, the high shear Fahraeus-Lindquist effect, plasma skimming, and other aspects are covered.

The next two weeks are spent discussing the human circulatory system. After describing the general features — volumes, flow rates, vessel sizes, locations of laminar and turbulent regimes — we consider the structure and properties of vessel walls. The various kinds of wall components, their effects on vessel stability, and their roles in modifing flow pulsations are discussed.

Application of Bernoulli's equation to various parts of the circulatory system are demonstrated in class (these are approximate analyses, neglecting pulsations). Here we show how high pressure is created in aneurisms, why low pressure prevails in stenoses, what the theoretical horsepower of the heart should be, and so forth. Typical homework problems dealing with circulatory system dynamics are cited in Table II.

ARTIFICIAL HEARTS AND VALVES

This subject area, involving many fluid flow problems, is treated next. At this stage of the course the students are anxious to learn about real hardware, and they find this topic quite satisfying from that standpoint. Some discussion of blood hemolysis, protein denaturation, thrombus formation, and the broad subject area of biomaterials comes first. Then various designs for heart valves, total heart replacements, and partial heart substitutes (ventricular boosters and bypasses) are discussed from engineering and physiological viewpoints. A life-sized model of the human heart is displayed and passed around to familiarize the students with the organ under discussion. The section of Eugene Guccione's paper[9] dealing with these devices is handed out for reference. Also, the film "The Human Heart" (another CBS "21st Century" production) is shown. This excellent film contains demonstrations of artificial heart construction, surgical implantation of heart assist devices and interviews with noted surgeons (Barnard, Debakey).

BIOLOGICAL MASS TRANSPORT

The second half of the course concentrates on topics involving mass transport phenomena to a large degree, especially membrane transport. We begin by reviewing the basics of ordinary, or passive, transport—diffusion resulting from concentration, electrical potential, or pressure gradients (no carriers, no biological energy consumption). This material is familiar to the student from earlier coursework.

Next we consider the structure, composition, and permeation properties of biological membranes. The importance of lipid solubility, presence or absence of "pores," and effects of solute character are pointed out. Facilitated and active transport mechanisms are discussed in some detail. With respect to the former, equations are written for the system O_2-hemoglobin-oxyhemoglobin to illustrate the effects. With respect to the latter, little of a quantitative nature can be written. However, details of proposed "Na-K pump" mechanisms are scrutinized.

Having obtained a background in passive, facilitated, and active transport the student is then ready for consideration of the natural lungs and kidneys and their artificial counterparts.

KIDNEYS—REAL AND ARTIFICIAL

Two lectures are spent on the physiology of the natural kidneys. Impressive data are given which convince the student of the tremendous capacity, selectivity, and efficiency of the human kidneys. Countercurrent concentration of urine via active transport is discussed in detail. This material gives the student the proper perspective toward the next subject — artificial kidneys.

Leonard and Dedrick's paper, "The Artificial Kidney — Problems and Approaches for The Chemical Engineer"[5] provides a good reference here. The major kinds of artificial kidneys in current use (coil, flat plate, hollow fiber) are reviewed, and their operating characteristics discussed. Advantages and disadvantages of each type are made clear. Mathematical descriptions of these devices are formulated on a simplified basis. Consideration is also given to modeling the artificial kidney-patient system as a whole (using a compartment model for the patient). Rough calculations of treatment times for typical patients and dialyzers are also performed. An excellent film (F7) showing actual clinical and home dialyses complements the lectures nicely. Demonstration units of coil and hollow fiber artificial kidneys, set up and run with "blood" (colored water), are used here also. Finally, some mention is made of "novel" and alternative approaches to uremia e.g., fixed-bed sorption devices, ultrafilters, peritoneal dialysis.

LUNGS—REAL AND ARTIFICIAL

The course format here is virtually identical to that relating to real and artificial kidneys. Two lectures on the physiology of the natural lungs are given, with emphasis on the kinetics of O_2-CO_2

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Solution

The obvious question relating to the marketability of a new cigarette filter is the cost of the absorbent per pack of cigarettes. Using the volume of charcoal in a Lark filter, the assumption that the new adsorbent could be used in the existing plastic cap on Doral cigarettes (or an equivalent specially manufactured cap), and the present market price for zeolites (the most expensive of the solid acids under consideration), we calculated that the incremental cost of the filter would be less than ½ cent per pack. Hence, the project was deemed to be sufficiently reasonable to define how the effectiveness of the new filters could be tested.

To determine how tars and nicotines are evaluated for cigarettes, in one day we called without success, the following:

(1) The U. Mass. Public Health Department; (2) The Mass. Dept. of Public Health; (3) the U. Mass School of Pharmacology; (4) The FDA office in Boston; (5) The U.S. Treasury, Alcohol and Tobacco Dept.; (6) The R. J. Reynolds Tobacco Co.

Finally we called the Tobacco Institute Testing Laboratory, where we talked to a laboratory technician who gave us a complete discussion of the gravimetric technique used as well as literature references describing the test.

That night we looked up the Journal of the Association of Official Analytical Chemists to find the specifics of the tar and nicotine test. We found that a smoking machine is used to test 10-20 cigarettes to obtain an average tar and nicotine level. The smoke is drawn through a commercially available filter unit; a volume of 35 ml. of smoke is puffed for a duration of 2 secs, once each minute. The filter paper is weighed before and after 10-20 cigarettes are smoked, the weight gain representing total tars, nicotine and moisture. The filter paper is soaked in an isopropanol-ethanol solution for extraction of water; the water content of the solution is determined by gas chromatography. The solution is then steam distilled to remove alcohol, and the nicotine then steam distilled from the tars; the nicotine content of the distillate is measured by infrared absorption at three wavelengths. The amount of tar is obtained by difference.

It became quickly apparent that we could neither duplicate this procedure in our laboratory nor afford the expense and time delay of sending our experimental filters to an independent testing laboratory. However, in reviewing the reported magnitudes of the tar, nicotine, and water levels on the filter paper, we realized that the water represents only 20-25% of the weight gain of the filtered paper. Since we were interested in significant improvements in tar and nicotine levels (e.g. up to 90% reduction of present levels), it appeared likely that simple measurements of the total weight gain of the filtered paper would be sufficient to indicate filter performance; the involved analysis procedure could be used to confirm the performance of those filters which were superior in our simpler tests, and those detailed tests would be performed by the Tobacco Institute Testing Laboratory.

Having established that our solid acid adsorbent concept was economically feasible and that a simple and inexpensive testing program could be initiated, we next turned to the patent literature to determine if such concepts had been previously invented. Much to our chagrin, we found not only 200 patents disclosing cigarette filters but also a 1958 patent covering the use of zeolites in cigarette filters and several more recent patents improving on this idea (e.g. changes to prevent the zeolite from drying out the tobacco, to prevent the adsorption of low molecular weight aromatics contributing to taste, etc.). At this stage, after about two man-days of effort, the project was abandoned.

Even though this project was terminated after only two days, the activity was of value to the student. They had learned to rapidly define the critical steps in an investigation, to simplify complex tasks for initial screening purposes, and to rapidly assimilate information in an unfamiliar field. We suggest that these are among the diagnostic arts important to the successful practice of engineering. Other important areas, such as the methods the student would use to sell his idea to tobacco company management and the relative importance of marketing, were not covered in detail with this problem. These items are more logically pursued with other, more successful, projects.

CONCLUSIONS

Obviously it would be nice to be able to say that several projects were brought to a successful completion during the course. However, the students appreciate the fact that an actual attempt at entrepreneurship will make artificial university time schedules meaningless, and they were willing to continue their efforts throughout the summer. Similarly, it might be of interest to describe the projects that appear to have sufficient promise that we are willing to supply our own capital to finance them, but one thing an entrepreneur learns very early in the game is to never reveal promising ideas until they have been exploited and sold! Nevertheless, we hope to make some successful case studies available in the not too distant future. □

COONEY (Continued from page 165)

exchange across the respiratory membrane.

For a discussion of artificial oxygenators, no suitable reference has yet been found. A chapter by Galletti[8] in the Advances in Biomedical Engineering and Medical Physics series has been used. However, this treatment is not aimed at the novice and is not appropriate. A welcome addition to the to the biomedical literature would be a paper containing illustrations and describing the available oxygenator designs (film, disc, membrane, bubble) in simple, clear terms. The mathematical modeling of oxygenators is normally given some treatment, but not any extensive elaboration. This is an area which soon becomes complex and is best left for advanced courses.

. . . the students construct a plastic model "Human Anatomy Kit" . . .

TERM PROJECTS

The term projects, which may be selected by the student (the choice of topic is largely left to the student, subject to the professor's approval) in lieu of taking the final examination, have proven to be popular and interesting. Typically, they consist of ten page paper reflecting in-depth reading or analysis of some biomedical topic, or a report on an experimental investigation or on a computer study.

Last year reports were received on: experimental studies on primary perception by plants (e.g., galvanic response to distant "threats"); computer studies on countercurrent heat transfer in the leg and on artificial kidney-patient systems; and papers on biorythyms, mathematical analyses of pulsatile blood flow, and modeling the effects of anabolic steroids on the body.

ASSESSMENT OF THE COURSE

This course has been favorably received and has generally sparked the interest of the students. About half of the students sign up for the advanced course. The author's impressions of the course are several. First and foremost, as the course now stands, a large number of topics is covered in only 14 weeks and, consequently, the treatment of many topics is too superficial. After deducting from each week the time required for quiz giving, quiz discussion, homework discussion, film showing, etc. too little lecture time remains for the amount of material involved. This problem could be alleviated by shifting some topics to the follow-up course. While this would make the first course less of a survey and be disadvantageous to those students who take only the first course, some shifting is imperative.

Secondly, the course seemed a bit too qualitative to the author. Under pressure of time, many mathematical formulations were omitted and the course was overly accented towards physiology *per se*. By shifting some material to a second semester, this problem could be ameliorated.

A third problem, mentioned earlier, was the lack of a really suitable text. This problem will hopefully be solved by the gradual development of a complete set of handouts for the course.

CONCLUSION

The reader, especially if he teaches in the same field, may have different views as to course content. However, the present syllabus seems reasonable and appropriate for chemical engineers. Additionally, a number of important topics omitted from the first course (e.g., nerve impulse transmission, physiological control systems, etc.) are conveniently covered in a second course.

As a preparation for advanced work the course seems to be effective. Several seniors have chosen to pursue advanced work in formal biomedical programs or in medical schools, and they consider the course to have been appropriate.

To the author it is exciting to be engaged in teaching at the interface of two great disciplines. Hopefully, this paper will serve to further the institution and development of similar courses in many more chemical engineering departments than presently offer such. □

REFERENCES

1. Guyton, A.C., *Textbook of Medical Physiology*, 4th edition, Saunders, Philadelphia, 1971.
2. Bischoff, K. B., "A Chemical Engineering View of Bioengineering," AIChE Student Members Bulletin, 11(2), 9 (1970).
3. Wissler, E. H., "A Mathematical Model of the Human Thermal System," CEP Symposium Series 62, No. 66, 66 (1966).
4. Bischoff, K. B., and Brown, R. G., "Drug Distribution in Mammals," CEP Symposium Series, 62, No. 66, 33 (1966).
5. Leonard, E. F., and Dedrick, R. L., "The Artificial Kidney—Problems and Approaches for the Chemical Engineer," CEP Symposium Series, 64, No. 84, 15 (1968).
6. Burton, A. C., *Physiology and Biophysics of the Circulation*, Yearbook Medical Publishers, Chicago, 1965.
7. Whitmore, R. L., *Rheology of the Circulation*, Pergamon Press, Oxford, 1968.
8. Galletti, P. M., "Advances in Heart-Lung Machines," in *Advances in Biomedical Engineering and Medical Physics*, Vol. 2, S. N. Levine, ed., Interscience, New York, 1968.
9. Guccione, E., "Biomedical Engineering," Chem. Eng., January 30, 1967.
10. Ruch, T. C., and Patton, H. D., eds., *Physiology and Biophysics*, 19th edition, Saunders, Philadelphia, 1965.
11. Lightfoot, E. N., *Biomedical Transport Phenomena*, AIChE Today Series, AIChE, New York, 1969.
12. Keller, K. H., and Leonard, E. F., *Applications of Chemical Engineering to Problems in Biology and Medicine. Part I. Engineering Analyses of the Functions of Blood*, Twelfth Advanced Seminar, AIChE, New York, 1968.
13. Middleman, S. *Transport Phenomena in The Cardiovascular System*, Interscience, New York, 1972.