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A TEACHING AID FOR PHYSIOLOGISTS – SIMULATION OF KIDNEY FUNCTION

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INTRODUCTION

In setting out to develop a simulation that can be used for teaching physiology students there are three important problems which must be solved.

(a) The physiological system to be modelled may be complex and ill-defined.
(b) Testing the validity of the model may be difficult due to the lack of suitable experimental data.
(c) The computer system used for the simulation must have good display and interaction facilities that can be readily made available in an undergraduate laboratory.

This paper describes how these problems were overcome in setting up a model of the facultative water transfer mechanism of the mammalian kidney.

THE PHYSIOLOGICAL SYSTEM

The overall purpose of water transfer is to maintain the body fluids at a constant level of osmolality. This involves the movement of water from the nephrons into the vasa recta. During this movement the water passes through the medullary interstitial space lying between the nephrons and the capillaries. Two types of transfer are identified. The first is a constant reabsorption of water from the proximal portions of the tubule, the second is a variable reabsorption from the distal tubule and collecting duct to the vasa recta. These movements are shown by arrows 1 and 2 on Figure 1 which gives a block diagram representation of the kidney. The variable or controlled reabsorption is of main interest in this simulation. The concentration of solutes in the medullary interstitial space, particularly urea and sodium in conjunction with the level of certain hormones in the blood, control the transfer rate. The average human kidney has a volume of 150 ml and contains approximately 10^6 nephrons. The solute concentration of tubular fluid and interstitial fluid is not uniform. At steady state a concentration gradient exists across different parts of the interstitial space which is maintained by a complex movement of urea (arrow 3, Fig. 1) and sodium (arrows 4 and 5, Fig. 1) between the tubules, the interstitial space and the capillaries. In a dynamic situation, where the level of urine generation is changing, the concentration in the medullary interstitial space also undergoes considerable change.

The immense number and minute size of the nephrons make measurements of different processes taking place along the length of a nephron extremely difficult. As a result, renal physiologists are by no means united in explaining all aspects of the facultative water transfer. Modelling is not, therefore, just a matter of setting up a series of equations to represent the system. It also involves trying different hypotheses which seek to explain the system and attempting to establish which of them is most likely to be the correct one. A major aspect of this project was the establishment of a consistent set of hypotheses.

SIMULATION PHILOSOPHY

In view of the uncertainty and sparsity of the data available in this case it was thought impractical to develop a series of detailed models of the micro processes involved and then attempt to put them together in a large and complex macro model. Instead, the model was built up in terms of the broad principles of operation in order to give a reasonable representation of overall behaviour. Where necessary, more detailed models of subsystems were embedded in the macro or "crude" model. The second important philosophy on which the model is based is that of aggregation. This is necessary in view of the large number of nephrons. The model being presented here is a compartmental one based on total flows between compartments, uniform average concentrations within compartments and negligible diffusion times across compartments. This latter simplification is justified because of the small physical dimensions of the nephrons leading to diffusion times very much smaller than other time constants involved in the system.

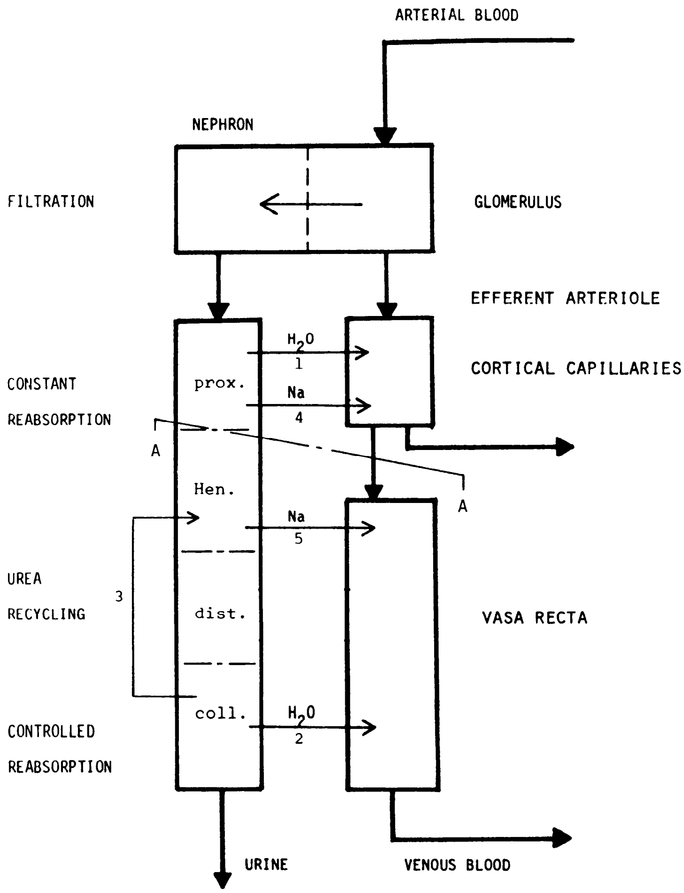

Fig. 1. Block diagram representation of the kidney. The processes represented in the simulation are those lying below the line AA.

Because of the complexity of the kidney and the uncertainty surrounding some aspects of its operation, it was necessary to base the model on a number of assumptions and limit the scope of representation. These assumptions, some of which are controversial, are listed below. A detailed discussion of these assumptions and the basis for making them is given in previously published papers (3-5).

The assumptions are:

(a) Ingested water and solutes rapidly equilibrate with the body fluids following absorption and this results in a proportional change in solute concentrations in the blood.

(b) Following fluid ingestion there is no change in the glomerular filtration rate or in the rate at which Na, urea or water are reabsorbed from the proximal convoluted portion of the tubule.

(c) The flow rate into the distal tubule is constant.

(d) All variations in the water reabsorption rate occur in the distal tubule and collecting duct.

(e) There is a dual action of the antidiuretic hormone (ADH) in the water reabsorption mechanism.
The first action of ADH is to alter the permeability of the tubular epithelium of the distal tubule and collecting duct.
The second action of ADH is to modify the vascular tone at the entrance to the vasa recta. This action regulates the flow of blood and hydrostatic pressure in the vasa recta.

(f) There is some increase in interstitial fluid volume during diuresis.

(g) The recycling of urea results from passive transfers along concentration gradients. No active transfer of urea is involved.

(h) The transfer of sodium out of the ascending limb of the loop of Henle is the major source of medullary sodium. This rate of transfer of sodium is not affected by the level of ADH.

(i) The removal of sodium from the medulla is by equilibration with blood flowing in the vasa recta.

As a result of assumptions (b) and (c) above, the simulation makes no representation of the kidney functions occuring prior to the pars recta of the proximal tubule. Figure 1 described in block diagram form the processes represented by the simulation.

Blood solute changes induced in the model are limited to the physiological range over which the glomerular filtration rate is unaffected in a normal kidney. Figure 1 indicates the processes represented by the simulation.

SIMULATION FACILITIES

Using a modification of BASIC known as REALTIME BASIC which was developed in the Electrical Engineering Department of the University of Melbourne a NOVA 1210 minicomputer was used to set up the model. The NOVA was equipped with 16 K of store and a Tec 4012 visual display unit (VDU). In addition, facilities were available which permitted outputs to be plotted directly on XY recorders. Program turn-around times of one minute were achieved, and the language permitted the simultaneous use of the VDU or one or more XY recorders as output devices. The interactive nature and fast turn-around time of this system provided a useful medium for both developing the model and making it a useful teaching tool.

THE MODEL

The model was set up in component block or transfer function form. This was done to maintain the identity and logical order of component processes in order to facilitate the overall development of the model. As mentioned earlier, some individual processes are not clearly understood and fundamentally different mechanisms needed to be investigated in the search for best results. Access to component processes was therefore essential. It also allows for subsequent modification of the model as new ideas become accepted.

The parameters of the model were established where possible by reference to the literature, and where this was lacking by a "best fit" approach. The model was tested by comparing its behaviour against published experimental results. Two types of test were used.

(a) An input/output test in which the urine flow rate generated by a given single-dose ingested water load was recorded (2).

(b) A drip feed test which permitted measurement of internal variables of the kidney system (1).

It was necessary to test and reject a number of hypotheses concerning the internal processes of the kidney before a unique model could be established which satisfied both test procedures. The fact that some hypotheses were not consistent with overall kidney behaviour lends confidence to the final model structure. However, aspects of it must remain controversial until supported by physiological experiment. A comparison between simulation results for the test (a) and published experimental data are shown on Figure 2. These curves were obtained by direct plotting from the computer onto an XY recorder.

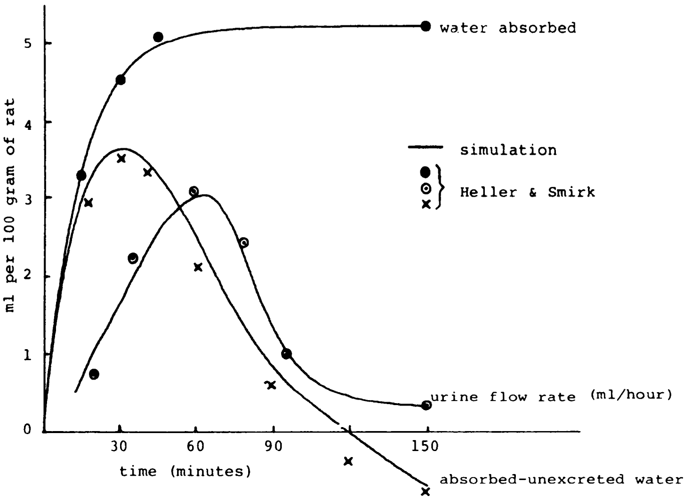

Fig. 2. Diuresis induced by large-dose water load. Comparison of simulated and experimental results. These curves where obtained by using an XY plotter as the output device.

PROGRAMMING THE MODEL AS A TEACHING AID

One advantage of a simulation as a teaching aid in physiology is that processes which take hours to happen in nature can be condensed into minutes on the model. This means that many experiments under a wide range of conditions can be simulated in one laboratory session.

A second important advantage is that the student can observe changes in internal variables of the organ function being simulated. Often such observations are quite impossible to obtain by a direct test in a teaching laboratory due to the technical difficulties involved in the experimental procedure.

Yet another advantage arises from the fact that the use of a simulation avoids the problems often encountered in experimental work where results are affected by uncontrollable factors. In humans this often takes the form of psychological factors. For example, normal release of antidiuretic hormone, which plays an important role in kidney function, can be disturbed by nervousness or sudden fear experienced by the subject. This would produce a distortion of an expected "normal" test result.

While it offers these advantages, if the model is to be of value for instruction purposes the student must have confidence in it as a reasonable representation of events which occur in nature. The preliminary section of the program is aimed at achieving this. In order to operate the program the student requires no knowledge of computer programming. A short text can be used to guide him through the sequence and indicate the instructions required to initiate displays or change variables. Interaction with the program is through the keyboard of the VDU. The introductory sections of the text can use diagrams to show the essential physiological detail of the kidney and then the extent to which this detail is represented by the model. Figures 1 and 3 are representative of these diagrams. Figure 3 will be familiar to physiology students but they may not be accustomed to representation of kidney operation in terms of a block diagram. A direct comparison of the two diagrams will assist them in correlating these two forms of representation.

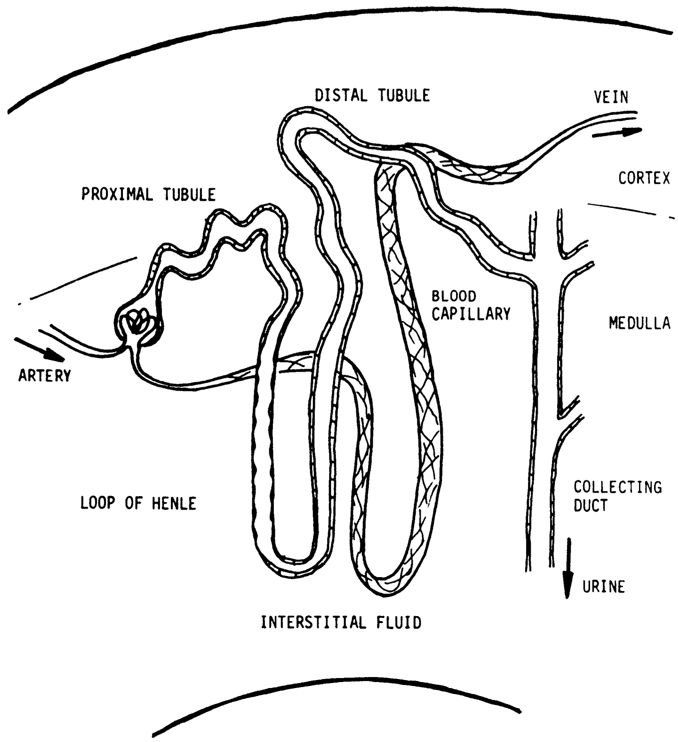

Fig. 3. Diagram representing the general form of the nephrons in the kidney and their relationship with capillaries of the vasa recta.

The first section of the program enables the student to compare the results of a simple physiological experiment and the computer simulation of that experiment. In this experiment the student drinks a litre of water and then measures at half hourly intervals the rate at which this excess water load is being removed by his kidneys. The urine flow rate curve obtained is then compared with that generated by the model under the same large ingested dose conditions.

In the subsequent section of the program the student is given more direct control over the model and guided through a more complex exploration of the operation of the kidney. By this means it is possible to gain an appreciation of the way in which the flow rates, pressures, and osmolalities within the kidney vary in response to normal changes in body fluid conditions.

Kidney variables which may be directly observed on the simulation are listed below.

The variation in blood osmolality.

The variation in the level of antidiuretic hormone in the blood.

The variation in urine flow rate.

The variation in total urine osmolality.

The variation in urea concentration in the urine.

The altered urea recycling between the collecting duct and the loop of Henle during diuresis.

The lowering of total medullary osmolality during diuresis.

The contribution of urea and sodium movements to the variation in total medullary osmolality (Fig. 4).

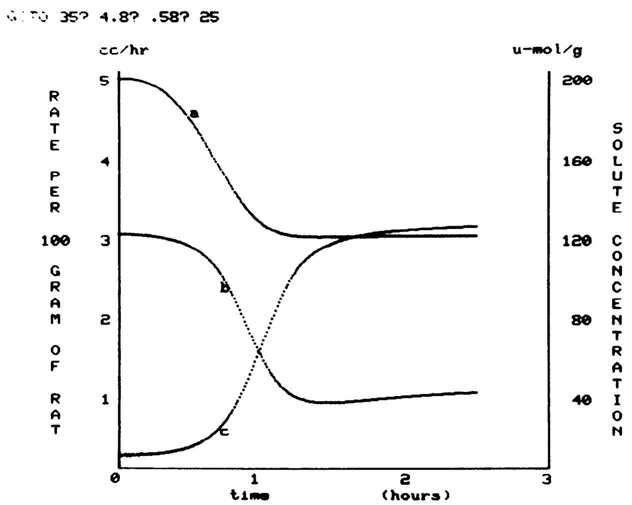

Fig. 4. Photograph of a typical display generated by the program. This display represents changes in sodium (a) and urea (b) medullary concentration resulting from a gradual onset diuresis. This corresponds to the drip feed test of Atherton et al (1968).

In the physiological experiment in the first section of the program, the student only observed the overall output of the experiment which was the urine generation rate. By repeating the simulation of that experiment and selecting for display appropriate variables from the list above, it is possible to observe internal responses of the kidney resulting from the onset of a normal diuresis.

Another experiment which can be simulated by the student is the drip feed test as described by Atherton et al. (1). Once again internal variations associated with the gradual onset of diuresis can be observed. Such phenomena as the exaltation of urea are more easily seen in such a test. Figure 5 illustrates typical diagrams which can be obtained on the VDU screen during these simulation runs.

The model may also be used to demonstrate some aspects of abnormal kidney behaviour. The model provides facilities for representing the following abnormalities.

Reduced osmoreceptor sensitivity to blood osmolality change.
Reduced sensitivity to antidiuretic hormone of the tubular epithelium and the vascular tissue in the vasa recta.
Diminished activity of the sodium chloride transport mechanism in the loop of Henle.
Increased renal venous pressure.

Some of these theoretically possible sites of malfunction can be directly correlated with clinical disorders while others are suspected sites in some kidney disorders. By studying the performance of the model using altered settings of individual parameters, the student can demonstrate for himself how malfunction to varying degrees at any one site may influence the overall kidney performance. Since the model displays in about one minute the outcome of a time consuming experimental procedure, many facets of the osmo-regulatory process of the kidney can be explored in one laboratory session.

In so far as it has been tested, the model gives a reasonable representation of kidney dynamic behaviour under conditions of changing body fluid osmolality. However, it is important to stress to the students that the model is an approximate representation of only certain aspects of kidney function. It must be recognized that the model has limitations and cannot be taken as an absolutely exact definition of what is happening in the real kidney. Despite these limitations, the model can play a useful role as a teaching aid in that its use can familiarize the student with the general characteristics of dynamic changes taking place in kidney behaviour as a result of body fluid changes. In addition to its use for teaching purposes, the authors believe that the model has considerable potential as an experimental tool.

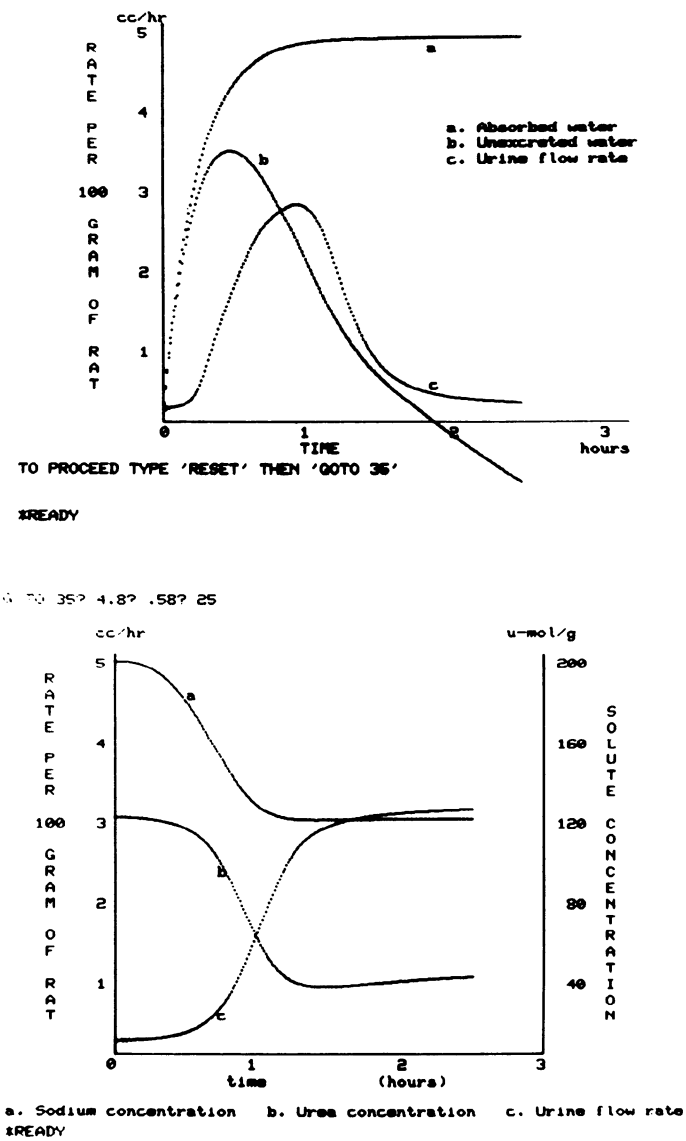

Fig. 5. Photographs of typical displays generated by the program.

In conclusion, the development of the model which forms the basis of this teaching aid has been an interesting and challenging interdisciplinary project. Controversial points have arisen in the development of the model, and these have been discussed in previously published papers (3-5). A concise definition of the complete model in its present form can be made available by the authors on request. Program listings can also be provided. The program can be used with only minor modification on any computer system using a version of BASIC as a programming language and with facilities for communicating with a visual display unit and/or XY plotter. The user needs no special knowledge of computers beyond some experience in using the language BASIC. The program can easily be converted into FORTRAN where the computer system permits the use of this language. Programming in FORTRAN would offer the advantage of increased speed of execution.

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LETTER TO THE EDITOR

Dear Editor:

I have been receiving The Physiology Teacher and it has been very useful to me in preparing course outlines and laboratory experiments for medical students taking physiology.

My department is constantly trying to improve the level of teaching Physiology and trying to make it a more attractive subject to study.

With the recent curtailment in imports we are having a big problem of furnishing our laboratory with basic instrumentation. Local companies are hesitant to industrialize physiology equipment just to cater for few physiology laboratories in the country. Consequently we are forced to make our own and improvise.

In this context I am appealing through the pages of your journal. If any of my colleagues could send me laboratory set-ups, multiple choice questions, and schematics of drop counters, constant temperature baths, digital thermometers, stimulators, etc. which they have designed for their laboratories, the help would be appreciated.

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PHYSIOLOGICAL SIMULATION: AN ASSESSMENT OF ITS ADVANTAGES AS WELL AS ITS LIMITATIONS

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As computing facilities become accessable to more people and at lower costs, it is becoming more attractive to use computer simulations in the teaching of physiology. In fact, as the technology advances some use of computer simulations for training may become mandatory (15). This presentation is made in three parts: the first section reviews some of the advantages to be gained by the use of computer simulations in support of conventional educational methods. The second topic discusses the evaluation of simulation programs for teaching purposes. The third portion of the paper deals with some limitations of the simulation approach. The latter emerged in the course of evaluating several cardiovascular-renal computer simulations under contract from the National Institutes of Health (17).

ADVANTAGES OF USING COMPUTER SIMULATIONS

The advantages to be gained in the use of computer simulations relate to a variety of activities as indicated below.

Faculty Time

Traditional educational methods require faculty and staff to teach and train students in all the topics covered in a course, from those which are conceptually simple but require practice to master, to those which are conceptually complex and require extensive thought and understanding. By designing simulations to take over the straight-forward tasks and to assist in the understanding of elements of more complex tasks, the faculty can recover time. This time could be used to prepare and lecture on more complex issues or to devote to research which typically includes student involvement.

The potential for this recovery of time has been amply demonstrated. Alpert and Bitzer (2) reported, in 1970, on a program written to test the feasibility of replacing some lecture time in a medical science course with program interaction time. Students who used the computer programs needed only one third to one half as many lecture hours as those students who relied solely on lectures. Attia et. al. (3) tested a case-simulation program for teaching cardiopulmonary resuscitation with first month anesthesiology residents at The Massachusetts General Hospital. Residents using the program learned significantly more than their classmates who only had access to textbooks and tutors.

Laboratories

Laboratory instruction is typically intended to accomplish at least two purposes: a) to develop particular skills in the students, and b) to present problem-solving situations which the student may later encounter and thus provide solutions (or guidelines) for those situations. While some activities must be dealt with in a laboratory, e.g. dissection and instrumentation, many can be dealt with by using computer simulations. When evaluation of results is of paramount importance, the use of computer assisted instruction (CAI) can be invaluable. Instead of spending time performing tests (which may require elaborate equipment and time consuming preparations) and writing conjectures on their results, students can request the necessary tests and then apply their conjectures to a model of the system under consideration, thus maximizing the cognitive aspects of the exercise.

Student Involvement

At least three motivational factors affect a student's learning: a) the nature of the teaching environment, including the amount of individual attention; b) the presence of opportunities to test the newly-learned material in a life-like situation; and c) the opportunity to explore a broad range of related topics. As argued persuasively by Hoffer et. al. (13), medical students are required both to amass knowledge and to develop competance in the application of that knowledge. Only the former is taught in a well-structured fashion; the latter is taught by exposure and experience in a clinical setting which is limited by the realities of life. There is no control over the selection of patients, the stage of their illness, or their time of arrival at a hospital or clinic. Further the mix is often atypical of what is likely to be found in private general practice, and worse — for teaching purposes — either the situations are emergencies which leave little room to discuss choice of treatment, or the maladies are so complicated that the patient's care cannot be entrusted to an inexperienced student. Thus, supervised practice in a clinical setting is necessary but severely limited. Computer simulations which place the student in complete control of a patient, and which can present rare clinical diseases at the touch of a button, are a helpful solution to much of this problem. These solutions extend to computer-controlled mannequins such as Gordon's (9, 10), or Abrahamson's (SIM-I) at the University of Southern California School of Medicine (1, 5). While medical students may present a somewhat extreme example, students preparing for any form of laboratory-associated career can benefit from such computer-based learning opportunities.

New Topics

Many topics can be taught via simulation programming which could not be taught otherwise. Using medical students as an example again, it is obvious that a patient with an acute illness cannot be placed in the care of an inexperienced medical student. Conversely, a student can be permitted considerable latitude in exploring the dynamic parameters of a disease in a simulated patient. For example, a student could deliberately withhold treatment in such a simulation to observe the natural course of a disease process. That type of experience might be of benefit in later practice as a guide for assessing the progression of a patient's disease and selecting among therapy alternatives. Additionally, the student could gain valuable experience with procedures requiring elaborate or expensive equipment without incurring any actual cost or subjecting a patient to possible training errors. Thus, a simulation can provide experiences that would not be ethical in a real-life situation or might only occur infrequently in practice.

EVALUATING COMPUTER SIMULATIONS

Before adopting computer simulations for curricular use, there are at least four questions which should be considered in a program evaluation:

1. Does the simulation provide a useful learning experience for the student?
2. What range of physiological responses are simulated?
3. What assumptions have been made in designing the simulation?
4. Are the simulation equations based upon physiological processes as currently understood, or are the equations empirical formulas developed to fit observed effects?

Teaching Level

Whether a simulation demonstrates physiology at an appropriate level for a student and whether it provides a useful learning experience are crucial concerns which are often difficult to resolve. With respect to the first concern, the simulation must not overwhelm the student with physiological detail yet it must represent physiology faithfully. (This concern is dealt with more fully in subsequent sections.) The second concern is essentially a methodological one and as such does not have a single clear-cut answer. In order to provide a useful learning experience, several factors must be present; motivation to participate in the experience, challenge to make the participation worth the effort, review to consolidate present knowledge, and new material to either increase knowledge or to extend understanding by demonstrating new relationships between known material. The balancing of these factors is subjective however some basic requirements do hold. Simply submitting prescribed data to a simulation is not likely to stimulate student interest unless some frame of reference is available to enhance the feeling of involvement. Interactive simulations provide more motivation because the student is able to make a series of inputs to the simulation, follow a sequence of events, and attempt to achieve a desired outcome. Management to achieve a final outcome or exploration of a particular scenario can provide an appropriate challenge. The involvement of using knowledge as well as acquiring and determining the need for new information is obvious in such contexts. Those programs which provide a seemingly new experience each time they are engaged contribute more to motivation than those which are less versatile.

Range of Response

Physiology is customarily defined as the science dealing with the normal vital processes of human beings and animals. For our purposes it will be useful to make distinctions between the terms 'normal' physiology, 'abnormal' physiology, and patho-physiology. Normal physiology will be used to describe physio-chemical processes operating within their homeostatic limits, abnormal physiology will be concerned with processes which are operating outside their homeostatic limits in the absence of an identifiable pathological agent, and patho-physiology is the study of processes affected by the intervention of diseased or degenerative conditions.

The physiological interrelationships which exist in normal physiology may change dramatically in certain abnormal states. This is in part because physiological actions are generally controlled by a multiplicity of other interlocking physiological processes. Some processes exert a large absolute effect which provides a gross adjustment while others exert a small absolute effect which provides only fine-tuning. For example, pH balance is controlled by the renal, pulmonary, and blood buffer systems. While the blood buffer system has the smallest absolute effect it is adequate to control the blood pH under resting conditions. Following exertion, the capacity of the blood buffer system is exceeded and the pulmonary system is called upon to restore acid-base balance. For conditions which occur over a longer time period the renal system can provide more sustained adjustments.

It is insufficient to state that a particular relationship exists between a number of factors within a defined range if the model can operate beyond that range. The formulas which describe the relationships between factors must describe them accurately over the full range that the simulation operates, not simply a 'normal' range or a 'range of interest'. In fact, most simulations do not attempt to define the range of their appropriate response (17).

The simulation should prevent itself from entering situations it is not equipped to handle. This requires each set of equations to check its input parameters. If any input is outside the permissable bounds, the simulation should reject the user input, print a message explaining the program's action, and restore the simulation to the condition it had before the unacceptable input was made.

Assumptions

When functioning in a research capacity it is permissable, if not desirable, for a physiologist to speculate in describing a physiological process. A trained researcher can construct a simulation reflecting a particular viewpoint about how some physiological process works and use it to test a hypothesis or to predict what to look for in laboratory experiments. In a teaching situation, however, such latitude can be dangerous. A naive student is often unable to distinguish an invalid result from a valid one. The background and perspective of experience is lacking, and the student is apt to accept everything as fact. The assumptions of a simulation must be as well documented as possible and should be clearly stated to the student. Like the range of operation, this is not customarily specified (17).

Formulation of Equations

A crucial question is whether the simulation programming reflects physiological processes, or simply displays the results of certain specified circumstances. To examine this question adequately it is necessary to consider the structure of simulation programs. Simulation programs can be divided into three categories; pseudosimulations, empirical simulations, and physiological simulations.

Pseudosimulations use a question/answer format to branch from physiological state to physiological state. While such programs can be quite complex there is no actual mathematical simulation involved. The question/answer structure only allows the user to branch to specific sets of circumstances for which particular parameter values are available. While some minor modification is possible, the parameter values are not computed, rather pre-assigned values are employed. Examples of this type of simulation are Cardiopulmonary Resuscitation (12) available via the Health Education Network, Inc. (HEN) from The Massachusetts General Hospital and CASE (11) available via HEN from The Ohio State University.

Empirical simulations are based on an integrated set of mathematical equations which represent a non-physiological system. The values of the parameters of the simulation are determined at any given time by solving the set of simulation equations. The vast majority of equation-based simulations available today fall into this category, including many programs which purport to demonstrate real physiological systems. Examples of empirical simulations are MACMAN (8, 14, 16), MACPUF (7, 16), and MACPEE (6, 16) developed at MacMaster University in Ontario, Canada and Cell Membrane, a simulation game which is used in the teaching program at The George Washington University Medical Center (16).

Physiological simulations differ from empirical simulations by faithfully representing real physiological systems in all their known detail. If the simulation is able to mimic the real system in every detail, then it is a true physiological simulation. Despite the vast amount of physiological knowledge available to the designers of simulations today, few physiological systems are fully understood and therefore there are few candidates for the designation true physiological simulation. Typically only portions of systems are fully understood and therefore simulations which limit htemselves to those areas tend to be quite restricted in scope. An example of a physiological simulation is the Cargille/Dixon model of the human menstrual system (4). This model was developed by exploring the literature and restricting the formulation of equations to documented relationships as much as possible. Further, the documentation within the model stated all assumptions and sources; as well as sources of conflicting data and viewpoints (see Figure I).

From the above discussion of the types of simulations which exist, and the realization that some programs share features of more than one type, it should be obvious that it is important to know, and to inform the students, what type of simulation is being dealt with. Pseudosimulations and physiological simulations can be used freely providing they meet the other criteria for being useful programs. Empirical simulations must be used with caution to ensure that the student remains within the 'physiological' bounds of the program.

Since simulations have been shown to be an effective instructional media, and since current knowledge in many areas of physiology is insufficient to allow true physiological simulations to be written for them, it is practical to accept some empirical simulations. It is undesirable, however, to accept empirical simulations in those teaching seetings where there is no opportunity to point out their limitations.

LIMITATIONS OF COMPUTER SIMULATIONS

The authors were recently involved in a project which evaluated several simulation programs (17). The results pointedly illustrated a major problem prevalent in simulation programming. The remainder of this article will discuss this difficulty and suggest a method to minimize its occurence.

Empirical 'Short-Cuts'

As we know them, the processes of physiology are quite complex. To simulate such complex processes using a digital computer requires a considerable investment of computer resources. These resources include central processing unit time, memory, and mass-storage. Briefly, this means that a complex simulation can be costly to run. This cost has typically been of prime importance in the development of simulations to the point that sometimes cost has been more important than accuracy (the reasons for this are not relevant to this article). The result of this situation has been for authors to attempt to group series of physiological processes into simple all-inclusive formulas. We call these formulas empirical approximations or simply, short-cuts. While these short-cuts have frequently been necessary to produce a functional simulation, the programs generally conceal this internal simplification or make no attempt to restrict the use of the simulation to those circumstances where the short-cuts appropriately represent the physiology they replace. Additionally, this approach ignores a primary teaching objective: to teach the student the process, not just the results of the process. Figure 2a provides an illustration of a stylized physiological pathway and figure 2b shows how an empirical short-cut equation might represent it. Table 1a provides an example of an empirical short-cut equation actually observed in a program attempting to simulate renal physiology. The large number of 'ignored' parameters (Table 1b) makes it obvious that the relationship is acceptable only under a very restricted set of circumstances.

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NOTE  ----------------------------------
NOTE
NOTE                          FSH
NOTE
NOTE  ----------------------------------
NOTE
NOTE
R     FSHPR.KL=18.2(100/(1+4.7*(HILL (.6*EBC.K,2.8)+.1*PBC.K)))
NOTE                          FSH PRODUCTION RATE (MIU/DAY)
NOTE*
NOTE* DEFINITION:
NOTE*   FSHPR IS THE NUMBER OF MIU OF FSH SECRETED BY THE
NOTE*   PITUITARY PER 24 HOURS, EXCLUSIVE OF THE FSH CONTRIBUTE
NOTE*   BY THE MIDCYCLE SURGE.
NOTE* ENGLISH TRANSLATION OF THE DYNAMO EQUATION:
NOTE*   THE FSH PRODUCTION RATE DURING THE NEXT INTERVAL IS EQUAL
NOTE*   TO 18.2 TIMES 100 DIVIDED BY 1 PLUS 4.7 TIMES THE QUANTITY
NOTE*   (.6 TIMES THE PRESENT ESTROGEN BLOOD CONCENTRATION AS IT
NOTE*   APPROACHES AN UPPER LIMIT OF 2.8 PLUS .1 TIMES THE
NOTE*   PRESENT PROGESTERONE BLOOD CONCENTRATION).
NOTE* DATA MODELLED:
NOTE*   1.   FSH PATTERN.
NOTE*      ROSS ET AL: REC PROGR HORMONE RES 26:1, 1970. FIG 9
NOTE* SUPPORTING EVIDENCE:
NOTE*   1.   FSH PATTERN.
NOTE*        FAIMAN ET AL: J CLIN ENDOCR 27:1711, 1967.
NOTE*        MIDGLEY ET AL: J CLIN ENDOCR 28: 1699, 1968.
NOTE*        MORI: J ENDOCRINOLOGY 42:55, 1968.
NOTE*   2.   INVERSE RELATIONSHIP OF E AND FSH
NOTE*        VAITUKAITIS ET AL: J CLIN ENDOCR 42:55, 1968.
NOTE*   3.   INVERSE RELATIONSHIP OF P AND FSH.
NOTE*        INSERT REF.
NOTE* CONTRARY EVIDENCE:
NOTE*   1.   FSH PATTERN.
NOTE*        SAXENA ET AL: J CLIN ENDOCR 28:519, 1968.
NOTE*   2.   INVERSE RELATIONSHIP OF E AND FSH.
NOTE*        FSH RISE FOLLOWING E ON DAY 10 OF THE CYCLE NOTED
NOTE*        CARGILLE ET AL: J CLIN ENDOCR 36:87, 1973.
NOTE* ASSUMPTIONS:
NOTE*   1.   FSHPR IS ONLY EFFECTED BY EBC AND PBC.
NOTE*   2.   CODE C. AT E LEVELS LESS THAN PROG, E IS 6X MORE EFF
NOTE*        THAN P IN SUPPRESSING FSH, NG FOR NG.
NOTE*   3.   CODE C. E AND P ARE ADDITIVE, NOT SYNERGISTIC, IN
NOTE*        SUPPRESSING FSH.
NOTE* LOCAL STRUCTURE – THIS ELEMENT IS EFFECTED BY:
NOTE*   EBC          (ESTROGEN BLOOD CONCENTRATION)
NOTE*   PBC          (PROGESTERONE BLOOD CONCENTRATION)
NOTE* LOCAL STRUCTURE – THIS ELEMENT EFFECTS:
NOTE*   FSHBC        (FSH BLOOD CONCENTRATION)
NOTE* COMMENT:
NOTE*   THE COEFFICIENT 18.2 EMPIRICALLY ADJUSTS THE RANGE OF FSH
NOTE*   LEVELS TO COINCIDE WITH THE NORMAL MEAN BLOOD LEVEL.
NOTE* ------------------------------------
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Fig. 1 Portion of the Cargille/Dixon model of the human menstrual cycle. This is the program documentation for one of the follicle stimulating hormone (FSH) equations.

Accepting the constraints of today's computer technology, it is inappropriate to suggest that all the factors involved in a physiological process must necessarily be present in a simulation, although this would be the ideal method. It is appropriate, however, to require that the simulation document its departures from physiological processes and restrict its own

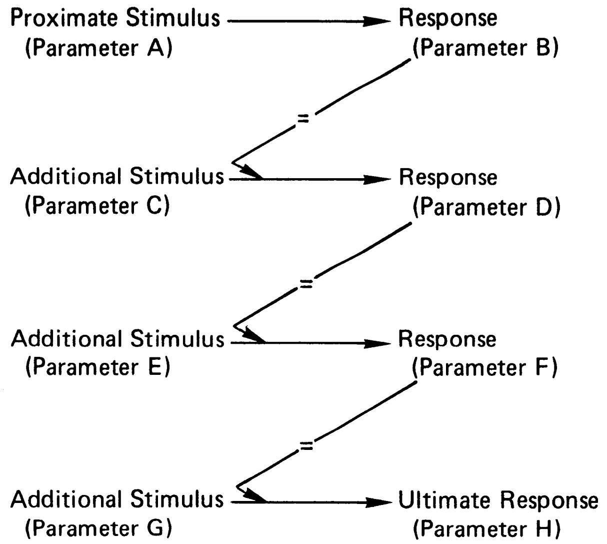

Fig. 2a. Stylized Physiological Pathway

Fig. 2b. Empirical Simulation of Physiological Process.

Note that the empirical simulation has simplified the physiological process by eliminating any modulating effects of the additional stimuli C, E, and G. In any circumstance where C, E, or G would significantly alter the ultimate response (H) the empirical simulation will give erroneous results.

TABLE 1a. *'Short-cut' parameters used to determine urinary output of a substance.*

Parameters
Circulating blood level of excretable substance
Urine Flow
–Urine Concentration of excretable substance

TABLE 1b. *Some of the 'process-oriented' parameters that should be considered in a determination of urinary output.*

Parameters
Circulating blood level of excretable substance
Arterial blood pressure
Renal blood flow
Glomenular Filtration rate
Proximal tubular function
Counter Current phenomena
Distal tubular function
Anti-diuretic hormone levels
Collecting duct exchanges
Urine flow
Urine concentration of excretable substance

Obviously the three parameters in Table 1a can only produce realistic answers under very restricted conditions for a restricted number of substances.

operation to insure that it is always functioning within the range where it faithfully represents physiological processes. A systematic approach which could help the programmer decide when to eliminate physiological interactions with minimal effect on the accuracy of the simulation would be very helpful.

A Systematic Approach

In designing a simulation the first step must be to define the system to be simulated. For a physiological simulation this involves gathering a comprehensive collection of articles, monographs, books, etc. which reflect the current knowledge of the system. This collection is then employed to construct a diagrammatic chart indicating all documentable parameters and relationships. The relationships can be indicated by lines from one parameter to another with an arrow to indicate the direction of the effect in the relationship's normal range. A separate chart is constructed listing each relationship with notes, formulas, and bibliography.

Once constructed the diagrammatic chart can be used as the basis for subsequent development, the ideal simulation would use the diagrammatic chart without modification. To reduce the complexity of the chart it is examined for stimulus/response relationships. Where no other parameters mediate the relationship the stimulus/response parameters can be removed from the chart by connecting the input parameters of the stimulus side of the relationship to the output parameters of the response side of the relationship. This process can continue to the elimination of many stimulus/response relationships and while the simulation would become increasingly imprecise, the programmer would be aware of exactly where those imprecisions occur. Further, the simulation would always model the total defined system with all pathways closed, albeit simplified. Physiology can be divided into a number of logical subunits each of which can be treated in this fashion. By allowing free overlap and interchange between the subunits a number of simulations can be developed which can be connected to create simulations covering progressively larger areas of physiology. Such a series of simulations might be quite valuable if coordinated with the sequencing of systems taught in an accompanying course.

The transition from diagrammatical chart to formulas consists of coordinating the original equations with the chart alterations. Where dissenting views or no formulas are present, some compromise must be worked out; however, the documentation must clearly state the dilemma, the sources of the dissenting views, and the compromises. The use of a table of values should be avoided except as a last resort.

To be sure, this method entails a considerable amount of effort to each step. However, this process carries the benefit that every increment can be offered for peer review. Different groups could concentrate on different physiological systems, and changes could be implemented with minimal effort as new findings emerged. As with any research endeavor, future revisions would be suggested by gaps and contradictions in the literature. Simulations are not easy to develop; but until they are programmed to reflect adequately the complex interrelationships of real physiological systems, they will not demonstrate the subtleties of those systems or achieve their full potential as learning experiences.

ACKNOWLEDGEMENTS

The authors wish to express their gratitude to Mr. Victor E. Church for reviewing this paper and to Mrs. Sun-Ying Yeh for assisting in manuscript preparation.

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APS FALL SCIENTIFIC MEETING

October 9-14, 1977
Diplomat Resort and Country Clubs
Hollywood, Florida

Scientific sessions will be scheduled from 9 a.m. to 4:30 p.m. Monday through Friday, with the exception of Wednesday afternoon. Each half-day period will consist of one symposium and simultaneous sessions of volunteer papers presented either in slide or poster sessions. The Bowditch Lecture will take place on Tuesday and the Society Business Meeting will be held on Thursday.

PROSPECTS FOR GRADUATE EDUCATION AND JOB OPPORTUNITIES IN PHYSIOLOGY†

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This paper presents best guesses as to the number of professional physiologists in the U.S., the number of graduate students, their support, numbers needed for replacement and possibilities for growth.

Several sets of data agree that professional animal physiologists comprise about 7 percent of basic biomedical scientists. The most accurate tabulation is probably that in the 1976 report of the National Research Council on Personnel Needs and Training for Biomedical and Behavioral Research. Table 1 lists the numbers in various biomedical professions as of 1973; the entries add to less than the total biomedical population because certain categories are omitted as not relevant to our discussion. In 1973 out of 26,380 basic medical professionals (47,271 biomedical scientists), 3,380 were rated as physiologists. By extrapolation for an annual growth of about 5 percent, the current number (1977) is estimated as slightly above 3,800. This checks well with membership in APS in which the numbers of persons whose primary profession may not be physiology appears to be balanced by physiologists who are not APS members. We can, therefore, take the figure of 7 percent of total biomedical scientists and slightly fewer than 4,000 as our professional population.

Employment figures compiled in 1976 are given in Table 2. Nearly 75 percent of physiologists are in academic positions. The number in industry, especially in pharmaceuticals, is surprisingly small.

The age distribution of physiologists (Table 3) is not favorable for employment of the present 30-40 year age group. There will be several qualified young physiologists for every tenured position opened by retirement of an older member.

TABLE 1. *Identified professional Ph.D.'s in selected areas 1973*

Biomedical Science	Total	47,271
Physiology		3,380
Biochemistry		7,442
Anatomy		1,672
Pharmacology		2,374
Biophysics		1,206
Microbiology		3,812

Physiologists are 7% of total biomedical scientists, 12.8% of basic medical scientists.
Data selected from Table 3.2 page 41 of NCR Report 1976.

TABLE 2. *Employment of physiologists in 1976*[1] *(Percentages)*

Academia			Non-Academic Employment			
Medical Schools	Universities	Other	Business	Pharmaceutical Industry	Govt.	Other
35	33	6	4	2	9	13

Data supplied by National Research Council.

[1] Editor's note: Distribution by employment of members of the American Physiological Society was recently published in The Physiologist, Vol. 20(2):17, April 1977.

The total number of physiologists in training is more difficult to ascertain than the number of practicing physiologists. According to the NRC survey only 38 percent of students who begin graduate training in physiology complete the Ph.D. requirements. This high attrition may result from the entrance of many premedical students into graduate programs in physiology. Some of these students succeed in obtaining admission to medical or dental school, others give up the struggle and drop out of graduate training.

In 1975 some 3,892 Ph.D. degrees were awarded in basic biomedical science. Of these 315 or 8 percent were considered to be in physiology. On the basis of our population figure of 7 percent the number would be 292. It is reasonable to take 300 as an average annual number of doctorates who consider animal physiology as their primary discipline, even though the degree may bear a different label.

TABLE 3. *Age distribution of physiologists in 1973 (Percentages)*

<30	30-39	40-49	50-59	60-69	>70
5.7	44.5	31.5	11.5	6.5	0.4

From Table 3.2 of NCR Report.

TABLE 4. *Total Predoctoral Students in Physiology*

Predoctoral Student		Ph.D's Awarded
Estimate for 1975:		
Biomedicine	23,365	3,984[1]
Physiology	1,635[2]	292
Calculation from 1974 support tables:		
Federal	544[3]	
Non-federal	804	
Self	401	
Total	1,749	

Data calculated from Table 11.2 of NRC 1976 report.

[1] If Ph.D's awarded = 1/6 of total (23,365) predoctoral biomedical students.

[2] If physiology students = 7% of total (23,365).

[3] 367 NIH and 262 other Federal Fellowships and Traineeships.

Table 4 presents estimates of total numbers of physiology graduate students. If 6 years are required from entrance to completion of a Ph.D., on the basis of 300 Ph.D.'s annually, there are currently 1,635 physiology graduate students. From tables indicating sources of financial support the number is 1,749 which is in reasonable agreement. Hence we conclude that there are 1,650-1,700 graduate students in physiology for an annual production of about 300 Ph.D.'s.

†Paper presented at the annual meeting of the Chairmen of Departments of Physiology, April 4, 1977.

Sources of support for predoctoral students in basic biomedical science are shown in table 5a. In 1974 the total NIH support in basic biomedical sciences was for 5,244 students of which 367 were estimated as being in physiology. This represented a decline of 13.2 percent between 1972 and 1974. However, at the same time support by universities and state funds increased by 17 percent and self (or wife) support increased by 19.9 percent. It is difficult to estimate the training grant support for physiology by the various National Institutes of Health because of different designations. Table 5b shows that for the National Institute of General Medical Sciences (NIGMS) the total number of trainees in the new program in systems and integrative biology plus the old physiology program is currently 279 or 6.8 percent, a value close to our earlier estimate of 7 percent for physiologists in basic biomedical sciences. Thus training grants in NIGMS support about 17 percent (279 out of 1,675) of graduate students in physiology. It is concluded that support from training grants has shown a modest decline during the past few years but that this has been more than compensated by increases in institutional and individual (self) support. If training grants were completely abolished there would remain some 1,395 graduate students in physiology. The decline in training grants may be more important qualitatively than quantitatively in that the departments receiving these grants are rigorously screened; other types of support are not so controlled.

To estimate the number of positions available due to retirements, deaths and transfers out of academic physiology, some attrition value must be assumed. On the basis of 3,800 professional physiologists, an attrition of 5 percent would require 190 new physiologists annually. This is a generous estimate and the true attrition rate is probably smaller. However, even this estimate is 100 fewer openings than the annual Ph.D. production.

It must be concluded that *for replacement alone, at least one out of every three Ph.D.'s in physiology will not find a position.* This is a frightening prospect for graduate education in physiology.

It is most unlikely that many competent young people who are highly motivated to become physiologists will stop their professional training because of a 1:3 balance against employment. This prediction is supported by the observed increase in local and self-support. Also departments across the country are not likely to reduce their graduate enrollments by one-third. The only solution to the preceding dismal dilemma is to create new needs for physiologists. What are the prospects for such new opportunities which would provide some 100 openings per year?

First, some expansion of needs in medical education is probable. The NRC report clearly shows that since 1962 the number of medical students and the number of clinical faculty have increased much more than has the number of basic science faculty. Further increases in numbers of students are projected for many medical schools. Also, there seems to be a trend away from the "fad" of teaching basic sciences in the departments of medicine and some trend toward reinstatement of more laboratory instruction. Thus, to match the increase in clinical faculty and students and to provide a better curricular balance, more physiologists will be needed. In part, the slower increase in physiologists than in clinical faculty results from our committment to cellular and molecular physiology. This is fine for research but our students should be prepared to teach the systems and organ physiology which clinicians need.

TABLE 5a. *Primary support for predoctoral students in Biomedical Sciences (1974)*

	Totals	Type of Support		Change 1972-1974
Total Federal	7,770			-13.6
Total NIH	5,244	Fell/Tr	3,746	-13.2
		RA	1,364	
		TA	49	
		Other	85	
Total Non-Federal	18,893			+16.2
Total Institution/ State	11,414	Fell/Tr	1,522	+17.0
		RA	2,001	
		TA	7,231	
		Other	654	
Self, Loans, etc.	5,736			+19.9

Calculations based on NCR Report and on information supplied by NIGMS.

TABLE 5b. *Predoctoral trainees supported by NIGMS in selected biomedical subjects*

	1975	1976 and 1977		
Biomedical Engineering	137	110		
Systems and Integrative Biology	48	79	(Physiology)	279 or 6.8%
		34	(Bioengineering Systems)	
Physiology	255	166		
Microbiology	222	156		
Anatomy		114		
Biochemistry		389		
Cellular and Molecular Biology	351	524		
Total for biomedical sciences	4,015			

Data supplied by NIGMS.

Paramedical programs continue to proliferate, e.g., programs to train "doctors' aids", and these will require more instruction in physiology. Finally, in non-human medicine, specifically veterinary medicine, there is much public pressure for expansion. Unfortunately some schools of veterinary medicine have failed to appreciate their need for professional physiologists. The number of new positions for teachers of physiology to medical students, paramedical students and potential veterinarians cannot be estimated from available data but some expansion seems probable.

A second area of possible expansion is in general university departments. The number of professional physiologists in departments of biology is relatively small. In general, the rewards in such departments have been less than in medical schools, but as a profession we have much to offer. There is real need for the teaching of sound physiology in biology departments. As professionals, we must expand our teaching in cellular and comparative physiology, in biophysics and in biomedical engineering and must be prepared to offer more courses to undergraduate students. Demographic data show the number of young people of college age will decline during the next decade, hence administrators who calculate staff needs from "full time equivalents" are not likely to expand university faculties very much. Some expansion in ongoing (adult) education is inevitable.

A few institutions are moving toward a British type of medical curriculum in which qualified undergraduates are enrolled early in a medical program. There is good reason for offering basic medical science to some upperclass college students. This trend will likely increase the total number of students taking physiology and thus increase the need for teachers.

A serious consequence of attrition in academic positions is the loss of the powerful influence of young professionals in research. The originality of young investigators is well known and to reduce their numbers in research will be a national loss. One proposal under NSF consideration is for that agency to provide salary for faculty who are within six years of retirement provided that the university uses equivalent funds to hire young scientists. Early retirement alone is not the answer because this deprives departments of the wisdom and talent acquired with years of service.

A third expansion is outside of traditional academic positions. We have trained our Ph.D.'s to be carbon copies of ourselves. This trend to self-replication is satisfying for the mentor but it does not provide the breadth which is needed if our graduates are to seek positions outside of academia. Many problems of modern society could well use the viewpoints and techniques of physiologists. Unfortunately, matching training and trainees to problems of society is difficult. A few examples may be mentioned. In environmental science there has been very little use of physiologists, yet problems of adaptedness to the environment are well known to physiologists. We seem not to have trained properly to interface with ecologists. Problems related to adaptation include aspects of food production and effects of man-made toxins. The number of physiologists in pharmaceutical companies and in federal agencies such as FDA is surprisingly small. Drug abuse is another area where physiologists could make more of a contribution. Matching food production to population growth is an urgent need and too few physiologists are now working in nutrition, animal (including fish) husbandry and population control. The energy problem is most urgent and in some aspects of its solution physiologists should be used. Not only can our graduates be of service in these fields but they will often find as much satisfaction in solving applied problems as in basic research.

It is essential that graduate programs be broadened so that physiologists can be useful in non-academic positions. Also it is essential that our profession, perhaps our societies, should publicize what physiologists might contribute toward solution of problems of society. We need better popular writing and speaking.

Despite the possible expansion of openings for physiologists as just described, it is unlikely that we can continue to place the 300 or more Ph.D.'s produced per year. The logical conclusion is that our graduate programs must emphasize quality rather than quantity and must cut back in number of Ph.D.'s produced. This is difficult but we have a responsibility to our profession, to our students and to society to produce only the best. Admissions must be more carefully scrutinized. Training programs must provide more breadth while not losing depth in research. The problem of quality control has been often discussed by APS councils but any serious consideration of accreditation has been avoided. Yet we know that some physiology departments are offering doctoral programs which are narrow and non-rigorous. Perhaps a statement of what is needed in a proper graduate program to train physiologists for the future should be issued by APS. It is difficult to set a figure of desirable reduction in number of Ph.D.'s produced but a decrease by 15-20 percent is not unreasonable.

My conclusions are as follows: We can no longer act selfishly as we did in the sixties. If there is no expansion of opportunities only two in three of our Ph.D.'s will find appropriate employment. Further reduction in NIH training programs will not reduce the total number of graduate students significantly and it may result in serious reduction in quality. There can be some expansion in employment opportunities if we are aggressive in promoting physiology as a useful profession. How far this expansion can go is uncertain, hence we would be wise voluntarily to reduce our graduate training programs in such a way as to emphasize quality rather than quantity.

BOOK REVIEWS

Signal Analysis and Pattern Recognition in Biomedical Engineering (G.F. Inbar, editor) John Wiley & Sons, Keter Pub. House Jersualem Ltd., 1975

Three years ago, an International Symposium on Signal Analysis and Pattern Recognition in Biomedical Engineering was organized by the Julius Silver Institute of Biomedical Engineering Sciences and held at Technion-Israel Institute of Technology, Haifa, Israel. The Proceedings, were published a year later, and are now reviewed (two years after that) in the Physiology Teacher, because they contain certain very straightforward papers of particular value to teachers and graduate students not only in neurophysiology, but in other areas as well. The thoughtfulness of these presentations and the candor of the brief discussions are certain to involve any physiologist in basic issues of methodology and interpretation. Since much of physiology is still phenomenological rather than analytical, there is a widespread anxiety about appropriate methods capable of generating a more basic understanding of physiological functions. Signals and patterns are all we have to go on. From these we work back to some descriptor of the system.

It is almost a given that physiological data, usually contain mixed (or confounded) information which are recorded as an "output" time-series. If conclusions are to be drawn about process, where at least two effects appear comingled, "In general, it is impossible to obtain guidelines about the scale of the first effect without establishing the magnitude of the second", Sayers, p. 4. Again, Stein questions Adey on the basic strategy of brain research, p. 119, as follows: "In a state where there is this much controversy about mechanisms of rhythms which we have known for forty years, I wonder if the right approach is to use the full armamentarium of computional techniques . . . Maybe what is really needed is to get down to some basic work and find out what the mechanisms really are." To which Adey responds by describing a possible mechanism, as he sees it. In doing this, a testable hypothesis is presented and the illustration transforms into questions of validation and generality. This reviewer finds such exchanges exciting and a far cry from "survey" monographs. We do not feel pushed to believe every suggestion. Hence the breadth and the richness, both of the biological phenomena investigated and of the diverse techniques of signal analysis, are preserved.

The book begins with three general chapters on patterns and signal analysis, from three points of view. Then, part two considers computer processing (four chapters). Part three is on brain processing of signals, considered as a set of problems in pattern recognition. Finally, there are four chapters on modeling specific data processing problems, including redundancy and multi-channel information transfer.

Just the titles of the chapters are intriguing — "Science and Judgement in Biological Signal Analysis", a very carefully developed plea for an analysis of phase-spectral patterns in addition to amplitude spectra, by B. McA. Sayers. "A Journey into the Brain" turns out to be experiences with the Friedman scheme for increased sensitivity of signal detection by template matching, from A. Abeles. Abeles is able to record from 60 cells in the cylinder 1500μ long and 40μ wide as an electrode is inserted, with minimal or no affect of the electrode itself on spike activity. Thus the concept of silent cells in the brain has to be questioned. Gath and Inbar describe their procedures for "Automatic Analysis of Motor Unit Firing Patterns" which, depending on the coefficients of variation for the separate processes, may be able to separate as many as ten concurrent oscillatory processes.

There are chapters on human motor control systems by R.B. Stein, on sophisticated analysis of the EEG by W.R. Adey, each with consideration of clinical implications. Caceres discusses computerized electrocardiography and there is a chapter on "Estimation of Cardiac Output from Respiratory Data" by Etsyon, Chayan, Itzkovitz and Bursztein from Haifa. The topics represent a tantalizing mixture of superb state of the art reports which are ideal starting points for students interested in where physiology will go in data processing in the next decade. There is a real revolution underway, with which the standard teaching department has difficulty. One of the ways to understand the widening world is through books such as this one.

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Regulation Of Depressed Metabolism And Thermogenesis (J. Janský and X. J. Musacchia, editors). C. C. Thomas, 1976. ($23.75)

This book is derived from introductory lectures presented at the Satellite Symposium, "Depressed Metabolism and Cold Thermogenesis," held in conjunction with the XXVIth Congress of the International Union of the Physiological Sciences. The symposium was held in Prague in 1974.

The coverage of the book is quite broad but major emphasis has been placed on the regulation of non-shivering thermogenesis, and brown fat (BAT) metabolism in particular. The book contains 14 chapters contributed by recognized experts in this field. Each chapter is clearly written and complete within itself. However, the sequence of the chapters might have been rearranged for better continuity.

The initial three chapters deal peripherally with the subject of non-shivering thermogenesis but provide a review of the recoding of electrical signals as they proceed from the peripheral thermoreceptors to the cerebral cortex; the thermo-integrative function of the hypothalamus, and the question of cold adaptation in the human. Other chapters characterize the diversity of experimental approaches to an understanding of non-shivering thermogenesis and BAT metabolism. Studies of the changes in composition of BAT cell membranes and BAT cell mitochondria during hibernation and stimulation by norepinephrine are described. The interaction of norepinephrine with receptors of BAT during calorigenesis is brought into focus, as is the possibility that thyroid hormones may play a permissive role in norepinephrine-induced calorigenesis. Several chapters emphasize the importance of organs other than BAT in the increased thermogenesis induced either by cold exposure or by administration of norepinephrine. An important metabolic role for skeletal muscle in non-shivering thermogenesis of the cold acclimated rat now seems likely.

During onset of hibernation in the hamster, turnover of serotonin in brain increased 14 fold compared with that observed prior to hibernation. It is suggested that the activation of serotonergic pathways at this time favors increased heat loss in preparation for hibernation. The question remains as to which hibernating process is critically related to the increased turnover of serotonin.

A chapter on induced hypothermia (80:20 helium-oxygen mixture) pursues the thesis that survival time in hypothermia can be lengthened if the time for induction of hypothermia is reduced (by shaving the hair) and if glucose is infused into the hypothermic hamster to maintain blood glucose at 40 to 50 mg%. Under these conditions, hypothermic hamsters (rectal temperature 7°C) survived for 100 hours. Renal filtration and tubular secretion were measured in hypothermic hamsters by means of $^{99m}T_C$-labelled red cells (filtration) and ^{131}I-hippuran (secretion). At rectal temperatures below 9-10°C, renal function was minimal. During rewarming, secretory function appeared to occur at temperatures where no filtration was observed. This interesting technique offers the opportunity to investigate more completely renal function during hypothermia in other species.

The authors dedicated this volume as a tribute to the contributions of two distinguished investigators to the field of temperature regulation, Dr. J. S. Hart and Dr. L. D. Carlson. A tribute to Dr. Hart was written by Dr. F. Depocas and a tribute to Dr. Carlson was written by Dr. A.C.L. Hsieh. Those who knew Drs. Carlson and Hart will be pleased both with the written tributes and the book dedicated to them.

This book should be of interest to all those in the field of thermoregulation and especially to those interested in hibernation, hypothermia and brown fat metabolism. Although the importance of this fascinating tissue for temperature regulation and its role in hibernation remain unclear, the significance of this volume may be in its attempts to highlight those areas of brown fat research where additional studies are needed.

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Introduction to Research in Medical Sciences, A. Cuschieri & P. R. Baker, Churchill Livingstone, London & New York, 205 pages and 10 pages of indices 1977 (Soft cover $10.50)

This is a book that would be of value to anyone contemplating research in the biologic or panmedical sciences, altho its messages are directed to the young graduate in medicine who would elect to do investigative work. The book reflects the research experience of the authors, one of whom was a clinician.

A broadly based introduction to research in so small a book would necessarily be limited in the material to be covered, and this is especially true of the chapter on laboratory animal care and of the chapter on basic techniques in animal experimentation. But the chapters on physicochemical properties of matter, on analytical techniques, on *in vivo* measurement of biologic phenomena, on clinical trials, and on analysis of data were very well epitomized.

A working knowledge in the basic sciences is presumed, but after each chapter a number of references are given so that the student may review those areas in which he may need more information.

The book fills a need in that it covers all aspects of research in the panmedical sciences. It would be especially valuable to those investigators who would participate in the guidance of developing scientists.

N. R. Brewer

Discovery Processes in Modern Biology Edited by W. R. Klemm with thirteen contributors to individual chapters. 334 pages and 4 pages of indices. Krieger Publishing Co., Huntington, New York, 1977

As if inspired by Watson's *The Double Helix* this book stresses the human side of research. Each of thirteen authors writes his own partial autobiography. They tell of early experiences that directed them to their way of life, and of the frustrations and the ecstasies that are the human part of discoveries. The book is written in non-technical language, but throughout the reader is impressed with the ability of good scientists "to see what others have looked at all along without really seeing."

All of the authors are still living and are still active. Each contributes in his own style. Although each author is an individual, there were some common denominators.

(1) Each had a hunger for knowledge and a talent for creativity.
(2) In each case there was a long "incubation period" of active work in an area of investigation before the great creative period developed.
(3) Each of the scientists was subjected to a great deal of criticism of their work.
(4) As is true in all scientific effort, there was the emphasis that the failure of an experiment is not a waste. What is learned is that one more approach will not work, and often, in trying to learn the reason for the failure there may be uncovered a hitherto unrevealed mechanism.
(5) Throughout the book the importance of basic science is emphasized.

N. R. Brewer

EDUCATION

Graduate enrollment decreased in five of six major fields between fall 1975 and 1976, according to a survey of 354 graduate schools conducted by the Graduate Record Examinations Board for the Council of Graduate Schools. Master's and doctorate enrollment increased 2.7% in the biological sciences but declined in every other field.

	Public	Private	Total	
	1976	1976	1976	Change from '75
Education	155,501	29,846	185,347	−5.4%
Humanities	61,989	18,940	80,929	−4.4%
Social Sciences	101,435	41,495	142,930	−1.8%
Physical Sciences	38,264	12,617	50,881	−0.2%
Engineering	33,383	17,341	50,724	−1.3%
Biological Sciences	71,751	17,081	88,832	2.7%

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