

AC 2008-1467: PHYSIOLOGY CONCEPTS AND PHYSIOLOGY PROBLEMS FOR BIOMEDICAL ENGINEERING STUDENTS

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Physiology Concepts and Physiology Problems for Biomedical Engineering Students

Abstract

Physiology is a core element of an undergraduate biomedical engineering curriculum, although programs differ in whether the biomedical engineering faculty or biology faculty teach these courses, and in whether physiology is taught in stand-alone courses or incorporated into other courses. Here we first present an analysis of the concepts and topics in physiology that are viewed by biomedical engineering faculty and by representatives of industry as being most important for biomedical engineers to learn. We also provide information on the importance of other topics in biology for the biomedical engineering curriculum. Biomedical engineering students need to be able to work with quantitative aspects of physiology and need practice applying engineering concepts to physiological systems. However, many physiology texts appropriate for undergraduates avoid quantitative analysis, and provide few problems to develop the students' use of mathematics or engineering tools in the context of physiology. As a result, we have begun the development of a resource of quantitative homework problems from which individual problems can be selected and linked to any physiology course.

1. Introduction

Physiology is a core element of an undergraduate biomedical engineering curriculum, with 98% of accredited US biomedical engineering and bioengineering undergraduate programs requiring an identifiable course in physiology.¹ Indeed, the requirement for physiology is a defining difference between biomedical engineering curricula and biological engineering curricula, most of which require microbiology but not physiology.² However, knowing that a course is required does not define the content that is delivered to the students, so we have surveyed representatives from academia and industry to establish what topics in physiology are regarded as being most important for biomedical engineers to know. One can argue that all physiological systems are related, and in an ideal world all biomedical engineers might be required to learn about all systems. This is not always practical within the crowded undergraduate engineering curriculum, and our analysis allows programs to prioritize the topics that are covered.

Biomedical engineering programs also tend to require coursework in biochemistry, molecular biology, cell biology and genetics, and a few require coursework in bioinformatics. We have found that 88 % of accredited US programs require biology courses in addition to physiology.¹ For this reason, we have also identified the topics that are viewed as important in these other areas of biology, although somewhat more coarsely than physiology, which has been our focus.

While physiology is an important topic, instructors are faced with the difficult job of finding a text and other resources that are appropriate for their students (generally sophomores or juniors). The problem with all existing textbooks at this level (not an exaggeration) is that they contain few quantitative relationships, few, if any, problems to solve, and no sense of how

mathematics or engineering topics relate to physiology. Each of these deficiencies exists despite the fact that research in physiology is highly quantitative. Publishers generally claim that the market is too small for an entry level quantitative physiology book (D.U. Silverthorn, personal communication). There are some simulation packages and computer labs that attempt to address this shortfall, particularly in the neural and cardiovascular areas, but large areas of physiology are not served in this way. A number of books are also available that contain problems, and for reference, a selection of these is provided in Table 1. Integrating their problems into a course is never easy, however, and in the authors' experience, problems taken from other sources generally require modification. Consequently, experienced instructors gradually build up their own stock of problems, at great effort. The paucity of problems that are easy to access has prompted us to begin the development of a resource for biomedical engineering, with the further advantage that it uses the novel and powerful learning technology developed by the VaNTH (Vanderbilt-Northwestern-Texas-Harvard/MIT) Engineering Research Center in Bioengineering Educational Technologies, which can be accessed electronically and has several learning advantages, which are discussed below.

Table 1. Selection of books containing quantitative physiology problems			
Problem Books			
Michael, JA and Rovick, AA	<i>Problem Solving in Physiology</i>	Prentice Hall	1999
	Problem solving strategies; conceptual problems; some relatively simple quantitative problems		
Tiger, S, Kirk, JK, and Solomon, RJ	<i>Mathematical Concepts in Clinical Science</i>	Prentice Hall	2000
	Very simple mathematical concepts with which engineering students should already be familiar		
Davidovits, P	<i>Physics in Biology and Medicine</i>	Elsevier	2001
	Relatively easy (no calculus) problems in biomechanics, fluids, heat and temperature, membrane physiology		
Areas of Physiology			
Johnston, D and Wu, SM	<i>Foundations of Cellular Neurophysiology</i>	MIT Press	1995
	Text with a wide range of problem difficulties. Solutions provided		
Mines, AH	<i>Respiratory Physiology, 3rd ed</i>	Raven	1993
	Text with solved problems suitable for BME or medical students		
Koushanpour E and Kriz W	<i>Renal physiology: principles, structure and function</i>	Springer	1986
	Comprehensive text including solved problems		
Weiss, TF	<i>Cellular Biophysics. V.1. Transport; V.2 Electrical properties</i>	MIT Press	1996
	Comprehensive text with problems from simple through advanced (those needing differential equations); not solved		
Advanced Books			
Keener, J and Sneyd, J	<i>Mathematical Physiology</i>	Springer	1998
	Modeling, differential equations, other math applications in physiology. Solutions to exercises not provided.		

2. Methods - Identifying important concepts in physiology and other areas of biology

The VaNTH ERC has done a Delphi Study^{3,4} to identify important topics in the biomedical engineering curriculum^{5,6}. We used the ZoomerangTM survey tool (www.zoomerang.com) to ask participants in the first iteration of the study how important it was to include each of 274 individual topics in the required undergraduate biomedical engineering curriculum. The topics comprised 11 engineering domains, physiology, and four other areas of biology. Each concept was presented as a questionnaire item and was rated on a 5 point Likert scale, with 5 indicating “very high importance for all bioengineers”, and 1 indicating “very low importance for all bioengineers.” A rating of 3 represented “moderately important,” and an additional category was provided for “No Opinion.” For each domain, respondents were asked about their level of expertise on a similar five point scale. A full analysis of this work is beyond the scope of the present paper, and only the results for biology and physiology will be presented here. The concepts for these areas were based on analysis of the contents of standard physiology and biology texts, as well as domain-specific taxonomies developed by VaNTH researchers. Physiology was investigated in some detail by including 82 topics. A few topics were simply identified as a system “overview,” and a few others might more properly be categorized as anatomy rather than physiology. To keep the length of the survey reasonable, other areas of biology, including biochemistry (8 topics), cell biology (7 topics), molecular biology and genetics (13 topics) and bioinformatics (8 topics) were queried at a coarser level. The exact wording used for each topic, and the raw data containing average ratings by industry and academic participants, are available⁷ and are given in the appendix of this paper. Ratings of the topics were analyzed in several ways, as described below.

Because of its length, each participant was asked to complete just half of the full survey, although a few individuals completed both halves. The biology concepts (biochemistry, cell, molecular, bioinformatics) were in Part 1 of the survey, and were rated by 42 participants from academia and 25 from industry. The physiology concepts were in Part 2 of the survey and were rated by 35 participants from academia and 22 from industry. Both the company and institutional affiliations of the respondents were broad, with the participants’ backgrounds and expertise covering all areas queried. The sixteen companies and 33 universities from which the participants were drawn are listed in Tables 2 and 3.

Companies	Areas of Expertise
Abbott Laboratories	Biomaterials
AstraZeneca	Biomechanics
Baxter Healthcare	Bioinformatics
Boston Scientific	Bioinstrumentation
Cardiodynamics	BioMEMS
Cleveland Medical Devices	Biotransport
Datasciences, International	Cellular Biomechanics

Dentigenix, Inc.	Computational Modeling
Table 2 continued	
Companies	Areas of expertise
Depuy, a Johnson & Johnson Company	Control Systems Engineering
ESTECH Least Invasive Cardiac Surgery	Fluid Mechanics
GE Healthcare	Medical Imaging
Intel, Corp.	Medical Optics
Materialise, Inc.	Signal Processing
Medtronic, Inc.	
Tyco Healthcare	
Underwriter Laboratories	
United States Air Force	

Table 3. Universities Represented in Biomedical Engineering Key Content Delphi Study, Round One (n_{Academia} = 77)	
Arizona State University*	Stanford University
Binghamton University	Syracuse University*
Boston University*	SUNY - Stony Brook
Columbia University	Tulane University*
Devry University	University of Akron*
Duke University*	University of Cincinnati
Florida International University	University of Illinois, Urbana-Champaign*
Illinois Institute of Technology	University of Iowa*
Johns Hopkins University*	University of Michigan
Marquette University*	University of Minnesota*
Milwaukee School of Engineering*	University of Pittsburgh*
MIT	University of Rochester*
NJIT	University of Texas - Austin*
NC State University*	University of Toledo*
Northwestern University*	Vanderbilt University*
RPI*	Virginia Commonwealth University*
RHIT	
*ABET accredited at time of survey. 21 of 37 accredited programs participated.	

3. Delphi study results

3.1 Data analysis

Table 4 shows the average self-rating of expertise in each domain, and the average percentage of topics that were given ratings of “no opinion” in each domain. Consistent with the

longstanding importance of physiology to the field of biomedical engineering, this was the area in which participants judged their expertise to be highest, and correspondingly, the area where they chose the “No Opinion” response least often. Next to physiology, both groups had greater expertise in biochemistry and in cell biology than in molecular biology & genetics or bioinformatics. (Note that a value of 3 still indicates moderate expertise.) In the latter two areas, the fraction of “No Opinion”’s was above 25% for industry. It was generally participants who had lower expertise who chose not to give opinions on particular topics, so the expertise of those participants whose ratings are considered below was higher than the average expertise in Table 4.

Table 4. Average self-rating of expertise in the domains examined and percent of questions receiving a response of “No Opinion” as opposed to a Likert scale value. Self rating was on the scale of 1 – very low expertise, 2 – low expertise, 3 – moderate expertise, 4 -high expertise, 5 – very high expertise. The percentages were determined by obtaining the percentage of “No Opinion” scores for each question, and then averaging these values across the domain. It was observed that the percentage was relatively consistent across a domain.				
	Academia		Industry	
	Average Expertise	% No Opinion	Average Expertise	% No Opinion
Biochemistry	3.08	19	3.08	19
Cell Biology	3.31	15	3.04	16
Molecular Biology & Genetics	2.74	13	2.59	28
Bioinformatics	2.29	23	2.54	26
Physiology	3.79	7	3.90	11

It is cumbersome to report the values for ratings of each concept by each participant, but simply taking the average value for a concept across the population has two limitations. First, an average is not necessarily valid for a non-interval scale such as a Likert scale. In order to make the averages more meaningful, we chose to identify the value of 3 as “moderately important,” rather than “no opinion,” so, while the distances between the elements of the scale are not necessarily equal, they are at least monotonic. Second, simply taking an average value loses the variation within the academic and industry groups, but representing an error measure for all concepts would also obscure trends in the figures and tables that follow. One way to represent the variation is to use histograms of responses to individual questionnaire items. Such histograms are shown in Figure 1 for a small number of items. Figure 1A shows histograms of the two most highly rated concepts by industry and the two most highly rated by academia in the Physiology domain, with average ratings of about 4.5. Figure 1B shows concepts with ratings in the midrange of the Physiology concepts based on their average ratings, with values about 3.75, and Figure 1C shows concepts that were near the bottom of the scale, with an average rating of about 3.0. Concepts were chosen for this analysis solely on the basis of their average ratings, not on histogram shape, but within each section of the graph, the histogram shape is rather consistent. The concepts rated most highly received few if any low values and therefore have the highest priority for inclusion in the curriculum. The ones rated in the 3.74 to 3.79 range elicited an almost uniform distribution of responses between 3 and 5, and were pulled down from a rating of 4 by just a few respondents who judged these concepts to be of low importance. Concepts with averages in this range would seem to be strong candidates for inclusion in the

curriculum. The ones with the lowest averages had essentially normal distributions centered on a value of about 3, with as many individuals rating them as very unimportant as those rating them very important. Based on t-tests, a rough measure because the criterion of normality was not always met, ratings of concepts in Fig 1A were found to be statistically different than those in Fig 1B ($p < 0.05$), and those in Fig 1B were different than those in Fig 1C ($p < 0.05$). P values for most of the tests were much less than 0.05.

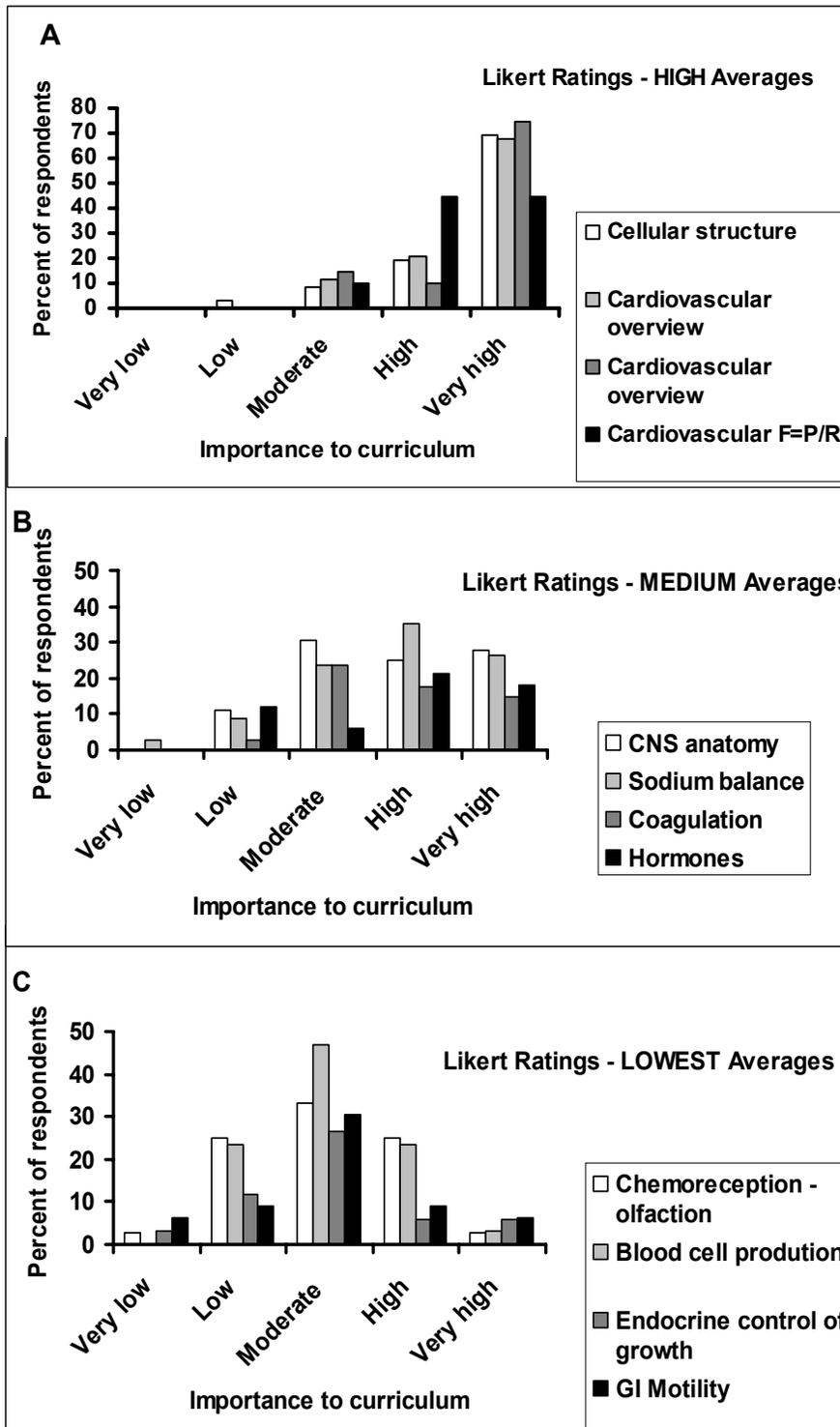


Figure 1. Histograms of ratings of selected concepts in the physiology domain. The ordinate shows the percentage of respondents judging the importance of the concept at the level indicated on the abscissa. A - The two most highly rated concepts by academia, and the two most highly rated by industry. Average ratings of 4.35 to 4.60. B - Two concepts ranked in the middle of the list of physiology concepts by academia and two by industry. Average ratings of 3.74 to 3.79. C - Concepts ranked near the bottom of the physiology concepts in terms of average score by academia and by industry. Average ratings of 3.00 to 3.06. In all cases the two darker bars are industry's ratings and the two lighter bars are academia's rankings.

3.2. Physiology concepts

Figure 2 shows average ratings of all concepts by academia and industry in the Physiology domain. Each point represents one topic. Twenty-one topics had ratings, aggregated across industry and academia, of 4.0 or greater. Twelve had ratings of less than 3.2. The full list of concepts, organized by overall rating, are given in the Appendix and are online.⁷ The appendix lists the concepts at the level of detail with which they were presented to the participants.

There are several points to be made from these data. First, industry and academic ratings are very similar for most topics, tending to cluster along a line of unity slope. While there was diversity in the rating of each concept within groups (Figure 1), there was only one concept for which the average rating between the two groups was significantly different at $p < 0.05$. This was “Platelets and Coagulation (e.g., hemostasis - platelet aggregation, coagulation; anticoagulants),” which was rated at 3.75 by industry and 3.22 by academia. Of the 82 concepts, only four additional concepts were rated differently by industry and academia at a less stringent criterion of $p < 0.1$. Second, as noted above, within physiology, all topics were considered to be at least moderately important, but there were clear preferences for certain concepts. Third, the most highly rated concepts were from a few areas of physiology: cellular, cardiovascular and neural were the most highly represented, with respiratory and renal concepts also in the top twenty. The concepts rated lowest tended to be in the areas of gastrointestinal function and endocrinology. (The lowest rated concept, “Hormone evolution,” was not further defined, and was expected to receive a low rating. It was included in the survey as a check that participants were evaluating each concept on its own merits.)

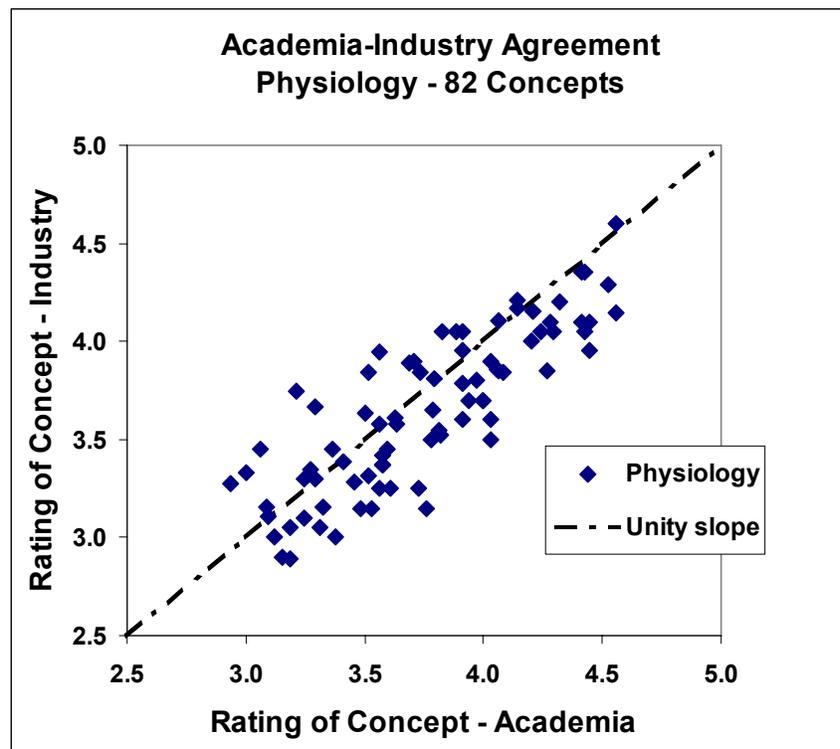


Figure 2. Average ratings of all physiology concepts by academia and by industry.

3.3 Biology concepts

Figure 3 shows the average ratings by industry and academia of the 37 concepts in the three biology domains considered, plus bioinformatics, and the Appendix lists all the concepts. For convenience, Table 3 lists the concepts on which the aggregate industry-academia rating was 4.0 or higher. Industry and academia generally agreed on the importance of these concepts, although not as well as in physiology. There was a significant difference ($p < 0.05$; t-test) between industry and academia in one topic in biochemistry, one in molecular biology, and two in bioinformatics. Using a less stringent cut-off ($p < 0.1$), three more topics were judged differently, two in bioinformatics and one in molecular biology. Disagreement on the ratings of topics in cell biology was the smallest. Biochemistry, cell biology, and molecular biology & genetics had almost equal numbers of concepts in the highly rated list.

Figure 3 shows that bioinformatics was judged least important by both academia and industry. Neither our academic nor industrial sample contained many experts in bioinformatics, but of those who did rate these topics, the industry group considered every topic more important than did academia. The four topics rated above 3.5 by industry (in abbreviated form) were: 1) Databases - Interfaces and Structures; 2) Familiarity with Online Databases; 3) Biological networks; and 4) Microarrays.

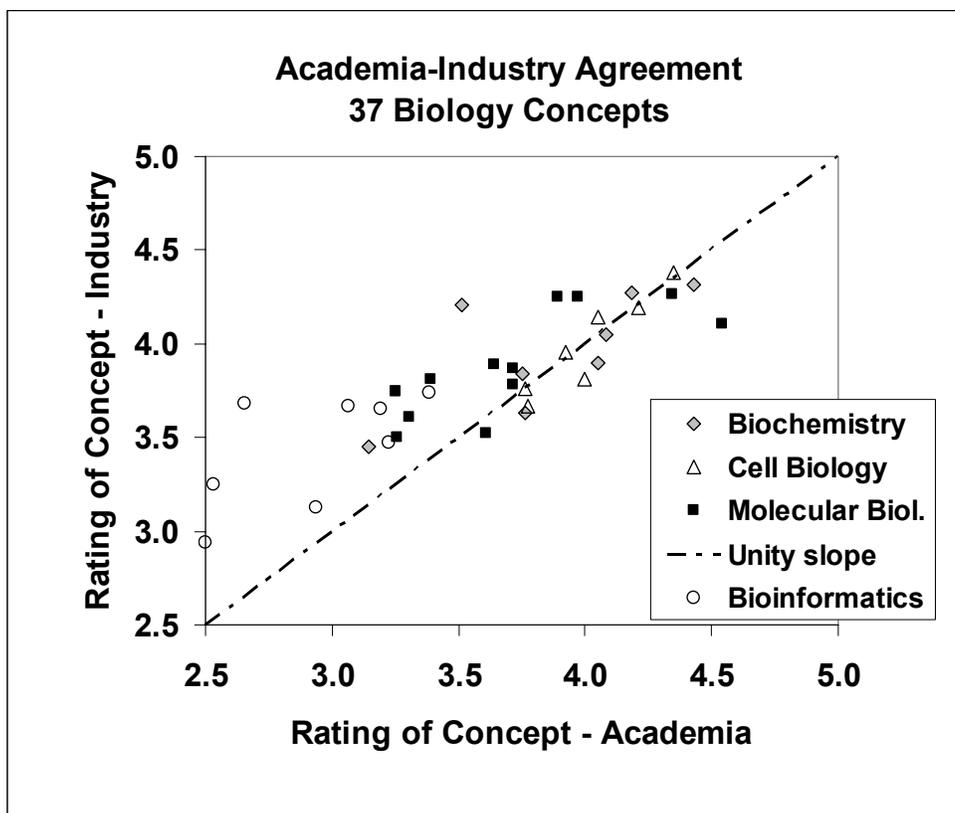


Figure 3. Average ratings by industry and academia of concepts in biochemistry, cell biology, molecular biology and genetics, and bioinformatics.

Table 3. Biology Concepts with Ratings of 4.0 or Greater		
Concept	Domain	Average Rating
Cell Organization, Organelles, Cellular and Molecular Architecture	Cell Bio	4.5
Synthesis, Structure and Function of Biologically Important Macromolecules (e.g., nucleic acids, DNA, RNA; amino acids, proteins; carbohydrates; fats)	Biochem	4.4
Flow of Genetic Information (i.e., DNA to RNA to Protein)	Mol. Bio	4.3
Properties of Genes and Chromosomes	Mol. Bio	4.3
Biochemistry of Water (e.g., polar properties; interactions with ions, small molecules, and macromolecules; hydrophobic and hydrophilic effects; vdW interactions)	Biochem	4.2
Structure and Function of the Plasma Membrane (e.g., membrane proteins; endo- and ectocytosis; phagocytosis; pinocytosis; transport)	Cell Bio	4.2
Cellular Interactions with the Environment (e.g., signal transduction, cell signaling; adhesion; motility; cell-matrix interactions)	Cell Bio	4.2
Properties and Structure of DNA	Mol. Bio	4.1
Properties and Structure of RNA	Mol. Bio	4.1
Structures and Properties of Interacting Macromolecules (e.g., hormone-receptor; substrate-enzyme; protein-DNA; immunoglobulin-antigen)	Biochem	4.1
Cellular Biosynthesis and Energetics - Mass and Energy Balances (e.g., ATP energy and transfer; aerobic glycolysis; anaerobic glycolysis; electron transfer chain)	Biochem	4.0

4. Quantitative Physiology Problems

Recognizing the importance of certain areas in the physiology curriculum, and the paucity of quantitative problems, we have initiated a project to create problems that can be done by students electronically and independent of a particular textbook. This project uses the powerful Courseware Authoring and Packaging Environment (CAPE) and Experimental Learning Management System (eLMS) that has been developed by the VaNTH ERC⁸. CAPE/eLMS problems have many features which differentiate them from problems made available through other learning management systems such as Blackboard. In a CAPE/eLMS problem, the student interacts continuously with the computer. When a student enters the answer to a problem, he or she receives feedback immediately on whether he or she is correct, and feedback can be provided, often in the form of diagnostic feedback that can tell the student what type of mistake he or she might have made or what to check for when trying again. Another important feature is the ability of the system to adapt to the needs of the learner. If a student needs practice, or more hints, the software can provide multiple attempts. If the student can do a problem immediately, the delivery pathway adapts and does not force the student into unnecessary practice. The author of CAPE/eLMS problems has the opportunity to randomize variables so that no two students get exactly the same problem, forcing each student to produce a unique solution. The CAPE/eLMS system saves a complete record of interactions for each student, so that the instructor can diagnose where a student or, extrapolating, a class, is having difficulty. Problems are graded automatically by the system, freeing teaching assistants for more valuable work. CAPE/eLMS handles a wide range of problems, and can accept text answers, multiple choice answers, fill-in-the-blank answers, and true-false answers. Special plug-ins facilitate the use of interactive graphics.

We have focused to date on producing problems in cardiovascular physiology, cellular physiology including membrane transport, and salt and water balance. Further development of problems will take advantage of the knowledge from the Delphi Study, so that problems are developed around the most important concepts. In order to make the problems compatible with many physiology classes, they contain some tutorial information for the student's reference. The problems are designed to be quantitative, although most of the problems currently require only algebra. In addition to using CAPE/eLMS as a platform, the problems use features of the How People Learn philosophy⁹ and challenge-based instruction^{10, 11} as a learning science underpinning. For instance, in a problem on salt and water balance, the challenge is "Why is it bad to drink seawater?", and, rather than giving the student all the necessary information, the student is prompted to supply some of the information. A simplified version of this problem is available as a freely accessible demonstration.¹² The problems available as of January, 2008 are listed in Table 4, along with their main learning objectives. In addition, other VaNTH authors have written problems in neuroscience and in renal physiology that will be incorporated.^{13, 14}

More problems are under development and testing, with the goal of developing a large suite from which problems could be drawn to accompany a year-long physiology course. Each problem will be accompanied by a description of the content covered in the problem. The problems can be assigned from any institution via an eLMS Blackboard plug-in, which makes the utilization very easy for both the instructor and student, and alternative methods can also be arranged if Blackboard is not available. Beta testers and additional problem developers are encouraged to be involved at the present stage, when access can be given at no charge. Ultimately, to support the expense of the servers and programmer time, it will be necessary to charge students a fee, much as a supplementary problem book would have a charge.

Table 4. CAPE/eLMS Physiology Problems	
Problem Title and Description	
1	Seawater
	Whole body mass balance on salt and water, with constraints on osmolarity
2	Salt and Water Control Diagrams
	Review of endocrine interactions in control of salt and water balance
3	Man vs. Wild
	Loss of fat, muscle, and weight during starvation
4	Urea Transport
	Passive mechanisms in membrane diffusion
5	SodiumPotassium (transport energetics)
	Energetics of the Na ⁺ /K ⁺ ATPase
6	Calcium Transport
	Thermodynamic minimum in intracellular Ca ⁺² via Ca ⁺² pumping
7	Osmolarity
	Osmolarity and tonicity of replacement fluids
8	Blood flow and velocity
	Calculations of flow and velocity in arterial tree
9	Pressure flow resistance
	Effects of resistance and vessel branching on flow

4.1 Description of problems

Four of these modules will be described in a little more depth. The **Seawater Problem** is almost completely numerical and requires multi-step calculations. Students are required to realize that in addition to drinking water and obtaining water in food, the individual in the problem produces water by metabolism, and, in addition to losses in sweat and urine and feces, there is insensible evaporation. Then, knowing all the daily input and output volumes and osmolarities, except for urine, and given the maximum osmolarity of urine of about 1200 mOsm/L, they can arrive at the final body osmolarity and total body water. It turns out that drinking seawater is seemingly beneficial, provided that its osmolarity is less than 1200, prompting a final part of the problem where additional factors are brought out. The important additional factors are that a large part of the urine osmolarity is due to urea, and that the high Mg^{+2} and SO_4^- levels in seawater cause diarrhea.

In contrast, the **Salt and Water Control Diagram** problem requires students to create a feedback diagram for salt and water balance by filling in qualitative, static relationships among variables, serving as a review of this complex system. Two steps of the control diagram problem are illustrated in Figure 4. The question on the left requires students to enter a text answer to the question “what hormone increases when osmolarity increases?” The frame on the right occurs later in the problem and gives multiple graphical choices for another block in the diagram. When a student completes the question for one of the transfer functions in the system, the part of the full diagram completed to that point is shown.

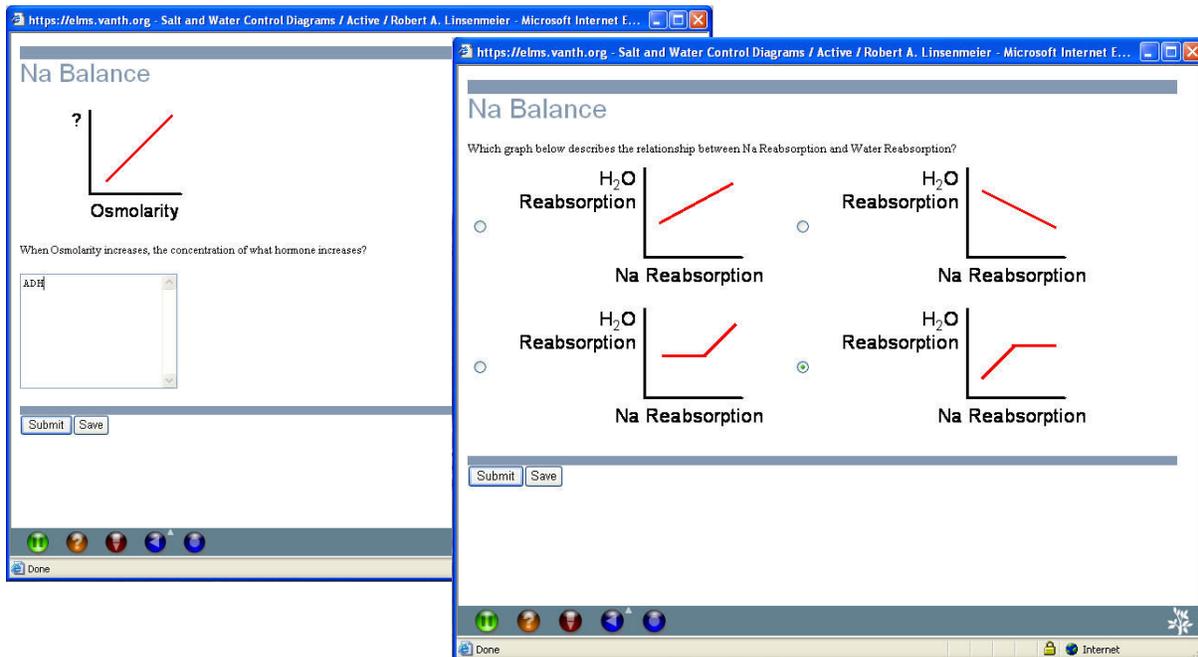


Figure 4: Screenshots of two stages in the Control Diagram problem.

The **Blood Flow and Velocity** problem asks students to make predictions about what will happen to both flow rate and velocity when an arterial stream divides into arterioles, and then takes the students through numerical calculations of flow and velocity to illustrate the decrease in velocity that occurs as blood moves into a bank of parallel vessels. The **Pressure-Flow-**

Resistance problem first addresses the question of the relative resistance of the pulmonary and systemic circuits, and then has students use the relations among velocity, diameter, and pressure drop to calculate relative resistances of individual vessels of different sizes, and the resistance of a bank of small vessels.

4.2 Assessment of Problems

Two types of assessment have been done. First, in a biomedical engineering systems physiology course, we evaluated performance on exam questions testing concepts that students should have learned in the Seawater and Control Diagrams problems. We compared a control group that did the problems with pencil and paper with a treatment group that used CAPE/eLMS. To prevent contamination across the groups, these homework problems were done in studio settings where students had access to each other, and to a teaching assistant. Students performed almost equally well on relevant exam questions when they used the CAPE/eLMS system as when they used pencil and paper, although performance with CAPE/eLMS was slightly worse in both cases (effect sizes of 0.35 and 0.4).¹⁵ However, these were the first head-to-head tests of CAPE vs pencil and paper, and no comparison was made between homework vs. no homework at all. In the subsequent year, CAPE/eLMS was used in an asynchronous mode (i.e. outside of class) and the performance on the exam was the same.

The second method of evaluating the problems was with surveys taken immediately after the completion of the problems. This was done for Seawater and Control Diagrams in the biomedical engineering course in 2007 (n=37), and for the two blood flow problems in an Animal Physiology course taken by junior and senior biology majors in 2007 (n= 19 and 24). In the BME course, the problems were counted in the grade, and in the biology course they were optional. Responses to selected questions from the survey are shown in Table 5. The percentage of students responding Agree or Strongly Agree is shown as “Agree” in the table, and the percentage responding Disagree or Strongly Disagree is shown as “Disagree” in the table. The percentage giving a neutral opinion is omitted.

	Seawater		Control Diagrams		Flow and velocity		Pressure flow resistance	
	Agree	Disagree	Agree	Disagree	Agree	Disagree	Agree	Disagree
The problem was difficult	48	9	21	15	58	8	53	16
I will review this problem before the exam	70	9	68	9	71	17	68	16
I found this problem useful.	70	12	68	3	58	21	63	26
I liked doing this on the computer more than with a traditional method	39	39	41	15	25	29	32	47

In general about half of the students rated the problems as difficult and less than 20% did not find them difficult. On all problems, many more students found the problems useful than not useful, presumably for teaching or reinforcing concepts, or giving them practice. Further evidence of the utility of the problems is that approximately 70% of students said they would review their work before an exam. Interestingly, on three of the four problems, the percentage

who liked doing the problem better on the computer was similar to the percentage who did not especially like this method. The one exception was the conceptual Control Diagrams problem.

5. Discussion

5.1 Delphi Study

This analysis of physiology and biology topics is the first that we are aware of. We found agreement between responses from academia and industry participants, not only that some topics are more important and others less important, but in general on the rank order of the topics. Perhaps this is not too surprising, because the highly rated topics primarily reflect the traditional fields that biomedical engineers have worked in (cardiovascular, respiratory, renal, and neural). Fields in which few biomedical engineers are currently involved were rated lower, although there may be opportunities in these as well. No topics in physiology, aside from our one “ringer” on hormone evolution received an average rating below “moderately important.” It is possible that our participants only used the top half of the scale, so that concepts rated 3 should be considered unimportant. However, participants did use the full range of the scale for some items (see Figure 1), so we believe that our participants felt that biomedical engineers should ideally have a rather comprehensive physiology exposure. Beyond this generalization, there is no clear break in the ratings that allows one to rule in, or rule out, particular topics.

Key concepts in physiology may be organized differently than we have proposed here. A thoughtful analysis that is especially relevant for bioengineers is the organization proposed by Feder¹⁶ in terms of physiology principles, rather than topic areas. The thirteen major conceptual headings in this framework include ideas on large ideas such as 1) maintenance, growth and reproduction, 2) exchange and equilibrium among compartments, and 3) physical mechanisms of exchange through surfaces, and 4) the role of the environment as the source of required mass and energy. Each of the ideas has several sub-headings that flesh out the major concept. While it would be difficult for students to appreciate this organization until they have had some specific physiology content, it may prove valuable for bioengineers who want to make sure that all the major ideas are covered, but who cannot teach in each organ system. A useful next step might be to generate a matrix in which Feder’s concepts are mapped onto those in the Delphi Study.

The biology part of the survey showed that biomedical engineers are no longer expected to learn just physiology, and need some level of biochemistry, molecular biology & genetics, and cell biology as well. Industry appeared to be ahead of academia in identifying an important role for biomedical engineers in bioinformatics. Investigating these issues in more detail may be worthwhile in the future.

While we refer to this work as a Delphi Study, we have only done one round of investigation on the topics discussed here. Typically, a Delphi Study involves questioning an audience, obtaining ratings on the questionnaire items as well as obtaining ideas for new topics to query, and going back to the audience for at least one more round of questioning in order to try to achieve convergence across the population. We were encouraged by the similarity of responses by academic and industrial participants, and did not receive many suggestions for new topics, so we elected not to engage in a second round of questions on biology and physiology. Instead, we focused our attention in the second round of the Delphi Study on achieving

consensus in engineering domains. There are at least two limitations of not continuing with the physiology part of the Delphi study. First, while there is agreement based on the average values between groups, for many topics there was a substantial spread in opinions within both the academic and industrial group. Multi-round Delphi studies are intended to reduce this variability. Assuming that the average responses did not change, however, it is not clear that there would be a practical purpose in reducing the variability. Second, and more important, the current survey asked simply about topics. It did not ask what the learning objectives should be for each topic, ask what level of proficiency a student should have with each topic, or give any guidance about how to teach each topic. Thus, another round of study could be to identify what a student should be able to do with each topic.

5.2 Physiology Problems

The importance of quantitative physiology for biomedical engineers and the paucity of appropriate resources for learning it have led us to work toward a resource of problems that will be generally available. The utility is not restricted to teaching biomedical engineers, and may benefit educators in biology and medicine as well. The development of a full resource of problems is still at an early stage. While we have not yet demonstrated clear learning gains by assessing performance on exam problems, learning to use CAPE/eLMS system in the most effective way requires time and experience. The extensive education literature shows that students learn more from frequent formative assessment,⁹ especially if we can diagnose their errors, and learning gains have been demonstrated for similar modules.^{11,13} CAPE/eLMS responds immediately, unlike traditional homework, which is not returned for a week, and often contains little feedback from instructors. Evaluating learning with just one exam question related to the CAPE problem is difficult, in terms of matching the exam question closely to the learning objectives of the CAPE problem without repeating the same problem, and this may partially account for the fact that students using CAPE/eLMS were a little weaker on the exams. A further benefit of CAPE/eLMS is that faculty can obtain information more easily on where their students are having difficulty, which they are often not cognizant of.^{17, 18}

The survey data are encouraging. Students believed that all of the problems tested so far were useful. The spectrum of attitudes toward liking and not liking the problems on the computer will require further study. We have some data correlating students' attitudes with their exam performance that suggest that the ones toward the bottom of the class like these problems better and may be the ones who benefit most. Some additional clues to the diversity of opinions are suggested by the fact that a conceptual problem (Control Diagrams), rather than a numerical problem (Seawater), was the one on which the students had a clear preference for the computer. Control Diagrams is very difficult with pencil and paper and may especially benefit from the staged way that it is done with CAPE/eLMS. Of course, we would like all the students to be at least neutral about the format in which they do their homework, or ideally, prefer the computer format, which works to improve their understanding during the problem session. Analyzing which students gain from these problems, how to best construct them in terms of remediation and adaptive delivery, and which types of problems work best, are all subjects for future research.

As we gain experience with creating problems in this medium, the existing problems will improve. The CAPE/eLMS system is flexible enough to handle a wide range of approaches, and

it already shows benefits. We believe that further construction of new problems, targeted toward the most important concepts and the most difficult concepts can strongly aid in the teaching of quantitative physiology. We encourage others to begin using the problems and assisting in developing the resource.

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APPENDIX: Delphi Study results for the biology domains sorted by domain and average rating (1 = unimportant; 5 = very important). A = average academia rating; I = average industry rating; Ave = aggregate average rating. The average standard deviation per item in the Delphi Study was 0.9.

		A	I	Ave
BIOCHEMISTRY				
1	Synthesis, Structure and Function of Biologically Important Macromolecules (e.g., nucleic acids, DNA, RNA; amino acids, proteins; carbohydrates; fats)	4.43	4.32	4.37
2	Biochemistry of Water (e.g., polar properties; interactions with ions, small molecules, and macromolecules; hydrophobic and hydrophilic effects; vdW interactions)	4.18	4.27	4.23
3	Structures and Properties of Interacting Macromolecules (e.g., hormone-receptor; substrate-enzyme; protein-DNA; immunoglobulin-antigen)	4.09	4.05	4.07
4	Cellular Biosynthesis and Energetics - Mass and Energy Balances (e.g., ATP energy and transfer; aerobic glycolysis; anaerobic glycolysis; electron transfer chain)	4.05	3.90	3.98
5	Methods for Determining Macromolecular Structure (e.g., NMR; X-Ray Crystallography; Spectroscopy - Mass, Infra-red, Raman; Microscopy - light, electron, atomic force; Circular Dichroism; radionucleotide labeling)	3.51	4.21	3.86
6	Enzyme Kinetics (e.g., catalysis; factors affecting enzyme activity; allosteric binding; graphical representations)	3.75	3.84	3.80
7	Metabolic Networks and Pathways (e.g., G proteins; protein kinases; secondary messengers; anabolic pathways)	3.76	3.63	3.70
8	Molecular Design (e.g., homology modeling and ab initio prediction of molecular interactions: protein-small molecule; protein-protein; protein-DNA)	3.15	3.45	3.30
BIOINFORMATICS				
1	Microarrays (e.g., DNA microchips; DNA microarrays; protein microarrays)	3.39	3.74	3.56
2	Biological Networks (e.g., genetic networks; protein/gene networks; signaling pathways)	3.19	3.65	3.42
3	Familiarity with Online Databases (e.g., PDB; GenBank; KEGG; SwissProt)	3.07	3.67	3.37
4	Proteomics (e.g., the large scale study of gene-expression products at the protein level; applications of protein electrophoresis and mass spectroscopy)	3.23	3.47	3.35
5	Databases - Interfaces and Structures (e.g., MySQL, relational tables, simple queries, PERL, CGI, DBI)	2.66	3.68	3.17
6	Alignment and Similarity Analysis of DNA, RNA and Protein Sequences (pairwise alignment - dynamic programming; BLAST; Psi-BLAST; Substitution Matrices - PAM, BLOSUM; Profiles; multiple sequence alignment; profiles)	2.94	3.13	3.03
7	Structural Prediction and Molecular Design (e.g., homology modeling and ab initio prediction of macromolecular structures and interactions: the protein folding problem; protein-small molecule; protein-protein; protein-DNA)	2.53	3.25	2.89
8	Determination and Analysis of Phylogenetic Trees, Molecular Evolution	2.47	3.00	2.73
9	Comparative Genomics (e.g., ortholog and paralog genes; gene fusion events)	2.50	2.94	2.72
CELL BIOLOGY				
1	Cell Organization, Organelles, Cellular and Molecular Architecture	4.58	4.38	4.48
2	Structure and Function of the Plasma Membrane (e.g., membrane proteins; endo- and ectocytosis; phagocytosis; pinocytosis; transport)	4.26	4.14	4.20
3	Cellular Interactions with the Environment (e.g., signal transduction, cell signaling; adhesion; motility; cell-matrix interactions)	4.21	4.19	4.20
4	Cell Determination, Differentiation, Growth and Death	3.92	3.95	3.94
5	Cellular Respiration and the Mitochondrion	4.00	3.81	3.90
6	Cytoskeleton and Cell Motility	3.97	3.67	3.82
7	Cellular Division and the Cell Cycle (e.g., mitosis; meiosis)	3.76	3.76	3.76

APPENDIX, Continued		A	I	Ave
MOLECULAR BIOLOGY AND GENETICS				
1	Flow of Genetic Information (i.e., DNA to RNA to Protein)	4.54	4.11	4.32
2	Properties of Genes and Chromosomes	4.34	4.26	4.30
3	Properties and Structure of DNA	3.97	4.25	4.11
4	Properties and Structure of RNA	3.89	4.25	4.07
5	Protein Translation, Regulation, and Post-Translational Regulation	3.71	3.87	3.79
6	DNA Replication and Repair	3.64	3.89	3.76
7	Regulation of Gene Expression in Eukaryotes	3.71	3.79	3.75
8	DNA Microarrays	3.39	3.81	3.60
9	Genetic Rearrangements: Recombination, Crossover Events, Transposition	3.61	3.53	3.57
10	Analyzing, Constructing, and Cloning DNA (e.g., Restriction Enzymes; DNA Sequencing; Recombinant DNA - plasmids, cloning vectors, YACs, lambda phage; Site-directed Mutagenesis)	3.25	3.75	3.50
11	Viruses	3.25	3.75	3.50
12	Biochemistry of Nucleic Acids	3.31	3.61	3.46
13	Regulation of Gene Expression in Prokaryotes	3.26	3.50	3.38
PHYSIOLOGY				
1	Overview of the Cardiovascular System (e.g., anatomy; functions)	4.56	4.60	4.58
2	Tissues of the Body (e.g., extracellular matrix; cell junctions; epithelia; connective tissue; muscles and nerves)	4.53	4.29	4.41
3	Pressure, Volume, Flow and Resistance (e.g., pressure and volume; pressure and flow; resistance and flow; flow rate and velocity of flow)	4.43	4.35	4.39
4	Overview of the Respiratory System (e.g., thorax; lungs; airways of the conducting system; alveoli and gas exchange; pulmonary circulation)	4.41	4.35	4.38
5	Cellular Anatomy (e.g., cell membrane; cytoskeleton; cytoplasm; nucleus; organelles)	4.56	4.14	4.35
6	Cellular Metabolism (e.g., chemical energy - ATP production; enzymes and catalysis of reactions; cellular respiration, mitochondria; synthetic pathways)	4.44	4.10	4.27
7	The Heart as a Pump (e.g., electrical conduction in the heart; pacemakers and heart rate; ECG; cardiac cycle; pressure-volume curves, stroke volume; cardiac output; homeostatic control of heart rate; control of stroke volume)	4.32	4.20	4.26
8	Overview of the Kidney (e.g., anatomy and functions)	4.41	4.10	4.26
9	Electrical Signals in Neurons (e.g. role of ions; properties of action potentials; the Na ⁺ /K ⁺ pump; chemical factors affecting electrical activity)	4.43	4.05	4.24
10	Membrane Dynamics (e.g., membrane structure and composition; transport across membranes; osmosis; membrane potential)	4.44	3.95	4.20
11	Communication, Integration and Homeostasis (e.g., cell-to-cell communication; receptors and signal transduction; homeostasis; control pathways)	4.28	4.10	4.19
12	Cardiac Muscle and the Heart (e.g., structure of the heart; properties of cardiac muscle cells; excitation - contraction coupling in cardiac muscles; action potentials in myocardial cells)	4.21	4.15	4.18
13	Organization of the Nervous System	4.14	4.21	4.18
14	Gas Laws (e.g., partial pressures; gas flow; Boyle's law; solubility of gases in liquids - Henry's law)	4.29	4.05	4.17
15	Skeletal Muscle (e.g., anatomy and types of fibers; regulation of contraction - troponin and tropomyosin; metabolism; fatigue; tension, fiber length and summation of twitches; the motor unit)	4.14	4.17	4.15
16	Blood Vessels (e.g., vascular smooth muscle; arteries and arterioles; capillaries; venules and veins; angiogenesis)	4.24	4.05	4.15
17	Cell-to-Cell Communication (e.g., the synaptic interface; neurotransmitters; postsynaptic responses; disorders of synaptic transmission)	4.20	4.00	4.10

APPENDIX, Continued		A	I	Ave
18	General Properties of Sensory Systems (e.g., receptors; sensory pathways; sensory transduction; stimulus coding and processing)	4.06	4.11	4.08
19	Processes of the Kidney (e.g., filtration, reabsorption, secretion and excretion; volume and osmolarity changes in the nephron)	4.26	3.85	4.06
20	Mechanics of Body Movement (e.g., isotonic and isometric contractions; bones, joints, levers and fulcrums; muscle disorders)	3.91	4.05	3.98
21	Cardiac Muscle (e.g., atrial muscle; ventricular muscle; excitatory and conductive muscle fibers; cardiac muscle as a syncytium - gap junctions; action potentials in cardiac muscle)	3.88	4.05	3.97
22	Blood Pressure (e.g., in the systemic circulation; in the arteries; estimation of; factors influencing; dependence on blood volume)	4.03	3.90	3.97
23	Cells of the Nervous System (e.g., neurons; glial cells)	4.09	3.84	3.96
24	Pathogens of the Human Body (e.g., bacteria and viruses; life cycle of a virus)	4.06	3.86	3.96
25	Functions and Processes of the Digestive System	4.06	3.85	3.96
26	Control of Body Movement (e.g., nervous reflexes; autonomic reflexes; skeletal muscle reflexes; integration of movement within the central nervous system; control of movement in visceral muscles)	3.82	4.05	3.94
27	Anatomy of the Urinary System (e.g., gross anatomy; the nephron)	3.91	3.95	3.93
28	Distribution of Blood to the Tissues (e.g., exchange at the capillaries; velocity of blood flow; capillary filtration and re-absorption)	3.97	3.80	3.88
29	Hormones (e.g., discovery of; distinguishing between hormones and other chemicals in the body)	3.91	3.79	3.85
30	Ventilation (e.g., conditioning of inspired air; pressure changes during; inspiration/expiration; intrapleural pressure, lung compliance; surfactant, role in alveoli; airways resistance to air flow)	4.00	3.70	3.85
31	Gas Exchange in Blood (e.g., oxygen transport; hemoglobin; oxygen-hemoglobin dissociation curve; factors affecting oxygen-hemoglobin binding; carbon dioxide transport)	4.00	3.70	3.85
32	Regulation of Blood Pressure (e.g., the baroreceptor reflex; orthostatic hypotension)	3.94	3.70	3.82
33	Filtration (e.g., anatomy of the renal corpuscle; filtration; glomerular filtration rate and its regulation)	4.03	3.60	3.82
34	Plasma and the Cellular Elements of Blood (e.g., plasma; cellular elements)	3.71	3.90	3.80
35	Anatomy of the Immune System (e.g., lymphoid tissues of the body; cells of the immune system)	3.79	3.81	3.80
36	Anatomy of the Central Nervous System - CNS (e.g., the spinal cord; the brain - brain stem, cerebellum, diencephalon, cerebrum)	3.74	3.84	3.79
37	The Eye and Vision (e.g., anatomy of the eye and optic tract; optics - focusing light on the the retina; phototransduction; signal processing in the retina; visual processing in the CNS)	3.69	3.89	3.79
38	Fluid and Electrolyte Balance - Homeostasis of Volume and Osmolarity	4.03	3.50	3.76
39	Reabsorption (e.g., transepithelial transport; saturation of renal transport)	3.91	3.60	3.75
40	Smooth Muscle (e.g., smooth muscle fibers; chemical control of smooth muscle contraction)	3.56	3.95	3.75
41	Anatomy of the Digestive System (e.g., gross anatomy; histology of the GI tract)	3.79	3.65	3.72
42	Resistance in the Arterioles (e.g., myogenic autoregulation; local control of; reflex control of)	3.81	3.55	3.68
43	Brain Function (e.g., neurotransmitters and neuromodulators; the hypothalamus; emotion and motivation; learning and memory; language; personality)	3.52	3.84	3.68
44	Excretion (e.g., using clearance to determine renal handling of a substrate)	3.82	3.53	3.67
45	Gas Exchange in Tissues (e.g., role of myoglobin)	3.78	3.50	3.64
46	The Ear - Hearing (e.g., sound waves; transduction of sound; middle ear; the cochlea and the inner ear; sound transduction through the cochlea; sound discrimination; auditory pathways; hearing loss)	3.63	3.61	3.62

APPENDIX, Continued		A	I	Ave
47	Efferent Peripheral Nervous System - Somatic Motor Division (e.g., anatomy, the neuromuscular junction)	3.64	3.58	3.61
48	Somatic Senses (e.g., classification; detection and transmission of tactile sensations; pathways for transmission of signals into the CNS)	3.56	3.58	3.57
49	Efferent Peripheral Nervous System - Autonomic Division (e.g., the adrenal medulla, autonomic neurotransmitters and receptors, sympathetic and parasympathetic branches, control, disorders)	3.50	3.63	3.57
50	Regulation of Ventilation (e.g., role of neurons in the medulla; chemical control; mechanoreceptor reflexes; higher brain control)	3.59	3.45	3.52
51	Control of Hormone Release (e.g., trophic hormones; endocrine reflexes; negative feedback in endocrine reflexes; hormone interactions)	3.58	3.42	3.50
52	Water Balance and the Regulation of Urine Concentration (e.g., overview; role of the kidneys; receptors and reflexes; osmolarity; loop of Henle; antidiuretic hormone)	3.73	3.25	3.49
53	Platelets and Coagulation (e.g., hemostasis - platelet aggregation, coagulation; anticoagulants)	3.21	3.75	3.48
54	The Ear - Equilibrium (e.g., anatomy and function of the vestibular apparatus; equilibrium pathways)	3.29	3.67	3.48
55	Classification of Hormones (e.g., peptides; steroids; amines)	3.58	3.37	3.47
56	Energy Balance and Metabolism (e.g., temperature regulation; fed and fasted states; regulation of metabolic pathways)	3.58	3.37	3.47
57	Sodium Balance and the Regulation of Extracellular Fluid Volume (e.g., dependence on aldosterone; control of aldosterone secretion; angiotensin II; atrial natriuretic peptide)	3.76	3.15	3.45
58	Acid-Base Balance in the Body (e.g., why pH is regulated; sources of acids and bases; buffer systems; renal compensation in acid-base disturbances; disturbances of acid-base balance)	3.61	3.25	3.43
59	Regulation of Potassium Excretion and Potassium Concentration in the Extracellular Fluid (e.g., overview of renal excretion; secretion in the late distal and cortical collecting tubules; factors that regulate secretion – concentration in plasma, aldosterone, tubular flow rate, hydrogen ions)	3.52	3.32	3.42
60	The Lymphatic System (e.g., disruption of capillary exchange - edema)	3.37	3.45	3.41
61	Cardiovascular Disease (e.g., risk factors; hypertension)	3.56	3.25	3.40
62	Endocrine Control of Metabolism - Pancreatic Hormones (e.g., the endocrine pancreas; insulin; glucagon; dual regulation of metabolism by insulin and glucagon)	3.41	3.39	3.40
63	Innate Immunity (e.g., phagocytosis; barriers to chemical and physical agents; the inflammatory response)	3.46	3.29	3.37
64	Digestion and Absorption (e.g., overview; of macromolecules - carbohydrates, proteins, fats; nucleic acids; vitamins and minerals; water and electrolytes; in the large intestine)	3.53	3.15	3.34
65	Integrated Control of Volume and Osmolarity (e.g., disturbances of salt and water balance; homeostatic response to dehydration)	3.48	3.15	3.32
66	Red Blood Cells (e.g., structure, surface antigens - blood type; hemoglobin; life cycle; disorders)	3.27	3.35	3.31
67	Immune Response Pathways (e.g., responses to bacterial and viral infections; allergic responses; recognition of self and non-self; immune surveillance)	3.29	3.30	3.30
68	Integration between the Immune, Nervous, and Endocrine Systems (e.g., stress and the immune system)	3.24	3.30	3.27
69	Blood Cell Production (e.g., control of hematopoiesis - cytokines, growth factors and interleukins; hormonal regulation of - thrombopoietin, erythropoietin)	3.06	3.45	3.26
70	Acquired Immunity (e.g., lymphocyte life cycle; B and T lymphocytes; natural killer lymphocytes; antibodies)	3.32	3.16	3.24

APPENDIX, Continued		A	I	Ave
71	Motility (e.g., GI smooth muscle; patterns of contraction; movement of foods through the GI tract)	3.38	3.00	3.19
72	Secretion (e.g., of digestive enzymes; of mucus; of fluids and electrolytes)	3.31	3.05	3.18
73	Regulation of GI Function (e.g., enteric nervous system; digestive hormones; paracrines in the GI tract)	3.24	3.10	3.17
74	Chemoreception - Smell (e.g., olfactory membrane; stimulation of olfactory cells; transmission of smell signals into the CNS)	3.00	3.33	3.17
75	Endocrine Pathologies (e.g., hypersecretion; hyposecretion; abnormal tissue responsiveness; diagnosis of endocrine pathologies)	3.09	3.16	3.12
76	Integration of GI Function (e.g., secretions in the stomach; events following ingestion of a meal)	3.19	3.05	3.12
77	Chemoreception - Taste (e.g., primary sensations of taste; threshold for taste; taste buds and their functions; transmission of taste signals into the CNS)	2.94	3.28	3.11
78	Neurally Mediated Aspects of Metabolism (e.g., the adrenal glands; thyroid hormones)	3.10	3.11	3.10
79	Endocrine Control of Growth (e.g., growth hormone; tissue hormone; bone growth; calcium balance)	3.12	3.00	3.06
80	Micturition (e.g., physiological anatomy and nervous connections of the bladder; transport of urine - kidney, ureters, bladder; reflex; facilitation or inhibition of, by the brain; abnormalities of)	3.19	2.89	3.04
81	Behavioral Mechanisms in Salt and Water Balance (e.g., thirst; salt appetite; avoidance behaviors)	3.15	2.90	3.03
82	Hormone Evolution	2.41	2.63	2.52

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