Challenge-Based Instruction in Biotransport

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Abstract

An introductory physiological transport course was recently redesigned to take advantage of the benefits of challenge-based instruction. In this mode of instruction a series of specific challenges are introduced throughout the semester. The challenges are based on real problems in biotransport and are designed to motivate students to discover a solution. For example, principles of diffusion and chemical reaction can be introduced by asking why cells are so small. Many important concepts in heat transfer can be discovered by asking students to play the role of a consultant in a murder trial in which the time of death needs to be estimated. Newtonian and non-Newtonian fluid mechanics can be introduced by asking how bacteria and other inspired contaminants are cleared from the respiratory system. In general, students will not have sufficient knowledge to solve the challenge as initially presented. They must consult several resources to help them understand which conservation principles apply, which constitutive relationships are appropriate, and which parameters are most important. Students are then asked to use this new information to develop a model that is appropriate for the challenge. They start this while still in the classroom so they can get help from their classmates and from the instructor. In developing a model from first principles for each case, they become familiar with the process, learn when to use a microscopic versus macroscopic balance, and should better appreciate the origins and limitations of generalized equations used to describe transport phenomena, such as the Navier-Stokes equation. Since the challenge-driven method puts students in the position where they need to determine which parts of the taxonomy are relevant to the challenge, it is hoped that this approach will better prepare students for the workplace and for life-long learning.

Introduction

Physiological Transport (BME 210) is a required course in the biomedical engineering curriculum at Vanderbilt University. Students normally take this course during their junior year. The course objective is to provide the fundamental principles and biological applications of momentum, heat and mass transfer. The course has followed a traditional approach, characterized by the presentation of lectures and instructor-centered problem-solving during the class period. The lectures normally covered material in the same sequence as it appeared in the textbook, and the textbook topics followed the traditional taxonomy of transport phenomena. Students were generally passive during classroom sessions and student problem solving was performed exclusively outside the classroom. Thus, the traditional method provides an

environment that is largely knowledge-centered, with some summative assessment, but with little attention to formative assessment, learner-centered activities, or community involvement.

Many recent advances in learning science are summarized in the book "How People Learn" (HPL).[1] A key finding, referred to as the "HPL framework", is that the most effective learning environments are those that are knowledge-centered, assessment-centered, learner-centered and community-centered. This premise was initially based on K-12 observations. Preliminary results indicate that HPL is effective in undergraduate bioengineering instruction as well.[2] The primary objective of this study was to modify BME 210 so that it conforms to the HPL framework. This was done by replacing the taxonomy-based mode of instruction with challenge-based modules. Each module is based on one or more challenges dealing with applications that are generally familiar to the students.

The challenges are designed to include portions of the taxonomy that students have not yet studied. They cannot solve the challenge without additional information. Thus, students are urged to begin each module by forming groups and generating ideas about just what additional information they are going to need before they can solve the problem. This feature distinguishes challenge-based instruction from problem-based instruction, where students have previously been exposed to those aspects of the taxonomy needed to solve the problem. An effective challenge will entice students to conduct their own research and will often involve at least one revision. The role of the instructor is to guide the students through this process, providing useful information when they appear to hit a dead end (i.e., "A time for telling"[3]).

An electronic polling system with the capability of displaying summaries of student responses has proven to be very useful in providing formative assessment to students in an introductory biomechanics course[4]. This system can be used to test student's preconceptions or to assess student's understanding and misunderstanding of material after listening to a lecture. It not only informs the student about his/her knowledge of the topic, but also informs the instructor about the comprehension of the class as a whole, allowing the instructor to review material that is not well understood. A polling system, the Personal Response System (PRS)[5], was introduced in BME 210 and used in most classroom sessions to assist with student assessment.

Methods

A significant challenge in organizing an HPL-based course is deciding how to design the course so that a limited number of challenge-based modules effectively expose students to all of the important aspects of the taxonomy. One method that has proven to be effective in redesigning a biomechanics course[6,7] is to construct a spreadsheet in which the important course concepts are listed in rows and the proposed modules are listed as column headings. Each spreadsheet cell represents the potential application of a specific concept in a module. A cell marked with an "X" indicates that a module relies on a specific portion of the taxonomy.

The concepts to be covered in the introductory transport course at Vanderbilt are listed in Tables 1A (basic transport phenomena and fluid mechanics concepts) and Table 1B (mass and heat

transfer concepts). I began by proposing approximately 30 potential modules, and

Module --->	Factors that influence the design of a heart-lung machine	Cell Volume Regulation	Determinants of Cell Size	Estimation of Post Mortem Interval	Cilia and Mucus Transport, Cystic Fibrosis	Asthma, COPD, Pulmonary Function Testing	Cardiorespiratory Compliance: Windkessel, pulmonary circulation, lung zones, respiration	Blood Rheology: Hemolytic Anemia, Sickle Cell Anemia	Inert gas transport, anesthesia	O2 & CO2 Exchange	Rapid reaction apparatus	Tracer studies & pharmacokinetics	Designing components of a heart-lung machine	Thermal Comfort (not covered 2003)
Transport Taxonomy	F,M,T	F,M	M	T	F	F	F	F	M,F	M,F	F	M	M,F,T	T,M,F
Basics														
Continuum Concepts	X		X		X			X					X	
Molecular transport analogies	X				X								X	X
Interfacial transport analogies	X					X					X		X	X
Modeling Concepts	X	X	X	X	X	X	X		X				X	
Shell balances/ conservation principles	X	X	X	X	X	X	X	X	X	X	X		X	X
Boundary/Initial Conditions	X	X	X	X	X	X	X	X	X	X			X	X
Dimensional Analysis				X							X		X	
MATLAB/ Alternate solution methods		X	X	X		X			X				X	
Fluid Mechanics														
Pressure	X	X			X	X	X	X	X	X	X		X	
Osmotic pressure		X												
Hydrostatics		X				X	X							
Shear stress	X				X	X	X	X					X	
Viscosity	X				X	X	X	X	X		X		X	
Fluid Resistance/Conductance	X	X				X		X	X		X		X	
Compliance		X				X	X	X						
Starling Resistor/ collapsible tube						X	X							
Membrane Conductance, Filtration, Porosity, Darcy's Law		X							X	X				
Newton's Law of Viscosity	X				X	X	X	X					X	
Non-Newtonian Biofluids					X			X						
Macroscopic Conservation of Mass	X	X				X	X	X	X	X			X	X
Macroscopic Conservation of Momentum	X					X	X		X	X				
Macroscopic Mechanical Energy Eq	X					X	X				X		X	
Macroscopic unsteady state flow		X					X					X		
Laminar vs. Turbulence, hydraulic diameter, Reynolds Number						X					X		X	X
Friction Factor, Moody Diagram, Friction Loss Factor											X		X	
Microscopic mass shell balance - continuity			X		X	X	X	X	X	X			X	
Microscopic momentum shell balance					X	X	X	X					X	
Sheet/film flow						X	X	X	X	X				
General microscopic mass balance - continuity					X	X		X	X	X			X	
General microscopic momentum balance					X	X		X		X			X	
Navier-Stokes Eq					X	X							X	
Velocity profile					X	X		X			X		X	
Sheet/Tube flow - Hagen-Poiseuille	X				X	X	X	X	X	X	X		X	
Entry flow						X					X		X	
Flow in tubes with non-circular cross-sections.											X		X	
Flow in networks						X	X						X	
Measuring pressure, flow						X	X	X						

Table 1A. Basic and fluid mechanics taxonomies covered in each module.

finally settled on the fourteen listed in Tables 1A-1B, since these adequately covered all of the material normally presented in the course. Due to time constrains, the last module (Thermal Comfort) was not offered.

VOS Observations

The VaNTH classroom Observation System (VOS)[8] was used to assess the degree of "HPL-ness" of this course relative to two other courses taught during the same semester by different instructors. The VOS assessment was based on six to ten classroom observations in each course.

PRS Questions

The Personal Response System (PRS)[5] was used to obtain student preconceptions and provide students with formative assessment in all challenges. Whenever a large fraction of the class

(>40%) missed a formative assessment question, the concept was revisited in detail before moving on to the next topic.

Module --->	Factors that influence the design of a heart-lung machine	Cell Volume Regulation	Determinants of Cell Size	Estimation of Post Mortem Interval	Cilia and Mucus Transport, Cystic Fibrosis	Asthma, COPD, Pulmonary Function Testing	Cardiorespiratory Compliance: Windkessel, pulmonary circulation, lung zones, respiration	Blood Rheology: Hemolytic Anemia, Sickle Cell Anemia	Inert gas transport, anesthesia	O2 & CO2 Exchange	Rapid reaction apparatus	Tracer studies & pharmacokinetics	Designing components of a heart-lung machine	Thermal Comfort (not covered 2003)
Transport Taxonomy	F,M,T	F,M	M	T	F	F	F	F	M,F	M,F	F	M	M,F,T	T,M,F
Mass Transfer														
Equilibrium, Donnan equilibrium		X		X										
Concentration	X	X	X					X	X	X		X	X	
Interfacial equilibrium, solubility, interfacial transport			X		X			X	X	X			X	X
Partial pressure			X					X	X	X			X	X
Henry's law			X					X	X	X		X	X	
Diffusion, Fick's Law	X	X	X					X	X	X			X	X
Diffusion through layers			X					X	X	X			X	
Nernst Eq		X												
Chemical reaction			X					X		X		X	X	
Oxyhemoglobin dissociation curve								X		X			X	
Convective mass transfer		X	X		X			X	X	X		X	X	X
Passive membrane solute transport		X	X					X	X	X			X	X
Carrier-mediated and active transport		X												
Blood-tissue/lung gas exchange								X	X	X		X	X	
Macroscopic species mass balance	X	X	X					X		X				X
Unsteady-state compartmental analysis		X							X			X		
Microscopic species shell balance			X						X	X			X	
Generalized microscopic solute equation			X										X	
Initial/boundary conditions		X	X			X	X	X	X	X		X	X	
Concentration profiles, total mass flow			X						X	X			X	
Mass transfer coefficients, Sc, Nu			X										X	X
Heat Transfer														
Conduction, Fourier's Law	X			X									X	X
Temperature-dependence of processes and physical properties		X			X									
Insulation				X									X	X
Microscopic thermal shell balance				X									X	
Thermal boundary/initial conditions	X			X									X	X
Heat generation	X			X										X
Macroscopic thermal energy balance	X			X									X	X
Lumped analysis, compartmental analysis				X								X		
Temporal & Spatial Temperature differences, Heisler Charts				X										
Dimensional analysis, convective heat transfer coefficient, Nu, Pr				X									X	X
Forced and free convection	X			X									X	X
Shell & Tube heat exchangers	X												X	
Radiation heat transfer														X
evaporation, insensible heat loss														X
Heat trasfer with change of phase														X

Table 1B. Mass transfer and heat transfer taxonomies covered in each module.

Results and Discussion

Modules

Brief descriptions of thirteen modules are presented below. The number of 50 minute sessions spent on each module is given in parentheses.

Factors influencing the Design of a Heart-Lung Machine (3 sessions). The purpose of this module is to introduce students to the basic concepts of physiological transport phenomena by presenting them with a realistic design problem that might face a practicing biomedical engineer. The Challenge: A company is considering designing and producing a heart-lung machine for use in open heart surgery. You have been recruited to inform them of the major system variables and

system components that they must consider in their design. The students recognize that the system must include a pump to provide momentum to the blood as it traverses the device, a heat exchanger to heat the blood back to body temperature, and a mass exchanger that removes carbon dioxide and adds oxygen. The students are told that the company is impressed with their recommendations and has decided to hire them to design and build the machine. They are introduced to two possible approaches: an empirical approach, where the final design is determined by experimental trial and error, and a theoretical approach, based on development of mathematical models of each system. They are asked how they might develop a mathematical model of a physical system. A familiar example of electrical circuit modeling is reviewed. At the same time, new concepts and definitions, such as a continuum, mass fraction, mole fraction, flux and gradient are introduced. These lead to mathematical expressions for empirical observations such as Ohm's Law, Fourier's Law, Fick's Law, and Newton's Law of viscosity. Conservation laws, convective transport and interfacial transport mechanisms are also introduced in this module. The module concludes with a definition of the overall heat transfer coefficient and an estimate of steady-state heat transfer through the walls of the pump in the heart-lung machine. Students emerge from this module with a much better understanding for many of the factors that need to be considered in designing a heart-lung machine and will return to a more detailed treatment of this design in the final module presented in the course.

Cell Fluid Volume Regulation (4 sessions). Key objectives of this module are to show how fluid and solutes move in and out of cells and to illustrate the critical role of active transport in the regulation of cell volume. The module begins with the following challenge: "If the cell membrane is a water-insoluble lipid bilayer, how can fluid or water-soluble substances pass in or out?" Students discuss this and reject the premise that the membrane is a continuous bilayer. Instead, many integral proteins, such as aquaporin, provide specific pathways for water and water-soluble substances to move in and out of cells. This raises the question as to which driving forces are responsible for the movement of fluid and solutes into and out of the cell. Students eventually agree that both hydrostatic pressure and osmotic pressure regulate fluid flow through membrane pores. A formal definition for osmotic pressure is introduced and an unsteady-state problem involving osmotically driven flow through a semipermeable membrane is solved. Students are asked to set up a model that can predict cell volume changes vs. time after macromolecules are released into the cytoplasm. They find that this will generally lead to cell lysis, and so a new challenge is introduced: "Are passive transport mechanisms consistent with experimental measurements made in cells that show no net transmembrane hydrostatic or osmotic pressure difference, but a net difference in transmembrane electrical potential?" This leads students to consider charge-related ion flux, the Nernst equation, and Gibbs-Donnan equilibrium. Ultimately, the students conclude that cell volume would increase indefinitely without the regulating action of the sodium-potassium pump, and that cell death leads to cell lysis.

Determinants of Cell Size (5 sessions). The objective of this module is to introduce students to the shell balance approach for finding concentration profiles in consuming tissue. The module illustrates how diffusion of critical metabolites can limit cell size. The main challenge: "Why are cells so small? What factors limit the ultimate size of cells." Students learn to use macroscopic and microscopic approaches to answer relevant questions. Students find the concentration profile for oxygen in the case where oxygen is consumed at a constant rate per unit volume for

rectangular, cylindrical and spherical cells. They learn to apply Henry's law at the interface between cell wall and cytoplasm, learn the difference between homogeneous and heterogeneous chemical reactions, and apply zeroth order, first order and Michaelis-Menten kinetics. They conclude that cell size is constrained by the ability of oxygen to diffuse to the center of the cell.

Postmortem Interval (4 sessions). Students found this module to be fun and interesting because they could relate it to popular TV shows based on crime scene investigations. The challenge statement is presented in Figure 1. The students were asked to justify the use of an empirical relationship used by forensic pathologists. They found that they can get a similar relationship using a lumped analysis heat balance. They discover, however, that the pathologist used a heat transfer coefficient based on cooling in air, while the correct heat transfer coefficient must be based on cooling in water. A new estimate of the time of death would appear to clear the defendant of the crime. However, use of this more accurate heat transfer coefficient invalidates the use of a lumped analysis. Body temperature varies both with radial position and with time. Students derive the partial differential equation that governs temperature and Heisler charts are introduced and used to estimate core temperature. Other confounding factors, such as asymmetry of heat loss from the body are discussed. The take-home message of this module is that models are only as accurate as the information provided and the validity of the assumptions made in their construction.

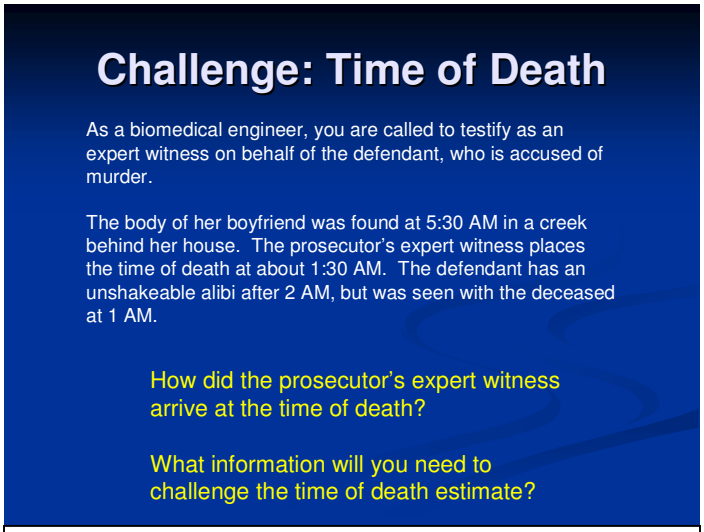

Figure 1. Postmortem Interval Challenge.

Respiratory Clearance (3 sessions). Key challenges: "What mechanism is responsible for clearing contaminants from the respiratory system and why doesn't mucus flow down the airways instead of upwards toward the mouth?" Students model mucociliary transport using experimentally measured mucus thickness and velocity at the upper surface of the periciliary layer. They are shown how shear stress can be interpreted as a momentum flux and are introduced to various relationships between momentum flux and shear rate, defining Newtonian and non-Newtonian fluids. It is shown that if mucus behaved as a Newtonian fluid that its viscosity would need to be more than 100 times that of water if it were to have an upward flow similar to the measured value. This is not consistent with measured values of viscosity. However, mucus behaves more like a Bingham fluid with a yield stress sufficient for the entire mucus layer to move upward as a plug, sweeping contaminants caught at the airway-mucus surface out of the respiratory system.

Asthma & COPD (2 sessions). The Challenges: "Why do asthmatics find it difficult to breathe? How can we quantify the severity of the disease? Can we as biomedical engineers design tests

that can help diagnose the disease and monitor its progression?" The primary objective of this model is to derive the Hagen-Poiseuille equation for flow through a tube, showing the high sensitivity of fluid resistance on tube radius. Concepts of laminar vs. turbulent flow are introduced, operation of a pneumotachograph is explained and a pulmonary function test based on forced expiration is described.

Biological applications of collapsible and compliant tubes (5 sessions). The challenge is to determine the influence of compliance on pressure and flow in the cardiovascular and respiratory systems. The effects of airway compliance on inspiratory and expiratory resistance are examined. Starling resistors are discussed and many biological applications, including flow limitation during forced expiration in collapsible airways and blood flow in lung zones are discussed. The Windkessel model is introduced and the regulatory effect of arterial compliance on blood pressure is examined. A simple resistance-compliance model of respiration is introduced and students use the model to examine the effects of pleural pressure, alveolar compliance, airway resistance and respiratory frequency on minute volume.

Blood Rheology in Sickle Cell Anemia (3 sessions). Sickle Cell Anemia, a disease familiar to most students, is used to examine the rheological properties of blood. Students are introduced to physical explanations for the dependence of apparent viscosity of blood on shear rate, hematocrit value, and vessel diameter (Fahreaus-Lindquist effect). In addition, the dependence of viscosity on oxygen tension in sickle blood is discussed. The Casson model for blood flow is introduced and compared with the Newtonian model for flow in blood vessels of various diameters.

Inert Gas Exchange (2 sessions). Diffusion and convection of inert gases and respiratory gases are treated in this module. The challenge: "How should we adjust the partial pressure of an anesthetic gas in inspired air to bring the blood concentration to a value necessary to induce a desired level of sedation?"

O_2 and CO_2 Exchange (2 sessions). The challenge is to estimate the pulmonary capillary length required to bring the blood gas partial pressure to within 1% of the alveolar partial pressure for O_2 and CO_2. The oxygen demands of the heart are presented and it is shown that the dissolved oxygen in the blood is not sufficient to supply the heart. The significance of hemoglobin and the shape of the oxyhemoglobin dissociation curve are discussed.

Design of a rapid reaction apparatus (2 sessions). The challenge for this module is presented in Figure 2. Students had not been exposed to pressure-flow relations in rectangular ducts. They use the Buckingham Pi Theorem to construct relevant dimensionless variables. Charts are provided for laminar flow situations in

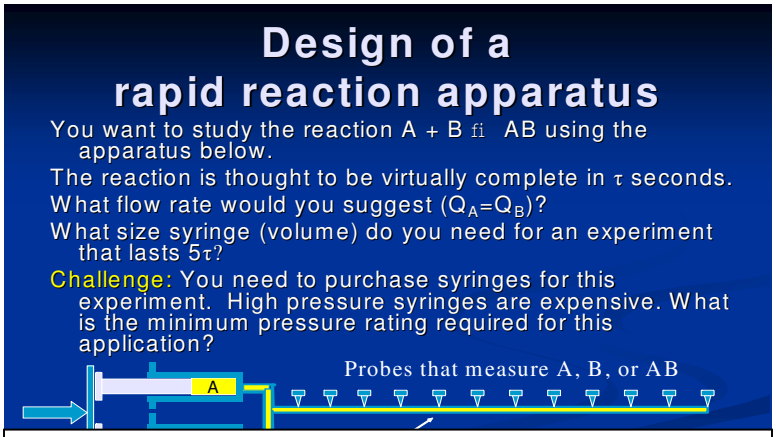

Figure 2. Rapid Reaction Challenge.

non-circular ducts. The friction factor, hydraulic diameter, and Moody chart are introduced for turbulent flow in ducts. The mechanical energy equation and friction loss factors are used to find pressure drops across fittings. Entry length effects are also considered.

Compartmental Analysis and Pharmacokinetics (3 sessions). The first challenge is to develop tracer methods for estimating total blood flow to the brain, for estimating blood flow to gray and white matter, and for estimating the gray/white tissue volume ratio. The Stewart-Hamilton equation is derived and a compartmental analysis is employed, along with the "peeling off exponentials" approach for extracting multiple time constants from a tracer curve. The second challenge deals with an intravascular bolus administration of a drug. The challenge is to find the maximum dose and time between injections such that the drug concentration does not drop below the minimum effective concentration and does not rise above the maximum safe concentration.

Designing Components of a Heart-Lung Machine (3 sessions). At the end of the semester, we returned to the design of the heart-lung machine proposed in the first module. The students had been exposed to most of the taxonomy needed to undertake such a design, including minimum pump size and the gas exchange requirements. However, several new topics are presented including shell and tube heat exchangers, and detailed treatment of convective heat transfer coefficients. We also derived and simplified the generalized partial differential equations of continuity, species conservation, thermal energy and the Navier-Stokes equation.

PRS Effectiveness

The topic of osmotic pressure was introduced as part of the cell volume regulation module, which was covered early in the semester. A single homework problem was assigned, then a series of PRS questions were asked in the next class meeting (Figure 3). The class did well on the homework problem, but their response to three of the PRS questions showed that many did not fully understand the concepts of osmotic pressure and the flow of water or solutes through

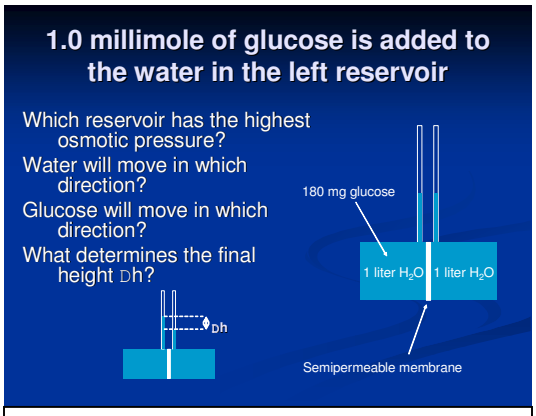

Figure 3. PRS Questions.

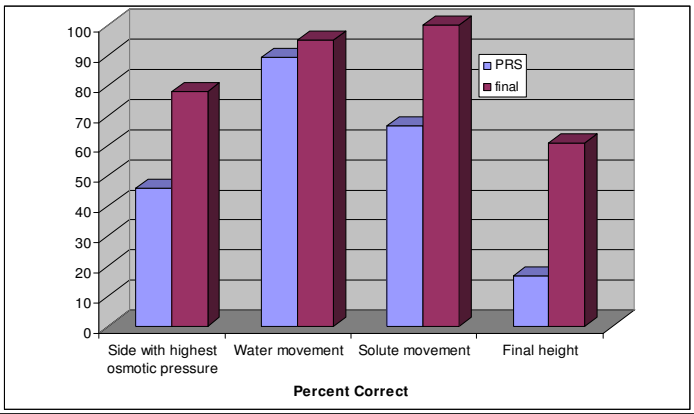

Figure 4. PRS Response vs. Response on Final Exam.

semipermeable membranes. In light of their poor performance, the material was reviewed immediately after asking the PRS questions, but the topic was not revisited again in the course. Equivalent questions were asked on the final exam. The students did remarkably better on the final exam, despite the fact that more than two months had transpired since the PRS questions

were reviewed (Figure 4). These results indicate that students who miss a PRS question tend to pay more attention to the explanation the second time around. Hence the PRS system appears to be very effective in providing *formative* assessment, in the true sense of the word.

VOS Observations

Results from the VOS classroom observation system (Figure 5) show little difference in the level of knowledge-centeredness in BME 210 (HPL) relative to other non-HPL courses taught in the same semester. However, a significantly greater amount of student-centered, assessment-centered, and community centered activities were observed in the HPL course relative to either of the non-HPL courses. The course labeled "non-HPL1" used the PRS system for assessment, but was not a challenge-based course. The four classifications are not mutually exclusive, so the percentages in Figure 5 can add to over 100%. These observations confirm that the challenge-based course more closely adheres to the HPL framework than the other two courses.

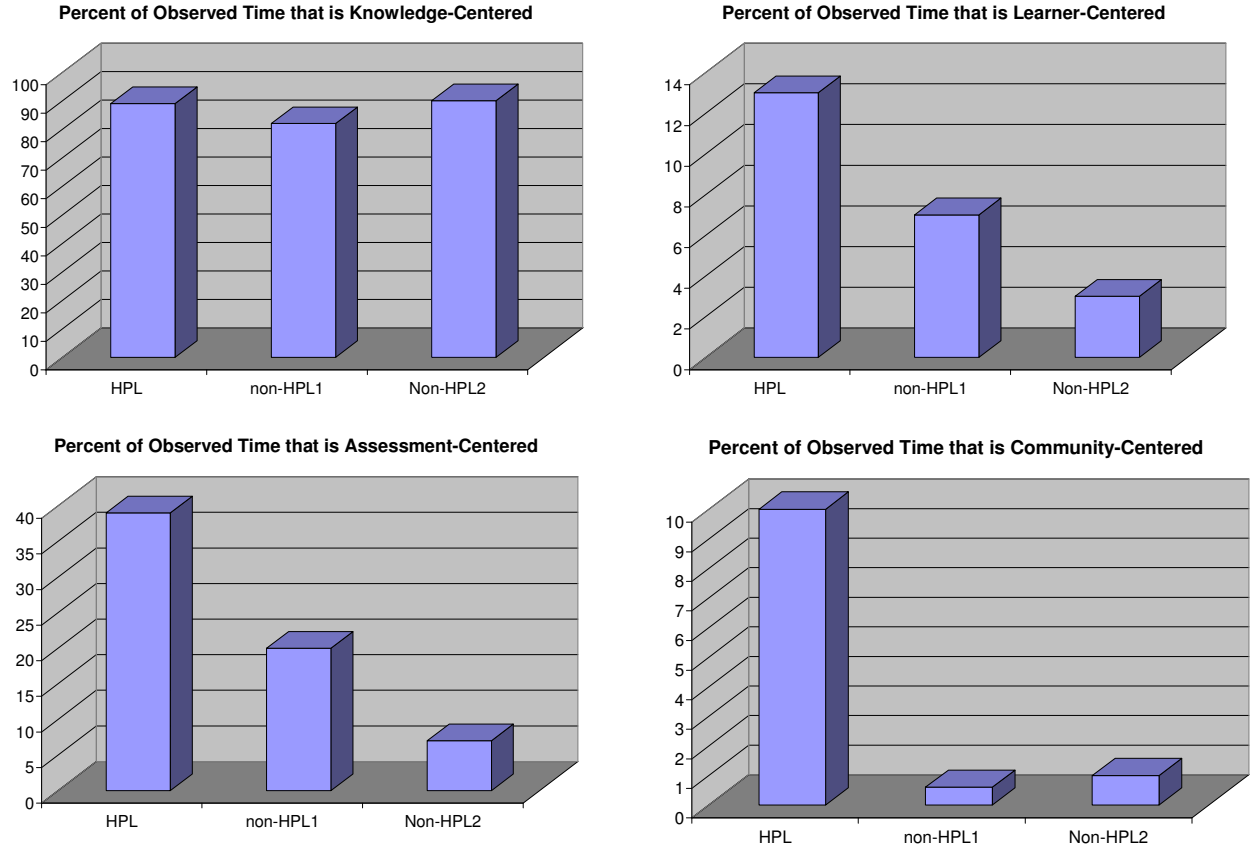

Figure 5. VOS Classroom Observations.

Module Effectiveness

The same topics normally taught in BME 210 using the traditional approach were effectively covered using a challenge-based approach. The primary advantage of this approach is that students become more involved, and hopefully more interested, in their own education. Some students find it difficult to jump around in the textbooks as challenges are presented. They are

generally quite comfortable with the familiar education model of moving linearly through the book, chapter by chapter. However, they soon recognize that real life challenges draw on multiple aspects of the taxonomy and they become more comfortable with using the textbooks, library, and the internet as resources.

Transformation of an entire course from a taxonomy-based to a challenge-based mode of instruction in a single semester is not the norm and is not recommended. Ordinarily new modules would be introduced each year until the course is eventually converted to the HPL model. The author has experience in teaching a challenge-based biomechanics course[6,7,9], which made the transformation somewhat easier. Nevertheless, the transformation was not as smooth as anticipated. Some classroom time previously devoted to lectures must be removed to make room for interactions in the classroom. In the case of the biomechanics course, many in-class lectures were converted to online lectures, providing the needed time. In the case of BME 210, the classroom time was freed by relying more on textbook assignments to provide supplementary information. Even then, there was not enough class time to cover the Thermal Comfort module.

Future Directions

In general, the modules were quite effective, so only minor changes will be necessary in the second offering of the course. However, in the next offering, I will devote a significant effort to preparing online lectures and additional resources, thus allowing more time for classroom interactions and opening enough class time for inclusion of the Thermal Comfort module.

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