An Experiment to

INTRODUCE MASS TRANSFER CONCEPTS USING A COMMERCIAL HOLLOW FIBER BLOOD OXYGENATOR

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The relatively new field of biomedical engineering emerged from interdisciplinary collaborations between engineers, life scientists, and physicians, and is the fastest growing discipline at most universities.[1] As a result of the aging population and growing focus on health issues, the demand for improved medical equipment and devices is rapidly increasing. According to the Department of Labor Statistics, biomedical engineers are expected to have employment growth of 23% between 2014–2024, in comparison with the average of 7% for all occupations.[2] It is also noteworthy that biomedical engineering has achieved greater participation of women in comparison with other engineering disciplines: In 2015, 40.9% of biomedical engineering bachelor's degrees were obtained by women, compared with an overall average of 19.9%.[3] While many biomedical engineers obtain a bachelor's degree from an accredited biomedical engineering program, a viable alternative relies on an undergraduate degree in a traditional engineering discipline complemented by technical electives related to biological sciences.[2]

Chemical, mechanical, and electrical engineers play an important and expanding role in this promising field because the core disciplinary principles are critical to biomedical mainstays such as the design of artificial organs. In an international study of career preferences of chemical engineering students, bioprocess and biomedical industry jobs received the highest ranking by a large margin in Australia and New Zealand, Canada, the United Kingdom, and the United States.[1] To provide engineering students with the skills directly relevant to the evolving needs of the biomedical industry, this paper describes a freshman laboratory experiment that is part of a larger effort to integrate biomedical content throughout the chemical engineering curriculum.[4-10] This paper presents a laboratory experiment in which students characterize man-made, life-saving oxygen transfer in a hollow fiber blood oxygenator in order to understand how engineering principles impact the design and operation of a heart-lung system.

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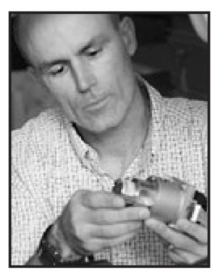

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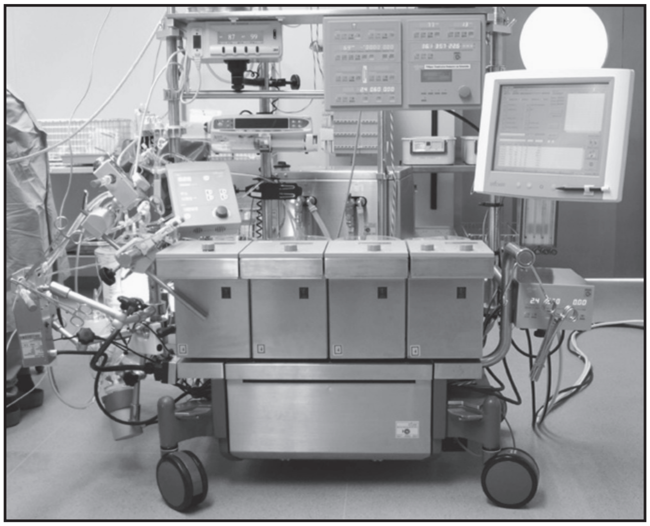

Figure 1. A clinical heart-lung machine. Reprinted from J. Schulze, "Herz-Lungen-Maschine im OP," Wikimedia <org/wiki/File%3AHeart-lung-machine.jpg>, vol. GFDL (<http://www.gnu.org/copyleft/fdl.html>), CC-BY-SA-3.0 (<http://creativecommons.org/licenses/by-sa/3.0/>), 2006.

The experiment was implemented within the Learning-for-Use framework[11] to increase students' experience with authentic engineering activities and promote deeper understanding of content.

CARDIOPULMONARY BYPASS

More than one million cardiopulmonary bypass procedures are performed each year[12] for surgeries including heart transplantation, coronary artery bypass, valve repair or replacement, and aneurysm repair.[13] In cardiopulmonary bypass (CPB), also known as extracorporeal circulation, the heart and lungs are temporarily removed from the circulation system. A heart-lung machine performs the function of the heart and lungs, allowing the heart to be still during the surgical procedure. Heart-lung machines have four functions: They pump the blood, oxygenate the blood, partially remove carbon dioxide from the blood,[14] and regulate the temperature of the blood.[15] A clinical heart-lung machine is shown in Figure 1.[16] Figure 2 shows the cardiopulmonary functions performed by a heart-lung machine.

Early heart-lung machines relied on bubble oxygenators to control blood gas levels. These have largely been supplanted by membrane oxygenators in modern heart-lung systems[17] in which the rate of oxygen transfer is directly proportional to the membrane area. Blood oxygenator membrane units are flat or hollow fiber membrane (HFM) units with at least 1 m^2 of surface area.[18,19] The units described in this paper have 2.5 m^2 of available membrane surface area.[20] Blood cells are delicate and are easily damaged by shear forces. Therefore fluid mixing is achieved through the geometric configuration of the oxygenator design rather than through high blood velocity.[21,22]

During bypass surgery on a typical adult patient, approximately 200 cm^3 (STP) CO_2/min must be transferred out of the blood and 250 cm^3 (STP) O_2/min must be transferred to the blood by the blood oxygenator. Excess loss of carbon dioxide causes alkalosis ($pH > 7.45$) while too little will cause acidosis ($pH < 7.35$).[23] Figure 3 shows the typical concentrations of blood entering and leaving the oxygenator.

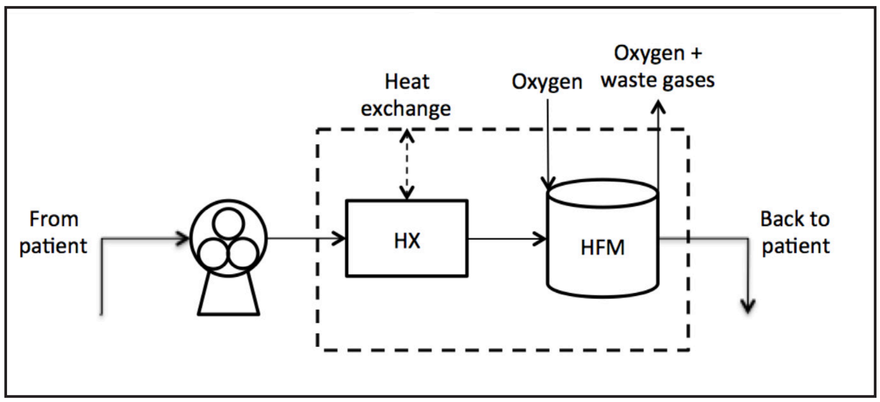

Figure 2. Unit operations in a heart-lung machine. Gas transfer is accomplished via membrane oxygenators, which have largely supplanted the bubble oxygenators used in early cardiopulmonary bypass (CPB) systems.[17] Heat exchange (HX) is required to maintain the desired body temperature. Heat exchanger and membrane are commonly combined into a single, disposable unit.[13]

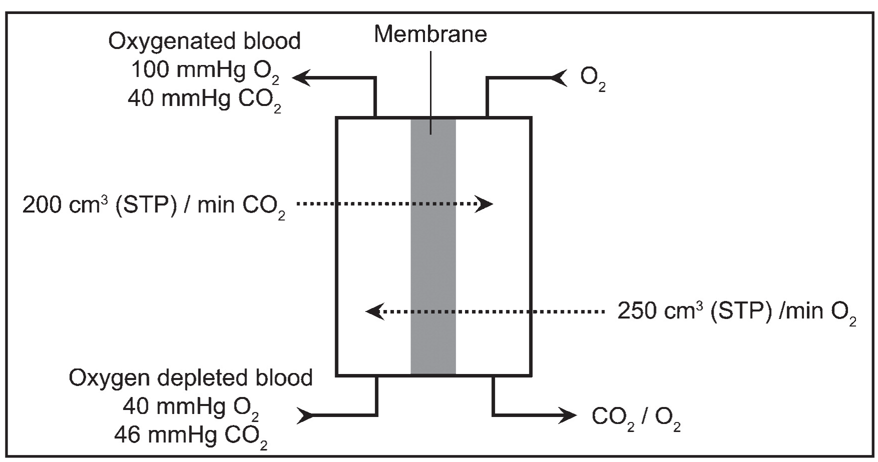

Figure 3. Membrane with gas transfer and concentration (partial pressures) values. As in the lungs, carbon dioxide is not completely removed to prevent alkalosis.[18]

Blood flow to the deeply anaesthetized patient during CPB is typically kept in the range of 2 – 4 L/min, which is less than the average resting flow rate of 5 L/min.[18] The ideal pump for CPB is capable of delivering physiologic blood flow against high resistance, without damaging blood. Positive displacement roller pumps and centrifugal pumps are the two most common types of pumps used for CPB; both are commonly used for routing procedures, although centrifugal pumps are preferred for prolonged circulatory support. The advantages and disadvantages of roller pumps and centrifugal pumps are reviewed by Tayama, et al.[24]

A heat exchanger is used to control the blood temperature and overall body temperature. A body temperature of 34 °C – 37 °C (normothermic) is used for some procedures; others require a reduction of the temperature to hypothermic conditions (<34 °C).[25] Normothermic operation is associated with increased oxygen demand due to the temperature dependence of metabolic processes.[26]

EDUCATIONAL CONTEXT

In 2009, Rowan University and Cooper University began a partnership that created a new four-year medical school, The Cooper Medical School of Rowan University. Vigorous collaboration between Rowan's College of Engineering and The Cooper Medical School provides a foundation for excellence in health and biomedical research by maintaining the infrastructure and expertise for interdisciplinary synergy and collaboration. Rowan University is uniquely poised to develop an innovative undergraduate curriculum that affords students the opportunity to pursue a versatile and traditional engineering discipline (*i.e.*, chemical, mechanical, electrical and computer, or civil), while simultaneously acquiring scientific knowledge and hands-on experience relevant to biomedical applications. Learning modules related to artificial organs, drug delivery, biometrics, and tissue engineering have recently been integrated into all levels of the chemical, mechanical, and electrical and computer engineering curricula.

The experiment was part of the Freshman Engineering Clinic I course at Rowan University. All students in the College of Engineering at Rowan University are required to participate in an eight-semester multidisciplinary course sequence called Engineering Clinic. Freshman Engineering Clinic I and II are offered in the fall and spring respectively, and each is a 2-credit-hour course. The class meets twice per week: one 50-minute meeting in a classroom, and one 165-minute meeting in a laboratory. Students from five engineering disciplines—biomedical, chemical, civil, electrical and computer, and mechanical—are enrolled in the course. There are currently 16 sections of the course offered with approximately 18–24 students from mixed disciplines in each section. Teams of students participate in a semester-long, multidisciplinary project that introduces students to a variety of introductory engineering topics and requires the application of science and mathematics concepts. While each instructor is free to choose a different project and pedagogical implementation, the common technical topics include unit conversions, statistics, problem solving, engineering design, and safety. Ethics, teamwork, and communication are also heavily emphasized in this course.

In the Fall 2012 semester, a heart-lung design project was introduced in one section of the Freshman Engineering Clinic I course at Rowan. This design project was adapted from a heart-lung curriculum described by Haar[27] that was originally designed for high school students. The details of the implementation of the project for Rowan's Freshman Engineering Clinic are described in more detail in Reference 28 but a brief description here is helpful for understanding the context in which the experiment was implemented. In this project, teams of students are challenged to design, build, and test their own heart-lung systems made from inexpensive, readily available materials. They are initially given minimal information about the function of heart-lung machines or criteria and constraints for their system; these are established through an open-ended design process over the course of one semester. The learning process is scaffolded through three cycles of semi-structured experiments investigating fluid flow, heat transfer, and mass transfer; this knowledge of transport phenomena is integrated with physiological and clinical considerations and applied to the design of heart-lung systems. The project offered rich opportunities to introduce a variety of engineering principles, was well received by students in the freshman course, and resulted in good learning outcomes; however, students' ability to apply science and engineering principles to the design of an engineering system was identified as a key area in need of improvement. While students performed well on assignments related to physiologic considerations, fluid flow, heat transfer, and mass transfer, their design reports did not adequately reflect synthesis of these concepts into their heart-lung design. For example, some teams included background information on the rate of oxygen delivery required during heart surgery, but neglected to calculate the rate of oxygen transfer in their own systems or to consider this as a criterion for evaluating their heart-lung designs.

Given an opportunity for informal feedback on the project, a theme that emerged was the desire for exposure to "real" lab equipment such as a commercially available blood oxygenator that would be used in an engineering research lab. The heart-lung experiment described in this paper was developed to provide a hands-on introduction to science and engineering principles using a laboratory blood oxygenation system, with the aim of improving students' ability to incorporate scientific and engineering principles into their heart-lung system designs.

While this experiment was implemented within the context of a semester-long heart-lung design project, it would be very suitable as a stand-alone experiment in an introductory first- or second-year chemical engineering course.

TABLE 1 Learning-for-Use strategies mapped to the blood oxygenator context			
LfU Step	LfU Strategy	Activity	Explanation
Motivate	Create demand	Structure of the mass transfer cycle of the project (consistent with overall project structure)	To design their oxygenators successfully, students must understand the relationship between variables that they can apply to their own designs
	Elicit curiosity	Pre-test	The pre-test and subsequent discussion of predictions elicits curiosity about blood oxygenator design and the factors affecting mass transfer
Construct	Observe	Non-intrusive investigation, hands-on experiment	Learners non-invasively investigate the design of the commercial blood oxygenator and speculate on rationale for design choices. In the hands-on experiment, they observe patterns and relationships among variables as directly perceivable phenomena
	Communicate	Instructor explanations	Instructor explains concepts of mass transfer resistance and introduces mass balance equations
Refine	Reflect	In-class group discussion	Students reflect on the experimental observations and design features of the commercial blood oxygenator and try to explain to others (see Appendix I)
	Apply	Design	Learners apply the mass transfer principles learned to the design of their own blood oxygenator

PEDAGOGICAL FRAMEWORK

Within an engineering context, Felder and Prince[29] present strong evidence that inductive teaching methods are more effective than traditional deductive teaching methods. Their review of inductive methods includes case studies, discovery learning, and project-based learning. The case for project-based learning throughout the engineering curriculum is compelling. In comparison to traditionally taught students, students who participate in inductive learning experiences are more motivated, demonstrate better communication and teamwork skills, and have a better understanding of issues of professional practice and how to apply their learning to realistic problems.[30-32] The effectiveness of purely constructivist, highly unguided approaches to teaching has been debated in the literature. For example, Kirschner, et al.[33] underscore the importance of providing guidance to mitigate heavy demands on working memory that impede the accumulation of knowledge in long-term memory.

This experiment was implemented within the context of guided inquiry, a constructivist-based approach in which learners are presented with a problem to solve and the instructor facilitates and supports the process of discovery and interpretation. To provide the scaffolding necessary for deep learning and knowledge transfer, the Learning-for-Use (LfU) framework described by Edelson[11] was used. The LfU model is a three-step process characterizing the development of knowledge for useable understanding: motivation, knowledge construction, and knowledge refinement.

In the LfU framework,[11] motivation is used specifically as it relates to acquiring knowledge or skills in a particular setting in which the student is already engaged. During knowledge construction, new knowledge structures are linked to prior knowledge. During knowledge refinement, knowledge is reorganized, connected to other knowledge structures, and reinforced. Ultimately the knowledge must exist in a procedural form so that it can be applied in other contexts. Table 1 shows how these three steps are mapped to the blood oxygenator context. This approach to laboratory instruction differs from the conventional deductive approach in which students first learn the underlying theory and test the strength of theoretical models as predictors of real-world behavior.[34]

During the semester-long heart-lung project, about three weeks were allotted to each of the design-build-test (DBT) cycles (fluid flow, heat transfer, and mass transfer), and an additional two weeks were allotted to optimization of system performance and preparation for the final challenge day. The commercial blood oxygenator experiment was part of the three-week module on mass transfer. Other activities performed during this module focused on the DBT cycle in which students added oxygenation to their heart-lung system. In the DBT cycle, students used aquarium pumps to oxygenate water and investigated the effect of air stone surface area and water flow rate on oxygen transfer.

EXPERIMENT

Objectives

After completing this experiment, students should be able to:

- *Define engineering and medical terminology relevant to mass transfer in heart-lung systems*
- *Calculate the rate of oxygen transfer from experimental measurements, using a mass balance*
- *Predict the effect of system variables such as temperature, flow rate, and membrane area on mass transfer rate*
- *Explain possible reasons that a mass balance does not close*

- *Evaluate design alternatives related to components and operating conditions of a heart-lung system*
- *Synthesize understanding of medical, science, and engineering knowledge into design and operation of the simple laboratory heart-lung system that was the basis of the semester-long project*

Heart-lung system

Figure 4 shows the blood oxygenator testing system used in this experiment. The blood analog fluid (water) is deoxygenated in a tank using a nitrogen sparge, and the fluid is circulated through two hollow fiber membrane modules in series and back to the tank. In the first membrane module the fluid is oxygenated by contact with oxygen. In the second membrane module the fluid is deoxygenated by contact with nitrogen. In a clinical setting the deoxygenation would be accomplished through the patient's metabolic processes. Gas flows on the tube side of the membrane module, and liquid on the shell side. Gas and liquid flow rates are changed individually to determine their effects on oxygen transfer rate.

Oxygen sensors measure the oxygen content of the gas and liquid streams entering and exiting the oxygenator. The flow rate of blood analog is controlled by a potentiometer on the pump and read on a flowmeter mounted on the front panel. Gas flow rates are measured and controlled by flowmeters with built-in valves. The flow measurement devices were specifically chosen to require students to practice unit conversions—the liquid flow rate is displayed in GPM, the gas flow rate in SCFM, and oxygen concentration is mg/L. The gas delivery pressure is monitored, and a manometer is used to measure the pressure drop across the membrane modules.

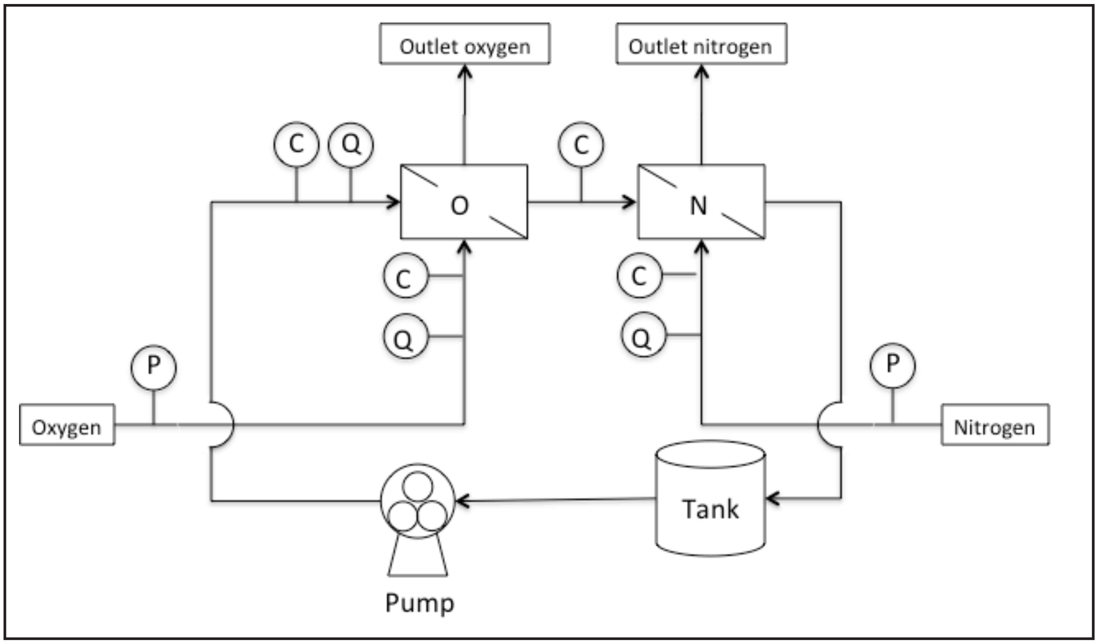

Figure 4. *The blood oxygenator testing system showing the two hollow fiber membrane modules used for gas exchange (Module O oxygenates the blood analog; Module N deoxygenates the blood analog). Concentration (C) measurements are taken at the inlet and the outlet of each hollow fiber membrane module. Gas pressure (P) is measured on the oxygen and nitrogen inlet streams, and liquid flow rate (Q) is measured on the blood analog inlet stream.*

TABLE 2
List of major equipment information with costs to project.
Valves and fittings are listed for their total cost.

Component	Make	Model	Typical Cost (USD)
Table	Fisher	Smart table	Available (*)
Pump	Watson-Marlow	701U/R	1300 (*)
Membrane units	Medtronic	Affinity NT	100 (**)
Valves and fittings	McMaster-Carr	(various)	550
Oxygen-in-gas sensor	Alpha-Omega	OXY-SEN	900
Dissolved oxygen sensor	Mettler-Toledo	InPro6050 and M300 O2	2300

(*) – Available laboratory equipment
(**) – Donated by Medtronic

The major components of the system are listed in Table 2. The pump used was a standard peristaltic pump available in the laboratory. The Watson-Marlow 701U/R model has been discontinued, but a comparable pump can be found on ebay for

TABLE 3
Gas and liquid flow rates defining each of the four runs. The different flow rates allow individual study of the effect of each on mass transfer rate.

	0.45 L O_2/min	**0.91 L O_2/min**
3.8 L BA/min	Run 1	Run 2
7.6 L BA/min	Run 3	Run 4

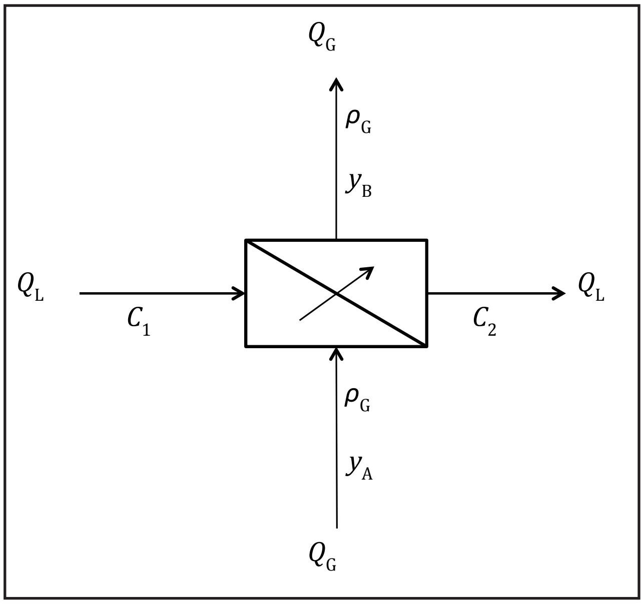

Figure 5. Blood oxygenator labeled with variables used in Eq. (3). Arrow in the center indicates oxygen mass transfer across membrane, which may be calculated using Eqs. (1) and (2) for the liquid side and gas side, respectively.

about $1,300. A centrifugal pump could be purchased from a supplier such as Cole Parmer for under $500. The Medtronic Affinity NT®Blood Oxygenator has a membrane surface area of 2.5 m^2, static priming volume of 270 ml, and range of blood flow from 1-7 L/min. Blood oxygenators can be found on ebay for under $100.

Procedure

Before beginning the experiment, each team met briefly with a graduate assistant for an orientation that covered safety and standard operating procedure. After completion of the orientation, students were able to run the system independently. Students worked in teams of 3–4 during the experiment and to produce the laboratory report. The entire experiment required about 60–75 minutes of student time in the laboratory.

At the start of operation flow rates of the blood analog (BA) and gases were set and the system was run for several minutes to allow steady state to be achieved. At this point, the oxygen concentrations in the inlet and outlet gas and liquid streams were measured. The flow rates were then changed and the process was repeated. Students performed runs in triplicate using four possible combinations of high and low gas and liquid flow rates (see Table 3).

Analysis: mass balances in blood oxygenators

Figure 5 shows a schematic diagram of the blood oxygenator around which a mass balance is written.

The rate of oxygen transfer to the incompressible liquid is

$$\dot{m}_L = Q_L (C_2 - C_1) \tag{1}$$

And the rate of oxygen transfer from the gas is

$$\dot{m}_L = Q_G \rho_G (y_A - y_B) \tag{2}$$

where Q is the flow rate, C is the mass concentration of dissolved oxygen in the liquid, y is the volume fraction of oxygen in the gas phase, and ρ is density. Assuming that the change in gas density is negligible and that the change in liquid flow rate is negligible, the gas and liquid mass transfer rates can be equated:

$$Q_G \rho_G (y_A - y_B) = Q_L (C_2 - C_1) \tag{3}$$

Each side of Eq. (3) represents the mass flow rate of oxygen across the membrane.

Redundant measurements allow both the liquid side and gas side mass transfer rates to be calculated from measured values of concentration and flow rate. These two values of the oxygen transfer rate across the membrane should be identical, but in reality almost never are; students are required to think critically to generate possible explanations for a mass balance that does not close.

Blood is a shear thinning and viscoelastic fluid; its rheological properties can be simulated using a blood analog fluid.[26,35] At lower shear rates (above the yield stress and below 100 s^{-1}), blood behaves as a power law fluid. At higher shear rates (above 100 s^{-1}), blood behaves as a Newtonian fluid. Blood in circulation in the major arteries and veins is often assumed to behave as a Newtonian fluid,[36] where at 37 °C, the blood viscosity relative to water is about 3.0. In this introductory experiment, non-Newtonian effects are not considered, and water suffices used as the blood analog (BA). McIver, et al.[37] present a related educational experiment to investigate the mass transfer of blood analog fluids in hollow fiber blood oxygenators based on Re-Sc-Sh correlations. A description of the rheological properties of blood is provided in the context of chemical engineering education by Purdy, et al.[9]

Students recorded the raw data in their laboratory notebooks and performed a complete set of hand calculations for one run before leaving the lab.

For the laboratory report, students calculated the liquid side and gas side mass transfer rates at each of the four operating states shown in Table 3. For a given run, the difference between the liquid side and gas side mass transfer rate was around 8-10%, and students used the mean value in their analysis. The most likely explanation for the discrepancy between calculated gas and liquid side mass transfer rates is that the pulsated liquid flow from the peristaltic pump caused variation in the liquid flow rate as measured with a rotameter.

Students explored the effect of the gas flow rate and the liquid flow rate on the mass transfer rate by preparing column graphs (Figure 6 and Figure 7). To reinforce statistical concepts, one graph used error bars that represent standard error bars, which allowed students to conclude whether the difference between two means was not statistically different; the other graph used 95% confidence intervals, which allowed students to conclude when the difference between means is statistically significant.

The conclusions shown in the figures—that mass transfer rate is independent of gas flow rate and is directly proportional to liquid flow rate—agree with literature. Wickramasinge, et al.[35] have extensively studied the operation of hollow fiber membrane modules such as these and found gas flow rate variations do not affect the rate of oxygen transfer. At typical clinical conditions, pure oxygen flows on the gas side of the membrane, and because the membrane is hydrophobic, its pores are also filled with pure oxygen. Thus, the concentration gradient exists in the boundary layer on the liquid side of the membrane, causing the dominant resistance to exist within the liquid boundary layer. This boundary layer resistance depends on liquid flow rate but not gas flow rate.

After the students have completed their calculations and prepared their graphs, concepts related to mass transfer resistance are treated inductively in class. The class discussion was structured such that students established connections between prior knowledge and new observations; explored analogies between heat, mass, and momentum transfer using familiar examples; and constructed an understanding of transport concepts through inductive methods of analogy, prediction, and generalization. The treatment was at an introductory level, but students were able to construct principles that explain their observations.

ASSESSMENT

The assessment considered knowledge gains directly related to the experiment as well as the gain in procedural knowledge that is usable by learners. To assess the effect of the experiment on knowledge gains directly related to the experiment, a pretest/post-test comparison design was used. To assess the usability of the knowledge gained by students, end-of-semester design reports by the treatment group were compared to those by the comparison group.

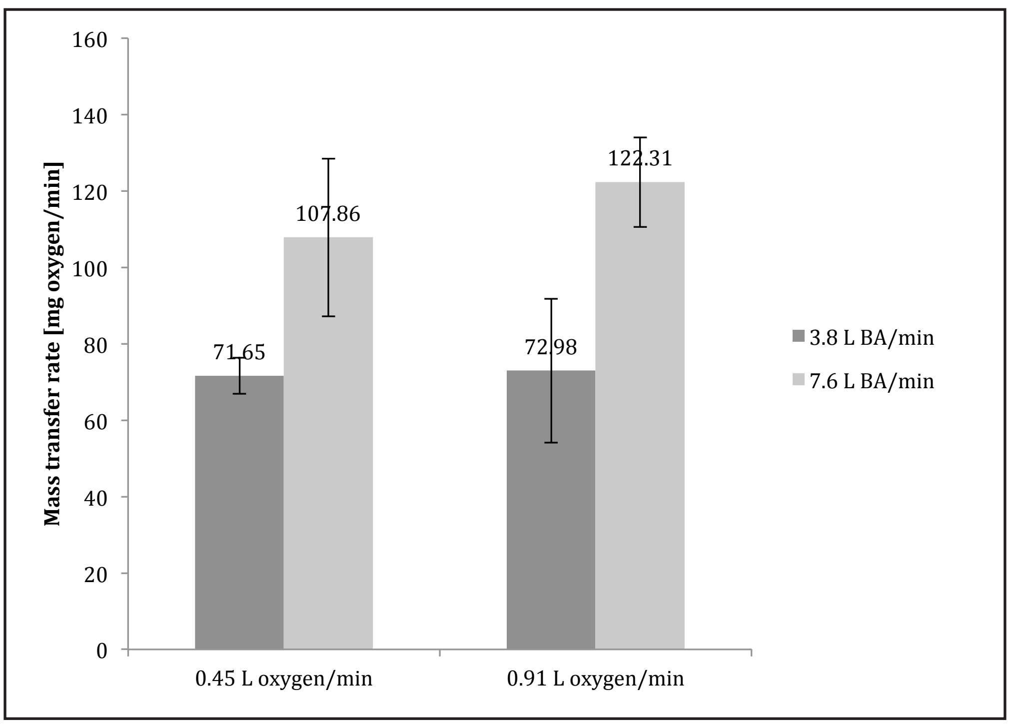

Figure 6. *Mass transfer rates for all four operating conditions listed in Table 3 showing confidence intervals on mean values. Each value is an average of the gas and liquid side mass transfer rates based on three trials. Error bars are 95% confidence intervals. The non-overlapping 95% confidence intervals allow students to conclude that the difference between means is not significant, and therefore the blood analog flow rate does not affect the mass transfer rate under these conditions. In the legend, BA refers to blood analog.*

To measure and compare learning outcomes, a pretest and post test were administered to two groups of students. One class section (n=21) served as the treatment group that performed the mass transfer experiment described here; another class section (n=23) served as the comparison group that did not perform the experiment. Both sections performed the same semester-long project during the course in which they designed, built, and tested a simple model of a heart-lung machine in a challenge-based module. Class content and home assignments were coordinated among the two sections to be the same. Thus, the experiment described here was used to enhance the students' understanding of science and engineering concepts, data analysis, and engineering design as applied to a blood oxygenator beyond the understanding derived from participating in the project. A limitation to this methodology is that in a highly interactive classroom it is not always possible to coordinate the timing of all discussions across the treatment and comparison groups, because discussions can be initiated by the class participants.

The pretest and post test comprised 11 questions that target students' understanding related to: (1) the application of mathematics, science, and engineering principles, ABET A; (2) designing and conducting experiments, analyzing and interpreting experimental data, ABET B; and (3) designing a system or component to meet specific needs, ABET C. The pretest was administered in the second week of class before students began working on their semester-long project. The post test was administered at the end of the semester, 3–4 weeks after the completion of the experiment and two weeks after completion of the project. The test questions were designed to address lower and higher levels of cognition (Anderson and Krathwohl, 2001). Test questions were a mix of six multiple-choice questions, four verbal short-answer questions, and one mass balance question. The test questions are provided in Appendix II. Question 1 was removed from the analysis due to an error in the phrasing, which made the correct choice ambiguous.

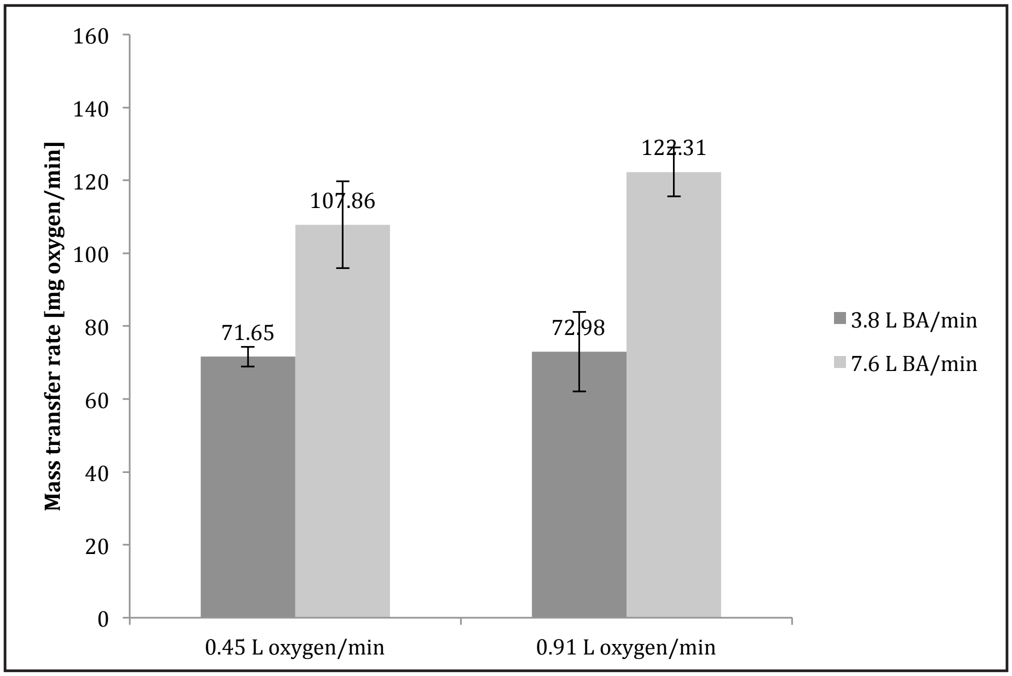

Figure 7. *Mass transfer rates for all four operating conditions listed in Table 3 showing standard error of mean values. Each value is an average of gas side and liquid side mass transfer rates based on three trials. Error bars are standard error. The overlapping standard error bars allow students to conclude that the difference between means is significant, and therefore the oxygen flow rate does not have an effect on the mass transfer rate under these conditions.*

Correct answers to multiple-choice questions 1-6 were awarded one point and incorrect answers were awarded zero points. Question 7 was an open-response question; its solution involved determination of the rate of mass transfer between phases. One point was awarded for mathematical representation of the three streams involved, one point for recognizing that the mass transfer rate was equivalent to the product of concentration and volumetric flow rate, and one point for applying the correct mathematical signs to indicate input or output terms. Question 8 asked for the three main functions of the heart-lung machine, and one point was awarded for each correct response. Question 9 asked why a very high blood flow rate should not be used to enhance mass transfer in a blood oxygenator, and one point was awarded if students identified a reasonable response directly or indirectly related to blood shear. Question 10 asked for a typical flow rate used in a blood oxygenator. The question was worth two points; one point was awarded for a response indicating a reasonable flow rate and one point for justification based on physiologic reasoning. Question 11 asked what body temperature is maintained during open heart surgery. The question was worth two points. One point was awarded for a correct answer indicating a temperature within a reasonable range, and one point was awarded for an explanation that was based on the body's demand for oxygen.

Two students were absent on the day the pretest was given to the treatment group. The mean pretest score of the treatment group (n=19) was 30.92% (SD=12.05%) and the mean pretest score of the comparison group (n=23) was 34.51% (SD=9.58%). The pretest scores of the treatment and the comparison group were compared using an independent, two-tailed Students t-test at a 95% confidence level. In the two groups, there was a statistically significant difference between the treatment and comparison based on pretest scores (p=1.7e-4).

The mean post-test score for the treatment group (n=21) was 76.49% (SD=15.30%), compared with the mean post-test score for the comparison group (n=23) which was 52.98% (SD=11.96%). The post-test scores of the treatment and the comparison group were compared using an independent, two-tailed Students t-test at a 95% confidence level. A statistically significant difference was found between the means of the two groups (p=2.1e-6).

The class average normalized gain was computed and used to evaluate knowledge gain as recommended by Hake.[38] The class average normalized gain is defined as the average actual gain divided by the maximum possible average gain:

$$\frac{\text{avg \% post} - \text{avg \% pre}}{100 - \text{avg \% pre}} \tag{4}$$

The class average normalized gain is one way of considering pre-test differences. Figure 8 shows the class average normalized gain on each question for the two groups. On almost every question, the gain and normalized gain were higher for the treatment group in comparison with the comparison group. The exception to this was the average normalized gain for question 8, which asked about heart-lung machine function and operation. However, heart-lung function and operation was mentioned briefly in the treatment section's class prior to the administration of the pre-test, which resulted in an artificially high pre-test score on question 8. Thus, the normalized gain for the treatment group is unreliable for that question. Hake[38] considers a normalized gain of 0.7 or higher to be considered high. A medium normalized gain is defined as 0.3–0.7, and a low normalized gain is below 0.3. The treatment group achieved high normalized gains on questions 4 and 7 and medium normalized gains on questions 2, 3, 5, 6, 9, and 10.

The effect size (Cohen's d) was used evaluate the magnitude of differences between groups based on pretest and post-test

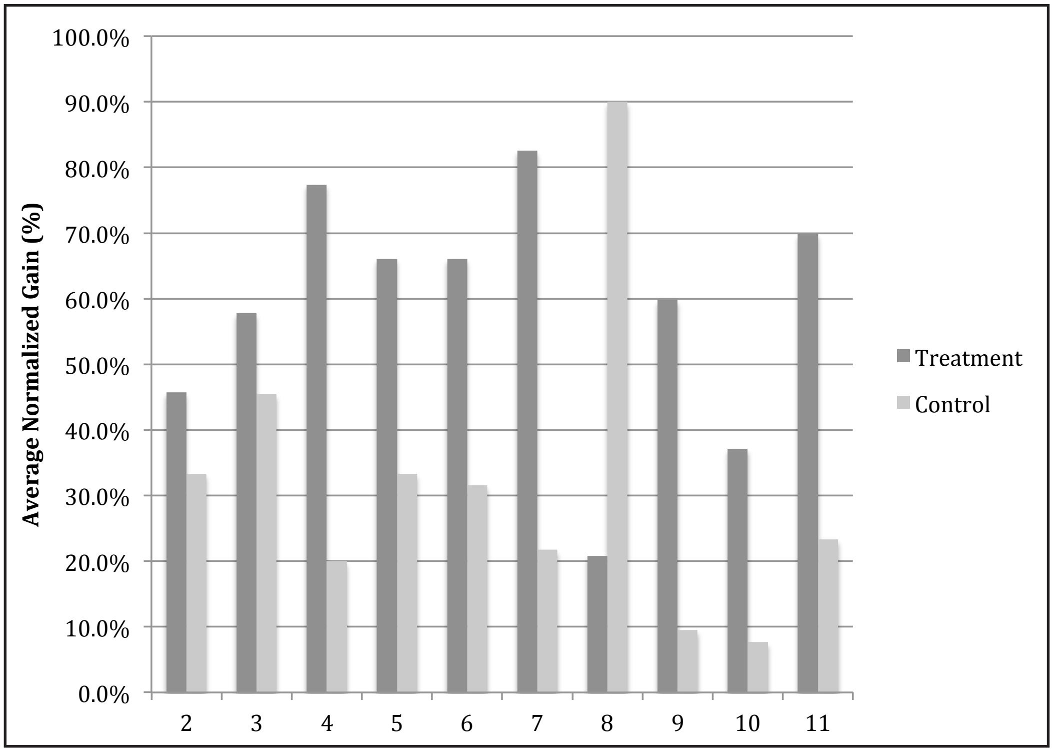

Figure 8. *Average normalized gain for each question on the test.*

TABLE 4

Design report rubric showing performance of teams in the comparison group (C) and the treatment group (E) against several performance indicators. The performance indicators were evaluated on a 4-point Likert scale: No evidence, Below expectations, Meets expectations, and Exceeds expectations. The numbers reflect the number of teams receiving each rating. Because all of the teams provided some evidence on each performance indicator, the level of "no evidence" is left out of the table. A positive shift in performance is seen with the comparison group in comparison with the treatment group.

	Below expectations		**Meets expectations**		**Exceeds expectations**	
Performance Indicator	**C**	**T**	**C**	**T**	**C**	**T**
Applied knowledge of heat transfer, mass transfer, fluid flow to the solution of an engineering problem	3	0	2	4	1	2
Identified realistic constraints in the following categories: economic, ethical, and medical	2	1	3	3	1	2
Developed technically feasible alternative solutions	4	1	1	3	1	2
Analyzed solution using engineering principles	2	1	2	2	2	3
Compared and evaluated alternative solutions using criteria and constraints	2	0	2	3	2	3
Recommended one of the solutions	0	0	5	4	1	2

scores. The calculated effect size of d = 2.06 is well above the criterion for large effect size suggested by Cohen,[39] indicating that the treatment had a large effect on student performance in the post test.

A design report rubric was used to assess the performance of each team in the comparison group (C) and the treatment group (T) against specific performance indicators. Elements of the rubric deemed directly relevant to this experiment are shown in Table 4. The performance indicators shown in the left column of the table were evaluated on a 4-point Likert scale: no evidence, below expectations, meets expectations, and exceeds expectations. The numbers in the table reflect the frequency of the rating received by teams in each group. Because all of the teams provided some evidence on each performance indicator, the level of "no evidence" is left out of the table. A positive shift in performance is seen with the treatment group vs. the comparison group. This suggests that the treatment group surpassed the comparison group in acquiring knowledge in a form that was retrievable and usable in a context beyond the isolated experiment.

CONCLUSION

This paper presents a hands-on experiment to introduce lower-level engineering students to mass balances in a two-phase system, using a laboratory blood oxygenation system as an example. This experiment builds on Rowan's previous efforts to integrate biomedical topics and hands-on experiments into the engineering curriculum.

The effectiveness of the experiment was assessed by comparing learning outcomes between a treatment group that performed the experiment and a comparison group that did not. Both sections performed the same semester-long project during the course in which they designed, built, and tested a simple model of a heart-lung machine in a challenge-based module. The project comprised three DBT lab modules that focused on fluid flow, heat transfer, and mass transfer functions of a student-designed heart-lung machine. The clinical blood oxygenator experiment described in this paper was performed by the treatment group during the mass transfer module. Thus, the assessment demonstrates the effectiveness of the experiment in enhancing learning outcomes beyond the understanding derived from participating in the project.

The treatment group that performed the experiment showed improved learning outcomes relative to the comparison group in knowledge directly related to the experiment. The group that performed the experiment scored significantly higher on the post test and achieved higher average normalized gain between pretest and post test than the comparison group; the effect of the intervention (Cohen's d) was 2.06. Further, this knowledge acquisition translated into a better ability to incorporate engineering principles into the design of a heart-lung machine in a semester-long project, when the performance of the treatment group was compared with that of the comparison group.

The introduction of the commercial blood oxygenator experiment into the heart-lung design project provided an opportunity to integrate the Learning-for-Understanding framework into the mass transfer module of the project. LfU offered scaffolding for learning in a guided inquiry project through a cycle of creating demand, eliciting curiosity, fostering knowledge construction, observation, communication, reflection, and application. The improved pre/post gains of the treatment group suggests that knowledge construction through inductively sequenced observation of phenomena followed by communication of concepts resulted in enhanced learning outcomes. The activities comprising the refinement of knowledge (reflection and application) were designed to facilitate the transformation and reorganization of knowledge structures for future retrieval and use. The improved performance of the treatment group with respect to applying engineering knowledge to their own heart-lung system designs suggests that the refinement of knowledge helped students activate their knowledge in a new context.

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REFERENCES

1. Shallcross, D.C., "Career Preferences for Undergraduate Chemical Engineering Students," *Education for Chemical Engineers*, **1**, 30 (2006)
2. U.S.D.o.L. Bureau of Labor Statistics. (29 December, 2015). *Occupational Outlook Handbook*, Biomedical Engineers (2016-17 Edition ed.). Available: <http://www.bls.gov/ooh/architecture-and-engineering/biomedical-engineers.htm>
3. Yoder, B., "2015 ASEE Profiles of Engineering and Engineering Technology Colleges," Washington, D.C. (2015)
4. Farrell, S., and R.P. Hesketh, "An Introduction to Drug Delivery for Chemical Engineers," *Chem. Eng. Ed.*, **36**(2), 198 (2002)
5. Farrell, S., R.P. Hesketh, and M. J. Savelski, "A Respiration Experiment to Introduce Chemical Engineering Principles," *Chem. Eng. Ed.*, **38**(3), 182 (2004)
6. Farrell, S., R.P. Hesketh, and M.J. Savelski, "Hands on the Human Body! Exploration of Heat Work and Power," *Chem. Eng. Ed.*, **39**(1), 30 (2005)
7. Farrell, S. and J. Vernengo, "A Drug Delivery Experiment Using Alginate Microspheres," *Chem. Eng. Ed.*, **46**(2), 97 (2012)
8. Mosto, P., M.J. Savelski, S. Farrell, and G. Hecht, "The Future of Chemical Engineering: Integrating Biology into the Undergraduate Chemical Engineering Curriculum," *Chem. Eng. Ed.*, **41**(1), 43 (2007)
9. Purdy, C., J. Vernengo, and S. Farrell, "Teaching Fundamental Concepts of Rheology within the Context of Sickle Cell Anemia," *Chem. Eng. Ed.*, **48**(3), 143 (2014)
10. Vernengo, J., P. Schwalbenberg, and S. Farrell, "Undergraduate Design and Structure-Property Characterization of Biomaterials," in Biomaterials Society Annual Conference, Denver, CO (2014)
11. Edelson, D.C., "Learning-for-Use: A Framework for the Design of

Technology-Supported Inquiry Activities," *J. Research in Science and Teaching*, **38**, 355 (2001)
12. Kaplan, J.A., D.L. Reich, and J.S. Savino, *Kaplan's Cardiac Anesthesia*, 6th ed., St. Louis: Saunders (2011)
13. Lillehei, W.C., "Historical Development of Cardiopulmonary Bypass in Minnesota," pp. 3-20 in *In Cardiopulmonary Bypass: Principles And Practice*, G.P. Gravlee, R.F. Davis, M. Kurusz, and J.R. Utley, eds., Philadelphia: Lippincott Williams Wilkins (2008)
14. Stoney, W.S., "Evolution of Cardiopulmonary Bypass," *Circulation*, **119**, 2844 (2009)
15. Hessel II, E.A., "Circuitry and Cannulation Techniques," in *Cardiopulmonary Bypass: Principles and Practice*, G.P. Gravlee, ed., Philadelphia: Lippencott, Williams Wilkins (2008)
16. Schulze, J., "Herz-Lungen-Maschine im OP," Wikimedia Commons <https://commons.wikimedia.org/wiki/File%3AHeart-lung-machine.jpg>, vol. GFDL (<http://www.gnu.org/copyleft/fdl.html>), CC-BY-SA-3.0 (<http://creativecommons.org/licenses/by-sa/3.0/>) 2006
17. Chatterjee, S., and A. Miller, *Biomedical Instrumentation Systems*, Cengage Learning, Clifton Park, NJ (2010)
18. Stamatialis, D.F., B.J. Papenburg, M. Girones, S. Saiful, S.N. Bettahalli, and S. Schmitmeier, "Medical Applications of Membranes: Drug Delivery, Artificial Organs and Tissue Engineering," *J. Membrane Science*, **308**(134), 1 (2008)
19. Haworth, W.S., "The Development of the Modern Oxygenator," *The Annals of Thoracic Surgery*, **76**, S2216 (2003)
20. Zhang, J., T.D.C. Nolan, T. Zhang, B.P. Griffith, and Z.J. Wu, "Characterization of Membrane Blood Oxygenation Devices Using Computational Fluid Dynamics," *J. Membrane Science*, **288**, 268, 1 February 2007
21. Cloutier, P., R. Olsen, S. Roller, C. Plott, A. McLevish, M. Li, M. Laxen, J. Knoll, and G. Hake, "Deairing Oxygenator for Treating Blood in an Extracorporeal Blood Circuit," US8518259 B2 (2013)
22. Carpenter, W.L., R.W. Olsen, M.J. Hobday, A.L. McLevish, C.J. Plott, R.E. Briscoe, P.J. Cloutier, A. Thapa, M. Li, et al., "Radial Design Oxygenator With Heat Exchanger," ed: Google Patents (2013)
23. Brown, T.L., H.E. LeMay, B.E. Bursten, C. Murphy, P. Woodward, and M.E. Stoltzfus, *Chemistry: The Central Science*, 13th ed., Upper Saddle River: Prentice Hall (2014)
24. Tayama, E., S.A. Raskin, and Y. Nosè, "Blood Pumps," in *Cardiopulmonary Bypass: Principles and Practice*, G.P. Gravlee, R.F. Davis, M. Kurusz, and J.R. Utley, eds., 2nd ed., Philadelphia: Lippencott Williams and Wilkins (2000)
25. Toenz, M., T. Mihaljevic, L.K. Segesser, E.R. Schmid, H.I. Joller-Jemelka, P. Pei, and M.I. Turina, "Normothermia Versus Hypothermia During Cardiopulmonary Bypass: Controlled Trial," *Annals of Thorac Surgery*, **59**, 137 (1995)
26. Wickramasinghe, S.R., C.M. Kahr, and B. Han, "Mass Transfer in Blood Oxygenators Using Blood Analogue Fluids," *Biotechnology Progress*, **18**, 867 (2002)
27. Vonder Haar, Z.D., T.M. Bayles, and J.M. Ross, "Engineering in Healthcare: A Heart Lung System," in ASEE Annual Conference, Vancouver, BC (2011)
28. Farrell, S., T.M. Bayles, and P. Kieran, "An Adaptable and Transferrable Project Based on a Heartlung Machine Design Challenge," in *Proceedings of the 2016 ASEE Annual Conference*, New Orleans (2016)
29. Prince, M.J., and R.M. Felder, "Inductive Teaching and Learning Methods: Definitions, Comparisons and Research Bases," *J. Eng. Ed.*, **95**, 123 (2006)
30. Dym, C.L., A.M. Agogino, O. Eris, D.D. Frey, and L.J. Leifer, "Engineering Design Thinking, Teaching and Learning," *J. Eng. Ed.*, **94**, 103 (2005)
31. Mills, J.E., and D.F. Treagust, "Is Problem-Based or Project-Based Learning the Answer?" *Australasian Journal of Engineering Education* (2003) Available: <http://www.aaee.com.au/journal/2003/mills_treagust03.pdf>
32. Galand, B., and M. Frenay, *L'approche par Problèmes et par Projets dans l'Enseignement Supérieur: Impact, Enjeux et Defies*, Louvain-la- Neuve: Presses Universitaires de Louvain (2005)
33. Kirschner, P.A., J. Sweller, and R.E. Clark, "Why Minimal Guidance During Instruction Does Not Work: An Analysis of the Failure of Constructivist, Discovery, Problem-Based, Experiential, and Inquiry-Based Teaching," *Educational Psychologist*, **41**, 75 (2006)
34. Feisel, L.D., and A.J. Rosa, "The Role of Laboratory Experiments in Undergraduate Education," *J. Eng. Ed.*, **94**, 121 (2005)
35. Wickramasinghe, S., J. Garcia, and B. Han, "Mass and Momentum Transfer in Hollow Fibre Blood Oxygenators," *J. Membrane Science*, 208 247256, pp. 1-2, (2002)
36. Truskey, G.A., F. Yuan, and D.F. Katz, *Transport Phenomena in Biological Systems*, 2nd Ed., Upper Saddle River, NJ: Pearson (2009)
37. McIver, K. ,T.L. Merrill, and S. Farrell, "An Experiment to Introduce Mass Transfer Correlations: Characterizing Mass Transfer in a Commercial Hollow Fiber Blood Oxygenator Using Blood Analog Fluids," In preparation, 2016
38. Hake, R., "Interactive Engagement Versus Traditional Methods: a Six-Thousand Student Survey of Mechanics Test Data for Introductory Physics Courses," *American J, Physics*, **66**, 64 (1998)
39. Cohen, J., *Statistical Power Analysis for the Behavioral Sciences*, 2nd Ed., Hillsdale: Lawrence Earlbaum Associates (1988)

APPENDIX I: DISCUSSION QUESTIONS

After conducting the experiment, students perform data analysis and bring basic calculations/graphs to class. They also read a patent for a Medtronic oxygenator[22] (background and summary) prior to coming to class.

1. Review the flow diagram.
2. Review mass balance equations and assumptions. Do the assumptions (incompressible liquid, negligible change in gas and liquid flow rates, negligible change in gas density) seem reasonable?
3. What are the sources of experimental error? Which measurement do you think contributes the greatest uncertainty? (The measurement of liquid flow rate is likely to contribute the most error. The peristaltic pump causes pulsation error in the rotameter.)
4. When operating at low gas flow rate, what effect did doubling the liquid flow rate have on
    a. The "blood" oxygen concentration difference between inlet and outlet? (The concentration difference decreased slightly)
    b. The rate of oxygen transfer to the "blood"? (The mass transfer rate increases significantly)
5. Did you observe the same trend when operating at the higher gas flow rate? (The concentration difference did not change significantly, but the gas transfer rate increased when the liquid flow rate increased).
6. When operating at low liquid flow rate, what effect did doubling the gas flow rate have on
    a. The "blood" oxygen concentration difference between inlet and outlet? (The concentration difference is about the same.)
    b. The rate of oxygen transfer to the "blood"? (The rate of oxygen transfer did not change significantly).
7. Did you observe the same trend when operating at the higher liquid flow rate? (Yes)

8. Discussion of resistances: observations show that liquid side mass transfer resistance dominates. Changing the gas flow rate has little effect because the gas side resistance is already minimized.

9. Increasing the liquid flow rate increases the rate of oxygenation of the "blood." Would there be any limit on the flow rate that should be used? Why? (Discuss damage to blood cells.)

10. Discuss design of blood oxygenator—what features promote good mass transfer? (Large membrane area and geometric configuration.)

11. What function of the clinical blood oxygenator did we NOT use in this experiment? (The heat exchanger was not used in our experiment.)

12. Based on what you know about the temperature dependence of oxygen solubility in water, would you place the heat exchanger before or after the membrane oxygenator? (Students explored temperature dependence of gas solubility in the DBT lab. Gas transfer will be more effective if the blood is cooled prior to oxygenation.)

13. How does the oxygenator design consider the amount of blood that is removed from the patient's body? (The design minimizes the "priming volume," so that the amount of blood removed from the patient is minimized.)

APPENDIX II: PRE/POST TEST QUESTIONS

1. What does "mass transfer" mean?
   a. A net movement of mass from one location to another
   b. The process of changing mass into weight
   c. Movement of mass between phases
   d. Bulk flow of mass moving across a system boundary

2. An adult human blood flow rate through the heart is approximately:
   a. 1 L/min
   b. 5 L/min
   c. 8 L/min
   d. 10 L/min

3. If the membrane area in a hollow fiber oxygenator is doubled, the rate of oxygen transfer to the deoxygenated blood contacted by oxygen would
   a. Decrease by a factor of 2
   b. Stay the same
   c. Increase by a factor of 2
   d. Increase by a factor of diameter squared

4. The term describing dissolved oxygen movement through a liquid such as blood, from a high concentration to a low concentration:
   a. Rediffusion
   b. Perfusion
   c. Associated rediffusion
   d. Diffusion

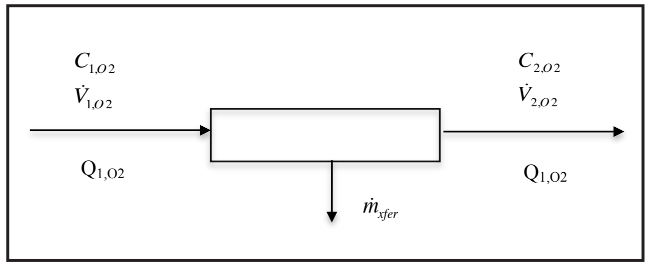

Figure A1.

5. In a hollow fiber membrane oxygenator, pure oxygen flows at a high flow rate through the tubes. The membrane is thin and oxygen fills the pores of the membrane. On the other side of the membrane (shell side), blood flows through the unit. How could the mass transfer rate of oxygen to the blood be increased?
   a. Increase the gas flow rate through the oxygenator
   b. Increase the liquid flow rate through the oxygenator
   c. Decrease the gas flow rate through the oxygenator
   d. Decrease the liquid flow rate through the oxygenator

6. The solubility of a gas in a liquid
   a. Increases as the temperature increases
   b. Does not depend on temperature
   c. Decreases as the temperature increases
   d. Decreases as the pressure increases

7. Write an equation for the rate of oxygen transfer to blood in a hollow fiber oxygenator. In the diagram Figure A1, C is the concentration of oxygen in the blood (mg/L), Q is the volumetric flow rate of the blood (L/min), and $\dot{m}$ is the rate of oxygen transfer to the gas (mg/min).

8. What are three functions of a heart-lung machine?

9. There are some benefits to using a higher blood flow rate of blood in a hollow fiber blood oxygenator. Yet it is not desirable to operate the blood oxygenators at the fastest flow rate the pump can achieve. Why?

10. What is a typical flow rate used in a hollow fiber blood oxygenator during open heart surgery for an adult, and why?

11. What body temperature is typically maintained by the heart-lung machine during open heart surgery, and why? ❐