

A SIMPLIFIED MODEL OF HUMAN ALCOHOL METABOLISM

That Integrates Biotechnology and Human Health Into a Mass Balance Team Project

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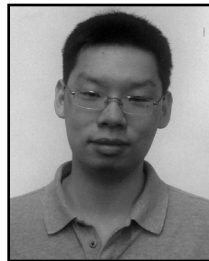
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Chemical engineers are important players in meeting the growing challenges of the 21st century, particularly in the areas of biotechnology and sustainable development. Most chemical engineering curriculums (including ours), however, still generally consist of a single path, through a set of fundamental courses, which teaches a necessary set of standard skills.^[1-3] The challenge for chemical engineering is refocusing some topics to create a program of study that has an overall modern feel, integrated with the strong tradition in the core values and fundamental skills that allow chemical engineers to be the important players in these emerging fields.^[2] In our Mass and Energy Balances course, we felt it was critically important to provide our sophomores with a clear understanding of the unique role of chemical engineering in the biotechnology field as well as illustrate the impact of these efforts on human health. This goal was reinforced by a survey of career interests given the first day of class; nearly 30 percent of our students had career interests in biotechnology.

Another common theme in our survey data was the desire to positively impact society. Research shows that students learn better if they are actively engaged in the material^[4,5] and if they find the content relevant to their own career interests.^[6] Research also shows that tying problems back to the “human element” engages student interest and enhances learning.^[7] Thus the logical choice for us was to add a group project to the course that reinforced fundamental skills and addressed an emerging area of biotechnology, since cooperative learning projects are an effective strategy in engineering education.^[8,9] There are examples in the literature for adding biotechnology material to labs,^[10] including it in the curriculum as a new course or as an added elective,^[11,12] incorporating it in other courses at later stages in the curriculum in a more applied

way^[13] (*i.e.*, unit operations laboratories), or as an addition to freshman engineering “exploration” classes,^[10,14] but there is a paucity of educationally rich biotechnology projects for a sophomore-year, required, core chemical engineering lecture course. Thus, there is a need to fill this place in the curriculum with biotechnology topics that also reinforce the fundamental skills students will need in later classes—*i.e.*, mass balances and multiple reaction processes—as part of cohesively strengthening and modernizing the overall undergraduate chemical engineering program of study.

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We therefore created a project on the mass balance of alcohol in the human body that has students posing as engineers at a pharmaceutical company that is developing a drug to dissuade alcoholism. The project structure includes engineering design, testing, evaluation, and exploration. We chose human alcohol metabolism for several reasons: 1) while many college students are aware of alcoholism, they are not likely to fully understand the underlying chemistry and causes of the resulting negative physiological effects; 2) modeling the human body as a chemical plant gives students a chance to apply and practice their mass balance skills on an analogous but different system, beyond the more traditional chemical processes in the curriculum; 3) scaling down the human model to microscale to simulate a “body-on-a-chip” illustrates a hallmark skill of chemical engineers while incorporating modern biomedical research applications; and 4) comparing the effects of a genetic mutation that alters alcohol metabolism with a hypothetical drug designed to thwart alcoholism (based loosely on a commercially available drug, Antabuse)^[15] engages students in evaluation and exploration. Student feedback on the course evaluation (90% response rate) indicated that the students perceived that the course projects helped them apply the course skills and concepts to more complex problems (95% of respondents) and increased their awareness of the range of topics and scales in the chemical engineering discipline (92% of respondents). (See Table 1).

PROJECT FRAMEWORK

Student teams create a mass balance model of ethanol metabolism in the human body using computer spreadsheets to calculate mass flow rates to and from key organs. The project requires only knowledge of multi-unit mass balances and chemical reactions in the steady state; parameters are designed to create reasonable physiological results in this model. The

project is divided into four parts (engineering design, testing, evaluation, and exploration) that chemical engineers would perform in a pharmaceutical or biotechnology company.

In the design phase, students model the organs handling oxygen and liquid intake, chemical breakdown, and waste removal as simple black-box process units. Students then test their model using an established basis and monitor variables such as blood alcohol concentration (BAC) and blood acetaldehyde concentration. An additional test considers changes due to a genetic mutation, the alcohol flush reaction—a physiological syndrome resulting from different enzymatic degradation of ethanol in some Asian populations compared to those of European descent.^[16] For the evaluation phase, student groups are assigned various hypothetical drug formulations, each altering different parameters in their mass balance model, and are asked to analyze the effects of their drug to determine its efficacy. Formulations can vary from detrimental to beneficial, leading students to develop analytical skills and engineering judgment as they assess the drug performance and describe their analysis. Finally, to expose students to current research in biotechnology, we ask students to scale their model from human proportions down to a microscale lab-on-a-chip device, a so-called “body-on-a-chip,” used for *in vitro* drug testing as an alternative for human and animal testing.^[17-19]

CONCEPTUAL MODEL—DESIGN PHASE:

Turning Organs Into Chemical Process Units

Alcohol metabolism and clearance in the human body occurs by the combined action of multiple organ systems. Alcohol enters the digestive system and passes to the circulatory system. The bloodstream carries the ethanol to the liver where a fraction is chemically degraded into acetic acid. Eventually, a portion of the unreacted alcohol exits the body

TABLE 1
Student Feedback on Effectiveness of Project in Connecting to “Real-World” Engineering and Reinforcing Course Skills

Data source (response rate)	Question	Response scale	Response grouping	Percent responses
Course evaluation (90%)	Did the projects help you relate the course material to real engineering applications and facilitate applying the course concepts and skills to a more complex problem?	5 = very much so 1 = not much	3 and above	95%
Course evaluation (90%)	Did the group project topics give you a sense of the variety of topics and range of scale of problems addressed by the chemical engineering discipline?	5 = very much so 1 = not much	3 and above	92%
			4 and above	85%
Independent evaluators survey (39%)	I understand how the skills and concepts I am learning might be applied to real-world engineering challenges.	Strongly agree to strongly disagree	Agree or strongly agree	76%
Independent evaluators survey (39%)	I can think of more career opportunities for chemical engineers today than when I first started this course.	Strongly agree to strongly disagree	Agree or strongly agree	81%
Independent evaluators survey (39%)	I can understand how the course projects relate to real-world engineering issues.	Strongly agree to strongly disagree	Agree or strongly agree	78%

through the urine and in exhaled breath. Mathematical models linking the mass flow between the various organs can be used to determine the blood concentration of ethanol and metabolic byproducts such as acetaldehyde and acetic acid. Research studies have shown good correlation between transient mass balance models and observed blood alcohol responses in human subjects.^[20,21]

Figure 1 maps the organs for material intake, chemical decomposition, and waste processing into a flowsheet. We assumed steady state, with a constant input rate of air, ethanol, and water. Stomach and intestine functions are integrated into a single process box (digestive tract) to model absorption of ethanol and water from the input. We reduce the bulk human metabolic and cellular respiration functions into two black-box unit operations, the metabolic processes box and the liver box. Lungs and kidney boxes serve as absorbers/exchangers and separators, respectively.

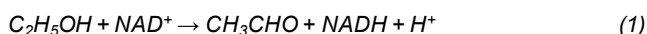
The average human male inhales 0.5 L of air per breath with ~14.5 breaths/minute. At 25 °C, the lungs can absorb ~20 mol% of inhaled oxygen into the bloodstream, primarily carried as dissolved oxygen or attached to the protein hemoglobin. Any excess oxygen and nitrogen not absorbed into the blood is exhaled along with some waste ethanol. For simplicity, students model the lungs as two process units (one for breathing in and one for breathing out) with a bypass stream for the excess air. Some ethanol is degraded and absorbed in the stomach along with water, but most liquid passes into the small intestines. We assume that 90 mol% of the ethanol and water passing through the digestive system is absorbed into the bloodstream.

Throughout the body, cells metabolize chemicals and create biomolecules in biochemical reactions. We approximate reactions as a single black-box process that will consume and produce the necessary metabolites as described in Box 1. Reaction parameters were chosen to make this process consume 30% of the oxygen fed into the metabolic process box (from lungs and recycled cleaned blood) and to generate 10 mol of NAD⁺ and 1 mol of NADP⁺ per mol of oxygen consumed. In addition, to make the mass balances realistic, we assumed 60% of the metabolites from the cleaned bloodstream entering the process were consumed.

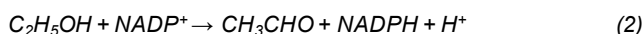
In the liver, ethanol is metabolized to acetic acid through a sequence of enzymatic redox reactions (Box 1). The single pass conversion in the liver of ethanol into acetaldehyde via the ADH and MEOS processes is 40%. This value was chosen to match BAC to realistic values. Ethanol consumed in the two competing reactions (the ADH and MEOS reactions) has an 87.5% selectivity for the ADH catalyzed process where selectivity is defined as the ratio between the extent of reaction of the ADH process to the overall conversion of ethanol to acetaldehyde; 99% of the acetaldehyde created by both reactions is then further degraded into acetic acid accord-

Box 1. Metabolic reactions used in the degradation of ethanol in the human body*

The main reaction that oxidizes ethanol (C₂H₅OH) into acetaldehyde (CH₃CHO) is catalyzed by alcohol dehydrogenase (ADH) and uses nicotinamide adenine dinucleotide (NAD):

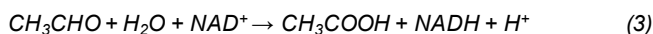


There is a second parallel reaction for converting ethanol to acetaldehyde known as the microsomal ethanol-oxidizing system (MEOS), involving nicotinamide adenine dinucleotide phosphate (NADP):



The MEOS process represents the main non-ADH pathway for ethanol degradation catalyzed by cytochrome P450 oxygenase enzymes.

In the final step, the acetaldehyde reacts to form acetic acid (CH₃COOH) in a reaction catalyzed by acetaldehyde dehydrogenase (ALDH):



*Summarized from references (16,20,21,23,26,27). See Glossary for definitions of these terms.

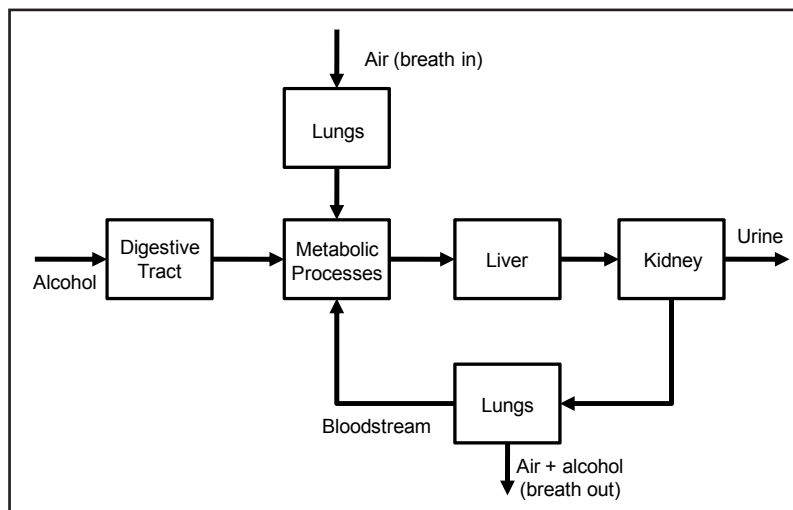


Figure 1. Schematic diagram of the simplified human alcohol metabolism model used in the project. The diagram illustrates the flow of alcohol and air through the body into the liver (where reactions take place), with the resulting products and remaining reactants flowing to the kidneys and lungs, and getting removed in the urine and breath. The metabolic processes box lumps the other metabolic processes occurring in the human body.

ing to this expression:

$\tau_{\text{ALDH}} = \tau_{\text{ALDH}} (\xi_{\text{ADH}} + \xi_{\text{MEOS}})$, where ξ are the extents of reaction for each reaction (Box 1) and τ_{ALDH} is the efficiency of the ALDH reaction. The specified parameters make the simplified mass balances follow a reasonable physiological response. This level of detail sufficiently captures the basic physiological results for our sophomore-level class; however, more complex models could be used for advanced students.

The kidneys and urinary tract are the body's primary waste removal organs for water-soluble metabolic wastes. We assume 90 mol% of the water and acetic acid and 97 mol% of the acetaldehyde output from the liver is removed by the kidneys. Ethanol is also removed via the kidneys: 1.3 gm ethanol/mL urine for every gm ethanol/mL blood. 20 mol% of the total oxygen present in the blood (after going through the liver and kidneys) is exhaled in the lungs. One gram of ethanol is exhaled in 2.1 L of air for each gram of ethanol per milliliter of blood.^[21]

To calculate the ethanol mass flow in the waste streams, students will need to reference the current blood alcohol concentration (BAC). It is important to clarify for students that ethanol is distributed in the total body water (TBW) volume within the body, which for the average male is 60 L of water,^[20] not just in the blood.^[22] The common notation used by law enforcement agencies, *e.g.*, 0.08%, is that of a percent gm/mL. Similarly, acetaldehyde is distributed amongst the TBW volume, and is normally measured in units of μM or $\mu\text{mol/L}$.^[21]

Using the above data, students develop mass balance equations in an Excel spreadsheet, capitalizing on the iterative ability to quickly determine steady state values of BAC and blood acetaldehyde concentration and to see the impact of changing various parameters and conditions.

ESTABLISHING CONTROLS AND BENCHMARKS—TESTING PHASE

The first control “experiment” students perform with their spreadsheets is determining the response of blood alcohol and acetaldehyde levels after consumption of a single beer.

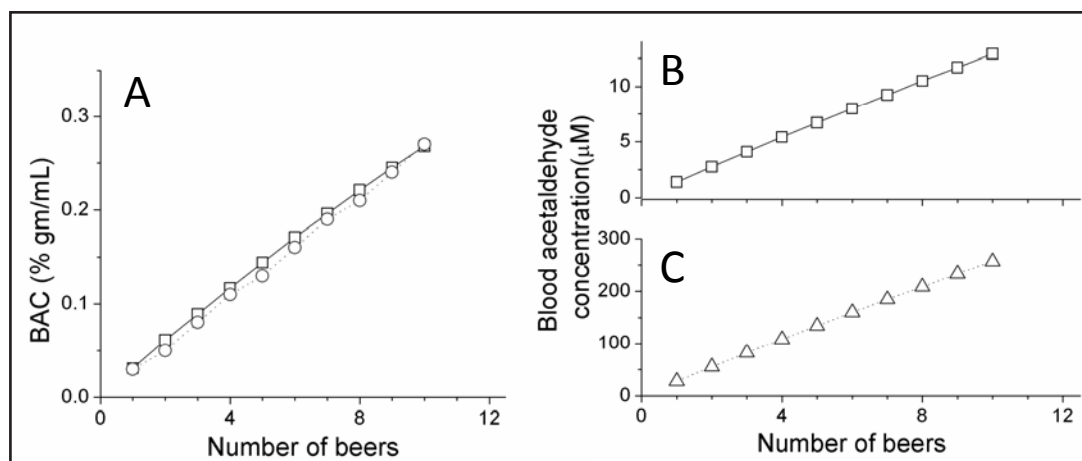


Figure 2. Blood ethanol and acetaldehyde concentration as a function of number of drinks consumed. (A) Increase in blood alcohol concentration (BAC) vs. number of beers consumed. A beer is defined here as a 355 mL drink with a 5% v/v concentration of ethanol. Squares represent results from the model using the default parameters, and circles represent data from the Virginia Institute of Technology police department for an average male weighing 140 lbs.^[28] Both the model and data end at 10 drinks for reasons described in the text. (B) Plot of blood acetaldehyde steady state concentration as a function of number of beers consumed for an average male weighing 140 lbs. and (C) for a male weighing 140 lbs. with alcohol flush syndrome (Δ). Notice that the vertical scale has changed significantly between the two plots on the right.

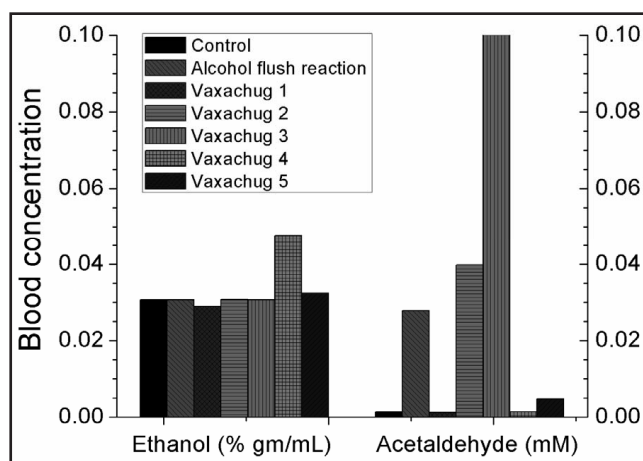


Figure 3. Vaxachug effectiveness results. The bar chart illustrates the effects of each Vaxachug formulation on blood ethanol and acetaldehyde concentration. The effects of the control case (one beer consumed per hour) and the alcohol flush reaction scenario are shown for comparison.

All student teams run this study and corroborate the results with each other and the teaching assistants to verify their models. Then, each student team determines the changes in these concentrations as a result of consuming various levels of a unique alcoholic drink assigned to each group and plots their results.

Next, students establish a benchmark against which to compare and assess drug performance. They are introduced to the alcohol flush reaction and adjust their model to mimic this syndrome. This will allow them to compare and contrast

the response of a patient taking a drug for alcoholism against the response of a person possessing the genetic mutation for alcohol flush.

Physiology of Alcohol Flush Reaction and Treatment for Alcoholism

While ethanol creates a number of effects on the central nervous system and is a known teratogen, the short-term effects of consuming alcoholic beverages are closely tied to the primary metabolic product of ethanol degradation, acetaldehyde. Chronic exposure to high levels of acetaldehyde causes irreparable liver damage. Acetaldehyde buildup is also partly responsible for the short-term physiological response to alcohol consumption typically referred to as “hangovers.” Studies of alcohol metabolism in some Asian populations revealed a missense polymorphism in the alcohol dehydrogenase (ALDH) enzyme which inhibits the rate of acetaldehyde degradation resulting in an alcohol flush reaction.^[16,21,23] The common physiological response to raised acetaldehyde levels is erythema of the face and neck, a noticeable reddening of the skin. Severe responses can result in drowsiness, headaches, and nausea. These symptoms can be artificially induced with drugs such as disulfiram (Antabuse), which artificially blocks the activity of the acetaldehyde dehydrogenase (ALDH) enzyme. The purpose of this medication is to artificially increase the alcohol sensitivity of a patient as a negative reinforcement treatment for alcoholism.

Model Output for Benchmarks Cases

Figure 2 shows results from the two control scenarios, each conducted using a basis of a pint of beer (a 355 mL beverage containing 5% v/v ethanol). Figure 2(a) compares the model’s predicted steady state BAC vs. beers consumed (using the default model parameters) with actual BAC data for an average male weighing 140 lbs. The model reproduces a realistic response to alcohol consumption up to an input of 10 alcoholic beers. At 11 beers, the model breaks down, due to complete consumption of the limited supply of oxygen and metabolites, resulting in negative molar flow rates in the model. While students should be made aware of this limit in the model, we note

such a high consumption rate would almost certainly result in severe health repercussions and would be beyond the scope of any comparable clinical study in humans.

Figure 2(b) shows the effect of the alcohol flush reaction which can be modeled as a decrease in the ALDH reaction efficiency from 0.99 to 0.8. This simple decrease in reaction efficiency results in a 20-fold increase in blood acetaldehyde concentration and recreates the alcohol flush response matched to concentrations found in previous clinical studies of this condition.^[21]

HYPOTHETICAL DRUG FORMULATION SCENARIOS—EVALUATION PHASE

In this portion of the project, the student teams evaluate the effectiveness of a hypothetical drug, referred to here as Vaxachug, designed to treat alcoholism by artificially reproducing the effects of the alcohol flush reaction. With the pretense of working as engineers for a hypothetical drug company, students must determine the efficacy and safety of their particular formulation. Students are instructed that a particular dosage of the drug will change how the body metabolizes alcohol, implemented in their models as changes to certain parameters. To increase the challenge, student teams were assigned different drug formulations, some of which achieve the desired effects, some of which create alternate side effects, while others achieve varying levels of success. Table 2 shows five possible drug formulations spanning functional, placebo, overactive, and side-effect prone. The drugs target and alter the function of several organs within the metabolic model resulting in changes to the BAC and acetaldehyde concentrations. Table 2 lists the necessary changes to the model parameters to simulate the effect of each drug. At this point in the project, students should be aware from working with the alcohol flush reaction example that the goal of Vaxachug is to raise acetaldehyde levels without significantly disturbing the other variables in the system (*e.g.*, BAC, metabolite concentration, intake, and waste function).

Figure 3 illustrates the effect of each Vaxachug formulation, compared to the control case, using the default model

TABLE 2
Drug Formulation Scenarios: Changes to Model Parameters to Simulate Each Drug

Vaxachug-1	(ineffective) Lung (exhale): breath alcohol content is 1 gm ethanol per 2.7 L of air for every 1 gm/mL in blood Digestive: 85% of ethanol and water is absorbed into bloodstream Liver: ADH and MEOS reaction selectivity is 85% Metabolic: 40% of metabolites consumed
Vaxachug-2 (functional)	Lung (exhale): breath alcohol content is 1 gm ethanol per 2.7 L of air for every 1 gm/mL in blood Liver: ALDH efficiency is 95% Liver: ADH and MEOS reaction selectivity is 85% Kidney: 85% of acetaldehyde from the liver is excreted
Vaxachug-3 (overactive)	Liver: ALDH efficiency 80%, Metabolic: 80% of metabolites consumed, Kidney: 90% of acetaldehyde from liver is excreted, Kidney: urine content is 0.9 gm ethanol per mL urine for every 1 gm/mL in blood
Vaxachug-4 (significant side effects)	Metabolic: 50% of metabolites consumed, Liver: ADH and MEOS reaction selectivity is 80%, Liver: ethanol single-pass conversion is 30%, Lung: breath alcohol content is 1 gm ethanol per 5 L of air for every 1 gm/mL in blood
Vaxachug-5 (ineffective due to competing effects)	Kidney: 99% of acetaldehyde from the liver is excreted, Liver: ALDH efficiency is 90%, Digestive: 95% of ethanol and water is absorbed into the bloodstream, Metabolic: 50% of metabolites consumed

The five drug formulations described here set the stage for multiple levels of analysis. They are designed to challenge students to go beyond simply solving an equation and collecting data and lead them to performing a more extensive analysis and drawing more thorough conclusions from the results.

parameters, and to the alcohol flush reaction scenario. As expected, the most significant changes in acetaldehyde concentrations occur in formulations that affect ALDH efficiency or ALDH recycle rates in the kidney. The Vaxachug-2 formulation increases the blood acetaldehyde concentration to 0.04 mM, comparable to the alcohol flush reaction scenario, but by altering the acetaldehyde recycle rates rather than acetaldehyde metabolism rates. Vaxachug-3 is considered an overactive formulation, because the combined effect of altering two critical acetaldehyde parameters spikes the blood acetaldehyde concentration to 0.1 mM, four times that of the alcohol flush reaction scenario. The Vaxachug-1, Vaxachug-4, and Vaxachug-5 formulations are ineffective, though the cause is different for each formulation. The Vaxachug-1 formulation specifically only alters parameters that have an insignificant or mild effect on the ethanol and acetaldehyde metabolism, therefore it acts like a placebo. Vaxachug-4 does have a significant effect on ethanol metabolism and the ethanol concentration in the breath, but does not significantly affect acetaldehyde metabolism. Vaxachug-5, however, does alter two parameters that affect the metabolism of acetaldehyde, but by decreasing the rate of acetaldehyde conversion to acetic acid and increasing its rate of removal from the system, the two effects nearly negate each other resulting in a small net change in blood acetaldehyde concentration. Depending on the severity of the response elicited by the particular drug formulation assigned to a team, students must judge its effectiveness for accomplishing its intended use and discuss relevant observations.

TEACHING POINTS

The five drug formulations described here set the stage for multiple levels of analysis. They are designed to challenge students to go beyond simply solving an equation and collecting data and lead them to performing a more extensive analysis and drawing more thorough conclusions from the results. We observed that the challenge and mystery of the

unknown motivated our students to delve deeper to figure out their formulation's attributes. The project structure guided the students towards analyzing their specific cases by comparing their results from the drug formulations to the response of the benchmark cases and of the alcohol flush scenario. All student reports showed this level of analysis and understanding.

The first level of analysis is determining the drug formulation activity. To accomplish this, students use their model to determine the ethanol and acetaldehyde levels. An insufficient analysis would conclude that any increase in blood acetaldehyde would constitute an effective drug. Students should realize that their data from the alcohol flush scenario provides a performance benchmark for their drug formulation. Using this benchmark, students can then differentiate between the different drug scenarios, identifying Vaxachug-2 and Vaxachug-3 as active formulations, while identifying Vaxachug-1, Vaxachug-4, and Vaxachug-5 as defective. At this point in the project, an instructor could reinforce the importance of control experiments and determining the significance of a result by comparing to known quantities or verified data.

A higher level of student analysis is determining how the changes in their model affect drug performance and explaining how this creates the results that are observed. Students in our class accomplished this in several ways. Some groups chose to model and analyze each parameter independently and determine which changes had the most significant effect and others chose to model combinations of parameter changes to determine which combination best matches the behavior of the entire formulation. Students who modeled parameters separately were able to differentiate between Vaxachug-1 and Vaxachug-5, which are both ineffective drugs, but because of different underlying mechanisms, illustrating that results that appear very similar could arise for different reasons and that thoroughly understanding how a system works is important in drawing the correct conclusion. This teaching point should be discussed following the project.

Although the primary focus is on how the drug affects acetaldehyde levels, there is room for creativity in designing model drug formulations with significant side effects to further promote student exploration and analysis. We have created several of these formulations. One example, Vaxachug-3, raises acetaldehyde levels far above the drug specifications. Several groups assigned Vaxachug-3 recognized that there could be potential health safety issues with the formulation, particularly because of the induced physiological symptoms resulting from high blood acetaldehyde levels. Another example, Vaxachug-4, reduces ethanol metabolism and decreases the amount of ethanol that leaves in the breath. Students in our class recognized that such a combination of effects could have a potentially lethal impact on drunk driving by increasing driver intoxication while also making detection by breathalyzer more difficult. Similarly, we had a formulation where acetaldehyde production is reduced and more ethanol

passes out in the urine. Here, some teams reported that the drug could potentially be marketed for an alternate purpose instead of its initially intended purpose; this drug could enable people to drink socially without feeling negative health effects associated with intoxication and thus they might be able to drive safely without any alcohol-induced impairment.

MICROSCALE ENGINEERING— Exploration of Current Biotechnology Research

Including research topics in the curriculum can effectively expose students to academic research and connect research to high-impact applications.^[24] Making connections to modern chemical engineering research and societal issues within the context of this project was achieved with a complementary exercise on drug testing platforms. We set the stage by explaining to the students that the most accurate way to assess the metabolism of an experimental compound in a human is to test its effect on human subjects. This assessment cannot be made until after the experimental compound is deemed safe, however. Therefore, animal testing models are often used as a substitute until safety is assured. This solution is not ideal for two reasons: 1) animal models are not exactly the equivalent of humans and 2) animal testing is unpopular. An alternative platform that circumvents these issues would be a welcomed advance that students can easily appreciate.

In this exercise, we introduce the concept of process scale down which opens a discussion on how microscale engineering, specifically “lab-on-a-chip” research in biotechnology, is pushing drug discovery research forward.^[17-19] A “body-on-a-chip” is a microfluidic device containing microfabricated bioreactors infused with living cell tissue used to mimic *in vivo* pharmacokinetics in humans experimentally. During

class, we showed actual devices (Figure 4, right side) and explained the connection between an experimental model of a biochemical process and the *in silico* model developed by the students. We asked students to find a scaling ratio between a human and a microscale body-on-a-chip.

Students are given the average blood flow rate in a human being: $Q_{\text{blood}} = 6 \text{ L/min}$. They are also informed that a typical polydimethylsiloxane (PDMS) on glass “body-on-a-chip” device can withstand $\sim 15 \text{ psi/cm}$ of pressure drop without delaminating (*i.e.*, when the PDMS and glass layers no longer adhere) and has channel cross-sections of $300 \mu\text{m}$ wide \times $20 \mu\text{m}$ tall. The students are provided an equation for parallel plate laminar flow:

$$Q_{\text{chip}} = \frac{H^3}{12\mu} \frac{dP}{dx} D,$$

where Q_{chip} is the volumetric flow rate, H is the height of the channel, D is the width of the channel, dP/dx is the pressure drop in units of pressure/distance, and μ is the viscosity of water at $0.001 \text{ Pa}\cdot\text{s}$. Once the students have calculated Q_{chip} , they can determine a scaling ratio between the human and microscale model, defined as $R = Q_{\text{blood}}/Q_{\text{chip}}$, where R is a dimensionless scaling number. Using this scaling ratio, students were asked to scale the volumetric flow rate of beer required to achieve the same effect as a single pint of beer in the human-sized alcohol metabolism model. These concepts (laminar flow, dimensionless numbers, and scaling) are a preview of future topics in upcoming classes and spotlight unique aspects/skills of the chemical engineering discipline. We encourage instructors to use this starting point to develop more extensive analysis or concepts that could be included in advanced classes.

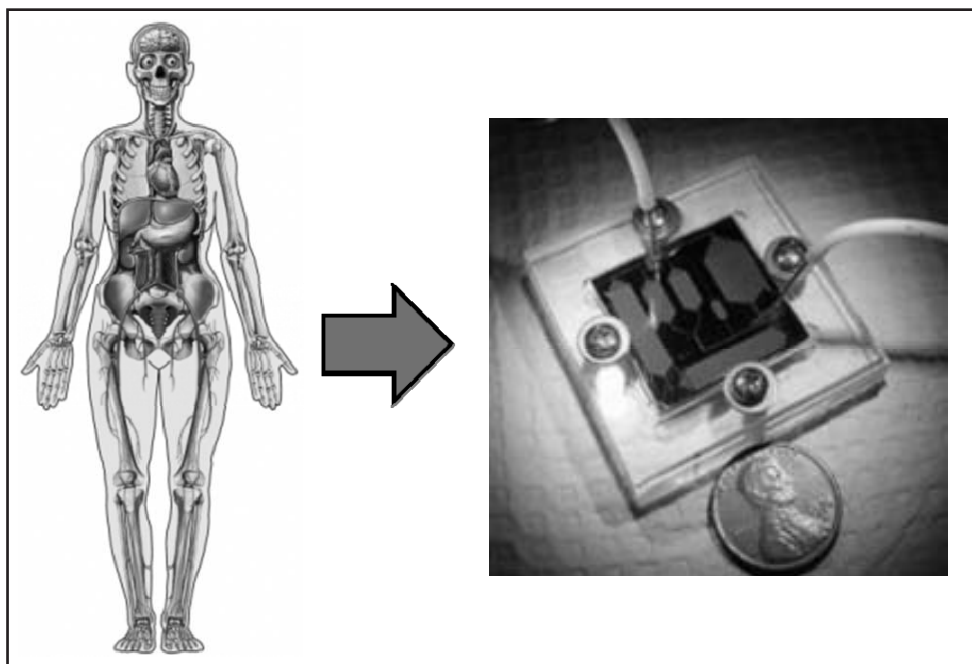


Figure 4. Scaling down the essential features of the human body to create an *in vitro* model for drug testing that accurately mimics the metabolism of chemicals ingested in the body. The small chip on the right contains chambers that mimic the organs in the body. Microfluidic channels containing a nutrient serum connect the chambers on the chip like blood flow connects organs in the body. Image credit: Michael Shuler, Cornell University, used with permission, also see Reference 2.

ASSESSMENT OF STUDENT RESPONSE AND CONCLUSIONS

Here, we described a biotechnology project developed for a sophomore-level mass balance class. All student groups successfully created the required spreadsheet, calculated the correct values for consumption of a beer and their assigned drink. Most groups correctly determined if their Vaxachug formulation was effective or not. Many groups went on to give very nice discussions of further implications. In an independent evaluation of the course, more than three quarters of the student respondents recognized connections to “real world” engineering and broadened their view of chemical engineering (Table 1). Generally, students rated their own and their team members’ project contributions highly, 6.4 out of 7 on average, and used various models for sharing the workload with varying degrees of success, as summarized in Table 3.

The project was well received by our students in its inaugural year. Student comments in course evaluations indicated that the integration of basic course skills, modern topics, and human health motivated them to explore various aspects of the project and this consequently enhanced their learning of core concepts while also stretching their analysis skills. This student quote echoes what we heard from many students: “I especially like the fact that the alcohol project integrated some bio aspects of chemical engineering because that’s what I believe I would like to go into (this project strengthened that notion).”

Readers may contact Prof. Daniel at sd386@cornell.edu for a detailed spreadsheet of the mass balances and a copy of the project statement used in class.

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GLOSSARY OF TERMS

ADH: alcohol dehydrogenase; an enzyme that catalyzes the conversion of ethanol to acetaldehyde in reaction 1 in box 1.

ALDH: acetaldehyde dehydrogenase; an enzyme that catalyzes the conversion of acetaldehyde to acetic acid in reaction 3 in Box 1.

BAC: Blood alcohol concentration.

Cytochrome oxygenase enzymes: A family of enzymes involved in the oxidation of organic molecules, including foreign organic molecules ingested by the organism.

Enzyme: A biological molecule that catalyzes biological reactions to increase the rate of reaction by reducing activation energy barriers or alternate reaction pathways.

Extent of reaction: The ratio of the molar reaction rate of a compound to its stoichiometric coefficient.

MEOS: Microsomal ethanol-oxidizing system; ethanol metabolism pathway that relies on cytochrome oxygenase enzymes to break down ethanol.

TABLE 3
Student Feedback on the Cooperative Learning Group Project Experience

Data source	Question/theme discussed	Response scale	Response grouping	Response average
Student peer evaluations for project groups	Evaluate team member’s contribution	Excellent 7	self	6.4
		Very good 6		
		Satisfactory 5	group members	6.4
		Ordinary 4		
		Marginal 3		
		Unsatisfactory 2		
		Superficial 1		
		No show 0		
Focus groups by independent evaluator	Reported theme that emerged from focus group discussions	“Many students also had positive group experiences, working smoothly with peers, dividing work according to the strengths of the group members, etc. They understood the value of group projects as a harbinger of the way things work in professional settings they will eventually be part of. Some expressed a sense of satisfaction at having conquered a difficult project.”		
Focus groups by independent evaluator	Reported theme that emerged from focus group discussions	“Students generally described their group project experience in either glowing or grueling terms . . . two models for group work seemed to emerge generally—doing all the project tasks together or doing project tasks independently and bringing the parts together at the end. Their contentment with group projects was largely associated with whether or not they were comfortable with the model used in their groups and whether or not everyone in the group bought into the model.”		
Course evaluation	Student quote	“... I especially like the fact that the alcohol project integrated some bio aspects of chemical engineering because that’s what I believe I would like to go into (this project strengthened that notion).”		

Metabolism: The summation of all reactions that take place inside an organism or cell.

Metabolite: A product or intermediate of a metabolic reaction.

Missense polymorphism: A single point mutation in the genetic code that results in the production of an enzyme mutant that has altered function. Missense refers to the modification in the code that results in a change in a single amino acid in the enzyme and impacts proper function.

NAD: Nicotinamide adenine dinucleotide; an oxidizing agent that participates in the conversion of ethanol to acetaldehyde in reaction 1 in box 1.

NADP: Nicotinamide adenine dinucleotide phosphate; NADP differs from NAD by an additional phosphate group in the molecule. NADP participates in converting ethanol to acetaldehyde by reaction 2 in box 1.

Pharmacokinetics: A branch of pharmacology that studies the adsorption, degradation, and elimination of substances in the body.

Selectivity^[25]: The ratio of moles of desired product formed to moles of undesired product formed. In this case, the selectivity of reaction 1 over reaction 2 is the ratio between the extent of reaction of the ADH process to the overall conversion of ethanol to acetaldehyde.

Single pass conversion^[25]: The ratio of the net amount of the reactant leaving the reactor unit (in – out) to the amount of reactant sent into the reactor unit.

TBW: Total body water.

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