How Drugs Work in the Human Body
Analysis of a Modeling Unit Used in a Second Year Algebra Class

Diana M. Fisher
Wilson High School
1151 SW Vermont St.
Portland, Oregon USA
(503) 916-5280 (phone)/(503) 916-2705 (fax)
dfisher@pps.k12.or.us or dmfisher@aracnet.com

Edward J. Gallaher, Ph.D.
Associate Professor
Behavioral Neuroscience MQ280
Oregon Health and Science University
Portland, OR 97201
(503) 418-4982
gallaher@ohsu.edu

Louis Macovsky, DVM
Research Associate
Behavioral Neuroscience MQ280
Oregon Health and Science University
Portland, OR 97201
(503) 418-4981
macovsky@ohsu.edu

Second-year algebra is a course ripe with topics for modeling experiments. Students in this course tend to be reasonably mature, in the 15 to 16 year range. Topics include linear, quadratic, exponential, logarithmic, polynomial and trigonometric functions. Students usually study these functions in isolation from one another.   It is not difficult, however, to add some examples where students create models that combine some of these simple functions and analyze the interesting dynamics that can result. One such example is a small unit on the study of pharmacokinetics.

The Sequence of Lessons:

The unit is studied midway in the year. The mid-year exam is given a few days early and the material for the second half of the year is delayed a few days.   The unit takes six class periods, four of which are 55 minutes in length, one 1.25 hours and one 1.5 hours in length.   Students have studied linear and exponential models in the first half of the school year. In those chapters they were required to build STELLA diagrams for various simple linear and/or exponential phenomenon, but they had not yet put the two types of growth patterns together in one model.

Day 1: The first lesson is a demonstration given by the teacher using a projection unit connected to a computer. Each student has a handout with three problem scenarios on it and space to draw graphs and diagrams and answer short questions. The teacher describes the first scenario and asks questions about how the diagram might be built. The first problem involves only exponential decay. A drug is already in the person's bloodstream and the model is used to determine the amount of drug in the body over time. Students predict what the model will look like. The teacher builds the model, with student suggestions, and the model is executed.   Students are expected to write the corresponding mathematical (closed form) equations, whenever appropriate (and not too complicated).

In the second scenario the patient is given a single intravenous injection. Students predict the graph. Students are then introduced to the command needed to simulate giving the patient an injection.

In the final scenario the patient must be connected to an IV (intravenous) drip (see figure 1, below), linear input with drug elimination as described above. Various modifications are made to the patients drug infusions/elimination. Students must maintain the drug level within a therapeutic range.

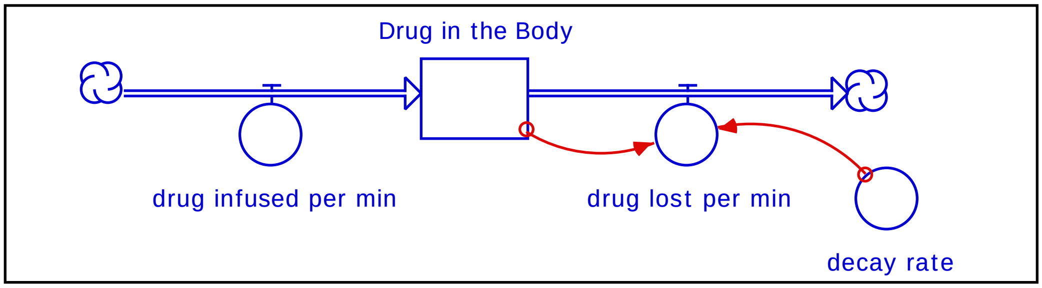


Figure 1

Since this lesson involves only demonstration by the teacher, it is the least exciting day of the unit, but it does serve to introduce some important components of the drug simulations that the students will use later. It helps remind students how to draw the diagrams, set up graphs, read graphs, etc., and the topic is interesting enough that the students are willing to participate for one class period.

Day 2: (1.25 hours) Since this lesson was actually after a short break of three days, the teacher reviewed the models from the first day and asked questions about the graphs produced by those models, to make sure the students remembered the material previously covered. Even without a break between day one and day two, a review is useful, since there are some subtle concepts that need to be reinforced before students proceed.

The second lesson has the students in the computer lab, each with a handout containing more scenarios. Students, individually, or in teams of two, start with a problem involving a doctor administering injections every four hours to a patient. The students are asked to analyze the simulations over a simulated 24 hour period.

The second scenario has the patient ingesting pills (see figure 2, below), which have an absorption rate to enter the bloodstream, and an elimination rate to exit the body. Again students are given multiple modifications to make and are asked to explain the simulated results. Finally additional components are added (body weight, volume of liquid in the body, etc.) so that it is possible to calculate, not just total drug in the body, but drug concentration in a given volume of blood.

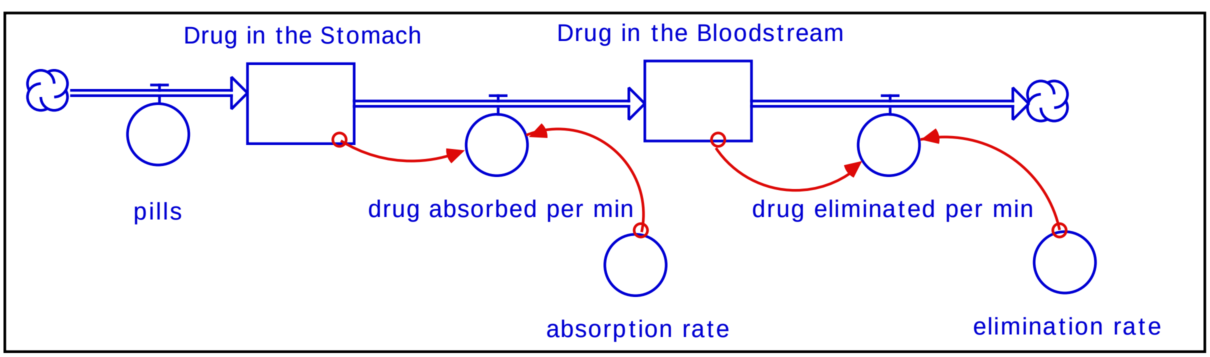


Figure 2

This day was much more engaging for students. The teacher moved around the room trouble-shooting computer problems and answering questions.

Day 3 & 4: (each 55 minutes) There was another short break of 4 days between day 2 and day 3. The teacher drew on the board, with student assistance, the final model diagram (see figure 3, below) from the lesson of day two. The diagram was reviewed carefully, since it was the core model to be used for day 3 and 4.

Again the students are in the computer lab. This time the scenario is the study of a 70 kg male drinking six twelve-ounce beers in two hours. A diagram (with equations) is given to the students, which they are to build and save on the computer. The handout that students are to complete has students study the blood-alcohol level of men of different weights, of women, of different alcoholic beverages, etc. They predict results then run the simulations and analyze what happens.

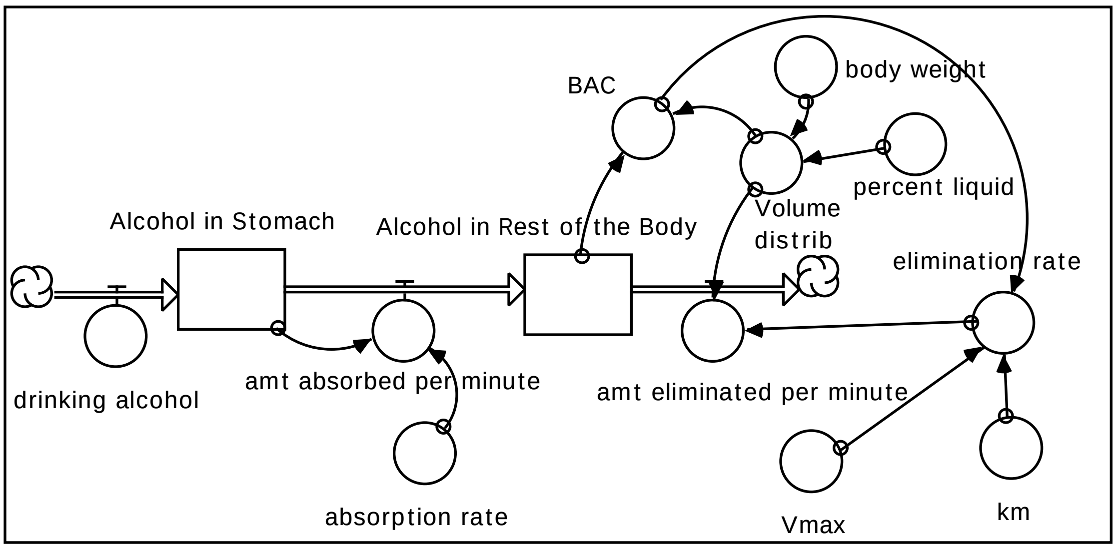


Figure 3

Day 5: (1.5 hours) The teacher has exchanged classrooms with the chemistry teacher so the lab for today can have access to running water and sinks. Dr. Gallaher and Dr. Macovsky arrived at the end of day 4 to set up 8 stations of a PK lab that they have designed and built with a National Institute of Health grant (#1 R25 RR12410). Each unit involves two tubs containing water. The tub the students work with has a constant inflow and outflow of water. Students have a handout that explains what they are to do and a place for them to record data. It also contains questions for them to answer after the lab is completed.

At the beginning of the lab Dr. Gallaher takes about 10 minutes to explain the lab background information. This information includes a brief introduction to pharmacology and dosage regimens, routes of administration, absorption and distribution of drugs throughout the body, and first-order exponential decay. This information was purposefully brief, allowing the students to experience the process of drug administration and elimination first-hand rather than via further didactic explanations.

The procedure is explained (quickly) a second time, to make sure the students know exactly what to do. Dr. Macovsky explains some precautions to take when collecting data. He also explains the procedure for analyzing the samples using the two computer stations set up in the classroom. The students are organized into groups of 4 and proceed to a lab station.

For the first of two exercises, each station has a 40 ml cup of blue liquid. Each cup had 2 or 4 or 6 blue pills pre-dissolved in the water. Students did not know the strength of the blue liquid at their station. The students fill a plastic syringe with all the blue liquid from their blue cup. They inject the blue liquid into their "patient" (a tub of clear water with a constant inflow equal to the constant outflow of liquid). Students take a reading from the outflow every 60 seconds, go to the computer station to get a reading of the concentration of blue drug, and record the information on their lab sheet. They line up the sample cups along the lab table in a row, also recording the reading on the lab paper under the cups.

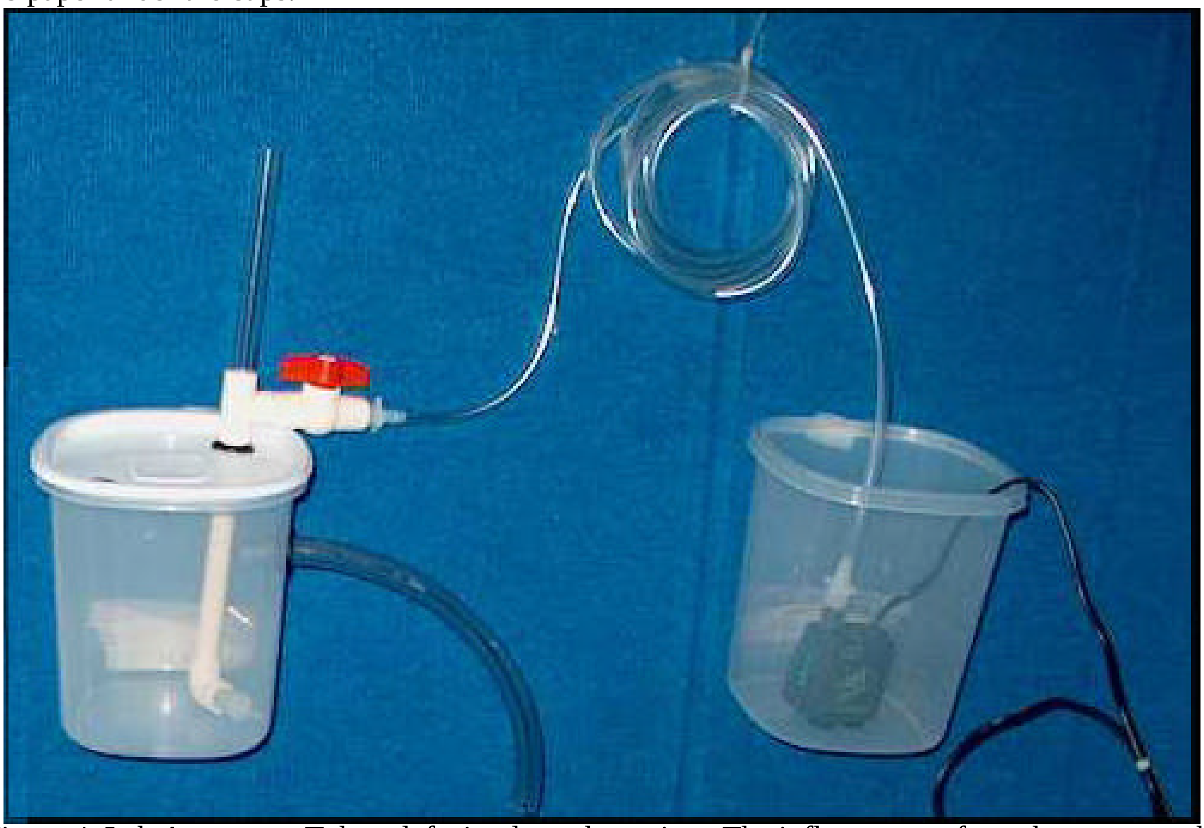


Figure 4: Lab Apparatus. Tub on left simulates the patient. The inflow comes from the pump on the right. The outflow drains from the tube that curves downward from the middle of the tub on the left.

The second exercise has the students adding blue pills to the tub of clear liquid and taking samples at irregular time intervals in order to try to keep their patient within a preassigned therapeutic level. Students are to try to maintain the therapeutic level using a minimum of blue pills and/or a minimum of drug administration. Some students discovered they could use the drug samples from the first experiment to informally gauge the drug level in their patient.

A video of segments this lab session was captured.

Day 6: (55 minutes) Dr. Gallaher returned on this day to debrief the PK lab session with the students and provide more summative information about the scenarios studied in this unit.

The Student Evaluation of the Unit

The day after the unit an evaluation sheet was given to students to get their immediate impression of the activities used in the lessons. The Group A class is comprised of 2 students age 14, 12 students age 15, 10 students age 16, and 1 student age 17. The Group B class had 1 student age 14, 22 students age 15, 3 students age 16, and 4 students age 17. Fifteen evaluation forms were returned from Group A and 25 evaluation forms returned from Group B.

The first five questions asked the students to select a number between 1 (not very helpful) and 5 (very helpful) with regard to how each day's activity helped them understand how drugs worked in the body.

Activity	% Group A selecting 3 or 4 or 5	% Group A selecting 4 or 5	% Group B selecting 3 or 4 or 5	% Group B selecting 4 or 5
Day 1 (lecture/demo/introduction)	100	66.7	73	50
Day 2 (students create small shot and pill models)	100	66	89	62
Day 3&4 (alcohol model)	94	75	77	50
Day 5 (PK lab)	100	87.5	100	88
Day 6 (lecture Dr. Gallaher)	86	57	79	58

Comments with regard to the five lessons included:
"It was a good experience, it helped the concepts come alive." "The labs were fun, but hard." "I like hands-on activities. The PK lab was the most helpful." "This was a fun way to learn." "The alcohol model helped a lot. It provided insight..."

Additional questions were asked as follows:

6. *Did you feel you learned important/useful information?*
   Group A : 94% yes; Group B:73% yes.
   Comments: "I learn visually." "Helps in real life. Learned you need to make good decisions on amounts when taking medication." "One of the first math lessons I can imagine using in real life." "Makes me think twice on how many pills and what intervals to take them." "Better than reading this." "Labs were fun."

7. *Did you gain a better understanding of linear versus exponential change because of the drug modeling lessons?*
   Group A : 62.5% yes; Group B: 61.5% yes

8. *Do you think the STELLA models helped you understand why the graphs of the drug level in the body had a particular shape?*
   Group A : 75% yes; Group B: 54% yes
   Comments: "I don't understand STELLA models." "We changed too many variables too quickly in the alcohol model." "Graphical representation of exponential functions were broken down into distinct pieces with specific purposes that could be easily understood." "I like equations better." "Showed how one small factor, body weight, greatly effects results." "Helped because we were directly involved and in control of all our simulations."

9. *Do you think this activity (all 5 lessons) were worth doing?*
   Group A : 81% yes; Group B: 92% yes
   Comments: "It was fun doing the lab and computer work." "Helps us to see how to apply math in the real world." "Educational and interesting at the same time." "No, (regular) homework is easier." "no, this is math class, not Biology, or my other science class. It's helpful if we do something mathematically." (Many responses that it was fun.)

Specific questions on the PK lab:

10. *Did you use your readings (cups of blue liquid) from your first experiment to help you decide the number of pills to give your patient during the second experiment?*

    Most students did not use the first experiment results to help them with the second experiment. Only 37.5% of Group A students and even fewer (16.7%) Group B students used their colored samples from the first experiment.

    How did this help you decide? A sample comment by students who used the results of the first lab to help them with the second: "By seeing the color of the water (in the tub for the second experiment) and the color of the sample (from the first experiment) we could approximate the level of drug in the body"

11. *How did the PK lab compare to science labs you have done in high school?*

    Some students replied that the lab was comparable to science labs, while others said it was very different. Most students replied that the lab was more understandable and definitely more fun to do. Quite a few students indicated they learned a lot and found the lab interesting and worth doing.

12. *For those students who have done the PK lab in middle school (previous experience with the lab), what did you get out of doing this lab a second time?*

    Students indicated mostly that they understood the lab better than before due an understanding of exponential functions now or because the STELLA models reinforced concepts they had learned before.

Overall, students indicated they really enjoyed the unit, learned useful information and felt it was worth doing.

The Teacher Evaluation of the Unit

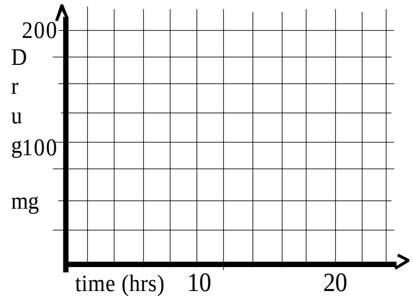
Observation

Students were on task almost all the time, so the sequence was timed reasonably well. There was enough variety in the type of activity, as well, to keep the students actively engaged. The lecture of the first day would not have worked well any other time, since introducing the drug topic was stimulating enough to overcome the less effective mode of instruction. The lecture allowed a review of the STELLA software, as well as an introduction to the model design, so it was an efficient first lesson. Having hand-on time for days 2 through 5 was very important for student motivation and accountability. It also allowed students to interact with each other in constructive ways, so making the lessons more relaxed. The final lecture was a good summation of the most important concepts studied but needs to have more student interaction.

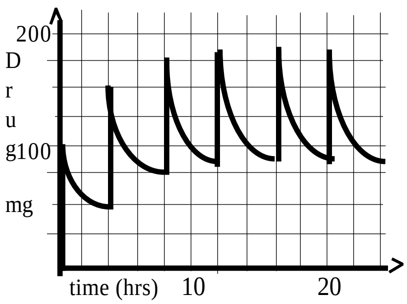
Quiz Question

A quiz was given within a week following the last day of the drug unit. There was one question on the quiz that dealt with the modeling concepts. It was difficult to create more questions that did not require students to work on the computer but still were not trivial questions, that they could answer via a paper-pencil quiz. It will take some more thought about how to expand the type of questions that would be appropriate for such a quiz.

The question on the quiz was: Sketch the graph of the drug level of a patient that receives a 100mg shot of antibiotic every 4 hours directly into his bloodstream. The half-life of the drug is 4 hours.

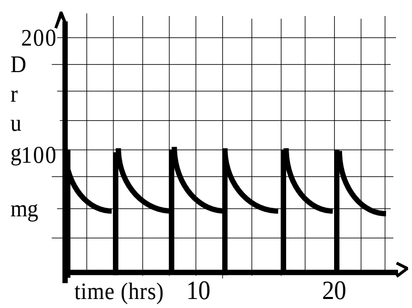


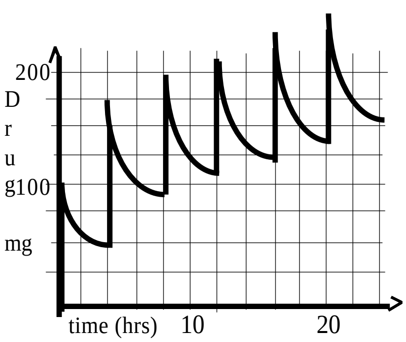
Student responses to this question on the quiz fell roughly into one of the following four categories:



The graph at the left shows the correct answer: Only 22.7% of Group A and 41.4% of Group B students got this question correct.

The graph at the right displays a frequent answer that was incorrect, not showing the increase in drug level with subsequent injections. 18.2% of Group A students and 6.8% of Group B students drew this graph or a graph with very similar behavior.





The graph at the left displays another frequent answer that was incorrect, showing an increase in drug level with subsequent injections, but not the leveling-off of the drug over time. 18.2% of Group A students and 24.1% of Group B students drew this or a very similar graph for their answer.

The final category contained graphs that were less than 50% correct in structure. 40.9% of Group A students drew graphs in this category, while only 27.6% of the students in Group B drew such graphs.

The results were disappointing and suggest more class review of the previous day's lesson is needed to solidify concepts.

Test Question

On the test subsequent to the quiz another question relating to the drug experiment was given:

A scientist gives a shot of 100 micrograms of a new antibiotic to a lab mouse and takes blood samples on the mouse every hour for 10 hours. She finds that 8% of the drug in the blood is gone each hour. Fill out the table below, recording how much drug left the body each hour and how much is left in the body. Then determine the half-life of the drug.

hours since shot	drug lost during hour	drug left in blood
0	0	1000
1	80	920
2		
3		
4		
5		
6		
7		
8		
9		
10		

half-life =

The results on this assessment question were better. 69.6% of Group A students and 65.5% of Group B students filled out the table correctly and determined the correct half-life. For those students who were only able to fill out the table correctly but not able to determine the correct half-life, 8.7% came from Group A and 20.7% came from Group B. For those students who could neither fill out the table correctly nor determine the correct half-life were 21.7% were from Group A but only 13.8% were from Group B.

The improved results could be due to the easier nature of the question to answer. Smart students could determine the correct process for completing the table just from the pattern shown and a recollection of some concepts from the chapter on exponential functions studied earlier in the year. The chapter covered the concept of half-life as well. It would have been better to design a question that would have more directly connected with the drug unit studied (as the quiz question did). But when students have access only to graphing calculators to answer questions, and not to computers, it is no small task to develop reasonable questions that comprise only part of a test or quiz that must be completed within a 55 minute class period. Still, it will be necessary to spend time developing good assessment questions for the unit.

Was the unit worth doing?

Since the STELLA modeling lessons had been created and used the previous two years, that segment of the preparation was not an issue. The items added this year were the PK lab and the final lecture by Dr. Gallaher. The students enjoyed the PK lab the most of any activity in the unit, so it was definitely worth doing. Had the lab handout, written by the instructor just two days before the lab, been designed better, the results would have been more useful. The handout will be improved, now that the instructor has been through the lab once. The lab equipment set-up was too time-consuming. Without Dr. Gallaher and Dr. Macovsky's significant effort, it would be too much to try to repeat alone. If the PK lab setup were streamlined, there is no question the lesson would be repeated. All of the work needed to monitor the students during the lab was not excessive, and could be accomplished by just the instructor. It was necessary to change classrooms with the chemistry teacher. He was very cooperative, so that presented no problems.

The students gained insight into an important dynamic that is directly related to their lives. The unit had enough variety and engaging activities to keep students attendant to the tasks required. It was worth the time and energy expended.

Possible changes for next year

Discussion between Dr. Gallaher and the instructor have centered around splitting the unit lessons up and doing the first two days earlier in the school year. The problem is that the students tend to forget information and it would probably be necessary to have at least one activity before the alcohol model to review the previously learned material. Adding more days to the unit is not an attractive option, given the curriculum constraints of a second year algebra class.

Remarks/observations by Dr. Gallaher

Given the familiar concept of studying topics as isolated disciplines, students found that conducting a laboratory exercise as part of a math class was a unique, and unexpected experience. I believe there is a real opportunity here to emphasize the relationships between math, science, and System Dynamics. However, this would be more effective if we were to introduce this discussion earlier in the year, separate and distinct from an exercise which includes performance expectations among students and instructors.

The PK-LAB is proving to be an excellent teaching device, but the apparatus needs to be simplified. The instructor expressed reservations about the time required to set up the apparatus, although this opinion was shaped in part from an unfamiliarity with the procedures and culture of a wet chemistry lab. We are convinced that future replications of this lesson plan will be easier as a result of this prior experience, but the fact remains that streamlining the equipment will reduce significant barriers for the busy teachers we are trying to recruit.

Despite the unfamiliarity with a chemistry lab environment, the instructor is a very experienced teacher. She has a good rapport with her students, but this rapport includes a no-nonsense approach to paying attention and doing good work. The students were very attentive (within the controlled chaos of any lab environment), and it was gratifying to see them actively (and effectively) engaged in the exercise within the first ten minutes. They efficiently divided up the necessary tasks, and during the each experiment there was a steady stream of students between the PK-LAB apparatus and the ‘clinical lab’ (laptop computers with Vernier Instruments conductivity detectors).

The modeling and lab exercises appeared to be rewarding for everyone involved. As instructors, we expected to find some issues that could be improved, but we were gratified with the productivity of the students. We received significant feedback from the students and from our own observations, and the materials will be modified and repeated next year.

Remarks/observations by Dr. Macovsky

(All remarks are in reference to the PK lab exercises.)

1. Students previously exposed to the laboratory apparatus in a middle school health class (Jackson Middle School) expressed a new or greater appreciation for the laboratory exercises.
2. The self-organization of team roles and leadership appeared to be quick and painless.
3. After a short period into the second exercise, students became aware of the delay or time lag in feedback between data collection and the decision on when and amount of dose.
4. Playing “doctor” was definitely a stimulation and incentive to pay attention to the exercise. Those students that had a parent in the health field expressed what seemed to be a greater appreciation for the second exercise.

Back to the Top