Abstract

The Biology Labs On-Line Project is an attempt to create simulations of important biology experiments that students normally cannot perform in typical undergraduate laboratories. All of the simulations have enough complexity that students have the flexibility to design and interpret their own experiments. The programs generate large amounts of data and are fast enough for students to do multiple experiments, creating the opportunity for students to get extensive practice at applying scientific methods. The simulations are all written in Java and are accessed over the World Wide Web, making them easily available to students anytime and anywhere. Nine of the simulations, covering the topics of evolution, Mendelian genetics, protein translation, human population demography, protein structure-function, human genetics, mitochondrial electron transport, cardiovascular physiology and photosynthesis are already finished, with six more planned for the summer of 2000.

1. Introduction

1.1. Pedagogical Motivation

A major lack in much current science instruction at the university level is appropriate active learning experiences. Students in many science courses still get too few opportunities to think and reason about scientific problems. Well-designed laboratory experiments provide the best means to give students the opportunity to learn about a science subject while developing the thinking skills most instructors have as a goal of their course. However, there are many limitations on the use of real laboratory experiments in an undergraduate or high school science course. Students in educational labs are severely limited by the time required for most serious investigations. A typical laboratory for a biology class will meet once or twice a week for two to three hours each time. This time constraint is a major barrier for introductory students as they try to learn how to be a scientist. Many important biological experiments take weeks, months or years to carry out, putting them well beyond the reach of the typical teaching laboratory. Many other barriers limit the choice of experiments in teaching laboratories, including a lack of appropriate equipment, insufficient funds for expensive reagents, restrictions on the use of hazardous chemicals and radioactive materials, a lack of technical skills by the students and ethical concerns.

As a result of these difficulties, most professors either concentrate on using laboratory time to provide students with an opportunity to practice being a scientist by carrying out inquiry based investigations, or demonstrate scientific principles by having students carry out carefully controlled experiments designed by the instructor. In both cases the main mechanism for students to learn the subject is the traditional lecture. A major trend in current attempts to improve science education is to try to replace static lectures with more active learning approaches. While there are many versions of "active learning," in the sciences an inquiry approach is frequently used. One version of this is the learning cycle method in which students explore a biological phenomenon before receiving any explanation from the instructor. Other aspects of the inquiry approach include having the students propose their own hypothesis and design, execute and interpret their own experiments to test their hypothesis (Lawson, et al, 1990, Uno, 1999). The National Research Council's Science Education Standards consider this the central strategy for teaching science (NRC, 1995). In addition to learning how to think like scientists, students learn the concepts and facts of a subject better when they have to apply the knowledge. While there are many ways to make the lecture more inquiry based, (see "Handbook On Teaching Undergraduate Courses" Uno, 1999), one very useful alternative is the use of simulations (Windschitl, 1998, Uno, 1999). To address these problems the Biology Labs On-Line Project has created several Java simulations of biological phenomena that can be used to supplement traditional laboratories and lectures, providing students with many more opportunities to learn by experimentation than is possible using traditional methods.
which calls for anywhere, anytime access to information. The project initially brought together biologists from throughout the CSU system and the CSU Center for Distributed Learning (CDL) to explore ways to use technology to improve learning in introductory biology courses. Later, multimedia developers from Addison Wesley Longman were added to the development team. A major goal of the collaboration was to allow students to learn as biologists do, i.e., by actively designing experiments and interpreting their results. Eliminating the time constraints of the traditional experiment, the simulations give students the opportunity to design and interpret experiments, to learn from their mistakes, and to revise and redo their experiments just like real scientists. The simulations are not designed to replace the traditional "wet labs" found in the normal biology course, but rather to extend the laboratory experience to subjects and experiments that cannot normally be done, or not done well enough, in a traditional laboratory. The simulations are also not multi-media presentations, stand-alone tutorials or on-line courses.

A key advantage of a simulation is the potential of allowing the student to design and carry out many more experiments than would be possible with real labs. This gives the student many more opportunities to practice the skills of hypothesis creation, experimental design and data analysis than can happen in the normal lab or lecture setting. A lack of underlying complexity is a problem with many of the currently available online educational simulations, which frequently allow only one real experiment. Thus, one of the design goals for the Biology Labs On-Line Project was to create simulations with enough underlying complexity that students would be able to do many different experiments. For example, the FlyLab has 29 different genes on four different chromosomes, allowing the possibility of literally millions of experiments. Similarly, the Evolution Lab, which uses two islands, each with 7 independent continuously variable parameters, provides the capability of millions of different possible experiments. In addition to the complexity in the starting parameters, each of these programs operates stochastically, so that even with identical starting conditions students will get different results. The large number of possible experiments and the speed at which each experiment can be carried out, five to ten minutes per experiment, means that students can get much more practice at designing and interpreting their own experiments than is possible in the traditional laboratory. This creates new possibilities for teaching some topics as students can now figure out the underlying principle on their own, with only minimal guidance from their instructor.

The FlyLab’s introduction to the topic of sex linkage illustrates how these simulations can be used in inquiry. After doing some genetic crosses that demonstrate normal Mendelian dominance and recessive inheritance patterns, students are asked to investigate one of the X-linked traits available in the simulation. The students are not told that the trait is X-linked, nor is the concept of sex linkage discussed prior to the assignment. The students can do as many different crosses as necessary to try to figure out what is going on. The ability to carry out many different experiments is a key to making this work, as that is the only way the students can eliminate many of their initial explanations for what is happening. Even for the many students who fail to solve this problem, the experience is very helpful, making them much more attentive when the genetic explanation is given in class.

Another goal of the BLOL Project was to design simulations that could be used to learn about key concepts in biology that are not normally used in traditional laboratories because of time, expense, hazards, etc. Examples of this are the Evolution Lab and DemographyLab, which simulate processes that take place over hundreds of years; MitochondriaLab, which simulates experiments that use toxic chemicals; TranslationLab, which simulates the use of radioactive isotopes; HemoglobinLab and LeafLab, which simulate the use of complicated and expensive measuring equipment; PedigreeLab, which simulates expensive mapping experiments using dozens of human families; and CardioLab, which simulates potentially lethal experiments on human subjects.

### 1.2. Design of BLOL and Comparison to Other Lab Simulations

Other laboratory simulation products exist, comparable in some respects to the BLOL Project. Stella, for example, is a general modeling tool, and Ecobreaker is a package that can be used to create useful simulations of ecology processes. The Bioquest Consortium sells a large number of simulations on CD, covering many of the same topics covered by BLOL. These simulations differ
from those in the BLOL Project, however, in that they have certain machine requirements (Mac, PC, Unix) and distribution difficulties. Our Java-based BLOL simulations, on the other hand, are platform independent and not tied to use within the actual science laboratory. The BLOL simulations have all been created in the Java programming language, so that they can be easily accessed over the web through any standard browser. This solves the problem of widely disseminating the applications, a common problem with most educational software. The Java application provides the user interface where students set the starting parameters for their experiment and get graphical feedback on their current settings. While each of the simulations is unique, all of them share many common interface elements and functions. In some of the simulations the Java program also calculates the results, while in others the input parameters are passed back to the server, where the real calculations take place. The students receive the results through the Java application.

The downside of using Java is that only individuals and schools with fairly new computers and software (Netscape 3 or better, etc.) and an internet connection can use the software. Another disadvantage of using Java is the inability of Java programs to save to disk or print. This limitation has been overcome through the use of a notebook that can be exported to a web page. All of the data tables, such as numbers of different types of progeny, or results of statistical calculations, can be imported directly into the notebook. After typing in their comments, students can export the notebook to a web page for printing, or to email to themselves or an instructor. The web page is temporarily stored on the server. Graphical images produced by some of the programs are also exportable to the notebook, where they can then be printed.

All of the programs share some common user interface elements, including a title bar with links to an introduction to the lab, help, sample assignments, the notebook, etc. While there is much diversity in how the different labs operate, most of them start in an input mode where the students design their experiment by adjusting different parameters, after which they run the simulation. The program calculates the results of the experiment, usually in a minute or less, and then presents the results in the output mode. In this mode there is a tabbed interface where the students choose which type of output they wish to view, a table of the data, a graph, the input values, etc. After analyzing their results they can import them into the notebook and then go back to the input mode to design another experiment. This ability to go back and forth quickly between the design of an experiment and the results is one of the powerful advantages of a simulation approach to teaching science.

1.3. Availability

For simulations to truly be useful as a primary mechanism for teaching the concepts of a course, they need to cover the majority of the key concepts in the course. The BLOL Project has produced nine different educational simulations covering the subjects of evolution, Mendelian genetics, protein translation, human population demography, protein structure-function, human genetics, mitochondrial electron transport, plant photosynthesis and respiration, and cardiovascular physiology. Current projects in progress and due to be finished by the summer of 2000 will simulate enzyme kinetics (EnzymeLab), the use of transgenic mice to study developmental genetics (TransgenicLab), phylogenetic reconstruction (CladisticsLab), population genetics (PopulationGeneticsLab), metabolism (MetabolismLab) and population ecology (PopulationEcologyLab). Thus, a significant portion of the major concepts introduced in a typical introductory biology course could be taught using a combination of real laboratories and these simulations.

Nine of the programs are currently available for beta testing and all fifteen should be finished by the summer of 2000. Descriptions of each of the labs can be found below. Current plans call for a $19.95 fee for access to all nine of the simulations and a lab manual with printed instructions and sample assignments. The fee is necessary to support the servers and for maintenance of the various programs as operating systems and computers change. Annual subscriptions to individual labs are available for $5.25 each, and there is also the option of getting the five genetics simulations, FlyLab, EvolutionLab, TranslationLab, HemoglobinLab and PedigreeLab, for $10.95. The web site for access to the labs and for current information on the labs is http://www.biologylab.awlonline.com/.

Below is a brief description of the finished simulations.
2. DemographyLab

The Demography Lab models human population growth for seven different countries around the world. Students can use this lab to investigate how differences in population size, age-structure, and age-specific fertility and mortality rates affect human population growth. Default values for seven countries—China, India, Japan, Mexico, Nigeria, Sweden, and the United States—have been incorporated into the program to allow comparisons between nations with very different demographics, such as Japan and Nigeria. In addition, students can change any of the parameters to create their own experiments. Initial population size can be set anywhere from two to six million. The proportion of males and females in each five year age group can be set independently of one another. Thus, the effects of a war or a disease that affects one sex or certain age groups can be modeled. The mortality rate for males and females in each five year age group can also be set independently so the effects of changes in health care can be modeled (by changing infant mortality rates or mortality rates for the elderly, for instance). The birth rate per female in each five-year age group can all be set for those ages in which birth rates are possible. Thus, the effects of birth control efforts or changes in marriage ages can be modeled. All of these parameters are adjusted using a simple graphical interface.

After running the simulation for 100, 200 or 300 years, students get summary statistics, such as life expectancy, birth rate, population growth rate, etc. They can view a line graph of population numbers over the course of their experiment, see a graphical representation of the population structure for every five years of the experiment, or examine the number of males and females in each age group for each five year period. With the program a variety of demographic phenomena can be demonstrated, such as exponential growth and decline, stable age structure, zero population growth, demographic momentum, dependency ratios, sex ratios and marriage squeezes.
3. **EvolutionLab**

Although evolution is the unifying theme of the biological sciences, it is perhaps one of the most misunderstood and difficult concepts to convey in a laboratory setting. The study of evolution is especially suited to computer simulations because evolution normally occurs over very long time intervals, large data sets are usually needed to understand it, and there are usually a number of important parameters that are difficult to control in real experiments.

EvolutionLab is a web based, interactive computer simulation designed to teach the basic concepts of natural selection and to convey the importance of time in the evolutionary process.

Students using EvolutionLab observe evolutionary changes in bird beak morphology in hypothetical populations of birds isolated on two islands. In the simulation, students can set the annual rainfall on island(s) containing finch populations, and then observe the effect of this environment on the evolution of the finches’ beaks. Students may also change several other properties of the bird populations, such as initial mean beak size, beak size variability, beak size heritability and mean clutch size, to determine their effect on beak evolution.

While the simulation is based on Darwin’s finches, changes in the species variables such as mean beak size, variability, heritability and clutch size create virtual species that can have properties similar to many other wild species. Students can investigate the parameters that are more likely to lead to the extinction of endangered species, see why some species might evolve faster than others, and examine many other facets of evolution. The program generates large data sets -- one run can produce 600 data points -- so students can learn how to analyze and interpret large amounts of data, unlike the situation in a typical lab. The great flexibility of the program should allow individual instructors to tailor student assignments to their particular preferences and provide students with a real opportunity to design their own experiments. Actively engaging students in exploring and studying evolution through this simulation provides another avenue for students to learn about evolution in addition to the traditional text and lecture explanations.

4. **PedigreeLab**

PedigreeLab generates a hundred pedigrees for each of the 23 different genetic diseases available, including dominant, recessive and X-linked diseases. Every student gets a unique set of pedigrees to analyze. Students can examine the pedigrees to determine the inheritance pattern of the particular disease. Once the inheritance pattern has been determined the student can choose a molecular marker, from over a dozen available markers, each with a known position on a chromosome, to study. The program will search through hundreds of randomly generated pedigrees to find 100 pedigrees meeting the criteria chosen by the student. Comparison of the presence of the disease trait to the presence of the molecular marker can be used to determine whether the molecular marker is linked to the disease trait and, if they are linked, give the distance between them. The program keeps track of the results from each pedigree they use and can determine the statistical significance of their results. They can use the molecular markers to map the disease gene to a particular chromosome or to a region of the chromosome. This is a key process in the current search for human genetic disease genes and is normally very difficult to explain to students. The program includes graphical views of the chromosomes, on which they can place a marker designating where they believe the disease gene is located. There are also graphical aids for understanding the pattern of inheritance they would expect if the marker was linked to the gene or was not linked. Having them actually go through the process of mapping a human gene can significantly improve their learning of these difficult concepts.
5. **FlyLab**

The FlyLab simulation is an update to the FlyLab originally created by Bob Desharnais. In the FlyLab, students design their own fruit flies by choosing from many different possible phenotypes for characteristics such as eye color, wing shape, body color, etc. They then mate their flies and analyze the progeny to determine the rules of inheritance for different traits. Each experiment is unique, and students can have up to 10,000 progeny produced from one mating. Offspring can also be mated, providing a wide range of different experiments. There are 29 different traits that can be studied in isolation or in various combinations so the number of possible experiments is in the millions. The traits are all represented graphically, allowing the student to observe the phenotypes directly. For instance, if the student selects the white eye mutation for the female parent, the picture of the female parent will have white eyes. After the mating, pictures of the different progeny are presented, along with numbers beside each picture to indicate the number of progeny of that type (number of females with white eyes, females with red eyes, etc.) The program includes a Chi Square calculator for doing statistical tests of the students' hypotheses, and a notebook for recording results, observations, hypotheses and conclusions. Students can import the numerical results from their crosses and statistical tests directly into the notebook.

Using this program, students can discover or study most of the important principles of Mendelian genetics, including dominant and recessive alleles, sex-linkage, lethal alleles, independent assortment, epistasis, linkage, gene order, linkage groups, and linkage maps. An advantage of the simulation is that students can discover these principles by doing the same sort of experiments as the original researchers, only much more quickly. The program is appropriate for a wide range of biology courses as the assignment determines the level of difficulty. Students can do statistical tests, but this is not required. They can do complicated crosses with multiple traits, or simple crosses with only one trait at a time. If students are confused by a complicated cross, they can always do some additional simpler crosses to try to figure out what is going on. They can also do additional crosses with the progeny from their crosses, and their progeny, etc. This ability to devise their own experiments and try many different permutations is a major strength of the FlyLab.

6. **TranslationLab**

So far, the BLOL project has produced two molecular biology simulations. The first, TranslationLab simulates some of the original experiments used to crack the genetic code, one of the key discoveries in molecular biology. These experiments rely on radioactive materials and difficult-to-produce RNA templates, so they can't be done in the normal biology lab. Students design and create simple RNA molecules in the simulation that they then translate in a virtual *in vitro* translation mix. The program shows a simple animation of the techniques that would be used to analyze the products of the translation and then gives them the amino acid sequence of any proteins produced in their experiment. The student must logically analyze the results of multiple experiments to deduce the properties of the genetic code, just as the original researchers did, only with the advantage of being able to do experiments in minutes that normally take months to carry out. Various properties of the code that can be determined using this simulation are the triplet nature of the code, the non-overlapping nature of the code, the degenerate nature of the code, codon assignments for each amino acid, and the existence and identity of stop codons.
7. HemoglobinLab
In the second molecular biology simulation, the HemoglobinLab, students investigate various aspects of the molecular biology of hemoglobin using case studies. The goal is for the student to learn how changes in the nucleotide sequence of a gene may affect the protein sequence, which may affect the structure of the protein, which may affect the properties of the cell, which may, in turn, affect the physiology of the individual. Students choose a case by selecting a patient from a pull down menu containing a list of over a dozen patients. For each case the students can examine the doctor’s notes about the symptoms and medical history of the patient, the color of a vial of the patient’s blood, and a microscopic sampling of the blood to determine changes in the red blood cells. They can run a sample of the blood on an electrophoresis gel to determine if there are physical changes in the globin protein, and determine the amino acid sequence of the protein, the student can go to the DNA sequence editor and try to alter the DNA sequence of the normal gene to see what type of DNA mutation would cause the changes found in the patient. The patients have a variety of mutations in the globin gene ranging from simple point mutations that change one amino acid, such as in sickle cell anemia, to deletions and insertions causing frameshifts, such as some of the thalassemias. The mutations cause many different patient phenotypes, such as anemia, brown blood, polycythemia (too many red blood cells), and purple skin color.

8. MitochondriaLab
Two biochemistry and cell biology labs have been completed, MitochondriaLab and LeafLab. MitochondriaLab simulates electron transport, proton gradients and oxidative phosphorylation in mitochondria. Students recreate the classic experiments that established the chemiosmotic theory as the mechanism for energy production in the cell. They add various substrates, such as pyruvate, succinate, etc. and inhibitors, such as malonate, cyanide, DNP, etc. to their virtual mitochondrial extracts and then measure the consumption of oxygen over time. The program produces a chart similar to what would be produced by a real oxygen electrode. Students use the chart, the known volume of the flask and the concentrations of the reagents added to determine oxygen consumed and the amounts of the substrates. From their results they can work out some of the steps in the electron transport pathway, and the mechanism by which chemical energy is converted into ATP molecules.

9. LeafLab
The LeafLab simulates the photosynthetic reactions in leaves. Students measure CO₂ consumption by leaves from six different plants, including both C3 and C4 plants. Students can vary wavelength and intensity of light, CO₂ concentration, air flow rate, temperature, and type of leaf and then measure the consumption of CO₂ in their simulated leaves. The program helps the student with the calculation of photosynthesis rate and has a sophisticated curve fitting function that lets students plot their data and then determine the shape of the best curve through the data. Students measure or study the light compensation point, the CO₂ compensation point, the connection between light and CO₂ consumption, photochemical efficiency, dark respiration, photochemical saturation, and the differences between C3 and C4 plants, sun versus shade plants and plants of different ploidy levels.
10. CardioLab
CardioLab simulates some aspects of cardiovascular function. Students can directly vary six different parameters that affect cardiovascular function, blood viscosity, blood vessel radius, heart rate, blood volume, systolic ventricle volume and venous capacity, and measure the effect of their changes on blood pressure, heart rate, stroke volume, blood volume and various nerve impulses. Concepts such as homeostasis, feedback, and compensation can be illustrated. Students can also do experiments on virtual patients with various health problems such as hypertension, congestive heart failure, mitral valvular stenosis, etc. The effects of different “real” interventions on both normal and diseased patients such as hemorrhages, exercise, dehydration, IV infusion, disruptive shock and treatment with drugs such as epinephrine, is also modeled in the simulation.

11. Assessment
The precursor to all of these labs is the original Virtual Fly Lab. This simulation of fruit fly genetics is now used in biology classes all over the world, and has created so much demand on the server hosting the program that there are now five different mirror servers. I field tested the FlyLab, EvolutionLab and TranslationLab in an upper division genetics course with encouraging results. 98% of the students in this course considered their FlyLab assignments useful in learning genetics; 83% found EvolutionLab to be useful; and 93% found TranslationLab useful. Some comments from the students are given below (Student comments refer to older names for the applications. Virtual Fly is now FlyLab, EvolveIt is now EvolutionLab and TranslateIt is now TranslationLab).

"Virtual Fly and TranslateIT were the assignments I got the most out of. I liked the way it made you systematically think to solve the problems."

"TranslateIt was enjoyable because it requires the student to investigate and solve the problem."

"TranslateIT gave me an excellent concept of how genes code for proteins through valuable experience. I could experiment and learn by trial and error to prove to myself that the book and what I was working on were in fact the same."

"It is a tie between TranslateIT and EvolveIT for most useful and as to how much I got out of them. They were easy to use, the help info was well defined and they both helped me see the larger concepts, 'big picture'."

"I liked the Virtual fly and EvolveIt activities because they allowed you to do some investigation on your own and they made you think about what was really happening, which made you understand the material better."

There were only a few negative comments, usually having to do with the difficulty of getting on-line and using the programs. Students who are uncomfortable with computers are at a disadvantage when using these simulations and special care must be taken to make sure they get the most out of the simulations. The only other negative comment was, "I liked TranslateIt the least because it made my head hurt."

While this is unfortunate, if the BioLabs project can produce more simulations that cause some students’ heads to hurt, then the project will be producing simulations that change, for the better, the way biology is taught.
12. Conclusion
The purpose of the BLOL Project is to try to find ways to use technology to improve biology education. The approach decided upon was to create a team composed of biology professors, graphic artists and programmers that would design and produce simulations of significant biological processes. While this approach greatly increases the expense of producing the simulation, it is hoped that the increased quality and complexity of the simulations will make them much more useful than the typical program produced by individual faculty, which typically are used in only a small number of courses. Eventually a publisher, Addison-Wesley-Longman, was also added to provide the marketing and support that would be needed if the programs were adopted by a large number of faculty. Initial tests have suggested that the programs can be very useful learning tools. Whether significant numbers of faculty will be willing to make the changes needed to incorporate these tools into their courses remains to be seen. With the rapid increase in the computing power available to students and the increased familiarity of students with using applications over the Internet, on-line tools such as the simulations produced by the BLOL Project will become more and more useful. Simulations such as these provide new tools to increase the use of the inquiry approach to teaching science. They will not, and should not, replace real hands-on laboratories. Finding the right balance and the proper way to use these new tools is going to take some time and experimentation by instructors (Jensen, 1998). Hopefully, they will at least consider the possibilities these new tools provide.

13. References

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