Using Classical Genetics Simulator (CGS) to Teach Students the Basics of Genetic Research

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Some experiments are not well suited to large introductory labs because of space, time and funding constraints. Among these are classical Mendelian genetics investigations. Cyber labs can overcome these constraints. Classical Genetics Simulator (CGS) gives students the opportunity to perform controlled crosses with model organisms much like a geneticist would do. CGS provides populations of *Drosophila*, *Arabidopsis* or mice with unknown patterns of inheritance and gives students the tools to design and perform experiments to discover these patterns. Students require an understanding of the what, why and how of solving genetic problems to successfully complete our cyber genetics lab activities.

Keywords: Mendelian genetics, simulator, classical genetics simulator (CGS), linkage, monohybrid, dihybrid

Introduction

In large introductory biology classes some labs are difficult to do because of space, time and funding constraints. Among these are classical Mendelian genetics investigations. As a result, we have turned to cyber labs. Working with the University of Wisconsin introductory biology program, Ben Adamczyk developed a Classical Genetics Simulator (CGS). CGS is web-based software that allows biology students to apply lessons in Mendelian genetics to real-world scenarios. Using CGS students can study the genetics of populations of model organisms, much like a geneticist would do in a modern laboratory. Instructors can set the parameters for the populations including the number and type of genes to investigate in a population, the modes of inheritance and gene linkage. It is then up to the students to determine which crosses to perform and how to interpret the data that they collect. Students cannot play CGS like a video game and expect it to give away any answers. Instead, CGS requires students to understand what they are doing, why they are doing it and how they should do it. CGS can be used as a primary laboratory module for introductory biology or genetics courses, or as a supplement to a hands-on genetics module with real organisms.

This paper will introduce you to the CGS program and provide you with two different examples of how we use it in large, introductory biology classes. It also provides the information you need to test the program for yourself, both from a student and an instructor perspective.

How can students get practice doing what geneticists actually do?

An obvious way for students to get practice doing what geneticists do is to conduct actual crosses. However there are problems with this when running student labs. For classes with hundreds of students setting up the stock organisms alone is costly. Doing the number of crosses required using real flies or *Arabidopsis* plants takes a considerable amount of time, especially if you want students to look at the results of several generations. In addition, when we use standard stock organisms, students often look up the genetics using online resources before running the experiments and therefore see no reason why they should run them.

Using CGS eliminates many of these problems. It is cost effective. Many generations of genetic inheritance can be studied without the time limitations that come with using live organisms. Organisms do not need to be created or destroyed. CGS is easy to use and can be customized for any biology course. Students cannot look up the answers because the genetics behind the traits are set by the instructor. Perhaps most important, to solve the problems, students need to use the same type of logic they would if they were using real organisms.

How do we prepare our students?

In most introductory biology courses, we use lecture and the textbook to describe how Mendel's experiments led to our understanding of how genes are transmitted from one generation to the next. We then show students how to solve a series of genetics problems and give them examples of how to use Punnet squares to do this. For example: We pose the following problem. Two mice each with the genotype Aa mate. What is the probability that any of their offspring will be aa? We indicate that we can use a Punnett square to solve this. We write the following on the board and then state that this shows the probability of having an aa offspring is ¼ or 25%.

	A	a
A	AA	Aa
a	Aa	aa

Most of our students will nod their heads as if they understand. However, what most of them take from this is that "the answer to that problem is ¼" and nothing more. Often this occurs because they do not understand how we set up the Punnett square. There are many assumptions we make in doing this including the following.

a) The two alleles, A and a, are located on a single pair of homologous chromosomes.

b) These homologous chromosomes (and therefore alleles) segregate at meiosis with one going ultimately to ½ of the gametes produced and the other going to the other half.

c) When we write A or a in the Punnett square we are indicating the alleles found in the male gametes (or the female gametes).

d) Filling in the Punnett square gives us all possible combinations of the male and female gametes and as a result, all possible genotypes of the offspring.

To be sure they understand, we find it is necessary to state all of these assumptions to our students. In addition we use a Punnett square that includes the alleles in eggs and sperm which helps our students see that the offspring genotypes are products of specific fertilization events.

Aa x Aa

	A	a
A	AA	Aa
a	Aa	aa

Following an explanation of the basics of autosomal and sex-linked crosses we provide our students with a handout titled "Solving Genetics Problems" (**Appendix A**). This handout lists the six different autosomal crosses possible for a gene with two alleles where one is dominant and the other, recessive. It also shows the six different sex-linked crosses possible for a gene with two alleles where one is dominant and the other recessive. In lab we try to convince our students that if they know how to solve these crosses, they can solve almost any cross. To drive this home, we have them solve a series of sample problems.

After going over a number of sample problems we ask, "Why do we need to know how to solve these types of questions? I.e., when in life is anyone asked to solve these kinds of problems?" The answer to this question is – about the only place a geneticist (or anyone else) solves these types of problems is in biology classes. That begs the next question – If geneticists do not work on these types of problems, what types do they work on? The answer is they work on problems that are messy. For example, a couple comes into a geneticist office. Are they more likely to say: "I think I'm Aa and my husband has a 50% chance of being Aa also. So I'm worried that my children may have..." Or do they say, "Both of my uncles had a genetic disorder on my side of the family and on my husband's side his mother had the disorder. One of his brothers has it now and we're worried that we might pass it on to our children." In other words, in humans, when they cannot actually test for specific alleles of genes, real geneticists do pedigree analyses. If they are dealing with animals or plants, they may do a series of controlled crosses to determine the genetics. This is what Mendel did. However, and this is a big HOWEVER – our ability to work out these real-life problems is based on a knowledge of theoretical Mendelian genetics. We look for similarities to theoretical genetic crosses in the pedigrees and in the controlled crosses in order to deduce the genetics. That is, we compare the results of different real-life crosses with those from theoretical crosses to determine how specific genes could be inherited, e.g. autosomal, sex-linked, etc.

How does CGS help students learn genetics?

The CGS program provides students with populations of organisms (*Drosophila*, *Arabidopsis* or mice) with specific phenotypes where the patterns of inheritance are unknown. In our labs, we set up a series of populations. The genetics behind the phenotypes become increasingly more difficult as the students progress through the populations. In each population, the number of genes and the type of inheritance (autosomal vs sex-linked, linked or unlinked) are set by the instructor. When students open a *Drosophila* problem, they get a field caught population of flies all of which may be unrelated. Students are required to set up and analyze a logical series of crosses to determine the genetics behind the fly phenotypes. Doing this requires that they really understand how genes are transmitted and why we would expect specific ratios of offspring. We can "see the light bulbs" go on as

the labs progress. This is also evident in student evaluations some of which are included below:

"The simulator assignment was most useful in helping to learn genetics because it required us to think critically and apply skills learned in lecture."

"The online simulator was at first extremely challenging to get used to, but once [I] had been able to play around with it, it was probably the most useful tool I used to learn about crosses and sex linkage."

Student Outline

What types of research problems did we develop using CGS?

At both the University of Alberta and the University of Wisconsin-Madison, we find that the benefits of using CGS as an anchor in our transmission genetics labs are many. As noted previously, CGS is cost-effective for large labs. Students can use CGS anywhere they have internet access because it is an online program. What is more important is that using CGS gives students the opportunity to develop the logic and thought processes needed to solve real-life problems in genetics. This experience promotes deep understanding. Overviews of how CGS is incorporated into our genetics labs are included below. The specific lab activities are included in the appendices.

Overview and Purpose of CGS-Based Lab at the University of Alberta

Our introductory genetics lab is directed at sophomore students. It is a large class (approximately 500 students a semester) with multiple lecture and laboratory sections. We use the Classical Genetics Simulator (CGS) to test students on concepts in transmission genetics. Students are assigned a take-home, simulator-based assignment to complete following two, three-hour labs held over two consecutive weeks. Theoretical concepts targeted by the assignment include Mendel's first and second laws, Mendel's principal of dominance, sex-linked genes, linkage, recombination frequency, breeding diagrams, and Punnett squares. Our simulator-based labs occur approximately half way through the semester. Students have attended labs focusing on fundamental genetic topics such as mitosis, meiosis, genes and alleles, mutation, and genotype to phenotype by this point in the course. As such, they have the relevant background knowledge to solve problems in transmission genetics.

The initial lab is a practical lab. Students score actual fruit fly (*Drosophila melanogaster*) offspring from a number of pre-set crosses. They use these data to determine the dominant trait for two different characters and the location (autosomal versus sex-linked) of the gene controlling those same characters by working through a series of focused analysis questions. Students are given time during lab to collect the data and complete these analysis questions. This lab not only allows students the opportunity to practice solving simple problems in transmission genetics it also gives them practical experience working with a key model organism in genetics.

The second lab begins by working through the remaining concepts in transmission genetics. We provide sample data from a number of dihybrid crosses and get students to work through a series of questions focusing them on independent assortment, linkage and recombination frequencies. This is followed by assigning the simulator-based assignment. We state the parameters of the assignment, introduce students to CGS and demonstrate it by working through an example simulator-based problem. Students have the remaining portion of the lab to first work through a practice simulator problem and then the actual assignment problems.

We find students gain most from these labs and thus the CGS assignment when they have the background knowledge to solve problems in transmission genetics and have practice solving the same. We give students the theoretical knowledge in the lectures and labs preceding our CGS-based assignment. We tell students what the CGS can do and how to use it in lab. We show students how to use the CGS using an example. And we encourage students to practice using the CGS in lab by giving them a practice problem. Student notes, sample data sets and analysis questions, instructions for using the simulator, and our assignment instructions including student worksheets, answer sheets and marking rubrics for the main simulator-based lab at the University of Alberta can be found in **Appendix B.** Notes for instructors are included in **Appendix C**.

Overview and Purpose of CGS-Based Lab at the University of Wisconsin-Madison

At the University of Wisconsin – Madison, our three-week genetics lab module is taught in the first semester of our two-semester introductory course sequence for majors. Similar to the University of Alberta, the majority of students in the course are sophomores. During the fall semester, about 800 students are enrolled in this course compared to about 300 in the spring semester.

Similar to the University of Alberta, our genetics lab module falls near the middle of the semester. Prior to the lab, students have been introduced to both molecular genetics and classical Mendelian genetics in lecture. During the first week of the module, students compare their answers to a set of prelab questions to help them develop the basic understanding and strategies needed to solve standard genetics problems. We follow this by discussing the type of work geneticists actually do. Then we introduce the research project. This research project is designed to allow students to determine whether specific phenotypic traits in a newly identified population of *Drosophila* (or *Arabidopsis*) are genetically determined. The research projects are described as follows:

Drosophila – Assume you are a geneticist. You have just returned from one of the more remote areas of the Hawaiian Islands. On the islands you collected specimens from different populations of fruit flies that were endemic (found only in this area). In this initial wild or field-caught population, the genotypes of the individual fruit flies and the mode of inheritance of the phenotypic traits displayed by the flies are not known.

Arabidopsis – Assume you are a geneticist. You are trying to learn more about the genes that control specific aspects of development in plants. Using *Arabidopsis* as a model plant organism, you add a mutagen to wild-type seeds in the hope of altering genes important for normal growth and development. When you grow the seeds and allow the plants to self-fertilize, you find several new phenotypes in the next generation that may be the result of genetic mutations.

You need to do controlled crosses in order to determine whether the new phenotypes (fruit fly or *Arabidopsis*) are genetically determined. If the traits are genetic, you also need to determine the mode of inheritance (sex-linked, autosomal, etc.). Please note that while fruit flies must outcross, i.e. mate with others of the opposite sex, *Arabidopsis* can either self-fertilize or be outcrossed.

Students work in groups of three to four. Each group begins with a Practice Problem designed to help them learn how to use the CGS program and to give them experience developing strategies for determining inheritance patterns. Following this each group is asked to determine the genetics of three newly discovered populations of organisms. The complete student lab activity and the instructors' notes that accompany it can be found in **Appendix D** and **Appendix E**.

How do students use CGS?

To use CGS, students need to know their instructor's "Course ID" and the "Student Account" that has been assigned to them. The first time they log in, CGS gives each student group a password. Students use this password to retrieve saved work and return to it at a later time if needed.

Figure 1. Student view showing the field caught population of flies in the practice problem.

The student interface for CGS is designed to be user-friendly, and students generally do not need a lot of instruction on how to perform crosses. A general guide with pictures can be found on the CGS web site at **http://www.cgslab.com/getstarted/**. A single-page condensed version of this, titled "CGS Quickstart Guide for Students" can be found in **Appendix F.**

To begin an investigation, students select a population to study. The flies in this population appear on a "sorting tray" (Fig. 1). Each fly is given a unique number. Various tabs and pulldown options give the students information about each fly's phenotype and the total numbers of flies with each phenotype. Individual flies can be selected and crossed by clicking and dragging to the crossing vial. Following each cross the offspring appear in a new "sorting tray."

Students can get a summary of the phenotype information for the flies in a given vial by clicking the "Analysis" tab (Fig. 2) and can add their own notes at the bottom of the screen. Students are told that they must include the following data for each cross.

1. What cross did you perform? Include details such as sex, phenotype, vial/cross number, etc.

2. What did you want to learn by doing the cross? In other words, what information could the proposed cross provide (e.g. is the gene in question located on an autosome or sex chromosome, etc.)?

3. What did the results of your crosses indicate about your assumptions and the genetics of the trait?

All data associated with the individual analysis screens, including added notes, can be collected together by clicking "View all data." These data can be copied and pasted into a word document and the results of specific crosses can be used as evidence to support the genetics the students propose for each population.

Figure 2. The "Analysis" screen includes summary information for the vial.

Materials

All materials for conducting the lab activities described can be found online at the URLs noted in the text of this article or in the appendices associated with this article.

Using the CGS web-based software requires a computer that has Flash capability and internet access.

Notes for the Instructor

What should instructors know before using either of the student labs described in this article?

Fairly detailed instructors' notes are included with each of our student lab activities (see **Appendices C and E**). Key points to note include the following.

a) Before you assign a CGS problem to your students, be sure to test the system by going on line to solve a practice problem yourself. Use the single-page "CGS Quickstart Guide for Students" (**Appendix F**) as you do this. Make any adjustments you feel are needed in these instructions as a result of your experience.

b) Solving the practice problem will not be easy or automatic even if you have a number of years experience teaching genetics. However, just because it is a little hard for you, don't assume that it is exponentially harder for your students.

c) Do not provide your students with a detailed strategy for solving the problems. Instead, give them questions they should be asking themselves as they do each cross. As noted above, we tell our students that for each cross they make they need to note the following.

1. What cross did you perform? Include details such as sex, phenotype, vial/cross number, etc.

2. What did you want to learn by doing the cross? In other words, what information could the proposed cross provide (e.g. is the gene in question located on an autosome or sex chromosome, etc.)?

3. What did the results of your crosses indicate about your assumptions and the genetics of the trait?

d) As you go from group to group and they ask questions, have your students refer to the handout on "Solving Genetics Problems." Use Socratic questioning as needed to help them. For example: What cross did you do? Which of the crosses on the handout are similar? If more than one is possible, how would you determine which one? What crosses would you need to make? What results would you need to find?

e) Bottom line - let your students learn by doing. Help them when they need it by asking the questions they should be asking themselves.

How can you set up a CGS account?

To request a CGS account, go to **www.cgslab.com/request**. An account is usually issued within 24 hours. New users will be issued an account with one free month of unlimited access to allow you to evaluate the software. After this trial period, you can renew your license on a semester or yearly basis (**http://www.cgslab.com/renew/rates.html**).

How adaptable is CGS? What can we control as instructors?

For step-by-step details on how to use CGS as an instructor, see the single-page "CGS Quickstart Guide for Instructors" in **Appendix G**. A more comprehensive manual is available to instructors at **http://cgslab.com/info/**. Click the **Instructor Resources** link from within CGS to access this material. Some of the key aspects are highlighted below.

With an instructor account, you can choose from a long list of basic and advanced genetics options and create either customized or randomized populations of organisms for your students. You can track the progress of your students. Students can save their work and return to it at any time from any computer.

An "Instructor Settings" screen (Fig. 3) allows you to set up new accounts. Within each student account, you can create a set of populations with specific phenotypes and modes of inheritance for students to analyze. Alternatively, you can set CGS to randomize these settings each time a new student logs in.

The genetic properties for each population can be selected using the instructors "dashboard" screen (Fig. 4). The slider on the left side of the screen allows you to create up to 10 independent populations for each student account. Up to four independent segregating traits (or genes) can be created per population. For each individual gene, a specific mode of inheritance can be selected from the drop-down menu, or a mode can be randomly assigned. Genes can also be linked to the same chromosome with a specified recombination frequency by using the drop-down menus.

CGS can randomize the mode of inheritance and phenotypes among students who log in with the same student account. This way, a small number of accounts can be sufficient for a large number of students.

How can instructors track their students' progress in CGS?

A "Track your students" option allows instructors to view answers (i.e. the genetics set for the students' populations), monitor student progress and retrieve lost student passwords (Fig. 5).
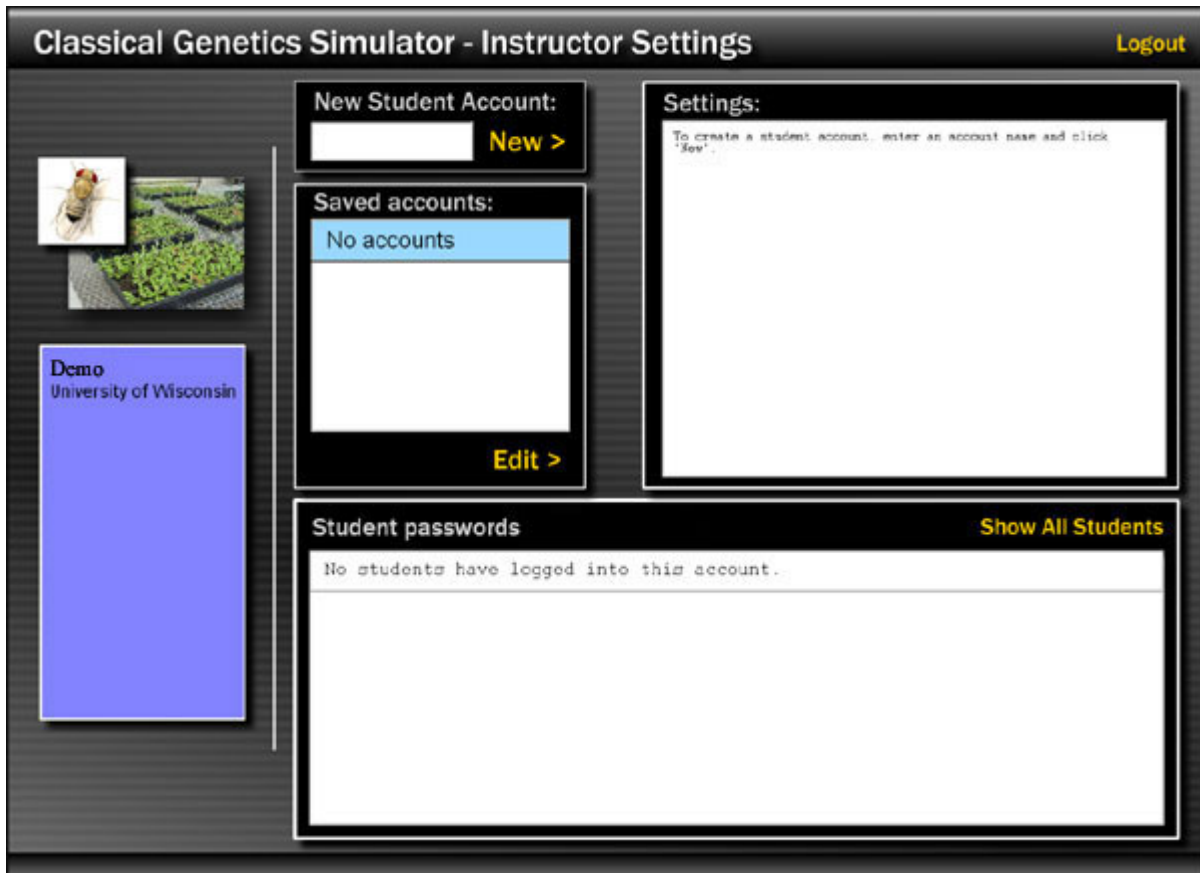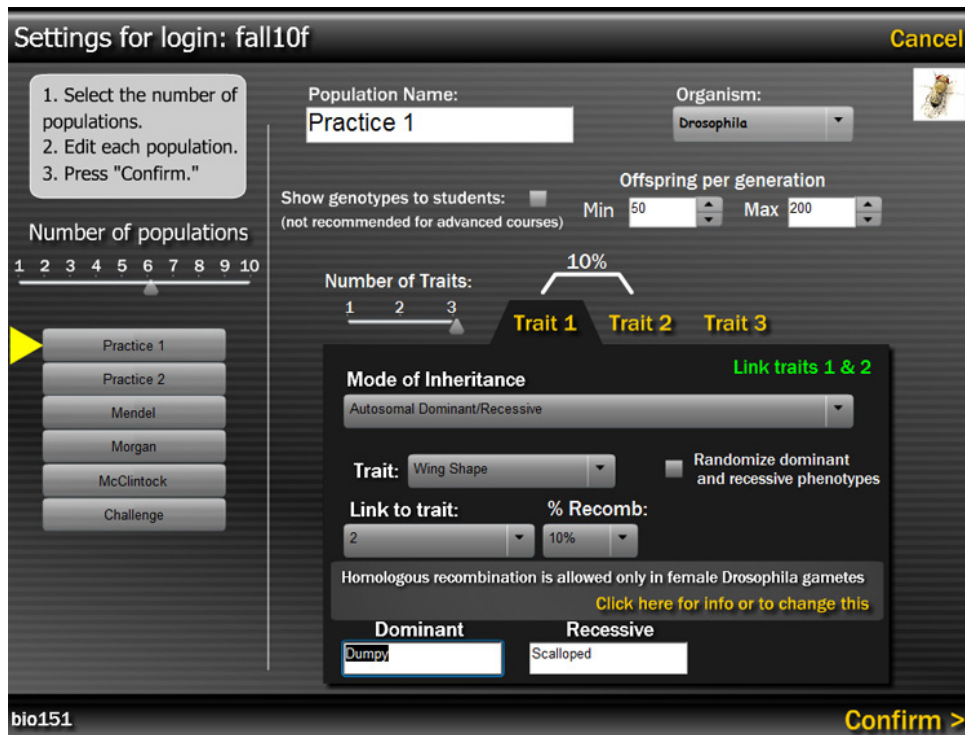
Figure 3. Instructor Setting Screen in CGS.

Figure 4. Instructor's "dashboard" screen allows instructors to set up a number of different populations each with its own genetic traits.
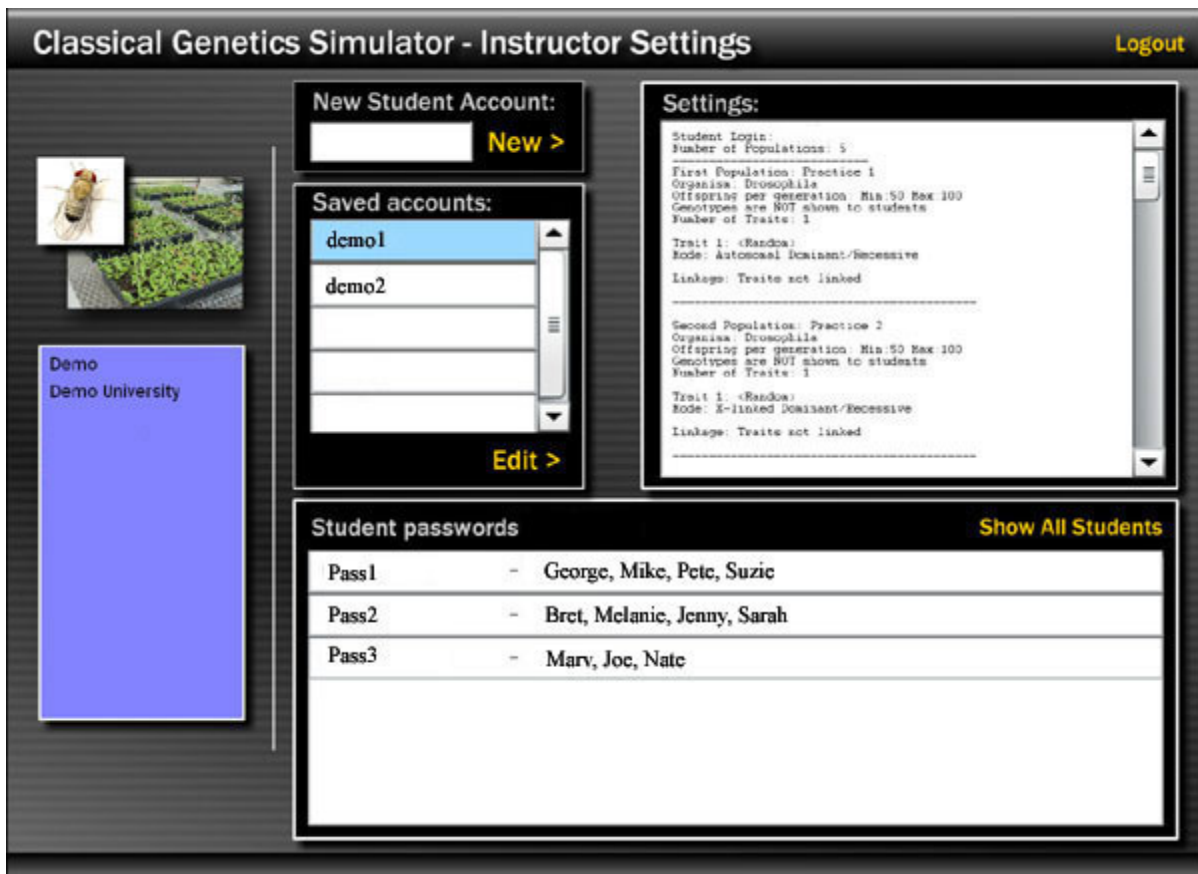
Figure 5. "Instructor Settings" allow instructors to monitor student progress and retrieve lost passwords.

Acknowledgements

About the Authors

Jean Heitz is a Distinguished Faculty Associate in Zoology at the University of Wisconsin-Madison and has worked with a two-semester Introductory Biology sequence for majors since 1978. Her key roles have been in development of active learning activities for discussion sections and open-ended investigations for laboratory sections. Jean has also taught a graduate course in "Teaching College Biology" and is the author of Practicing Biology: A workbook to accompany Biology by Campbell and Reece, 4th Edition and Practicing Biology: A workbook to accompany Biological Science by Freeman, 2nd edition (Benjamin Cummings, 2010).

Mark Wolansky earned a B.Sc. in Molecular Genetics and Heredity from the University of Alberta and a M.Sc. in Plant Biology also from the University of Alberta. He is currently the Laboratory Coordinator for the Department of Biological Sciences' core introductory genetics course at the University of Alberta. Prior to this position, Mark taught lectures and labs for small colleges located in and around Edmonton, Alberta, Canada. The fields he has taught in include genetics, cell biology, microbiology, and botany. Mark is a current member of ABLE and the Alberta Introductory Biology Association.

Ben Adamczyk earned a Ph.D. in Botany and a B.Sc. in Computer Science at the University of Wisconsin-Madison. While working with Jean Heitz as a Teaching Assistant for undergraduate introductory biology courses at Wisconsin, he developed the CGS application for use in their genetics laboratory module. Since completing his doctoral work Ben has been working at Genedata, Inc. in Boston, MA.

Appendices

All appendices are available in both Word and PDF format at
- **http://tinyurl.com/CGS-appendices** or at
- **https://mywebspace.wisc.edu/xythoswfs/webui/_xy-43592010_1-t_MpoVoSQ2**

Appendix A: Solving Genetics Problems

Appendix B: Student Lab Activities - University of Alberta

Appendix C: Instructors' Notes - University of Alberta

Appendix D:: Student Lab Activity - University of Wisconsin-Madison

Appendix E: Instructors' Notes – University of Wisconsin – Madison

Appendix F: CGS Quickstart Guide for Students

Appendix G: CGS Quickstart Guide for Instructors

Mission, Review Process & Disclaimer

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