Genetics Research Project Laboratory: A Discovery-Based Undergraduate Research Course

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Resource Justification:

Synopsis:

This resource is an example of a discovery-based undergraduate research course in genetics, using the course-based undergraduate research experience (CURE) model. During the first part of the course students perform designed experiments with the goal of learning laboratory techniques, experimental design, and key features of the model system. During the second part of the course, students perform original research. Two example lab manuals from different offerings of the course are given, one using *Drosophila* mutants in mitochondrial function and one using *Arabidopsis* hormone mutants. Representative results of the experiments and students' perceptions of learning are also included.

Introduction:

Student research is an experience with high impact on meaningful learning (Anderson et al., 2011) and a practice highly valued by future employers (Hart Research Associates, 2013). Research experience increases retention and interest in postgraduate education, even in first generation college students and minority students (Bauer et al., 2015; Elgren et al., 2006; Hathaway et al., 2001; Lopatto, 2004, 2006; Nagda et al., 1998). The benefit and importance of research experiences in undergraduate science is well established (AAAS, 2011; Lopatto, 2004), but in many institutions limited faculty time and resources make it difficult to give every undergraduate biology major an independent research experience. Alternatively, traditional science laboratory courses with prepared "cookbook" exercises can be replaced with discovery-based research courses that better promote student learning and engagement, as advocated by the President's Council of Advisors on Science and Technology (2012). However, implementing discovery-based research courses may present a challenge for faculty and administration, especially in small institutions where faculty research has modest support and where not many faculty are actively doing research (Healey and Jenkins, 2009).

Here we describe a discovery-based undergraduate genetics research course that provides research experience to a large group of students (up to 24 in a lab section) similar to that the students would receive in an independent project in a faculty member's lab. Just as with undergraduates who start research projects in our labs, in the project lab we guide them through the first few experiments with detailed instructions while they gain technical proficiency and an understanding of the intellectual basis of their project, then encourage them to proceed more independently. By the end of the course students are able to design, execute and evaluate an experiment on a topic of their choice. The course is taken concurrently with the introductory genetics lecture course by students in their sophomore, junior, or senior years. Both courses are required for the biology and biochemistry majors, but are sometimes taken by non-majors as well.

The laboratory course has evolved over the years, as both the organism used and the research questions investigated by students during the course have been closely aligned with the instructors' research programs. The originally-developed version of the course focused on *Arabidopsis* mutants altered in their responses to the plant hormone auxin. The currently-offered version of the course uses diverse mitochondrial and nuclear genomes of *Drosophila melanogaster* from a perspective of co-evolution of the two genomes and health homeostasis. Lab manuals for both versions are given here.

The description that follows refers to the current *Drosophila*-based version of the course, but the earlier version was similar in organization. The course is divided into two parts. The first part (about half of the semester) is composed of three designed experiments (experiments 1 to 3) that introduce students to the model system, hypothesis testing, data analysis and reinforce written and oral communications skills. During the second part of the course (experiment 4) students use the knowledge acquired in the first part of the course to develop their own novel independent research project using *Drosophila melanogaster*. Finally, students present their work in an oral presentation and in a research paper following the conventions of scientific papers in biology.

At the beginning of the semester, students are provided with a lab manual that carefully describes the goal of the course as a whole and of each experiment (see material provided to the students). The experiments stand alone but are designed to build progressively students' knowledge of the model system and of a variety of experimental techniques. Therefore, it is recommended to follow the particular order suggested in the lab manual and to read all the experiments to understand the goal of the course as a whole.

In addition to the explanation of the experiments, the lab manuals provide direction for use of micropipettors, calculation of dilutions, chi-square analysis, literature search strategy, guidance for information literacy, oral communication and written scientific reports. A description of student learning goals, expectations, and alignment of homework to the specific learning goals are also provided in the lab manual.

Approach/Method (Instructor Guidelines):

This course is designed for a class of 24 students maximum that meets for 2.5 hours twice a week. Throughout the semester, students work in pairs and maintain the same partner for all the experiments, including the independent project (experiment 4). Working in pairs allows students to learn how to collaborate, which is a fundamental skill in scientific research.

Ideally, the instructor will have the help of a teaching assistant (TA) since the experiments require significant preparation, especially for experiments 1 to 3. A tentative schedule of when to do the experiments and how to overlap several experiments is provided in the laboratory manual for laboratories that meet one and two times a week. Guidance for pre-class preparation for TAs and a list of representative topics from students' independent projects is also included in this submission. Instructions on how to do the experiments are given in the lab manual and in the guidance for instructors and TAs. However, our goal in describing the specific experiments and experimental material that we have used in teaching the genetics project lab is more to offer a general approach that may be valuable in teaching than to propose that other instructors should follow exactly the experiments outlined here. The approach we recommend is to develop specific experiments for use in a genetics project lab around the research interests and expertise of the instructor, or of a colleague. Many geneticists will have lines of mutants of a particular organism available and be familiar with several types of experiments--physiological, morphological, molecular, even cellular--to characterize the mutants. We suggest thinking about types of short and easily carried out projects that students might develop to characterize novel aspects of these mutants, and then work backwards to choose one to three common types of experiments that relate to such characterization. These basic experiments could be used to introduce students in the first part of the semester to the organism and experimental design, and give them some confidence in being able to carry out a small independent project.

Justification:

The rationale of this course is to help students to develop core competencies and review concepts learned in the genetic lecture class (which they are required to take concurrently). In particular the core concepts in this course are:

Experiment 1 and 2 → How do genes and genomes control development?

How can one deduce information about genes, alleles, and gene functions from analysis of genetic crosses and patterns of inheritance?

Experiment 3→ What is the molecular anatomy and function of genes and genomes?

The course overall→ How do the results of molecular genetic studies in model organisms help us understand aspects of human genetics and genetic diseases?

The course proposed here helps students to develop four of the six core competencies described in Vision and Change (AAAS, 2011): the abilities to apply the process of science, use quantitative reasoning, use modeling and simulation, and communicate and collaborate with other disciplines. This course does not explicitly address the ability to tap into the interdisciplinary nature of science or the ability to understand the relationship between science and society.

To help students understand what is expected from them, they are provided with a clear list of course objectives, student learning outcomes and an alignment with summative assessment. Calculation of grades is described in the lab manual provided to the students.

General Course Objectives

At the completion of this course, we hope that students will be able to:

1. Understand the genetic approach to biological problems and the use of molecular biology techniques to address biological problems
2. Understand key features of experimental design
3. Understand the importance of proper statistical analysis of experimental results
4. Understand the organization of the scientific literature and scientific databases
5. Communicate science and give presentations on scientific subjects

Student Learning Outcomes

At the end of this course, we hope that students will be able to:

1. Interpret primary research literature
2. Design and carry out novel research projects investigating genetics of an established organismal model system.
3. Describe and explain concepts used in research in genetics and molecular biology
4. Search for, collect, and evaluate scientific research articles relating to topics of interest.
5. Statistically analyze and evaluate novel research findings
6. Describe results in written papers and in oral presentations following established conventions for the field of biology.

Course goals, student learning outcomes and assessment alignment

<table>
<tr><th>Course objectives</th><th>Student learning outcomes</th><th>Assessment</th></tr>
<tr><td rowspan="2">Understand the key features of experimental design</td><td>• Interpret primary research literature</td><td>• Written and oral article responses</td></tr>
<tr><td>• Design and carry out novel research projects investigating genetics of an established organismal model system</td><td>• Independent project proposal
• Oral and written presentations of independent project (final lab report)</td></tr>
<tr><td rowspan="2">Understand the genetic approach to biological problems and the use of molecular biology techniques to address biological problems</td><td>• Interpret primary research literature.</td><td>• Written and oral article responses</td></tr>
<tr><td>• Describe and explain concepts used in research in genetics and molecular genetics</td><td>• Lab notebook and prelab summaries
• Written and oral article responses
• First lab report</td></tr>
</table>

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<tr><td>• Search for, collect and evaluate scientific research papers relating to topics of interest</td></tr>
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<tr><td>Understand the importance of proper statistical analysis of experimental results</td><td>• Statistically analyze and evaluate novel research findings.
• Describe the results in written papers and oral presentations following established conventions for the field of biology</td><td>Oral and written presentations of independent project (final lab report)</td></tr>
<tr><td>Communicate science and give presentations on scientific subjects</td><td>• Describe the results in written papers and oral presentations following established conventions for the field of biology</td><td>Oral and written presentations of independent project (final lab report)</td></tr>
</table>

Sample/Example:

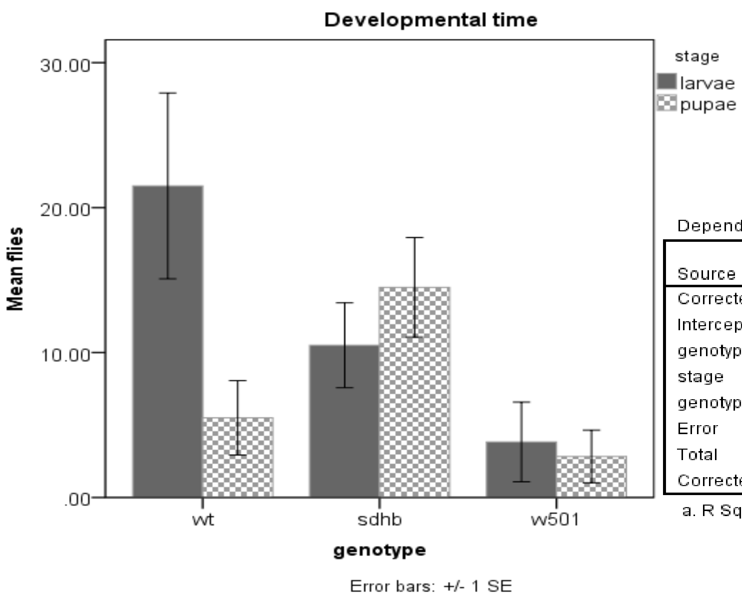
This course was taught using Arabidopsis for 7 semesters to about 250 students (most semesters two sections of the lab were taught). In its present Drosophila-based form it has been taught for 4 classes during three semesters to a total of approximately 94 students. Here we present the data obtained during one of these semesters (fall 2013). Results for experiment 1 are represented in Figure 1 to 4, experiment 3 in Figure 5. All the data were obtained and analyzed in class.

For the students' independent project (experiment 4), we provide a list representing topics of research. Note that the list is not a selection of the best titles, but instead is a complete list of all the research topics that students selected during one semester that the course was taught in this format.

Experiment 1:

Phenotypic characterization of mitochondrial haplotypes and mitochondrial mutations.

Defects of mitochondrial function cause damage to cells in tissue that have high energy requirement. Because fruit flies need a lot of energy to fly and climb, muscle tissue is highly affected by mitochondrial pathology. In this experiment students measure the developmental time (Figure 1), climbing ability (Figure 2), flying capacity (Figure 3) and the *in vitro* activity of succinate dehydrogenase (Figure 4) of control (*OreR: OreR*) and mitochondria altered strains *sdhB*^{EY12081} *(sdhB)* and *simW501;OreR (W501).*



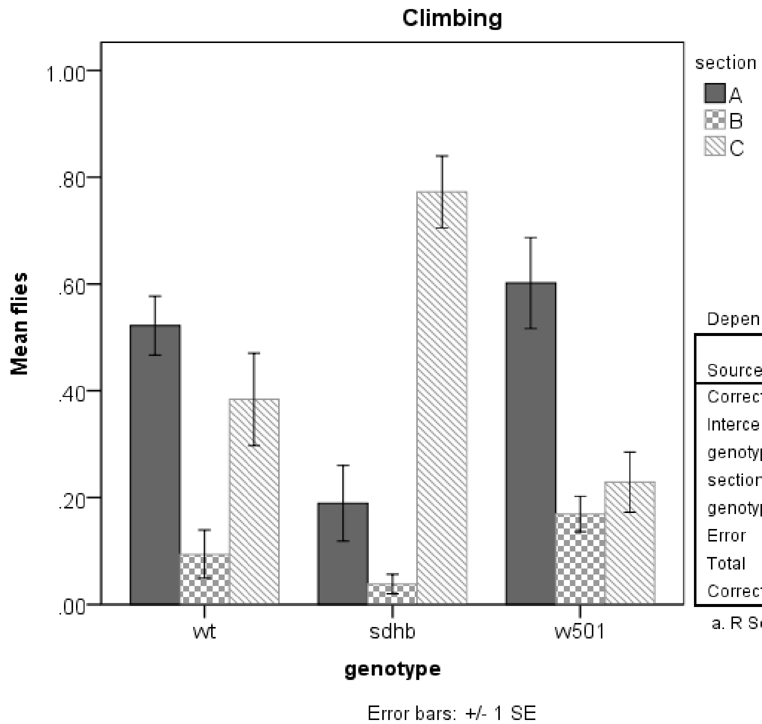
Tests of Between-Subjects Effects

Dependent Variable: flies

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	1572.556[a]	5	314.511	3.985	.007
Intercept	3441.778	1	3441.778	43.610	.000
genotype	753.556	2	376.778	4.774	.016
stage	169.000	1	169.000	2.141	.154
genotype * stage	650.000	2	325.000	4.118	.026
Error	2367.667	30	78.922		
Total	7382.000	36			
Corrected Total	3940.222	35			

a. R Squared = .399 (Adjusted R Squared = .299)

Figure 1: Representative results for developmental time measurements. The data are represented as the average number of individuals in stage of larvae and pupae for the three genotypes. Adjacent table represents the Analysis of Variance obtained using SPSS software.



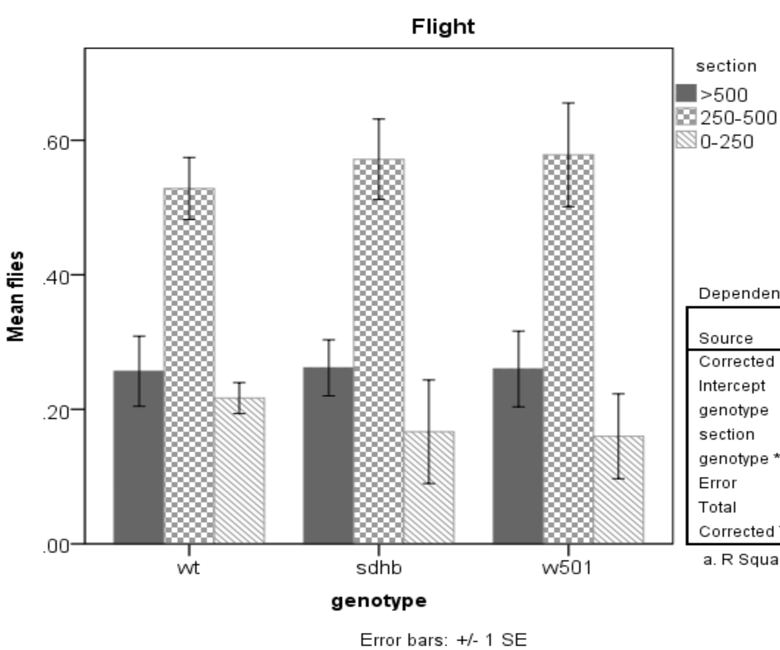
Tests of Between-Subjects Effects

Dependent Variable: flies

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	3.037[a]	8	.380	16.765	.000
Intercept	6.000	1	6.000	265.004	.000
genotype	.000	2	.000	.000	1.000
section	1.470	2	.735	32.452	.000
genotype * section	1.567	4	.392	17.303	.000
Error	1.019	45	.023		
Total	10.055	54			
Corrected Total	4.055	53			

a. R Squared = .749 (Adjusted R Squared = .704)

Figure 2: Representative results for climbing performance. The results shown are the proportion of flies that climbed section A (top), B (middle) and C (bottom) of the vial for each of the three genotypes. Adjacent table represents the Analysis of Variance obtained using SPSS software.



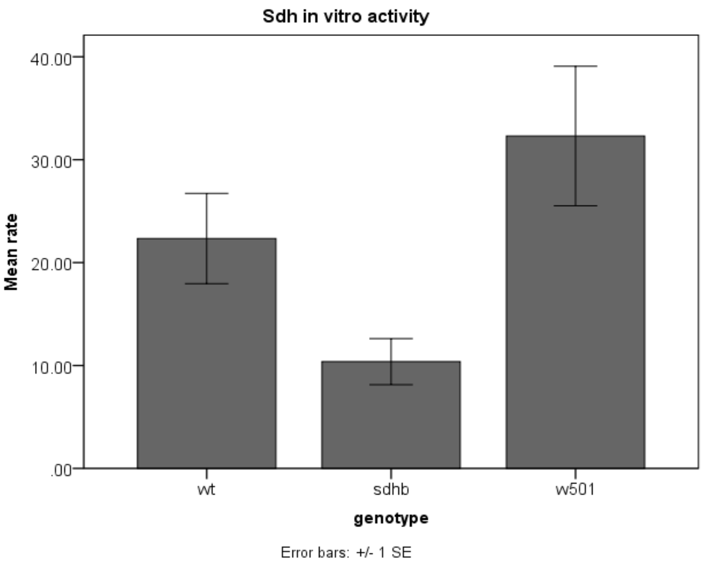
Tests of Between-Subjects Effects

Dependent Variable: flies

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	1.456[a]	8	.182	9.193	.000
Intercept	6.000	1	6.000	303.053	.000
genotype	1.111E-5	2	5.556E-6	.000	1.000
section	1.436	2	.718	36.256	.000
genotype * section	.020	4	.005	.258	.903
Error	.891	45	.020		
Total	8.347	54			
Corrected Total	2.347	53			

a. R Squared = .620 (Adjusted R Squared = .553)

Figure 3: Representative results for flight measurement. The data are represented as the proportion of flies that landed at section >500 (top), 250-500 (middle) and 0-250 (bottom) of the cylinder for each genotype. Adjacent table represents the Analysis of Variance obtained using SPSS software.



Tests of Between-Subjects Effects

Dependent Variable: rate

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	2136.766[a]	2	1068.383	4.418	.023
Intercept	12573.471	1	12573.471	51.993	.000
genotype	2136.766	2	1068.383	4.418	.023
Error	5803.975	24	241.832		
Total	21587.000	27			
Corrected Total	7940.741	26			

a. R Squared = .269 (Adjusted R Squared = .208)

Figure 4: Representative results for Sdh enzymatic activity. The data are represented as average rate of the enzymatic reaction for each genotype. Adjacent table represents the Analysis of Variance obtained using SPSS software.

In this experiment students characterize and idenfity the mitochondrial haplotypes of the strains *control, sdhB and w501*. To do so they use Polymerase Chain Reaction (PCR) and Restriction Fragment Length Polymorphism (RFLP). By PCR students amplify genomic DNA. By RFLP these DNA samples are digested by restriction enzymes and the resulting restricted fragments are separated by lengths using gel electrophoresis. Wild type control and *sdhB* strains have *D. melanogaster* mitochondrial DNA (mtDNA), while w501 strain has *D. simulans* mtDNA. Because *D. simulans* and D. *melanogaste*r mtDNA differ in sequence, RFLP bands show different digestion patters in an agarose gel (Figure 5).

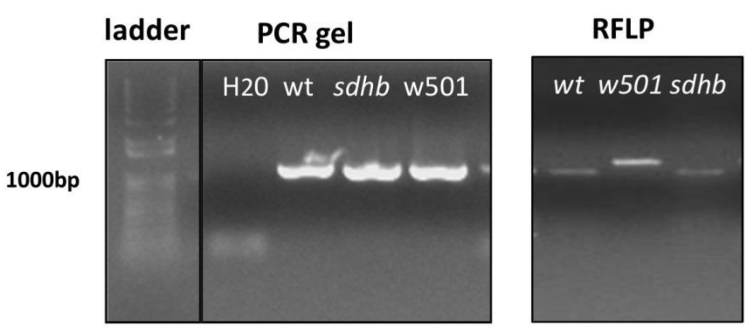


Figure 5: Representative results for PCR amplification and RFLP analysis in the genotypes.

Experiment 4: Independent Project.

Representative list of independent projects:

Topic by group
Varying concentration of Ethanol causes differences in Development in *Drosophila melanogaster*
Spicing it up in the mitochondria: Antioxidant ability of curcumin to increase resistance to ROS buildup succinate dehydrogenase deficiency*
Classical vs. Electronic Music: The effects on the lifespan of *Drosophila melanogaster*
The effects of color on the activity and preference of color of the *Drosophila melanogaster*
Effects of Hypoxia on the Expression of the *Antennapedia* Mutation in *Drosophila melanogaster*
Exposure to Chronic Noxious heat during early developmental stages causes *Drosophila melanogaster* to become resistant to heat and pain perceptions*
Effect of High Sugar Diet on *Drosophila melanogaster* climbing and Flying Ability
Non-tobacco hookah smoke shortens the lifespan of male, wild type *Drosophila melanogaster**
Effects of Vitamin B-12 on the capability of climbing in *Drosophila melanogaster*
The effect of calcium supplements on *Drosophila melanogaster* physiological capabilities
The effect of green coffee bean extract on the fecundity of female *Drosophila**

*****Students voluntarily presented their research the following year in the 11th Annual Research Conference, Adelphi University.

Students' perception of learning and benefits:

At the end of each semester students voluntarily and anonymously provided their perception of learning and benefits promoted by the course. We modified the Classroom Undergraduate Research (CURE) survey (www.grinnell.edu/academics/areas/psychology/assessments/cure-survey) using the online survey software SurveyMonkey (www.surveymonkey.com). On a scale from 1 to 4, with 1 being small gain, 2 moderate gain, 3 large gain and 4 very large gain, students' evaluations are summarized in Table 1 and 2 and Figures 6 and 7. Table 1 and Figure 6 represent their perception of the learning obtained from each element of the course. Table 2 and Figure 7 provide a representation of the benefits students may have gained from the research experience. The data are separated by the three semesters the course was taught, fall 2013, spring 2013 and spring 2015. Overall, students perceived higher learning from analyzing data (3.57) followed by their work in the independent project (3.43). On the contrary, critiquing other students' work was considered the element with lower learning (2.70) (Table 1 and Figure 6). Overall, learning obtained by specific elements of the course was rated higher in spring 2015 than in fall 2013, with the biggest different between semesters in the perception of the learning obtained by reading primary scientific literature and maintaining a notebook (Table 1 and Figure 6).

With regard to the benefits obtained after the research experience, students perceived a greater benefit analyzing data and other information (3.48) and understanding science (3.44). In contrast, clarification of a career was less benefited (2.81). Overall, students in the spring 2015 semester perceived a higher benefit from the course, with the biggest difference between the fall 2013 and the spring 2015 semesters being the ability to analyze data and other information and the understanding of the research process (Table 2 and Figure 7).

Overall, student perceived the project lab course very positively, averaging between a “large gain” and a “very large gain” on every possible benefit listed in Table 2 except for clarification of a career path. The results show a more positive response from students in spring 2015 than in either of the previous two semesters that the course was offered. This improvement may be due to a better communication of expectations between instructor and students as the instructor gained experience in teaching the course.

A similar assessment of the earlier Arabidopsis-based version of the course was not carried out successfully. In spring 2010 students in the class were encouraged to complete the Classroom Undergraduate Research (CURE) survey Out of the 20 students in the class, 15 students completed the pre-class survey at the start of the semester, but only 5 completed the post-class survey. The 5 students who did complete the post-class survey responded very positively about the perceived benefits of the class, but the sample size and response rate were too low to be meaningful so the results are not presented here.

LEARNING GAINED PER ELEMENT	FALL 2013	SPRING 2013	SPRING 2015	mean
the experiments organized by the instructor	2.92	3.13	3.29	3.11
the independent project	3.15	3.43	3.71	3.43
work individually	2.85	3.2	3.43	3.16
work as a whole class	2.77	2.8	3.43	3.00
work in pairs	2.85	3.6	3.71	3.39
became responsible for a part of the project	3.15	3.33	3.71	3.40
read primary scientific literature	2.62	3.07	3.71	3.13
present a research proposal	3.15	3.4	3.71	3.42
collect data	3.23	3.33	3.71	3.42
analyze data	3.31	3.53	3.86	3.57
present results orally	2.92	3.2	3.71	3.28
present results in written papers or reports	2.77	3.2	3.71	3.23
critique the work of other students	2.42	2.67	3	2.70
discuss reading materials in class	2.54	2.87	3.43	2.95
maintain lab notebook	2.23	3	3.29	2.84

Table 1: Students’ perception of learning gained per element of the course in the semesters of fall 2013, spring 2013 and fall 2015. 1 = small gain, 4 = very large gain.

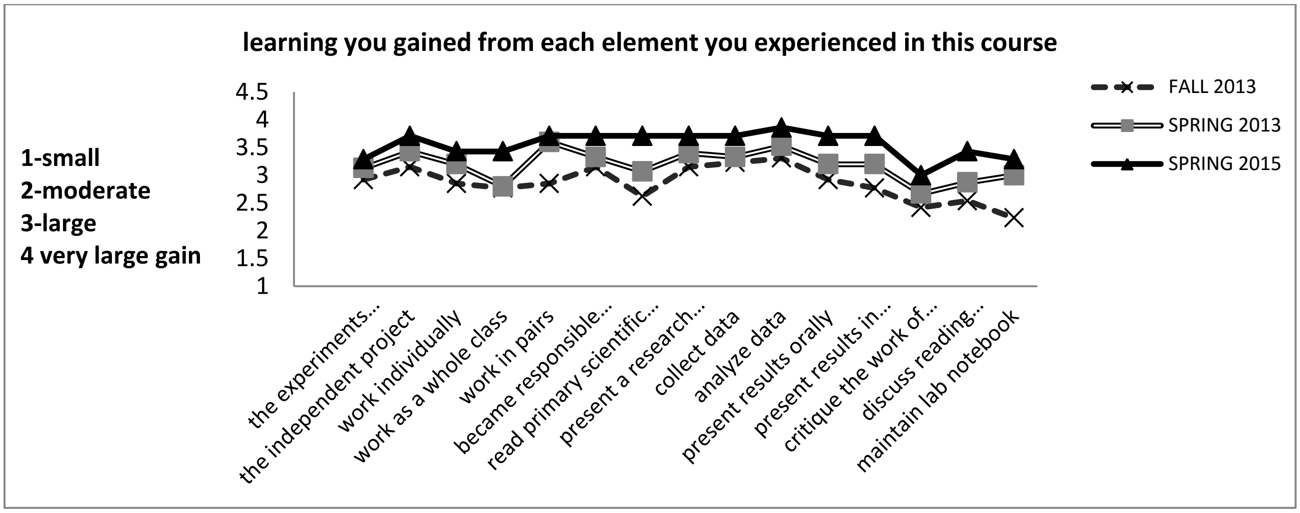


Figure 6: representation of the results in Table 1.

BENEFITS GAINED PER EXPERIENCE	FALL 2013	SPRING 2013	SPRING 2015	mean
Clarification of a career path	2.69	2.73	3	2.81
Skill in the interpretation of results	3.31	3.13	3.43	3.29
Tolerance for obstacles faced in the research process	3.23	3.13	3.57	3.31
readiness for more demanding research	3.38	2.93	3.71	3.34
Understanding how knowledge is constructed	3.31	3.2	3.43	3.31
Understanding of the research process	3.54	3.13	3.71	3.46
Ability to integrate theory and practice	3.46	3.14	3.57	3.39
Understanding of how scientist work on the real problems	3.38	3.2	3.71	3.43
Understanding that scientific assertions require supporting evidence	3.31	3.07	3.57	3.32
Ability to analyze data and other information	3.46	3.27	3.71	3.48
Understanding science	3.62	3.13	3.57	3.44
Learning ethical conduct in science	3.38	3.2	3.14	3.24
Learning laboratory techniques	3.31	3.13	3.71	3.38
Ability to read and understand primary literature	3.38	2.87	3.29	3.18

Skill in how to give an effective oral presentation	3.38	3.2	3.57	3.38
Skill in science writing	3.23	3.2	3.57	3.33
Self-confidence in understanding biology	3.23	3.33	3.43	3.33
Understanding of how scientist think	3.23	3.2	3.14	3.19
Learning to work independently	3.31	3	3.57	3.29
Becoming part of a learning community	3.31	3.13	3.43	3.29
Confidence in my potential to be a teacher of science	3.23	2.87	3.43	3.18

Table 2: Students' perception of benefit gained per experience in the semesters of fall 2013, spring 2013 and fall 2015.

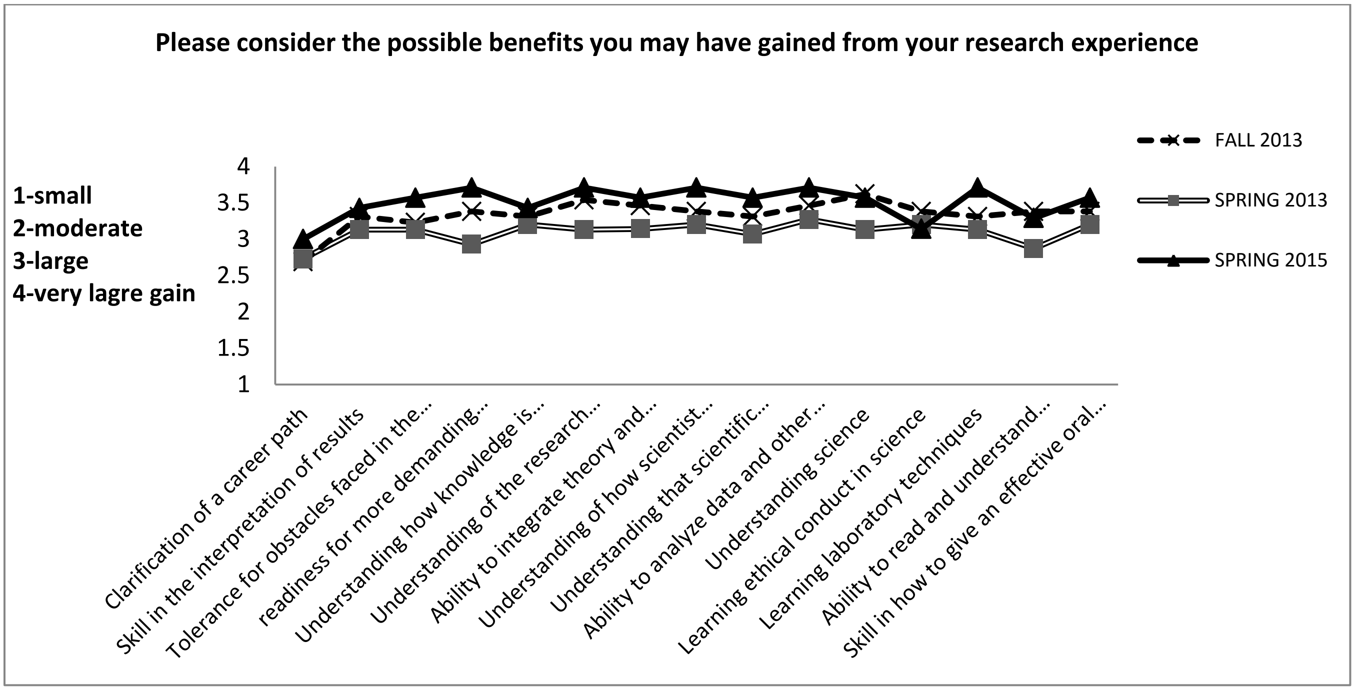


Figure 7: representation of the results in Table 2.

Challenges and successes:

This independent research laboratory course is one of the best ways we have found to motivate biology majors, as they become excited about their own idea and the potential of discovering something new. However, implementing the experiments requires moderate to intense preparation. This approach may be easier to implement in departments with technical assistant(s) and/or dedicated personnel that help the instructor with the preparation of the experiments.

We regard the overall design described here as generally applicable to teaching genetics labs. In contrast to classically-organized genetics labs, in which students carry out a series of unrelated laboratory exercises, in the project lab students analyze a single biological problem in one organism using several different approaches and techniques. The progression from straightforward guided experiments (presented with an emphasis on experimental design and hypothesis testing) to the concluding independent project mirrors the sequence used for training new students in research laboratories, and the focus on one problem in one organism give coherence to the semester's work. Although it may seem that students are being exposed to only a narrow spectrum of genetic experiments, in fact many connections can be pointed out with other areas of research. For example, the instructor can describe how the same molecular mapping techniques used to clone genes in *Drosophila* or *Arabidopsis* are used to identify the genes responsible for human genetic diseases.

This course has become a signature part of the Biology major requirements at Adelphi, bringing together as it does an emphasis on the scientific method, on experimental design, and on promoting students' ability to use the scientific literature and to carry out inquiry independently. During the genetic project lab, students practice and learn a number of basic lab skills including making solutions, doing dilutions, and using micropipettors, and also practice analyzing and presenting their results. The adoption of the same course format by several different instructors with different research interests, with equal success, demonstrates the flexibility of the overall design. Also, we have found there to be many advantages to developing the project lab around a faculty member's existing research program, including the ready availability of research materials and equipment and the instructor's deep knowledge of the topic, which aids in explaining the topic to students, in helping students develop and carry out their independent projects, and in troubleshooting.

Promoting Student Understanding and Acceptance of the Approach

The scientific background necessary for students to understand the experiments and succeed in the project lab course was complex and much more in-depth than most students had likely encountered before. The instructors explained this background to the students multiple times during the semester, gradually adding more complexity and detail as students gained familiarity with the concepts and terminology. The extensive background given in the lab notebook was also useful. The instructors increased student acceptance of this course's focus on a specialized area of research by explaining each experiment as an example of an aspect of the genetic approach (phenotypic characterization, genetic characterization, and molecular characterization) and by connecting the approaches used in lab to experiments discussed in the lecture part of the class. Not every student "bought in", but most did, especially as repeated exposure to the initially-novel terminology and practice with the techniques increased their comfort level. The commitment of time and effort required for the independent project also played an important part in fostering student enjoyment of the class; many students commented at the end of each semester that the class had indeed given them a research experience.

Acknowledgments:

The Genetics Project Lab as an investigative course focused on auxin physiology and genetics in *Arabidopsis thaliana* was originally developed by one of the authors (Hobbie) with funding from the National Science Foundation, DUE 0127035. Aram Stump in the department subsequently developed a version of the course using *Drosophila*. The most recent version of the course, focused on mitochondrial genetics and physiology in *Drosophila*, was developed by the other author (Villa-Cuesta) starting in spring 2013. We thank Dr. Stump for the ideas and insights that he contributed to the development of the course.

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