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Implementation of Genomics Research in an Undergraduate Course

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In the past ten years, numerous studies have assessed the effectiveness of undergraduate research on student success in retention, earning a degree, pursuing professional studies, and career success (American Association for the Advancement of Science [AAAS], 2009; Crowe & Brake, 2008; Fechheimer, Webber, & Kleiber, 2011; Gregerman, 2008; Hunter, Laursen, & Seymour, 2006; Lobav, Singer, George, Schweingruber, & Hilton, 2009; Lopatto, 2004, 2007, 2008; Narum, 2008); Russell, Hancock, & McCullough, 2007). Research, as it applies to the undergraduate level, can be broadly defined. California Polytechnic University - Pomona identifies the undergraduate research experience as “a spectrum of scholarly and creative activities that vary across disciplines, but all of which enhance student learning and better prepare students to be productive scholars, professionals, scientists, teachers, artists, and citizens” (UR Bronco, 2008).
Three types of methods, and their advantages/disadvantages, are described in the literature for engaging student participation in research projects. During the academic year, students typically participate in research projects on an individual basis with a mentoring faculty member (“apprenticeship model” Hunter et al, 2006). This model promotes a close mentor-student relationship, but the “complexity” of the relationship may be perceived as either positive or negative (Russell, et al., 2007). This method obviously requires significant faculty time and commitment (Pfund, 2009). The student, however, can often continue the research project in subsequent semesters and ultimately produce publishable data, a benefit for both the faculty member and the student.

National summer internships are widely available, but this method for engaging undergraduates in research can be expensive for both the students and the host institution since internships usually require external funding support from federal agencies, e.g., NSF Research Experiences for Undergraduates (REU), Department of Education DOE Science Undergraduate Laboratory Internships (SULI) and multiple scholarships and internships available through the National Institutes of Health (NIH) Undergraduate Scholarship Program (UGSP) and sponsored internship programs, e.g., Research Experience for Undergraduates (REU). These experiences expose students to faculty and students from many different locations, and often provide a more structured research environment. Summer internships, however, may not provide sufficient time to develop a research project, conduct experiments, and conclude of a research project (Butler, Dong, Snyder, Jones, & Sheets, 2008).

A third method is the integration of research in an existing laboratory course structure. However, labs often emphasize process skills, and lecture typically emphasizes content skills. To bridge the content/process gap, reform based teaching provides the best instructional strategy for the integration of lecture and laboratory in an individual course (McCormick & MacKinnon, 2004; Odell, et al., 2004; Raubenheimer, 2004; Scharmann, Stalheim-Smith, & James, 2004; Wright & Sunal, 2004).

There are significant “situational barriers” to a course-based research project (Dancy & Henderson, 2008). Faculty, for example, may lack the professional development needed to effectively promote active student learning, there may be time and space constraints in teaching laboratory facilities, and there may be a lack of support by university administration in valuing efforts to implement reform-based teaching (Dancy & Henderson). Nonetheless, there is significant evidence that demonstrates that these barriers can be minimized (Sunal, C. et al., 2008a; Sunal, C. et al., 2008b).

Ideally, an experience that engages students in a research project should have the following characteristics: (1) common methods used for the research are taught; (2) assignment of individual students to their own project is possible; (3) results from individual projects can be combined into a whole data set; (4) the research is technically simple; (5) there are minimal safety risks; (6) there is a high probability of success; (7) the research provides different levels of content accessible to multiple levels of student knowledge; (8) there are multiple learning outcomes; (9) there is a possibility that the project can be extended into other courses; and (10) there is a good potential for producing publishable results (Elgin, 2011).
Genomic sciences present an opportunity to do authentic research that meets the above ideal characteristics since both the “wet-bench” and “silico-bench” protocols are well established. Genomics is a rapidly changing science and, in many cases, students can participate in the same projects as those conducted at research-level universities and institutes (Shafer, et al., 2010). Genomics also appeals to students who are primarily interested in pursuing a medical profession because genomics is a key foundation of “translational research” (NIH Common Fund, 2011).

Several genomics/bioinformatics programs are available for the acquisition and analysis of authentic data that can be analyzed directly by students in a hands-on learning environment. These nation-wide projects in genomics education include the Genomics Education Partnership (GEP), Genome Consortium for Active Teaching (GCAT), DNA Learning Center at Cold Spring Harbor: Dynamic Gene and iPLANT-DNA Subway; Howard Hughes Medical Institute Science Education Alliance (SEA: phage hunters), American Society for Microbiology (ASM) Faculty Programs: Bioinformatics and Functional Genomics as well as Bioengineering and Bioinformatics Summer Institute programs. Most of these programs, however, require acceptance to comprehensive faculty development workshops for successful classroom implementation of activities. Professional development in reform teaching varies a great deal in these programs.

For faculty who have limited time and/or funds for genomics professional development, the Bio-Rad Cloning and Sequencing Explorer Series™ provide genomics activities designed for incorporation into an existing curriculum (Robinson, Lau, Porter, Wiseman, & Woodrow, 2008). Implementing the established protocols cloning and sequencing is relatively straightforward with the commercial product and therefore characteristics of a student research project are largely met. Key features of reform teaching methods, however, extend technical success into content success.

**Methods**

**Participants**

The study course, BIOL 4499 Selected Topics: Research in Genomics, was initially in Summer I semester, 2010. Sixteen students (junior and senior level) were enrolled. All students were biology majors or minors, and had previously completed the course, BIOL 3461 Genetics and Lab. Students enrolled in Research in Genomics, in order to fulfill degree requirements in either a research course or an elective course. Because this study was conducted in a standard educational setting, involving accepted educational practices, it was exempt from the university’s Institutional Review Board (IRB) committee review.

**Course Structure and Overview**

The course was offered in an eight week summer semester, meeting for three hours Monday through Thursday. Students self-assigned themselves into groups into five laboratory groups. One group consisted of four students, and four groups consisted of
three students. The curriculum outcomes and assessment methods for the course are shown in Table 1. The student grade was determined by participation (40%), quizzes and discussion assignments (10%), group laboratory notebook (10%), and a written research report (40%). There was an equal assessment of process (participation, laboratory notebook) and content knowledge (quizzes, discussion assignments and research report).

### Table 1

**Curriculum Outcomes and Assessment for BIOL 4499 ST: Research in Genomics**

<table>
<thead>
<tr>
<th>Course Outcomes</th>
<th>Assessment The objectives will be assessed by:</th>
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<tbody>
<tr>
<td>Upon completion of the course, students will be able to:</td>
<td></td>
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<tr>
<td>Interpret data to explain the concept of a gene.</td>
<td>quizzes, assignments, research project</td>
</tr>
<tr>
<td>Conduct multiple protocols to isolate and clone a gene fragment.</td>
<td>quizzes, laboratory notebook, research project</td>
</tr>
<tr>
<td>Use educational and research interfaces for genomic research.</td>
<td>quizzes, assignments, research project</td>
</tr>
<tr>
<td>Prepare a detail report of the activities conducted in class.</td>
<td>completion of a research project and report</td>
</tr>
</tbody>
</table>

The commercial product, Bio-Rad Cloning and Sequencing Explorer Series™, was used for all experiments. This series of experiments allow students to clone and sequence the GAPC gene, a gene that encodes an essential enzyme in glycolysis (one of the major biochemical pathways for glucose catabolism). Experimental protocols from the Bio-Rad series were posted on the university’s Blackboard virtual learning environment website. The summative evaluation was the research report. Students were provided a detailed rubric for each section of the report (see Figure 1). An optional part of the research report allowed anonymous group responses to questions about effectiveness of the experimental activities on research interest, content knowledge, higher-level thinking skills.

All of the students had enrolled in the BIOL 3461 Genetics & Lab course taught by the senior author. This course also is taught with a reform instructional strategy, and therefore, the students were familiar with the course structure and the instructor’s teaching style. In order to articulate the characteristics of the learning environment experienced in the genetics course, however, the following statements were included in the genomics research course outline:

A learning cycle format is used in this course. This learning/instructional strategy is student-oriented and therefore requires active participation in class activities. The instructor’s role is to guide discussion through small group discussion, question-answer discussion, and minimal formal lecturing. To prepare for class,
students must read the assigned readings, and the lab activity/results page. Failure to prepare for class will result in poor comprehension and inability to understand the instructor’s presentation of material.

The purpose of this course is to prepare students to conduct genomic research and gene annotation. Technology to be used includes educational and research interfaces for genomic research. Topics include meaning, structure and annotation of genes, genomic structure and function, research protocol and techniques to prepare plant tissue for genomic sequencing.

Figure 1: Course Outcomes and Assessments

Title: Cloning & Sequencing the GAPC gene
Group Names:
Report Sections:
  Abstract                      10 pts
  Introduction*                25 pts
  Materials and Methods        10 pts
  Results                      20 pts
  Discussion*                  25 pts
  References*                  10 pts

*Must include references to assigned readings and the Complete Cloning and Sequencing Explorer Series Curriculum Manual.

The Research Project will be prepared per group. It’s permissible to assign a section to a group member. However, each group member is responsible for reviewing/revising each section! Since this is a group grade, all members of the group are responsible for a complete, well-prepared Report.

The integration of lecture and lab facilitated the reform teaching strategy. The 5-E model of a learning cycle was used for the course structure: students engage in a topic, explore through experimental protocols, explain concepts, examine knowledge and extend knowledge by writing/completing the research report.

Each class day began with a process activity, e.g., experimental protocol. During natural breaks in the procedures, students were engaged in group discussions (i.e., explanation) of content knowledge. A collaborative quiz was assigned once per week. The last week was dedicated to collaborative group work to write the research report.

Results

All groups succeeded in conducting complex protocols for cloning and sequencing the GAPC gene as demonstrated by experimental results. The protocols, or process activities, included DNA isolation and purification, nested PCR to isolate genomic fragments.
containing the GAPC gene, ligation reactions to insert the PCR products into a plasmid; transformation of bacteria to amplify plasmid content; isolation and restriction enzyme analysis of plasmids, sequencing reactions, and simple sequencing analysis (BLAST) (see Figures 2-7).

Figure 2: African Violet leaves used for genomic DNA extraction.

Figure 3: Restriction Digest of GAPC gene isolated via PCR of genomic DNA.
Figure 4: Nested PCR lane 1 positive control, lane 2 Arabidopsis, lane 3 negative control, lane 4 the Begonia, lane 5 African Violet, lane 6 was left blank while lane 7 contained the molecular markers.

Figure 5: E. coli colonies transformed with ligation reaction with GAPC gene and vector.

Figure 6: Transformation Electrophoresis: The above illustrates the gel electrophoresis for transformation. Lane 1 contains the Arabidopsis, Lane 2 the Begonia, Lane 3 the African violet, and Lane 4 had the pGAP gene.
Figure 7: Chromatogram of African Violet with GAP primers.

The content activities involved discussions about pedigree analysis, interpreting evidence for gene structure and function, bioinformatics activities for the analysis of gene structure and function, use of databases to access information of gene function, and simple programs for analyzing biological and computational evidence for a protein coding gene. Quizzes assessed students’ knowledge of both process and content activities (Figure 8).

Figure 8: DNA Sequence of African Violet GAPC gene.

http://example.com/sequence.png

Figure 9: BLAST Report. The African Violet GAPC gene match was highly significant (Expect value = 1e^{-35}).

ref|NC_003070.9| Arabidopsis thaliana chromosome 1, complete sequenceLength=30427671 Features in this part of subject sequence: GAPC2 (GLYCERALDEHYDE-3-PHOSPHATE DEHYDROGENASE C2); NAD ... Score = 152 bits (82), Expect = 1e-35 Identities = 96/103 (94%), Gaps = 0/103 (0%) Strand=Plus/Minus Query 95 TCAGCTACTGAAAGCAGTTGATGGCGTGCCTGAAACTGAGGGAGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCTCCACACGCAGCTTGAAGCTGGTCTTCAATGAGGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCCAGCAGCACTGGAGCTGCCAAGGCTGTCGGAAAGGTGCTTCCA

Sbjct 4609193 TCAGCTACTGAAAGCAGTTGATGGCGTGCCTGAAACTGAGGGAGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCCAGCAGCACTGGAGCTGCCAAGGCTGTCGGAAAGGTGCTTCCA

Query 155 TCAGCTACTGAAAGCAGTTGATGGCGTGCCTGAAACTGAGGGAGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCCAGCAGCACTGGAGCTGCCAAGGCTGTCGGAAAGGTGCTTCCA

Sbjct 4609133 TCAGCTACTGAAAGCAGTTGATGGCGTGCCTGAAACTGAGGGAGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCCAGCAGCACTGGAGCTGCCAAGGCTGTCGGAAAGGTGCTTCCA

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Sbjct 4609193 TCAGCTACTGAAAGCAGTTGATGGCGTGCCTGAAACTGAGGGAGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCCAGCAGCACTGGAGCTGCCAAGGCTGTCGGAAAGGTGCTTCCA

Query 155 TCAGCTACTGAAAGCAGTTGATGGCGTGCCTGAAACTGAGGGAGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCCAGCAGCACTGGAGCTGCCAAGGCTGTCGGAAAGGTGCTTCCA

Sbjct 4609133 TCAGCTACTGAAAGCAGTTGATGGCGTGCCTGAAACTGAGGGAGGACTGGAGAGGTCGGGAGAAGAGCTGCTTCATTCAACATTATTCCAGCAGCACTGGAGCTGCCAAGGCTGTCGGAAAGGTGCTTCCA

8
Student groups rated process activities as “very useful” (> 90%) and content activities “useful” (70%) for increasing in research skills, enhancing content knowledge, practice using higher level thinking skills and positive collaborative learning (see Table 2).

Table 2

Anonymous Group Self Reports

<table>
<thead>
<tr>
<th>Activity</th>
<th>Increase in Research Skills</th>
<th>Enhanced Content Knowledge</th>
<th>Practice using Higher Level Thinking Skills</th>
<th>Collaborative Learning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolating Genomic DNA</td>
<td>2.8</td>
<td>2.6</td>
<td>2.8</td>
<td>2.6</td>
</tr>
<tr>
<td>PCR</td>
<td>2.8</td>
<td>3.0</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Ligation &amp; Transformation</td>
<td>2.6</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Electrophoresis</td>
<td>2.8</td>
<td>3.0</td>
<td>2.8</td>
<td>3.0</td>
</tr>
<tr>
<td>Content Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quizzes</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Discussion Questions</td>
<td>2.0</td>
<td>2.0</td>
<td>2.4</td>
<td>2.2</td>
</tr>
<tr>
<td>Supplemental Activities</td>
<td>2.1</td>
<td>2.1</td>
<td>2.1</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Students’ success with experimental protocols and high ratings on the effectiveness of the experimental activities on students’ skills indicate that it is feasible to implement a genomics research project in a laboratory course structure. The Bio-Rad Cloning and Sequencing Explorer Series™ commercial product effectively provided laboratory experiments that met research curriculum outcomes. Curriculum outcomes also can be achieved without purchase of the entire Bio-Rad Cloning and Sequencing Explores Series™ since individual modules can be purchased separately. Faculty with experience in basic molecular biology protocols can readily implement a cloning and sequencing project that partially utilizes supplies from Bio-Rad or from other commercially available reagents and supplies.
Figure 10: Genomics Quiz Questions, BIOL 4499 ST: Research in Genomics

1. What is a genome?
2. What is the structure of the genome in eukaryotes?
3. Define forward genetics. Define reverse genetics.
4. Explain the significance of the E-value. What is the relationship between a bit score and E-value?
5. Which of the 16 pair combinations gives the biggest percent difference between the genic and intergenic sequences? What pair combination is likely to indicate a coding sequence if found in high content?
6. What are the structural and functional features of a eukaryotic gene?
7. What are degenerate primers and why/how would you use them?
8. Why is it necessary to conduct two rounds of PCR in this lab?
9. Why is it necessary to purify PCR products? What type of chromatography is used to purify PCR products?
10. The protein GAPDH is necessary for cellular function and is highly conserved between organisms. Why is it probable that proteins needed for cell survival will be very similar (highly conserved) in many different organisms?
11. Compare/contrast GAPC, GAPC-2, GAPCP-1, GAPCP-2 and GAPDH.
12. Explain the following:
   a. The purpose of using ampicillin containing media for the growth of transformed E. coli.
   b. The purpose of the multiple cloning site located within the eco471R gene.
   c. The purpose of using exonuclease on the PCR product before ligation into the pJet1.2 vector.
13. Explain the outcome of the following steps in the plasmid isolation protocol:
   a. Resuspension solution
   b. Lysis solution
   c. Neutralization solution
   d. Wash solution
   e. Elution solution
14. If the ligation reaction resulted in a complete PCR product ligated into the Bgl II site, how many restriction fragments, and their sizes in base pairs, are expected to be observed after electrophoresis?
15. What are possible interpretations of obtaining two or more restriction fragments of the PCR product ligated into the vector?

Discussion

The characteristics of this research course matched several of those identified by the HHMI Bio 2020 Professor’s Council (Elgin, 2011), specifically: common methods for cloning and sequencing were taught; combining results from individual projects into a whole data set; the methods were technically simple; there were minimal safety risks; there was a high probability of success; the content was accessible to multiple levels of student knowledge; and multiple learning outcomes were met. The two student authors
also continued the research in independent studies projects on sequencing reactions and sequence analyses as well as BLAST analyses of the GAPC sequence.

The senior author benefited from 15-plus years of professional development, almost all of which was through Project NOVA (Wright & Sunal, 2004). Integration of a research project into a course format was seemingly effortless. Upon reflection, however, of the course structure, curricular activities, pedagogical content knowledge needed to determine learning outcomes and assessment of student performance, the impact of the professional development model became clear. As stated by Mason et al., (2010) reform teaching has distinct characteristics. Key features needed for the application of reform teaching in this genomics research course, are identified per reform characteristic:

- Reflects national science standards: Pedagogical content knowledge.
- Emphasizes student-centered activities: Professional development in active learning strategies.
- Utilizes inquiry-based pedagogy: Knowledge of research based evidence for reform.
- Builds on undergraduate students’ prior knowledge: Science content standards.
- Incorporates interdisciplinary learning and collaborative approaches: Participate in a community of scholars.

Summary and Conclusion

The integration of a research project in a course structure is feasible to structure and is effective in student process and content knowledge gains. Reform teaching not only supports the characteristics of a successful research project but informs both the teacher and the student nature of the research experience.

Author Note

Dr. Christy A. MacKinnon joined the Biology Department at the University of Incarnate Word, San Antonio, TX, in 1991. She currently serves as department chair, and holds the Sister Joseph Marie Armer Endowed Chair. Dr. MacKinnon earned her B.S. in Biology from the University of Michigan-Flint, and a M.S. in Plant Biology from Michigan State University, where she also completed teacher certification in secondary science. She completed a Ph.D. in Plant Biology from Colorado State University. Dr. MacKinnon’s scholarly interests have focused on the professional development of in-service science teachers and college faculty. This research has been conducted in collaboration with Dr. Dennis Sunal, Department of Education, University of Alabama at Tuscaloosa. She was a NASA Project NOVA Research Fellow from 2001-2006 and a NSEUS Fellow from 2008-2010. Dr. MacKinnon was the primary developer of the MA degree in Multidisciplinary Studies, School of Mathematics, Science and Engineering, UIW. This unique program integrates reform-based science teaching methods with standards based content. E-mail: mackinno@uiwtx.edu
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