Research Article

Educational Modules in Tissue Engineering Based on the "How People Learn" Framework

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Abstract

This paper describes an educational package for use in tertiary level tissue engineering education. Current learning science principles and theory were employed in the design process of these educational tools. Each module started with a challenge statement designed to motivate students and consisted of laboratory exercises centered on the "How People Learn" framework. The preliminary assessment of these modules supports their potential value in teaching tissue engineering laboratory exercises.

Keywords: tissue engineering, laboratory, rat, animal use in laboratory

Introduction

Tissue engineering is an emerging, dynamic, experimental science in which engineering and biological principles are used to develop techniques for improving or restoring the structure and function of pathologically altered molecules, cells, tissues, and organs. During the past several decades, extensive studies have been carried out in this area, and a number of tissue engineering techniques have been developed, such as gene transfer into tissues and organs, cell and tissue implantation, and artificial replacements of cells, tissues, and organs (Friedmann, 1993; Mitani and Caskey, 1993; Young and Dean, 2002). The usefulness and effectiveness of these techniques have been demonstrated in experimental research as well as in clinical applications. Bioengineers continue to make significant contributions to tissue engineering. Thus, it is necessary to establish and strengthen tissue engineering education programs in higher education institutions.

As part of the National Science Foundation-funded VaNTH (Vanderbilt, Northwestern, University of Texas, and Harvard/MIT [http://www.vanth.org/]) Engineering Research Center (ERC), faculty members have revised courses in the Biomedical Engineering (BME) Department at Northwestern University to enhance the learning experience of students. In this Center, BME faculty are working with learning scientists (Education), learning technologists (Computer Science), assessment experts (Education) and students to develop educational modules and tools for bioengineering education. Learning science, learning technology and assessment are continuously integrated into BME modules. In addition, the classroom and laboratory environments are restructured to support collaborative and reflective learning, and provide opportunities for students to practice skills expected in engineering practice.

We have developed an integrated lecture-laboratory approach to teach tissue engineering in which students have one laboratory that is specifically tied to a weekly lecture. This is different from the laboratory approach in many courses, where the laboratory is a separate, somewhat dissociated, part of the course. Additionally, since there are no textbooks available for teaching tissue engineering, there is an increasing demand for educational materials in this area. In consequence, we have developed seven educational modules based on the "How People Learn" (HPL) framework (Bransford *et al,* 1999). This paper describes these modules and makes suggestions for possible implementation. The modules can be accessed by contacting G. Birol, now at University of British Columbia (birol@science.ubc.ca).

Pedagogical Approach: the "How People Learn" (HPL) Framework used with the Legacy Cycle

The *How People Learn* framework, suggests that learning environments should consist of four primary elements (Bransford *et al,* 1999). Thus, an HPL environment should be:

- **Learner-centred:** The environment and class activities should take into account the knowledge, skills, preconceptions and learning styles of the learners;
- **Knowledge-centred:** The learning environment should help students learn with understanding by thinking qualitatively and organising their knowledge around key concepts;
- **Assessment-centred:** The environment should provide frequent opportunities for students to make their thinking visible so that their understanding can be refined as needed; and
- **Community-centred:** The environment should foster norms that encourage students to learn from one another, plus encourage faculty to do likewise.

Research has also shown that an HPL-informed instructional strategy promotes student learning of content (Greenberg *et al,* 2003; Pandy *et al,* 2004). Each tissue-engineering module presented here has been developed within the How People Learn framework using a pedagogical sequence called the **Legacy Cycle**. Figure 1 illustrates the legacy cycle as a method of solving complicated problems that most engineers use implicitly. It starts in phase one with an introduction of the challenge statement that describes the problem. In the second phase, students "generate ideas" about the challenge based on their prior knowledge. This is followed by "multiple perspectives," allowing experts to contribute ideas that students may not have considered and to guide students' initial learning. The next stage, "research and revise," allows students to pursue the areas they identified as useful and relevant. This stage usually consists of lectures, laboratories, demonstrations, homework, etc. "Test your mettle" is the stage in which students begin to express their newly discovered information and receive feedback from the instructor. Students may return to "research and revise" or earlier stages of the legacy cycle to improve their solutions after testing their mettle. Finally, students "go public" with their final answer to the challenge question. This is when they are graded: they are assessed formally in a final exercise such as a written examination or an oral presentation.

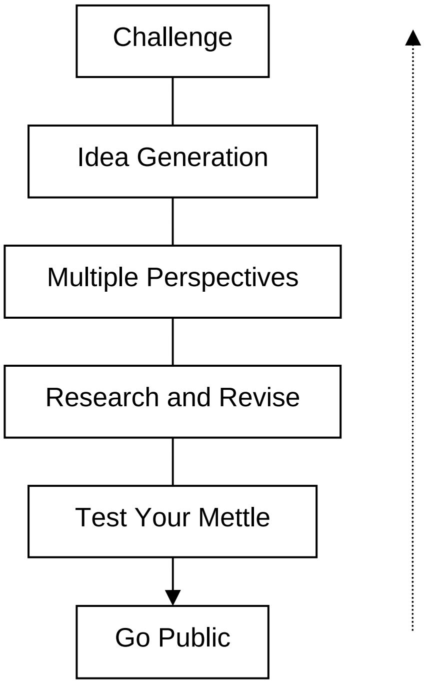

Figure 1 *A schematic representation of a legacy cycle*

The creation of challenge-based learning modules in engineering requires experts from diverse backgrounds. Our team consisted of domain experts who have the knowledge and expertise in tissue engineering, learning scientists who have a background in education, an expert in communication (one of the core competencies required of engineers), and assessment experts who can help construct evaluation of the learning.

Overview of the Tissue Engineering Modules

There are seven modules in the tissue engineering education package (see Figure 2). Each module is composed of a folder containing the following documents: *Important Note*, General *Tips for Writing a Report*, *Grading Criteria*, *Home Page*, *Sample Lab Report*, and *Sample Procedure*. Among these, "*Important Note"* and *"General Tips for Writing a Report"* are identical in all modules and are available as Supplementary Material via links. *Important Not*e gives an overview of the How People Learn (HPL) framework and how the advanced HPL learning tools were incorporated into the module. It also explains each of the phases, which are presented in the home page of each topic. *General Tips for Writing a Report* is a guide that outlines the sections to include in a technical report, namely an abstract, introduction, theoretical background, materials and methods section, results, discussion, conclusion, and references.

The remaining documents are unique for each module although all share the same style. The *Home Page* reveals the topic's targeted audience, presents the challenge, initiates class discussion, explains the homework assignment, and suggests topics for the in-class and out-of-class activities and timeline of each activity. A sample Home Page is provided in Figure 3. The *Grading*

Criteria is a guideline to report writing and can be used for grading. The *Sample Procedure* suggests an experimental procedure for that specific lab. The *Sample Lab Report* provides an example of how students are to present their work during their written presentation.

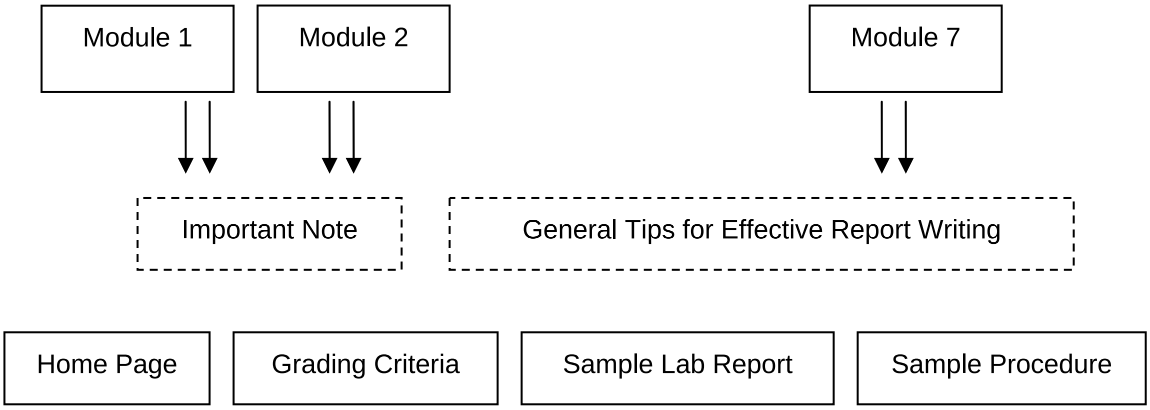

Figure 2 *Tissue engineering package structure. Boxes with dashed borders refer to material that is common among modules whereas solid-lined boxes refer to module specific material. The home page of each module provides links to associated materials*

The material in all modules is designed to be flexible. The instructor may decide to omit one or more activities if the learning objectives of that exercise do not fit the overall objectives of the course, or if the material is too difficult or easy, depending on the level of the course. The primary use of this package is in a tissue engineering course. The module can be used with a wide range of students, provided that the students know basic aspects of organic chemistry and molecular and cellular biology from previous courses. Each module's home page has a section called "targeted audience" to help instructors make informed decisions about the material to use.

Animal Anesthesia©

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Please read **Important note to the user** before start.

Targeted Audience

This module is appropriate for use in the following classes:
brain and cognitive sciences , biochemistry, biological sciences, biological engineering , biomedical engineering, biotechnolog, cell biology, chemical biology, chemical engineering, chemistry, developmental biology, health sciences and technolog, neuroscience, neurobiology, psychology, physiology, reproductive science, tissue engineering.

The Goal ***(~5 min of class time, day 1)***

At the end of this activity, students are expected to learn how to handle the rat and prepare it (or the animal to be used) for surgery.

Class Discussion ***(~20 min of class time, day 1)***

Instructor will lead the discussion by asking these questions:

1. How should you handle a live rat (or the animal to be used)?
   a. *What equipment may be helpful in handling the animal?*
2. How should you anesthetize the rat (or the animal to be used)?
   a. *Which drug(s)/ chemical(s) should you use? How much?*
   b. *On which part of the body? How long should you wait before starting the surgery?What should you do the rat keeps responding to stimulation?*
3. Are there alternative ways to anesthetize a rat (or the animal to be used)?
   a. *Pros and Cons?*
4. What are the safety issues?

Homework Assignment ***(~60 min of out of class activity)***

Find three sources that will help you achieve your goal. Be ready to discuss your findings in class. Below are some possible sources:

1. *Baker, Henry J., J. Russell Lindsey, Steven H. Weisbroth.* The Laboratory Rat. *New York: Academic Press, 1980.*
2. *Chiasson, Robert B.* Laboratory Anatomy of the White Rat. *Dubuque, Iowa: Wm. C. Brown, 1958.*
3. *Gram-Jones, Oliver.* Small Animal Anesthesia. New York: Macmillan, 1964.
4. *"Johns Hopkins Animal Care and Use: Procedures." October 11, 2001. Johns Hopkins University and Health System <www.jhu.edu/animalcare/rat.htm>.*
5. *Olds, Ronald J.* A Color Atlas of the Rat Dissection Guide. *New York: Wiley, 1979.*
6. *Sisson, Septimus.* The Anatomy of the Domestic Animals. *Philadelphia: Saunders, 1953.*

In-class Activity ***(~20 min of class time, day 2)***

Instructor will moderate the discussion based on the ideas that students bring to the class. The following are suggested topics to be covered during this discussion session:

1. Animal Handling
   i. Materials, Animal restraining tube
2. Animal Anesthesia
   i. Methods
   ii. Materials
   iii. Drugs/Chemicals
   iv. Methods of checking the level of anesthesia (stimulus and breathing)
3. Anatomy
   i. Rat (or animal to be used in the lab)

Through the class discussion, the students are expected to come up with the procedure for animal anesthesia. The finalized procedure may be distributed at the end of the class (here is the Sample Procedure).

Test Your Mettle ***(~120 min of class time, same day with in-class activity, day 2)***

Perform the lab under the instructor's supervision.

Go Public ***(~150 min)***

Students are to present their results in a written (or oral) report format. Please refer to General Tips for Effective Lab Report Writing and grading criteria for this activity. Include the ethical issue(s) you observed in your discussion.

Some questions that may be considered are:

1. Is the use of animals necessary for the learning environment?
2. How appropriate is it for undergraduate students to be using live animals in this class?
3. How are the animals maintained (housing, mental/ physical/emotional stimulation, food)?

Please refer to this *Sample Lab Report* for self- assessment.

Figure 3. *A Sample Home Page: Animal Anesthesia.*

Module Specifications

All of these modules, except the bioethics module, are laboratory sessions. Each module is designed to be self-contained and can be used alone or in combination with other modules, depending on the requirements and timeframe of the specific course. Each module contains a challenge statement to initiate the learning process. Modules are designed to be completed within one 1-hour discussion session and one 3-hour lab session. Throughout several activities, learners are specifically expected to do the following (the **bold** text after each objective shows how it maps onto the How People Learn framework):

- integrate their existing domain knowledge and skills, as well as knowledge of lab experiences, into experimenting with live rats **(learner centredness)**;
- use lab skills developed throughout the lab sessions by applying them appropriately to a new situation **(knowledge centredness)**;
- design an experiment related to gene therapy and implement it by considering alternatives, comparing and contrasting different gene transfer techniques, recognising the constraints and accommodating them in the plan, executing the proposed experiments, working efficiently in a team **(knowledge and community centredness)**;
- interpret experimental data by identifying the sources of error and variability in biological data, comparing them to expected results and literature, and drawing conclusions from the results **(knowledge centredness)**;
- document the results in a formal report using the communication skills developed throughout the lab sessions and highlighting focus, organisation, development, and style **(assessment centredness)**; and
- develop their awareness of the ethical issues involved in these modules in particular and tissue engineering in general (**community centredness**).

Module Content

This section briefly introduces the content of each module. Details regarding the first module, *Animal Anesthesia*, are provided as Supplementary Material via this link to illustrate how the modules work.

1. ***Animal Anesthesia (Home Page)*** highlights techniques to use live rats in laboratory. It explores handling and anesthetising animals and which drugs or chemicals to be used. Questions focus on the pros and cons of different techniques to anesthetise animals.
2. ***Blood Vessel Cannulation*** explores the function of the carotid artery and techniques of performing carotid artery cannulation, which involves identifying the vessel and discussing which chemicals are used for the procedure and why.
3. **Animal Fixation** discusses preparation of live rats or laboratory animals for histological analysis to fix their tissue. Questions raised include the different methods of tissue fixation and the pros and cons of each, how to drain the blood and store the tissue, and safety issues involving these techniques.
4. ***Histology*** involves differentiating the major rat organs by appearance, collecting tissue samples, dissecting the organs, fixing the tissue for histological analysis, straining and analysing the tissue, and safety issues.

The questions that are raised include discussing the different methods of fixation, the pros and cons of each chemical, understanding the chemical interaction during fixation, pros and cons of the different devices during dissection, and the specifications of the microscope.

5. ***Gene Transfer and Expression*** discusses transferring genes, which involves gene targeting, random gene transfer, preparing the tissue, using certain drugs and chemicals, and safety issues. Some of the questions raised include factors that affect gene transfection, how to estimate the percentage of the transfected tissue, and how to determine the success of transferring a gene.
6. ***Hypertension and Its Assessment*** introduces a disease model and explores the causes and diagnosis of hypertension in humans and animals, the effects of hypertension on the body, techniques of measuring blood pressure, and methods of creating hypertension in an animal model. Some of the questions raised are whether hypertension can be prevented or reversed, what equipment and tools are required to measure blood pressure, and recognising structural changes in the arterial system. This particular module is intended to be used as an application (i.e. a disease model) of the techniques introduced through previous modules.
7. ***Bioethics*** concentrates on issues involving biomedical research. Discussions focus on current laws and regulations, data collection, data selection, research design, conflict of interest, ownership and use of animals and humans in research.

Learning Objectives of the Modules

Each module has its own set of learning objectives, leading to four overall goals. For example, for the *Gene Transfer and Expression* module, the students will be able to:

- describe the mechanisms of gene transfer and evaluate various gene transfer techniques;
- use common gene transfer techniques and experiment with live rats;
- effectively write up their problems, procedures, and results in a technical report; and
- evaluate ethical dilemmas related to the use of animals in biomedical research and teaching.

Note that *Gene Transfer and Expression* and *Hypertension and Its Assessments* each has two laboratories, giving them two sets of objectives. Table 1 summarises the bioengineering learning objectives of each module. Every module contains a writing component to help students improve their ability to write clear formal laboratory reports.

Table 1 *Learning Objectives of the Tissue Engineering Modules*

Module	**Learning Objectives of the Module**
Animal Anesthesia, Fixation and Blood Vessel Cannulation	Know how to • properly handle a laboratory rat or other laboratory animal • anesthetise a rat or other laboratory animal • recognise rat anatomy • perform carotid artery cannulation • fix tissue samples for further histological analysis
Gene Transfer and Expression	Demonstrate the ability to • transfer genes via electroporation and liposome mediation • determine the expression level of a transferred gene • be familiar with the X-gal assay Know how to • use the electroporation equipment and the liposome method • prepare animals for this technique • prepare tissue specimens for X-gal assay • measure the density of gene-transfected cells • estimate the efficiency of gene transfection
Anatomy and Histology	Demonstrate the ability to • identify an organ and tissue • collect specimens • prepare tissue specimens for histological preparation • fix the tissue specimens for histological observation and analysis • section the tissue specimens • stain the tissue specimens • observe the tissue specimens • analyse histological data
Hypertension and its assessment	Demonstrate the ability to • create hypertension in a rat model • measure arterial blood pressure in a rat model • collect and prepare arterial specimens for structural observation and analysis • analyse the influence of hypertension on arterial remodeling
Bioethics	Demonstrate the ability to • Evaluate ethical dilemmas related to using animals in biomedical research and teaching

Necessary Materials/Equipment

A typical laboratory should be equipped with optical microscopes, including a fluorescence module, surgical microscopes, an electroporation apparatus, a cryo-microtome, cell culture incubators, and surgical tool kits. The cost of rats, chemicals, and lab supplies is approximately \$3,000 – \$4,000 (£1,600 -

£2,100; €2,300 – €3,100) for 8 groups of students (each group consisting of 3-4 students) per term.

Assessment Tools

Formal assessment of these modules can be carried out via laboratory reports. Each module's homepage is linked to a grading criteria sheet and a sample lab report for the instructor's convenience (refer to *Animal Anesthesia* Module's Home Page to see an example). The grading criteria sheet contains a rubric to help students develop the written communication skills they will need as professionals, some of which are among the newest Accreditation Board for Engineering and Technology (ABET) requirements. Since the writing assignment is completely integrated with the technical work, the writing instruction in these modules, like the technical instruction, is grounded in the HPL pedagogical framework.

Implementation

This section describes the tissue engineering course from which the content of these modules was originally obtained. The learning science principles were then integrated into the content to create these new modules, which now have a stronger pedagogical base.

Tissue Engineering (BMD ENG 346) is one of several courses currently being taught in the Biomedical Engineering Department at Northwestern under the tissue engineering specialisation that has been offered for the past ten years. The course focuses on *in vivo* molecular, cellular and tissue engineering; it emphasises the concepts, techniques and clinical applications of tissue engineering (Birol and Liu, 2002). The primary learning goals of the Tissue Engineering course are to help students do the following:

- understand the principles and concepts of molecular, cellular and tissue engineering;
- learn basic tissue engineering techniques;
- apply tissue engineering principles and approaches to practical problems;
- design and conduct an independent research project with a focus on a real life problem; and
- begin to develop lifelong skills such as adaptive expertise (Fisher and Peterson, 2001) (through an independent project) and written presentation and communication skills (through reports and project development).

Table 2 shows the outline of the course. Northwestern utilises a quarter system with each quarter lasting nine to ten weeks. The quarter-long course consisted of two class meetings per week, each Tuesday and Thursday. The Tuesday meeting (80 minutes) followed a regular lecture format where the class met in a classroom, and the Thursday meeting was the laboratory section where the students ran hands-on experiments. The instructor (S.Q. Liu) was present at all laboratory meetings since expert guidance was required to carry out these sophisticated experiments.

***Table 2** Tissue Engineering Course Outline*

Week	Lecture	Laboratory
1	Introduction to Tissue Engineering	Animal Anesthesia, blood vessel cannulation, tissue/organ identification, and specimen collection
2	Molecular Engineering: Introduction to gene therapy	Histological preparation, specimen sectioning, staining, and examination
3	Molecular Engineering: gene transfer	Electroporation- and liposome- mediated gene transfer into selected tissues
4	Molecular engineering: gene transfer	Examination of the expression of the transferred gene
5	Molecular Engineering: gene therapy for cardiovascular and pulmonary disease	Experimental hypertension
6	Cellular Engineering: biological basis of cellular engineering, cardiovascular engineering	Measurement of blood pressure in hypertensive animals and examination of the influence of hypertension on arterial structure
7	Cellular Engineering: neural cell engineering and nerve fiber regeneration, corneal engineering	Polymer implantation into selected organs and tissues
8	Cellular Engineering: Pancreatic cell engineering, hepatocyte engineering	Biological responses to implanted polymer materials
9-10	Organ Engineering	Independent project

The grading included daily exercises and lab reports (30%), an independent project (10%), a midterm examination (30%), and a final examination (30%). Student registration was limited to 30 to accommodate laboratory sessions.

The students performed a wide range of experiments that required specific skills and a sound knowledge of the topic, such as tissue and cell identification, vascular cannulation, specimen preparation, gene transfer into various tissue and organs, polymer implantation, and disease model creation. At the end of the quarter, students were asked to develop their own projects based on the experience, expertise, information from the literature, and interest they developed throughout the course. Teams of three to four students worked for a period of two weeks on their projects. The students were allowed to use the lab at any time in order to provide some flexibility with their busy schedules. This in fact promoted their interest in the topic, since they devoted time to their projects whenever they could. The projects helped students to achieve their learning objectives and the goals of the course. The intrinsic, challenge-based nature of the existing course helped us to create these new challenges which are grounded in learning science principles based on the “How People Learn” framework. To the best of our knowledge, this is the first time learning science has been formally embedded into educational materials in this area.

Summary of the Assessment Results of the Modules

A series of assessment tools were used to test the efficacy of these modules, and the results have been presented elsewhere (Yalvac *et al,* 2006). In brief, data were collected using assessment instruments specifically designed to measure the gains of the students' outcomes in 2004. The instruments were as follows:

- a student communication survey;
- a rubric for assessing content-knowledge given as a homework assignment; and
- a rubric for written communication in the laboratory report.

We used a quasi-experimental, non-randomised control group pre-and post-test design (Campbell and Stanley, 1966). Since the study participants were students enrolled in the tissue engineering course, they were all self-selected. Students were self-grouped into two sections of the laboratory, one of which was taught by an instructor who followed the traditional approach to teaching and the other who followed the HPL approach described in this article and elsewhere (Yalvac *et al,* 2006). A total of 33 students participated voluntarily.

Students in both groups demonstrated gains over the course. However, data showed that an HPL framework, used to improve science and engineering instruction, was exploited concurrently to teach written communication, including higher level writing skills such as argumentation and coherence. These gains were also supported by students' perceptions. Although the small numbers of students in the study preclude the appearance of some statistically significant differences, the data strongly suggest that the students' abilities to write lab reports were enhanced through a pedagogy informed by the HPL framework (Yalvac *et al,* 2006). The analysis of students' content understanding revealed no statistically significant differences across groups. This showed that the HPL approach to teaching did not prevent students in the HPL group from learning the content matter as well as the students in the traditional group.

Concluding Remarks

Tissue engineering is taught at many institutions. However, few are teaching it by using an approach with integrated lecture and lab experiments. Furthermore, these courses are not developed on the basis of learning science. That is why we developed, describe, and now recommend, the approach and modules in this educational package to be used in tertiary level tissue engineering education.

These modules were developed from lessons we learned throughout the years by observing students in the laboratory. This tissue engineering lab is their first exposure to live animal experiments and students are usually hesitant to handle the live animals (for example, rats) at the beginning of the quarter. One successful approach to this problem, which we incorporate in the modules, is to let them work in groups of three to four people and decide for themselves who will do each task during the experiment. We also observed that class discussions about the safety issues and the procedure precautions help students to be more comfortable in their practices. Some students raise their concerns about the use of animals in the laboratory, thereby offering an opportunity for the instructor to initiate a discussion on ethical issues on animal use in research and teaching.

We believe that a number of laboratory sessions are critical for students to develop the skills needed in this field, since the more the students are exposed to such experiments, the more they master the required skills and reflect on tissue engineering in a purposeful way. We also realise that the instructor's guidance is essential for a successful laboratory session (student to instructor ratio should be around 12:1).

In our modules, students are expected to write reports regarding their experimental procedure and findings; hence, written communication in engineering is another challenge they encounter. We designed student guidelines and instructional strategies to help students communicate effectively. Each formal lab report was evaluated, and feedback was provided so that students could reflect on their written communication strengths and deficiencies. We observed that students' written reports improved with time (see Yalvac *et al,* 2006).

A successful completion of an independent laboratory project where students would propose an experimental plan and carry it out provides the evidence that they developed the necessary laboratory skills and gained the knowledge to execute the experiment. In summary, we recommend the modules in this educational package for use in tertiary level tissue engineering education, since current learning science principles and theory were employed to develop effective learning tools by a team of experts in tissue engineering, learning science and assessment. We not only encourage others to try these modules, but to share their results with the community. Toward those ends, the authors are willing to share these modules with interested parties who sign an agreement with VaNTH (initially free of charge) — and to obtain more information on these modules and others generated through our Engineering Research Center at http://www.vanth.org/.

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