Is There Room in the Graduate Curriculum to Learn

HOW TO BE A GRAD STUDENT?

An Approach Using a Graduate-Level Biochemical Engineering Course

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How different is graduate education from undergraduate education? At the course level, the topics become more interesting and focused, and the problems become more challenging and time consuming. These differences aside, however, most graduate courses are very similar to those taken at the undergraduate level. For thesis-driven graduate programs, course work represents only a small portion of the degree sought, especially if one considers that courses are not compulsory in many institutions. Undergraduates may not always understand this aspect of graduate studies and therefore, the fact that the majority of learning at the graduate level must be achieved through self-discovery may be somewhat foreign to most students starting their graduate degrees. Furthermore, graduate training should prepare students to spearhead and carry out a research project, a skill that may or may not be developed at the undergraduate level.

To facilitate this goal, a number of institutions, including the École Polytechnique de Montréal (herein referred to as EPM), have added a mandatory research methodologies course in the graduate curriculum.1 At EPM this is offered as a general engineering course to all graduate students, regardless of the discipline of study (ING6900 – Méthodes de recherche). At the University of Waterloo (herein referred to as UW), such a formal course is still lacking and it remains up to the thesis advisor to provide this training to his or her students. Although such a course (ING6900) adds to the overall development of the graduate student, the methodology course focuses only on how to perform an efficient literature review and assists the student in writing a condensed research proposal. It thus lacks the applied nature of experimental research and, because of the general nature of the course, does not guide the student on how to go from identifying research hypotheses and objectives based on the state of the art to developing a proper research plan.

It has long been recognized that didactic aspects of courses have a positive effect on student comprehension.2,3 Despite this, there are few, if any, graduate lab courses at EPM and none at UW. It almost seems obvious that laboratory-based courses would be extremely valuable to graduate students.

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because of the importance of validating hypotheses experimentally at the graduate level. When preparing a graduate course, it is often desirable to design it in such a way as to tailor it to the specific size and ability of the class so that at least a minimum set of requirements are met by the end of the session. Graduate courses are special in that as little as one person or as many as a couple of dozen students may be taking the course at a given time; therefore it is possible to narrow the scope of material taught, and to explore these more thoroughly. An open-ended laboratory course is well suited for obtaining this flexibility.

The following describes a course that addresses many of the aforementioned issues while maintaining its identity as a graduate course on cell culture and modeling. Chemical engineering has seen an increasing presence of biology in the curricula[14] especially at the undergraduate level, a trend that is also being observed at EPM and UW. A course such as this, therefore, serves multiple purposes: to deepen and continue education in bioprocess engineering while providing a means for students to transition from an undergraduate to a graduate mindset. The course in its present form has been offered in the department of chemical engineering at EPM since 2004 and has integrated a number of concepts aimed at enabling students to first understand their role in research and then become better researchers. To achieve this, the course has amalgamated concepts also described by others[1,9,13] with a focus on the implementation of experiments proposed in a research plan.

OVERVIEW OF THE COURSE

The course is listed in the EPM graduate calendar as GCH6301/02 – Biosystems Engineering Cell Culture – Cell Culture and modeling (Ingénierie des bio-systèmes/Culture des cellules – Culture cellulaire et modélisation). It is meant to be a hands-on course working with a bioreactor and the cultivation of a microorganism, often E. coli, which is an obvious choice as a model system given the shortened study period and the costs associated with the implementation of experiments. This course poses an open-ended question without a defined problem. The students are asked to identify the current limitations that exist in a particular field, such as the production of protein in E. coli, evaluate the needs of the state of the art, and decide a course of action that is plausible given the somewhat limited resources available in a course setting. The choice of microorganism is dependent on the availability; in the past, students have benefitted from the close ties between EPM and the Biotechnology Research Institute of the National Research Council of Canada (Montréal, Québec, Canada), which has supplied various recombinant microorganisms for study.

This course satisfies one of the five courses required for thesis-based master’s and Ph.D. degrees at the EPM; however, this course is not mandatory. It is operated as a scaled-down research project run intensively for 5-6 weeks. Students are expected to dedicate all the time defined by the credits awarded for this course: 3 credits = 135 hrs or up to 27 hrs per week. The course, therefore, requires that the students be dedicated only to this course while it is being given. The students gain insight, however, into the type of research that can be conducted at the graduate level and gain a better understanding of the processes involved in a research-based graduate degree. This course also illustrates how training for a research-based graduate degree can be completed in a little over a month: from problem synthesis, statement of hypothesis and objectives, implementation and analysis of experiments, as well as defense of their work.

This course can be done with as little as three students; however, we feel that this is not an optimal size given the resources required in terms of teaching assistants discussed further on. Optimally, this course would be given to a group of between eight and 16 students, allowing the instructor to create groups of three to four students initially, with the possibility of combining groups as the course progresses.

Currently this course is given in the Spring term (May-June). Certain graduate students—especially those exiting their bachelor’s degree from EPM and UW—start at this time, which makes the placement of this course ideal, since it can then be taken in the first term of study. Students starting in the Fall or Winter terms would only get the opportunity to take this course in their second or third term, which is still early enough to benefit the student. Although it may be theoretically feasible to place this course in another term, there are a number of practical reasons that do not allow this course to be shifted to another semester, including the use of this laboratory for undergraduate teaching in Fall and Winter terms.

GENERAL OBJECTIVE

The general objective of this course is to transform the student from having an undergraduate mindset, which looks to textbooks for solutions, to a graduate mindset, which understands that textbook information is meant as a comprehensive review of the literature at an earlier point in time. Students are taught to understand that specifics and the state of the art are found in scientific peer-reviewed journal articles. This change in mindset aims to drive the students to question results or approaches that have led to earlier conclusions, and gain an appreciation for the overall scientific method.

A second aspect that is highlighted in this course is the difference between report writing and scientific communication. Not all schools permit “theses” by scientific publication, however a number of schools do. The benefit of such a format is that it maximizes the potential for good scientific work to reach the masses, with the drawback being that these types of theses do not necessarily read as well as conventional theses. With traditional theses, however, professors may lack detail or...
complete understanding of the student's work described in the thesis if the original author/student is incommunicado, which may happen more often than not, if the author has moved on and is working in industry and becomes overwhelmed with commitments that were not necessarily pre-existent while in academia. The ability to write a scientific publication is also of high importance. This is why the course emphasizes the preparation of a scientific manuscript at the end. It is often surprising that even though a student normally reads hundreds of papers and book chapters during their graduate degree, students often have difficulty writing a manuscript that has coherent structure and argumentation, a skill often lacking in engineering undergraduate students.

SPECIFIC OBJECTIVES

To achieve the global objective of the course, students are required to assimilate the accumulated literature in a specific field; develop, based on a scientific approach, a strategy to produce protein in a bioreactor; carry out the strategy in the lab; and validate the results. This approach results in general theoretical and practical knowledge that will permit the student to understand, prepare, operate, and optimize a bioprocess. More precisely, the student that takes this course develops an ability to: 1) understand the notion of aseptic techniques and learn how to apply them; 2) apply a scientific methodology to the study of cell culture/fermentation; 3) describe, explain, and model cellular phenomena; 4) operate a pilot-scale bioreactor; 5) learn how to determine bioprocess parameters that can be optimized; and 6) learn how to write and defend a scientific manuscript.

PREREQUISITES

This course involves intensive cell culture in a laboratory setting. A good foundation in biochemical engineering is needed and knowledge of biochemistry and cellular biology are assets, but are not necessary. General chemical engineering skills such as the ability to develop mass balances around a system, in this case around a bioreactor, are essential. Working knowledge of a computer coding language such as MATLAB, that will allow the simulation of the process, is also required.

Most chemical engineering undergraduates that have attempted this course have the pre-requisite skills upon entry into the graduate program; however, it becomes fairly obvious within the first couple of lectures whether or not a student has the required skills to take on this course and it becomes the responsibility of the instructor to discuss the situation with the student. In the past, we have had to ask students to withdraw from the class. Although we believe that this course has many general lessons that are important for graduate students, it is meant to be a graduate-level course in biochemical engineering. As such, although the lessons to be learned about graduate studies may be lessened if the student takes this course beyond their first year as a graduate student, the student will still benefit from taking an advanced biochemical engineering course.

COURSE SYNOPSIS

Using a heuristic approach, the principal problems encountered with in vitro cell culture are studied. The students are called upon to work together in teams to develop their knowledge in this field. Students survey the literature in a short period of time, present a summary of the literature highlighting what has been accomplished and at the same time identify areas that could benefit from further exploration. In consultation with the professor and the teaching assistant, the students assess what type of experimentation is feasible in light of the available resources; plan a course of action; perform a predetermined number of experiments that build upon previous work; analyze the data; choose a scientific journal appropriate for the work done; and write a scientific publication for that journal. Once the article is written, the project needs to be defended in front of a panel consisting of the professor and the teaching assistant(s). Figure 1 describes in more detail the general operation of the course since 2004.

REFERENCE MATERIAL AND AIDS

Several textbooks are recommended as complementary to the course[14-18] and can span different levels of experience depending on the strength of the class. All of the documents and class notes of an undergraduate course on Biochemical Engineering (GCH4650) are also made available to the students.

Lectures

During the first week, a seminar/lecture component is given to provide insight on the system to be studied. This includes major elements of biochemical/bioprocess engineering and relevant background information, for example characteristics of the microbial strain to be used. Practical and theoretical information is given based on need, which allows the course to be tailored to the directions the students want to take, while at the same time meeting the learning objectives set for the course.

Meetings/Discussion Groups

Frequent meetings are scheduled between the students and the teaching group. During these meetings, students are evaluated individually and in a group depending on their progress. Two formal presentations are required by the students to assess progress achieved in the course. Other meetings are scheduled on a daily basis to assist students in their reflections.

Teaching Assistants

Given that the maximum class size is approximately 15, justifying more than one teaching assistant is quite hard; yet, this course is highly dependent on the teaching assistant(s). Teaching assistants are a major resource for the students taking
Acquired knowledge
- Understanding of cell needs when cultured *in vitro*.
- Overview and selection of bioreactor configuration.

Acquired skills
- Identification of appropriate bioreactor given cell type.
- Critical evaluation of literature.

Week 1
- Presentation of objectives and organization of the course.
- Introduction to equipment used in cell culture:
  - Cell needs vs. what a bioreactor can offer
  - Distribution of the case study.
  - Distribution of previous year’s final report.
- The students present a critique of last year’s final report.
- The teaching group presents last year’s corrected report.

Week 2
- Students present a literature review
- The bioreactor is characterized experimentally in terms of:
  - Sterility
  - Hydrodynamics and mixing
  - Mass transfer
  - Shear stress
- Students define their experimental strategy in order to ensure that the cell needs are met by the bioreactor and culture strategy.

Week 3
- The teaching group remains available to the students.
- Students present data and their analysis from bioreactor characterization studies.
- Students define their culture strategy.
- Students perform bioreactor cultures, sample and data analysis.

Week 4 to 6
- The teaching group remains available to the students.
- Students may perform a second series of cultures to confirm specific findings.
- Students analyze the data collected and write a final report.
- Students defend orally their report on the last Thursday of the course.
- The final report is submitted to the teaching group, with revisions from the oral defense, on the last Friday of the course.

Acquired knowledge
- Behavior of cells in a bioreactor.
- Behavior of bioreactor during a culture.
- Basic analytical techniques.
- Development of appropriate experimental design.

Acquired skills
- Preparation, operation and sampling of a bioreactor culture.
- Critical assessment of experimental data.

Acquired knowledge
- Techniques for modelling cell culture.

Acquired skills
- Analysis of culture and process data.
- Situational of experimental data with respect to published literature.
- Drafting a manuscript.

*Figure 1. General operation of GCH6301/02 since 2004.*
the course. Although they may not be present at all times during the periods of experimentation, the teaching assistant(s) are essentially “on-call” for the students. If the teaching assistant does not have an existing relationship with the instructor, whether this is an advisor-student or mentor-protégé relationship, the assistantship task may be viewed as being overly demanding. In the past, however, the assistantship position has also served as a learning experience and in a way follows a recent Teaching Tip, which describes the benefits of informally sharing a course with a graduate student.

Over the years this course has been taught, several students who have taken this course have also moved on to become TAs and lecturers for the course. The importance of this circle should not be lost, as it fulfills many aspects of graduate education and is at the heart of the success of this course. Although this relationship has remained informal, this aspect of the course is similar to the mentorship programs suggested by others.

Not all students that have taken the course have the aptitude to take on such a teaching task, however. This assistantship requires a person that is flexible, approachable, resourceful, and able to think quickly.

**STUDENT EVALUATION**

Every student starts out with a grade of A or excellent. After each meeting, the students’ grade is subject to change to A (excellent), B (satisfactory), or F (fail). The grades can be individualized by attributing the grade based on the level of progress on the sub-objectives they have set for themselves or that were set for them in previous meetings. For example, if a student within a group has agreed to prepare a statistical design of experiments, to assess certain conditions with the least number of experimental runs then at the following meeting, this student would be individually assessed against this sub-objective. Furthermore, this student would also be graded within the context of the group for cohesion of that sub-objective with the ones set by the other members of the group. The evaluation process, therefore, assesses their progress within the group and allows for the individualization of grades. This evaluation is done by both the instructor and the teaching assistants individually, and following a discussion between the teaching staff, a final mark is given. The marking scheme of A/B/F was chosen because at EPM, the Ph.D. program requires students to maintain a minimum of a “B” in each course to stay in the program, and an overall average of “B” in the master’s program.

The second portion of the student’s mark is based on a final report in the form of a scientific manuscript. The group marks and the individual marks are combined to yield the student’s final mark. Fifty percent of the grade is awarded for the term performance (25% for their individual contribution and 25% for the advancement of the group) and 50% for the final manuscript (which is a group mark). As can be seen, there is a significant weight associated to group work in this course.

This course, from an evaluation perspective, is also of benefit to professors who are looking to assess a student’s potential as a graduate student; it allows the professor to evaluate the student’s abilities: from their thought process to their critical thinking and reasoning skills. Given that this course is generally taken before the fourth semester, which is also the deadline for a student to defend their research proposal for their doctoral degree, this may also serve in the future as part of the qualifying exam. In the past, EPM has had topical qualifying exams in Reactor Engineering, Polymer Engineering, or Biochemical Engineering, which have been recently disbanded. This is in line with many other chemical engineering departments that seem to be moving away from course-based qualification processes that emphasize coursework rather than research potential. The course described here could therefore be used as a topical qualification exam to assess research potential.

**THE CASE OF GCH6301/02 SUMMER 2004**

The pedagogical approach described here was first experimented with in 2004 and resulted in an unexpected level of success that encouraged us to continue in this direction in subsequent years. Summer 2004 brought together six motivated graduate students: four registered in the thesis-based graduate program, (two Ph.D. and two M.A.Sc. candidates), and two registered in the course-based master’s program. Two students were in their first semester, two were in their second, while the others were in their third and fourth terms.

Students were introduced to the production of GFP in E. coli under a temperature-sensitive promoter. The course followed closely the path described in Figure 1. Although the class was first split into two groups of three to assess the state of the art, the six students were combined into a single group for the development of research objectives and experimentation. This was also useful to follow and sample the bioreactor cultures, which were followed for more than 12 consecutive hours (a real industrial context). Teamwork in industry requires that all involved contribute and that a certain amount of confidence between team members exists. Similarly, this relationship must be understood by the graduate students. The Summer 2004 students obviously showed different scientific and technical skill levels, but what made this group stand out was the “chemistry” within the team allowing for very good interaction and communication. As a result, the project report/manuscript was also of high quality. It was also highly interesting to note at the “defense” that every team member was able to answer the questions adequately; showing that every student actively participated in the various aspects of the course including classroom concepts, the laboratory, and writing up the project. Moreover, due to the concepts and methodologies explored by the students, the manuscript submitted for the course was submitted, with a few modifications, to a scientific peer-reviewed journal. It should be noted that alterations to the manuscript did occur after the course.
was actually completed—driven by the students and not the TA or instructor. The instructor, however, remained available to the students for valuable feedback. Communication after completion of the course was done mostly through e-mail. Although initially rejected for publication, the manuscript was revised based on the reviewers’ comments, again driven by motivated students, re-submitted to another journal having a higher impact factor, and was accepted and published.

The manuscripts at these various steps, as well as the reviewers’ comments, have also found their way into later offerings of the course. In Summer 2006, students were also introduced to the production of GFP in E. coli under a temperature-sensitive promoter, still following the chronology described in Figure 1; however, this time the introduction was through the previous year’s report and manuscripts. This allowed the students to become familiar with the system very rapidly, question previous approaches, and situate themselves in the literature by using the reference list in the report. To really make the students gain an appreciation of the work conducted previously, they were asked to review and critique the article produced by the previous year’s class, identify strengths and weaknesses, and highlight ways to push the study further. This served as the first assignment upon which they could be evaluated. To further the students’ experience, the professor and teaching assistant went through these documents, helping the students highlight the strengths and weaknesses in both the scientific and editorial aspects associated with the manuscripts, as geared for a scientific journal. From this process, students were asked to propose what research they would like to perform in order to answer questions that may have arisen from the analysis of the manuscript, so as to better understand the bioprocess and maximize productivity of the system. These activities occurred in the span of two weeks. To further their understanding of the system, the students created simulations of the process using MATLAB. Here they were able to modify process parameters and see the effects of various changes. Following this, the students were brought to the laboratory setting and were asked to use pilot-scale equipment to test their hypothesis and determine the predictive capabilities of their kinetic model. Various strategies were used to sustain the production of GFP under the control of a temperature-sensitive promoter, in batch and fed-batch modes of culture.

The final outcome of this course obviously varies each year because of the composition of the group, as well as the “chemistry” between the members. The 2004 group revealed to be a “Grande cuvée” (an appropriate reference to a good year for wine, considering this is a biochemical engineering course). In any case, this approach has been highly stimulating for both the professor and for students taking this graduate course, who now strive to come up with similar advances through this course. Another exciting outcome of this course came from students who decided to switch from the course-based program to the thesis-based program, because of the hands-on aspects of the course.

COURSE CRITIQUE AND STUDENT FEEDBACK

Although the course (in name only) has existed since 2000, the approach taken today started in 2004. The course has therefore gone through many changes over the years, evolving as a result of student comments and course evaluations. Every time the course is offered, the students have the opportunity to submit a critique. The marking is on a scale of 0-100%, 100% being complete approval of the course, the content, and how it was taught. On average, the course evaluations have increased significantly—especially when examined against the first offering in the summer of 2000 when it was given as a fully theoretical course, built on the same framework as classical undergraduate courses. In the last few times this course has been offered, it was given the highest rating in all categories assessed in the course critique, a positive sign that this is a valuable learning experience even though it can be quite demanding. The most recent class to take the course unanimously gave it a 100% rating.

The most frequent student comments for pre-2004 offerings pointed to the lack of experimental work. Retrospectively, those that have taken the course more recently regard the high workload as extremely beneficial, concluding that they “have learned a lot in a very short time.” It can be said that this is mostly due to the many resources made available to the students, including the teaching staff.

It has been hard to truly quantify the mid- and long-term effect of the course. All graduate students who had taken the course in 2004 have graduated, except for one student still pursuing a Ph.D. degree (year 4). This 100% (expected) graduation level is very high compared to what is usually seen, however, given the limited number of students, the results may not be statistically significant. Furthermore, given that the instructor assesses the capabilities of the students in the first few classes, we cannot discount that selection may have played a role on the success of the students.

Following the completion of the course, those who continued in a thesis-driven program (M.A.Sc. or Ph.D.) did seem to show a better understanding of research project management, as well as the importance of the existing literature and of critical thinking. These students, we believe, also showed greater maturity toward research. Unfortunately, these assessments are all subjective. Our one true measure of success has been the continued student involvement after the course was finished, either by future involvement as teaching assistants or by continued efforts on drafting a publishable piece of work.

CONSTRAINTS, LIMITATIONS, AND FUTURE POTENTIAL

Timing and budget comprise the major constraints at EPM. This course was developed around infrastructure that was either kindly donated to the department of chemical engineering by the National Research Council of Canada, such as the 20L bioreactor, or that was available from Prof.
Jolicoeur’s laboratory. Much of the department’s equipment is also used for undergraduate training in the Fall and Winter semesters; therefore, the only time this course can be given currently is in the Summer term. Given the time of year that this course is given, it is expected that all students should have the opportunity to take this course before their 5th term, which is approximately the same timing given to complete the requirements of their comprehensive examination. It can therefore provide an additional indicator of the quality of the student, and be used as a practical component of the qualifying exam.

The major expenses for this course remain the cost of hiring teaching assistants. We have been fortunate to have had the constant support of the chair of the department, Prof. Robert Legros. In terms of material, cost is kept at a minimum by culturing bacteria, such as E. coli. As such, the major expenses for running these labs have been the cost associated with purchasing glucose and lactate assay kits.

As we start increasing the complexity of the course, given that we can use what previous classes have done in earlier offerings of the course as a new starting point each time, we may be faced with increasing expenses if we expect to explore novel aspects of the system. Another option may be to widen the focus of the course, for example including control theory to optimize the operation of a reactor. It is our intent to set up a series of variations, bringing in concepts like metabolic engineering, on-line and at-line monitoring and process control, and perhaps develop an advanced course in bio-process control within the control unit at the EPM.

Although this course is currently not a required course for all graduate students, we believe that it can be used in the training of students focused in other areas of chemical engineering. For example, students specializing in mass transfer, heat transfer, or rheology may benefit from taking this course, without having to actually change the content of the course. Extension to these adjoining fields may require additional expertise and buy-in from other faculty members in the department. Widening the focus, however, could pose fresh problems especially in trying to integrate students with varying backgrounds.

CONCLUDING REMARKS

We believe that this type of course is of crucial importance for three reasons: 1) it allows the incorporation of different concepts that should be assimilated by new graduate students and considered as key success factors for their own research project; 2) it allows the development of a productive graduate student, which is why we believe that room should be made in the graduate curriculum to ensure that there is an opportunity, early on, to experience being a graduate student; and lastly 3) this course can serve as an evaluation tool for graduate school potential.

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REFERENCES