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Teaching Genomics and Genomic Technologies to Biomedical Engineers: Building Skills for the Genomics World

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Abstract
During the last decade, the cost of sequencing DNA has plunged exponentially, primarily due to the development of new sequencing technologies. This change has impacted biomedical research, biotechnology, and pharmaceutical development. Additionally, it is beginning to change clinical practice. Students entering these fields need to have a basic understanding of the technologies that are used to explore the field of genomics and an understanding of the data they will encounter. Toward that end, I have developed and taught a genomics technologies and analysis course. Materials for replicating this course at other universities are available through github (http://bit.ly/GenAnal). An assessment of the effectiveness of this course is presented in this paper.

Introduction

During the last decade, the cost of sequencing DNA has plunged exponentially, primarily due to the development of new sequencing technologies. The first next-generation sequencing technology, the 454, began the race to $1000 genome in 2006 [1],[2]. This change has impacted biomedical research, biotechnology, and pharmaceutical development, and is also beginning to change clinical practice [3]–[6]. The development of personalized medicine, genetic biomarkers of cancer, and direct-to-consumer genetic testing are all the result of advances in DNA sequencing technologies.

Biomedical and bioengineering students often enter these fields. They will need to have a basic understanding of the technologies that are used to explore the field of genomics, and an ability to use the data they encounter. Bioengineers are uniquely positioned to address many of the challenges in the genomics field, as these challenges require individuals with skills in biology, computation, and design. Though there is literature describing genomics courses for first year undergraduates, nursing students and medical residents, none were found for engineering students[7]–[10]. Bioengineering students have more extensive training in mathematics and less in healthcare delivery than nursing students and medical residents, and therefore, a genomics course geared toward them would emphasize quantitative and technological aspects of genomics.

In this paper I present the structure of the course as well as a basic analysis of its effectiveness at preparing students for further exploration of the genomics space. This course focuses on the technological and computational aspects of genomics to enhance an engineering education.

Methods

Student Profile and Course Structure

This course is a 4-credit course that meets for two 80-minute lectures and a 3-hour computational lab each week. It is an elective course intended for advanced undergraduates and junior graduate students with backgrounds in bioengineering, though it is open to all advanced students in the university. In the most recent offerings, 60% were undergraduate students with most being bioengineering students 40% were bioengineering graduate students. The course currently accommodates up to 30 students with the size of the Mac computer lab on campus being the limiting resource. This course could be expanded by creating lab sections. Prerequisites for the

course include an undergraduate biology course or an equivalent that provides the basics of genes and genomes.

Students learn about the technologies that are on the market, or on the near horizon, for sequencing DNA. The course explores the technological advances that enabled the development of each of these tools, including back-engineering the constraints and criteria. We focus on the currently available tools including NanoString, llumina MiSeq and HiSeq, IonTorrent, Pacific Biosciences, and the Oxford NanoPore. With few technical prerequisites, students acquire skills to assess the strengths and weaknesses of each technology both in isolation and in comparison. Through guest speakers, they interact with leading members of the sequencing and genomics community in our city.

The course also has a hands-on genomic data analysis component. In this computational lab, the students are provided data from publicly available sites, and they perform analysis on this data. This includes genome assembly, gene expression analysis, and genome-wide association studies. In these labs, students use software that is currently used by researchers and professionals in the field. This allows students with little computational background to conduct quantitative analysis of large genomic data sets. As we have limited access to high-performance computing facilities, we mostly work with smaller datasets, though we discuss the computational needs for scaling data. It is not expected that students can write a program to analyze data, but they should be comfortable using a command line programs whether in Java, Python, MatLab or R. As this is a fast-changing field, we try to use the most current computational tools. Many of these are currently being developed in the programing language R. Therefore, students are introduced to R and R Studio in the course. These freely available tools run on Mac and Linux environments. Students complete analysis-based reports at the end of each analytical module.

Through a final project, students have the opportunity to explore and expand their interest in genomics. Students have chosen a variety of topics including: defining the criteria for a new type of sequencer, discussing the design of a genomics technology, and performing analysis on a novel data set. This project allows students to demonstrate mastery of a number of the learning objectives that are difficult to assess in exams. The course objectives for the course are listed in Table 1. These align with a number of the ABET student outcomes as indicated.

Though this course is not flipped, I am using some of these techniques to provide low–stakes assessments to help students acquire metacognition of their own learning [11], [12]. In particular, students take weekly online reading quizzes before class through the course Canvas site. Students are able to retake these quizzes up to five times to enable them to identify material they need to review. The quizzes are graded to incentive students to complete them. These quizzes provide low–stakes practice opportunities demonstrated to improve student learning [12]–[14]. In addition to providing feedback to the students about their learning, these quizzes identify areas that need extra emphasis in lecture [15], [16]. They are not intended to determine if students have met the learning objectives of the course, so are not used in evaluating the course.

Evaluation

Evaluation of the course is based on the final exam and surveys used to evaluate changes in student perception of the genomics field.

Table 1 Course Learning Objectives and ABET Outcomes

	Learning Objectives	ABET outcomes Up to 2017	ABET outcomes 2018
1	Identify and apply the genetic and biological terms that describe patterns of inheritance and genome contents.	A	1
2	Describe the types of libraries that are generated for DNA sequencing on genomic scales. Describe how to generate these libraries.	A	1
3	Distinguish between technologies being used to sequence DNA, and identify their strengths and weaknesses.	A,B	1,6
4	Describe the history, development, and engineering challenges of these technologies. Explain the technological and engineering principles that underlie them.	A	1
5	Determine what technology would be most useful for different biological and biomedical questions.	A,B	1,5,6
6	Perform analysis of genetic and genomic data with and without software.	A,K	6
7	Use common software to analyze different types of genomic data.	A,K	5
8	Identify limitations on current technologies, and define the criteria of current engineering problems in the field of genomics.	J	4
9	Discuss the opportunities and challenges posed by these technologies in the biomedical field	H	4
10	Understand the impact of high-throughput sequencing on the medical, computational, and bioengineering fields.	H,J	4

Exams were analyzed for mastery of learning objectives 1-9 (Figure 1). The exam illuminates areas for improvement in the course. Specifically, learning objectives 1 and 2 show low levels of mastery. As these were covered early in the course, the exam may not fully represent student understanding of these concepts.

The exam cannot well evaluate learning objective 10, so a survey was administered digitally to the students at the beginning and end of the class to evaluate this (Table 2). A two directional Wilcoxon Signed-Rank test was performed on the 11 surveys completed for both the beginning and end of course surveys (Figure 2).

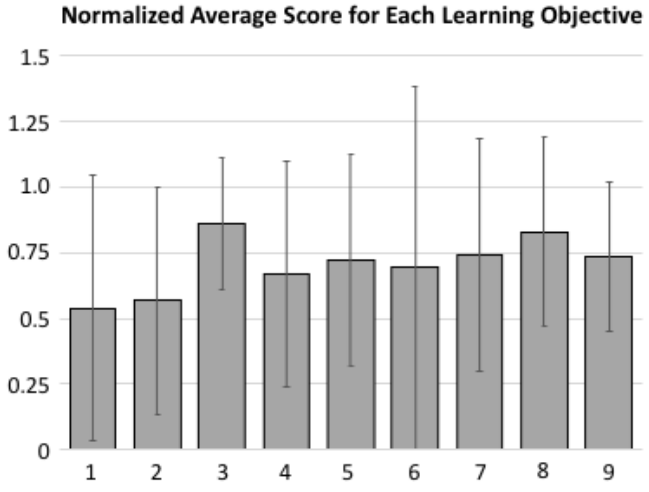

Figure 1 Normalized Average Scores for each Learning Objective. Student scores for each exam question in each learning objective were normalized to the number of points per learning objective. The average and standard deviation of the questions in each learning objective were calculated. In the graph, the bar represents the average and the error bars are the standard deviation.

Conclusions

This course successfully increased students' confidence in their understanding of genomics. In beginning and end of course surveys, students reported their confidence increased significantly in four different areas: the role of genomics in medicine, bioengineering, and biological research; and the role bioengineers play in genomics. Based on performance on the final exam, students demonstrated mastery of four of the learning objectives, 3,7,8, and 9. These learning objectives were the ones most recently taught or used most in the computational lab. Learning objectives 1 and 2 were not well mastered by many students, and 4, 5, and 6 were moderately mastered.

Table 2 Questions in Beginning and End of Course Survey

Question Number	Questions: On a scale of 1-6 (*1 being not at all to 6 being very well*)
1	How well do you think you could explain the role of genomics in the field of medicine?
2	How well do you think you could explain the role of genomics in the field of bioengineering?
3	How well do you think you could explain the role of genomics in the field of biological research?
4	How well do you think you could explain the role bioengineers play in development in the genomics field?

Future Goals

This course has met many of the goals. It has successfully introduced students to DNA sequencing technologies and genomic analysis. Students were able to identify appropriate technologies for different types of experiments. They were able to perform basic analysis and identify the challenges associated with these analyses.

To improve student mastery of the learning objectives that were not well met, I will be adding more discussion of the history and development of genetics as well as genomic technologies. We will spend more time discussing library production, and spend some time reviewing the early concepts again later in the course.

For those wishing to implement a similar course, I have posted my materials on github for public use (http://bit.ly/GenAnal). The computational laboratory component has been most useful for student understanding. Additionally, the students strongly benefitted from guest lectures by local industry and medical researchers in the field.

As this is meant to be an introductory course, students are not equipped to take roles as genomics experts. However, students appear to be equipped to appraise uses of genomic technologies and data, understand how genomics may influence their careers, and explore more advanced training in this area.

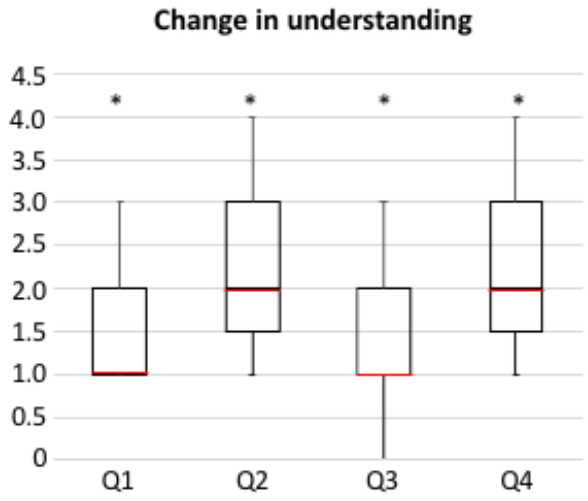

Figure 2 Self-reported Improvement in Understanding the Role of Genomics and Bioengineering. Student evaluations of their understanding of the roles of genomics and bioengineering. Median and first and third quartile are indicated by the whisker plot. Stars indicate a p-value of less than 0.01 in a two-directional Wilcoxon Signed-Rank test comparing beginning of class to end of class survey answers.

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