The Systems Biology and Bioengineering Undergraduate Research Experience at Vanderbilt University

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Abstract – We describe an ongoing program at Vanderbilt University centered on independent, long-term undergraduate research, the Systems Biology and Bioengineering Undergraduate Research Experience (SyBBURE). The program is loosely structured with the intention of enabling young students to fulfill the most basic and appealing aspect of scientific research: curiosity-driven experimental discovery and peer-to-peer communication of results. Microfluidics and biomicroelectromechanical devices are part of an exciting new wave of technology for studying biological systems and have proven well suited for training undergraduates in hands-on fabrication and laboratory experimental techniques. The encapsulation of idea generation, device design, fabrication and experiment within the experience of a single student leads to powerful opportunities for instruction in foresight, craftsmanship and outcome assessment – often with a redoubling of student motivation over time. SyBBURE is highly interdisciplinary, with faculty and staff project leaders from the Natural Sciences, Engineering, and Medicine. In notable cases the student-researcher becomes a bridge between basic bench research and more clinically focused laboratories. Short-term, high-risk, high-benefit projects that are inappropriate for grant-funded graduate students on a PhD track are ideal for undergraduates. The work can be demanding, so SyBBURE has significant attrition. We believe this is doubly effective as an early identifier of those students that might not be inclined to excel in graduate research, and rigorous preparation and credentialing for those students that are. SyBBURE efficiently identifies students with an inclination and aptitude for scientific research and prepares them for the challenges of a career in science. While quantitative outcomes cannot be obtained without a control group, independently assessed qualitative feedback suggests the program is highly effective in stimulating learning by actual problem-solving, cooperative approaches to science and communication of scientific problems and data.

Keywords: undergraduate research, innovation, challenge-based learning, microfluidics and BioMEMS

BACKGROUND & INTRODUCTION

Science, Education, Technology and the National Economy

Innovative workers are critically important in a highly competitive, technology-driven economy like that of the United States and an increasing number of other nations [Augustine, 4]. Companies need a steady flow of new or improved products to remain competitive and continue to employ a large workforce in the manufacturing sectors of the economy. Recent and widespread access to information among the growing economies of other nations has exposed

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Americans to the real wage structure of the rest of the world. As companies outsource larger amounts of their operations overseas, workers may have to compete more vigorously and live on lower wages. Rising energy and health care costs in the next decades also threaten to pinch corporate and private budgets [Samuelson, 31]. There is a tremendous need for significant advances in the health care, energy and technology sectors of the U.S. economy. The educational system must rise to meet this challenge and prepare excellent students capable of thinking and operating inside and outside of the classroom. To remain competitive, American graduates must be able to rapidly find and assimilate new information and bring it to bear on fresh and challenging real-world problems. They need to remain productive and engaged under quickly changing technological and market realities – at least as well as their overseas counterparts, if not better [Bransford, 6], [Clough, 9].

College students can be trained to think quantitatively and innovate if they perceive value in the training [Robinson, 29], [National Leadership Council, 24], [Bransford, 6], [National Research Council, 25]. Conversely, the wrong environment can stifle creativity. Students attend college primarily to secure jobs with better wages, but also to obtain and contribute to the body of knowledge. A college education helps them evaluate their prior beliefs and experiences and expose them to a wide range of new knowledge and information. This curricular education typically occurs by means of lectures, reading and examinations, and is summed up in the student's course grade point average (GPA) which is the primary focus of most students and their parents. Rarely is a student afforded the opportunity to see or experience the practice of research from which the textbooks and all scientific knowledge come. Laboratory and studio courses give the student a small sampling of the tools and methods of research, but the problems are often carefully chosen and scripted so that outcomes are predictable. This is a necessity because actual research experiments are too difficult and ill-behaved for a college laboratory class! There is presently not a place for creative, innovative thinking and real unscripted problem-solving in most college curricula, especially at large research universities, although this is the type of training most needed for innovation in the workforce [National Leadership Council, 24].

Discovery of the laws and mathematical underpinning of the natural world by the practice of research leads to valuable technological developments that can have lasting effects on the economies and societies of the world [Diamond, 11]; but research and innovation require an active learner with a broad knowledge base who is aware of the state of the art and is incentivized and equipped to improve it. Innovators are driven by internal, self-constructed visions of future possibilities. They actively increase their knowledge of how things presently are and constantly fine tune their vision of how things can be different and better. The ideas that stretch and extend between present status and future possibilities in the mind of the researcher are the fabric of invention. The imagination phase of invention occurs in discontinuous leaps and leads to futuristic, even unlikely, places, but the realization of the invention requires the steady hand and adroit skill of a craftsman. Only ideas that survive experimentation and prototyping have possible production value, and this requires fabrication of precise instruments and carefully strategized testing. The manual and intellectual toolbox required for this kind of work can be taught and learned [Paydarfar, 27], but is presently of little value to a college student – and can actually be a liability to the GPA. Students in science, technology, engineering and mathematics (STEM) disciplines can benefit greatly from vigorous training in real, unscripted innovation and experimentation as early in their career as possible. The reward system of the traditional classroom environment with lectures and examinations may discourage some students from developing a curious and inquisitive approach to life-long learning, instilling a life-long fear of getting the wrong answer instead. Experiments, on the other hand, encourage imagination and creativity.

Imagination is half of the equation for innovation, but careful instrumentation is equally indispensible [Bock, 5]. It has been demonstrated that students retain erroneous preconceptions about the natural world even after attending an excellent and clearly delivered lecture. However, they are able to replace them with correct knowledge if they are encouraged and rewarded for independent experimentation aimed at understanding the same subject matter. For instance, students with misconceptions of the way electricity causes a light bulb to glow who heard a lecture on the process failed to understand it until they were given a light bulb, wire and battery and allowed to experiment, with guidance [Annenberg Media, 2], [Annenberg Media, 3]. Through experimentation the student gains a deeper and more correct understanding of the world, but more importantly he or she begins to learn how to learn. Metacognition, the ability to recognize *how* we know what we know, is a key part of becoming a life-long learner. Instruction by real-world experimentation can pay large dividends by transforming students into the ultimate active learners – those that value learning and learn how to learn better.

Examples of tremendous advances arising from learning by imagination supported by experimentation are numerous. Consider briefly Nikolai Tesla's invention of the multiphase electric motor "to do the work of the world" or Thomas Edison's relentless pursuit of the perfect incandescent light bulb to light the night [Jonnes, 19]. Both of these scientists possessed great imaginations, but they were also intimately tied to the scientific instrumentation they used in the discovery process. In fact, the development of instrumentation and discovery of natural laws are often inextricably linked, even identical, processes. Michael Faraday, in discovering the principles of electromagnetic induction, was simultaneously building the rudiments of what would eventually evolve into the modern-day electric motor. In many cases the instrument becomes the discovery and vice versa. There are notable exceptions, of course. Most famously, Albert Einstein completed most of his work using only thought experiments and no laboratory [Isaacson, 17]. But his work began an age of theoretical physicists whose ideas were tested or sparked by data from experimentalists. Whether embodied in one scientist or distributed across many, no real valuable technological development is discovered or tested without experimentation, and experimentation absolutely requires precise instrumentation.

As compared to forty years ago, the ever advancing integration and computerization of consumer products, automobiles, and industrial and scientific instruments has led to a drastic reduction in the number of students with the technical skills required to build their own scientific apparatus [Sharkey, 33]. While high-school and college engineering design competitions, for example in robotics (http://www.bestinc.org/MVC/) or automobiles (http://students.sae.org/competitions/), are attempting to address this problem, college students have few opportunities to build instruments that they could then use in a meaningful research project. While there are texts on the art of building scientific apparatus (http://www.amazon.com/Building-Scientific-Apparatus-John-Moore/dp/0813340063), the problem is that few engineering, physics, or chemistry laboratories can provide the level of technical infrastructure, financial support, or patience that would allow undergraduate students to develop macroscopic pieces of mechanical hardware for ongoing research. In contrast, the introduction of rapid, low-cost soft-lithographic microfabrication of microfluidic devices [Duffy, 12] provides students with the tools to fabricate simple devices that can be readily incorporated into a wide variety of research problems, particularly at the interface between the physical and biological sciences, engineering, and medicine. We find that students with only a week or two of training are invigorated by being able to create devices whose function they can observe under a microscope, and that they can then use to answer their own, meaningful scientific questions.

Systems Biology, Microfluidics and BioMEMS

The 21st century is often heralded as the era of biotechnology [Rifkin, 28], [Grace, 14]. Indeed, mapping the genomes of many commercially valuable organisms (including humans) has already led to improvements in industries such as pharmaceuticals and agriculture. It is also clearly the age of nanotechnology, the study of devices and systems with features as small as one or a few nanometers. Biotechnology and nanotechnology have merged in research that falls under the broad category of "lab-on-a-chip" technology. Borrowing methods from the semiconductor manufacturing industry, microfluidic (MF) devices with tiny, cell-sized channels, chambers, traps, electrochemical sensors and actuators can be manufactured with relative ease. The devices have applications across a wide spectrum of disciplines. Some are used to manipulate and study individual cells of humans and other organisms, and these types of devices are known as biomicroelectromechanical systems (BioMEMS). **Figure 1** illustrates the multitrap nanophysiometer fabricated and used by SyBBURE students [Faley, 13]. The device traps and retains large numbers of adherent or nonadherent individual cells in spatially addressable traps for long-term study. SyBBURE students using this device have conducted independent studies of pinocytic loading [Hughey, 16], [Hughey, 15], calcium release activated calcium channel dynamics, toximetry [Kim, 22], [Ostrowski, 26], [Kim, 20], [Kim, 21], leukocyte sorting and labeling [Wertz, 36] and others [Jiang, 18], [DeLong, 10], [Clay, 8], [Chamberlain J., 7]. Many other types of devices have been made and used by undergraduate students, including mirrored pyramidal wells [Seale, 32], [Wright, 38], [Wright, 39] and devices for oxygen-sensing, electroosmotic flow [Wellstead, 35], and studies of chemotaxis and galvanotaxis [Skandarajah, 34], and multicellular bioreactors [Lu, 23].

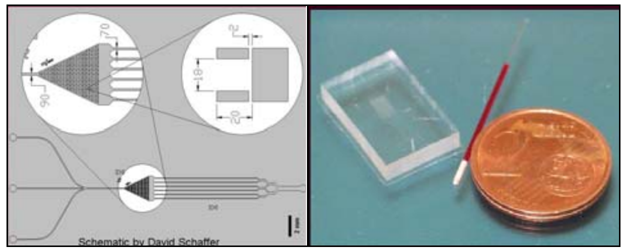

Figure 1: Left Panel – Schematic of the multitrap nanophysiometer (MTNP). 440 traps (inset) are arrayed in a 2 x 2 mm chamber with three inputs and one output. Right Panel – The MTNP device with a €0.02 (U.S. penny-sized) coin and a glass microtube containing 10 microliters of whole blood.

Traditional methods of biology using beakers, petri dishes and flasks are technology-limited to relatively large volumes. While the advances of biology and medicine under the traditional methods, including vaccines, antibiotics and nutrition, have been tremendous, many believe that BioMEMS technology is ushering in a new era of discovery in health care research. Researchers are beginning to understand that genetic polymorphisms underlying human populations lead to subtle, but important differences in cellular-level biology and ultimately in the health and well-being of individuals, particularly in their disease development and response to therapeutic intervention. Humans and other multicellular organisms are complex assortments of very large numbers of cells (approximately 100 trillion). Our coordinated bodily functions are ultimately controlled by communication between individual cells of the body using autocrine and paracrine signaling molecules. The holistic study of an organism, encompassing genetics and

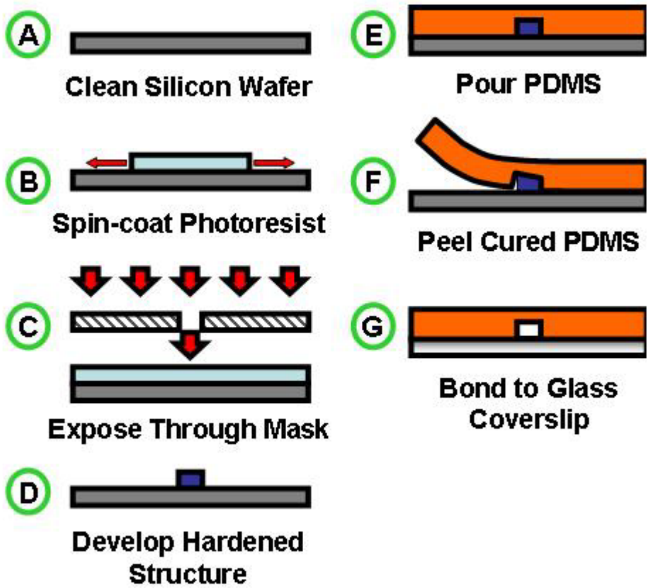

Figure 2: Overview of soft lithography.

molecular biology up to and including the level of the whole organism, is defined by some as systems biology [Wikswo, 37]. It is distinguished from traditional physiology by the instrumentation available to the systems biologist. BioMEMS and MF devices enable researchers to isolate small numbers of cells and control and manipulate their extracellular milieu of nutrients and signaling molecules [Wikswo, 37]. While the advantages of BioMEMS are many, the central advantage is the ability to precisely *organize the instrumentation at or below the size scale of an individual cell* and conduct studies with response times *on the time scale of the activity of a single cell*. This kind of instrumentation requires the fine craftsmanship and attention to detail that would have been familiar to Edison, Tesla or Faraday, and the potential for a revolutionary understanding of biology that would have appealed to Einstein. We have found that undergraduate students are fully capable of mastering many microfabrication methods and readily adopt them into their thinking about and solving of scientific problems.

The SyBBURE students receive training in the methods for soft lithography microfabrication illustrated in **Figure 2**. Using computer-aided design (AutoCAD, AutoDesk, Inc., San Rafael, CA) software, the student prepares a precise scale drawing of the device to be manufactured. Single or multilayered devices can be constructed from one or more separate, spatially registered drawings. The drawing is printed to a mask in one of three ways: 1) chrome on glass (Advance Reproductions Corporation, North Andover MA), 2) ink on mylar (Infinite Graphics Incorporated, Minneapolis, MN) or 3) on 35 mm film with an in-house printer (Polaroid Corporation, Concord, MA), in order of decreasing resolution. When a suitable mask is complete, sturdy chrome replicates on glass can be made using photolithography for device archival and backup. The pattern in the mask is transferred to a precision-thickness photoresist layer on a silicon wafer with ultraviolet photolithography. We use a commercially manufactured UV light source (EXFO, Canada), but inexpensive black light fixtures (Spencer Gifts, Egg Harbor Township, NJ) also work. The mask is pressed tightly against the wafer during UV exposure, sandwiching the photoresist and preventing leakage of light to unexposed areas. After exposure the wafer is chemically developed using a process similar to photograph development. Depending on the type of photoresist used (positive or negative) the pattern from the mask or its negative image remains on the wafer after development as a bas-relief structure of uniform height. This is the master device. A flexible silicone polymer (PDMS) is poured in liquid form onto the master device in the bottom of the petri dish. After curing, the master pattern has been transferred to the solid but flexible PDMS, which is cut and peeled away from the silicon wafer master and clamped or bonded to glass or other substrate. Punched holes enable coupling of the cell-sized channels to syringe pumps or gravity feed devices for cell loading and/or perfusion.

METHODS

SyBBURE Structure

The goal of the program is to stimulate and encourage original, independent and creative problem-solving skills in undergraduate students. We believe that immersion in unscripted, real-world problems is the fastest way for students to develop these skills. The SyBBURE environment is very unlike the classroom in the sense that the experience of each student is likely to be different and defined by the problem he or she decides to study. While all students receive training in the core competencies of microfabrication, even to the point of conducting actual experiments, the specific skill set required for their research is determined progressively by knowledge gained through experimentation and consultation with mentors and project leaders as well as other students. Admission to the program is normally by a competitive application process in the spring, and the complement of students is intentionally limited to twenty. Application is open to all undergraduate students regardless of major or year of study, though the majority of the group comprises students from physics, chemistry, biology and engineering majors. There are eight project leaders made up of faculty and staff from various disciplines. The program runs year long, and a few students enter and leave every semester. Usually the largest influx of students occurs in the summer. The training of this cohort marks the beginning of a year-long cycle that repeats the following spring. A typical student enters the program at the end of the freshman year and remains in the program until graduation, although excellent candidates are occasionally admitted as juniors or seniors, and several students have opted to return for part of the summer after graduation to complete their research projects.

A very important aspect of the program is its self-organization. The students are expected to help keep the program organized and professional. Since the students are given an unusual amount of freedom when they begin, they invariably start by wanting to "know the rules." Rather than finding rules, they learn to work in order to meet self-selected goals that are more motivating than rules would be. This self-motivation is encouraged by the near presence of high-performing peers. We encourage and reward self-starters and usually reprimand students only for not trying. The productivity of their peers in the form of papers, posters and public presentations is clearly a very strong motivator. Students tend to take their cues from the whole group, instead of a single "boss." This has the powerful effect of diffusing self-critical arguments from students that have not yet built their confidence, since it is more difficult to believe they are incapable of something their peers have mastered.

Training

The program begins with an intensive three-day orientation, where the students are briefly introduced to microfabrication and its relevance to biological research. Existing SyBBURE students present their research goals, methods and results first, and faculty and staff present their research thrusts next. Finally, students are randomly paired with a teammate and scheduled for hands-on training in the following two weeks. During orientation, speakers stress that the research program is very

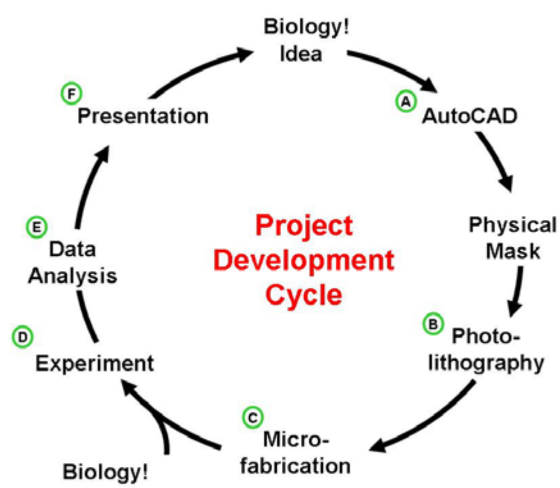

Figure 3: The project development cycle and major training areas.

unlike the classroom and that independent motivation is critical to success. Advice from former students is printed as quotations in the orientation booklet and invariably stresses the importance of self-motivation for success both in SyBBURE and future graduate work. Following orientation, students are intensively trained in the basics of microfabrication. The development cycle illustrated in **Figure 3** is roughly an accurate depiction of the cycle of BioMEMS innovation, and reflects the cycle by which people iteratively learn complex concepts [Roselli, 30]. Ideas for research projects arise from anyone, but normally more experienced researchers have more ideas. Most of the ideas in SyBBURE arise from the central advantage of BioMEMS and are explored through Items A-F (AutoCAD design, UV photolithography, microfabrication, microscopy, image analysis with ImageJ, etc.). Presentation skills are strongly emphasized, using Microsoft Power Point©, Publisher© and Word©, and include reference and bibliography management, figure creation and embedding and poster creation. In all cases SyBBURE faculty and staff attempt to find software and tools that are either ubiquitous or freely available on the internet. The objective of this training is to provide students with the basic accoutrements of research in microfabrication as well as the wider world of science.

Research Projects

The undergraduate research in SyBBURE is different from that of other undergraduate research experiences in several ways. First, the program runs concurrently with classes and the academic school year as well as during the summer. Students continue their projects in SyBBURE for three or more years beginning the summer before their sophomore year. This enables them to set and achieve long-term goals in their research. Second, students conduct their research independently as much as possible. After their initial training, the student is expected to set his or her own direction and goals with the minimal necessary guidance. This stands in stark contrast with summer research experiences, many of which are projects a graduate student could complete in a few days or weeks but instead are stretched over the whole summer. The long-term nature and self-motivated aspect of our program allows students the time required to make, identify, and correct their own mistakes, without risk of academic penalty. As one SyBBURE student stated in a presentation of his work to parents and alumni, “I am proud of my first picture of fluorescent cell goo, because it was mine and I then figured out how to handle the cells correctly.” Finally, as a consequence of the structure of the program the students and staff inevitably develop a rapport that often transcends the program in both space and time. The relationships are always grounded in the student’s research and data but reach into larger areas of the student’s professional life, such as plans for graduate education. Conversations (one-one and group) often meander over larger societal issues such as health care disparities; the progress, funding and review of science; and ethical issues of science and technology. Students are mentored by faculty, staff, and near-peers on how best to present what they have learned and accomplished as they prepare applications for graduate or professional schools, fellowships, and industrial jobs.

Poster Presentations & Talks

Regular communication of research efforts and results is a prominent part of the program. Students are expected to be able to make clear and concise presentations of their project, including its relevance to larger societal considerations. Upon entering the program, one to two students per week are required to give a brief presentation of their latest research results. Early presentations lack original scientific content, but students can give more or less professional presentations regarding the training they have received to date and receive feedback accordingly.

In the early stages this may include comments on simple presentation skills such as oration and slide structure and content; however, thus far we have adamantly refused to impose a presentation template on students, preferring imperfect but robust self-expression to a uniformly dictated format. We have been rewarded in this respect with student presentations that over time become astoundingly creative, interesting and informative to all in attendance.

Journal Club

The ability to rapidly find and assimilate published work in a given area of research is a key skill for any scientist. All researchers need to have a ready, working knowledge of the scientific literature in their field. With scientific research growing rapidly it is increasingly important to possess facile strategies for interaction with major sources of information. Researchers need to be able to find, judge and assimilate work that has been done in a given area as they develop their own research directions. To address this critical need, all students, faculty and staff meet once each week to analyze a research article from the literature. The article is usually chosen by a student and is emailed in advance to the entire group. To encourage reading the article before the meeting, all students are required to email their responses to general questions and questions they have about the reading to the entire group the day before.

At the meeting, the designated student presenter provides an overview and background for the paper, ideally including its relevance to his or her research and that of the group. They also answer the most frequently posed questions from the pre-meeting emails. The meeting then proceeds in two phases. In the first phase, randomly chosen small groups of two to three students cluster to discuss one or two figures or tables from the paper. In the second phase, a student from each small group explains the figure to the entire group in order of figure appearance in the paper. In this way, the responsibility for understanding and explaining the paper is disseminated to the students. The student-presenter position rotates through every student in the group. The pre-meeting email and the anticipation of being asked in front of peers to explain a particular figure or table help to motivate students to read the papers carefully in advance of the meeting.

RESULTS

While it has never been our intention to study student cohorts, and we have no control group for comparison, we have compiled some basic information about the program. Since the summer of 2006, SyBBURE has trained 63 Vanderbilt students, nine students from other universities and one student from a local high school. The SyBBURE program is privately funded, and additional students participate through NSF-REUs or other funding mechanisms such as the Vanderbilt School for Math and Science. Over the eight semesters thus far, the average number of students in the program at a time is 24, and the demographics are 68% male, 32% female, 95% Caucasian, 1% Hispanic and 4% African American. The 63 Vanderbilt students comprise twenty that are currently active in the program, 29 graduates, and 15 that voluntarily resigned or were not advanced in the program. Of the graduates, nine are in graduate school, twelve are in medical school, six are in industry and the whereabouts of one is not known. Twelve of the 15 that left the program did so after one or two semesters (mean 1.6 ± 1.0). Only three stayed with the program for three or more semesters before deciding to leave. The overall attrition rate is thus approximately 31% (15/48), although this number adjusts continually. Of the students with confirmed positions, the ratio of students in post-baccalaureate training to industrial jobs is 3.5:1.

All students in the first and second year SyBBURE Summer Program submitted a program survey. While some students did not answer all of the questions on the survey, most did and many provided detailed responses to several questions. From these responses, patterns emerge about what students learned by participating in the program, what they identify as its strengths and areas for improvement, and how their views and aspirations changed because of their involvement with SyBBURE. In their responses, students identified three main areas of learning (numbers in parentheses indicate total number of responses): 1) learning self-direction and motivation (10); 2) a better understanding of how scientific research works (6); and 3) the development of lab skills and techniques (5). In terms of the first area, students offering this response were very clear about what they learned. As one student puts it, "What you get out of research is what you put into it, self-motivation is key to making your project and research experience worthwhile." Another student similarly links self-motivation and the success of one's research, noting that "With SyBBURE, no one's going to tell you what you need to do to get things done. You have to go out there to ask people and do things yourself if you want results." Students linked the development of research expertise with their access to and interactions with mentors as well as their working relationship with peers. One student identified a "great aspect" as "the ability to interact directly with sources of expertise including faculty, staff, and senior students." Another student found "support from both the students and the professors with our projects. Having everyone packed in the same corridor made it easy to ask advice or consult with our peers if we were having problems." We thus identify the communal nature of the program as one of its strengths although the students didn't identify it directly as such.

Case studies

Student 1 (S1), Major: Biomedical Engineering, GPA: 4.0

S1 entered the program at its inception, but began research in the group as a freshman through an alternative funding source. He conducted studies on pinocytic loading of cells in microfluidic cell traps. S1 returned to the lab after graduation for approximately one month to complete his research. He presented his results twice at the annual fall meeting of the Biomedical Engineering Society (BMES) and a full paper at a small NIH meeting. He is also coauthor on a recent research publication and is currently in graduate school at a top rated west coast research university studying microfluidics and BioMEMS.

Student 2 (S2), Major: Biomedical Engineering, GPA: 3.43

S2 entered the program the summer before his senior year and conducted research on the effects of toxins at various concentrations on cell motion in a microfluidic device. S2 returned to the research group for approximately one month to complete his studies after graduation. He presented twice at BMES and had a paper accepted through a competitive peer review process at a specialty MEMS meeting. Working remotely, he applied the image-processing techniques he developed as an undergraduate to a research problem in cell motility that led to co-authorship in a peer-reviewed full research article. He is currently setting up a microfluidics fabrication facility to study adherent cell cultures at major Midwestern university and planning to attend medical school.

Student 3 (S3), Major: Biomedical Engineering, Minor: Math, GPA: 2.46

S3 entered the program the summer after her junior year. She conducted research on cell forces using antibody-coated microspheres. She presented her research at the annual meeting *of a local scientific society and is currently in graduate school at a prestigious Midwestern school researching microfluidics and bioMEMS.*

DISCUSSION

While it is impossible to know how the program is affecting students' career decisions, some observations suggest that the experience is helpful. The number of students that leave the program after only one or two semesters is much higher than those that wait longer to leave. The most common reason cited for leaving the program is concern over heavy course loads and the need to maintain a high GPA. The proportion of students that complete the program and continue to graduate or medical school is high. Also, students continuing in the program often grow more aggressive about pursuing their research and more vocal about their results. At least eight students in the last two years have returned to the lab after graduation to continue or complete their research projects, and two to three seniors have presented their research at local or national meetings each year. The students that continue also appear to become more adept at presentation of their results and more comfortable discussing them with other more senior colleagues.

A career in scientific research can be very satisfying, but also highly competitive [Anderson, 1]. Jockeying for authorship on publications, trying to keep a laboratory funded, worrying about having ideas "stolen" by competitors and getting tenure are all among the reasons undergraduates cite for being hesitant to continue research as a career. While all of these concerns are authentic and should be considered in their own contexts, college students have little exposure to the "real world" of academic research, and have difficulty gauging how well they might perform. Our view is that the essential job of the professor is to be innovative; challenge the established order; and introduce new technology, new methods and new thinking for the improvement of society. SyBBURE gives young students the opportunity to exercise these core skills at an important moment in their education – when they are trying to decide whether to pursue research as a career. In addition, SyBBURE exposes them to the realities of research: communication in conference presentations and publications; the business and management of science, including grant applications, patents, specification and purchasing of supplies and equipment, and team management; and most importantly, the service of science through teaching and research aimed at major societal problems. Collaborative, interdisciplinary research by definition requires scientists from disparate fields of study. The SyBBURE community is intentionally diverse in an effort to foster a sense of community among the nascent researchers.

Even without the institutional difficulties cited above, science as a career can be very difficult. Experiments "fail" more often than they "succeed." Experimental requirements can be harsh and may impose odd or long hours. The study of complex systems such as those in biology can be daunting and discouraging. However, these basic struggles are also the great appeal of scientific work. It is the very fact that one is working among the unknown laws and forces of nature that makes success so incredibly exhilarating and addicting. Scripted experiments are essentially glorified demonstrations. The development of skills to independently identify and correct errors and refine instrument designs and scientific hypotheses is a central part of SyBBURE. If the student pursues his or her own idea and finds success (even in an unknowingly reinvented technology), the effect is an instantaneous jolt of confidence and redoubling of effort. Students in this energetic state can be more easily instructed to strive for excellence in all aspects of their lives and their work, including strong interpersonal relationships, honorable life goals, personal integrity, careful work and effective communication.

Research in any area is subject to the same joys and frustrations outlined above. BioMEMS and lab-on-a-chip research benefits from being new and exciting on a national, even worldwide, level. This helps a good deal, because students feel much more connected with the happenings of science on a larger scale. Given the novelty of the field, it may be more likely that a student will make an original contribution to the field. At the time of this writing two SyBBURE students are coauthors on two scientific publications in major journals, two are co-inventors on a patent application and two are co-inventors on a patent disclosure. SyBBURE students have made dozens of poster presentations at local and national conferences and two full papers on which the student was first author have been accepted and appear in refereed conference proceedings. At least two graduates are considered local "experts" in microfabrication in their present position as graduate students.

SyBBURE employs one full-time faculty member and part-time effort from several scientific staff. In terms of dollars expended per student, it is an expensive program. While SyBBURE is not designed for implementation in the classroom, some observations in this regard are worthwhile. The core SyBBURE group has shown a tendency to attract other students in the form of volunteers, senior design teams, work study participants, NSF-REU programs and other funding sources, so the total cost per student is lower than the booked value. At least four graduates from the program have gone on to leadership positions in graduate school where they are training others in methods they learned in SyBBURE. It is difficult to estimate the impact this may have on research productivity. The supplies and materials for microfabrication are not necessarily expensive. We and others have used simple materials ranging from Silly Putty, Scotch Tape, Shrinky Dinks, black lights, screws, fishing line, hot glue and many other inexpensive items to help fabricate novel instruments. Finally, the energetic work of the students leads to valuable preliminary data for use in federal grant applications for student training.

CONCLUSIONS

The effects of sustained, independent research on undergraduate education are multiplicative. Students learn about their own capabilities and feel an immediate connection to the "big picture" of research and industry. This naturally increases their desire to broaden their knowledge base and helps them place their coursework in the proper perspective. Even if a course is not immediately relevant to their research, they may better identify with the knowledge presented in class as the results of research. It stands to reason that productive scientists from all ages chose to remain engaged in research because it can be very enjoyable. Furthermore, those same scientists may not have continued on their paths if they were required to sit in four or more years of lectures before making an attempt at research. We believe that thrill of research and discovery will draw the most motivated, innovative and capable students from an undergraduate community like a lighthouse can guide a ship to a harbor.

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