MICROFLUIDICS @ THE BEACH:
Introduction of Microfluidics Technology to the ChE Curriculum at Cal State Long Beach

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Microfluidics involves the study of the behavior of fluids at microscale, fluid manipulations, and the design of the devices that can effectively perform such manipulations. It has been widely applied to the miniaturization of analytical methods and chemical and biological processes because of its many advantages, such as significant reduction in analysis time, much lower sample and reagent consumption (in the nanoliter range or less), and enhanced system performance and functionality by integrating different components onto microfluidic devices.[1,2] These applications are usually called micro total analysis systems (μTAS) or lab on a chip (LOC).[3,4] Since its debut in the '90s,[5–7] microfluidics has made significant progress and gradually moved from pure research projects to commercialized products, such as Agilent Technologies' 2100 Bioanalyzer for biomolecule analysis, PerkinElmer Inc.'s LabChip systems for biomolecule analysis and drug discovery, and Fluidigm Corporation's BioMark system for real-time PCR.

Microfluidics is an interdisciplinary area that incorporates various technical branches, such as biochemistry, biology, chemistry, physics, and engineering.[8] As microfluidics finds increasing new applications, there is a strong need for general awareness and in-depth understanding in this growing area, especially for science and engineering education. Although some undergraduate courses exist, most microfluidics courses are offered to graduate students. They are mostly lecture-based and do not have hands-on sessions for students to put in action right away what they see/learn from class lectures. The major barrier to integrating hands-on sessions with lectures in microfluidics courses is the need for access to equipment in cleanroom facilities and the associated costs for supplies, such as silicon wafers and polydimethylsiloxane (PDMS), to

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fabricate microfluidic devices for educational purposes. As a result, these resources are generally for research personnel only. In addition, fabrication of microfluidic devices requires specific training to enable each individual to reliably make working devices, which is not feasible for a typical class of 20 to 30 students. To provide students with hands-on experiences in microfluidics, there have been efforts focused on developing more accessible systems and educational modules, *e.g.*, LabSmith's commercial SVM340 microscope,[9] shrink- film microfluidic devices by Nguyen, et al.,[10] Jell-O chips by Yang, et al.,[11] SmartBuild by Yuen,[12] and several reported chemical engineering laboratories.[13–15] These efforts have lowered the barrier to such integration.

In the past few years, we have seen an increase in job opportunities for engineers with skills relevant to microfluidics, such as microfluidic chip design, microfabrication, optical imaging, and programming languages for instrument control and data analysis. For such opportunities, we believe that chemical engineers have the edge over other engineering majors because of our required training in biology, chemistry, and physics, which matches the interdisciplinary nature of microfluidics. However, our current chemical engineering curriculum at California State University, Long Beach, does not provide our students with the necessary training for these skills.

We seek to address this gap by initiating a course development project for two new elective courses, Microfabrication and Microfluidics Technology and Microfluidics Technology and Its Applications, along with corresponding hands-on laboratory sessions. In this project, both undergraduate and graduate students were involved in the design of the laboratory sessions. They helped to convert some experiments in our ongoing research projects into the ones suitable for teaching by actually performing them and revising the protocol to fit our class needs.

In this paper, we present the contents and student feedback of the first course, Microfabrication and Microfluidics Technology, which was offered for the first time in the Spring 2013 semester as a cross-listed course for both undergraduate and graduate students.

FACILITIES AND RELEVANT COURSES AVAILABLE

California State University, Long Beach (CSULB; The Beach) is predominantly an undergraduate institution. We have been seeking to include microfluidics technology in the chemical engineering curriculum at the senior and first-year graduate level. Currently in the CSULB College of Engineering, there are several courses covering some relevant topics of microfluidics technology offered in the Department of Electrical Engineering (EE 435 Microelectronics, EE 436/536 Microfabrication and Nanotechnology, and EE 437 Multidisciplinary Nano-Science and Engineering).

TABLE 1
Course contents of ChE 432/532 Microfabrication and Microfluidics Technology

Format	Topic
Lecture	Course Introduction
	MEMS and its applications
	Fabrication technology
	Micromachining process
	Dip-pen nanolithography
	Mechanical analysis of MEMS structures
	Capacitive transducers
	Piezoresistive transducers
	Thermal transducers
	Microfluidics technology
Laboratory	Soft lithography
	Pressure-driven flow and mixing
	Homemade pH sensor
	Pattern fabrication onto copper-coated slides

However, these courses focus on the device fabrication, material characterization, and the standard photolithographic techniques used in the microelectronics industry. In addition, these courses do not come with laboratory sessions, because CSULB had neither a fabrication facility nor faculty members with microfluidics-specific expertise before 2009. To initiate our research program and this course development project, we have established the Microfabrication Laboratory, a Class 10,000 cleanroom, capable of fabricating polydimethylsiloxane (PDMS) and thiolene-based microfluidic chips using soft lithographic techniques[16] and the Analytical Instrumentation Laboratory capable of fluorescence microscopy and image processing for microfluidics applications. They have been fully functional since Summer 2010, and our students have presented their work from these two laboratories at various conferences, such as Southern California Conferences for Undergraduate Research (SCCUR), ASEE, and AIChE annual meetings.

COURSE CONTENTS

In this course, we introduce fundamental concepts involved in the design, construction, and operation of microelectromechanical systems (MEMS)-based devices and seek to provide students with working knowledge to get involved in this area of growing importance through both class lectures and related reading materials. In the laboratory sessions, our students get hands-on experience by fabricating chips and conducting experiments on flow in the channel. The topics covered are summarized in Table 1.

The objective of this course is to familiarize our senior and first-year graduate students with common microfabrication techniques and basics of microfluidics technology, and to prepare them for the sequential course, Microfluidics Technology and Its Applications. The expected course outcomes are as follows:

- *To understand the basic chemistry, materials, and processes of photolithographic pattern transfer, micromachining, and soft lithographic casting.*
- *To get familiar with the common CAD tool for mask layout and design, actual microfabrication process, and manipulation of fluids on the microfluidic chip through hands-on lab sessions.*
- *To understand the basic concepts of microfluidics, on-chip component fabrication, and chip-to-world interfacing.*
- *To design the microfabrication process flow for different types of microfluidic devices according to process compatibility and manufacturability, and the application needs.*
- *To get familiar with report writing and oral presentation for communication of technical information.*

The lecture and laboratory materials were developed with materials from various sources:

- *Textbook:* Fundamental of Microfabrication (Marc Madou, 3rd edition, *CRC Press)*
- *Articles in relevant journals, such as* Chemical Engineering Education, Journal of Microelectromechanical Systems, Analytical Chemistry, Microfluidics and Nanofluidics, Electrophoresis, Proceedings of the National Academy of Sciences, and Lab on a Chip
- *Ongoing research projects in the authors' labs*

In addition to homework assignments and exams, graduate students in this course are required to write term papers to review the latest progress in research areas involving microfabrication and microfluidics technology within the past five years (2008-2013 for this course offering). Undergraduate students are not required but highly encouraged to write term papers, so that they can get more familiar with literature survey and technical writing. The term paper requirements are as follows.

- *The paper should include abstract, introduction, working principle, latest advances, summary, and a list of cited publications (at least 10 peer-reviewed technical journal papers).*
- *Double-spaced pages excluding the reference list (15 pages for graduate students and eight for undergraduate students).*
- *12-point Times New Roman font and 1-inch margins*
- *Figures and tables should not occupy more than one-third of the area of each page.*

We also introduced Zotero (<http://www.zotero.org>) in this course to train our students on organizing technical references and preparing report bibliographies from their literature collections.

MATERIALS

Purchased from Amazon.com, Inc., (Seattle, WA, USA) were heat glue guns (Low Temp Mini; Adhesive Technologies, NH, USA), petroleum jelly (Vaseline jelly; Unilever United States, Inc., Englewood Cliffs, NJ, USA), gelatin (Knox Gelatin; Kraft Foods Group, Inc., Chicago, IL, USA), activated filter carbon (API; Mars, Incorporated, McLean, VA, USA), and pH paper strips (Scientific Equipment of Houston, Navasota, TX, USA). Food dyes (Smart & Final Stores, LLC, Commerce, CA, USA) and hydrogen peroxide (CVS Corporation, Woonsocket, RI, USA) were purchased from local stores. Copper-coated slides were ordered from EMF Corporation (Ithaca, NY, USA). Sodium hydroxide and hydrochloric acid were purchased from Thermo Fisher Scientific, Inc. (Waltham, MA, USA).

LABORATORY DESCRIPTION

To enhance the learning experience through teamwork, students were required to work on lab assignments in groups of two. As described below, the lab sessions were held over four weeks after all the lectures had been completed.

Week 1: Soft lithography

PDMS (polydimethylsiloxane) is a very popular material used to construct microfluidic devices and other components for applications in biology, chemistry, and engineering because of its great properties, such as optical transparency, biocompatibility and elasticity, and a simple fabrication process ("soft lithography").[17] However, fabrication of PDMS devices is not suitable for a teaching lab because of the cost of mold making and toxicity of the monomer and curing agent.

With low-cost, non-toxic materials, this session was intended to familiarize our students with the typical soft lithographic process. A collection of chip designs was drafted with the open-source Inkscape vector graphics editor (<http://www.inkscape.org>) and was printed on copy paper using an office laser printer (LaserJet 4050N; Hewlett Packard, Palo Alto, CA USA). These designs were cut from the sheet and placed in disposable Petri dishes. To make the molding master, heat glue guns were used to deposit molten plastic glue (~ 2 mm thick) to form desired patterns. To allow clean release of cast chips, petroleum jelly was evenly coated on the mold masters. The gelatin solution was prepared by dissolving 40 grams of the powder in 1 liter of boiling water and was later treated with activated filter carbon to produce a clear solution. To cast hollow channels, 50 mL of the clear gelatin solution was poured into each Petri dish with the designed mold with care to avoid any bubbles, and the whole assembly was allowed to set in the refrigerator. Access holes were punched on the hollow channels with coffee stirrers before they were reversibly sealed onto Petri dish covers to form working chips. The

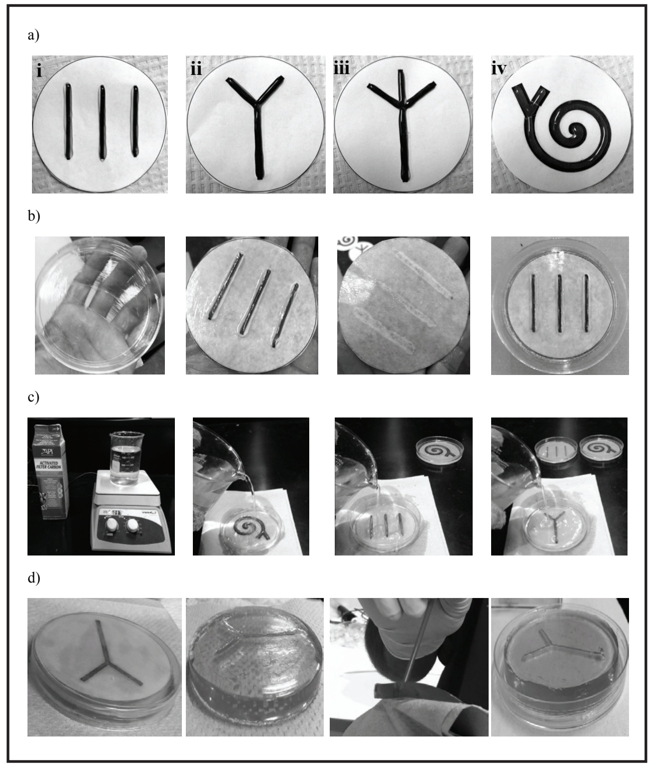

Figure 1. *Chip designs. (a) i. Straight channels for homemade pH sensors. ii.-iv. Different channel configurations for observing laminar flow and on-chip mixing. (b) Apply evenly a thin layer of petroleum jelly to both the bottom half of the Petri dish and mold, and then place the mold in the dish for casting. (c) Dissolve gelatin in boiled water, add activated carbon to make a clear solution, and then pour 50 mL of the gelatin solution into each prepared mold to cast the designed channel. The whole assembly is later placed in a refrigerator to solidify at 4 °C. (d) After the gelatin solution sets, the whole assembly is removed from the refrigerator. The gelatin channel is removed from the mold, punched with a coffee stirrer to make access ports, and carefully placed on a Petri dish cover to form a reversibly sealed chip for later experiments.*

general fabrication process is shown in Figure 1. Through this lab, our students could obtain a general picture of how lithographic techniques are used to fabricate microfluidic devices for desired applications.

Week 2: Pressure-driven flow and mixing

For better visualization of flow in the channel, we used milk and food dyes diluted with water (red and blue; 0.03 % v/v) for flow experiments. To demonstrate the pressure-driven flow, we asked students to load the colored fluids into their gelatin chips with syringes and to observe how the fluids moved in their channels and how their behaviors changed when the pressure was applied differently by changing the way they pushed the plunger. The students could see the fluids stopped moving soon after they stopped pushing the plunger. We also asked them to keep pushing the fluids into their channels while blocking the exit ports and to see the effect of pressure building up within their gelatin chips. The gelatin chips were reversibly sealed onto Petri dish covers. They got broken from the covers when the built-up pressure exceeded the limit of the reversible seal, which showed that the exit ports served as an easy way out for the air trapped in the channel to allow fluid movement.

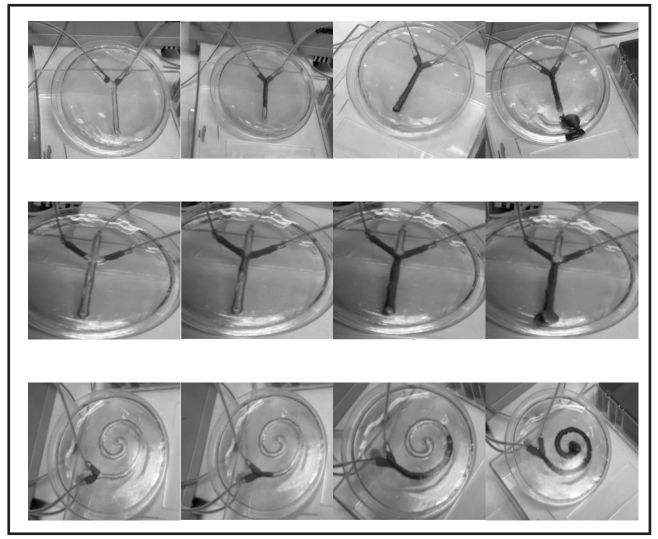

Figure 2. *Fluid mixing on different gelatin chips. Red food color, milk, and blue food color were used for better visualization, as shown in different grayscale shades. The channel cross section was 3 mm by 2 mm (W x H).*

In this experiment, we also demonstrated the mixing of fluids in channels on their gelatin chips. With this configuration, our students could directly visualize the laminar flow profile within the channels without using a microscope, as shown in Figure 2. They could see the formation of an interface between two colored fluids (red and blue) and mixing taking place along the channel length. To enhance our students' understanding of the flow profile, we asked them to calculate the Reynolds number (Re), the ratio of inertial forces to viscous ones, to confirm the laminar flow profile is the one they should see in such a configuration.

$$Re = \frac{\rho U_0 L_0}{\eta} \tag{1}$$

where ρ is the fluid density, U_0 is the characteristic velocity, L_0 is the characteristic length, and η is the shear viscosity of the fluid, respectively.[18] Given our channel dimensions (3 mm x 2 mm in cross section), water-based working fluids (ρ = 1.0 g/cm^3; η = 1.0 x 10^{-2} g/cm s), and a characteristic velocity of 1.0 cm/s, the Reynolds number was determined to be 24. This indicated that the viscous forces were dominant and the flow was within the laminar regime (Re << 2300) on our chips.

In addition to the Reynolds number to confirm the flow regime, we also asked students to identify the dominating mechanism for fluid mixing on their gelatin chips by calculating the Péclet number (Pe), which is the ratio of convective mass transport to diffusive mass transport.

$$Pe = \frac{U_0 L_0}{D} \tag{2}$$

where D is the diffusion coefficient. Given the average diffusion coefficients of food dyes (2.33 x 10^{-10} m^2/s),[19] the Péclet number was determined to be 103,004. This indicated that convective mass transport was the dominating mechanism for fluid mixing and the diffusive mass transport is negligible along the characteristic length (the hydraulic diameter of the channel) on the gelatin chips. As the channel width decreases, the effect of diffusive mass transport becomes more pronounced. Through calculations of these dimensionless numbers, our student could obtain a fundamental understanding of the flow regime and mass transport on a fluidic chip and thus could design microfluidic devices according to desired applications by identifying the dominating mechanism and changing parameters, such as characteristic length and velocity.

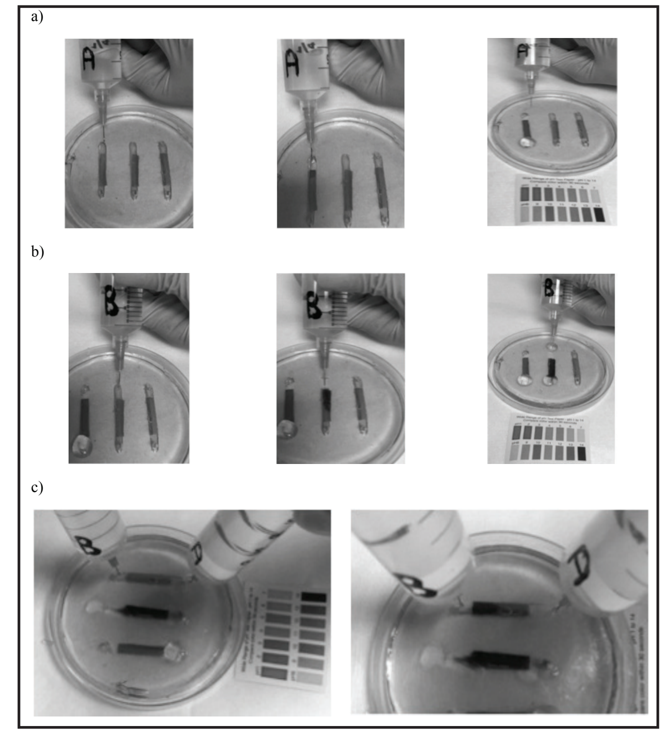

Figure 3. *Homemade pH sensor for acid and base detection. (a) 0.1 M HCl. (b) 0.1 M NaOH. (c) Neutralization test. The acid and base were loaded at the same time from the two ends of a channel. The test strip showed three grayscale shades, corresponding to different pH values.*

Week 3: Homemade pH sensor

To fabricate homemade pH sensors, pH paper strips were imbedded into chip channels before sealing onto Petri dish covers. Two syringes were used to load the acid and base, 0.1 M HCl and 0.1 M NaOH, into the channel. As indicated in Figure 3, the pH paper strips turned red in contact with the acid and purple in contact with the base, respectively. Through this lab, our students could see how to construct a simple device for chemical analysis. Another concept demonstrated here was parallelization, an important feature of microfluidics technology, because multiple reactions/assays could run simultaneously in different channels on a single chip. Herein, we introduced to our students the idea of "lab on a chip," which allows integrating multiple steps onto a single microfluidic device, ranging from sample pretreatment to final readout. In this case, both acid and base could be detected at the same time on a single gelatin chip, and the results could be read by color changes.

Week 4: Pattern fabrication onto copper-coated slides

Electrodes have been integrated onto microfluidic chips for various applications, such as electrochemical detection and electrokinetic manipulations of molecules for reactions/assays. For etching experiments, desired patterns were drawn on copper-coated slides with a permanent marker. With the ink serving as the resist, all excess copper was etched away with a 3:1 mixture of 3% H_2O_2 and 10 M HCl (Thermo Fisher Scientific, Inc., Waltham, MA, USA). The final copper pattern was revealed by washing away the permanent marker ink with acetone, as shown in Figure 4. Through this lab, students could learned the basic techniques of fabricating metal electrodes on a substrate.

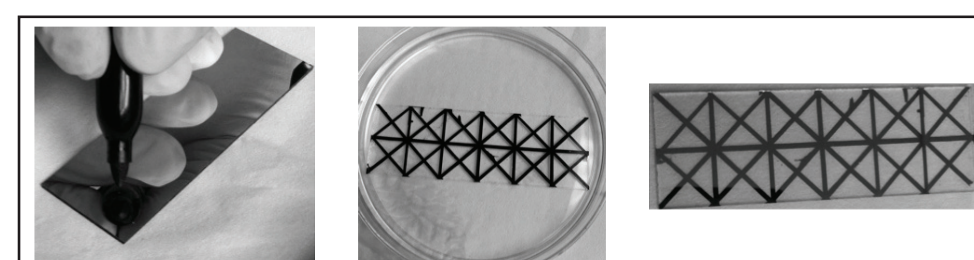

Figure 4. *Copper electrode fabrication. The desired design was first drawn on a copper-coated glass slide with a permanent marker. Unwanted copper was etched away in a 3:1 mixture of 3% H_2O_2 and 10 M HCl. To reveal the final copper electrodes, the permanent ink was washed away with acetone.*

COURSE ASSESSMENT

Besides the regular CSULB Student Perceptions of Teaching (SPOT) questionnaire, this course was also evaluated by an additional outcome survey at the end of the semester. We used a course outcome assessment survey form on a five-point Likert scale with 5 being Strongly Agree and 1 being Strongly disagree.[20] The criteria of each expected course outcome was included, and students could rate how successfully they reached the goal as described by the criteria (Table 2). The survey results are summarized in Figure 5. In general, our students responded very positively and were confident in what they had learned from this class, as supported by average scores ranging from 4.00 to 4.69 (out of 5.00). They were glad to be able to take the gelatin chips home as souvenirs and knew that they could make new ones easily to showcase what they learned using materials readily available around the corner.

After looking into individual criteria, the results indicated that our students felt less confident in Outcomes 3 and 4, as reflected in the scores of 4.06 and 4.00, respectively. From their comments, our students suggested that an adjustment in the topic coverage and labs would help them better understand the materials presented in this course. To address these comments to improve this course, we will prepare more detailed lecture slides to help walk our students through the topics presented in the textbook and focus on those more directly related to microfluidics technology. We will also increase the coverage of the device design and introduce more experiments demonstrating actual applications of the microfluidic devices in the field, such as sample separation and detection of biological/chemical agents.

CONCLUSION

We present in this paper our efforts and current progress to introduce microfluidics technology to the chemical engineering curriculum at CSULB. Although the first course offering was successful, there is still room for improvement. We have recently started in our department an instrumentation development project that employs 3D printing and open-source electronics to design and construct portable systems for chemical and biological assays. We plan to include the results from this project in the next course offering. A sequential course, Microfluidics Technology and Its Applications, is currently under development. It will focus more on theoretical aspects of microfluidics technology and its applications.

TABLE 2
Anticipated outcomes and performance criteria for the course assessment on a five-point Likert scale with 5 being strongly agree and 1 being strongly disagree

OUTCOME 1: To understand the basic chemistry, materials, and processes of photolithographic pattern transfer, micromachining, and soft lithographic casting.	
	Criterion 1.1: I have acquired a basic understanding of the chemistry, materials, and fabrication processes of MEMS through class lectures, in-class video demonstrations, and reading the textbook.
OUTCOME 2: To get familiar with the common CAD tool for mask layout and design, actual microfabrication process, and manipulation of fluids on the microfluidic chip through hands-on lab sessions.	
	Criterion 2.1: I am able to draw simple mask designs with the open-source vector editor, Inkscape.
	Criterion 2.2: I am able to fabricate simple microfluidic chips via soft lithography based on gelatin and paper.
OUTCOME 3: To understand the basic concepts of microfluidics, on-chip component fabrication, and chip-to-world interfacing.	
	Criterion 3.1: I understand the working principles of on-chip valves, transducers, and actuators through class lectures, in-class video demonstrations, and reading the textbook.
OUTCOME 4: To design the microfabrication process flow for different types of microfluidic devices according to process compatibility and manufacturability, and the application needs.	
	Criterion 4.1: I have learned how to select the materials and fabrication processes based on their compatibilities and applications through class lectures, in-class video demonstrations, and reading the textbook.
OUTCOME 5: To get familiar with report writing for communication of technical information.	
	Criterion 5.1: I have acquired the basic skills of using search engines (Google Scholar and journal websites) and bibliography manager (Zotero) to prepare my written report of reviewing technical papers in the past five years through class lectures and in-class video demonstrations.

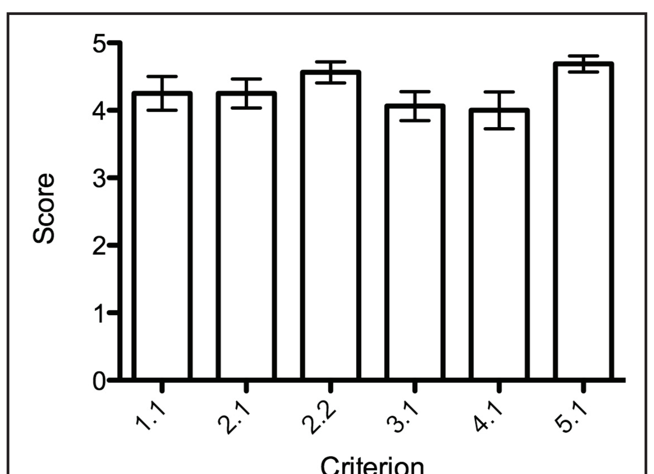

Figure 5. Student response to the course outcome survey. The average score for each criterion is shown here. All criteria are listed in Table 2.

These two elective courses are intended to expose our senior and first-year graduate students at CSULB to this exciting field of study and to provide them with working knowledge to get involved in this area. They will be first offered to students in our department as a pilot program and will later be offered to all science and engineering majors at CSULB after revising the course contents according the feedback from our students and faculty. Through these courses, our students will obtain not only the working knowledge of microfluidics technology, but also the written skills required for effective technical information exchange. We hope that in the future these two courses may excite more students to pursue advanced studies and careers in this area of growing importance.

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