AC 2007-2504: INTRODUCING MICROFLUIDICS TO ELECTRICAL ENGINEERS: AN INTEGRATED PROBLEM-BASED LEARNING EXPERIENCE

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Introducing Microfluidics to Electrical Engineers: An Integrated Problem-Based Learning Experience

Introduction

Microfluidics is a multidisciplinary field comprising of physics, chemistry, engineering and biotechnology that studies the behavior of fluids at the microscale and the design of systems that take advantage of such behavior. The behavior of fluids at the microscale differ from "macrofluidic" behavior in that factors such as surface tension, energy dissipation, and electrokinetics begin to dominate. Integrating microfluidics with sensors, actuators, or other electronics provides for new applications.[1-3] Even more importantly, the new fluid manipulation principles have enabled manipulation and detection of nanoliter fluid samples. The behavior of such systems has been extensively investigated and explored in so-called lab-on-a-chip (LOC) systems.[4,5]

Recently, expanding interest in scaling down to nanometer dimensions of the channels for fluid transport opened a new window for fundamental and applied studies of *nanofluidics*—studies of the characteristics of flow in nanoscale systems. From the applications point of view, nanofluidics represents an important step in developing LOC systems for small-scale analysis with high throughput. The small dimensions of LOC systems reduce processing times and the amount of reagents necessary for assay, substantially reducing costs. Sample volumes for a single experiment can be in the nano to picoliter range enabling the analysis of components from single cells and single molecules. It has been recently shown that nanofluidics has advantages in biological sciences, biophysical sciences (*e.g.,* DNA analysis) and chemistry.[6,7]

As previously stated, systems with microscale and nanoscale dimensions tend to behave differently than their macroscale counterparts, and the unfamiliar physics involved can require modeling and specialized training. Dozens of universities across the country have recently recruited faculty in the field of micro and nanotechnologies, specifically focusing on micro/nanofluidics and biomedical microtechnologies (or BioMEMS). These initiatives have brought the excitement of BioMEMS research to graduate studies and research programs in Electrical Engineering. While BioMEMS technologies have dramatically altered biomedical, pharmaceutical, and environmental research, they are yet to be successfully transferred to the undergraduate curricula.

Since microsystem technologies often employ techniques developed for the microelectronics industry, microfluidic devices were first fabricated in silicon, and later in glass, using standard photolithography and wet etching processes to produce planar microchannels.[8] However, new physical properties resulting from the small dimensions may dominate operation of micro/nanofluidic devices. Polymer microfabrication methods have replaced much of the established silicon and glass-based MEMS fabrication techniques,[9] due to complex fabrication procedures, geometric design restrictions, and costs associated with silicon and glass processes. The major advantages of polymers include a wide range of material characteristics, biochemical

compatibility, ease of processing, and lower cost. These characteristics make polymers the most promising substrate materials for applications in life sciences. A number of micro/nanofluidic systems have been demonstrated in polymers for biomedical applications, including miniaturized electrophoresis chips,[10-12] drug delivery systems, microfluidic mixers,[13-15] pumps and valves,[16] devices for cell or protein patterning,[17,18] and microfluidic switches.[19]

As we enter the 21st century, microfluidics and lab-on-a-chip technologies are still developing, with nanotechnology knocking at the door. Yet little has been done to transfer the micro/nanofluidics research to the undergraduate curricula. At University of Cincinnati, we are integrating state-of-the-art research in microfluidics within our graduate and undergraduate electrical engineering curricula via a laboratory course "Micro/Nano Fluidic Biochip Laboratory."

The current course offerings in the MEMS and BioMEMS areas at University of Cincinnati are described in Figure 1. Many undergraduate and most of the graduate students take both course sequences concurrently. The "MEMS sequence" is focused on principles of microfabrication and microsystem design, while the "BioMEMS sequence" is focused on biomedical application of MEMS and microfluidics. Each of the courses provides depth in both theoretical and practical topics. Typical enrollment in these courses ranges from approximately 12 students in the

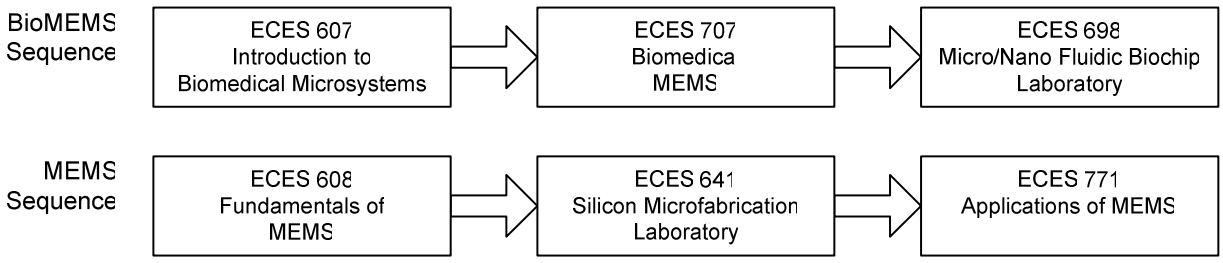

Figure 1. MEMS and BioMEMS courses offered at the University of Cincinnati.

graduate courses (700-level and above), to about 30 students in the dual-level lecture courses (600-level). The new laboratory course "Micro/Nano Fluidic Biochip Laboratory" is the last course in the "BioMEMS sequence." It was first offered in the spring 2006, with support from the National Science Foundation (DUE-0536799).

The "Micro/Nano Fluidic Biochip Laboratory" Course

The objective of the "Micro/Nano Fluidic Biochip Laboratory" course is to expose students to the rapidly emerging field of micro/nano fluidics. The course was designed to be ten weeks long, two hours of lecture, and four hours of lab per week. As a 600-level course it was dual-level, intended for the undergraduate seniors and first year graduate students in the Electrical Engineering program.

Some examples of topics covered in lectures include Navier-Stokes flows, pressure driven microflows, electroosmotic microflows, mixing and diffusion on micro- and nanoscale,

fabrication of micro/nanochannels, device packaging, and fluorescent flow characterization. These topics are listed in Table 1.

The topics and their sequence were selected with three criteria in mind. The first criterion was to introduce students to micro/nanofluidics. For most students, this was the first exposure to micro/nanofluidics. Thus, the first three weeks of the course were focused on introducing the critical concepts of microscale and nanoscale fluid flows. In these three weeks, students learned how to mathematically describe flow in a microchannel—a fundamental microfluidic structure that was revisited throughout the course.

The second criterion was not to overwhelm the electrical engineers by the highly-multidisciplinary nature of micro/nanofluidics. From surveys used during teaching of the *Introduction to Biomedical Microsystems* course,[20] we learned that by their senior year, electrical engineering students are very knowledgeable in electrical engineering topics, but only half of them have taken courses in mechanics and transport phenomena. Thus, the course topics were selected to gradually increase emphasis on mechanics and chemistry as the course progressed.

The third criterion was to make sure that lecture topics were aligned with the laboratory sessions. Laboratory sessions followed the iterative design cycle aimed at teaching students micro/nanofluidic system design. Thus, the theoretical aspects of micro/nanoflows were to be discussed early in order to be applied to the modeling labs. Fabrication and characterization topics were presented later in the course.

A unique aspect of the course was that we focused on an extended problem-based learning example of a microfluidic mixer that underlined all course activities. Rapid mixing of macromolecular solutions presents a significant challenge in microfluidics. Yet many miniaturized biochemical sensing techniques such as immunoassays or LOC-based devices for

Table 1. Lecture topics of the "Micro/Nano Fluidic Biochip Laboratory" course.

Week	Lecture Topic
1	Applications of Micro/Nanofluidics
2	Principles of Micro/Nanoscale Fluid Flows
3	Pressure Driven Flows
4	Electroosmotic Flows
5	Diffusion and Mixing
6	Design of Micro/Nanofluidic Lab-on-a-Chip (LOC) Systems
7	Fabrication Technologies for Micro/Nanofluidics: Masters & Embossing
8	Fabrication Technologies for Micro/Nanofluidics: Nanoimprinting
9	Packaging of Micro/Nanofluidic Systems
10	Flow Characterization Using Fluorescence

point-of-care (POC) medical diagnostics often require multiple mixing steps. Thus, successful development of a micromixer capable of passively mixing in a short distance is an active area of research and is of a significant interest to the microfluidics and LOC research communities.

At the first course offering in the Spring 2006, a large number of students expressed interest in the course. However, the enrolment was limited to twelve students. This was done for several reasons. First, we wanted close interactions between students taking the course, the instructor and teaching assistant (TA). This was especially critical since every student team was given the freedom to develop their own micromixer design, thus needing additional guidance outside the scheduled hours. Second, we were limited by the number of software licenses available to run the multi-physics modeling software CFD ACE+ (ESI-CFD Inc., Huntsville, AL) used to design and model the micromixers. Each student in the course was given a license, which permitted off-hours access and allowed student teams to spend additional time on their designs beyond the scheduled laboratory periods. Finally, we were limited by the available equipment to operate the lab. An inverted epifluorescence microscope (Olympus IX71) with a 12-bit CCD camera (QImaging Retiga EXi) was purchased with the NSF CCLI funds. Each student team was scheduled for blocks of time on the instrument to perform laboratory procedures. In addition, the use of the University of Cincinnati's state-of-the-art clean room facility to prototype the designed micromixers presented a challenge due to safety concerns arising from a larger student group.

The twelve students enrolled in the course represented both degreed programs within the Department of Electrical and Computer Engineering and the Department of Chemistry from the College of Arts and Sciences. Four students were female. Three students were undergraduate, nine were graduate. The students were divided into four teams of three, each including an undergraduate student. Working in teams allowed graduate and undergraduate students to work together to conduct laboratory assignments. The collaborative efforts provided opportunities for team members to learn from each other. Thus, students from differing backgrounds were able to teach one another. Each team used the modeling software CFD ACE+ to design and simulate their microfluidic mixer and characterize them experimentally using fluorescence microscopy. At the end of the term, in their seminar-style presentation, each student team discussed their device design, and compared experimental results with simulations.

The teaching style of the instructor included the use of PowerPoint presentations and a whiteboard. An interactive Web-based Blackboard e-Education platform operated by the University of Cincinnati was used to host the course materials (*e.g.,* PowerPoint slides, research papers). The system permitted quick and effective communication with students in the class through e-mail and announcements, and provided students with feedback on their lab assignments. To supplement these materials, students read journal articles related to the topics covered in class. The strategy was to expose students to the state-of-the-art and give them a flavor of what happens in the research environment.

Laboratory Modules

The course laboratory sessions were divided into three modules. These are detailed below:

Module 1: Modeling (weeks 1-4). In this module (see Table 2), students were introduced to the CFD ACE+ modeling software and learned the basics of microfluidic simulation through step-by-step tutorials we developed. CFD-ACE+ is the most advanced multi-physics software commonly used for accurate analysis of MEMS and micro/nanofluidic devices. It enables coupled simulations of fluid, thermal, chemical, biological, electrical and mechanical phenomena. CFD-ACE+ is currently used by over 400 major organizations worldwide, including DARPA and NASA. More information is available on the company website at http://www.cfdrc.com/serv_prod/cfd_multiphysics/software/ace/. This software package was selected due to its advanced capabilities, rapidly increasing popularity in industry and academia, and easy-to-use graphical user interface.

The tutorials initially helped students to model flows through simple geometries, such as the Y-mixer, followed by more complex geometries, such as the Tesla mixer,[21] and analyze the results to calculate mixing. In this module, students not only learned the basics of CFD ACE+ software through a series of tutorials, but used this knowledge to model their own designs. At the end of this module, students became comfortable using CFD ACE+ and generate a microfluidic device design they will fabricate and characterize in the subsequent lab modules. The University of Cincinnati College of Engineering computer laboratory facilities were used for this portion of the course.

Working in teams, students investigated effects of microchannel geometries on mixing. In the first 40 min of each lecture during the 3rd and 4th weeks, each student team made a 10 min presentation on their findings in the previous lab period. This permitted each team to receive feedback and guidance from the instructor and TA, as well as comments from other students enrolled in the course. This also facilitated all of the student teams to work together, helping each other with many useful discussions, and created an environment conducive to learning. By the end of the fourth week, the teams were asked to complete their final designs and submit a three-page report summarizing their findings.

Module 2: Device Fabrication (weeks 5-8). In this module (Table 2), students designed masks for microfabrication and then fabricated their micromixer designs. AutoCAD was used for mask layout design. All the four micromixer designs were incorporated in a single mask and sent out to an external vendor to make a high resolution chrome mask plate in the fifth week. The sixth week lab was conducted in the cleanroom where the students were a given a demonstration of the master fabrication procedure by the course TA using SU-8 lithography. Following the fabrication, the students spent the next week in a traditional laboratory learning the polydimethylsiloxane (PDMS) casting procedures. Each group was given one master Si wafer with their microchannels patterned on it. After PDMS casting, the groups then peeled the PDMS molds from the master and characterized their designs using conventional microscopic techniques. During the next laboratory period, the students were given a demonstration of PDMS-glass bonding process, to complete the microchannels, using a reactive ion etcher (RIE) commonly found in most cleanrooms. At the end of this module the groups were asked to submit a three-page report summarizing the fabrication process along with images of their fabricated designs. Students also gained first hand experience with fabrication of microfluidic systems and fabricated designs simulated in Module 1.

Table 2. Lab sessions of the "Micro/Nano Fluidic Biochip Laboratory" course.

No.	Lab	Description
1.	Microfluidic modeling I: CFD-GEOM	The students familiarized themselves with modeling with the CFD-ACE+ software using tutorials on how to model and mesh their designs. A TA guided them through the tutorials and was available for questions and trouble shooting.
2.	Microfluidic modeling II: CFD-ACE+/VIEW	The groups simulated the models using the CFD-ACE+ software. The parameters were given to the students and the simulation viewed with the CFD-VIEW. The groups were then taught how to visually represent their models and how to analyze the results.
3.	Device Modeling I	Each group chose a design to model and fabricate. The groups investigated the basic working principles and began their CFD modeling and simulations of the device within the operational scenario.
4.	Device Modeling II	Additional time to complete designs and analyze modeling results.
5.	Mask Design in AutoCAD	During the course of this session the students used AutoCAD to layout mask plates for the respective device geometries. At the end of the lab session each group was required to submit their AutoCAD designs in either the .dwg/.dxf format which was then checked by TA and sent out for fabrication.
6.	Fabrication I: SU-8 Master *(Cleanroom)*	The students worked in the cleanroom for this part of the class. SU-8 photoresist was patterned on clean silicon wafers using UV-lithography. The TA guided the students through the entire process of fabricating the SU-8 masters for the various microfluidic device designs.
7.	Fabrication II: PDMS Casting	The groups cast PDMS over the photoresist molds from the previous week. The cured PDMS molds were then be peeled and measured using optical microscopy.
8.	Fbarication III: Plasma Bonding and Packaging *(Cleanroom)*	The students worked in the cleanroom again. The PDMS molds were cleaned and holes for inlets/outlets were carefully punched. The PDMS molds were then be bonded to glass microscopic slides using plasma bonding to complete the microfluidic devices.
9.	Device Characterization	Devices were packaged into the custom device Plexiglas fixture having in-built tubing for inlets/outlets. Fluidic characterization was carried out using a dilute solution of fluorescent dye and water on an inverted epi-fluorescence microscope.
10.	Data Analysis	The experimental data from the previous class was analyzed using *ImageJ* software and compared with the modeling results. Additional time was used for further microfluidic testing as necessary.
	Final Report and Presentations	Results were presented in a final report and presentation during the finals week.

Module 3: Characterization (weeks 9&10). In this final lab module (Table 2), students packaged and fluorescently characterized the microfluidic devices fabricated in Module 2. The TA first demonstrated how to measure device behavior, while students themselves performed measurements on the microfluidic systems they fabricated. The devices were fixed in the microfluidics device holder specifically developed for rapid characterization of microfluidic devices[22] to connect tubing for inlet and outlet. While testing, one of the syringes was filled with a fluorescein solution while the other with water. The syringe pump was set to the flow rates corresponding to the modeling conditions and images of the microchannel at various positions downstream were captured for each design. Following this, the teams were given time to analyze the images and calculate mixing.

Overall, the course exposed students to polymer microfabrication technologies that are beginning to dominate microfluidics, as previously discussed. The course lectures complimented the laboratory sessions and included discussions of the microfluidics theory, microfabrication, and the practical issues encountered in the lab. This course provided students with the skill set they will need to pursue graduate work or a career in industry.

Results of Course Evaluation

The first offering of the course in the spring of 2006 was a considerable success. All students enrolled in the course participated in the course evaluation and responded to anonymous questionnaires at the end of each module. Questionnaires used a five-point Likert scale (5 being a *Strong Yes* and 1 being a *Strong No*). The means and standard deviations of the questionnaire responses are summarized in Table 3. The means range from 4.0 to 4.8, with relatively low standard deviations, indicating highly positive ratings. These results indicate that each module was successful in achieving its objectives.

A second method of assessment was provided by an anonymous course evaluation form at the end of the course employing a series of open ended questions addressing student experiences. All twelve students enrolled in the course responded to the evaluation on the last day of the course. A representative sampling of student responses to key questions has been summarized below. This questionnaire yielded very positive results overall.

In response to the question "What was the best aspect of the course?" students responded:

- *"We were given a specific problem to solve, thus we took ownership of the knowledge needed to find the best solution. The fact that we worked in teams and had a friendly competition with other groups also made it fun and interesting."*
- *"Hands on experience in the fields that [we have only discussed in other courses] is a very good thing."*
- *"We can use the simulation software, and practice the software with our own design…"*

In response to the question "What part of the course would you suggest improving and why?" students responded:

- *"It would be better of there is any way to fabricate microchannel [independently] without TA"*
- *"More time in lab; need more time with [TA] on device fabrication; expand course into two quarters: quarter one would be theory of design, quarter two would be fabrication and testing."*

A third method of assessment was provided by an informal interview of the entire class conducted by Dr. Cathy Maltbie of the Evaluation Services Center of the University of Cincinnati. This provided students with a comfortable forum with a third-party mediator to

Table 3. Summary of Questionnaire Results (5 is a Strong Yes, 1 is a Strong No; $N = 12$)

Question	Mean	Standard Deviation
Module 1: Modeling (weeks 1-4)		
Where the modeling tutorials sufficiently detailed?	4.6	0.5
Where the modeling tutorials relevant?	4.8	0.4
Did you have sufficient time to complete the tutorials?	4.6	0.5
Did tutorials provide enough background to allow you to work independently on your design?	4.4	0.8
Did you have enough time to model your design?	4.5	0.7
Was software available to you in the lab outside class hours?	4.6	0.9
What is your comfort level with this module?	4.3	0.7
Module 2: Device Fabrication (weeks 5-8)		
Did the fabrication protocols provide sufficient process detail?	4.8	0.4
Where the fabrication protocols relevant?	4.7	0.5
Do you understand the mask design process?	4.9	0.3
Did you have sufficient time to complete the mask design?	4.8	0.4
What is your comfort level with this module?	4.6	0.5
Do you feel sufficiently trained now to carry out the fabrication process by yourself?	4.2	0.8
Module 3: Characterization (weeks 9&10)		
Was the microscope demonstration sufficiently detailed?	4.3	0.7
Was the microscope demonstration clear?	4.3	0.7
Did you have enough time on the microscope to perform your device characterization?	4.2	0.7
Was the data analysis tutorial sufficiently detailed?	4.0	0.9
Was the data analysis tutorial clear?	4.2	0.8
What is your comfort level with this module?	4.3	0.7

provide their comments. Again, students expressed extremely positive comments, such as one below:

- *"This was one of the best classes I ever took, because I was able to see how device would be designed, simulated, fabricated and characterized. You could actually see something you were just reading about earlier."*

Conclusions

All of the student comments collected throughout the course in the form of ratings, questionnaires, and informal interviews support the conclusion that the course was a considerable success. In particular, students valued hands-on experience in the laboratory which is not provided to them in other MEMS courses. Specifically, the modeling aspect of the course gave them the opportunity to "learn by doing" as they explored multiple device designs. Hands-on work also allowed for testing the boundaries of possibilities, and therefore resulted in deeper understanding of the material. Some students even suggested splitting the course into two quarters to provide more hands-on experience. Both undergraduate and graduate students indicated that they appreciated the opportunities to see and experience "state-of-the-art" research in the classroom.

All three methods of assessment will be used to again evaluate the upcoming offering of the course in the spring of 2007. The initial success of our pilot program is encouraging, and suggests that the format developed in this course could be adapted to introduce engineering students to advanced multidisciplinary research topics.

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