A Three-Course Sequence in the Engineering of Fluorescence-Based Micro Total Analytical Systems

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Abstract *¾ We describe a three-course introductory sequence in fluorescence-based microanalytical systems. The series is aimed at beginning graduate students and advanced undergraduates who have an interest in MEMS and microelectronics. The first course is introductory with the objective of educating students in the basics of silicon microfabrication. Devices are produced. This course is more project- and product-oriented, with a strong technology component building on the first course. The second course has been offered twice, with drastically different formats as described in the article. The third course has been offered once. The ultimate goal of this course is to produce students capable of leading a team to produce a product. The objectives, methods, and assessment of each course are described.*

Index Terms ¾ Fluorescence. MEMS. Micro total analytical system.

I. Introduction

We have developed a three-course sequence of interdisciplinary graduate courses intended to give participants a hands-on introduction to the design and fabrication of Micro Total Analytical Systems (μTAS). The curriculum differs from previous MEMS-focused efforts [1] in that it empahsizes fluorescence-based sensing techniques. The curriculum is designed to take advantage of cutting-edge research into UV light-emitting diodes and photodetectors being carried out in the Jack Maddox Laboratory at Texas Tech University (TTU). The primary goals of the sequence are to: 1. Graduate engineers and scientists well founded in the issues and methods important to the burgeoning microelectromechanical systems (MEMS) area, with relevance to education in microelectronics, and 2. To prepare students to carry out research in scientifically interesting and technologically crucial areas relevant to microsensing. A team of faculty from the departments of Electrical Engineering, Mechanical Engineering, and Physics teach the classes, with significant input from faculty in Chemistry and Biology. Although the courses are not strictly or solely devoted to MEMS, the course sequence is locally referred to as MEMS 1, 2, and 3 and we retain this notation for this paper. While originally intended for first-year graduate students, the sequence has proven popular with juniors and seniors as well. In fact, it is proving to be a valuable tool for convincing our best engineering undergraduates to pursue a higher degree.

We structure the remainder of this paper as follows. Each course in the MEMS sequence is discussed. The format for the discussion is Objective, Methods, and Assessment. The latter refers to how we assessed the students in the courses. We then assess the overall success of the sequence.

II. Curriculum Development – MEMS 1

The first course in the sequence is officially titled *Introduction to MEMS and Microfluidics*. This course has been given a permanent course number in Electrical and Mechanical Engineering, and in Physics, and will be available on a regular basis (at least biannually, and preferably annually). It has been taught three times to a total enrollment of 41 students. Enrollment had to be restricted each semester to avoid overuse of the available laboratory. This offering is intended as a broad-based introduction to the tools of microfabrication for microelectromechanical systems (MEMS) and microfluidic systems. A textbook [2] and numerous literature references [3]-[5] are used for this course. It is designed to serve either as a stand-alone introduction to the field, or as the basis for further advanced study. The main objective of this course is to develop *core processing competency*. This entails knowledge of, and facility in, basic fabrication technologies. The emphasis is on silicon processing, including photolithography, thermal oxidation, evaporation, lift-off, and etching of metals and oxides. Also introduced are polydimethylsiloxane (PDMS) casting using ultra-thick negative photoresist molds, bulk silicon micromachining, doping and spin-on polymer coating. All students must learn and abide by safe laboratory practices; a policy enforced if necessary by dropping violators with a failing grade. This course is also used to develop oral communication and presentation skills. Finally, students are introduced to some fundamental issues in sensor design.

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The course is based on a series of interdisciplinary projects. Topics range from a chemoresistor for humidity sensing to a bulk-micromachined MEMS accelerometer. Students work in teams of three or four, with if possible at least one member each from the departments of Physics, Electrical Engineering and Mechanical Engineering. Figure 1 (upper) shows an array of student-fabricated humidity sensors prior to cleaving and packaging. Figure 1 (lower) shows an array of bulk micromachined accelerometer proof masses. Students perform most processing steps themselves, with critical steps such as photolithography repeated until each member of the team has had a chance. Laboratory staff members operate some equipment—such as the oxidation furnace and e-beam evaporator—but the student team is required to be present when their samples are loaded, processed and unloaded. Hands-on participation, when safety permits, is encouraged. Teams describe their project outcomes in joint presentations. These are required to include an outline of the underlying principles of the fabricated device, with references to archival journal publications. Presentations are videotaped, and made available to students who wish to improve their speaking style.

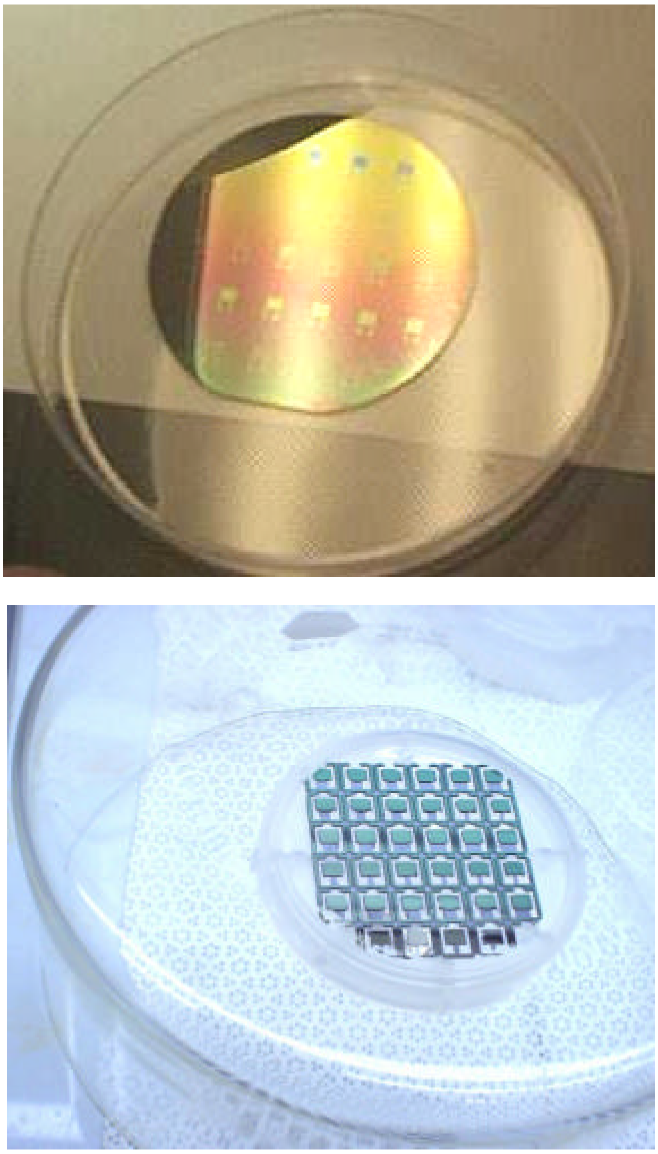


FIGURE 1.
2 inch wafers showing:
Upper panel: An array of microfabricated humidity sensors. Lower panel: An array of bulk micromachined silicon accelerometer proof masses.

The laboratory instructor (either a professor or a postdoctoral research associate) who supervises and assists with all projects assesses the students' progress in developing laboratory skills. To date, all students have completed the course no worse than competent at basic photolithography. Some have become expert in both the basic processes and such advanced topics as PDMS fabrication. Student presentations allowed evaluation of their understanding of device principles. Both laboratory skills and presentations are used to rate effort and teamwork. Not surprisingly, students with a record of academic success also excelled in the ability to research, digest and explain underlying device physics. However, students with less traditional skills were also able to display their strengths. For example, one resourceful student calibrated his team's humidity sensors using equipment purchased at a local Radio Shack and a tea kettle. Until then the standard procedure was just to breathe on the sensor and watch it respond.

The effectiveness of the course as a whole was assessed using responses to an extremely broad test given to the class before taking, and after completing, the course. The evaluation question was as follows:

> *"Describe a MEMS or microfluidic device. This may be an actual device, or one of your own imagining. What makes it a 'micro' system? How is it fabricated? What benefits accrue from making this device small? What challenges does this scaling present?"*

Pre-course testing showed that the students were largely ignorant of microfabrication and microdevices. Post-course, many of the students simply described the lab projects. However several showed that working at the microscale had sparked their imaginations:

- "My dream is to make a micro-condenser. In the present world, every system goes into micro-scale, due to the cause of vibrant/other effects, temperature may be built up in the device. We can use the micro-condenser to cool it down. The applicant for this may be in the computer industry/semiconductor industry."
- "I would imagine about microfluidic device that can physically separate chemical substances. Having very

small width, length, and in bulk. I think that having such a device we can separate urea from blood of kidney-failed people. We replace their kidneys by such a device. But making such a device will not be easy to many channels and so tiny in a small space. In addition to this mass separation system, this also takes space. But it is practical if we think of the size of the kidney. So this device can be implanted instead of kidney."

- "I think MEMS have a very bright application in medical devices, since it can be made small enough to put into human body without any sense. Like if people have stomach problems, there will be a sensor you can put into the stomach, then the sensor can feel the acidity of the liquid in the stomach or something else. That's wonderful. I think the material is important and in an idea situation, the sensor can exist for seventeen days, then it can resolve and goes away."

Since this first course was not intended to address sensor design, the generality of these responses is not disappointing. Rather, it shows that the material covered had opened these students to new possibilities, and spurred them to continue on in the sequence.

III. CURRICULUM DEVELOPMENT – MEMS 2

A. DEVELOPMENTAL MATRIX ORGANIZATION

The main objective of this course was to learn the necessary experimental techniques needed for μTAS. Then, the students integrate these techniques to produce a functional device. Another objective of the course was that the students should be able to work in a team with minimum supervision and able to make decisions regarding design and implementation of the processes necessary to create a functional device. Supervision was done by faculty in the lab, but on an as-needed basis.

TABLE 1.

Project grid used the first time MEMS 2 was offered.

Technology 1	Technology 2	Technology 3	Technology 4
Optics	PDMS	Structural Coatings I	Bonding I
Intensity Meas.	Glass and Silicon	Coatings II	Bonding II
Spectroscopic Meas.	Pumps and valves	Advanced Etch	Antigen Binding I
Systems Integration	Mixers and Injectors	Data Acq. and Control	Antigen Binding II

The MEMS 2 class utilized a project grid as shown in Table 1, designed to allow students to systematically rotate through a number of different sub-projects in the development of fluidic-based microanalysis systems. The grid is arranged into four columns that correspond to a broad topic. The rows describe the milestones of the projects, where as, the columns describe the technologies needed to implement a functional device by the end of the semester. Column 1 projects are optics based, column 2 involves fabrication of microfluidic structures, column 3 deals with specific chemical processing, and column 4 deals with both chemical and biological binding. The students assigned to initial teams were given a project from row 1. They were given three weeks to complete the tasks and then, they were moved diagonally on to the next row. This gave the students the opportunity to do a project in each of the different topic areas. The students gave presentations after each module and handed off the projects to the subsequent groups. This required that detailed passdown meetings and documentation were provided to the group taking over to ensure continuity and a minimization of redundant work. The ultimate goal of the students was to create a μTAS designed to: 1. Determine the concentration of fluoresceine in an unknown using fluorescence intensity. 2. Determine metal salt concentration in an unknown using chemiluminescence. 3. Determine epithelial to stromal cell ratio in an unknown based on fluorescence.

This course was designed by a team of five faculty from the Mechanical Engineering, Physics, Electrical Engineering and Biology. Faculty provided their expertise in the areas of microfluidic channel fabrication, pumps and valves, channel coating, wafer bonding, optical measurements and biological systems.

In column 1, the team's goal was to design an optical set-up capable of performing spectroscopic measurements. This group used an existing optical microscope and coupled it with a CCD camera and a spectrometer using fiber-optics and LabView programming to create an optical detection system. The system was tested for light detection using various microfabricated systems, e.g., liquid core waveguide (LCW) channels. In a LCW a low-refractive index (n_{LCW}) tube confines a water-based fluid. Since water has $n < n_{LCW}$, the water serves as a waveguide. In the second column, the students successfully microfabricated channels in PDMS, glass and silicon. They were able to prepare peristaltic micropumps in PDMS. They designed and implemented peristaltic pumps, and tested the pumps by measuring flow rates at several pump frequencies. In the third column, the task was to coat microchannels in PDMS, glass and silicon with Teflon AF [6] or nanoporous silica to create a liquid-core waveguide. Since Teflon AF sticks to almost nothing, the students developed surface modification technologies to improve Teflon bonding. The Fig. 2 shows the cross-sectional SEM of Teflon-coated microchannel in silicon. A plasma-deposited amorphous fluorocarbon (a-FC) was used

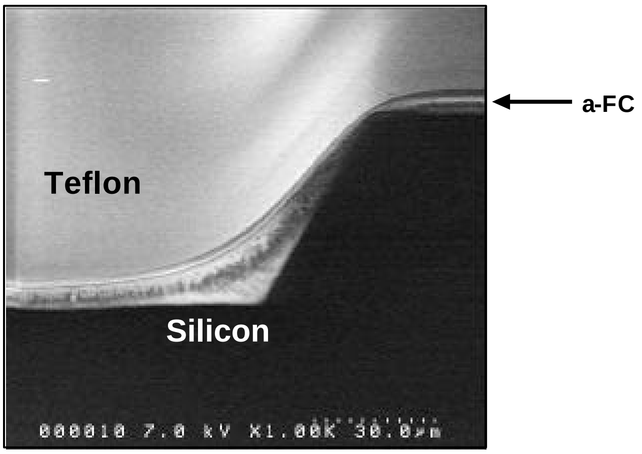


FIGURE 2.
Cross-section SEM of a-FC and Teflon AF coated microchannel.

to improve adhesion of Teflon to silicon. Nanoporous silica was prepared by sol-gel technique.

In the fourth column, the students performed various wafer bonding experiments in order to create sealed microchannels. They performed bonding of PDMS to glass by modifying the PDMS surface by oxygen plasma, thermal glass to glass bonding and anodic bonding of silicon to glass.

Finally, the students used these channels to experiment with capillary-based immunosensor technology. This involves integrating fiber optics and elements of the body's own immune system for a wide variety of applications. With this technology, a sensor can be designed to detect virtually anything for which the human body can create an antibody. For this experiment, channels in PDMS were bonded to Si wafer by oxygen plasma treatment. Since antibodies cannot bind directly to the PDMS surface, the surface was chemically modified. Figure 3 shows fluorescence tagged antibody bonded PDMS channel.

Oral presentations were the primary assessment tools and the evaluation was similar to the one described for MEMS 1. The MEMS 2 students were also assessed by judging the reproducibility, quality, functionality, elegance, simplicity, and appropriateness of the final process and product they made. Teams were judged based on the use of published research papers in design and implementation of the projects, written and oral parts of the presentations and the process by which they transferred the technological knowledge to other groups.

B. CLIENT/LEADER/TEAM ORGANIZATION

The second time we offered MEMS 2, we altered the methods significantly. We are using a novel mentoring scheme in which student teams in the second course of the sequence are directed and supervised in the laboratory by a team leader from the third and final course. The primary motivation for the changes to be described was that we now

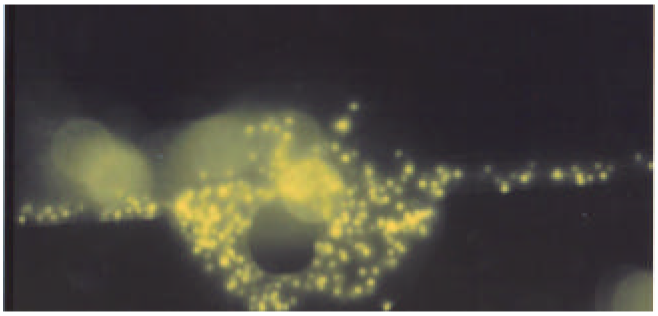
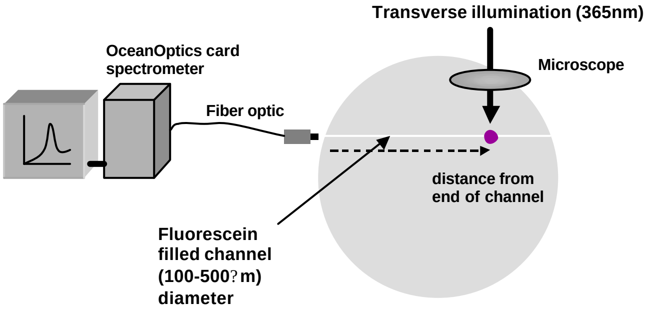


FIGURE 3.
Fluorescence tagged Cells bound to the inside of a PDMS channel.



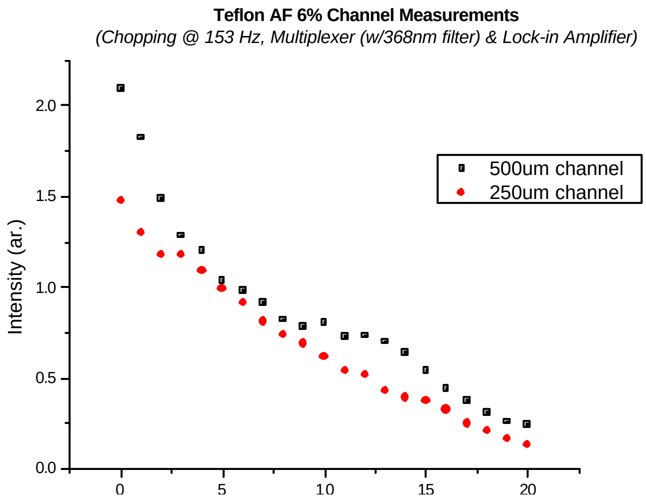


FIGURE 4.
Basic test setup for LCW experiments. Dependence of fluorescence intensity on separation between illumination source and detection. To be published.

had a set of students who had taken MEMS 1 and 2, and we anticipated strong peer instruction. We structured this course with a Client (or customer), Technical Team Leader, Team (CLT) relationship. The "Clients" were the course instructors, the Team Leader was a MEMS 3 student (to be discussed in the next section), and the Team was a group from MEMS 2. With this structure, the Clients specified a desired analytical system(s) with specific goals. The system architectures were to be guided by the optical illumination/detection scheme employed. These detection schemes, listed in Table 2, were studied preliminarily during the first iteration of MEMS 2 or as part of ongoing research projects.

TABLE 2.
Basic optical detection schemes assigned for MEMS 2 & 3.

DETECTION SCHEME	Embedded waveguide (commercial tubing)	Deposited waveguide (proprietary waveguide material)	Etched silicon microchannels
MEMS 2 Team composition (EE/ME/Phys)	0/2/1	1/0/1	2/0/0
MEMS 3 Team Leader (Major)	1 (ME)	1 (EE)	2 (EE)

The most important operational difference for the MEMS 2 Teams was that their principal contact was a peer. This provides an interesting advantage due to the lack of barriers between the Leaders and Teams. This is in contrast to barriers, real or perceived, between professors and students in courses with traditional structure. The key subject difference in this structure is that the teams are responsible for every technology necessary for their device, and do not transfer between device architectures (as in the preceding setup). Outside of the detection scheme assigned by the clients, the only other requirements specified were capabilities needed for the end users, which were the same as in the previous MEMS 2 course (fluorescence-based concentration, metal salt concentration, cell mixture determination).

The requirements were communicated to the Team Leaders by the Clients. Each Team Leader had the primary responsibility of communicating with their Team, although meetings were held in which all the instructors were available for clarification. The MEMS 2 Teams were required to make presentations to the Clients on a regular basis. The goals of these presentations were the same in the other cases discussed here, with the additional goal of checking for adequate communication between Team Leaders and Members. The Team Leaders were invited to attend, but not required. Feedback was given directly to the Team and also to the Leaders.

Assessment of the CLT structure was based on several factors. Individual team members and entire teams were given lab practical examinations (site visits) by the Clients. For example, automation needs motivated us to require rudimentary to functional knowledge of LabView. Individual practical exams were given following a reasonable period for the students to gain this knowledge. Presentations were used as an important guide for our assessments. Team Leaders were also asked to thoroughly assess Teams and Team Members. The specific questions asked on the assessment were:

1. (Assess Member's) Fabrication skills and laboratory contribution.
2. Analytical skills and design contribution.
3. Reliability, attitude, attendance, and team morale contributions.

These assessments were passed on to the Teams, following filtration by the instructors, to insure that tactful and constructive criticism were fed back. Positive comments included: "Always wanted to be involved and help out." Conceptual problems were also noted: "… was always willing to contribute to processing, but didn't understand the process parameters."

Instructors were interested in results. While all the teams succeeded in building functioning test devices, the application goals were never met. Test data from a deposited waveguide device are shown in Fig. 4. The data establish waveguide properties and discrimination against the illumination source. A publication on this project is in preparation [7].

IV. CURRICULUM DEVELOPMENT – MEMS 3

MEMS 3 has only been run in the CLT model with MEMS 2 Teams, as discussed in the prior section. This course was for students who had already completed the MEMS 1 and 2 courses. The primary objective of the course was to develop engineering team leadership skills. At this stage, we expect technical competency. However, we also expected the innovative design of new devices. In turn, each Teams was to handle all issues of fabrication and data collection with consultation and problem solving sessions from the Leaders. We also expected Leaders to help locate relevant literature, and help Teams understand literature as needed.

The methods applied have a strong overlap with the preceding discussion on MEMS 2. However, we expected the Team Leaders to do the primary design and integration work for their microsystems. The initial design was proposed to the Clients for approval or recommended/required change. The Team Leaders had to communicate "up" and "down" the technical ladder. Team Leaders were responsible for monitoring the Teams in the lab, but were encouraged to refrain from doing technical work for the Team. It was also their responsibility to check the Team presentations for content, accuracy, and scope.

Team Leaders were assessed through written final project reports, based on the outcomes of the projects, based on the Team presentations, and based on their abilities to utilize Team members in their respective strength areas. The

Teams also evaluated the Leaders based on the following instrument, which is intentionally open ended:
1. (Team Leader) Provided technical guidance, supervision, and training.
2. Motivated team projects and explained the “big picture”.
3. Set realistic goals and made optimal use of team manpower.
Mostly, responses were numerical on a 1-10 scale, and were high. Written comments on Team Leaders included: “I learned more from him than I ever have in a classroom setting.” This is precisely as expected. The negative comment on one Team Leader was echoed by several Members: “He spent minimal time with us.”

As with the MEMS 2 students, we were interested in the success of the project as measured by producing a functioning device. We were also interested in assessing the creative input of the MEMS 3 Team Leaders with regards to design and problem solving. To do this, the course instructors met and prepared nominal architectures addressing each device goal. These were not revealed to the students. We compared the designs produced by the MEMS 2/3 teams to these baseline designs in terms of functionality, elegance and manufacturability. We found that student teams produced extremely innovative solutions. For example, one group added integrated transmission/ absorption spectroscopy capabilities into their unit, to complement the required fluorescence measurement. We concluded that the MEMS 3 Team Leaders had developed strong independent design capabilities.

VI. DISCUSSION AND SUMMARY

The MEMS 1 course was highly successful at providing a good general background to Texas Tech students interested, or potentially interested, in MEMS, microelectronics, or research in the Maddox Laboratory. Success stories include one graduate currently working in the MEMS industry, one student who is now working in microelectronics industry, one student in an internship in a national lab, three students engaged in internships in microelectronics, and ten students currently involved in research.

The two MEMS 2 courses were also successful in their different formats. The technology matrix organization was extremely effective at educating students to attack problems from a core-technology approach and to work in teams. However, the inherent shuffling between product goals resulted in no products. These students were highly capable in the lab, following this course, and several of them followed up as team leaders in the next semester. The Client/Leader/Team organization to MEMS 2 and 3 was likewise successful at training the students in the methods needed to produce a product. Despite the fact that no final product emerged, each team brought their devices to the point of preliminary testing within the semester timeframe. Students in the MEMS 2 course showed marked improvement in their team coordination, presentation, and processing skills. Several of the MEMS 3 students learned to function effectively as team leaders. One might easily anticipate this structure to be hands-off for the instructor. To the contrary, it required a significant amount of effort from the faculty to insure smoothness of operation and for assessment. Peer instruction was considered the unknown factor, since we did not know how this would work within a course structure. From experience with research students, we do know that peer instruction is highly effective in the laboratory setting. We found this instructional method to be highly effective, and students echoed these findings. Obviously, course continuity is essential for this organizational method (i.e., one must have students at the senior MEMS 3 level to conduct the course this way). With this in mind, the obtained benefits of peer instruction can not be overstated

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