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## **AC 2012-3683: MICROFLUIDICS IN ENGINEERING, SCIENCE, AND TECHNOLOGY EDUCATION**

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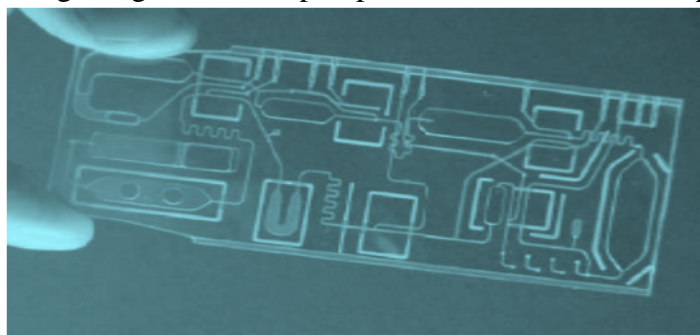
# Microfluidics in Engineering, Science, and Technology Education

## Abstract

We are integrating microfluidics laboratory experiments and projects into the Engineering Technology curriculum and high school science classes with the support of a Type 1 NSF TUES program. Microfluidics provides miniaturized fluidic networks for processing and analyzing liquids in the nanoliter to milliliter range. Microfluidics ‘lab on a chip’ technology offers many opportunities for teaching students CAD/CAM, rapid prototyping and microfabrication, fluid mechanics, heat and mass transfer, instrumentation and control, optics, sensors, robotics, automation, machine vision and image processing, and nanotechnology. The following activities, laboratory experiments and projects are described here: 1) the design, rapid prototyping, and characterization of microfluidic chips, 2) robotic manipulation and machine vision of ferrofluids in microfluidic channels, 3) the development a PID microcontroller polymerase chain reaction (PCR) system for medical diagnostics, and 4) microfluidic chips with multicolor LEDs to observe phototaxis (light-directed movement) of algae under a low-power microscope.

## 1. Introduction and Overview

Microfluidics is the miniaturization of fluidic processing systems for applications in chemistry, biotechnology, nanotechnology, clinical diagnostics, medical devices, sensors, and small-scale, customized production of materials [HABER 2006; FRANKE and WIXFORTH 2008; OHNO *et al.* 2008]. A fluidic network of channels, conduits, chambers, filters, and manifolds is defined in a substrate ‘chip’ made of plastic, glass, ceramic, or silicon (**Figure 1**). Typical feature sizes (e.g., channel width dimensions) range from 0.1 to several millimeters, with fluid processing volumes in the microliter to milliliter range. Flow control and fluid manipulation can be realized by integrating valves and pumps into the substrate, or implemented externally by interfacing or



**Figure 1:** Microfluidic chip. A fluid network is machined into a in a bonded plastic laminate.

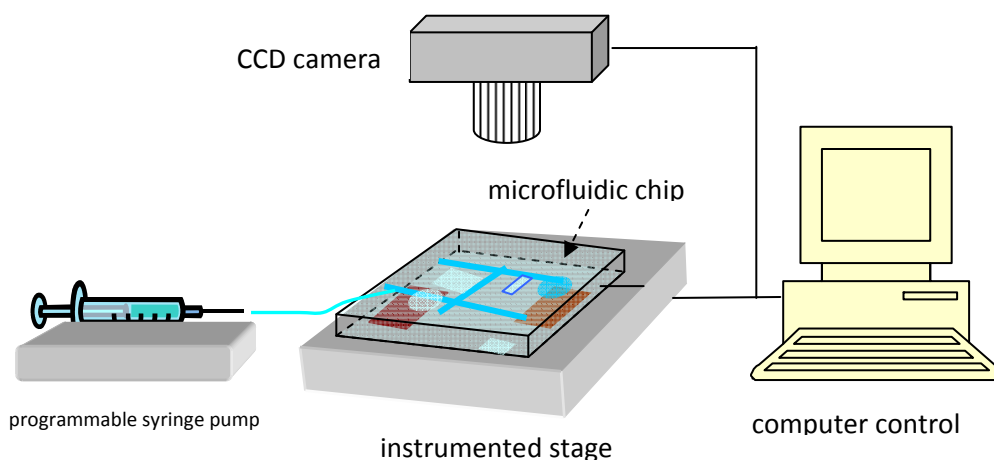
coupling the chip to various components for fluid actuation and flow regulation. To operate the chip, fluids are loaded through inlet ports and pumped through the microfluidic circuit formed in the chip. The chip can be instrumented with various sensors (e.g., thermocouples, pressure transducers, optical fiber probes, photodetectors) along with resistive heating elements, thermoelectric heaters/coolers, and electromechanical actuators such as solenoids. Chips made of transparent

materials can be imaged during operation with a CCD camera, either directly or with the aid of a low-power microscope. Imaging is facilitated by using colored dyes or fluorescent particles suspended in the fluids.

Microfluidics is an emerging technology that merits a prominent place in the engineering curricula due to both its expanding commercial and technical importance, and as a means to apply knowledge and skills from diverse engineering fields into projects with varying levels of sophistication and wide ranging applications. From an educational perspective, microfluidics offers many interesting and ‘real-world’ interdisciplinary engineering case studies, as well as demonstrations of basic science and engineering applications in fluid mechanics, heat and mass transfer, process control, image processing, microfabrication and prototyping, materials science, sensors and actuators, and nanotechnology. We are integrating microfluidics into the Engineering Technology curriculum with the purpose of giving students hands-on experience in applying their foundational knowledge and skills in solving and addressing problems and challenges in areas of miniaturization, medical diagnostics, and process control and instrumentation.

Microfluidics experiments to supplement courses or as topics for Senior Design projects are attractive due to their relatively low cost, small working space requirements, safe operation, and the opportunity to give students projects for which they have complete control from conceptualization through design, prototyping, and testing. Moreover, microfluidics is an effective vehicle to introduce engineering students to biology topics since simple-to-make microfluidic devices can be used for immunoassays, clinical diagnostics and other biochemical assays, cell cultures, nucleic acid extraction, hybridization and amplification; studies of enzyme kinetics and protein binding, cytometry, and cell sorting.

**Figure 2** shows a typical benchtop setup for microfluidic experiments. The chip is placed on an instrumented stage that may include thermoelectric elements for controlled heating and cooling, resistive heaters, thermocouples, and/or pressure sensors that are in intimate contact with the chip. In microfluidic chips capped with a flexible membrane, diaphragm valves, one shot pumps, and peristaltic pumps can be readily implemented using solenoid actuators to flex the membrane. Alternatively, many interesting and useful microfluidics experiments can be done with simpler monolithic (no moving parts) chips using programmed syringe pumps to deliver liquids to the chip inlet ports at a controlled flow rate.



**Figure 2:** Experimental set-up for microfluidics experiments.

**2. Rapid Prototyping of Microfluidic Chips.** Microfluidic chips can be made as laminates of plastic films such as acrylic (PMMA), polycarbonate (PC) and other polymers. These materials are generally low in cost, widely available in thicknesses ranging from 0.1 mm to several millimeters, and easy to machine with a mill or (in the case of PMMA) laser cutter. For



**Figure 3:** Benchtop CO<sub>2</sub> laser cutter for prototyping microfluidic chips.

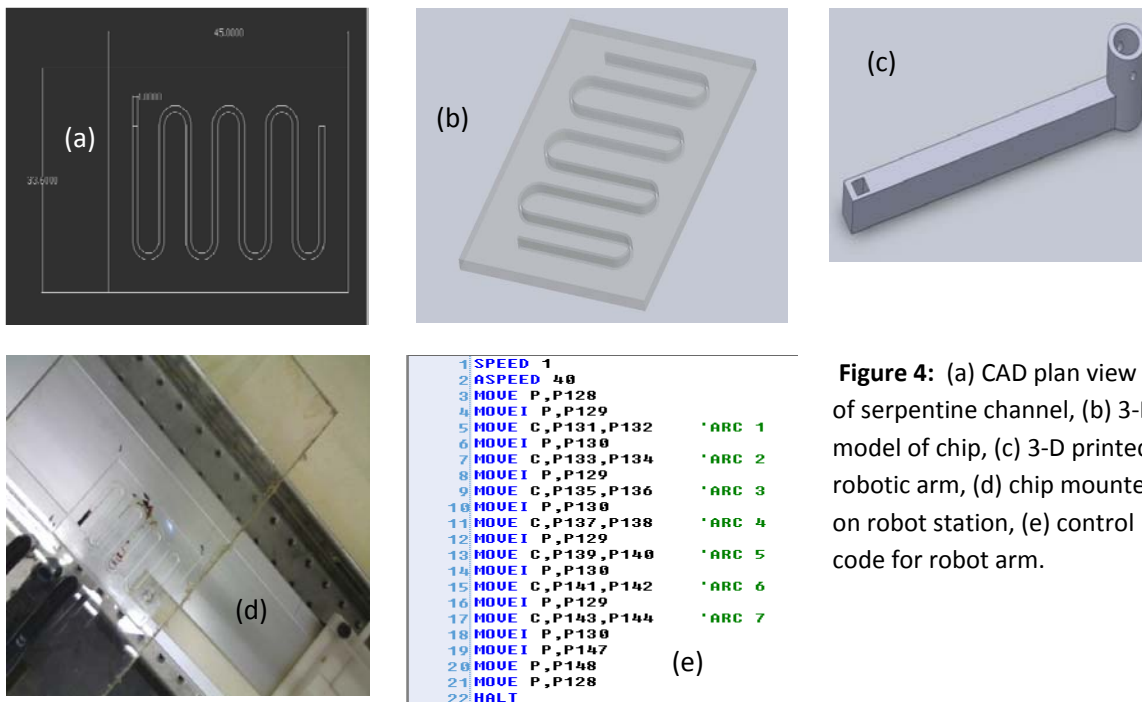
many applications, functional and useful systems can be made as a three-layer laminate comprising a middle layer cut-through with a fluidic network of mixing and reaction chambers, fluid reservoirs, filters, and manifolds interconnected with a conduits. The machined middle layer microfluidic circuit is enclosed by bonding with top and bottom sheets. For our work, a microfluidic circuit is designed using CAD (AutoCAD™ or SolidWorks™) and fabricated with benchtop CO<sub>2</sub> laser (Universal Laser Systems, Scottsdale, AZ Model ULS 350, 50 Watts power, see **Figure 3**). The laminate can be bonded by adhesives, including double-sided tapes that can be patterned along with the plastic stock, solvent bonding, various adhesives, thermal/pressure bonding, microwave bonding,

or ultrasonic welding. The laser machining is characterized by three laser parameters: laser power, laser cutting speed, and pulses per laser distance traveled. These parameters need to be optimized for each material and stock thickness, and will determine the laser kerf (cutting width) which will translate into the smallest feature length possible (about 0.1 to 0.2 mm). The quality of the cut can be assessed with a machine vision system (COGNEX, Natick, MA) where a CCD captured image is analyzed for average width (dimensioning) of channels and their variation (tolerancing), and other geometric features. We are also exploring the use of a stylus roughness measurement or laser light scattering surface roughness measurement on assessing the laser-cut surfaces of chips cleaved along the length of a cut to expose the lateral sidewalls of channels. Such optimization studies are good candidates for practical Design of Experiments (DOE) case studies. More detailed modeling of the polymer laser cutting, as relevant to microfluidics fabrication of microfluidics, is discussed by BLACK [1998], SNAKENBORG *et al.* [2004], and ROMOLI *et al.* [2011].

The bonding process to make the laminate out of the plastic layers is also a useful case study for engineering optimization [TSAO and DEVOE, 2009]. As mentioned above, there are numerous approaches to bonding polymers for microfluidics devices, each with several process variables. Criteria for assessing bonding methods include ease of use, potential contamination (e.g., adhesive compounds), highest temperature compatible with plastic materials or pre-loaded reagents, and most importantly, bond strength as observed by highest pressure the chip can withstand without delaminating or springing leaks and non-blocking of narrow channels as might occur due to flow or deformation of the chip materials or clogging with adhesives and solvent-plastic compounds. Development and optimization of polymer bonding for microfluidic devices provides many instructive projects in Design of Experiments (DOE), Response Surface

Methodology, Taguchi methods and Six Sigma [see for example, HSU and CHEN 2007; UMBRECHT *et al.* 2009].

**3. Robotic Manipulation of Ferrofluids in a Microfluidic Circuit.** As described above, many microfluidic systems utilize micropumps integrated into the chip or external syringe pumps to propel fluids through the microfluidic circuit. Alternative means of fluid actuation and flow control are of interest to reduce the number of external connections to the chip, improve control, and simplify valving or chip design. Ferrofluids are suspensions of magnetic  $\sim 10$  nm diameter nanoparticles suspended in a light hydrocarbon liquid (educational kits are supplied by Ferrotec, Inc., Bedford, New Hampshire). Slugs or boules of ferrofluids can be externally manipulated (without physical contact) in a microfluidic circuit by a strong permanent in close proximity to the chip [PAMME 2006; SUN *et al.* 2007]. As part of the laboratory for Fluid Mechanics, students designed and fabricated an acrylic chip (**Figures 4a** and **4b**) with a serpentine flow channel ( $\sim 1.0$  mm width) along with an ABS plastic robot arm extension (**Figure 4c**), designed with SolidWorks™ and prototyped on a 3-D printer) to hold a neodymium (NdFeB) magnet (K&J Magnetics, [www.kjmagnetics.com](http://www.kjmagnetics.com)) that pulls a 1 to 5  $\mu\text{l}$  ( $\text{mm}^3$ ) slug of ferrofluid through the channel. The magnetic holder was mounted on the arm of a YK250 Yamaha SCARA robot with 4 degrees of freedom. The control code for the robot is shown in **Figure 4e**. The channel was coated with sprayed-on fluorosurfactant (Novec™ ECG-1700, 3M, St. Paul, MN) to hinder the hydrophobic ferrofluid from wetting the acrylic channel, thus remaining as an intact slug rather than dispersing into small droplets as it moves through the channel.

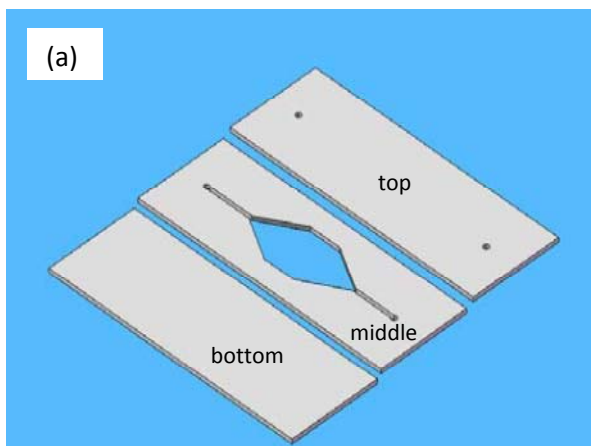


**Figure 4:** (a) CAD plan view of serpentine channel, (b) 3-D model of chip, (c) 3-D printed robotic arm, (d) chip mounted on robot station, (e) control code for robot arm.

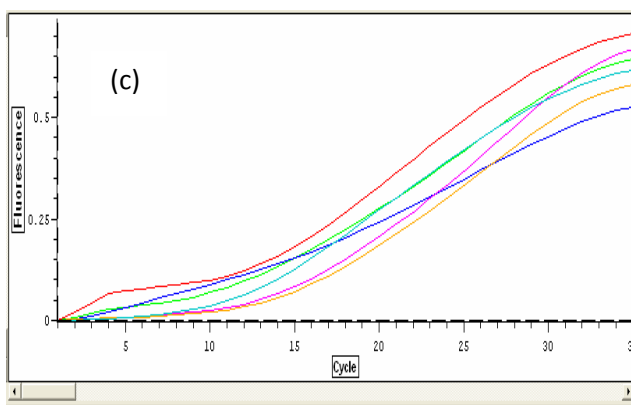
**4. Chip PCR.** The polymerase chain reaction (PCR) is an enzymatic amplification process that makes multiple sequence-specific copies of nucleic acids (DNA and RNA). PCR has had a tremendous impact on biomedical research and medical diagnostics. PCR and analogous

processes serve as basis of much biotechnology including genetic engineering, gene sequencing, and molecular diagnostics. Further, PCR is an important application of microfluidics to biotechnology. Our interest in PCR is three-fold. First, the principles of PCR are easy to grasp and underscore key fundamental concepts in biology such as detection of biomarkers as a diagnostic for disease, sequence-specific hybridization of nucleic acids, kinetics of enzymatic reactions, and fluorescence-based detection of analytes. Second, implementations of PCR rely on precise temperature cycling and temperature control, and serve as an instructive example combining temperature measurement, process control, and regulated heating/cooling. Third, a PCR chamber can function as the main process around which more sophisticated microfluidic systems can be designed to incorporate sample metering, cell lysis, nucleic acid extraction, and multiplex detection of several target analytes. Such a device would integrate all the steps of typical medical molecular diagnostics in a single microfluidic device.

A simple 25- $\mu$ l microfluidic chamber PCR chip was designed and prototyped with the CO<sub>2</sub> laser in acrylic as shown in **Figure 5a**. Double-sided tape (3M) was used to bond the chip. The ‘chemistry’ of PCR has been greatly simplified by the availability of specialized, commercially produced reagents. PCR on a chip can be easily done with lyophilized beads containing pre-measured PCR reagents (e.g., illustra™ Pure-Taq Ready-To-Go-PCR beads (GE Healthcare), along with Control DNA and primers (Takara Biosystems, Madison, WI) that can be quickly reconstituted with water and pipette into the chip. A fluorescent dye (SYTO Green, Invitrogen, Carlsbad, CA) added to the PCR reaction creates a real-time fluorescence signal. The fabricated PCR chip is shown in **Figure 5b** with two small (1.5-mm disc) discs of Whatman (GE Healthcare) cellulose-based FTA™ paper included in the chamber to extract DNA from samples. These DNA-binding materials can be washed by flowing (50% ethanol-50% water) wash solution through the chamber prior to PCR, yielding concentrated, relatively pure DNA template immobilized on the discs for subsequent PCR amplification. This mimics a typical application for a microfluidic point-of-care diagnostics chip where DNA is extracted from a clinical specimen and subjected to PCR. A rising fluorescence signal (see below) constitutes a positive test result. The chip was thermally cycled using a Peltier module powered through an H-bridge circuit controlled by a Accutherm FTC 100 PID controller. Students learned about PID feedback control by programming and tuning the controller to produce the 55 °C (30 sec)-65 °C (1 min) -95°C (30 sec) cycling needed for PCR. An Arduino microcontroller version of the control circuitry is under development as a student project. The progress of the PCR reaction (which indicates the amount of DNA amplified as a test result), can be monitored by measuring the green fluorescence of the reaction excited by a blue LED, see for example **Figure 5c**.



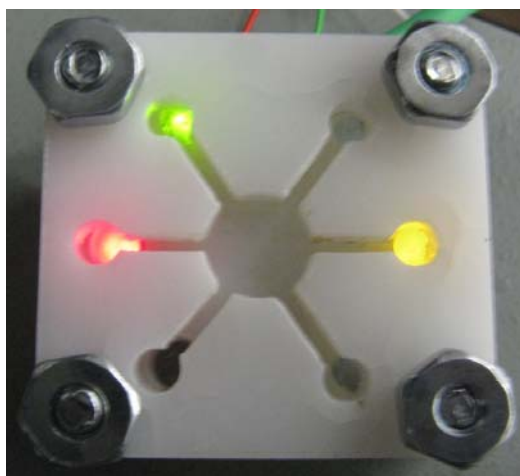
(b)



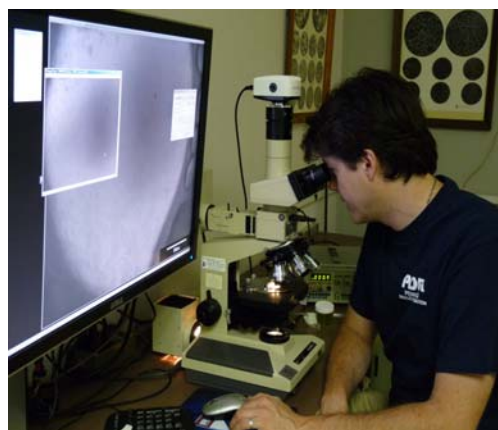
**Figure 5:** (a) CAD design of single-chamber PCR chip; (b) prototyped acrylic (PMMA) microfluidic PCR chip. Chip includes two cellulose membranes for extracting DNA from samples (c) fluorescence as a function of PCR cycle number for six PCR experiments.

**5. Microfluidic Device for Observing Algae Phototaxis.** Microfluidics implementations of microbiology experiments afford better control of cell culture conditions, stimulation/manipulation of cells, and facilitate image processing for cell counting and analysis of cell behavior. We developed a microfluidic observation chamber for use under a low-power optical microscope with CCD camera imaging to analyze the response of algae populations to light. This activity was part of an NSF-sponsored program (Research Experience for Teachers) to host secondary school science teachers in our laboratories with an aim of disseminating current research activities to high school students. This project demonstrated how several topical engineering fields (microfluidics, CAD/rapid prototyping, image processing, and solid-state lighting) could be applied to better study a biological phenomenon. Beginning biology students are typically introduced to the light microscope, cell culture, and the microbiology of simple organisms such as algae, but the treatment is very qualitative. Further, there is perennial interest in learning more about photosynthesis in microorganisms as a possible route to biofuels. In this work, we studied the feasibility of making a microfluidic observation chamber that would enable studying the phototaxis (movement in response to light) behavior of algae under more controlled conditions than is normally possible in a Petrie dish or similar vessel. An acrylic chip (both white and clear layers) was designed and fabricated by the students using AutoCAD and laser machining. 1.5-mm diameter blue, green, yellow, and red display-type LEDs were fitted into wells so that various lighting effects can be realized. The chip shown in **Figure 6** allows students to investigate the effects of pulsed vs. steady light, light color, and light intensity on the

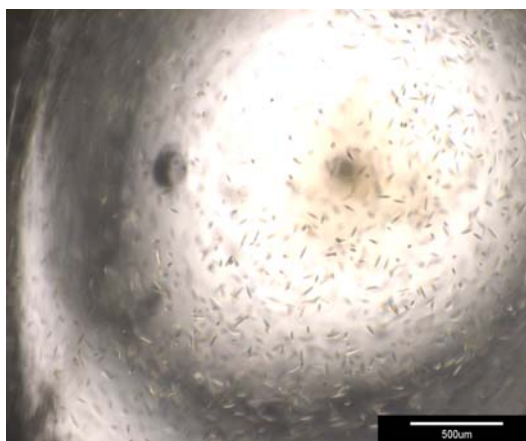
response of algae. Cell cultures of *Euglena* algae were obtained from Carolina Biological (<http://carolina.com>). Because of the large number of cells and the statistical behavior of cell movement, it may be difficult to ascertain trends and rank effects, especially as the device allows many different lighting conditions. Image capture by video or time-lapse still images lets students track the movement of algae over time under various lighting conditions. Students can use *ImageJ* (a public domain, open-architecture, Java-based image processing program, downloadable at <http://rsbweb.nih.gov/ij/>) utilizing common image formats (.TIFF, .PNG, .GIF, and .JPEG) with tools to count cells and perform other parameterizations and feature recognition of captured images. As a result, students can better appreciate the stochastic nature of biological phenomena and the use of image processing and statistical descriptions.



(a)



(b)



(c)

**Figure 6:** (a) A microfluidic cell chamber is fitted with LEDs of several colors which can be pulsed or varied in optical intensity. (b) This 'chip' is designed to fit on the stage of a microscope. (c) An inexpensive CCD camera can be used to monitor the movement of algae in response to light.

**6. Discussion.** There is a tremendous range of applications for microfluidics—from the simplest single-chamber chips to complex networks of fluidic components interfaced with a wide range of sensors and MEMS devices. Microfluidics is truly a microcosm for many fields of science, engineering, and technology. Almost any benchtop chemistry or biology procedure is a good candidate for microfluidics implementation. Moreover, we believe microfluidics is an effective way to introduce engineering and technology students to biomedical engineering.



Engineering technology students, with their skills in CAD/CAM and prototyping, instrumentation, sensors and transducers, and microcontrollers can play an important role in the future of microfluidics. This opportunity can be addressed by integrating microfluidics into the curriculum as a supplement to existing courses, and as topics for Senior Design projects, for which several examples are reported here.

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