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MAKER: Utilizing 3-D Printing of Nanotechnology Design Project Prototypes to Enhance Undergraduate Learning

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Introduction

The first-year engineering program at The Ohio State University provides honors students with the option to undertake a research and development design project with a focus on lab-on-a-chip (LOC) and nanotechnology applications. The course is the second in a series for first-year engineering students in the Fundamentals of Engineering for Honors program. This project is an alternative to a robot design-build course which has a focus on mechanical engineering and computer programming. As LOCs and nanotechnology have many applications in medicine, many students that enroll in this course are Biomedical Engineering and Chemical and Biomolecular Engineering majors.

In tandem with the development of a microfluidics chip for research on cell attachment, the teams of three or four are also tasked with designing a device capable of detecting disease from a blood sample. This project must be able to capture and detect a specific analyte of interest from a collected blood sample. This analyte must be able to be found in the blood and indicative of a specific disease state (inflammation, heart disease, cancer, HIV, etc.).

Well-defined micro- and nanoscale channels can provide better understanding of fundamental fluid transport at the dimensions relevant to bacteria, viruses, proteins, DNA, and other nanoscale analytes. The ability to understand and manipulate materials at this size scale is valuable for chemical and biological applications. Another challenge lies in the specific detection of these analytes, and a number of strategies have been developed harnessing various physical phenomena (e.g. fluorescence, magnetic properties, electric fields, enzymatic reactions, etc.) to provide means of analyte detection. The students must choose an appropriate medical application for their chip such as the diseases discussed above, and design a device that incorporates required characteristics to make a useful, clinically relevant device.

Additionally, students are given ideal characteristics, required features, required constraints, and specific tasks to guide their design. Students also conduct a technical literature review toward the beginning of the semester to develop familiarity with literature search tools and strategies. The final step in this design process is the production of a full documentation and design package, which includes a full CAD working drawing set, as well as a poster presentation at a formal research forum.

Project Details

Specifically, students are given a detailed problem statement with objectives, ideal characteristics, required features, required constraints, and specific tasks. Excerpts from the problem statement are given in this section. The acronym for the device the student teams create is the "**N**anofunctionalized **A**ssay **N**ested in an **O**nboard **L**aboratory **Y**ielding **S**pecific **E**xpeditious **R**esults" or NANOLYSER. The project objectives are as follows:

1. Exposure to various fields of engineering – specifically, how nanotechnology approaches can be utilized for various applications in many fields
2. Experience in essential time management, task scheduling, and project management skills
3. Experience in following a research & design cycle – brainstorming, idea inception, sketching, literature research, preliminary and final designs, CAD modeling, and 3D printing of a prototype
4. Experience in conducting a literature search – learning both how to locate relevant scholarly journal articles from peer-reviewed journals as well as how to read them critically
5. Exposure to an interdisciplinary team-based work environment
6. Exposure to the developing fields of microfluidics and nanotechnology

Strategy and Problem Statement

Microfluidics Device Incorporating Nanoscale Features/Technologies for Detection of Biomarkers in Blood

In tandem with the development of a microfluidics chip for research on cell attachment, your CENSE team (**C**ell **E**ntrapment and **N**ovel **S**ensing **E**ndeavors) is also tasked with designing a device capable of detecting disease from a blood sample. This project, deemed the **NANOLYSER** (**N**anofunctionalized **A**ssay **N**ested in an **O**nboard **L**aboratory **Y**ielding **S**pecific **E**xpeditious **R**esults) chip, must be able to capture and detect a specific analyte of interest from a collected blood sample. This analyte must be able to be found in the blood and indicative of a specific disease state (inflammation, heart disease, cancer, HIV, etc.).

Well-defined micro- and nanoscale channels can provide better understanding of fundamental fluid transport at the dimensions relevant to bacteria, viruses, proteins, DNA, and other nanoscale analytes. The ability to understand and manipulate materials at this size scale is valuable for chemical and biological applications. Another challenge lies in the specific detection of these analytes, and a number of strategies have been developed harnessing various physical phenomena (e.g. fluorescence, magnetic properties, electric fields, enzymatic reactions, etc.) to provide means of analyte detection. You are to choose an appropriate medical application for your NANOLYSER chip such as the devices discussed above, and design a device that incorporates the following characteristics to make a useful, clinically relevant tool.

Ideal characteristics of a well-designed device include the following:

1. Ability to process and diagnose using a single drop of blood (~0.05ml)
2. Chosen analyte (protein, antibody, virus, cell, DNA, etc.) must be able to be found in bloodstream
3. Choose/define what property will be used to separate/isolate the target analyte from blood
4. Incorporate a separation method within device microchannels/microfluidics to deal with cellular components of blood
5. Choose/define what nanoscale detection strategy will be employed to detect presence of target analyte
6. Incorporate detection method into microfluidic circuit
7. Thorough description of technology (fluorescence, FET, MRI, etc.) that will be used with your chosen detection strategy

8. Low cost materials (especially for disposable device designs)
9. Simple to operate (does not require extensive training to use)
10. Processes in a timely manner (less than 8 hours)
11. Explanation of advantages that your detection device offers and why your device is preferable to current analyte detection systems (increased efficiency or accuracy, decreased costs, etc.)

You are to propose a micro- and nanofluidic circuit design and layout to carry out the separation and detection of your specific biologic analyte from collected blood sample.

Required features:

1. Fluid circuit to load blood sample
2. Fluid circuit to load any reagents needed
3. Fluid circuit for separation/capture of analyte
4. Nanoscale strategy for specific detection of analyte
5. Ability to interface appropriately with requisite technology for reading sample
6. All fluid movement will be either electromotive, pressure driven, or capillary force
7. Appropriate valves where needed to control flow
8. If reusable, cleaning and sterilizing approach
9. Chip must be able to plugged into a "reader" that is capable of gathering data from chip using selected detection method(s) (e.g. must have light transparent section for collecting fluorescence data or electrical connection for field effect sensing)

Required constraints:

1. Appropriate processing techniques for producing nanoscale, microscale, and other features should be identified where they exist.
2. Human interaction with the device is limited to: (a) loading blood sample and reagents, and (b) inserting the chip into a reader and/or pump. If you decide to use an external reader/pump (i.e., fluorescence reader), you must explain how the external device works and include specific parameters (i.e., size, wavelengths used for a fluorescence reader, pressure applied for a pump).

Specific Tasks:

This is a theoretical design project, and you will be asked to document your design and its development throughout the semester through the following:

1. A set of working drawings (prepared in SolidWorks) describing your device. The working drawings are to include at least:
    a. a 3D assembly of the completed device
    b. an exploded 3D assembly of the completed device
    c. 3D assemblies of all significant components of the device
    d. individual part drawings for each fluidic circuit properly dimensioned
    e. layout of each layer present in any 3D features
    f. a bill of materials
2. 3D printed version of your final device (optional)
3. Full documentation of the research process and drawings in the Project Notebook
4. A final report detailing your design incorporating the following:

a. your design philosophy and considerations
b. a complete description of each feature (or circuit) and how it operates in your design
c. advantages your design offers over current detection methods
d. the fabrication techniques required for your device
e. a complete list of materials, time, and costs required to fabricate your device
f. a description of any unresolved issues or special difficulties in your design
    i. For example, did you have to design things for which you are unsure precisely how they will work?

Application

Students delivered a poster presentation over their nanotechnology based lab-on-a-chip design to judges that consisted of faculty, graduate students, and former course participants. During these presentations they used the 3D models as supplements to both their posters and a corresponding short oral presentation. One example can be found in Figure 1 below.

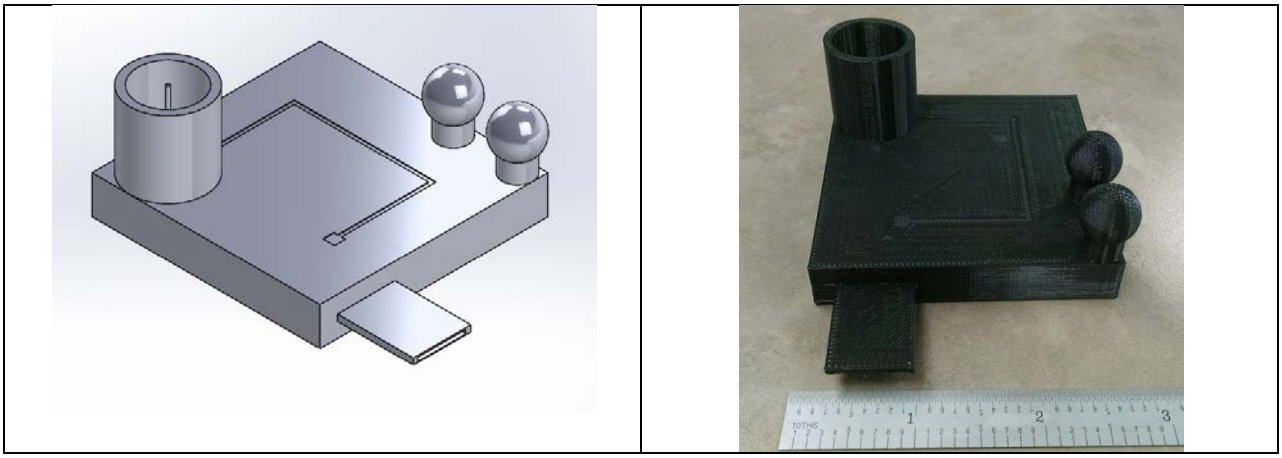

Figure 1: 3D Model (SolidWorks) and Physical Model of Student NANOLYSER

The typical group produced a scale-model of their design, either as one whole piece or as a series of components that could be assembled or disassembled as needed. Groups also opted for "cut-out" models where micro- and nano- scale features were exaggerated and made to stand alone. This allowed groups to show the concepts and features that made their designs unique and how design elements could fit together to achieve a desired diagnostic process. There were suggestions given to students for possible 3D model ideas, but there were no specific requirements given beyond reasonable use of the available resources.

The entire process was optional but all thirteen groups in 2015 had at least one part 3D printed. In 2016, fifteen of the sixteen groups opted for at least one 3D printed component. Two more examples of student 3D printed NANOLYSERS can be found in Figure 2 on the following page.

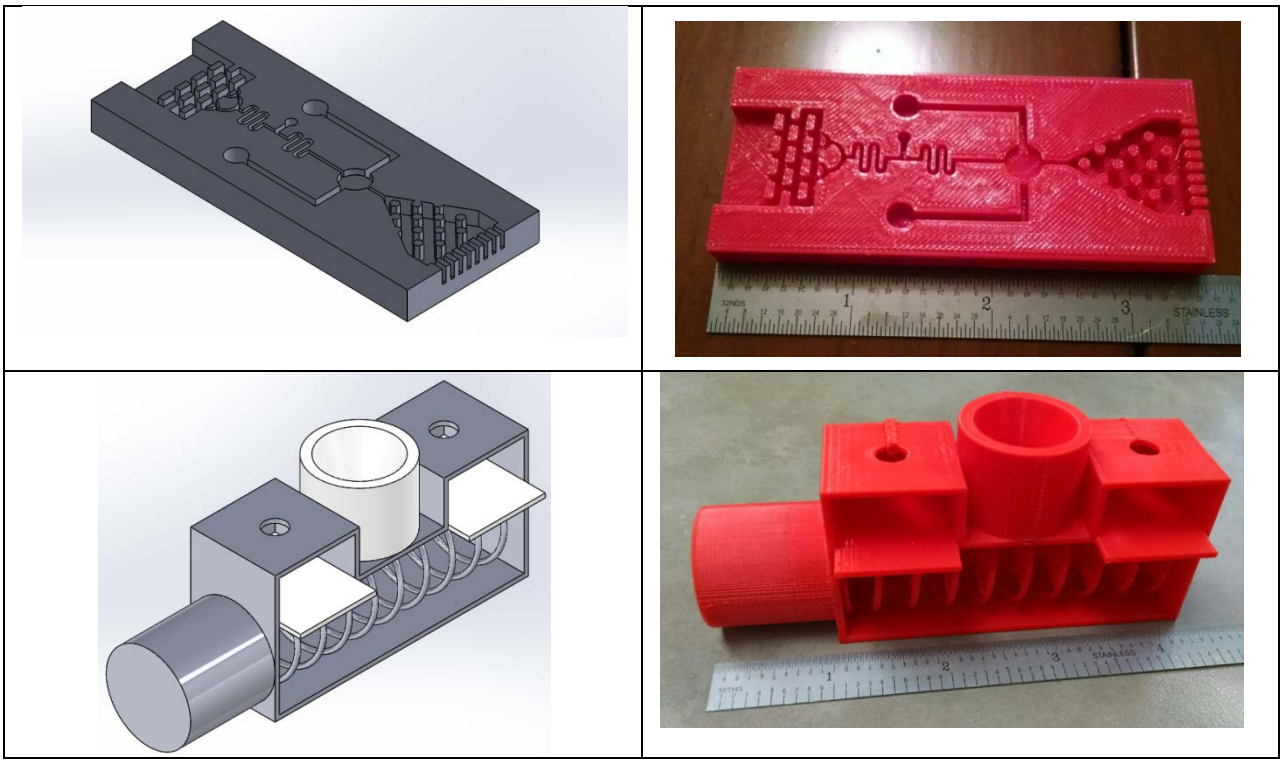

Figure 2: 3D Models (SolidWorks) and Physical Models of Student NANOLYSERs

Methods

All 3D printing for the course was done using the MakerBot Replicator 2 model printer using 1.75mm diameter PLA filament. There were approximately ten of these printers available for use which greatly increased the amount of models that could be produced in a given time frame. The printers were maintained by program laboratory supervisors and the printing was done by undergraduate teaching assistants.

Students submitted both SolidWorks part files or assembly files (.sldprt or sldasm) as well as creating ".stl" files of all parts to be made. These files could also be made by SolidWorks. Both file types were required as the ".stl" files could not be as easily edited in the event the instructional team needed to modify parts. Student ".stl" files were opened in MakerBot Desktop software which then allowed changes to scale and orientation of the object. Additionally, settings such as the print infill, layer height and the presence of rafts (a flat "base" printed by the machine that the part is built on) or supports (automatically added structures that allow large overhangs to be successfully made) could be controlled in this software.

Whenever possible, parts were positioned as not to need supports because even when removed they often left noticeable blemishes on the part surface. If this was not possible, the part was positioned so that supports were minimal or in areas that were less critical to function. Rafts were generally not preferred as the raft required material which was eventually discarded,

increased print time, and occasionally led to difficulty removing the raft from the rest of the object. The standard infill used in prints was 10% and the standard layer height was 0.20 mm. For parts that required more detail a 0.10 mm layer height was used and for more simplistic parts a 0.30 mm layer height was sufficient.

Students were given two possible submission dates for any files to be 3D printed. The first of these ("Round 1") was on a Wednesday two weeks before their final presentation. This allowed time for the instructional staff to look over any submissions so that any last minute corrections could be made if necessary. The 3D printing occurred over that weekend and then parts were returned to students the following Monday. The final deadline ("Round 2") was that Wednesday, approximately one week before the final presentation. This allowed students who wished to tweak their 3D printed designs a second opportunity to have parts made while still being open to groups that did not submit by the first date. The printing process occurred again over that weekend with parts returned the following Monday, similar to the first submission date. The next day was the poster presentation so no further revision was possible by that point.

In order to have a quick return time for the 3D printed designs a team of four undergraduate teaching assistants worked over each week and weekend to make sure that all submitted parts were completed and returned. Printing time was limited primarily to weekends because class was held in the room that contained the 3D printers during the week. Having multiple TAs allowed for more possible run time for the machines since someone must be present to start each print. Typically each team's design was scaled in a way that it took less than three machine hours to produce. If time allowed, larger designs would also be made.

Teams used the available printing resources as follows in 2015:

Round 1 Only	Round 2 Only	Both Rounds
6	3	4

Teams used the available printing resources as follows in 2016:

Round 1 Only	Round 2 Only	Both Rounds
8	2	5

It appeared that some teams used the opportunity for revision provided to them but the largest portion of groups did not. Groups that took both opportunities for printing generally went for more cut-out, exaggerated features for the 2nd submission. There was no correlation between number of parts submitted or when parts were submitted and the overall scores on the poster presentation.

Students generally reacted very positively to the opportunity to design parts for 3D printing and to have these parts available for use in a presentation setting. To quantify this, an anonymous survey was sent to all sixty-two students who completed the course in 2016. Of those who participated in this optional survey (N=33), 91% believed having 3D models increased the quality of their presentation and 88% believed 3D models enhanced the communication of design features and ideas to their audience. The remaining percentage in each case thought there was little impact of 3D models, no responses indicated there was a negative effect in either area.

Student comments in the survey were mostly positive and cited being able to show "relative size to [...] judges" as well as providing "a visual way to understand fluid flow" as some of the benefits and that is was preferable in some instances as opposed to "lean[ing] over the table and point[ing] to the poster" to show design features. In addition, students reported a sense of satisfaction of seeing their designs in "real-life, especially when you design your pieces to fit together and they work".

Conclusions

By producing physical models of lab on a chip designs students are able to show off often complex micro- and nano- scaled design elements at a poster showcase without relying exclusively on 2D drawings and verbal explanations. This reduced potential misunderstandings between students and observers who weren't as familiar with the project, such as a judge. The entire 3D printing program was implemented with a handful of teaching assistants using retail-grade 3D printers and allowed for students to get printed designs back within five days of part submission. Future work may investigate the connection between the quality of the 3D printed parts and final presentation scores or sub-scores. While there was no correlation between quantity of parts and final presentation scores, by subjectively ranking each submission in terms of quality a correlation may be found.