SANTA CLARA UNIVERSITY

DEPARTMENT OF COMPUTER ENGINEERING DEPARTMENT OF MECHANICAL ENGINEERING DEPARTMENT OF BIOENGINEERING

Date: November 24, 2016

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Maxwell Abrams Cynthia Le

ENTITLED

3D Bioprinter

BE ACCEPTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREES OF

BACHELOR OF SCIENCE IN COMPUTER SCIENCE AND ENGINEERING BACHELOR OF SCIENCE IN MECHANICAL ENGINEERING BACHELOR OF SCIENCE IN BIOENGINEERING

Thesis Advisor
Thesis Advisor
Department Chair
Department Chair

3D Bioprinter

by

Maxwell Abrams Cynthia Le

Submitted in partial fulfillment of the requirements for the degrees of
Bachelor of Science in Computer Science and Engineering
Bachelor of Science in Mechanical Engineering
Bachelor of Science in Bioengineering
School of Engineering
Santa Clara University

3D Bioprinter

Maxwell Abrams Cynthia Le

Department of Computer Engineering Department of Mechanical Engineering Department of Bioengineering Santa Clara University November 24, 2016

ABSTRACT

The 3D Bioprinter project aims to create a 3D bioprinter that can improve the capabilities of high school teachers to engage students in STEM education. In order to accomplish this goal, the team is working to expand functionality in SE3Ds product line to allow for a better student and teacher user experience and the execution of more interesting experiments. The 3D Bioprinter projects main goal is to create a modular incubating box with a variety of sensors to allow for custom environments per experiment, a clear interface to control the settings, and an automatic image capture system. As the project increases functionality, it also will keep the final deliverable as low cost as possible. These additions to the current SE3D 3D Bioprinter will increase effectiveness in the classroom and allow the target audience, high-school students, to better engage in STEM education activities.

Keywords: 3D Printing, Bioprinting, STEM, Education, Control Systems, Incubation

Acknowledgments

Acknowledge the contributions of the sponsor, university staff, other students, faculty, and other persons who were of assistance. This section is optional.

Table of Contents

1	Intr	roduction	1
	1.1	Problem Statement	1
	1.2	Background and Related Work	2
	1.3	Objectives	4
2	Poo	quirements	6
4	2.1	Functional Requirements	6
	$\frac{2.1}{2.2}$	Non-Functional Requirements	6
	$\frac{2.2}{2.3}$	Design Constraints	7
	2.3	Design Constraints	1
3	\mathbf{Use}	Cases	8
	3.1	The Box	8
	3.2	Feasability Study	10
4	Svs	tem Sequence Diagrams	11
_	4.1		 11
	4.2		 11
5	-	8	12
	5.1	8	13
	5.2	1	13
	5.3		17
	5.4	8	17
		•	17
		5.4.2 Justification of Technologies Used	18
6	\mathbf{Sys}	tem Design- Feasabiltiy Study	19
	6.1		19
	6.2	· ·	19
	6.3		19
			19
			19
	6.4		19
7	Test	ting Plan	20
8			21
	8.1		21
	8.2		21
	8.3		21
	8.4	V	21
	8.5		21
	8.6	Manufacturability	21

	.7 Sustainability	21
	.8 Environmental Impact	21
	.9 Usability	21
	.10 Lifelong Learning	21
	.11 Compassion	21
9	Conclusion	22
10	References	23
11	Appendices	24

List of Tables

1.1	Current Bioprinter Problems and Senior Design Project Solutions	2
1.2	Comparison of Existing 3D Bioprinters	3

List of Figures

3.1	Use Case Diagram for The Box
5.1	Initial Incubator Prototype
5.2	Mock up of home screen
5.3	Mock up of temperature setting
5.4	Mock up of light intensity setting
5.5	Mock up of image capture setting
5.6	Mock up confirming experiment begin
5.7	Mock up of status screen during an experiment
5.8	Mock up of how a dish is added in the middle of an experiment
5.9	Mock up of how current status screen reflects addition of a dish
5.10	Mock up of export images to a USB drive

Introduction

1.1 Problem Statement

STEM (science, technology, engineering, and math) fields are a primary focus in education, because there is increasing need for students who have the technical skills to solve real-world problems. A major challenge that many STEM educators face is engaging students in the classroom. The education technology (ed-tech) startup, SE3D, hopes to solve this challenge by bringing 3D bioprinting technology to high school classrooms. Although SE3D has already produced a working prototype, the printer only has basic capabilities and requires further development.

The 3D bioprinter senior design team aims to create a 3D bioprinter that can improve the capabilities of high school teachers to engage students in STEM education. Implementing 3D bioprinters into high schools will generate increased understanding and interest in biology, research, and technology for the students who will soon be Americas doctors, technicians, and scientific pioneers.

In order to accomplish this goal, the team is expanding SE3Ds product line to improve student and teacher user experiences and to expand the possibilities for biological experiments. Table 1.1 shows how SE3Ds current printer can be improved to meet these goals.

Table 1.1: Current Bioprinter Problems and Senior Design Project Solutions

Problem	Solution			
Printer lacks advanced features: automated	Develop a separate, modular incubation unit			
camera, temperature control and humidity reg-	(The Box) with an automated camera and hu-			
ulation	midity and temperature controls			
- Limits capability of experimentation	- Analysis and printing can occur in parallel			
	since functions are not in same physical space			
	- Automatic image capture to analyze experi-			
	ment over time			
	- Simple user interface to configure and run ex-			
	periments			
Printer only prints with one material	Design and implement low cost dual extruder			
- Limits print designs				
Motion control system relies on specialized 3D	Create custom software environment - Dis-			
printer software and feature-limited hardware	tributed control board system to accommodate			
- Duet Control Board only supports basic 3D	extra control features Run on built-in computer			
printing operations	- Keep low-cost with Raspberry Pi			
- External computer necessary for control				
Operator must manually calibrate syringe ex-	Implement auto-calibration software of the sy-			
truder	ringe extruder			
- Room for human error				

The goals in Table 1.1 are subject to the following criteria:

- 1. Usable in a high school lab environment by both students and teachers
- 2. Safe for all users
- 3. Low cost

1.2 Background and Related Work

The current bioprinter produced by SE3D, the r3bEL, is marketed towards high school science classes. It prints using a single 5 mL syringe that has to be manually loaded by the user, put into the head of the bioprinter, and calibrated by hand to begin printing. It currently has the capability to print enzyme, alga, and bacterium 2D arrays, chocolate, and cells and scaffolds for 3D tissue engineering. The r3bEL printer can print four 3x3 array tray experiments in about 3 minutes. After it is finished, the experiment must remain on the bed of the bioprinter until it finishes culturing. The user gathers data form the experiment by constantly taking pictures of the experiment as it cultures. To capture more consistent and higher quality images, an SE3D employee created a separate box that block out external light and has its own light source. This small box has a removable ceiling, lined with LEDs, and holds a single Petri dish. A small hole in the ceiling allows a mobile phone camera to be placed over it to capture images of the experiment as it cultures, though it still requires

an individual to operate the camera and capture each image.

Table 1.2: Comparison of Existing 3D Bioprinters

	Features							
Printers	UV Curing	Multi Material	Simple UI	Self Cleaning	Auto Calibration	Modular Incubation	Used for Education	Price
RegenHu	X	X		X	X			250K+
Bio3D		X					X	*
Aether 1	X	X+		X	X			9K+
Inkredible	X	X	X					10K
BioBots	X	X	X					10K
SE3D		~	X		~	X	X	3K

Kev

X: has feature

X+: has advanced features ~: project stretch goal *: value unknown

Although the team is enhancing the functionality of SE3Ds 3D Bioprinter, there are currently many similar products that are already available for purchase. Below are the bioprinters shown in Table 1.2 with an explanation of their key features and price ranges.

RegenHu: 3D Discovery Printer

RegenHu produces a professional printer priced at 250,000+ USD. It supports a wide range of funcationalities and applications. It is primarily used for optimal processing of a broad biomaterial/bioactives portfolio. The device prints using cell-friendly Ink-jet and thermopolymer extrusion using a 2-component printhead. In addition, it has a high precision temperature controller for biomaterial culturing.

Bio3D Technologies: Bio3D Explorer series

Three-dimensional bioprinters have also been developed internationally. Bio3D Technologies in Singapore has a series of printers in their Explorer product line. Designed for educational purposes, the Bio3D has 1 to 4 printing heads available and is lightweight and foldable with a full metal frame. The device is suitable for a wide range of applications and materials. The price was not listed online.

Aether 1 3D Bioprinter

Aether has a 3D bioprinter that begins with a base unit cost of 9,000 USD. The product includes 8 syringes, 2 hot ends, and 10 extruder print heads. It has the widest range of usable materials for printing, from oils to plastics. The device has many useful attachments, like a UV curing light for biomaterial prints. Its extruders are pneumatic-driven.

CellInk: Inkredible Printer

In Palo Alto, California, CellInk manufactures a research grade bioprinter, Inkredible. Inkredible is priced at 10,000 USD for the base version of the printer. It focuses on assisting tissue engineers who use their custom bioink line to create hydrogel structures that allow for efficient mammalian cell culturing. It has been optimized to print skin and cartilage tissue and uses UV lighting to cure the biomaterial. The printer has a clean chamber and heated cartridges.

BioBots 3D printer

BioBots has a desktop 3D printer capable of printing tissues out of living cells. The base model price of BioBots 3D printer is 10,000 USD. It is small and portable to allow for ease of use. In addition, the device has a dual heated, pneumatic driven extruder system for precise printing and uses replaceable syringes for easy material changing. Blue light technology is used to safely cure the biomaterial. BioBots is based in Philadelphia; however, they ship internationally.

After reviewing these printers, it is clear that they are all capable of completing the biological experiments that SE3D desires. The one aspect that they all do not meet, however, is that they are priced much higher than the average high school laboratory budget. Furthermore, these printers require high levels of knowledge in order to operate, which is not a reasonable expectation of high school students. To improve this aspect, the UI must be simplified and easy to use for people with less than a high school education. The closest competitors are Inkredible and BioBots, which are low cost and have simple user interfaces. The 3D Bioprinter that the team is working on improves on this problem by providing the necessary functionality at a more reasonable price closer to 3,000 USD.

1.3 Objectives

The 3D bioprinting team consists of mechanical engineers, computer engineers, and bioengineers. To accomplish the project goals, the team has split the project into three parts: The Box, 3D Printing Feasability Study, and a bioengineering experiment. The bulk of this document will focus on the software components for The Box and 3d Printing feasability study, as that will be where the computer engineering work is applied.

- The Box:
 - 1. Meet with Maya, SE3D CEO to define requirements for the incubating box

- 2. Make design decisions for functionality included in the box and physical and structural designs
- 3. Develop prototypes of box, user interface, and controls, allowing users to customize the box environment, begin and end experiments, and automatically capture a series of photos
- 4. At every stage of development, run tests for proper software and hardware compatibility
- 5. Share prototype with users in a classroom setting for feedback
- 3D Printing Feasability Study
 - Auto-Homing of Extruder
 - Multi-Material Extrusion

Requirements

The requirements section defines and qualifies what our 3D printer feasability study and the incubating box must do. We communicated with SE3D to determine the requirements.

2.1 Functional Requirements

Functional requirements define what the system must do.

The incubating box system will:

- support timed image capture at a pre-specified image per time interval
- have an interactive user interface
- allow user to monitor and control light, temperature, and camera settings
- $\bullet\,$ allow users to download captured images
- allow users to save settings as custom environments to be used later

The 3D printer feasability study system will:

- show feasability of auto-homing of SE3D's syringe
- show feasability of adding a multi-material printing module to an open source printer

2.2 Non-Functional Requirements

Non-functional requirements define the manner in which the functional requirements need to be achieved.

The system will be:

• User friendly and intuitive

- Safe
- Secure
- Reliable

2.3 Design Constraints

Design Constraints are non-functional requirements that constrain the solution instead of the problem.

The system must:

- function without being connected to a desktop or laptop computer
- be low- cost

Use Cases

Use Case diagrams dene tasks that users will perform to achieve a certain goal when using our incubating box and 3d bioprinter system.

3.1 The Box

Set up new environment

Save environment settings

Begin new experiment

Add another dish to existing experiment

Export images from experiment

Figure 3.1: Use Case Diagram for The Box

- 1. Name: Set up new environment
 - Goal: Prepare The Box to have the proper settings for the experiment that the user wants to run
 - Actors: Student, Instructor

- Pre-conditions: No other experiment is currently running
- Steps: Either load settings that have been previously saved, or enter custom light, temperature, and image capture settings.
- Post-conditions: The Box is at currect environment settings for the experiment.
- Exceptions
- 2. Name: Save environment settings
 - Goal: Save temperature, light, and image capture settings to prevent repetition in the future
 - Actors: Student, Instructor
 - Pre-conditions: User has input custom temperature, light, and image capture settings
 - Steps: User clicks 'Save Custom environment' and enters an appropriate name
 - Post-conditions: Future users will now be able to load this environment for future experiments
 - Exceptions: n/a
- 3. Name: Begin new experiment
 - Goal: Begin timer and image capture on current incubated experiment
 - Actors: Student, Instructor
 - Pre-conditions: User has entered proper environment settings, selected which petri dishes
 are present, and has placed petri dishes in The Box. The Box has been brought to proper
 temperature.
 - Steps: Click 'Begin Experiment'
 - Post-conditions: Timer and image capture begins
 - Exceptions: n/a
- 4. Name: Add another dish to existing experiment
 - Goal: Add another dish to a experiment that is already running
 - Actors: Student, Instructor
 - Pre-conditions: An experiment must be running in The Box
 - Steps: User places dish in the box. Clicks on the appropriate petri dish to begin timer and image capture of new dish

- Post-conditions: New petri dish is added into the experiment and final end time is extended to accommodate
- Exceptions
- 5. Name: Export images from experiment
 - Goal: Download images captured during the experiment of a single petri dish for analysis
 - Actors: Student, Instructor
 - Pre-conditions: A USB drive has been inserted and detected
 - Steps: Click 'download images' button, Select the relevant dish, click 'download'
 - Post-conditions: Images transferred onto the USB drive
 - Exceptions

3.2 Feasability Study

System Sequence Diagrams

- 4.1 The Box
- 4.2 Feasability Study

System Design- The Box

The Box is a stand alone, modular incubator that will be used to let certain SE3D experiments culture over an extended period of time. It will provide a custom lighting environment that allows consistent lighting conditions for the camera to effectively document the experiments. The box also will have temperature control capabilities to adjust temperature levels for each of the relevant SE3D experiments. The box will support nine petri dishes at one time.

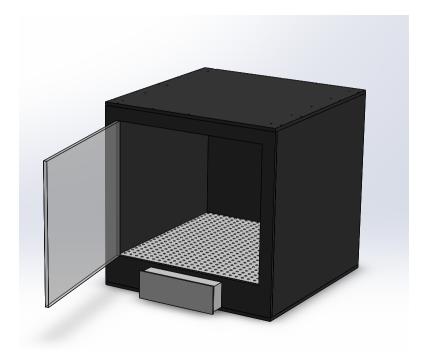


Figure 5.1: Initial Incubator Prototype

Figure 5.1 shows a initial drawing of the plans for the physical incubating box. At the top of the box, there will be a touch screen that allows users to interact with the controls of The Box.

5.1 Architectural Design

5.2 Conceptual Model

The user interface for The Box consists of screens in which the user can configure the boxs settings for the current experiment, begin and end experiments, and download images that are collected during the experiment. The user interface shall perform the following:

- 1. Run off of a microcomputer
- 2. Allow users to choose custom light, temperature, and image capture settings
- 3. Allow users to save a set of environment settings
- 4. Allow users to load a previously saved environment
- 5. Organize all images from a single experiment into a folder per petri dish so that they each can be exported to USB

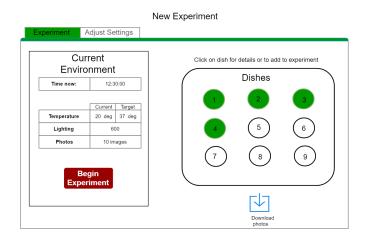


Figure 5.2: Mock up of home screen

The user interface mock-ups shown in Figures 5.2 through 5.5 step through a typical sequence of steps a user would take when using the system. The first screen show, in Figure 5.2, is the default home screen that is shown when a experiment is not running. The home screen shows current environment status of the box. If a user would like to begin a new experiment, he would first select the dishes that will be initially placed into the incubator by clicking on each numbered circle that corresponds to a specific location inside of the physical box. Figure 5.2 shows dishes 1-4 will be present in the experiment.

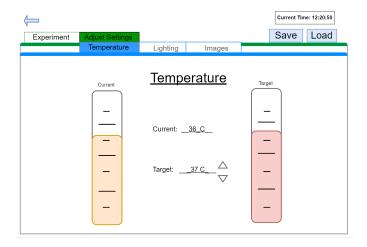


Figure 5.3: Mock up of temperature setting

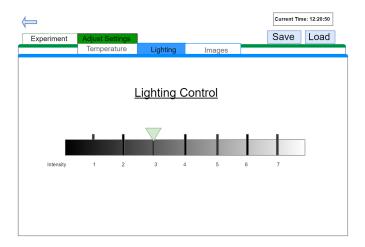


Figure 5.4: Mock up of light intensity setting

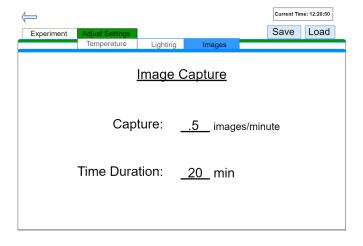


Figure 5.5: Mock up of image capture setting

Next, to customize the environment, the user would click adjust settings to be taken to the settings panel, shown in Figures 5.3 through 5.5. The user can choose to load a previously saved set of environment settings or provide a new set of environment settings. In each of these panels, the user can choose the appropriate temperature, light, and image capture settings for the system. After, he can choose to save the set of settings to be used in the future.

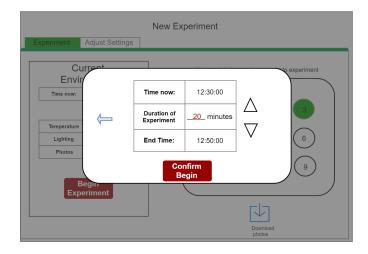


Figure 5.6: Mock up confirming experiment begin

Once the settings are appropriately chosen, the user navigates back to the home page to begin the experiment. The user clicks the 'Begin Experiment' button and a confirmation screen will pop up to allow users to specify how long the incubating box will maintain the environment. This is shown in Figure 5.6.

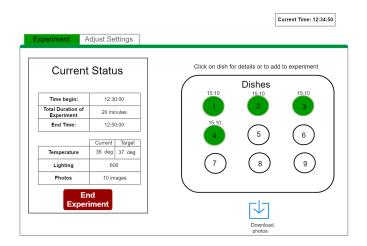


Figure 5.7: Mock up of status screen during an experiment

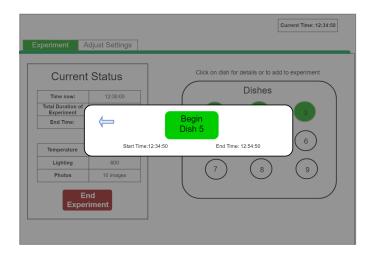


Figure 5.8: Mock up of how a dish is added in the middle of an experiment

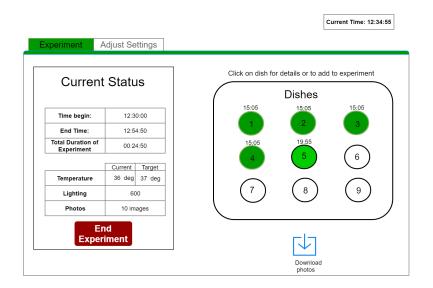


Figure 5.9: Mock up of how current status screen reflects addition of a dish

As seen in Figure 5.7, users will be able to monitor the experiment in real time and see how much time is left in the experiment as well as the current incubator conditions. If another dish needs to be added into the incubator in the middle of a running experiment, the user will add the dish into the box, then click on the corresponding circle on the screen. Figure 5.8 shows Dish 5 being added into the experiment. After the dish is added, the current staus screen is updated appropriately to reflect the change- specifically in the duration of experiment and end time sections as well as in the 'Dishes' graphic. This is show in Figure 5.9.



Figure 5.10: Mock up of export images to a USB drive

After an experiment is finished, users will export the images captured by USB. After a USB drive is inserted and recognized by the system, the user can click 'Download Photos' on the status screen. A pop-up will allow the user to choose which dish's images the user would like to export. In Figure 5.10, the images of Dish 1 will be exported to the USB drive.

5.3 Technologies Used

5.4 Design Rationale

5.4.1 Justification of User Experience

We decided a touch screen interface was the most effective solution for the most enjoyable user experience for both high school students and instructors. A touch screen interface provides better image quality and intuitive interaction for users. Users are familiar with touch screens because of the popularity of touch screen smart phones and other screens.

The user interface is optimized for a touch screen experience. Since users will be using fingertips to navigate the interface, instead of a mouse cursor or stylus, all functions are tied to simple and prominent buttons. We kept the interface as simple as possible, only showing options and information that are necessary. Since we anticipate that we will have about a 5 in. screen, a simpler interface allows users to more easily navigate the system. In addition, since our users will be high school students, limiting the options they have on each screen reduces confusion on what to do next and lowers the chance of error due to unintentional clicks of other buttons.

There is minimal direct user input of values to reduce the need for on-screen keyboards that can be hard to navigate on a small screen. Instead, numbers are increased or decreased with up and down arrows, images, text, and color highlighting are used for signaling if certain dishes are selected or in use, and sliders are used in configuration. Reducing direct user input reduces the likelihood of human error.

We chose not to include preloaded experiment settings that users can choose from after speaking with Maya from SE3D. Allowing users to input their own settings provides more flexibility for the user to customize experiments and create their own experiments. Since there are only a few criteria to set-light, temperature, image capture, and duration of experiment- it does not add too much overhead in set-up time. Users will have the option to save a certain combination of environment settings to use in the future. Thus, the 'preloaded experiment' feature is emulated here- an instructor could set up a desired environment before class begins and save it to the system. Students can then load the environment that was set up by their instructor.

5.4.2 Justification of Technologies Used

System Design- Feasabiltiy Study

- 6.1 Architectural Design
- 6.2 Conceptual Model
- 6.3 Design Rationale
- 6.3.1 Justification of User Experience
- 6.3.2 Justification of Technologies Used
- 6.4 Technologies Used

Testing Plan

Societal Issues

- 8.1 Ethical
- 8.2 Social
- 8.3 Political
- 8.4 Health and Safety
- 8.5 Economic
- 8.6 Manufacturability
- 8.7 Sustainability
- 8.8 Environmental Impact
- 8.9 Usability
- 8.10 Lifelong Learning
- 8.11 Compassion

Conclusion

References

Appendices