TEAM 12 Design Assignment

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3. Design

3.1. Design Context

3.1.1 Broader Context

Area	**Description**	**How our Project Relates**
Public health, safety, and welfare	How does your project affect the general well-being of various stakeholder groups? These groups may be direct users or may be indirectly affected (e.g., solution is implemented in their communities)	This method of DNA synthesis uses UV light to break down and bond the DNA. If not regulated the UV light could be too intense and prolonged exposure could lead to potential harm of users such as geneticists or other scientists
Global, cultural, and social	How well does your project reflect the values, practices, and aims of the cultural groups it affects? Groups may include but are not limited to specific communities, nations, professions, workplaces, and ethnic cultures.	Development of DNA synthesis technology assists with researchers who are attempting to keep up with the increasing data storage demand year to year. DNA can be a viable solution for containing copious amount of data in a single structure
Environmental	What environmental impact might your project have? This can include indirect effects, such as deforestation or unsustainable practices related to materials manufacture or procurement.	Data centers are currently used to hold the digital information for companies such as Amazon or Facebook. DNA storage capabilities could reduce the required space and therefore the required energy to store data, from the size of a data center to the size of a small room.
Economic	What economic impact might your project have? This can include the financial viability of your product within your team or company, cost to consumers, or broader economic effects on communities, markets, nations, and other groups.	This product reduces the cost of current DNA synthesis by using simpler components. This would allow bioinformatics personnel the opportunity to budget more resources towards storing data in DNA. This process could also eventually be used by geneticists for patients who require some form of gene therapy.

3.1.2 User Needs

- Geneticists need a cheaper way to synthesize DNA that will end up saving them money and time in the end.
- Doctors need a way to store DNA safely and efficiently.

3.1.3 Prior Work/Solutions

There are no DNA 3D printers on the marketplace currently. Although, there are a few companies that can perform DNA synthesis. The first of these companies are San Diego-based Molecular Assemblies, Ansa Biotechnologies, and Paris-based DNAScript. Currently a single character in a genetic sequence costs roughly $1 to print, or $1 per base pair. In perspective, if you wanted to print the entire sequence of a human, it would cost around $2 billion.

3.1.4 Technical Complexity

1. The design consists of three major systems, each consisting of multiple components working in tandem to complete the desired function.
    a. Anycubic Photon Mono 3D Printer
        i. Monochromatic LCD screen
        ii. UV light module with magnifying lenses
    b. Microfluidic System
        i. Flow cell fabrication
        ii. Fluigent controller and switches
        iii. DNA oligo pools
        iv. Vacuum pump
    c. Software/GUI
        i. WPF
        ii. C#
        iii. XAML
2. The DNA synthesis process requires the use of several scientific principles which can be realized using the above components.
    a. UV light polarization via control of liquid crystal display
    b. DNA oligomer denaturing via UV light
    c. DNA phosphoramidite synthesis
3. The problem scope contains multiple challenging requirements that match or exceed the current solutions or industry standards.
    a. More affordable alternative to the current industry processes
    b. Accuracy of DNA sequencing to reflect the current industry standard
        i. Minimal substitutions, omissions, or additions of DNA base pairs during sequencing
        ii. Proper dispersion of UV light exposure to all regions of the flow cell
    c. User friendly interface to allow for ease of use
        i. Variability in DNA strand array size
        ii. Easy input of desired sequence

3.2 Design Exploration

3.2.1 Design Decisions

1. Connection between the LCD and the computer will be made via an HDMI to MIPI adapter connection.
2. The variables users will have control over within the software will consists of array size, individual position size, and position spacing
3. The sequence of DNA base pairs as well as the selection of intermediate chemical compounds used for cleaning the surface of the flow cell will be determined once the setup of the microfluidic system is complete.

3.2.2 Ideation

Several considerations were taken into account when determining the best course of action for the connection and control of the LCD screen. The ideas were generated through brainstorming sessions during team meetings and new ideas continued to be generated as we gained more background information from our advisor. The following options were considered for this decision in the design:

1. Connection to the 3D printer directly via USB port
2. Connect to a Raspberry Pi or the 3D printer itself through the Wifi capabilities of both
3. Use of a Raspberry Pi to control the LCD and connect via MIPI port
4. Connection between the LCD and computer via an HDMI to MIPI adapter
5. Various alternative LCD screens with built in HDMI connections

3.2.3 Decision-Making and Trade-Off

For each of the options we went through and researched the current products available on the market to determine its viability. We also took into account financial considerations since one of the major goals of our project is to create an affordable design. The different variations of LCD screens were more expensive than our current screen so we wanted to find a method to make it work without the need for a new part. Research was done on the wifi connection and USB connections to the 3D printer and it became evident that extensive reconfiguration of the microcontroller would be required to control the LCD and allow for an image file to be passed through the printer to the LCD. This option was mainly in consideration because it did not require us to dismantle the printer. The Raspberry Pi option was appealing because it had the simple software available. The only issue was that it required an adapter and it required introducing an additional part to our system. We determined the best option was to go with the HDMI to MIPI adapter which could connect the LCD directly to the computer and cut out any additional controllers, secondary components, or difficult software reconfigurations. This option allows for the LCD screen to essentially act as a second monitor to our computer and we can project any image we want to the screen for the purposes of DNA synthesis.

3.3 Proposed Design

The current design has been broken down into three major sub-components. Those being the LCD screen and UV light control, the user interface, and the microfluidic system. Each member of the group has been designated a role in designing at least one of these components.

LCD Screen/UV Light Control

The different iterations of LCD screen control methods we have tried have been outlined in the above sections. We have tested the LCD screen with HDMI to MIPI adapter and found this method of interfacing with the LCD screen works well. Further testing is being done to determine the intensity of UV light being produced by the light module when it passes through the LCD. This will be an important factor in determining the time of exposure for the DNA base pairs when they pass through the system. The UV light is the catalyst for the bonding reaction so the testing will ensure it has enough energy to break the protective molecules on the DNA which prevent it from bonding uncontrollably.

User Interface

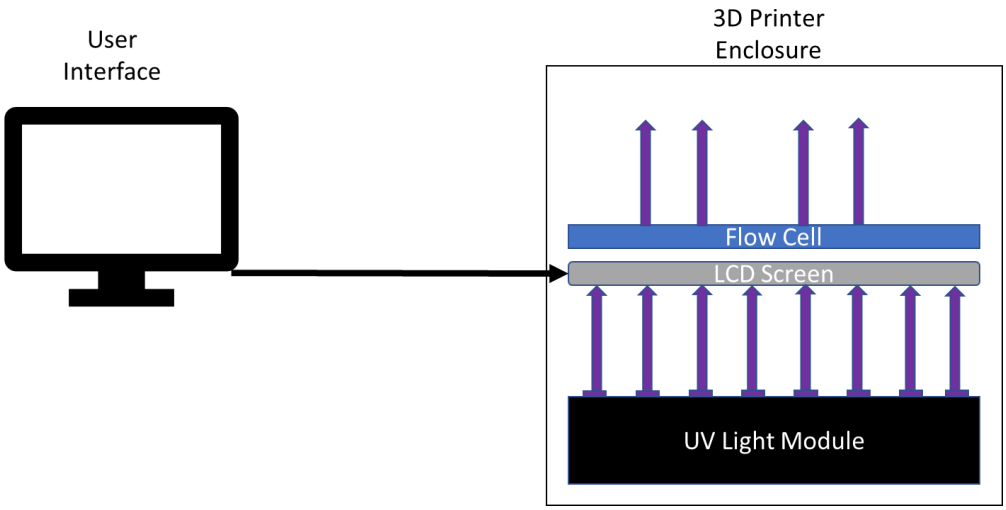
For the software application that users will visually interact with we decided to go with a WPF framework application that uses C# for the backend functionality and XAML for the GUI. Currently, it displays a white matrix on a black background as this is the basis for what our project will look like and what we will base the rest of our code on. We are in the process of implementing/testing receiving user input that will be used to determine the size of the matrix, size of the individual cells, as well as a few other minor aspects.

Microfluidic System

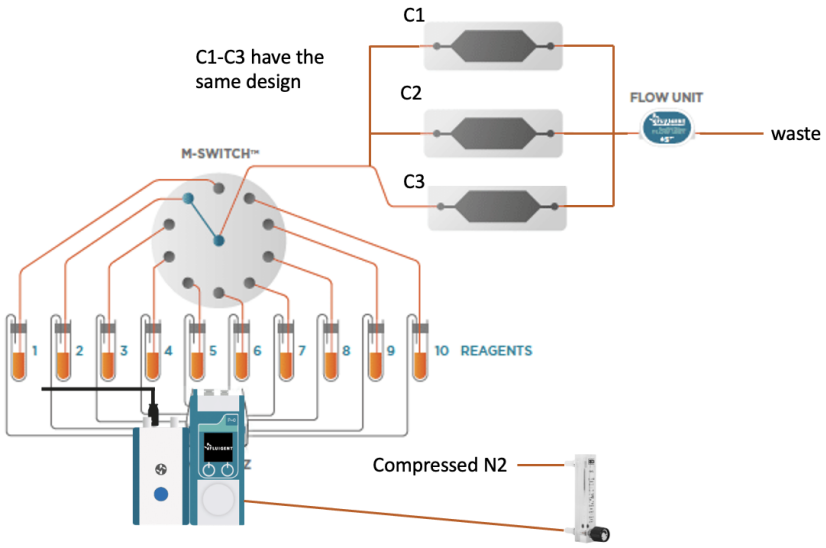
This subsystem is still in the early stages of development and has been heavily research based. A schematic for the overall design of the microfluidic system has been sketched out to be referenced during assembly. Most of the parts have been obtained, but the flow cell is required to be custom fabricated. A 3D rendering of the model is currently being developed and the goal is to fabricate it in the early weeks of next semester.

3.3.1 Design Visual and Description

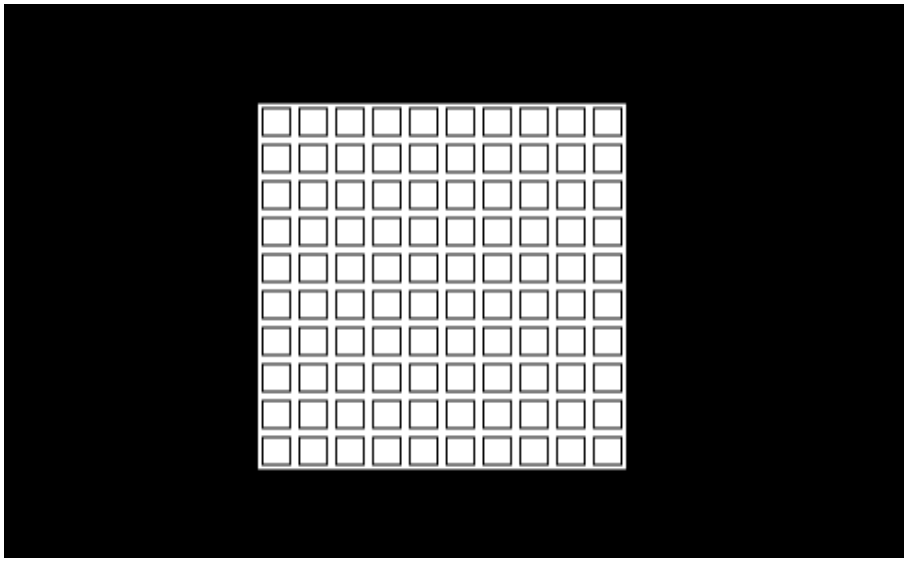
The diagram below depicts the interaction between the user interface and the LCD screen. The array parameters and digital information are uploaded into the designed software. The digital information will be divided up into two-bit segments, each of which will be correlated to any given DNA base pair based on its value. The software will then break the string of data down into relatively equal segments to fill each of the positions on the array. The segments will be parsed layer by layer in each of the array locations and an image will be generated to be passed to the LCD screen. The images will configure the LCD screen in a way which selectively lets the UV light through and into the flow cell where it will initiate the bonding between the DNA base pair and the growing DNA segment.



The microfluidic system is shown in the image below. There will be a total of ten chemical compounds which will be used throughout the bonding process of each layer of the DNA segments. The rotating M-Switch in the middle of the diagram will rotate at each step and open up the channel between the reagents and the flow cells. During that time the other wells will be replenished. The flow cells are the components labeled C1-C3 and will be the location where the bonding will occur. The entire system will be operated using a vacuum and compressed air to push the reagents through the system.



Primitive example of the User Interface. This is just a simple look of what we are basing our current code off of. Each cell in the matrix will eventually be separated (surrounded by black to match the background) and also be able to switch colors to completely blend in with the background. Also, as mentioned above, we are currently working towards receiving user input to allow the entire matrix to be customizable to the DNA standards that they want.



3.3.2 Functionality

The DNA synthesis is initiated by a user dictating the array size, which is the number of DNA segments created, position spacing, and size for their desired sequence. The digital information which is to be encoded by the DNA is translated by assigning a two-bit value to each of the four base pairs. Each time a different base pair is introduced to the flow cell a new black and white image will be displayed on the LCD screen. The white locations will allow UV light to pass through and thus allow bonding to occur between the current base pair and the DNA strand being synthesized in that position of the array. This process will be repeated for each base pair at any given level until the desired strand length is reached. Once completed the individual strands can be bonded together to create one coherent strand containing all of the digital information.

The current design has not reached its fully functional form, but in theory once all of the components are integrated together it should be able to perform the task. The accuracy of the DNA synthesis is still in question and some alterations may need to be made in order to correct this issue.

3.3.3 Areas of Concern and Development

One of the major areas of concern is the accuracy of the DNA synthesis process. Bonding errors, such as omissions, additions, or substitutions, are potential issues to arise if the surface of the flow cell is not properly cleansed between each base pair being introduced or insufficient light allowing for the activation of the bonding reaction. This issue will be addressed by determining the best compounds to use as intermediate fluids to cleanse the surface of each DNA base pair. Extensive testing will also be done to determine the accuracy of the process and where errors are occurring. These solutions will come in the late stages of the project as we are currently working on integrating each subsystem together.