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Development of a Hydrogel Extruder

Mechatronic Project 478
Final Report

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Executive summary

Title of Project

Development of a Hydrogel Extruder

Objectives

To design and construct a hydrogel extruder, as well as a 3D printer body, with the capability of printing three dimensional shapes (of reasonably complex geometry).

What is current practice and what are its limitations?

Its current practice is to make hydrogel structures for tissue engineering and biomedical research. Its limitations include its printing speed due to curing limitations and print resolution.

What is new in this project?

A hydrogel printer will be designed and made with the ability to create prints with different kinds of hydrogel and curing methods with a focused calibration of the system to be able to print with a selected test gel to show the design as a working concept.

If the project is successful, how will it make a difference?

The project will make a difference by adding new knowledge to the methods of 3D printing (and curing) with hydrogels for medical application as well as provide medical researchers with a new research tool to help create cell cultures and 3D environments to simulate cell growth.

What are the risks to the project being a success? Why is it expected to be successful?

Risks that may prevent the project completion include budgetary and time constraints as well as finding a cheap, easy-to-access hydrogel/surrogate to test and calibrate the printer.

What contributions have/will other students made/make?

This is the second iteration of this project, and future students will use this research as a foundation to build more functional and effective printers that are better tools for tissue engineering and biomedical research.

Which aspects of the project will carry on after completion and why?

In future applications, the design can be improved, and additional functionality can be added such as implementing additional methods of forced gelation.

What arrangements have been/will be made to expedite continuation?

Carefully documenting all details regarding the design (mechanical, electronic, and firmware) as well as conducting and recording an experimental observation to calibrate the printer to a specific gel, and show the printers abilities.

ECSA self-assessment

GA 1. Problem solving

The project will heavily require problem solving through creating solutions to problems like finding a cheap hydrogel alternative for testing, the issue of printing speed due to slow curing rates by investigating and implementing a method of forced and accelerated hardening.

GA 2. Application of scientific and engineering knowledge

The project will require the application of many fields of science and engineering. It will use knowledge of fluid mechanics to describe the rheological properties of a selected hydrogel which will be used to define the requirements and parameters of the extruder, which will require a mathematical description of the fluid. Designing the extruder and printing gantry will utilize physical knowledge of strengths and materials by implementing a system that can withstand the induced and static loads. This knowledge will required mathematics and numerical methods to model and describe the effects from these fields of science.

GA 3. Engineering Design

A detailed design process will be conducted in this project for both designing the machine (mechanical) and embedded system (electrical). This process will include a literature review to gather knowledge required to understand the functionality of the system, a concept generation where three concepts for each subsystem will be developed, followed by an evaluation of the generated concepts that will be used to select the concepts for each system, and a final design will be developed.

GA 5. Engineering methods, skills and tools, including Information Technology

This attribute will be achieved through the need for mathematically understanding the rheological properties of liquid hydrogel (fluid mechanics), using Inventor as a means of CAD to implement the skill and method of machine design, using an integrated development environment to engage in the design and programming of embedded systems to implement methods of control systems, and using numerical methods for modelling and processing raw data with MATLAB.

GA 6. Professional and technical communication

The project will include a final report that will clearly and professionally communicate its contents using language intended for its target audience (those trained in the field of mechatronics), that will make use of a literature review (which for this attribute, gives the engineering sufficient knowledge in biomedicine to understand the context/application of the project), graphical aid (CAD drawings, electrical diagrams, and experimental results), design and experimental methodology.

GA 8. Individual, Team and Multidisciplinary Working

The project will demonstrate this attribute by utilizing knowledge from many fields of science and engineering (thermodynamics, fluid mechanics, electronics and embedded systems design, and mechanical design) and requiring careful planning of the project timeline (with a Gantt chart) and project costs (with a budget) to ensure that all the many project deliverables are achieved.

GA 9. Independent Learning Ability

The project will demonstrate independent learning ability due to the need to apply advanced knowledge of material science (properties of hydrogel), electrical and mechanical (regarding the gantry and extrusion system) design from various academic sources such as textbooks and research papers.

Acknowledgements

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Constants

$L_0 =$	300 mm	

Variables

Re_D	Reynolds number (diameter)	[ ]
x	Coordinate	[m]
$\ddot{x}$	Acceleration	[m/s^2]
θ	Rotation angle	[rad]
τ	Moment	[N·m]

Vectors and Tensors

$\vec{v}$	Physical vector, see equation ...

Subscripts

a	Adiabatic
a	Coordinate

Abreviations

DEM	Discrete Element Method
FEA	Finite Element Analysis

Chapter 1

Introduction

1.1 Background

Starting from the big picture, gradually narrow focus down to this project and where this report fits in.

1.2 Objectives

The objectives of the project (in some cases the objectives of the report). If necessary describe limitations to the scope.

1.3 Motivation

Why this specific project/report is worthwhile.

Chapter 2

Literature review

2.1 Tissue engineering

2.1.1 Definition and Background of Tissue Engineering

Tissue engineering can be defined as the "the application of principles and methods of engineering and life sciences toward fundamental understanding of structure–function relationships in normal and pathological mammalian tissues and the development of biological substitutes to restore, maintain, or improve tissue function" (Skalak and Fox, 1988).

The concept of replacing dysfunctional tissues and organs has been around for millennia, with the first nose transplants occurring as early as 1000 B.C. in ancient India (Saltzman, 2004). In recent centuries, major advances in organ transplantation have taken place – even transplants of organs supplied by donors. These strides include tooth transplants, successful skin grafts (which became commonplace in the 1800s), and even the first successful heart transplant which took place in South Africa, 1967 (Saltzman, 2004).

Despite the rapid advancements in organ transplantation in recent centuries, all transplants involving organs from donors have a common issue. The problem is that the tissue/organ in need of replacement requires the availability of viable tissues or organs from a donor and in modern times the demand for tissue/organ replacement far exceeds the available supply from donors (Saltzman, 2004). This problem can be alleviated using tissue engineering.

Through tissue engineering, the demand for useable and available donor tissues is mitigated by creating viable tissues (and even organs) through artificial means. This replacement tissue is formed by creating a three-dimensional scaffold to take on the shape of the space of the human (or organism) that needs to be filled with new tissue. These scaffolds can be acellular or seeded with cells prior to formation. The acellular scaffolds rely on the body's natural ability to regenerate the cells for normal function. Whether seeded or regenerated from the body, the scaffolds (with its contained cells) are intended to replace the functionality of the old or damaged tissue (Olson *et al.*, 2011).

2.1.2 Scaffold Requirements

The main purpose of artificial scaffolding in tissue engineering is to mimic the environment and behaviour of the tissue being replaced. To create artificial scaffolding that recreates these same conditions, the scaffolding needs to be biocompatible, biodegradable, have sufficient architecture and have the same mechanical properties as the native extracellular matrix (O'Brien, 2011).

The scaffolds must be biocompatible with the cells. This means that the cells should be able to migrate through the scaffold material and be able to function normally within this artificial EM (extracellular matrix). This criterion also means that the engineered tissue should result in minimal immune response from the body once it is integrated (or implanted) with the host tissue (O'Brien, 2011).

The artificial scaffolds must be biodegradable since the scaffolds are not meant to be permanent implants. The scaffolds are intended to be gradually broken down and slowly replaced with a new extracellular matrix that is formed by the seeded or host's natural cells. To ensure that the tissue continues to function normally and remain undamaged, the by-products of the scaffold's degradation must be non-toxic (O'Brien, 2011).

The architecture of the scaffolds should be sufficient to allow for the cells to exist inside the matrix. This means that it should have an interconnected porous structure, and it should be highly porous. The reason for this, is so that the structure can allow for the diffusion of nutrients to the cells and the diffusion of waste products from the cells through the EM (O'Brien, 2011).

The scaffold's mechanical properties should match that of the native extracellular matrix or that of its intended purpose. This involves selecting materials (for scaffolding) that have similar stiffness (Young's modulus), hardness, etc. The importance of matching mechanical properties to the scaffolding can differ depending on what the engineered tissues intended purpose is. For example, if its function includes a structural role (as would be the case with bones and cartilage), then it is important to ensure it has enough stiffness and strength to not break upon usage. It should also be noted that the artificially formed matrix should have sufficient mechanical properties for it to remain undamaged when being implanted. In addition to this, it is important to ensure that the scaffold's mechanical properties do not get chosen at the cost of the scaffold porosity as this can result in the engineered tissue having difficulty in allowing vascularization and cell infiltration resulting in conditions where the cells cannot exist over time (O'Brien, 2011).

2.1.3 Scaffold Fabrication Methods

There are many methods of fabricating scaffolds. These techniques for creating scaffolds differ according to the material used to create the scaffold and depending on whether the seeded cells can survive the scaffolding formation process. The formation process also needs to ensure that the produced scaffolds meet

the requirements for being used as engineered tissue (it must be biocompatible, porous, etc.). These varying methods can be split up into conventional and advanced methods (Dutta *et al.*, 2017).

Conventional techniques include particulate-leaching, extrusion, molding, thermally induced gelation, gas foaming, etc. (Dutta *et al.*, 2017). These processes can be used in combination to manufacture scaffoldings that meet the previously identified scaffold criteria and can work together to form more advanced manufacturing techniques.

Advanced methods include 3D printing, electrospinning, emulsion templating, and designed self-assembling peptides:

- 3D printing allows for the computer aided design of scaffolding and then the formation of these designs through additive manufacturing methods such as Fused Deposition Modelling, Stereolithography, and Laser Sintering; this style of fabrication is particularly useful for rapid prototyping, developing scaffolds with complex geometries, and having control over the macroscopic properties of the artificial matrix structure (Dutta *et al.*, 2017).

- Electrospinning involves using an extruder with an electric field to produce ultrafine nanofibers to form the extracellular matrix; this method is very useful for creating scaffolds with fibrous nanoporous materials with high precision (Dutta *et al.*, 2017).

- Emulsion templating uses phase separation to form tertiary pores to create scaffolds with a hierarchical pore structure; emulsion templating is useful for creating scaffolds with a porosity gradient (Dutta *et al.*, 2017).

2.1.4 Scaffold Materials

The material used to form the extracellular matrix depends on the application of the tissue that is being engineered. These possible materials include linear aliphatic polyesters and other synthetic polymers, natural macromolecules, inorganic materials, and hydrogels (Ma, 2004).

Linear aliphatic polyesters, such as PGA and PLA, are a group of biodegradable plastics that break down due to the hydrolysis of ester bonds. There are also other synthetic materials such as PPF and tyrosine-derived polymers that are used in bone engineering (Ma, 2004).

Natural macromolecules, like proteins polysaccharides, are often used in tissue engineering. Examples of fibrous proteins that are used to create tissue is collagen and silkworm silk. Collagens have useful properties and is therefore often used as a major component of EM scaffolding although it has potential issues with pathogen transmission and less controllable biodegradability; silk (from silkworms) is a useful tissue replacement option in certain instances due to its desirable tensile properties but has issues with cytotoxicity and slow

degradation. Polysaccharides such as alginate, chitosan, and hyaluronate (these examples are or can be used to create hydrogels) are also useful in creating porous solid-state scaffolds (Ma, 2004).

Inorganic materials that fall into the categories of porous bioactive glasses and calcium phosphates are used in the fields of bone and mineralized tissue engineering due to their ability to support cell adhesion, growth, and differentiation (Ma, 2004).

Hydrogel polymers (like PEGs, alginates, etc.) are also a desirable option for producing extracellular scaffolds because they can be easily made to form structures of complex shapes/geometries, they can be seeded with cells, have solidification rates that are controllable (to some degree) and can often be implemented through procedures that are minimally invasive (Ma, 2004).

2.2 Hydrogel

2.2.1 Introduction to Hydrogels

Hydrogels are three-dimensional polymeric networks that are hydrophilic and therefore capable of containing large quantities of water while keeping their structural integrity (Peppas *et al.*, 2000). Hydrogels have many desirable properties that make it useful in many applications (even outside of tissue engineering).

The network structure of hydrogels is comprised of homopolymer or copolymer chains. These chains attract water, but the overall polymer network is still insoluble due to chemical and/or physical (entanglements, crystallites, etc.) crosslinks. Crosslinks are the tie points where the adjacent or neighboring chains are joined together. These crosslinks allow for the network structures to be solid and have some degree of structural integrity (Peppas *et al.*, 2000).

Hydrogels can be used in many applications. Due to their resemblance to the properties of natural extracellular matrices of tissue (as they are porous, enzymatically degradable, soft in consistency, biocompatible, and have high water content), they are an attractive option for applications within the medical and pharmaceutical sectors. Their biocompatibility (contributed to by its capacity to hold large amounts of water) allows it to make contact lenses, biosensor membranes, artificial heart lining, artificial skin materials, and drug delivery systems (Peppas *et al.*, 2000).

2.2.2 Classification of Hydrogels

Hydrogels can be classed in many ways and there are many kinds of hydrogels with different applications within the fields of medicine or tissue engineering.

Hydrogel can be classified according to its polymer source, physical properties, ionic charge, biodegradability, or its method of crosslinking. With regards

to classifying these gels according to their source, they can either be natural, synthetic, or hybrid polymer hydrogels (Li *et al.*, 2020).

Natural hydrogels are a form of natural polymer (or biopolymer) as they are derived from organisms. These can be further classed into polysaccharide hydrogels (such as alginate which comes from brown algae), glycosaminoglycan hydrogels, and polypeptide/protein hydrogels (the most common example of these include collagen and gelatin hydrogels) (Li *et al.*, 2020).

Synthetic hydrogels are artificially created and come in the form of polyacrylamide (PAAm), poly(ethylene glycol) (PEG), and poly(vinyl alcohol) (PVA) hydrogel. PEG derived gels are the most used synthetic hydrogels in medicine due to their hydrophilic nature and excellent biocompatibility (Li *et al.*, 2020).

Hybrid hydrogels are made from a combination of natural and synthetic materials. The reason for this is that synthetic and natural gels on their own tend to have limited mechanical strength but through the combination of natural and synthetic materials this problem is rectified to allow improved and tunable mechanical properties as well as allow for the addition of other desirable characteristics to the gel product (Li *et al.*, 2020).

2.2.3 Properties of Hydrogels

Since there are countless types and forms of hydrogel, in this section, the properties of specific examples of hydrogels, relevant to the context of extrusion-based 3D printing with the intention of engineering tissue, are considered. These examples are GelMA (gelatin methacrylate), PEGDA (poly(ethylene glycol) diacrylate), Alginate, and Matrigel.

- Biocompatibility – all four of these hydrogels are highly biocompatible but only some are naturally able to adhere to cells. GelMA and Matrigel support cell adhesion; PEG-based hydrogels and Alginate naturally have poor cell adhesion, and this can be rectified by incorporating cell-adhesive peptides (Li *et al.*, 2020).

- Biodegradability – GelMA, Alginate, and Matrigel are enzymatically degradable. If the necessary enzymes are not available to degrade Alginate, it can also be ionically degraded while immersed in an aqueous solution with Na+ ions. PEG-based gels are not degradable and need to be chemically modified to become biodegradable (Li *et al.*, 2020).

- Water retention – PEGDA, GelMA, and Alginate are all very soluble (in water and other solvents) and capable of holding large amounts of water (Li *et al.*, 2020). Matrigel needs to be chilled for it to be more easily soluble (Merceron and Murphy, 2015).

- Crosslinking method – PEGDA and GelMA (with a photoinitiator) are made to cure via photo crosslinking when irradiated by UV rays. Alginate is ionically crosslinked by divalent cations like Ca2+ (Li *et al.*, 2020). Matrigel,

however, is thermally crosslinked (which is reversable). It is a liquid at low temperatures (around 4°C), and it forms a solid matrix at higher temperatures of around 37°C (Merceron and Murphy, 2015).

- Rheological properties – the rheological properties of hydrogels often depend on its temperature, concentration is a solute, and molecular weight. Before gelation, PEGDA is found to be a Newtonian fluid (to a certain shear flow rate) and its viscosity increases as its molecular weight increases (Brikov *et al.*, 2016). Both GelMA and Alginate, on the other hand, are non-Newtonian fluids that exhibit shear-thinning behaviour, meaning that their viscosity reduces as its shear rate increases (Gregory *et al.*, 2022). The viscosity of GelMA also varies depending on temperature and concentration. Its viscosity decreases as its temperature increases and its concentration decreases. The viscosity of GelMA, therefore, is very low when flowing at temperatures above 30 °C (significantly less than 1 Pa · s), but at cooler temperatures (less than 30 °C) its viscosity drastically increases (Adhikari *et al.*, 2021). For example, a solution with the GelMA concentration of 10% at 26 °C has a viscosity of roughly 168 Pa · s, which is a very large increase in viscosity (CELLINK, 2020).

2.3 3D Printing Hydrogel

As extrusion-based 3D printing has continued to grow as a method of engineering tissues with hydrogel, many companies have developed state-of-the-art hydrogel 3D printers for biomedical applications. The most advanced and notable bioprinters of today include the CELLINK BIO X printers, the RegenHU 3DDiscovery™ Evolution, and the Allevi 3 printer. To get an idea of the state of the art of hydrogel printers, this subsection will discuss the capabilities of the BIO X printer.

The BIO X 3D printer is developed by a company called CELLINK. It is capable of extruding and printing with many kinds of bioinks including GelMA, PEGDA, Alginate, etc. for application in biomedical research and has a print resolution of 1µm (CELLINK, 2025).

The BIO X has interchangeable and attachable printheads for different forms of gel extrusions including a pneumatic, syringe pump, thermoplastic and inkjet printheads. The printing bed and printheads are temperature controlled (to account for the wide-ranging rheological properties of different hydrogels). The printers also include UV LED attachments for photo-induced crosslinking and implement a UV ray-based system (with smaller wavelengths than for curing) for sterilizing the printing environment in between prints to ensure biosafety standards are met (CELLINK, 2025).

Chapter 3

Stakeholder Requirements

Number	Stakeholder	Description	Priority
SR1	End-user	The system must be able to extrude hydrogel to create 3D shapes structures out of hydrogel	must-have
SR2	Design	The printer should be able to precisely and smoothly adjust the position of the extruder	must-have
SR3	Design	The extruder must be able to precisely control the flow rate of hydrogel being extruded	must-have
SR4	End-user	The extruder must be sterilizable and able to contain and extrude hydrogel without compromising its useability through contamination	must-have
SR5	End-user	The printer must allow for tuneable parameters	must-have
SR6	End-user	The system should have parameters that are tuneable in real time	optional
SR7	Design	The printer should have a repeatable performance for a set combination of parameters	must-have
SR8	End-user	The system should include at least one method of solidifying the gel that is synchronized during the printing process	must-have
SR9	End-user	The system should have the physical ability to print with a large variety of different types of hydrogels	optional
SR10	End-user	The printer should be user-friendly with a reasonable degree of simplicity to operate	must-have
SR11	Safety	The system should be safe to handle with minimized risks to the health and safety of its users	must-have
SR12	Financial	The system must be able to be designed and built within a budget of R6000	must-have
SR13	Experimental	The system's performance must be well documented by means of experimental validation	must-have
SR14	Experimental	The system should be able to send live sensory information for experimental feedback	optional
SR15	End-user	The system can have two extruders for more useful prints	optional

Table 3.1: Stakeholder Requirements

Chapter 4

Engineering Requirements

Chapter 5

Functional Decomposition

Chapter 6

Mechanical Design

Unless the chapter heading already makes it clear, an introductory paragraph that explains how this chapter contributes to the objectives of the report/project.

6.1 Extruder Design

6.1.1 Concept Generation

Concept 1

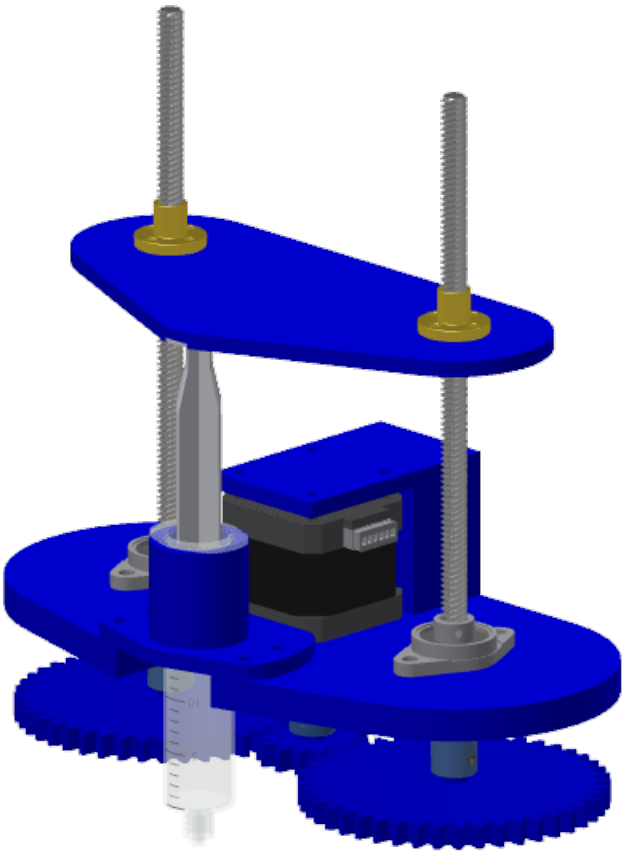

Figure 6.1: Concept 1 Syringe-Based Extruder

Concept 2

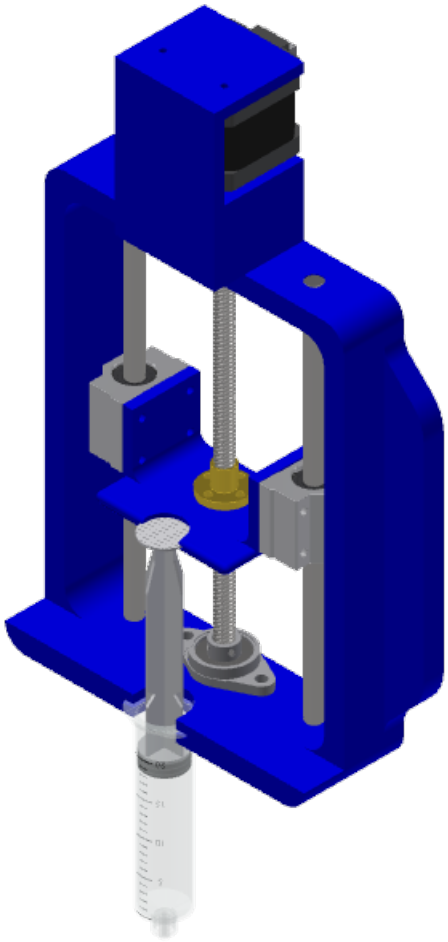

Figure 6.2: Concept 2 Syringe-Based Extruder

Concept 3

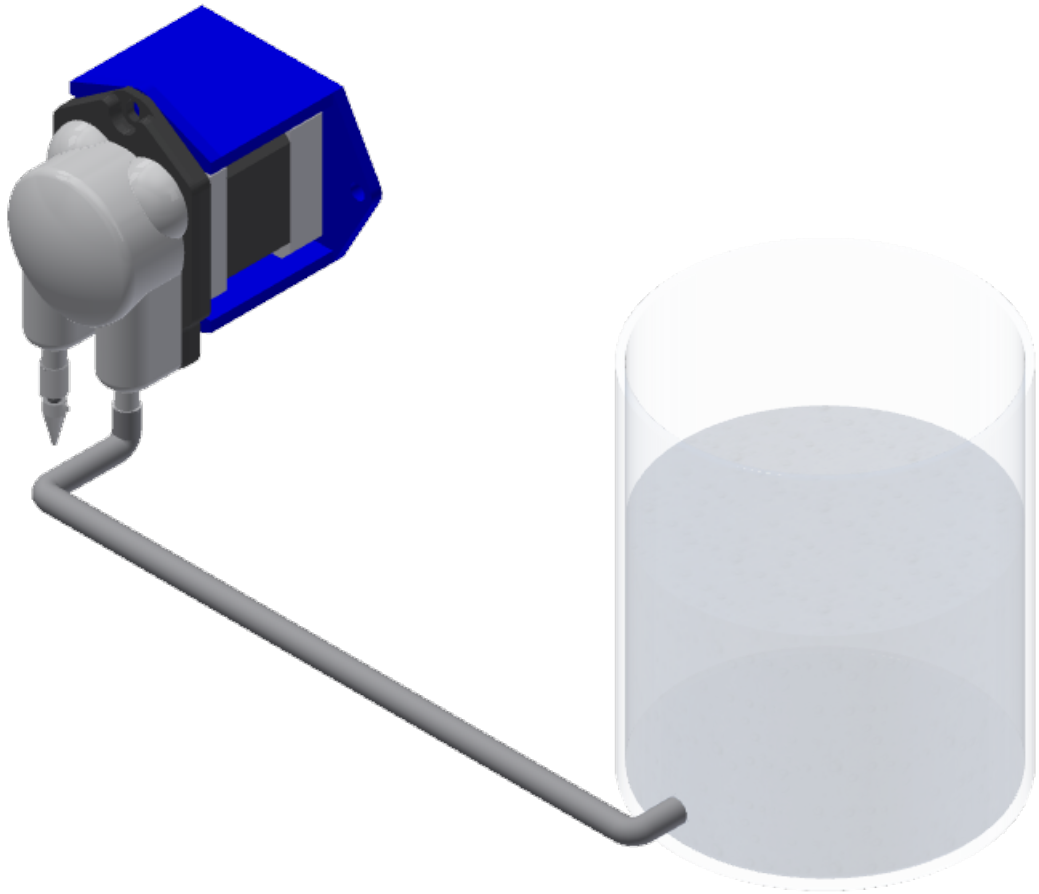

Figure 6.3: Concept 3 Pump-Based Extruder

6.1.2 Concept Evaluation and Selection

6.1.3 Final Design

6.2 Gantry Design

6.2.1 Concept Generation

Concept 1

Concept 2

6.2.2 Concept Evaluation and Selection

6.2.3 Final Design

6.3 Final Assembled Bioprinter

Chapter 7

Embedded System Design

7.1 System Description

7.2 Hardware Design and Implementation

7.2.1 Hardware Block Diagram and Description of Interaction

7.2.2 Power Supply

7.2.3 Memory Storage and Programmer Circuit

7.2.4 Stepper Motor Setup

7.2.5 Load Cell Circuit

7.2.6 Thermocouple Circuit

7.2.7 FET Switching Circuit

7.3 Software Design and Implementation

7.4 Measurements and Results

Chapter 8

Experimental Design

8.1 Materials and Methods

8.1.1 Materials

The bioprinter's printing parameters are adjusted using a computer which behaves as an interface and the prints produced in each trial of the experiment are measured using a measuring tape and digital vernier caliper. This experimental setup is shown below in Figure 8.1:

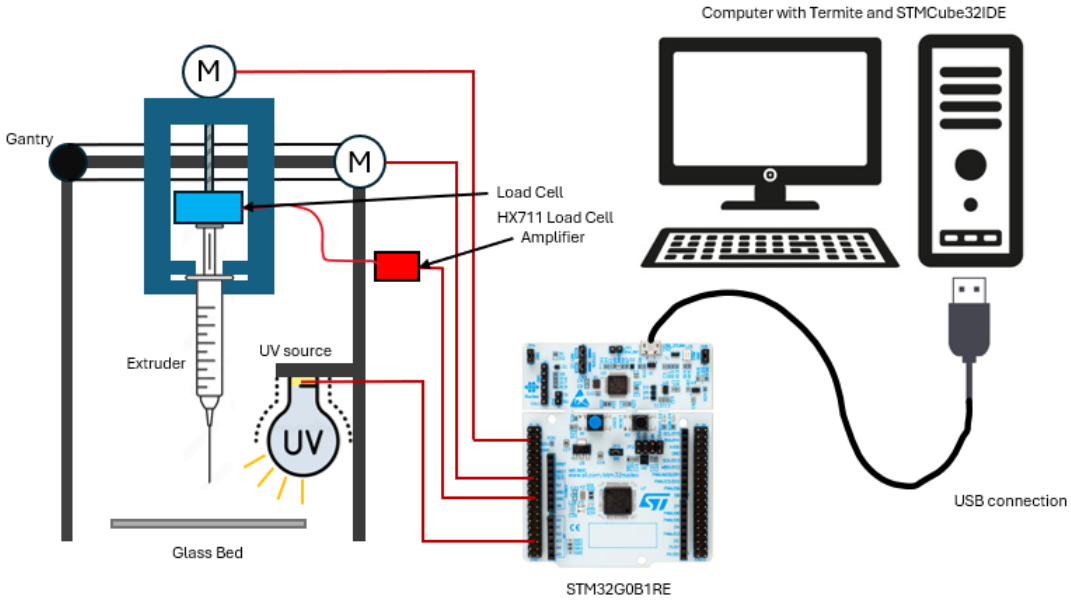

Figure 8.1: Experimental Setup (please change pic)

8.1.2 Equipment Specifications

GelMA Specifications

Bioprinter Specifications

Software

8.1.3 Methods

Experimental Setup Procedure

Test Procedure

8.2 Discussion of Results and Conclusion

Chapter 9

Conclusions

Appendix A

Calculations

A.1 Syringe Calculations

Given:

$$\text{Inner diameter of barrel } (\text{ID}_1) = 20\,\text{mm}$$
$$\text{Length of barrel } (\text{L}_1) = 80\,\text{mm}$$
$$\text{Inner diameter of nozzle } (\text{ID}_2) = 0.2\,\text{mm}$$
$$\text{Length of nozzle } (\text{L}_2) = 20\,\text{mm}$$

Cross-sectional areas:

$$A_1 = \pi\left(10 \times 10^{-3}\right)^2 \approx 314 \times 10^{-6}\,\text{m}^2$$
$$A_2 = \pi\left(0.1 \times 10^{-3}\right)^2 \approx 31.4 \times 10^{-9}\,\text{m}^2$$

Max extrusion speed at nozzle:

$$v = 5\,\text{mm·s}^{-1} = 5 \times 10^{-3}\,\text{m·s}^{-1}$$

Volumetric flow rate:

$$Q = v \cdot A_2 = (5 \times 10^{-3}) \cdot (31.4 \times 10^{-9}) = 1.57 \times 10^{-10}\,\text{m}^3\text{·s}^{-1}$$

Assumed viscosity:

$$\mu = 10\,\text{Pa·s}$$

Poiseuille's Law:

$$\Delta P = \frac{8\mu LQ}{\pi r^4}$$

Total pressure required:

$$P_B = P_{\text{atm}} = 101\,325\,\text{Pa}$$
$$P_A = \frac{8 \cdot 10 \cdot 0.08 \cdot (1.57 \times 10^{-10})}{\pi(0.01)^4} + \frac{8 \cdot 10 \cdot 0.02 \cdot (1.57 \times 10^{-10})}{\pi(0.0001)^4} + 101325$$
$$= 900\,919\,\text{Pa} = 900.919\,\text{kPa}$$

Required force:

$$F = P \cdot A_1 = (900\,919) \cdot (314 \times 10^{-6}) = 282.889\,\text{N}$$

Design force (with safety margin):

$$F_{\text{design}} = 300\,\text{N}$$

Appendix B

Experimental results

List of references

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