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## Practical Work Portal

Report Year 2023



Employment at University Of Auckland, Faculty Of Engineering

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**Assigned Marks : 25 / 25 (Grade : A)**

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**Hours Verified : 400**

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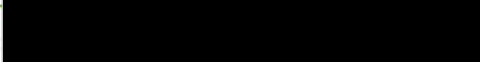

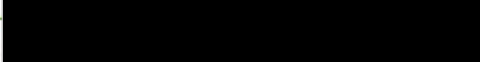
Section One	<b>Passed Section</b> If you pass Section One you still need to pass Section Two.			<b>Failed Section</b> If you fail Section One you will be asked to resubmit the report.			5/5
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Section Three Part A : Structure of the Report	Excellent	Above Average	Satisfactory	Room for Improvement	Below Average	No Marks	5/5
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Section Three Part C : Presentation of the Report.	Excellent	Above Average	Satisfactory	Room for Improvement	Below Average	No Marks	5/5

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No additional time added.

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#### Administrator Details

Verified Hours

Hours Type

08 December 2022

# Practical Work Report



Department of Engineering Science and Biomedical Engineering  
The University of Auckland

Company: The University of Auckland Department

Address: 

Supervisor: 

Employment Period: 23 November 2020 to 25 February 2021

## Summary

During the summer of 2020-2021, I had the privilege of working at the University of Auckland's Department of Engineering as a Research Assistant in the fields of Biomedical Engineering, and Chemical and Materials Engineering. My time was split between the Auckland Bioengineering Institute (ABI) and the Chemical and Materials Department. The ABI at 70 Symonds Street contains the offices of academics specialising in Engineering Science and Biomedical Engineering departments. It comprises a number of academics who work on various projects, both independently and collaboratively. The Chemical and Materials department is on 20 Symonds Street in the heart of the city campus of The University of Auckland. The faculty separates into groups that facilitate the study of many different areas such as biomaterials and food materials.

I worked as a Research Assistant under the supervision of [REDACTED] [REDACTED] [REDACTED] (Engineering Science and Biomedical Engineering) and [REDACTED] [REDACTED] [REDACTED] (Chemical and Materials Engineering). The project that was assigned to me was to develop a mathematical model for cells in the eye, and to investigate the effects of different topographies and environmental factors. I also had the opportunity to work with different students in the lab extracting proteins that were relevant to my project.

Through this internship experience, I have gained valuable skills such as laboratory etiquette, data analysis, report documentation, and reviewing academic writing. Additionally, collaborating with people who were working on different projects related to mine taught me the importance of communication and flexibility.

This internship has been very valuable for my personal growth as an engineer and student, and has given me the opportunity to learn from experienced academics. Having worked alongside academics of various stages of study, my experience as a research assistant has allowed me to consider the possibility of further study in biomaterials and mathematical modelling.

## Acknowledgements

All glory, honour, and power to God who created all things and sustained me through the internship.

I would like to thank my supervisors: [REDACTED] [REDACTED] and [REDACTED] [REDACTED], who guided me through my projects with feedback and encouragement. Their input has been most valuable to my progress both within the project, and in my professional development.

I would also like to thank my team members: [REDACTED], [REDACTED], [REDACTED], [REDACTED], and [REDACTED], who welcomed me into their team and gave me advice whenever I asked questions.

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# 1 Introduction

The Auckland Bioengineering institute is a world-leading research institute that facilitates the application of mathematical and engineering sciences to biology. Many of these projects involve studying and treating diseases, and creating innovative technology to improve the quality of life. The Institute's building is at 70 Symonds Street, Grafton. There are supervisors from diverse backgrounds of study such as biological mathematics, artificial intelligence, signal processing, and many more. The ABI also facilitates postgraduate study and undergraduate research projects.

I had the privilege of working under the supervision of [REDACTED] and [REDACTED] as a Research Assistant from November 2020 to February 2021. The project I was given involved mathematical modelling of cells and biological tissue under the effects of different topographies and environmental factors. This involved reading academic writing about human eye anatomy and limbal stem cells, as well as reading documentation on PhysiCell - an open-source customisable cell model programme in C++. At the same time, I experimented with different cell models in PhysiCell and accompanied team members in the lab to learn more about the cells I was trying to model.

My work as a Research Assistant has given me insight to the working life of a professional academic and researcher. Through my work, I have gained technical skills such as C++, laboratory techniques, and data analysis, as well as a broadened knowledge of limbal tissue and cell physiology. Furthermore, I have gained efficacy in reviewing documentation and research, and applying the relevant knowledge to my project. I have also developed important soft skills such as the ability to communicate effectively through written, verbal, or presented mediums, and learning to adapt and solve problems that arise throughout a project. Overall, this internship experience has been both challenging and inspiring in my growth as a Biomedical Engineer.

## 2 Company Information

### 2.1 Workspace Layout

The University of Auckland Faculty of Engineering is a large 12-storey building in the centre of Auckland CBD on Symonds Street. The lower floors up to floor 4 consist of student lecture halls and study areas, whereas the upper levels contain office spaces where academics and postgraduate students work.

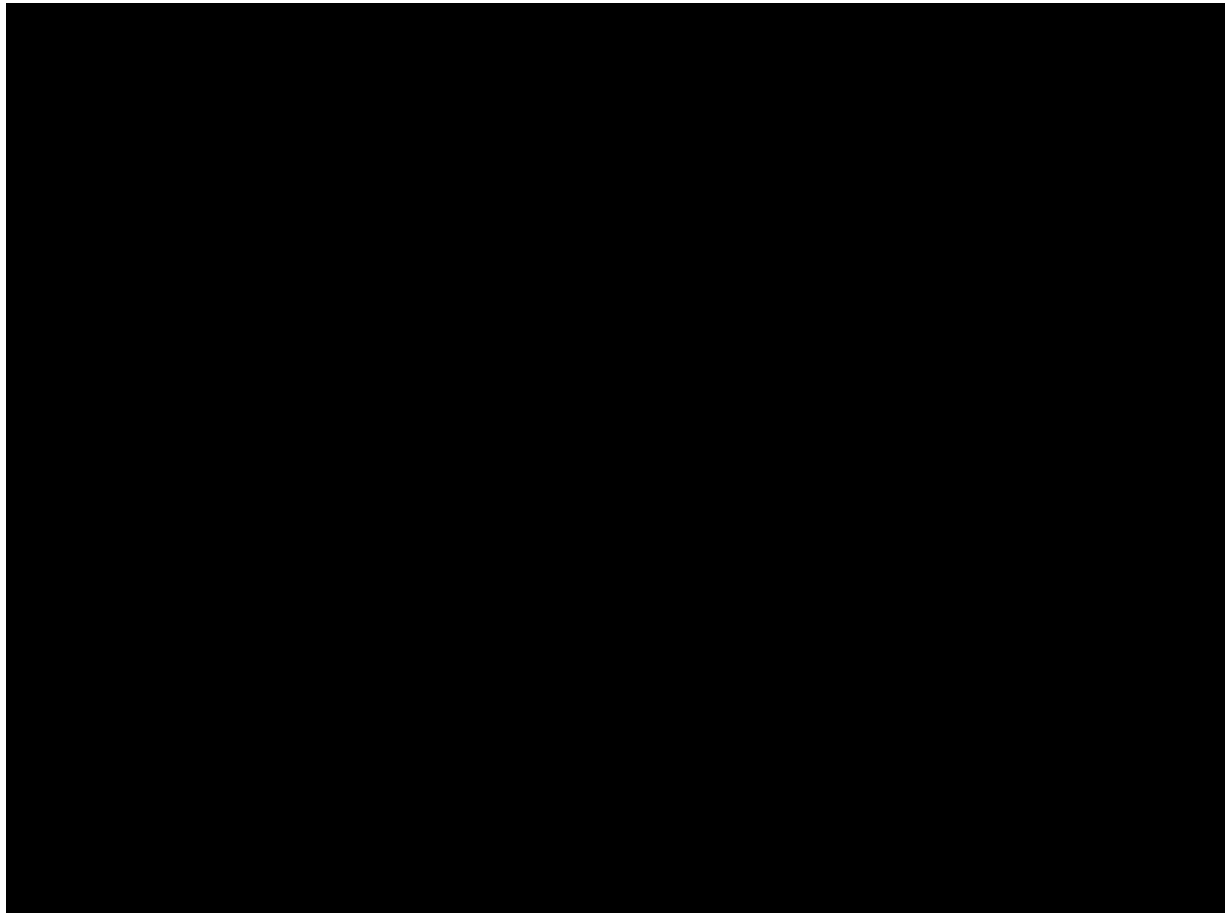


Figure 1: The University of Auckland Engineering building

The floors in the building are subdivided into different specialisations. The building contains a mixture of both open-plan office spaces, individual offices for professors, common rooms, and laboratory or workshop spaces. The bottom floor of the building contains workshop spaces for mixed-disciplines (MDLS), in addition to lecture halls and various study areas for undergraduate students. Floors one to four also contain lecture halls and study areas, as well as common areas and tutorial rooms. Above floor four, the spaces become more specialised, with labs and tutorial rooms dedicated to one particular engineering discipline. These spaces are often occupied by postgraduate students and professors. On these floors, there is a corridor running through the centre of each floor, allowing ease of access to all the necessary facilities.

Floor ten, which is the Chemical and Materials Engineering faculty, was the place where I spent most of my time. The floor is mainly made up of a large open-plan office space where the postgraduate students work. On the opposite side of the corridor, there are labs for testing, as well as small offices for individual professors. There is another larger laboratory on floor nine in which the majority of my laboratory work was done. The common room is also located on floor nine.

## 2.2 Workspace Facilities

Inside the open-plan office area, the office desks are laid out in groups, and each team occupies a group of desks. This layout enables individuals within teams to collaborate easily and interact with each other effectively. The open-plan layout of the office also enables different teams to easily communicate with each other, as some teams are working on similar projects.

The common room on floor nine is a communal space with microwaves and fridges, and furnished with modern sofas, coffee tables, and bar stools. There are also various cafes and food vendors across the road which offer a variety of options.

The desk where I spent the majority of my time was a shared desk on floor ten with a PhD student on the team. I was given a chair and various items of stationary, and the monitor and desktop computer were available for my use whenever the PhD student was absent. I mostly worked on my personal laptop, as all the relevant files were saved on my device.

I also had weekly meetings with the other supervisor of the project whose office is located in the ABI. The ABI is similarly structured to the general Engineering building, where there are offices on every level, as well as classrooms and spaces for students to study.

## 2.3 Staff Organisation Structure

There are over a thousand postgraduate engineering students studying at the University of Auckland, not including the large number of qualified academics and professors. Each different specialisation under the general Faculty of Engineering is split into different areas of research. Within these areas, there are teams which are led by senior academics such as my supervisors, who oversee the study and research done by postgraduate students and research assistants. There are also opportunities for teams or individual researchers to collaborate, as there is often some overlap between areas of research that are similar.

I had the privilege of working alongside three PhD students on the team, as well as a postdoc researcher and another research assistant. The team was led by our supervisor who is a senior lecturer. Each team member's projects were centred around the topic of biomaterials, as this was the area in which our supervisor specialised in. My project was about biomaterials and it overlapped two areas of



study: Chemical and Materials Engineering and Biomedical Engineering, hence my other supervisor was a lecturer in the ABI.

## 3 Work Experience

This internship was based on individual-based modelling of limbal stem cells using PhysiCell - an open-source software based on C++ which uses BioFVM solvers to solve complex biological ODEs and PDEs required in cellular processes.

The overall goal of my research project was to create a computational model of limbal stem cells, with respect to factors such as topographies, external environmental changes, and the presence or absence of various chemicals. To make this goal more achievable, my work was divided into different sections:

- Literature review and documentation study
- Modelling cells in vitro
- Laboratory work and other team activities

Being a research internship, the vast majority of my time was spent in the literature review and documentation study section, explained in more detail in Sections 3.1 to 3.4. My findings were used to generate graphics and results, which are explained in Section 3.5. The remaining time was spent in the laboratory and with my team, explained in Section 3.6.

### 3.1 Learning about different cellular models

#### 3.1.1 Compartmental models

In the beginning of the internship, I was given the task of researching the different existing computational models that could potentially be used to model limbal stem cells. I was given a review written by my supervisor which was helpful in differentiating the different types of models, as all of them are highly complex mathematically. Compartmental models such as the Cellular Potts model consists of a lattice or matrix, where each cell is represented by a cluster of lattice sites. These models have been used to represent cell growth, migration, signalling, and division. However, with this type of model, the accuracy and resolution decreases as the size of the model increases, as the model tries to account for processes such as growth and death without modelling the underlying mechanisms by which these processes occur.

#### 3.1.2 Individual based model

Individual based models have either an ‘on-lattice’ or ‘off-lattice’ framework for the model to be based on. The on-lattice model is similar to the compartmental model, where each cell is represented by one site in the lattice or matrix. Movement and interactions between cells can be modelled, but the growth and size of the cells is difficult to determine from this model. The off-lattice model can be either vertex-based or centre-based. These types of models are able to capture the dynamics

of discrete cells using energy and kinetics equations or functions. PhysiCell is a centre-based model that encodes equations relating to cell to cell adhesion, cell growth and division, secretion of substances, etc. Many of these parameters can be changed depending on the properties of the cell being modelled, and equations can be added or removed depending on what is needed.

### 3.1.3 Continuum model

The Continuum model is different from the discrete models previously described as it is based on conservation principles and constitutive equations for entire cell populations rather than interactions between individual cells. These equations are also used within Compartmental and Individual based models, but the Continuum model is more holistic and less complex than the other two models, as it does not require detailed calculations of every single cell.

## 3.2 Investigating existing computational models

### 3.2.1 CompuCell3D

The computational model CompuCell3D is an existing computational model that is based on the Cellular Potts model. The software is open-source and is still under development. After investigating some documentation on how to create models using this software, I made a decision to stop as the time taken to create a basic model would be greater than PhysiCell, with a lower accuracy and complexity.

### 3.2.2 PhysiCell

PhysiCell is an open-source individual-based model that models all kinds of different cells, from individual cells to large colonies with many intercellular interactions. The software uses C++ and graphics that show the change in behaviour over time can be generated using Python or ImageMagick. There is also an extensive documentation that explains how to use the software, as well as demonstrations using various templates and default models.

## 3.3 Learning PhysiCell

### 3.3.1 Learning C++

Since PhysiCell is coded in C++, an understanding of the language was required for me to successfully use this template to create my own models. The tutorials that were recommended to me were online tutorials by learncpp.com and W3Schools, which equipped me with a basic understanding of the syntax and structure of the language. Once I was able to read and gain a basic understanding of the code inside the PhysiCell files, I moved on to PhysiCell tutorials and documentation.

### 3.3.2 Learning how to change and add parameters

There are several tutorials on the PhysiCell online website that instruct users on how to set up the program on a device, and examples of how to use templates and change parameters [1]. These tutorials were helpful in setting up my PC for using PhysiCell, and debugging problems. I was also able to follow demonstration tutorials to create models that PhysiCell developers had already created as defaults or examples [2]. These tutorials showed how to build, run, and view sample models. Through these tutorials I learned that all the parameters in the model, including equations that encoded environmental factors and cell behaviour, were located inside the “.xml” file. Every model contains a “.xml” file which is referenced within the “.cpp” and “.h” files: the files used to run the model. To familiarise myself with the existing models that PhysiCell has developed, I ran the “biorobots-sample” model. To display the output, I used ImageMagick to gifs out of the SVG files that are output from the simulation. The graphics and observations will be discussed in Section 3.5.

I later came across a more comprehensive documentation of PhysiCell called the “User Guide” [3], which contains lots of information about how to navigate and use the software. Sections 7 to 14 of the document gave detailed explanations of how to open and run models, how to change different parameters and their effects on the model, and how to create graphics that result from the model. By reading and altering the “.xml” files of example models from the PhysiCell default projects, I was able to alter parameters such as growth rate and migration, as well as add my own parameters as desired. In addition to learning a lot about how to use the PhysiCell software, I also learned many things about the life cycle of cells. Much of my time at the internship was spent studying this document and learning the complexities of PhysiCell, and debugging the code whenever an error would occur.

### 3.3.3 Writing custom code

When downloading PhysiCell, one of the projects included is the “template2D” model. This model is a blank model with no existing cells and only default parameters. My custom code is all within the template2D folder in sample\_projects. The files inside the folder that I edited are: custom.cpp, custom.h, and PhysiCell\_settings.xml. When PhysiCell runs, it copies these files into the custom\_modules and config directories inside the main PhysiCell directory.

These are the main sections of code I edited within my own model from *template2D*:

Inside custom.cpp there are 4 pre-existing functions: *create\_cell\_types*, *setup\_microenvironment*, *setup\_tissue*, and *my\_coloring\_function*. All other functions that have been added onto the end are custom functions that I’ve written.

*create\_cell\_types* is a function which defines the different cell types in the simulation. You can create new cell types here and customise their parameters. You can also call custom functions, e.g.

```
motile_cell.functions.update_phenotype           =  
motile_cell.increase_proliferation;
```

The pre-written code defines a default cell, and when other cells are created, this default cell is copied to make new cell types. After the new cell type is created, parameters are customisable by hard-coding values, or calling them from the *PhysiCell\_settings.xml* file. I've created 4 different cell types: motile, bob, TA (transit amplifying), and fred, each with different parameters and custom functions.

*setup\_microenvironment* is a function which uses the *PhysiCell\_settings.xml* file to set up the microenvironment. All of this is automated within the pre-written code. In addition, you can overwrite the automatic microenvironment by writing custom code, e.g. `get_default_microenvironment()->update_dirichlet_node(1226, 1, 100);`

Within this function, the only custom code I added were the dirichlet nodes that are activated using the *dirichlet\_center* boolean. This was added when I was experimenting with the glucose microenvironment for centripetal migration using chemotaxis up the glucose gradient.

*setup\_tissue* creates cells using the cell types that have been created in *create\_cell\_types*. For each individual cell, you can choose its position, size, motility, etc. Section 9 of User Guide explains more on how to customise your cells.

I also declared several booleans at the beginning of the file, which selects which simulation I want to run. Each simulation plots different cell types in positions that test or model different things.

### 3.3.4 Generating graphics and observations

A graphics simulator is required in order to visualise the outputs generated by the model. Initially, I used ImageMagick, the programme recommended by the PhysiCell documentation. This is a free downloadable graphics software that produces a simulation in the form of a gif. I found that this software was difficult and time consuming, so I decided to investigate other ways of producing simulations.

After talking to my supervisor, I found out that a previous intern of this project had already created a graphics simulator in Python that generates graphics in an mp4 format, and is faster than ImageMagick. I was able to successfully run this on my own PC, generating mp4 videos of the model simulations.

From these graphics, I was able to make observations and conclusions about the different models and parameters that were experimented with.

## 3.4 Researching limbal stem cells

### 3.4.1 Limbal stem cell life cycle and growth factors

Limbal epithelial stem cells are located at the edges of the cornea, at the limbus, and are believed to divide every two to three weeks to provide cells that migrate to the centre of the cornea for growth and repair after injury [4].

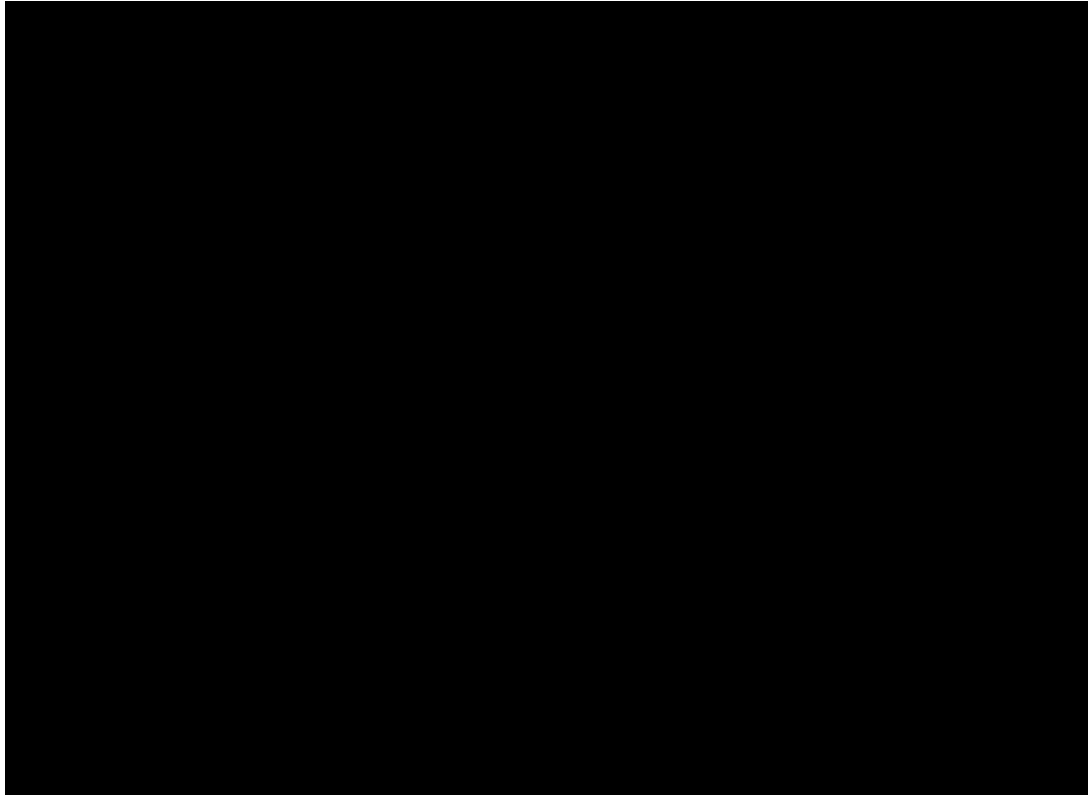


Figure 2: Diagram of the life cycle of a corneal epithelial cell, from limbal stem cell to corneal epithelial differentiated cell.

As shown in Figure 2, when the need arises, the limbal stem cell divides and the resulting cell becomes a transient amplifying cell, dividing quickly and migrating towards the centre of the cornea. These cells will eventually turn into corneal epithelial differentiated cells, which help to repair the damaged cornea. Currently, the reason for migration of cells toward the centre of the cornea is unknown, but is thought to be due to a chemical gradient.

A potential problem that could arise that prevents the cornea from effectively repairing itself is deficiency of limbal stem cells. Possible causes of this are congenital diseases, large chemical and thermal burns, multiple ocular surgeries, contact lens wear, and ocular surface inflammatory diseases. In these situations, limbal stem cells are less able to proliferate and repair the cornea. As a result, our research team has been working on ways to aid cell growth and division. They have discovered that the crystallin protein that can be extracted from fish eyes is a material that promotes cell growth and division when limbal stem cells are in close proximity. The team have

been working on the extraction and purification process, as well as finding ways to incorporate it into hydrogels to create a favourable environment for cells to grow on. This study will lead to applications on patients to help their corneas repair themselves more effectively.

### 3.4.2 Applying research to a PhysiCell model

Using the information gathered from research papers and the team's data, I was able to create a basic model of limbal stem cells. The stem cells exist only at the edge of the cornea, then transit amplifying cells are created from division of the stem cells.

After creating the basic model, I added cell migration at a specified rate and stochasticity towards the centre of the cornea. Within the microenvironment, I added a constant chemical gradient along which the cells migrate. I also added a rate of apoptosis as the cells that die are replaced by new cells as they reach the centre of the cornea. A video graphic was generated that includes this screenshot:

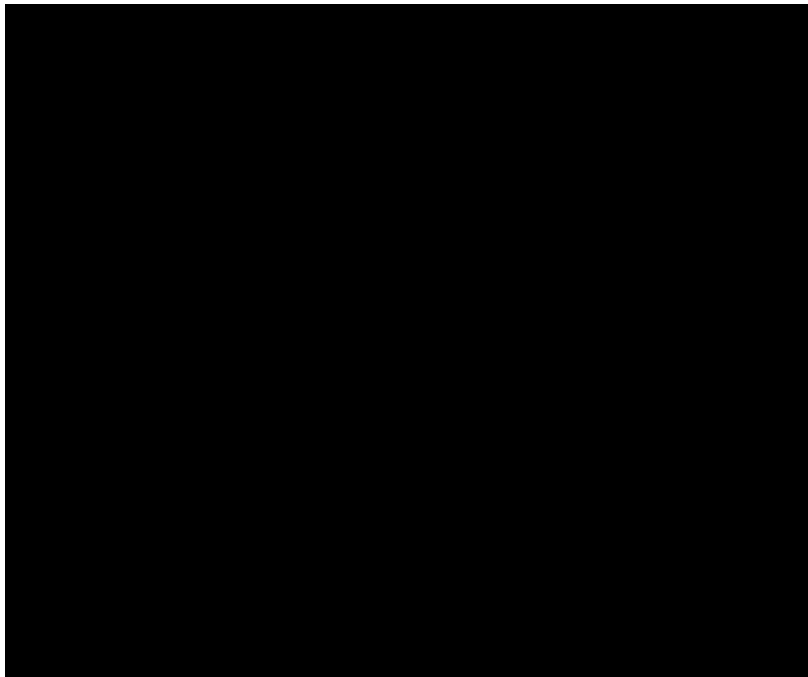


Figure 3: Basic model with transit amplifying cells migrating towards the cornea centre.

There were many other environmental and cellular parameters that I experimented with, such as cell to cell adhesion, secretion of chemicals, cell differentiation, chemotaxis, topographies, and presence of a binding motif. The latter two were the most complex as they required creating a new type of cell to represent different textures and substances in the hydrogel, and the crystallin protein, respectively.

An initial goal of the project was to model how the cells would react to different topographies on hydrogels. To model this, I created a new cell variety with zero movement and placed them in specific locations to imitate different patterns on the hydrogel. I experimented with the adhesion level so that cells would either move

towards or away from the pattern. I also placed these topography cells into different formations: spiral and grid, to see if any particular topography was more favourable for growth.

To model the crystallin protein's effect on limbal stem cells, I used the cells I created for the topography experiments and altered them to cause increased growth and division in the transit amplifying cells. The resulting graphics are interesting as they show the pattern of movement and growth of cells as they react to the different topographies in which the crystallin protein is placed.



Figure 4: Crystallin protein in a grid formation, with transit amplifying cells placed randomly.

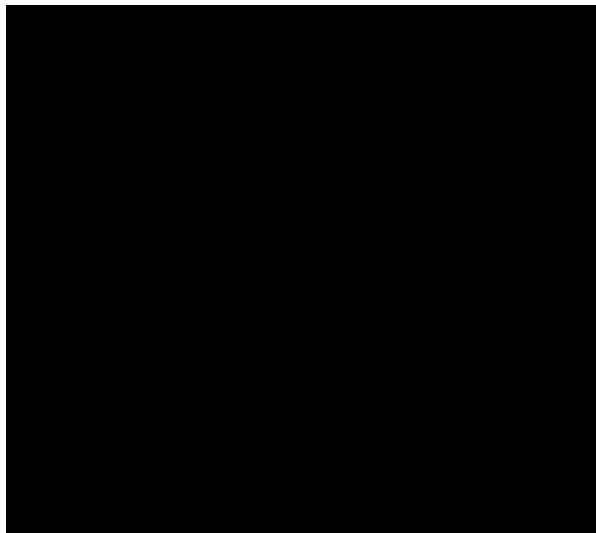


Figure 5: Crystalline protein placed in an eight-way spiral, with transit amplifying cells placed in a circle.

## 3.5 Other activities

### 3.5.1 Team meetings

As well as the PhysiCell coding and limbal stem cell research that was part of my project, there were also other activities that took place, such as meetings, presentations, and report writing. Weekly group meetings took place on Monday or Tuesday mornings to connect socially with each other and report our activities and findings for the previous week. During these meetings, there would often be a presentation from a member of the group who would talk more in depth about the project they were working on. These presentations were an ideal time for feedback and questions which would guide the team member through the next steps in their projects.



### 3.5.2 Laboratory work

On several occasions, I was given the opportunity to work with another summer student in the laboratory in the Chemical and Materials Department. They had been working on extracting and purifying the crystallin protein from fish eyes, and I was able to assist them in their laboratory work. Although my time in the laboratory was brief, I was able to help handle chemicals and use various pieces of equipment such as the magnetic stirrer, centrifuge, and Milli-Q water system.

### 3.5.3 Presentation

On the 9th of February 2021 I gave a presentation that explained and summarised my project and the conclusions I made [5]. Because the group were from diverse backgrounds in science and engineering, I began by giving an explanation of what mathematical and computational modelling is. I then talked about how modelling is relevant to limbal stem cells and the crystallin protein, and gave examples of the models I had done. To conclude, I summarised my findings from the different models I created and gave suggestions for future work, which I intended to continue working on in the final few weeks of the internship.

### 3.5.4 Report

During the last week of the project, my supervisor requested for me to write a report to hand on to any future students who hope to continue my work. I therefore wrote a document summarising all of the reading and tutorials I gathered my research from, the processes and methods through which I created my models, and the conclusions I made from them [6].

## 4 Reflective Appraisal

My internship experience as a research assistant at the University of Auckland has been very rewarding and enjoyable. I have gained many valuable professional skills through interacting with more experienced academics and learning from their feedback. I have also been able to experience the working life of an academic, which has encouraged me to consider a career in postgraduate studies. The work that I undertook also challenged me to be self-driven in my research and through reading and experimenting with the cell models, I have learned a great extent about mathematical modelling. Furthermore, through assisting the other summer student in the laboratory, I was able to gain experience in the lab and learn about the skills and equipment needed for handling different chemicals and for protein extraction.

Through my team's guidance and feedback, I have learned the importance of constant communication and acknowledgement of their advice. Their knowledge and resources on the topic of biomaterials was very helpful, as the relevant information was more readily accessible than if I had tried to search for it myself. Furthermore, I was shown that communicating my questions and issues with my team members is more effective in solving problems than attempting to figure out the solution myself. Oftentimes, following their experienced advice was the best way to solve problems.

My experience as a research assistant also revealed to me the realities of working in academia. Because the field of my study is so broad and there is a vast amount of knowledge that I was yet to understand, at times I felt very overwhelmed by the broad scope of my project. However, this taught me to be patient with reading articles and studying documentation, as I found that my knowledge of the topic would grow over time.

Working on a code-heavy program that is not extremely user-friendly, such as PhysiCell, gave me many practical engineering skills+. Not only was I required to self-learn how to use the software in a new language, but I also gained the skills and patience in self-learning a new programming language: C++. This project has greatly advanced my programming skills and ability to pick up new programming languages. I am much more familiar with the syntax and semantics of C++, and I am now confident in learning new programming languages without the need for external mentoring.

I was also fortunate enough to gain access to the laboratories and learn about common laboratory equipment and etiquette. I was exposed to the practical challenges of using the laboratory such as contaminations and time and spaces constraints. This experience was a valuable opportunity as the vast majority of engineering workspaces have research laboratories, and having used the equipment already, I am more equipped to work effectively in laboratories in any future work.

Overall, this summer research internship has widened my knowledge of scientific and engineering research, and has increased my knowledge of how to communicate,

solve problems, and be self-driven in my work. Through this experience, I have also learned to greatly appreciate the practices of patience, life-long learning, and humility, which are all skills that are beneficial to my professional career as a Biomedical Engineer.

## 5 Conclusions

The University of Auckland has given me valuable insight into the fields of Academia and Research. The self-driven yet collaborative working style was uniquely challenging as I was required to set my own goals and resolve unexpected problems that were exclusive to my project, and therefore difficult for others to help solve. The team aspect of the project, where several people were working on different projects within a similar field, enabled a balance of working independently, whilst still receiving assistance and advice from various team members and my supervisors.

The key skills I have gained are:

- Collaboration skills such as communicating with team members and supervisors to ensure that my work remains relevant to my goals, and the goals of the team.
- Understanding the relevance and importance of the work that an academic does, and the advantages such as time flexibility, as well as challenges such as specific jargons that are exclusive to the field.
- Practical engineering skills such as mathematical modelling, coding languages (C++ and Python), literature review, and knowledge of physiology at the cellular level.
- Proper laboratory skills, etiquette, and procedures, related to handling chemicals, biomaterials, and specialised laboratory equipment.

This internship has not only expanded my theoretical knowledge of academic research, but it has helped me to understand the necessity of this field of work, and the applications that it has to the real world. In the future, I hope to continue developing my professional skills as an engineer, and give back to the community through my work.

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## 7 Appendices

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Figure 2: Diagram of the life cycle of a corneal epithelial cell, from limbal stem cell to corneal epithelial differentiated cell.

Figure 3: Basic model with transit amplifying cells migrating towards the cornea centre.

Figure 4: Crystallin protein in a grid formation, with transit amplifying cells placed randomly.

Figure 5: Crystalline protein placed in an eight-way spiral, with transit amplifying cells placed in a circle.