Dissertation:

**Introduction (Aim: 571/600 words)**

Background Information:

The cells which line our blood vessels are called Endothelial cells (EC), which form the Endothelium layer. This layer of cells are able to repair themselves after injury, which is essential to good health, however, the repair process becomes slower with age due to the cells becoming senescent.

These cells are generally in a confluence, therefore a larger number of cells are no longer dividing, however, when they’re wounded, such as an atheroma, the confluence is broken and the cells leave this phase to continue dividing, repairing the damaged tissue. This process is slower in elderly patients due to many senescent cells, or if the same area is damaged a second time after repair. This is due to scar tissue being less capable of mitosis and repair.

Aims and Objectives:

The main aim of this project is to monitor the affect ageing has on the ability for blood vessels to heal after being scratched. The implications of this project will help professionals further understand the process of wound healing and to provide further insights into the conditions affecting the deadly disease atherosclerosis, which can lead to strokes and heart attacks.

The way the main aim will be implemented requires the development of an agent based model to encapsulate the key behaviours associated with endothelium cells, including: cell proliferation, apoptosis, and senescence. This model will record the time taken for the wound to repair itself, and observe any emergent behaviour that takes place through the mitosis and movement of the cells. For the basis of producing this agent based model, I’ll be developing on top of already developed code by Marziha Tehranis’ code, giving the agents and environment differing behaviours.

I’ll be observing the difference between elderly and younger cells to see how much, if any, age affects repair time.

Interestingly, this project has ample room for expansion; some of these aims include: modelling the problems associated when the endothelium layer doesn’t sufficiently repair in time, and the effect on endothelium repair after successive tears (allowing significant scar tissue to build up) showing the differences in speed and process of the repair.

Constraints:

Unfortunately, this aims of this project are currently hindered by several constraints that agent based models inherently possess.

So far in my testing of Marzihas code, it has become obvious that the level of computing power on my personal computer is only capable of modelling areas of around 0.1mm2 within a reasonable amount of time, without many agents. However, when I increase the area to the size desirable for the project, 1mm2, the number of interactions between all the agents is too large and therefore not feasible.

Another constraint on this project is the lack of specific and accurate data I can use as parameters within the program, which can end up leaving the simulation less useful.

 Summary of Report:

Over the next few pages, I’ll go through the literature I’ve read to date, picking out any data that could be used as parameters, go through the current state of Marzihas code and how I’ll adjust it to this project. Next, we’ll discuss in detail the aims and objectives, what will not be covered and why, and any experiments or tests I’ll be carrying out at the end of the project. Finally, I end on a conclusion on what’s been found so far, my achievements to date and a project plan to take through into semester 2.

**Literature Review (Aim: 561/1500)**

Within our bodies, there are several systemic factors, such as: obesity, heredity factors and age that contribute to the ill-health of a person <Warboys>. The areas that seem to cause the greatest deal of harm tend to be at branches within the blood vessel, where there is a turbulent flow of blood<Warboys>. At these sites, we tend to see an increase in senescent cells which can increase the time taken for a wound to heal. Evidence shows that with an increase in age, there tends to be an increase in the number of senescent cells, leading to long term health problems such as atherosclerosis or plaque formation, potentially breaking off a capillary, causing heart attacks or strokes

The Endothelial Cell Cycle:

Firstly, it’s important to fully understand the mechanisms by which our ECs divide and any biological factors that can change its behaviour.

* Time taken
* Cell growth and division
  + Increase size in G1
  + During mitosis they become spherical?
  + Split into 2 equal size daughter cells
  + All above sup points are simplification and we can either go deeper with A level knowledge or leave as is
* Age
  + The effect on healing?
* Factors

Senescent Cells:

* Slow down surrounding cells
  + How?
* Undergo apoptosis?
* Stay in quiescent state for a long time, then why move over?
* What size do they grow to?
  + How long does this take?

Environment:

The type of environment that is most interesting to us is that involving low sheer stress.

* - Environment within Blood Vessel<?>
* Low Sheer Stress <?>
* Physiological environment within blood vessel
  + Assuming physiological Ca2+ levels.

Atheroprone Sites:

Not all ECs within our blood vessel have the same physiology behaviours; this is due to the differing environmental factors within the vessels, discussed above. This leads to parts of our blood vessels under going higher levels of injury than others. In fact, the main disease this project is aimed at further understanding, atherosclerosis, is rather specific, and can be most commonly be found at the bends or branches of arterial trees <Chaudhury>. These bends and branches are known as atherosusceptible sites, which have enhanced proinflamitory activation, due to the constant activation of c-Jun N-terminal kinase (JNK)<Chaudhury>. These atherosusceptible sites therefore have a higher rate of injury and cell turnover compared to EC at atherprotected sites <Chaudhury 5-7>. Analysis by Chaudhury et al showed that the ECs at Atheroprone sites express proteins that respond to lipopolysaccharides by priming for apoptosis and proliferation<Chaudhury>. They also state that wherever JNK1 is active is where apoptosis and EC turnover occur in arteries.

I will therefore be looking at branches and bends within my model as they are the areas where there is the highest level of turbulence and concentration of JNK; leading to the greatest injury of the endothelium wall. Which, in turn has the greatest concentration of EC apoptosis and proliferation.

Review of Agent Based Software:

So far, I have found several computer programs that use agent based modelling to allow realistic modelling of biological behaviours. The first program is SPARK …

The other program, is … by Marziha Tehrani

Overall, I’ve decided to use Marzihas programme as it already has solved the mathematics behind the complex and possible recursive overlapping interactions between cells once they divide by mitosis or move around.

**Requirements and Analysis (Aim: 17/1000)**

Aims and Objectives

Areas not Covered

Evaluation of Current Work

* Test1 - vary age

**Conclusion, Progress, and Project Plan (Aim: 42/600)**

Conclusion

Progress

* Achieved to date

So far to date, I’ve managed to translate Marzieh’s code from python 2 in to python 3, refactored to PEP8 and run a few test simulations with nothing changed.

* Anticipate changes to the code.
  + Random number of proliferating cells
  + In confluence
  + Then remove a strip
  + Plot number of cells / time?

Project Plan