Development of An Agent-Based Model Capturing Cellular Interactions Associated with Heart Attacks

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Under the Supervision of: Dr Dawn Walker

Introduction:

Background:

The cells which line our blood vessels are called Endothelial cells, 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 due to scar tissue being less capable of mitosis and repair.

Description of Project:

My project is to model the effect of tearing the single layer of Endothelium cells lining our blood vessels, record the time taken for the wound to repair itself, and observe the behaviour of the dividing mitotic cells.

I'll be observing the difference between elderly and younger cells to see how much age affects repair time, and the subsequent problems associated when this layer doesn't sufficiently repair in time.

Further to the effect of age on repair, my project will also model the repair of the Endothelium layer after successive tears. This will show the effect of scar tissue on the speed and process of repair.

To form the basis of my project, I will be using and adapting Python code provided by Marzieh Tehrani, a PhD student. This code already handles the biomechanics involved in ensuring two or more cells are sufficiently apart (not overlapping) and the potentially recursive effects of this.

Literature read to date:

➢ Joyce, N. C. (2012). Proliferative capacity of corneal endothelial cells. Experimental eye research, 95(1), 16-23.

➢ Walker, D. C., Hill, G., Wood, S. M., Smallwood, R. H., & Southgate, J. (2004). Agent-based computational modeling of wounded epithelial cell monolayers. IEEE transactions on nanobioscience, 3(3), 153-163.

➢ Kwak et al (2014). Biomechanical factors in atherosclerosis: mechanisms and clinical implications. European Heart Journal. 35, 3013-3020.

➢ Chandhury et al ATVB (2010). C-Jun N-Terminal Kinase Primes Endothelial Cells at Atheroprone Sites for Apoptosis. Journal of the American Heart Association. 30, 546-553.

➢ Warboys et al ATVB (2014). Disturbed Flow Promotes Endothelial Senescence via p53-Dependent Pathway. Journal of the American Heart Association. 1079-5642.

Analysis:

Some of the problems I've found so far in analysing this project, include, understanding Marzihas' code, as it's lacking sufficient commenting and documentation. Another problem I face is insufficient Biological background knowledge. Only having an A level in Biology means that many of the terminologies used, I haven't covered before, leading to a large proportion of time required to fully understand the Biological systems going on within the Endothelial layer. The final problem I can see myself having with the project is where to get the figures used for the Biological modelling. This will probably involve reading through papers, taking out the key figures, however, sometimes these numbers aren't 100% known and are estimated in the paper itself. Therefore, I expect to adjust these numbers significantly during testing.

To overcome these problems, I'll be using the programming language Python, versions 3.5.2, Anaconda, version 4.2.0, and the IDE Spyder, version 3.0.0. I've decided to proceed with Python as it's a powerful Object Orientated Programming language, with a large community of scientist providing substantial libraries for me to utilise. This also means I'll have an easier time merging any of Marzieh's code with my own.

Plan of Action:
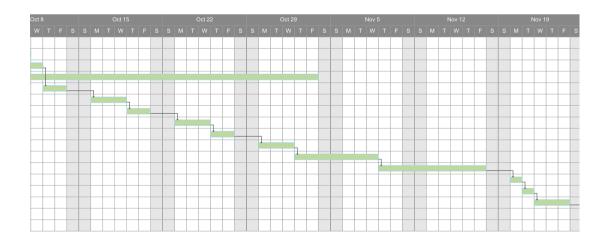
Description Stage

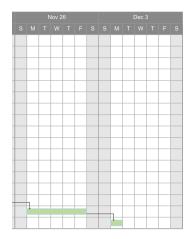|	Task Name	Duration	Start	Finish	Sep 24								Oct 1										
					S	M	T	W	T	F	S	S	M	T	W	T	F	S	S	M	T
1	Define Project	9d	09/26/17	10/06/17																	
2	Get feedback on Defining Project	1d	10/10/17	10/10/17																	
3	Understand Agent Based Model	3d	10/09/17	10/11/17																	
4	Understand Marzihas Code	20d	10/09/17	11/03/17																	
5	Understand Proliferative Capacity of Corneal Endothelial Cells	2d	10/12/17	10/13/17																	
6	Understand Endothelial Cells at Atheroprone Sites for Apoptosis	3d	10/16/17	10/18/17																	
7	Understand Biomechanical Factors in Athersclerosis	2d	10/19/17	10/20/17																	
8	Understand Disturbed Flow Promotes Endothelial Senscence	3d	10/23/17	10/25/17																	
9	Start Introduction	2d	10/26/17	10/27/17																	
10	Start Requirements and Analysis	3d	10/30/17	11/01/17																	
11	Start Literature Survey	5d	11/02/17	11/08/17																	
12	Tidy Up / Complete Survey And Analysis To Date	7d	11/09/17	11/17/17																	
13	Hand in Draft Survey And Analysis	1d	11/20/17	11/20/17																	
14	Get feedback on Survey And Analysis	1d	11/21/17	11/21/17																	
15	Make Changes to Survey And Analysis	3d	11/22/17	11/24/17																	
16	Formalise and Finish off Survey And Analysis	5d	11/27/17	12/01/17																	
17	Hand in Survey And Analysis Stage	1d	12/04/17	12/04/17																	