

A COMPUTATIONAL MODEL OF INTIMAL HYPERPLASIA

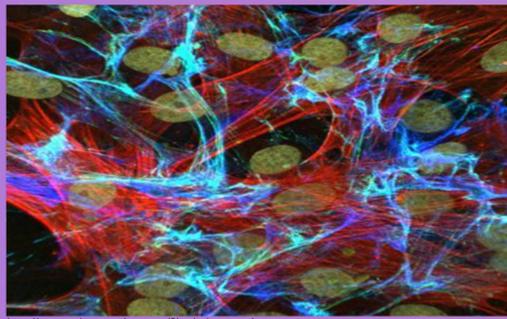
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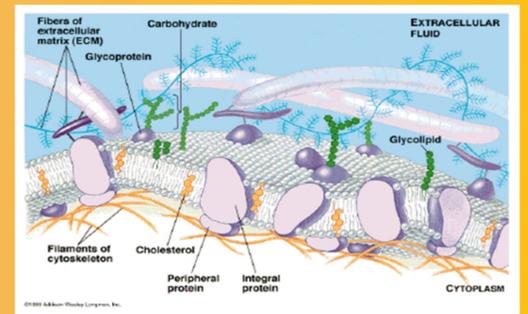
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https://info.ornl.gov/sites/rams09/m_jaime/Pages/Home.aspx



<http://www.sciencecodex.com/files/sciencecodex-oZsXUw08Fbda46Z.jpg>



<http://de.geocities.com/asternberghof/CellMembraneModel7.gif>

Background

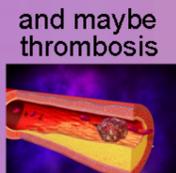
Intimal hyperplasia (IH) is the thickening of the tunica intima caused by vascular smooth muscle cell (VSMC) proliferation and migration from the medial layer to the intimal layer of the arterial wall. IH is a general response to arterial injury which may proceed bypass surgery or balloon angioplasty. IH after angioplasty is a main component of restenosis (secondary narrowing of artery).



http://healthhobbyfirst.com/graft/2007/00/04/quadruple_bypass_for_gpr.jpg

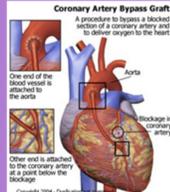


<http://scienceblogs.com/5enatiem/images/atherosclerosis.jpg>



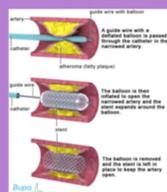
<http://z.about.com/d/oreate/1/0/D/p/4/0168.jpg>

which requires



http://images.healthcenteronline.com/heart/images/cabg_bypass_creat.jpg

or



http://hvd.co.uk/images/fact-sheet/coronary_bypass_427600.jpg

but beware of intimal hyperplasia

Research Objectives

- Create computational model of cell migration in response to multiple biochemical signals
- Include effect of matrix degrading enzyme (MDE) activation on extracellular matrix (ECM) proteins during VSMC migration
- Use C++ language to create the model and incorporate new components into previous hybrid discrete continuous model

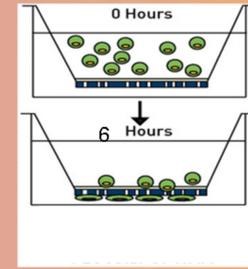
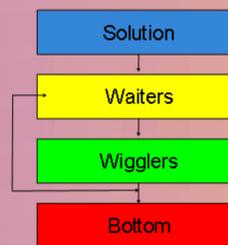
Methodology

Boyden Chamber experiment is the physical basis of the simulation model. Partial differential equations are developed to simulate the experiment.

Boyden Chamber



http://www.neuroprobe.com/images/products/BMC_BF312.jpg



<http://www.bmgbiotech.com/images/lan144-1.jpg>

- Consists of two compartments separated by porous filter (matrix) coated with collagen
- Conceptually, cells exist in one of four states

Mathematical Modeling

Traditional approach for computational modeling is to solve a simultaneous set of partial differential equations.

$$\frac{\partial n}{\partial t} = D_n(\nabla^2 n) - \nabla \cdot (\psi(c)n \nabla c) - \nabla \cdot (\chi(e)n \nabla e) + p_n - d_n$$

$$\frac{\partial c}{\partial t} = D_c \nabla^2 c + p_c - u_c - d_c$$

$$\frac{\partial m}{\partial t} = D_m \nabla^2 m + p_m - d_m$$

$$\frac{\partial e}{\partial t} = p_e - d_e$$

$n \rightarrow$ cell density
 $c \rightarrow$ chemoattractant concentration
 $m \rightarrow$ MDE concentration
 $e \rightarrow$ ECM concentration

Expected Results

- Positive correlation between chemoattractant concentration gradient and number of VSMCs that migrate
- Positive correlation between MDE concentration and the rate at which VSMCs migrate
- Matrix degrading enzymes effect development of IH
- Adding ECM and MDE equations produce more precise data

Future Research

- Optimize parameters to achieve more accurate results
- Add extracellular matrix (ECM) deposition to simulation
- Parallelize code
- Add cellular apoptosis and proliferation to the simulation

References

- Boyden, S.. The Chemotactic Effect of Mixtures of Antibody and Antigen on Polymorphonuclear Leucocytes. *Journal of Experimental Medicine*. 115 3 (1962).
- Dexter, N. C., K. L. Kruse, J. J. Nutaro, R. C. Ward. A Computational Model of Cell Migration in Response to Biochemical Diffusion.
- Budu-Grajdeanu, P., R. C. Schugart, A. Friedman, C. Valentine, A. K. Agarwal, B. H. Rovin. A Mathematical Model of Venous Neointimal Hyperplasia Formation. *Theoretical Biology and Medical Modelling*. 5 2 (2008).
- Nutaro, J. J., K. L. Kruse, R. C. Ward, E. O'Quinn, M. Woerner, B. Beckerman. A Discrete Cell Migration Model.

