‘Developing Models of the Blood Brain Barrier’

Gavin Fullstone

Supervisors: Prof. Giuseppe Battaglia (Biomedical Science), Dr Jonathan Wood (Sheffield Institute for Translational Neuroscience), Professor Mike Holcombe (Department of Computer Science)
Blood Brain Barrier

- Physically prevents the passage of almost all molecules
- Protects the brain from disease causing organisms and the immune system
- Only specific transport of certain molecules possible

Science, 2002, 297, 1116-1118

Neurobiology of Disease, 2010, 37, 13-25
Laminar Flow in a Blood Vessel
Validation: Zebrafish Embryos

Fli1 (endothelial marker): GFP zebrafish embryo at 3 days post-fertilisation
The Effect of Cell Size Changes on Dynamics of the NFκB pathway

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Supervisors: Prof. Eva Qwarnstrom (Cardiovascular Science), Prof. Mike Holcombe, Dr Sheila Francis (Cardiovascular Science)
The NFκB Pathway

- Key immune pathway

- Implicated in cancer, autoimmune disease and atherosclerosis

Stimulation e.g. Immune Signals, Bacteria, Cell Damage

NFκB

Regulation e.g. Cell Death, Cell Proliferation, Cell Activation
Observation: Cells Shrink after IL1 Stimulation

IκB-eGFP Hela Cells, before Stimulation

IκB-eGFP Hela Cells, 10mins Stimulation
Question

How does the change in cell size and shape affect the dynamics of the NFκB pathway?
What we did?

- Cell could shrink by up to 20% volume (cytoplasm only)
- Ran models with and without shrinkage
- Demonstrated that at multiple levels of regulation the pathway operates faster
- Consequently, negative regulation of the pathway also occurs faster
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