Marc Sturrock
University of Dundee
e-mail: msturrock@maths.dundee.ac.uk

Spatio-temporal modelling of the Hes1 and p53 pathways

The correct localisation of transcription factors is vitally important for the proper functioning of many intracellular signalling pathways. Experimental data has revealed that many pathways exhibit oscillations, both temporally and spatially, in response to certain external stimuli. Negative feedback loops are important components of these oscillations, providing fine regulation for the factors involved. In this talk, mathematical models of two such pathways–Hes1 and p53–are presented. Building on previous mathematical modelling approaches, we derive systems of partial differential equations to capture the evolution in space and time of the variables in the Hes1 and p53 systems. Through computational simulations we show that our reaction-diffusion models are able to produce sustained oscillations both spatially and temporally, accurately reflecting experimental evidence and advancing previous models. The simulations of our models also allow us to calculate a diffusion coefficient range for the variables in each mRNA and protein system, as well as ranges for other key parameters of the models, where sustained oscillations are observed. Furthermore, by exploiting the explicitly spatial nature of the partial differential equations, we are also able to manipulate mathematically the spatial location of the ribosomes, thus controlling where the proteins are synthesized within the cytoplasm. The results of these simulations predict an optimal distance outside the nucleus where protein synthesis should take place in order to generate sustained oscillations.
Using partial differential equation models, new information can be gained about the precise spatio-temporal dynamics of mRNA and proteins. The ability to determine spatial localisation of proteins within the cell is likely to yield fresh insight into a range of cellular diseases such as diabetes and cancer.

References

[1] M. Sturrock, A. J. Terry, D. P. Xirodimas, A. M. Thompson, M. A. J. Chaplain, *Spatio-temporal modelling of the Hes1 and p53-Mdm2 intracellular signalling pathways* Journal of Theoretical Biology **273** 15–31.