

## “Hopf Bifurcation in a Gene Regulatory Network Model: Molecular Movement Causes Oscillations”

Gene regulatory networks, i.e. DNA segments in a cell which interact with each other indirectly through their RNA and protein products, lie at the heart of many important intracellular signal transduction processes. In this talk we analyse a mathematical model of a canonical gene regulatory network consisting of a single negative feedback loop between a protein and its mRNA (e.g. the Hes1 transcription factor system). The model consists of two partial differential equations describing the spatio-temporal interactions between the protein and its mRNA in a 1-dimensional domain. Such intracellular negative feedback systems are known to exhibit oscillatory behaviour and this is the case for our model, shown initially via computational simulations. In order to investigate this behaviour more deeply, we undertake a linearized stability analysis of the steady states of the model. Our results show that the diffusion coefficient of the protein/mRNA acts as a bifurcation parameter and gives rise to a Hopf bifurcation. This shows that the spatial movement of the mRNA and protein molecules alone is sufficient to cause the oscillations. Our result has implications for transcription factors such as p53, NF- $\kappa$ B and heat shock proteins which are involved in regulating important cellular processes such as inflammation, meiosis, apoptosis and the heat shock response, and are linked to diseases such as arthritis and cancer. Implications for the multiscale modelling of cellular systems will be discussed.