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Spatio-temporal modelling of gene regulatory networks: The role of molecular movement

Abstract

Gene regulatory networks (GRN), 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 will present and analyse mathematical models of various GRNs using partial differential equations (PDE) and stochastic PDEs. We will then analyze 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 one-dimensional domain. Such intracellular negative feedback systems are known to exhibit oscillatory behavior and this is the case for our model, shown initially via computational simulations. In order to investigate this behavior 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-kappaB 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.