

Diffusion Driven Oscillations in Gene Regulatory Networks

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Many key cellular processes, such as cell division and apoptosis, must be precisely timed, and **gene regulatory networks** (GRNs) play an important role in maintaining these. A GRN may be concisely defined as a collection of DNA segments in a cell which interact with each other indirectly through their RNA and protein products. These interactions control the rate of transcription (mRNA production) in a cell and consequently translation (protein production). GRNs therefore typically rely on feedback mechanisms to function. Proteins may bind to gene-sites in the nucleus and alter the transcription rate. If the binding reduces the transcription rate there is a negative feedback which leads to oscillatory behaviour in both mRNA and protein levels. This has been observed experimentally both spatially (e.g. by observing fluorescently labelled molecules in single cells) and temporally (e.g. by observing protein/mRNA levels over time). Mathematical modelling of GRNs has focussed on determining the conditions which lead to such oscillatory behaviour. The spatial aspects of such models have been found to be of key importance with computational modelling demonstrating that spatial movement of the molecules is a critical component of GRNs [1, 2, 3, 4], while, in fact, it has been proved rigorously that the diffusion coefficient of the protein/mRNA acts as a bifurcation parameter and gives rise to a Hopf-bifurcation [5]. In this talk we show results from numerical simulations of PDEs which model (a) the well-known GRN, the Hes1 system [6], and (b) synthetic GRNs e.g. n-gene repressilator and activator-repressor systems [7]. Our specific interest concerns the role of location i.e. the relative position of sites for transcription and translation in a cell. We show that there is an optimum range for the distance between an mRNA gene-site and a protein production site in order to achieve oscillations [8]. By incorporating the idea of production sites into such models we show that the spatial component is vital to fully understand GRN dynamics.

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