Dissecting the dynamics of a simple genetic oscillator

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Abstract

Oscillatory activity of genetic networks underlies a wide range of developmental and physiological processes. During vertebrate development, certain embryonic tissues are spatially segmented in a highly dynamic process termed somitogenesis. Central to this process are cell autonomous oscillations in the transcriptional state of a number of genes; these oscillations are spatially coordinated by intercellular signalling. The period of these oscillations is rather short (20–120 min, depending on species). Genetic data suggest that the oscillations are generated by negative feedback loops, and mathematical modelling confirms the general plausibility of this idea. However, the short period of the oscillations imposes quite strict constraints on both the biochemical parameters of the underlying genetic circuits and on the amplitude of oscillations that can be generated by these circuits. Starting from arguably the simplest circuit that can support sustained oscillations (a single gene negative feedback circuit), I will explore the dynamical effect of each basic biochemical process known to be involved in the operation of the circuit (for example, movement of transcription factor between the cytoplasm and nucleus). The mathematical analysis highlights the potentially critical role of transcription factor dimerisation in the generation of short period oscillations with a physiologically reasonable amplitude. More generally, it provides important justifications for specific model reductions that are important in reducing the complexity of more complex oscillator models.