Emergence of Coordination in Genetic Networks from Low-Level Pulsing in Transcription Factors

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ABSTRACT

Cells live in changing, uncertain environments, exposed to sudden increases in the concentration of stressors. In order to survive, cells cannot depend solely on sensory responses, which have a delay associated with them, instead they need to anticipate future changes. However, the continuous synthesis and maintenance of general stress response mechanisms has a high energy cost for the cell. To resolve this, cells can rely on phenotypic diversity, where only a few cells carry the burden of expressing resistance mechanisms, effectively bet-hedging against the sudden appearance of a stressor. Phenotypic diversity can be produced by fluctuations in gene expression and is observed in many stress response mechanisms. In this study, we show another general role of noise in gene expression. By simulating a transcription factor that activates several downstream genes (single-input module) we discovered that when the concentration of the regulator is kept at low levels, as in the absence of stressors, infrequent bursting in downstream genes is observed and that these bursts can be coordinated. We compared an activator with fixed expression to an activator with pulsing dynamics. With one downstream gene, there is little or no difference observed between the two activators. However, when several downstream genes are studied together, the pulsing activator is able to coordinate them with a higher probability than the fixed activator, while maintaining the same cost for the cell. Furthermore, this cost can be tuned by modifying the frequency, duration and amplitude of the pulses of the activator, providing the cell with a flexible mechanism for tuning the dynamics. This coordination may not be exclusive to stress response mechanisms and has the potential to provide an advantage in all single-input modules where coordination and low levels of the regulator is desired.