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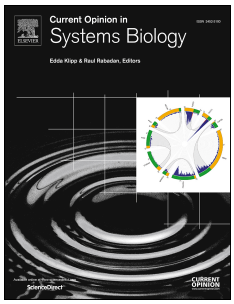

Living with noise: on the propagation of noise from molecules to phenotype and fitness

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Living with noise: on the propagation of noise from molecules to phenotype and fitness

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Abstract

In single cells, all molecules fluctuate in concentration because synthesis and degradation events occur asynchronously in a probabilistic manner. Since molecules generally influence multiple reactions, concentration fluctuations can propagate through the entire molecular circuit of a cell. This causes single isogenic cells to vary in their phenotypic properties, which affects the fitness of the associated genotype. Currently, we have a good understanding of how fluctuations arise and propagate in small molecular circuits. Convincing experimental observations exist of fluctuations in the growth and fitness characteristics of single cells. Yet, we have a poor understanding of which molecule concentration fluctuations cause emergent fluctuations in the phenotype of a single cell, how extensive fluctuation propagation is, and what its effects on fitness are. In this opinion paper, we discuss those aspects of current single-cell systems biology.

Box 1: Definitions and insightful relations

Stochasticity: A system is stochastic if random fluctuations occur in its variables. This means we can assign probabilities to variable values. A deterministic system does not show fluctuations. See Figure 1 and 2.

Fluctuations: A fluctuation is the deviation in the value of a variable of a single cell, such as a concentration or generation time from the mean value across all cells. So, for cell i a fluctuation is defined as $\delta x_i = x_i - \langle x \rangle$, with $\langle x \rangle$ as the mean value of one of its variables. Since fluctuations can be negative and positive, the mean size of fluctuations is calculated from the mean squared deviation, denoted by $\langle \delta^2 x \rangle$, which equals the variance of x across all cells. The standard deviation equals $\sqrt{\langle \delta^2 x \rangle}$ and is therefore a measure of fluctuation sizes. See Figure 2.

Noise: noise is a measure for the significance of fluctuations, defined as the squared coefficient of variation (CV^2). Accordingly, the noise equals $CV^2 = \frac{variance(x)}{mean(x)^2} = \frac{\langle \delta^2 x \rangle}{\langle x \rangle^2}$.