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Characteristic variability of co-regulated genes

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Populations of genetically identical cells exhibit significant variability even when grown in constant conditions. This cell-to-cell variability is the result of a varying intracellular milieu, as well as noise arising from probabilistic birth and death events of any molecule of interest. Because the network of molecular interactions within a cell is only sparsely characterized, it is difficult to make rigorous predictions about the variability of any given cellular component. Here we show that non-identical but co-regulated reporters can be used to rigorously infer properties of their upstream dynamics from static snapshots of naturally varying cells. Analytically proving covariance relations for classes of systems, we derive correlation constraints that can be used to detect the presence of feedback. Furthermore, we demonstrate how the variability of co-regulated fluorescent proteins with unequal maturation times can be used to identify genes with cell-cycle dependent transcription rates or detect oscillating genes. Finally, we show that such correlation constraints can be rigorously exploited even in the presence of experimental artifacts, such as molecular undercounting, making our theoretical results directly applicable to commonly used experimental techniques like fluorescent in-situ hybridization.

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