

Signatures of regulatory synergies in intrinsic biological noise

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THE past decade has seen remarkable advances in understanding of how genetic regulatory modules process information, particularly in prokaryotes. Extending this systems perspective to higher organisms requires a better understanding of how eukaryotic genes combine information from multiple transcription factors to give context sensitive responses. However, few synergies between regulators have been delineated to date because elucidating them can be experimentally challenging. In this talk, I will discuss a class of fluctuation-based relations that connect the moments of the distribution of molecular copy numbers of the regulators and the product of a gene to the derivatives of its *cis*-regulatory input function (CRIF), the quantitative mapping between the transcription factor concentrations and expression. These relations are useful because they enable statistics of naturally arising cell-to-cell variations in molecular copy numbers to substitute for traditional manipulations for probing regulatory mechanisms. This idea will be illustrated with applications to combinatorial and cooperative regulatory scenarios.