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An Evolutionary Perspective on the Role of Extrinsic Noise in Filtering Transcript Variability in Small RNA Regulation in Bacteria

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Abstract : Cell-to-cell variations in transcript or protein abundance, called noise, may give rise to phenotypic variability between isogenic cells, enhancing the probability of survival under stress conditions. These variations may be introduced by post-transcriptional regulatory processes such as non-coding, small RNAs stoichiometric degradation of target transcripts in bacteria. We study the iron homeostasis network in Escherichia coli, in which the RyhB small RNA regulates the expression of various targets as a model system. Using fluorescence reporter genes to detect protein levels and single-molecule fluorescence in situ hybridization to monitor transcripts levels in individual cells, allows us to compare noise at both transcript and protein levels. The experimental results and computer simulations show that extrinsic noise buffers through a feed-forward loop configuration the increase in variability introduced at the transcript level by iron deprivation, illuminating the important role that extrinsic noise plays during stress. Surprisingly, extrinsic noise also decouples of fluctuations of two different targets, in spite of RyhB being a common upstream factor degrading both. Thus, phenotypic variability increases under stress conditions by the decoupling of target fluctuations in the same cell rather than by increasing the noise of each. We also present preliminary results on the adaptation of cells to prolonged iron deprivation in order to shed light on the evolutionary role of post-transcriptional downregulation by small RNAs.

Keywords : cell-to-cell variability, Escherichia coli, noise, single-molecule fluorescence in situ hybridization (smFISH), transcript
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