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Gene expression noise and robustness of signaling in bacterial chemotaxis¹

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Stochastic variations in protein levels are one of the major sources of noise affecting biological networks. Since networks involved in gene regulation and signal transduction must have a defined input-output relation, they can be expected to have undergone evolution for inherent robustness against such perturbations. Chemotaxis of a model bacterium *Escherichia coli* – a mechanism that allows motile cells to follow chemical gradients in the environment – has one of the most thoroughly studied signaling networks in biology. Combining theoretical and experimental analysis, we investigated robustness of this network to intercellular variations in expression levels of chemotaxis proteins, or gene expression noise. The single-cell levels of different chemotaxis proteins showed strong co-variation, which implies that stochastic variations in transcriptional control are the main source of the noise. We demonstrated that the pathway is indeed robust to such kind of perturbations by testing the effect of concerted overexpression of all chemotaxis proteins on the pathway output. Using computer simulations and theoretical analysis, we determined the network design features responsible for robustness and showed that the experimentally established network in *Escherichia coli* has the smallest topology that is sufficiently robust to allow a majority of the individuals in a population to maintain a correct pathway output.

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