Cascading Non-Local Noisy Readouts Improves Precision of Gradient Response

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Gradient response circuits frequently involve a weakly diffusible molecule. Using a simple model that combines noise of individual cell readouts with non-locality mediated by the exchange of a pathway intermediate between neighbors, we demonstrate that this cell-to-cell communication improves the precision of gradient response. Further, although each noisy readout locally leads to loss of information, in the non-local case cascading of readouts can in fact improve the decision-making accuracy. We illustrate these results using the segment patterning system of the fruit fly, whose multi-tier feed-forward architecture provides an example of a cascade of noisy readouts.

***Keywords* — morphogenesis, gradient response, noise, precision.**

REGULATORY processes such as transcriptional control are intrinsically noisy. Quantifying this noise and determining how biological systems are nevertheless capable of making reliable developmental decisions has attracted much attention.

Cell-to-cell communication is a plausible general mechanism for mitigating the noise in individual decisions, and indeed many gradient response circuits involve a weakly diffusible molecule as one of the intermediates. The early embryonic development of the fruit fly is a particularly appealing model system to test these ideas, since here communication is mediated by a very simple mechanism, namely diffusion of protein products in the syncitium. Spatial averaging was suggested as a mechanism for improving precision of protein expression [1] and, more recently, as a mechanism mitigating instrinsic transcriptional noise [2]. We present new experimental evidence showing that spatial averaging indeed has a measurable effect on the precision of mRNA expression profiles: the observed noise level is lower than the theoretical curve of maximally efficient local noise filtering (Fig. 1).

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Previous theoretical work has investigated the effect of diffusion on the precision of expression boundary [3]. Here we extend this work by explicitly defining a distinction between the information content of a signal, and the amount of information it can transmit downstream. The former is determined by signal precision, while the latter is affected also by dynamic range. We show that optimizing decision-making accuracy is not the same as optimizing precision of expression. In presence of cell-to-cell communication, this tradeoff between signal precision and dynamic range makes cascading noisy readouts the optimal gradient response strategy, where optimality is defined in terms of transmitted information content.

More generally, we comment on the role of cell-to-cell communication in solving morphogenesis problems and the cost of establishment of structural information within a system.

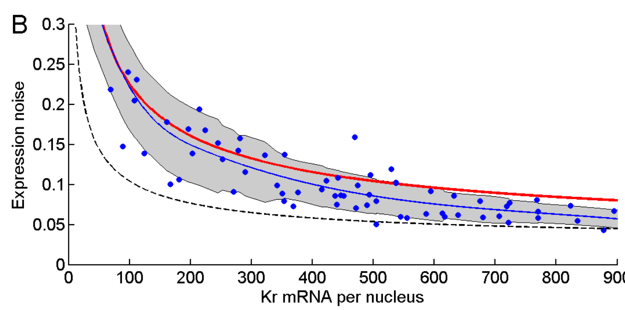

Figure 1. Measured expression noise of Kr mRNA profile is below the theoretical curve of maximally efficient local filtering (in red).

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