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The many ends of a never-ending story: Deriving the Drosophila gap gene system by ab-initio optimization

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Early embryogenesis is driven by complex spatio-temporal patterns that specify distinct cell identities according to their locations in the embryo. This process is remarkably reproducible, even though it results from regulatory interactions that are individually noisy. Despite intense study, we still lack a comprehensive, biophysically realistic model for at least one biological system that could simultaneously reproduce quantitative data and rigorously explain the emergence of developmental precision. Moreover, traditional approaches fail to provide any insight as to why certain patterning mechanisms (and not others) evolved, and why they favor particular sets of parameter values. We address both questions during early fly embryo development. Previous work has shown that the gap gene expression patterns in Drosophila optimally encode positional information. We therefore asked whether one can mathematically derive the gap gene network—without any fitting to data—by maximizing the encoded positional information. To this end we constructed a generic, biophysically accurate spatial-stochastic model of gene expression dynamics, where genes respond to morphogen input signals and mutually interact in an arbitrary fashion, and optimized its parameters for positional information. Firstly, our results show how the experimentally observed precision can be achieved with basic biochemical processes and within known resource and time constraints. Secondly, we show that multiple optimal solutions exist and systematically explore their characteristics. Finally, we show that some of the optimal solutions closely correspond to the real Drosophila gap gene expression pattern. To our knowledge this is the first successful ab-initio derivation of any biological network in a biophysically realistic setting. Our results suggest that even though real biological networks are hard to intuit, they may represent optimal solutions to optimization problems which evolution can find.

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