Constraints, objectives and tradeoffs in morphogen-mediated patterning

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Gradients of diffusible morphogens orchestrate precise pattern formation during animal development. Conserved, complex regulatory circuitry is found in most morphogen gradient systems, including elaborate feedback and feed-forward circuits, with contributions by co-receptors, diffusible inhibitors, multiple morphogens, and regulated uptake. It has been hypothesized that such mechanisms further "strategic" goals—robustness, speed, noise-filtering, flexibility, adaptability, etc. Mathematical and computational studies have shown how some of these mechanisms can indeed contribute to the robustness of patterning. Yet largely neglected have been the tradeoffs that often occur between strategies for achieving different goals. For example, we recently showed how strategies for achieving robustness to uncertainty in morphogen production typically interfere with strategies for overcoming cell-to-cell variability in morphogen response ("spatial noise"), and vice versa [Lander, et al. 2009, CSH Perspect. Biology 1, a002022]. Spatial noise should be especially troublesome at the far edges of morphogen gradients (where morphogen concentration is low), a prediction we have confirmed experimentally in the fruit fly larval wing imaginal disc. One consequence of a tradeoff between robustness and noise-tolerance is a limit on the maximum distance over which a morphogen can pattern, a constraint that is indeed observed. Recently, we have begun to elucidate tradeoffs among strategies for achieving robustness to uncertain production rates of morphogens, receptors and co-receptors. In my talk, I will attempt to use the need to balance such tradeoffs as a basis for understanding the peculiar regulatory machinery of the fly wing disc *decapentaplegic* gradient, one of the most intensively studied morphogen gradient systems.