

DEVELOPMENT

Robust but responsive protein gradients

Gradients of chemical signal are thought to be important in conveying positional information both in individual cells and in whole organisms. Two papers recently published in *Developmental Cell* show that the establishment of such gradients in two different systems displays the complementary properties of plasticity and robustness.

Reeves *et al.* monitored the establishment of the dorsal–ventral nuclear gradient of the Dorsal protein in live early *Drosophila melanogaster* embryos using a fusion of Dorsal to the Venus fluorescent protein. The authors found that the nuclear concentration of Dorsal fluctuated in a manner that coordinated with cell division; the dorsally positioned cells start interphase with ‘too much’ nuclear Dorsal and actively transport it out of the nucleus, whereas ventral cells commence interphase without enough nuclear Dorsal and actively transport it into the nucleus during interphase. This is consistent with nuclear envelope mitotic breakdown, resulting in the equilibration of Dorsal concentration across the nucleus and cytoplasm in mitosis; the nuclear concentration gradient is then established in the cells during interphase. Despite these oscillations in the nuclear concentration of Dorsal, a remarkably consistent, although shallow, Dorsal nuclear gradient is achieved across the embryo over time.

Analysis of the expression of several Dorsal target genes using multiplex *in situ* hybridization revealed that target gene expression also fluctuates until nuclear cycle 14. In response to the puzzling question of how such a dynamic and shallow nuclear gradient of Dorsal can result in a stable graded expression of genes, particularly at the tail end of the gradient, the authors propose a time-averaging model. They propose that noise in this system allows the gradients to respond

to environmental or genetic perturbations and that this plasticity may be crucial for the implementation of gene expression domains.

Saunders *et al.* investigated what it is that makes an intracellular gradient robust. Imaging of the *Schizosaccharomyces pombe* Pom1 protein using the fluorescent fusion protein Pom1–Tomato confirmed that Pom1 forms concentration gradients in these cells and that the concentration of Pom1 is highest at the tips and lowest in the middle. This gradient is thought to regulate cell division. Time-lapse imaging showed fluctuations in the localization of Pom1, but time-averaging resulted in a smoother gradient profile. Through confocal imaging of fluorescence recovery after photobleaching (FRAP) and fluorescence correlation spectroscopy (FCS), the authors showed that Pom1 localizes to the plasma membrane in multiple forms, including in a fast-diffusing form and in slower diffusing clusters. The authors propose a two-state model of gradient formation in which Pom1 forms unstable clusters in a manner that is nonlinear with respect to protein concentration. Such nonlinear cluster dynamics, together with time-averaging, maintains a robust gradient despite the presence of large fluctuations.

Protein gradient formation and establishment is thus likely to be a more complex process than first thought, as these studies show that gradients must be able to both respond to and be resistant to noise.

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ORIGINAL RESEARCH PAPERS Reeves, G. T. *et al.* Dorsal–Ventral gene expression in the *Drosophila* embryo reflects the dynamics and precision of the Dorsal nuclear gradient. *Dev. Cell* 16 Feb 2012 (doi:10.1016/j.devcel.2011.12.007) | Saunders, T. E. *et al.* Noise reduction in the intracellular Pom1p gradient by a dynamic clustering mechanism. *Dev. Cell* 16 Feb 2012 (doi:10.1016/j.devcel.2012.01.001)