

Dynamic Gene Circuits Control *Drosophila* Embryogenesis

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WE have conducted a systems-level analysis of differential gene activity in the early *Drosophila* embryo. These studies have led to the elucidation of a comprehensive gene regulatory network governing embryonic patterning, and have identified a number of unexpected design features:

1. The double-negative gate is a common network motif used by the early embryo. Instead of simple activation, many genes display restricted activities due to localized inhibition of global repressors. Examples include localized Notch signaling and inhibition of apoptosis.
2. Many key developmental control genes contain stalled RNA Polymerase II (Pol II) prior to their activation. Quantitative confocal imaging analyses suggest that genes containing stalled Pol II are activated in a synchronous fashion, while genes lacking stalled Pol II are induced in a stochastic fashion. Stalled Pol II appears to suppress transcriptional noise prior to the coordinate induction of gene expression.
3. Target enhancers that are regulated by diminishing levels of a regulatory gradient contain a fixed arrangement of binding sites. This regulatory “grammar” ensures a stable output pattern of gene expression in response to a changing gradient. Such enhancers possess the properties of bipolar junction transistors.