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Gene Regulatory Networks in Embryos Depend on Pre-existing Spatial Coordinates

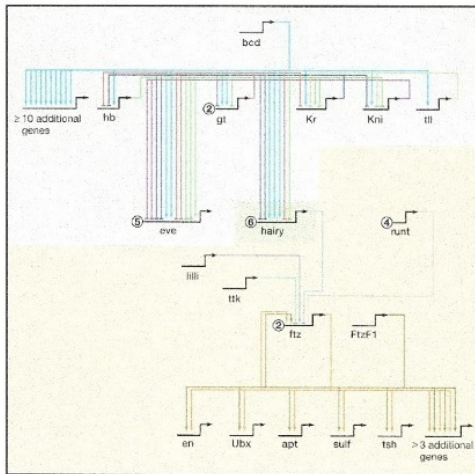
Abstract #347

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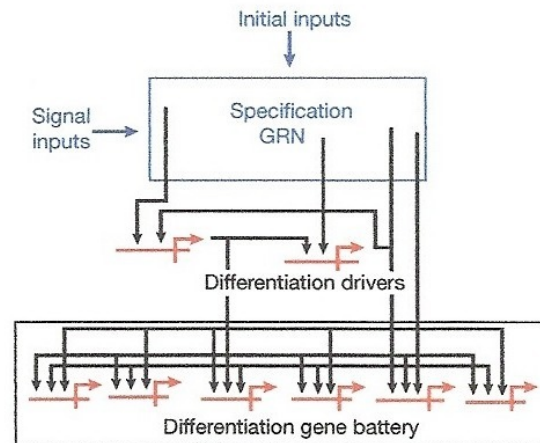
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The development of metazoan embryos requires the precise spatial deployment of specific cellular functions. This deployment depends on gene regulatory networks (GRNs), which operate downstream of initial spatial inputs (E. H. Davidson, *Nature* 468 [2010]: 911). Those initial inputs depend, in turn, on pre-existing spatial coordinate systems. In *Drosophila* oocytes, for example, spatial localization of the earliest-acting elements of the maternal GRN depends on the prior establishment of an anteroposterior body axis by antecedent asymmetries in the ovary. Those asymmetries appear to be derived from cytoskeletal and membrane patterns rather than DNA sequences, and there is evidence that some cytoskeletal and membrane patterns can be inherited independently of the DNA. I review that evidence, suggest that such patterns provide developmental information that must precede the operation of GRNs, and discuss possible implications of that information for evolutionary theory.

GENE REGULATORY NETWORKS IN DEVELOPMENT



Sean B. Carroll, "Evo Devo and an Expanding Evolutionary Synthesis: A Genetic Theory of Morphological Evolution," *Cell* 134 (2008): 25-36.



Eric H. Davidson, "Emerging properties of animal gene regulatory networks," *Nature* 468 (2010): 911-920.

THE INITIAL INPUTS FOR GENE REGULATORY NETWORKS INCLUDE SPATIAL ASYMMETRIES THAT ARE ALREADY PRESENT IN THE ZYGOTE.

"Ultimately, the beginning of spatial information in the embryo often traces back to asymmetrically distributed molecules deposited in the egg during its production in the ovary that initiate the formation of the two main axes of the embryo (so the egg did come before the chicken)."

"In almost all animal groups there are two kinds of mechanism used to start the process by which given parts of the egg become given parts of the embryo. First, there are internal anisotropies built into the egg during oogenesis that result in asymmetric distribution of various macromolecule(s) attached to the egg cytoarchitecture. Second, there are cues that result from the advent of the sperm in fertilization."

Sean B. Carroll, *Endless Forms Most Beautiful: The New Science of Evo Devo* (New York: W. W. Norton, 2005), p. 116.

Eric H. Davidson, *The Regulatory Genome: Gene Regulatory Networks in Development and Evolution* (Amsterdam: Academic Press, 2006), p. 90.

In a *Drosophila* oocyte, even maternal effect genes are expressed within an already-established body plan.

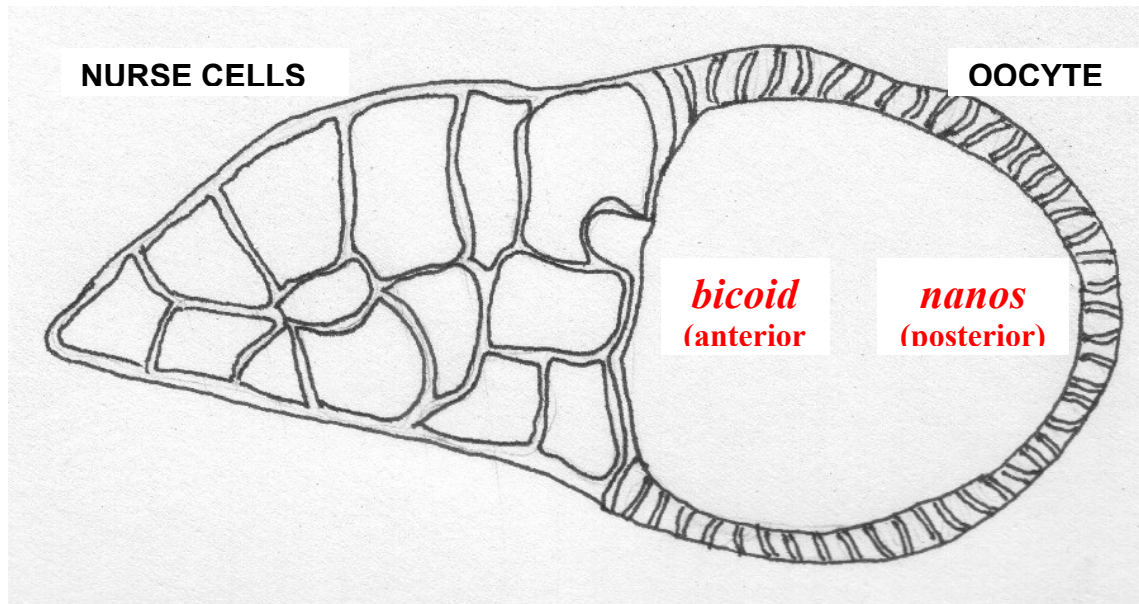


Illustration by Lucy Wells

For example, the stable localization of *bicoid* and *nanos* depends on targets that are spatially specified by antecedent cytoskeletal and membrane patterns.

William E. Theurkauf & Tulle I. Hazelrigg, "In vivo analyses of cytoplasmic transport and cytoskeletal organization during *Drosophila* oogenesis: characterization of a multi-step anterior localization pathway," *Development* 125 (1998): 3655-3666.

Kevin M. Forrest & Elizabeth R. Gavis, "Live Imaging of Endogenous RNA Reveals a Diffusion and Entrapment Mechanism for *nanos* mRNA Localization in *Drosophila*," *Current Biology* 13 (2003): 1159-1168.

Uwe Irion & Daniel St. Johnston, "Bicoid RNA localization requires specific binding of an endosomal sorting complex," *Nature* 445 (2007): 554-558.

Musa M. Mhlanga, et al., "In vivo colocalisation of oskar mRNA and trans-acting proteins revealed by quantitative imaging of the *Drosophila* oocyte," *PLoS One* 4 (2009): e6241.

These targets provide the initial inputs for gene regulatory networks.

SOME MEMBRANE PATTERNS CAN BE INHERITED INDEPENDENTLY OF THE DNA.

“Composition of cellular organelles and their membranes is constant from one generation to the next. This latter property of organelles, when considered with the fact that membranes do not form *de novo*, has led to the proposal that cell membranes and their constituent proteins have *temporal continuity* and, as such, may account for at least part of the epigenetic spatial memory which is present in cells. It has been proposed that genetic memory and spatial membrane memory interact whenever new proteins are inserted into membranes and that, insofar as membranes do not form *de novo*, it is the preexisting spatial memory encoded in a membrane that brings new proteins to its surface... Realizing that genetic memory is one-dimensional, along a DNA molecule, whereas spatial memory is likely to be two-dimensional, along membrane surfaces, and three-dimensional within the cellular interior, it is probable that spatial memory is more complicated and diverse than genetic memory.”

Robert O. Poyton, “Memory and Membranes: Expression of Genetic and Spatial Memory During the Assembly of Organelle Macrocompartments,” *Modern Cell Biology* 2 (1983): 15-72.

According to Poyton’s hypothesis, although the molecules in a membrane pattern may be encoded by DNA, the membrane pattern itself pre-

exists their synthesis. It's a bit like painting by numbers. The protein "paints" are encoded by DNA sequences, but where they end up on the membrane "canvas" depends on the antecedent pattern.

EVOLUTIONARY IMPLICATIONS

- 1. Changes in the architectures of gene regulatory networks are probably insufficient to account for major evolutionary changes. The initial inputs must change as well.**
- 2. Evolutionary developmental biology needs a more adequate explanation for the sources of spatial asymmetries—including membrane patterns— in the zygote.**
- 3. Those spatial asymmetries are probably not derivable simply from DNA sequences in the parental genome.**