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FlyWeb is a research project in progress. Work in progress is red textboxes:
-Figures identified but not yet digitized are noted along with REFS.
-Pathways where data is available but not yet correlated are marked "End of the Line – For Now"
- Proposed changes to the CootieFly programs on the basis of new data are noted.
-The literature review is constantly ongoing. References for upcoming additions are added to the REFS list as they are processed.

The "**Computing the Egg**"Project ([CompEgg](#)) uses Boolean-based PC programs to compute transcriptional programs to study gene interactions and effects of mutants on developmental programs.

Programs: John W. Bodnar
Digital Scholar: Brian Rogers

Funded in part by Howard Hughes Memorial Institute Digital Scholars Program

SUMMARY

While development is a single hierarchical process, scientists tend to study it one level at a time - molecular, cellular, or organismal. Data and theory are available to integrate focused molecular, cellular, and organismal models into a single hierarchical model for development of the *Drosophila* embryo. The overall model links the transcriptional cascade with the mitotic and phenotypic fate maps to trace hierarchical mechanisms of development from the genotype in the egg to the phenotype in the larva.

Phenotype = Organismal Level - Events that determine organismal structure begin as cells differentiate and form the functional organs or structures in the embryo or adult. The organs can be identified through their physical characteristics or phenotype. Therefore, we can describe embryogenesis as an organismal process and map cell fates by following phenotypes

Mitotic Domains = Cellular Level - Cellular events begin with cell divisions that program compartments of cells in the developing embryo. The compartments in the cellular program can be identified as groups of cells that share a common developmental program. Early in *Drosophila* embryogenesis compartments can be seen as mitotic domains that divide synchronously as the embryo develops. Therefore, we can describe embryogenesis as a cellular process and map cell fates in compartments by following the mitotic domains.

Transcriptional Cascades = Molecular Level - Molecular events begin with morphogens (either proteins or mRNAs) stored in the egg that program a transcriptional cascade. The biochemical steps in the molecular program can be identified as combinations of transcriptional activators and repressors (usually termed transactivators) or signal transducers that control the fates of each cell's progeny. Therefore, we can describe embryogenesis as a molecular process and map cell fates by following the transcriptional cascade.

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The organismal program for Drosophila embryogenesis begins with the genotype and assigns a phenotypic fate map consisting of the cell types throughout the larva. Growth studies of various sorts (from gynandromorphs to laser ablation of eggs;) have allowed the assignment of maps indicating where individual cell types or organs in the Drosophila larva or adult originated in the fertilized egg. By looking for changes or deletions of larval structures as one changes the genotype or destroys individual cells in the blastoderm, one can link genotype to phenotype – providing important information about the beginning and end of the cascade but unfortunately without providing information about what occurs between.

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The cellular program for Drosophila embryogenesis begins with the cellularization of the blastoderm and by means of synchronous cell divisions assigns a mitotic fate map consisting of cellular compartments in the larva (based on Foe (1989)). After rapid nuclear divisions to form the syncytial blastoderm, newly formed cells comprise a cellular blastoderm that arrests in G2 of the 14th cycle. During the subsequent two hours, most cells pass through mitosis of their 14th cycle, with groups of cells in different regions of the embryo dividing at different times. Foe (1989) studied cell divisions in the gastrulating embryo using anti-tubulin staining in situ to discriminate between mitotic cells (with tubulin in mitotic spindles) and interphase cells (with tubulin in cytoplasmic filaments), following the synchronous divisions of about thirty different "plaid patches" of cells throughout the embryo, and compiling a catalog for these "mitotic domains" (Foe, 1989). She suggested that "the challenge this presents is to discover which are the important genes (colors) that endow each interesting square of the plaid with its instructions. Cataloging the morphogenetic performance of various domains produces a list of consequences, and cataloging gene expression patterns will produce a corresponding list of potential causes (Foe, 1989)".

Transcriptional Cascades = Molecular Level - Molecular events begin with morphogens (either proteins or mRNAs) stored in the egg that program a transcriptional cascade. The biochemical steps in the molecular program can be identified as combinations of transcriptional activators and repressors (usually termed transactivators) or signal transducers that control the fates of each cell's progeny. Therefore, we can describe embryogenesis as a molecular process and map cell fates by following the transcriptional cascade.

The molecular program for Drosophila embryogenesis begins with the egg and, by means of a transcriptional cascade, assigns a transcriptional pattern consisting of stripes of gene expression at the cellular blastoderm (based on principles reviewed in Bodnar, 1997). The fertilized *Drosophila* egg goes through a series of rapid nuclear divisions within a syncytial cytoplasm of the egg. The nuclei divide synchronously, and after nine divisions most nuclei migrate to the outer membrane (leaving behind the centrally located yolk nuclei) to form a syncytial blastoderm. The nuclei continue to divide synchronously in a single layer along the membrane and after thirteen nuclear divisions are enclosed by individual cell membranes (forming a cellular blastoderm). When the egg is laid, it contains morphogens - proteins (transcriptional activators and repressors or signal transduction proteins) or their mRNAs that were deposited in gradients from the anterior, posterior, or ventral surfaces. (Proteins that bind DNA to regulate transcription are generically termed "transactivators." This term can be confusing since "transactivators" often repress transcription. Therefore, we will use the term "transregulator" to describe DNA-binding proteins that regulate transcription - either activation or repression). After the 6th nuclear division, transcription is begun in the blastoderm, and the morphogens control expression of new transregulators which in turn regulate each other as well as new ones in a cascade. In any particular region of the developing syncytial blastoderm the identity of transregulators expressed in the cascade depends on the particular combination of morphogens stored in the egg in that region. The result is a pattern of expression for transregulators that form a series of stripes in both the anterior/posterior (A/P) and dorsal/ventral (D/V) directions.

The cells in the *Drosophila* embryo are committed to their ultimate fate when the cellular blastoderm is formed. Cell-cell interactions will modify these fates, but the overall body plan is determined independent of cell-cell interactions when all the nuclei are contained within a single cytoplasm. Certainly, short and long range interactions are seen among the nuclei as transregulators are expressed in differing regions of the common cytoplasm, but since the nuclei are enclosed within a single membrane, newly secreted morphogens and associated signal transduction pathways are not used until the cellular blastoderm forms. Therefore, it appears that the combinations of transcriptional factors that become enclosed within a particular cell at the 14th cycle are programmed by previous history of transcriptional activation defining the fate of that cell (Bodnar et al., 1989).

Victoria Foe (1989) has suggested that "if the accumulated product of each early pattern gene contributed to the cells that expressed it a unique color, then, just prior to gastrulation, the blastoderm sheet of cells, each cell with a mix of colors, would appear clothed in an exceedingly complex plaid...It must be that the special combination of genes that cells in a particular group express impels them to act at a particular time in a particular way." One can map the ultimate fate of the growing cells in terms of the combination of factors their progenitors contained in the "plaid" pattern at the cellular blastoderm. Thus the final cellular fate is based on the "plaid" formed by combination of "colors" in the A/P and D/V stripes for all the transcriptional activators in the individual cells of the cellular blastoderm.