Virtual Embryos As Tools For 3D Gene Expression Analyses

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BDTNP
Berkeley Drosophila Transcription Network Project

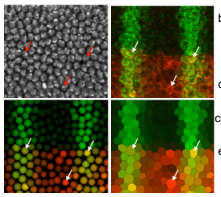
Introduction

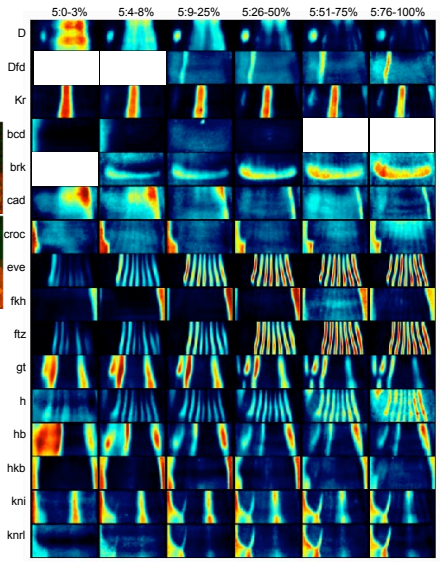
The Berkeley Drosophila Transcription Network Project (BDTNP) is a multidisciplinary collaboration studying the developmental regulatory network of Drosophila blastoderm embryos. One component of this project (Luengo et al., Genome Biology 7:R123, 2006) maps the full 3D blastoderm expression patterns of 37 principal developmental regulatory genes and hundreds of their targets at cellular resolution, and uses these data to model potential regulatory interactions. We have developed an automated pipeline and methods for producing these data. Both the algorithms and the data are freely available at:

http://bdtnp.lbl.gov/

Collecting the Data

The 3D, full blastoderm images are analyzed and accurately converted into PointCloud files by an automated algorithm.

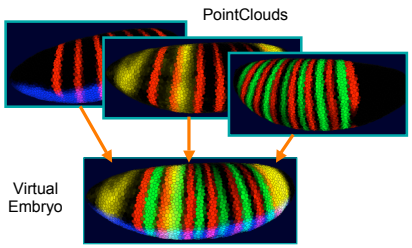


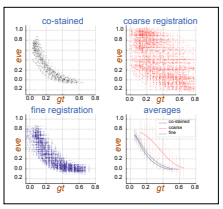


We currently have data for 24 of the principal regulators and over 80 putative target genes, the latter selected using BDTNP ChIP-chip binding data and BDGP expression data.

Generating Virtual Embryos

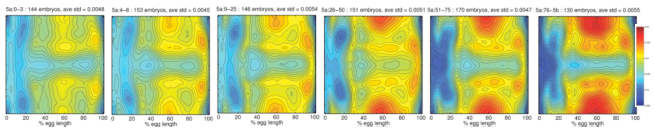
Because each imaged embryo contains expression information of only two genes, expression data from hundreds of embryos are mapped onto a virtual embryo to allow many genes' expression to be compared and modeled within each cohort. These virtual embryos contain nuclei placed to match the average density pattern and embryo shape for each cohort.





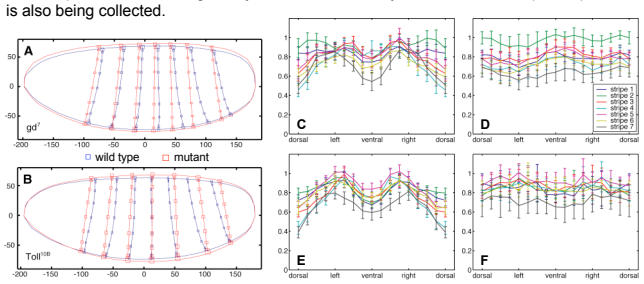
(Fowlkes et al. in preparation)

Density changes through time (Keränen et al., Genome Biology 7:R124, 2006)

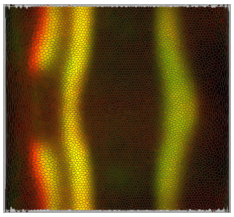


Mutants & Other Species

Gene expression data in regulatory factor mutant embryos and other *Drosophila* species is also being collected.



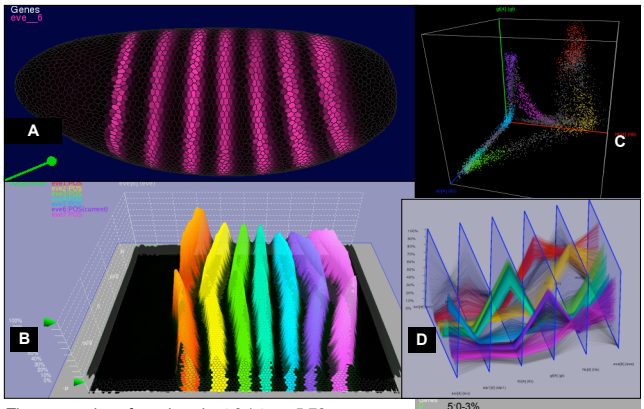
Dorsal-ventral signals affect the anterior-posterior pattern formation (Keränen et al., Genome Biology 7:R124, 2006). In dorsalized gd[7] mutants the ventral *ftz* stripes resemble wild type dorsal *ftz* stripes (**A**), whereas in ventralized Toll[10B] mutants the dorsal *ftz* stripe positions resemble the wild type ventral *ftz* stripes (**B**). The intensity profiles of the stripes lose the dorsoventral polarity (**D**, **F**) that is seen in wild type looking embryos (**C**, **E**).



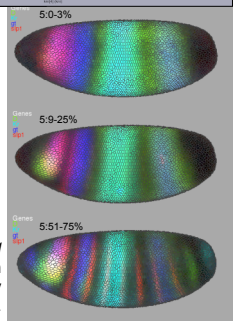
Unrolled view on comparison of *gt* mRNA expression in *D. melanogaster* (green) and *D. pseudoobscura* (red) aligned on *eve* mRNA expression (below). Note the relative positions of anterior *gt* stripes.

Uses of Virtual Embryos

The use of standardized virtual embryos allows temporal comparison within each nucleus between earlier expression of regulators in one cohort and the later expression of target gene patterns in another cohort, as well as better estimates of the developmental increase in complexity.



The expression of *eve* in cohort 6 (stage 5:76-100%) (**A**, **B**) compared to the expression patterns of gap genes in cohort 4 (stage 5:26-50%) (**C**, **D**). The expression levels of each *eve* stripe can be visualized and analyzed separately (**B**), and the relative expression levels of their putative regulators can be then studied in the corresponding nuclei either by analyzing their clustering in 3D scatter plots (**C**) or by observing the multigene expression profiles in parallel co-ordinate view (**D**) that also can contain 1D spatial information.



For example, the spatial expression of *D*, *Kr*, *gt* and *slp1* change during stage 5. In virtual embryos, such changes in multiple genes can be computationally analyzed in a standardized environment.