35th Biological Systems Simulation Conference, US Water Conservation Laboratory, Agriculture Research Service, Phoenix AZ, 19-21 April 2005 (Abstract of Oral Presentation).

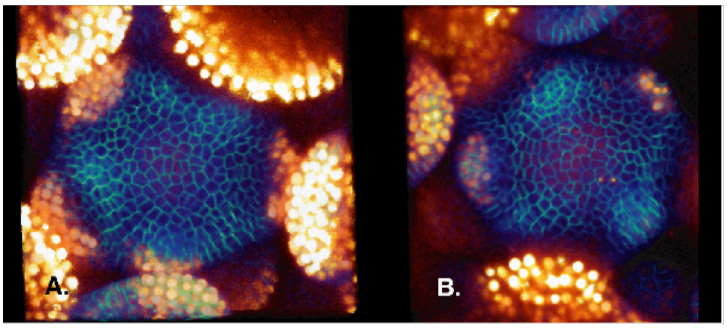
Developmental Modeling of the *Arabidopsis* Shoot Apical Meristem by the Computable Plant Project

Bruce E. Shapiro[1]*, Vikas Agrawal[2], Victoria Gor[1], Marcus Heisler[2], Henrik Jönsson[3], Elliot M. Meyerowitz[2], Eric Mjolsness[4], G. Venugopala Reddy[2]

[1]Jet Propulsion Laboratory, California Institute of Technology, Pasadena, CA USA, 91109
[2]Division of Biology, California Institute of Technology, Pasadena, CA USA, 91125
[3]Complex Systems Division, Lund University, Lund, Sweden
[4]Department of Information and Computer Science, University of California, Irvine, CA 92697
*Corresponding author, E-mail: bshapiro@caltech.edu

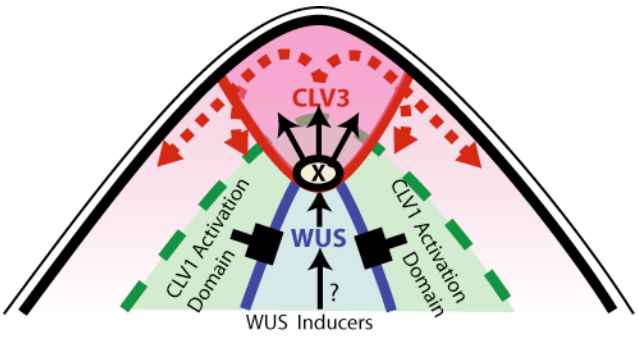
The computable plant project is developing an end-to-end research and modeling framework for the *Arabidopsis* SAM (shoot apical meristem). We observe several cell type specific markers for growth and differentiation in real-time in live plants with a dedicated confocal laser scanning microscope. Using a combination of computational modeling and image processing techniques we then infer specific transduction pathway data and fit mathematical models to produce two- and three- dimensional visualizations of the growing SAM, including phyllotactic and leaf-vein development. In particular, we have developed several GFP (Green Fluorescent Protein) variants that allow us to observe various meristem and floral primordial features including both cell plasma membranes and cell nuclei as well as track specific cell lineages over time. Our aim is to determine the spatial and temporal relationships between the expression of different genes in an effort to understand how primordial cells are progressively specified. These markers will allow us to correlate gene expression changes with cell growth over time. Thus far the live imaging technique has led to the development of a spatial and temporal map of cell division patterns. We have observed that primordium development is a sequential process linked to distinct cellular behavior, and that the amount of cell division is comparable in regions of the SAM where successive primordia arise. Changes in cell division orientation are associated with initial outgrowth of a flower primordium. These changes are followed by a rapid burst of cell expansion and cell division that transforms a flower primordium into a flower bud. We are developing software to automatically extract cell positions from time-lapse observations; integrating this information with inferred pathways, it should be possible to produce forward simulations that predict and visualize meristem growth.

The three-dimensional reconstruction starts from "stacks" of horizontal sections, such as those shown to the left. These show pPIN1: PIN1GFP (shown in blue) in combination with pFIL: dsRED N7 (shown in yellow) at two time points 33 hours apart, and illustrate the budding of new floral meristems (A: initial view, B: final view). Such sections are combined to produce four-dimensional visual-izations (3 spatial dimensions plus time) using various programs we have developed.



JPL-CL#05-0565

In any 3D image stack there is a correspondence problem: which cells in one image correspond to which cells in the adjacent cross-section? Cell membranes that are transverse to the image are clearly visible, but it is possible to miss nearly horizontal walls that lie between sections and must be inferred. With a time-course of 3D stacks the formation of floral meristems, cell growth, movement, and division all complicate the problem. Nuclear locations are inferred from a gradient descent-based algorithm on image intensity; the correspondence between successive images was found for those nuclei that did not divide using a Softassign algorithm. We are currently investigating the use of the Delaunay triangulation and Voronoi diagrams (two geometrical constructions from Computer Science) to identify near neighbors and cell walls.



Cellerator is used to design signal transduction networks (STN) based on known or hypothesized biochemical interactions and gene regulation. A model based on gene expression imagery of key regulatory proteins in the SAM's development is shown here. WUSCHEL (WUS), a homeodomain transcription factor expressed in the rib meristem activates an unknown protein, X, which in turn induces CLAVATA3 (CLV3) in the sub-epidermal layer. CLV3 is believed to be the ligand for CLAVATA1 (CLV1), a receptor kinase, that in turn is hypothesized to inhibit WUS. Other WUS inhibitors may also exist. Input to Cellerator is via a set of arrow-based reactions representing the network; Cellerator translates the STN into a system of differential equations. An automated code generator reads the Cellerator SBML model and generates and links an efficient simulation engine. Spatial dynamics are described by a network of point-localized cells joined by "spring" dynamics. Ellipsoidal and polyhedral cell models with stress/strain tensors are being developed.

The work described in this abstract was performed at the California Institute of Technology and funded by NSF Grant 0330786.

References

Jönsson H, Shapiro BE, Meyerowitz EM, Mjolsness ED, 2003. "Signaling in Multicellular Models of Plant Development, " In S. Kumar and P.J. Bentley (Es.) "On Growth, Form, and Computers", Academic Press.

Meyerowitz, EM, Genetic control of cell division patterns in developing plants, 1997. Cell, 88:299-308 (1997).

Mjolsness ED, Jönnson H, Shapiro BE, Meyerowitz EM. 2003. Modeling plant development with gene regulation networks including signaling and cell division," in Bioinformatics of Genome Regulation and Structure, eds R. Hofestaedt and N. Kolchanov, Kluwer.

Rangarajan A, Yuille AL, Gold S, Mjolsness E, 1999. Convergence Properties of the Softassign Quadratic Assignment Algorithm. Neural Computation 11:1455-1474.

Shapiro BE, Levchenko A, Meyerowitz EM, Wold BJ, Mjolsness ED, 2003. Cellerator: extending a computer algebra system to include biochemical arrows for signal transduction simulations,. Bioinformatics 18:677-678.

Venugopala Reddy G, Heisler M, Ehrhardt DW, Meyerowitz EM, 2004. Real-time lineage analysis reveals oriented cell divisions associated with morphogenesis at the shoot apex of Arabidopsis thaliana. Development 131, 4225-4237.