The Computable Plant: Annual Report, 6/2006-5/2007

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1. Introduction

Following last year's Computable Plant project breakthrough in modeling and understanding phyllotaxis at the molecular level [Jönsson et al. 2006], 2006-7 was devoted to consolidating our gains in shoot meristem, preparing for a much more detailed level of modeling of that tissue, and expanding the effort in a preliminary way towards other tissues in *Arabidopsis*. The phyllotaxis model combines the key ingredients of autoregulated and polarized transport of auxin between cells by PIN1, and the growth and mechanics of cells and tissues, to create a dynamical pattern formation system for floral meristem primordia. *Consolidating our gains* included the incorporation of AUX1 into auxin-PIN1 two-dimensional modeling (described in Section 2.1 below), creating new mathematical frameworks for complex developmental models, extensive dissemination by writing review articles and lecturing around the world (listed in Section 7), and adding to the list of software and other information released on www.computableplant.org. *Preparing for more detailed models* included assembling a 3D finite-element modeling system for plant cells (Section 4.2). *Expanding the effort* involved analyzing *Arabidopsis* sepal (Section 3.1) and root imagery, comparing root and shoot pattern formation models, and preliminary mechanical models of *Arabidopsis* embryo. These and other technical points are covered in Section 2, 3, and 4 below.

There are several essential social processes in the Computable Plant (CP) project as well. The primary one is the outreach project for high school science teachers at the Huntington Botanical Gardens, described in Section 6. We presented this project to a wider audience in Washington DC with the display booth "The Computable Plant: Modeling Plants and Plants as Models" at the National Science Foundation budget rollout in February, 2007. At the research level, we held the annual CP research meeting in Corona del Mar California, with attendance by most of our foreign collaborators, and we established a new connection with the UK Center for Plant Integrative Biology (CPIB) project in root imaging and modeling, both described in Section 5.

Supported personnel included Marcus Heisler, Bruce Shapiro, Adrienne Roeder, Vijay Chickarmane, Patrick Hung, and Sean Gordon (Caltech); Tigran Bacarian, Ashish Bhan, Pawel Krupinski, Guy Yosiphon, Elaine Wang, David Orendorf, Todd Johnson (UC Irvine); Martha Kirouac (Huntington); and visitors Vitali Likhoshvai, Sergei Nikolaev, Nikolai Podkolodny, and Nadezhda Omelianchuk from the Institute for Cytology and Genetics (Novosibirsk, Russia) while visiting UC Irvine. A very rough allocation of people to roles this past year is shown in Table I. Key collaborators such as Henrik Jönsson (Lund University) are not listed in Table I unless they received at least travel support from the project, which is nevertheless critically dependent on their contributions.

Table I: CP participant roles, 2006-07

	image analysis	biological expertise	modeling	software	mathematics	outreach
Caltech /JPL	Burl Heisler Roeder	Gordon Heisler Meyerowitz Roeder	Heisler Hung Shapiro	Hung Shapiro	Chickarmane	Gordon Meyerowitz
UCI/ICG	Bacarian Mjolsness	Omelianchuk	Baldi Bhan Krupinski Likhoshvai Nikolaev	Bacarian Johnson Krupinski Podkolodny Orendorf Yosiphon	Likoshvai Mjolsness Sadovsky	Wang
Huntington						Kirouac

Reference

Henrik Jönsson, Marcus Heisler, Bruce E. Shapiro, Elliot M. Meyerowitz, Eric Mjolsness. "An auxin-driven polarized transport model for phyllotaxis". Proceedings of the National Academy of Sciences, 13 January 2006.

2. Biological Modeling

2.1. Auxin modelling in the shoot apical meristem

One notable feature of our auxin transport model (Jönsson et al., 2006) is that when the model is modified to include the experimental result that PIN1 transcription is auxin regulated, the resulting auxin distribution patterns are not stable. Secondly, simulations of auxin distribution in the meristem indicate that if PIN1 is predominantly expressed in the L1, auxin levels should be lower there than in cell layers below, assuming synthesis and degradation is ubiquitous. However RT PCR and microarray results have shown that the auxin influx carrier AUX1 is also auxin regulated and expressed in the meristem. Expression analysis of AUX1 mRNA using in situ hybridization as well as visualization of a functional YFP-AUX1 reporter protein indicate that AUX1 is predominantly expressed in the L1 layer of the meristem and upregulated during the early stages of primordium specification. We therefore have extended our model to incorporate AUX1 and to have both AUX1 and PIN1 regulated by auxin. Simulation results show that the incorporation of auxin-regulated AUX1 restores stability to the model when PIN1 is also auxin regulated. We conclude that AUX1 probably functions redundantly with closely related AUX1-like proteins to both maintain auxin levels in the meristem epidermis and stabilize auxin distribution patterns generated by PIN1 mediated auxin gradient models [1].

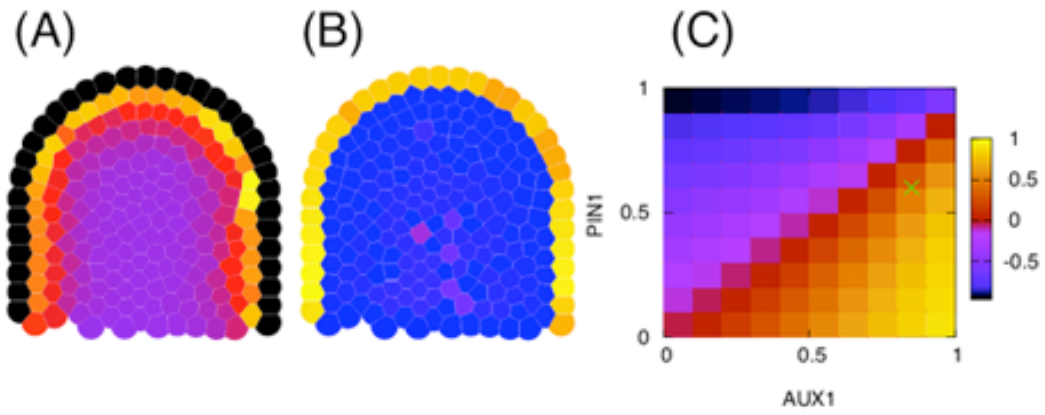


Figure 1.

Auxin localization dependence on asymmetrically expressed PIN1 and AUX1 in a longitudinal section simulation. A) and B) show the auxin concentration in the cells (where the walls in-between have been left out). A) In a model only explicitly including the efflux mediator PIN1, the equilibrium auxin concentration is high beneath the epidermal layer when the PIN1 is expressed in the epidermal layer. B) A model that also includes an asymmetric influx mediator, results in auxin mainly within the epidermal layer. C) Restrictions on the asymmetry of the influx/efflux mediator expressions apply to achieve high auxin concentrations in the epidermal cells. The color-coding represents the measure $(a_{epi} - a_{int})/(a_{epi} + a_{int})$ where a_{epi} (a_{int}) is the average auxin concentration in the

epidermal (internal) cells. The axes show the asymmetry where 0 is uniform expression in all cells and 1 is expression in epidermal cells only (taken from [1]).

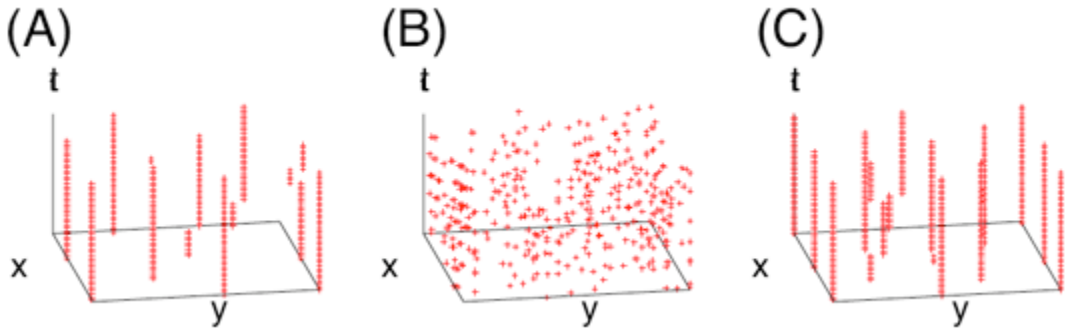


Figure 2.

Auxin peaks in simulations on a static square lattice of cells with walls in-between. The simulations are started from a close-to-homogeneous auxin distribution. Parameter values are described in the text. (A) Model without auxin-induced PIN1 and AUX1. Some minor rearrangements occur, in a stable pattern. (B) Model with auxin-induced PIN1. The pattern is unstable as the peaks move around in the cell tissue. (C) Model with both PIN1 and AUX1 induced by auxin. This results in a stable pattern (taken from [1]).

2.2. Investigation of local signalling for determination of PIN1 polarity.

A central tenet of our auxin transport model is that cells signal to their neighbours their auxin content such that cells can position PIN1 according to the relative auxin concentration in neighboring cells. To start to test this hypothesis we investigated the effects of local cell ablation using a micro-pulsed laser beam. We have found that PIN1 responds to local ablation events by polarizing away from wounded cells (Fig 3.). This response does not appear to be position specific and is not emulated by other membrane-localized proteins such as AUX1 or PINOID. Interpreting this in terms of our model, if we assume dead cells are incapable of signaling positive auxin concentrations to their neighbors the result that PIN1 polarizes away from ablated cells should be emulated by our model and simulations so far bear this out. Surprisingly however similar responses are seen in *monopteros* (mp) mutant plants. MP encodes an Auxin Response Transcription Factor (ARF) thought to be required for auxin transcriptional responses in the meristem. The observation that PIN1 reorientations occur despite the lack of MP function suggests that either these reorientations do not require auxin induced transcription or that other MP-like genes function somewhat redundantly with MP to mediate the response.

Elements of the cytoskeleton are also known to respond to wounding. Wounding experiments on injured pea roots indicated that cortical arrays of microtubules (MTBs), originally aligned with their helical axis along the apical/basal axis of the root, reorient their axis to be perpendicular to the wound edge [2]. This occurs within five hours, which is a similar time frame to the reorientation observed for PIN1. To investigate the similarity in response between PIN1 and MTBs in response to wounding we conducted laser ablations of cells while imaging a GFP-MAP4 marker line in the Arabidopsis meristem. MTB orientation was observed to respond to wounding by reorienting the helical axes radially from wounded cells within 5 hrs (Fig.4) confirming that MTB behavior displays striking similarities to PIN1 behavior in response to wounding. Furthermore we noticed that MTB orientations throughout the meristem epidermis appear to be very similar to the orientation of PIN1 polarity suggesting that either these cellular components influence one another's behavior or that they may share upstream regulatory factors. We are presently examining PIN1 and MTBs together to gauge the extent of their co-alignment in detail and are investigating possible causal interactions.

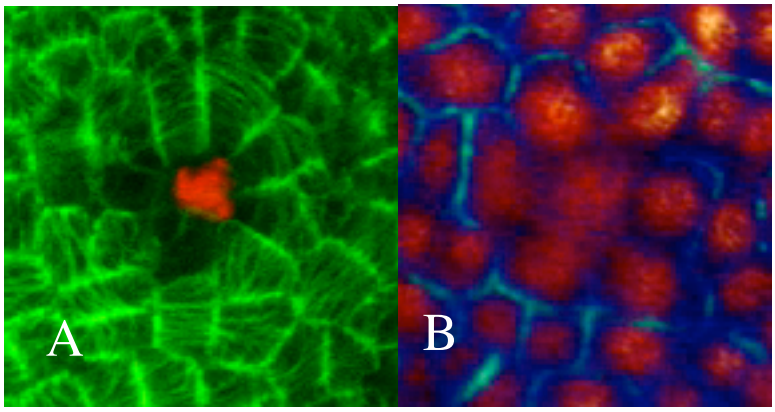


Figure 3.

Confocal projections showing similar orientations of microtubules and PIN1 in response to single cell laser ablations. A. Single cell ablation showing microtubules (green) and ablated cell marked by propidium iodide staining (red). B. Single cell ablation showing PIN1 fused to green fluorescent protein (GFP) (blue) and nuclei marked with nuclear localized dsRED fluorescent protein.

References.

1. Heisler, M.G., and Jönsson, H. (2006). Modeling auxin transport and plant development. Journal of Plant Growth Regulation *25*, 302-312.
2. Hush, J.M., Hawes, C.R., and Overall, R.L. (1990). Interphase Microtubule Reorientation Predicts a New Cell Polarity in Wounded Pea Roots. Journal of Cell Science *96*, 47-61.

2.3 Models for other *Arabidopsis* tissues

As a result of the CP project, our collaborators at Novosibirsk have undertaken a mathematical modeling comparison between auxin/PIN network dynamics in shoot and root, applying S. Fadeev's homotopy-method software for finding attractors in large systems. First results of this comparison were presented at the annual CP meeting and in a paper in press (Section 7). Future work in the area may be further enhanced by three-way interaction with the new CP-like project at the University of Nottingham (Section 5). In addition, a theoretical model of root mechanics was developed and is in press (Section 7.)

3. Image Analysis

3.1 Development of the sepal epidermis

We have recently expanded our analysis to include not only the meristem, but also the organs it produces which make up the body of the plant. The shoot apical meristem produces floral meristems, which in turn produce the floral organs starting with the sepals. The sepals are the outermost, green, leaf-like organs that protect and cover the flower while it is developing. Currently we are focusing our analysis on the development of the sepal epidermis, which forms a complex pattern of cells with different sizes (Figure A). Variation in cell sizes is observed throughout much of the *Arabidopsis* epidermis and is not a specific feature of sepals. We have chosen to focus on the sepal epidermis for this study in part because it is accessible for imaging in the living plant.

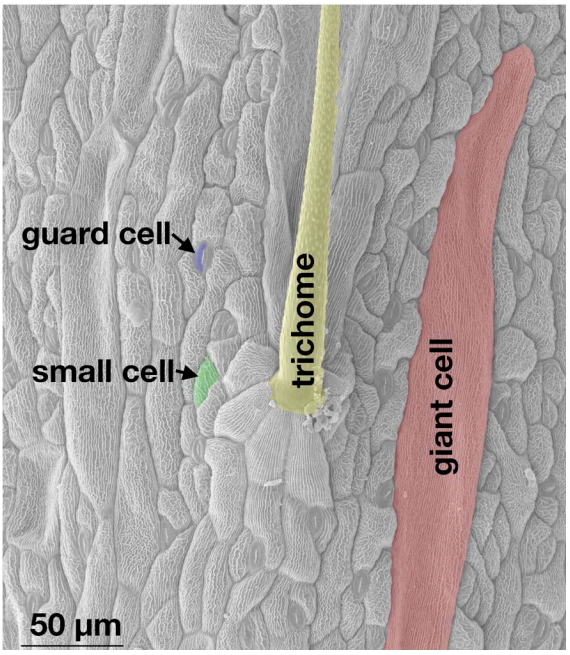


Figure A: Complex pattern of different sized cells in the sepal epidermis

Scanning electron micrograph of the mature sepal epidermis showing the wide variation in cell sizes from giant cells (one example false colored red) to small cells (one example false colored green). The sepal epidermis also includes specialized cell types such as trichomes (hairs, false colored yellow) and guard cells (one example false colored blue), which flank the stomatal pore.

The variation in cell sizes raises a number of fundamental biological issues including the question of how differences in the sizes of neighboring cells are generated. Do some cells expand faster than their neighbors? In plants, this possibility seems unlikely because the cell walls of the neighboring cells are glued together at the middle lamella, which necessitates the coordination of wall growth between neighboring cells.

Alternatively, do some cells stop dividing and continue to expand thus becoming larger than their neighbors, which expand at the same rate, but continue to divide?

3.1.1 Live imaging: (Adrienne Roeder)

One of the best ways to determine how the variations in cell size arise in the sepal epidermis is to watch the process in living plants. To observe the development of the epidermal cells specifically, we have generated a new fluorescent reporter, ML1::H2B-mYFP, in which an epidermal promoter is used to drive the expression of histone 2B fused to YFP, which marks the nuclei of all the epidermal cells. We have imaged a living sepal on the plant every 12 hours for several days as the sepal grows (Figures B and C).

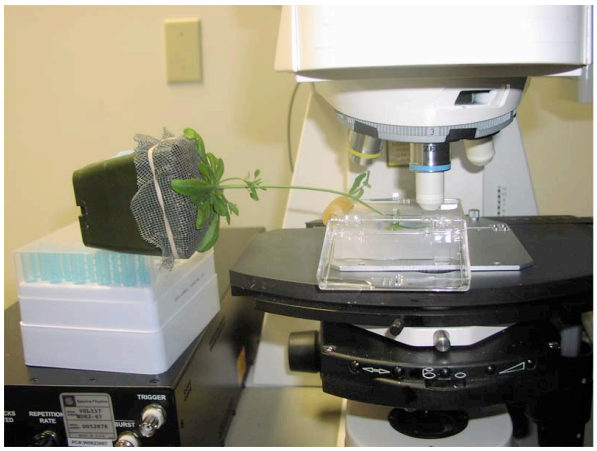


Figure B Live imaging of a sepal
The plant is positioned sideways such that the sepal can be placed under the objective lens (in this case a water dipping lens with the sepal under water in the small box). The plant is returned to the growth room to develop in its normal vertical position for 12 hours between images.

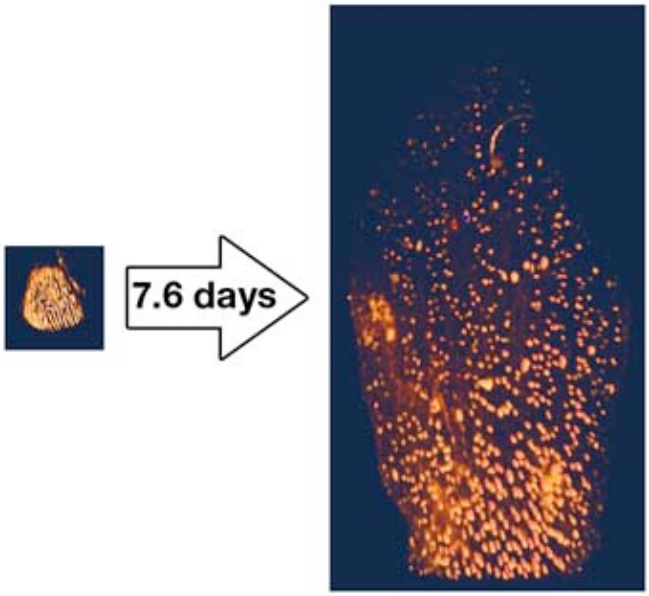


Figure C: Live imaging of nuclei in the developing sepal epidermis.
A developing sepal was imaged every 12 hours for 7.6 days. The nuclei marked in red and blue in the fist image are the same nuclei marked in red and blue in the final image. Both of these nuclei have started endoreduplication before the first time point and neither of these nuclei divides during the 7.6 days of analysis.

Our first observation from our images is that larger cells have nuclei with increased DNA contents and that the increase in DNA is roughly proportional to the overall cell size. Just as a whole range of cell sizes is observed in the mature sepal epidermis, a corresponding range in DNA contents of the nuclei is present. The increased DNA contents of these nuclei have been generated through a specialized cell cycle called endoreduplication. In the normal cell cycle, the cell grows, replicates its DNA once and divides once so that each daughter cell has the same DNA content (2C) and approximately the same volume as its mother did. In contrast during endoreduplication, the cell grows and replicates its DNA, but does not divide resulting in a cell with twice the DNA content (4C) and twice the volume. Once a plant cell has entered endoreduplication, it is no longer capable of dividing. Cells can undergo multiple rounds of endoreduplication resulting in DNA contents of 8C, 16C, 32C, etc and volumes to match. This suggests that the variation in the size of sepal epidermal cells results from regulating their timing of entry into endoreduplication such that large cells enter endoreduplication first, undergo the most rounds of replication, and hence reach the largest sizes whereas smaller cells continue to divide and maintain their smaller size (Figure D).

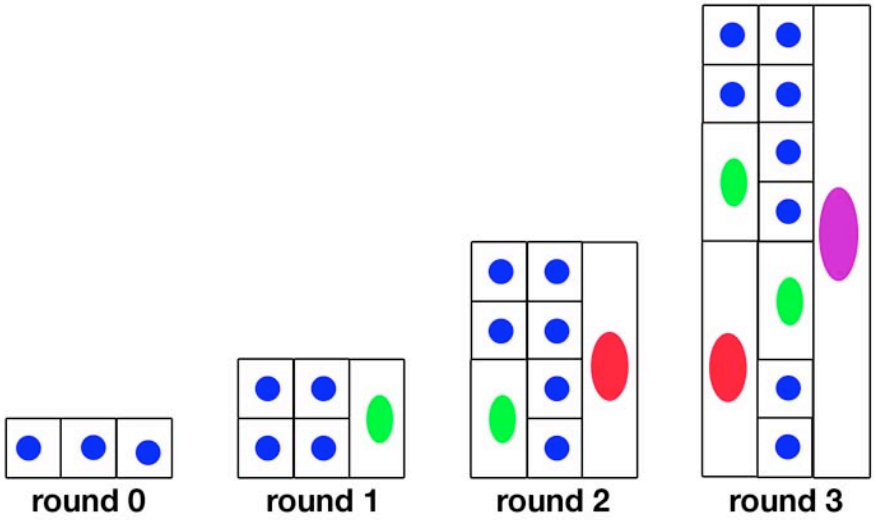


Figure D: Different times of entry into endoreduplication generate cell size diversity.

Imagine three small 2C (blue nuclei) neighboring cells at division round 0, which are all approximately the same size. These cells grow to twice the volume and replicate their DNA. The two cells on the left divide in round 1 to become 2C cells again, but the cell on the right enters endoreduplication retaining its 4C DNA content (green nucleus) and its larger size. In the next round the cell on the right must endoreduplicate again reaching 8C (red). Most of the remaining cells divide, but the cell on the lower left also enters endoreduplication and becomes 4C. Thus by the end of round 2 a large cell, medium cell and several small cells have been generated. The process continues in round 3 further enlarging the endoreduplicating cells and allowing more cells to enter the pathway.

Tracking cells in our live images confirms this hypothesis. The nuclei of the cells that become giant cells can be identified early in the sepal development because they already contain more DNA and visually appear larger than the surrounding nuclei indicating that they have started endoreduplication. Furthermore, these giant cells do not divide throughout the remainder of the development of the sepal, while the neighboring small cells can be observed to divide (Figure C).

3.1.2 Nuclear surface extraction: (Michael Burl)

Initially the analysis of the sepal images was done by hand, but to automate the process we created a program to extract the surfaces of the nuclei from confocal image stacks in 3D. The size of the nucleus is correlated with the DNA content, so this program complements our other nuclear segmentation programs which extract the center of the nucleus. First the boundaries of the nuclei from each 2D image in the stack are detected and converted to smooth contours (Figure E and F). Then the contours are linked in the z-dimension such that all the contours belonging to one nucleus are associated (Figure G). Next a surface is triangulated from the contours (Figure H). Finally for 3D visualization of the data, the surfaces are written into a file that can be displayed in the

commercial 3D rendering program Amira (Figure I). The extracted surfaces have been overlaid upon the original data in Amira for validation.

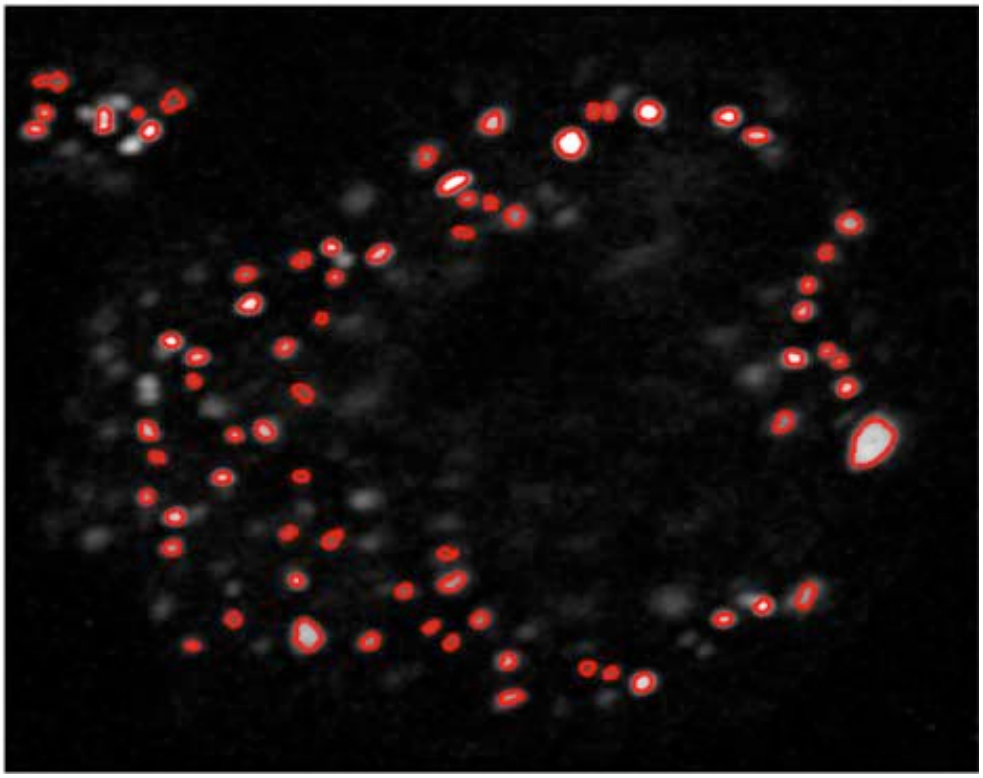


Figure E Extraction of smooth contours surrounding each nucleus from a single stack level.

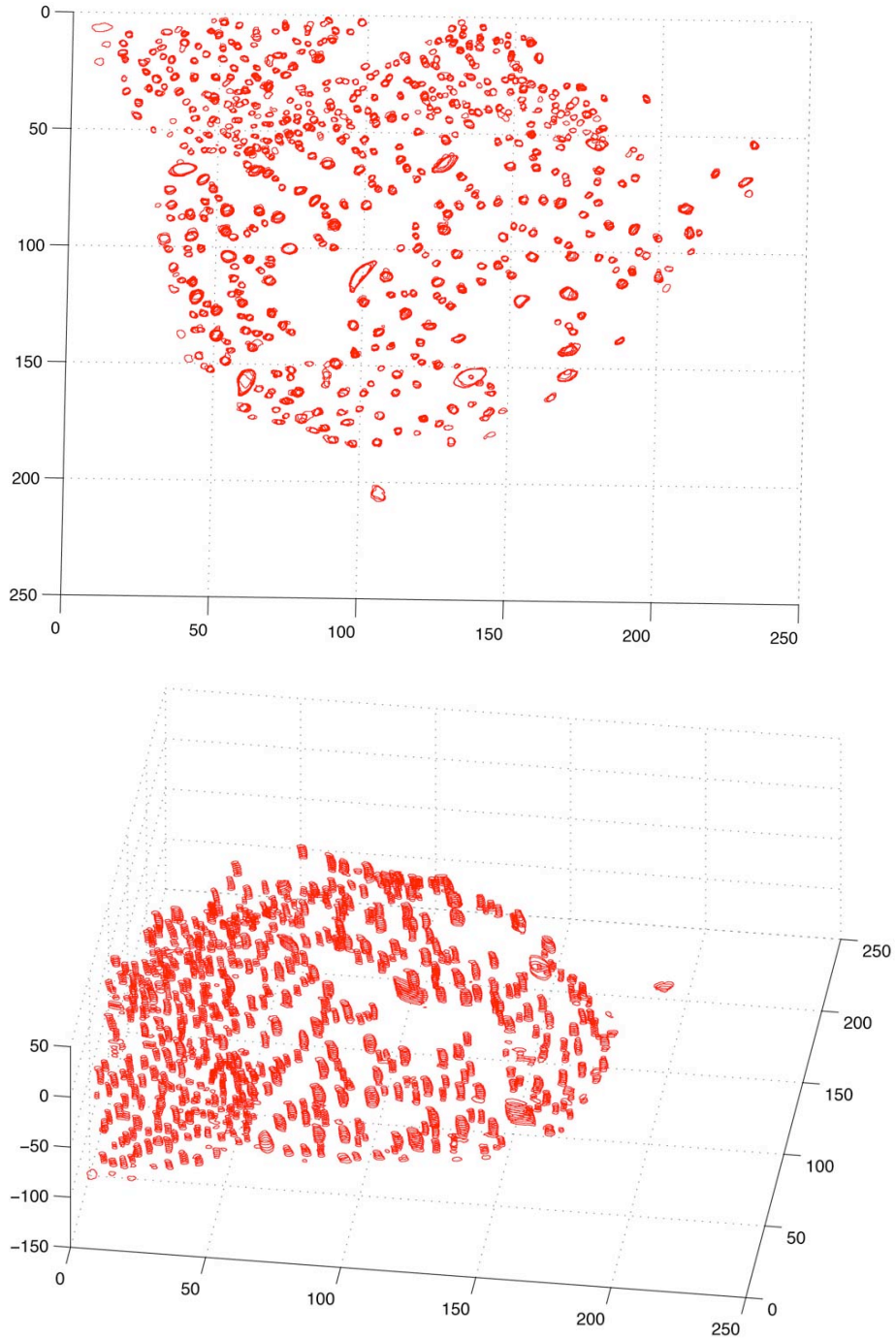


Figure F: Extraction of nuclear contours from all stack levels.

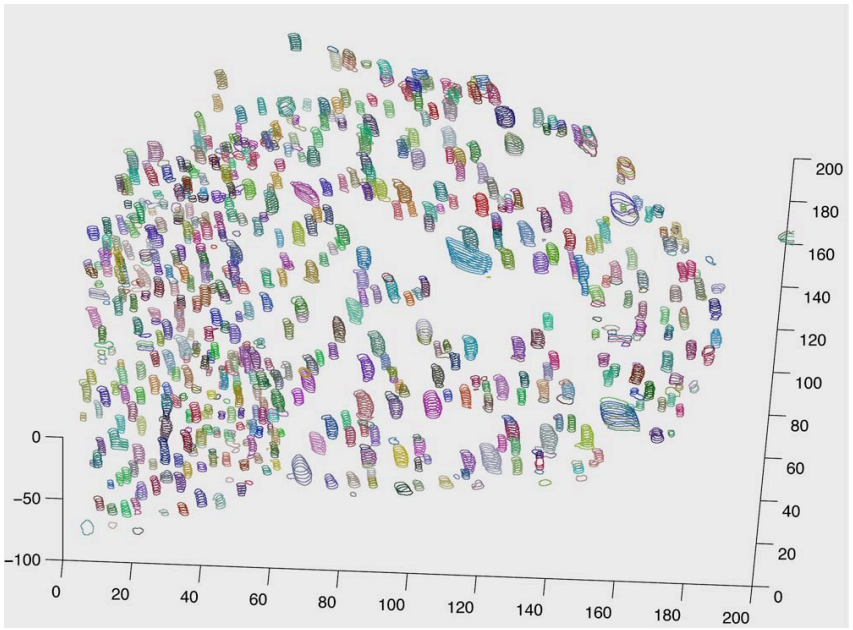


Figure G: Z-linking of contours

The contours from a single nucleus are in 3D space are linked together in 3D space. Assigning a consistent color to all contours from the same nucleus illustrates the association.

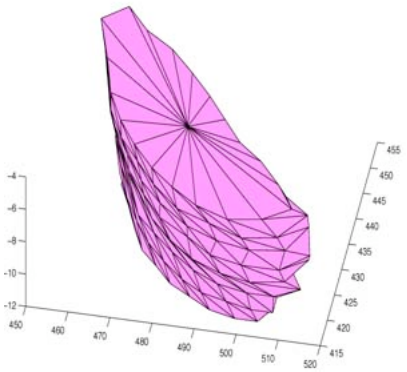
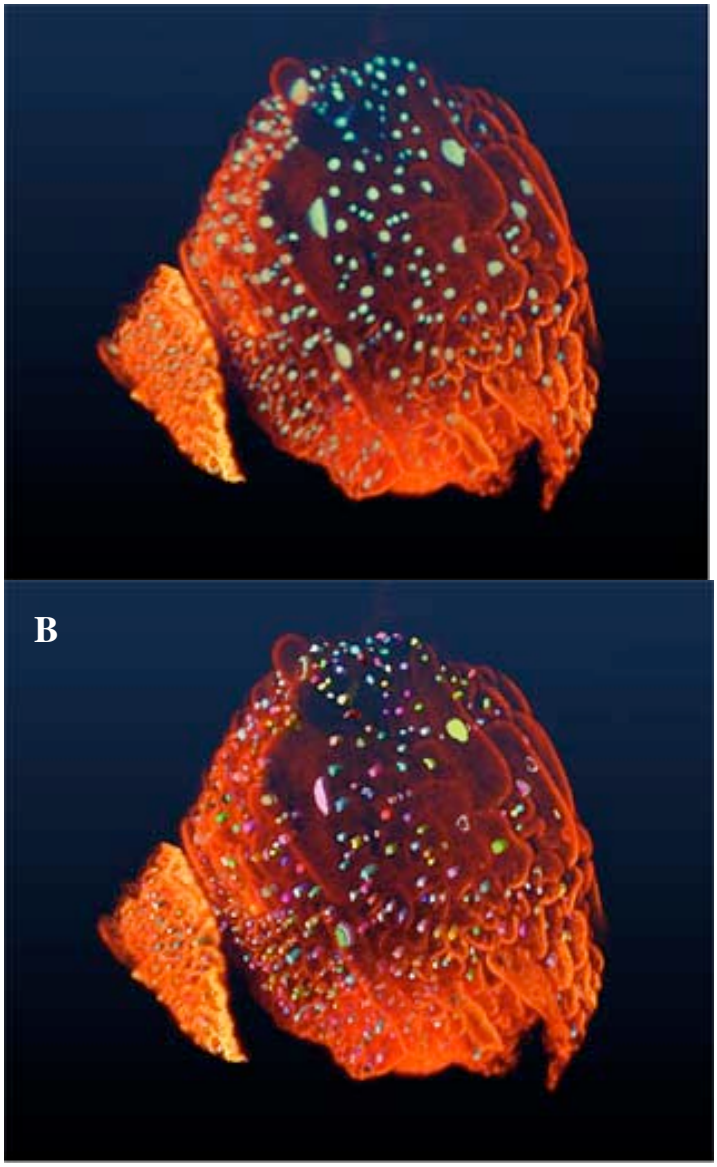


Figure H: The surface of the nucleus is triangulated from the contours. Here we show the triangulation of a single giant cell nucleus.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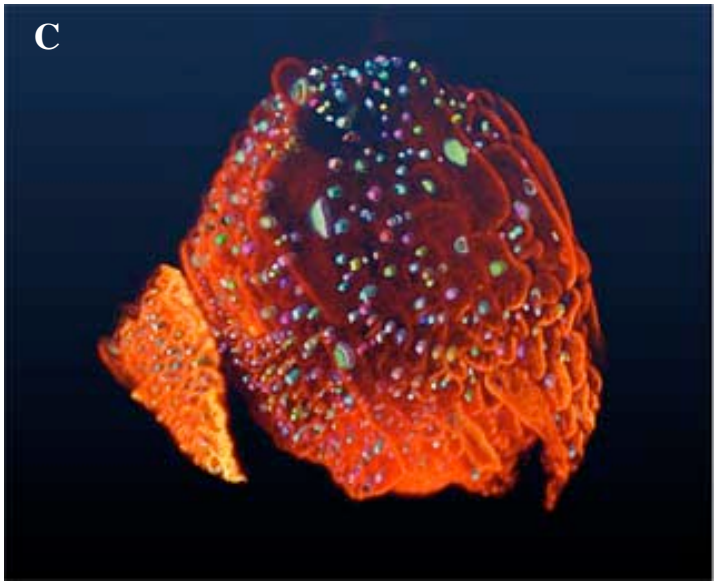


Figure I: Display of the extracted nuclear surfaces in Amira.

(A) The original image data with the plasma membranes shown in red and the nuclei shown in green.
(B) The extracted nuclear surfaces overlaid on the membrane data.
(C) The extracted nuclear surfaces overlaid on the membrane and nuclear data showing that the extracted nuclear surfaces match the real nuclei.

3.1.3 Nuclear volumes histogram: (Michael Burl)

In addition to extracting the nuclear surfaces in 3D, we would like to be able to determine the DNA content of a nucleus from a projection of the confocal stack. We extracted the area of each nucleus and used that to approximate the volume of the nucleus. We would expect the volume to be directly proportional to the ploidy (number of copies of DNA) of the nucleus, so we would expect the calculated nuclear volumes to fall into discrete categories separated by powers of 2. A histogram of the approximated nuclear volumes shows peaks that are about one unit apart on a log base 2 scale as expected (Figure J). We are currently evaluating the ploidy levels of the sepals through standard biological methods so that we can validate our results based on the images.

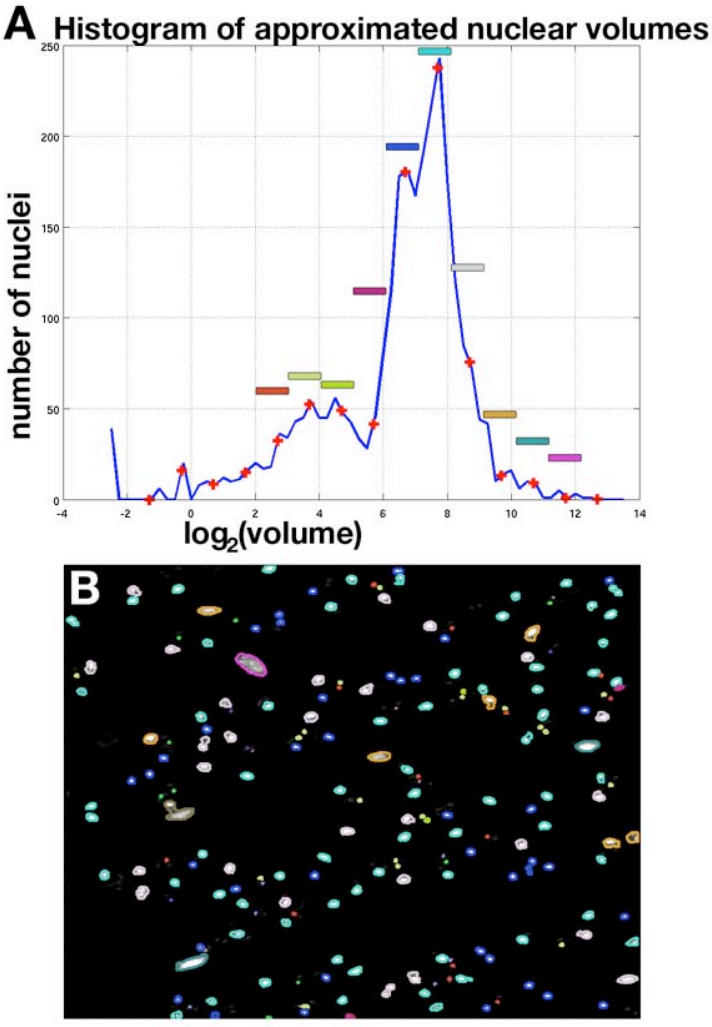


Figure J: Histogram of approximate extracted nuclear volumes.
(A) Histogram showing the number of nuclei that fall into each of the volumes.
(B) The contours surrounding nuclei in the image have been colored to reflect their volume as shown by the color bars on the histogram.

Progress toward the problem of recovering 3D mathematical descriptions of the cell compartments from CLSM image stacks was also achieved. Starting from 2D segmentations of the cell compartments in each stack level (e.g., from watershed or similar algorithms), we construct an affinity graph. Each segmented region is a node in the graph. A weighted edge is created between a given node and nodes in adjacent stack levels, with the weight based on the projected area of overlap. Spurious edges in the graph are pruned by enforcing a mutual best match constraint similar to the left-right constraint used in stereo vision algorithms.

The resulting graph is used with the 2D segmentations to create a consistently-labeled voxelization of the volumetric data. A frequently used algorithm from machine learning, known as a support vector machine (SVM), is used to recover the best planar separating

surface between voxels with different labels. Aggregating the planar separating surfaces for a particular label (and correctly orienting the normals to the plane) allows recovery of a polytope model (set of linear inequalities) capturing the 3D structure of a cell compartment. Future work will extend this technique to two more difficult situations: (i) cases where cells are on the exterior surface of the plant and (ii) cells where one of the walls is parallel with the optical slice plane.

3.1.4 Geometric model of the sepal epidermis: (Vijay Chickarmane)

To determine whether there is any pattern to the positions of large cells and small cells in the sepal epidermis we are currently building a geometric model of epidermal cell growth. In this model all of the cells grow at the same rate, but we can alter the division versus endoreduplication pattern. We can use this model to test various hypotheses about how the pattern is generated. For example, our null hypothesis is that the pattern of entry into endoreduplication is purely random and cells of each size should be randomly spaced throughout the sepal. By generating this pattern in the model we can see that it does not appear to match the actual sepal data. In real sepals we often see giant cells concentrated toward the top of the sepal, not scattered throughout. In addition, giant cells frequently occur adjacent to one another. Now we are testing an alternate hypothesis in which one cell entering endoreduplication can recruit a neighboring cell to do the same.

3.2 Image analysis software tools

2.3.1 Cell tracking (Tigran Bacarian)

In solving he problem of correct identification of nuclei on a raw 2D or a stack of 3D data image one has to overcome the usual problems of shot noise, variation in absolute brightness and contrast throughout the image and existence of alien objects on the image. Morphological reconstruction was found to be the most robust method for use as a base for initial cell identification. The preceding gray-level dilation of an image uses specific structural element consisting of disc (sphere) of a minimum nucleus “blob” size of ground level and a central level “spike” of a minimum “blob” height. The noise and background artifacts are effectively eliminated while following reconstruction restores the original size and shape of each “blob”. Nuclei are then individually segmented with by their flat local “blob” maxima.

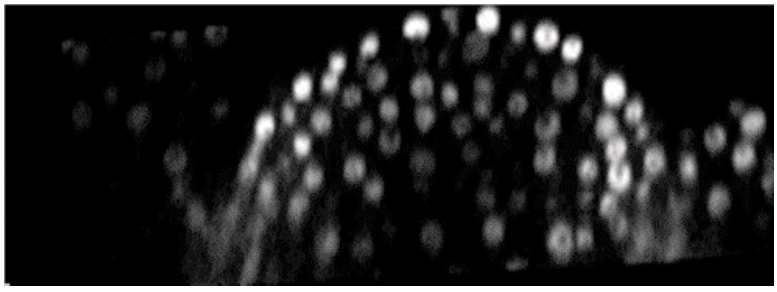


Fig.1 A fragment of a vertical section from 3D Arabidopsis data stack

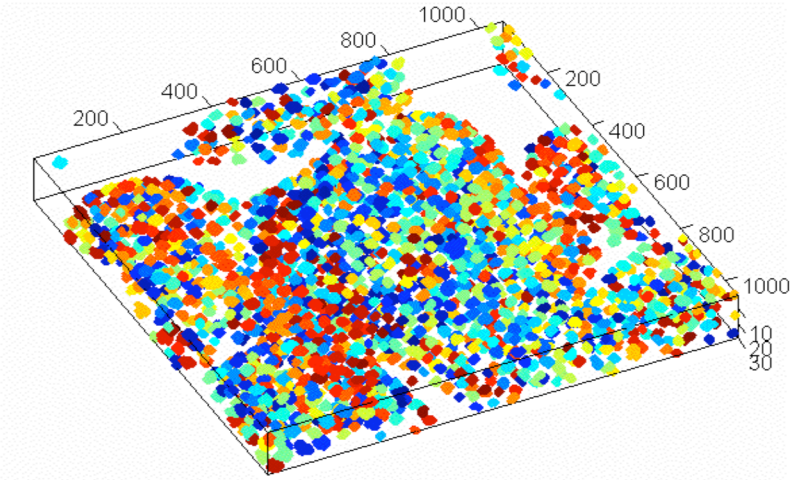


Fig. 2 Individually segmented nuclei from raw data on a 3D diagram.

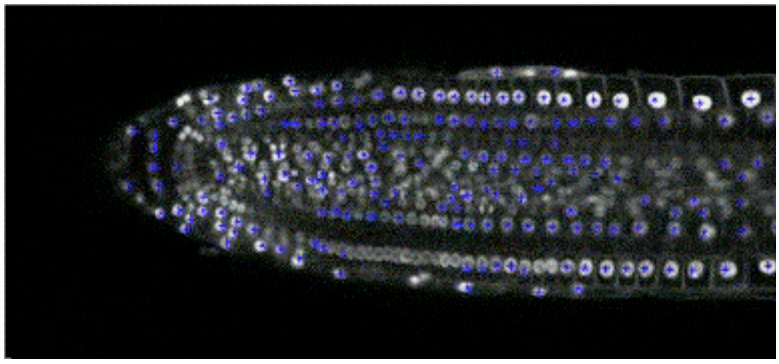


Fig. 3 2D slice of a growing root with blue dots marking identified nuclei. Original data: Ben Scheres, U. Utrecht.

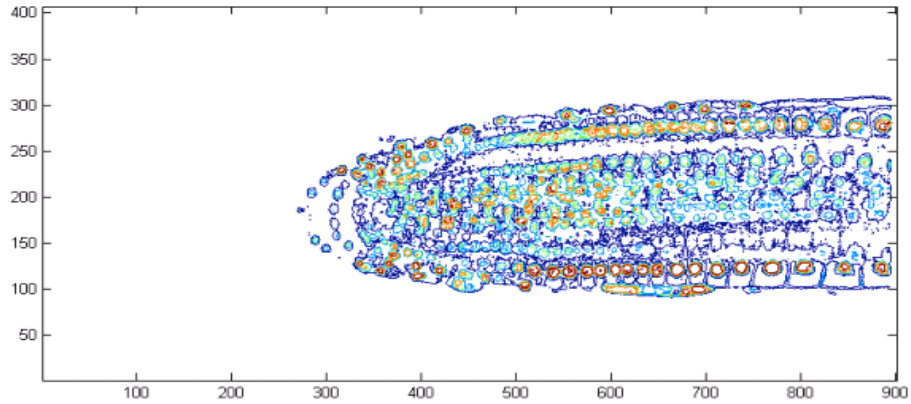


Fig 4. Level plot from the original data exhibiting noise and artifacts that must be removed.

The software encompassing the previous work on cell segmentation, tracking, data extraction, and the infrastructure of all supportive operations has been gathered in two

software packages available on the Computable Plant project's web-site www.computableplant.org: "segtrack" and "sassign". The latter package is the C/C++ tracking code with Matlab interface, whereas the former is the collection of Matlab operations for rest of the image processing tasks. Fig. 4 illustrates the velocity and the strain rate maps obtained after segmentation, tracking, smoothing/extrapolation and data extraction steps for the time-series of the growing root image data (original data from Ben Scheres, University of Utrecht).

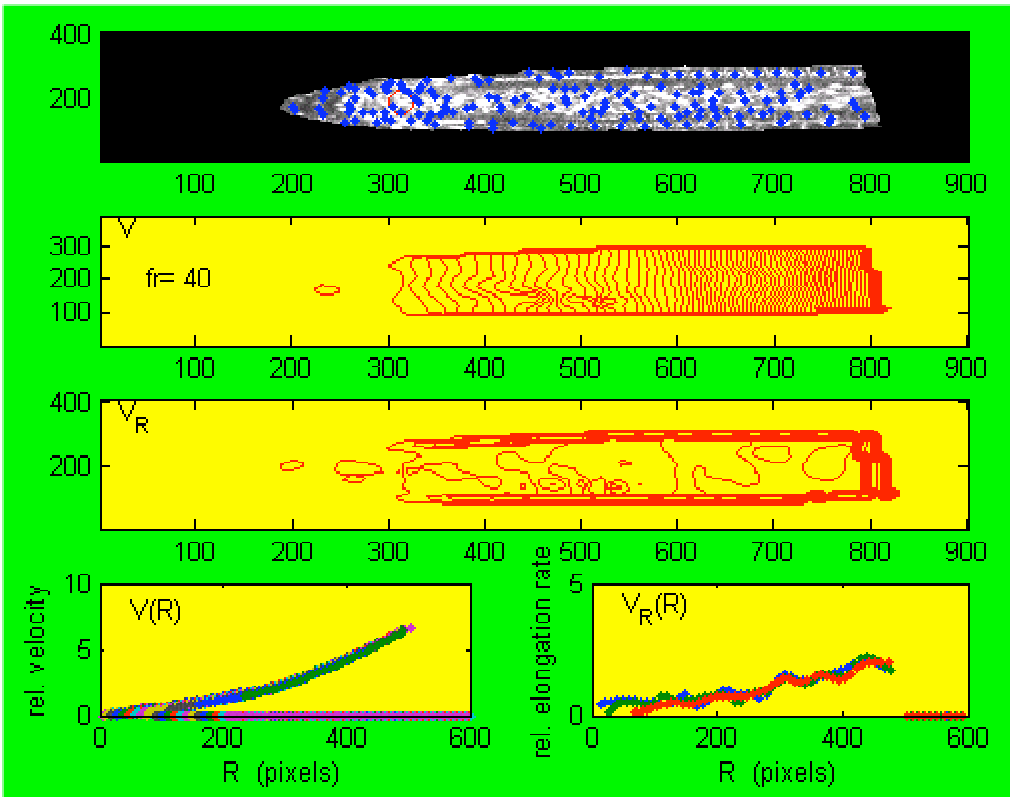


Fig.4 Velocity and strain rate contour level maps with appropriate plots vs. distance to the quiescent center (the red circle on the top pic.) for the growing root.

3.2.2 Convex cells extraction from volumetric data (Patrick Hung)

A software tool is being developed for the extraction of cell geometries and topologies from noisy confocal images. Given an image stacks with the cell walls highlighted from the background, optimal separating planes between pairwise connected cells are computed, intersection of planar half-spaces so defined provide convex polytopic descriptions of the single cells. Two dimensional prototypes suggest that this method is robust to relatively poor quality data. Nevertheless, a GUI postprocessing tool is envisioned to enable biologists to manually correct obviously spurious or missing features from the algorithmic output.

4. Mathematical and Software Tools for modeling

4.1 Mathematical tools for modeling

We are developing several interrelated mathematical frameworks that are aimed at the modeling challenges posed by biological development in general and plant development in particular. The most fundamental and general of these reached journal publication this year: the Dynamical Grammar framework [Mjolsness and Yosiphon 2007]. This framework models biological processes using a generalized form of chemical reaction notation in which the "reactants" are objects with parameters or attributes that affect their probability per unit time to undergo any particular reaction. For example, molecules may need to approach within a certain distance to undergo a chemical reaction, and cells may need to grow to a threshold size before undergoing a cell-division "generalized reaction". This reaction notation is mapped to a time-evolution operator that specifies dynamics which can be deterministic, stochastic, discrete, continuous, spatial, graphical, or any mixture of these characteristics. This great flexibility makes the mathematical framework especially suitable for modeling complex, multiscale systems as encountered in developmental biology. There is a proof-of-concept implementation of Dynamical Grammars which has been used to implement the weak spring mechanical model used in the full phyllotaxis model. We have recently used this software to model other stem cell niches including *Arabidopsis* root and mouse olfactory receptor neurons, proving that plant modeling can have non-plant modeling spinoffs.

A more specialized framework for application to plant developmental modeling was introduced as a poster at the International Conference for Systems Biology in Yokohama. In this case, the continuum limit is taken of cellularly compartmentalized models of autoregulated transport of auxin by PIN1, within the background of a growing tissue whose growth is regulated by a localized regulatory network. The resulting model family may be called "lively surfaces" [Mjolsness JPGR 2007] since they combine active geometry and local information processing and communication. This framework is not well explored yet.

Another specialized mathematical modeling method was described for modeling molecular complexes such as transcription and signal transduction complexes [Mjolsness BIB 2007], both of which have an important future in multiscale mechanistic models of development, with particular exploration of transcription complex modeling [Mjolsness JBCB 2007].

4.2 Software tools for modeling

4.2.1 Finite Element Modeling (Pawel Krupinski)

Mechanical properties of plant cells, next to Gene Regulatory signals, are thought to be an important factor in cell development and growth. Mechanical models of cells often simplify the task by reducing dimensionality to two dimensions, or by working with simple geometries, suitable for analytical studies. While such approaches are valuable for

developing a general understanding of the principles governing mechanical interactions within a cell, Finite Element Models (FEM) offer an attractive alternative because they are able to handle multiple cells and realistic geometries. At the same time, FEM allows to incorporate different material models for plant walls, including anisotropic, composite array of cellulose microfibrils and viscoplastic materials. FEM also makes it possible to extract not only the global deformation of a collection of cells, but also local information about stresses and strains within each cell wall. These quantities can be important for modeling of cell growth and division.

Solutions obtained by FE analysis can provide the equilibrium state of the system under external loads and prescribed deformation, as well as small time step updates describing displacements and velocities at each of the discretization nodes. The latter can be useful as part of a large-scale model of plant tissue, in which mechanical updates are interconnected with Gene Regulatory Networks and provide spatial and topological information utilized by GRN algorithms.

The starting point for FEM is definition of the geometry of the cellular complex. This can be done either by providing 3D positions of cell nuclei, in which case cell compartments are created as Voronoi cells of the point set, or by supplying complete description of cells' nodes and faces in predefined file format. Such cells have polyhedral shape which corresponds to e.g. meristem cells in *Arabidopsis thaliana*. Cells whose shape is not polyhedral, e.g. *Arabidopsis thaliana* embryo cells, can be described by allowing multiple polygons per wall. In next step cell walls are created as plates whose thickness is either specified for each cell or is a fraction of cell size. The whole complex is meshed and node loads are calculated from given turgor pressures and prescribed boundary conditions. After processing the FE solution is obtained and results are written for visualization in a post-processor. Currently the VRML file format is supported as the default visualization. More formats will be added in the future.

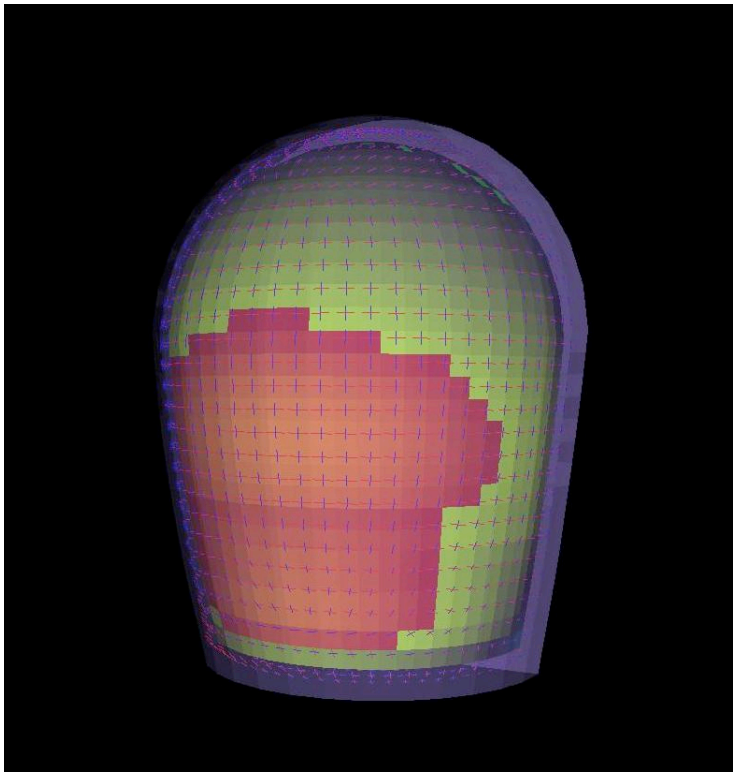


Figure 1
Stress pattern from FEM model of 2-cell *Arabidopsis thaliana* embryo growing under turgor pressure. Surface coloring represents value of Von Misses stress (red-high, green-low). Crosses give principal direction of surface stress.

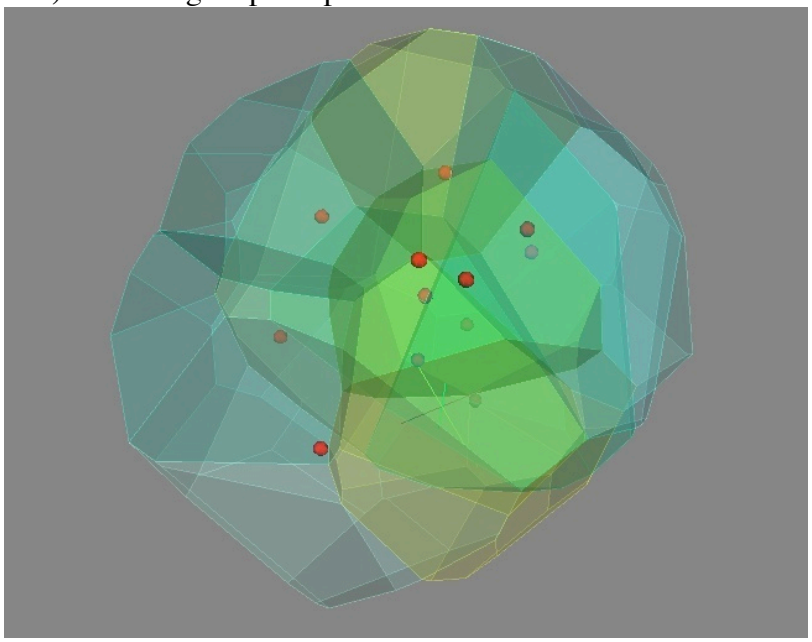


Figure 2
Cluster of 11 cells obtained from Voronoi diagram of nuclei positions (red dots).

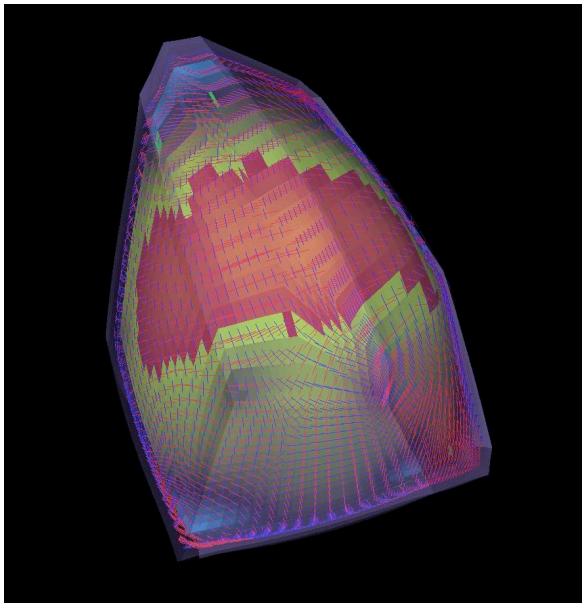


Figure 3
Stress pattern in FEM model of polyhedral cell expanding under internal turgor pressure.

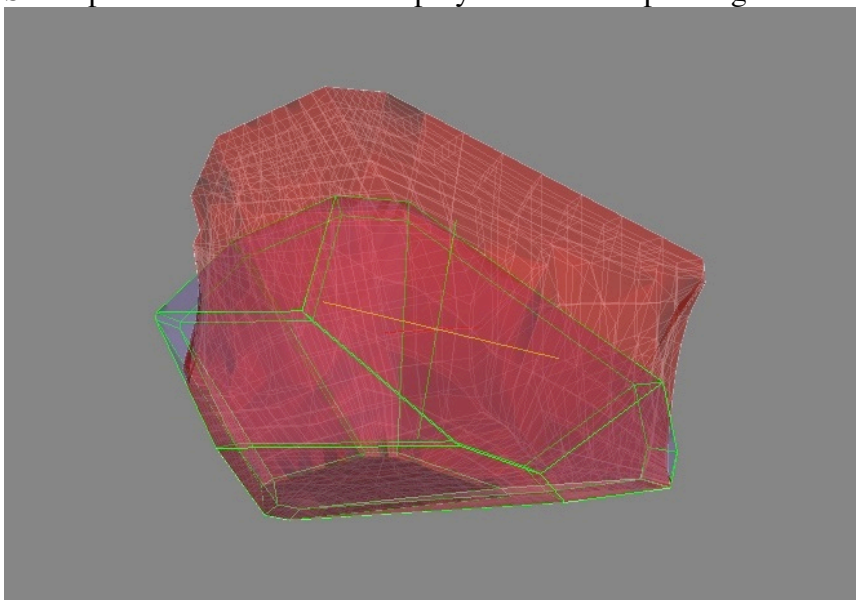


Figure 4
Deformation in FEM model of polyhedral cell stretched and twisted 30º along vertical axis. Original cell is shown by the green outline; the deformed cell is in red.

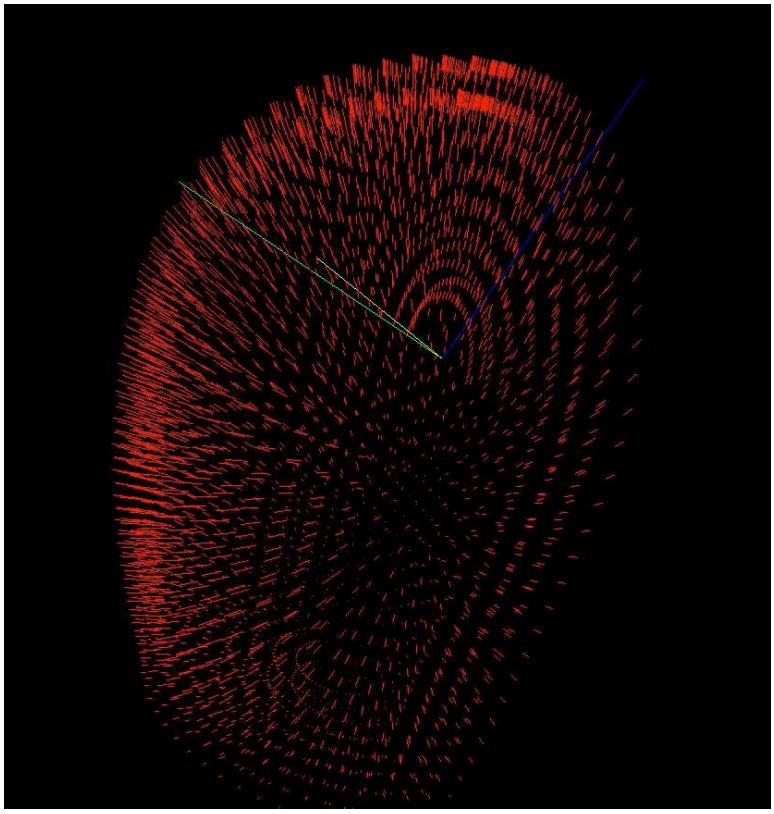


Figure 5
Main growth direction (green line) of FEM model of two-cell *Arabidopsis thaliana* embryo extracted by Principal Component Analysis of growth vectors of discretization nodes (in red).

4.2.2 "Tissue3D" FEM package (Alexey Vorobyov)

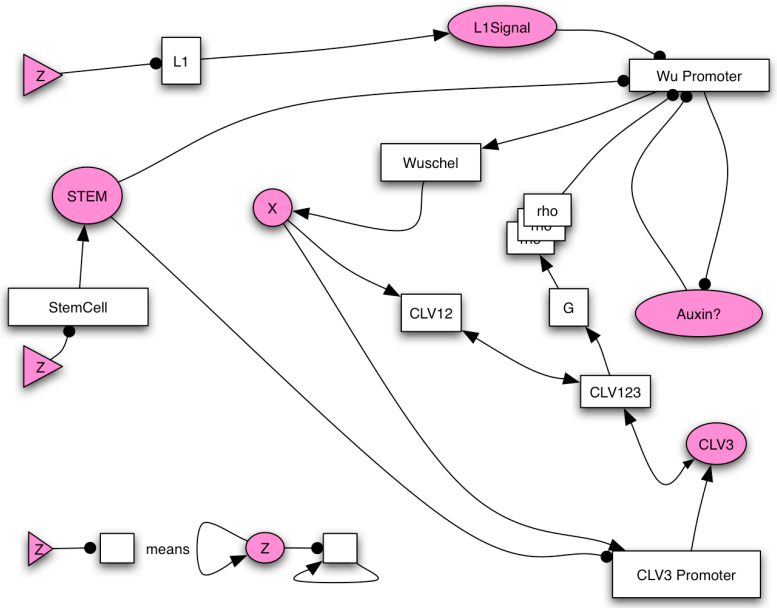
The main efforts this year were directed on testing, verification and performance improvements of the *Mathematica* Tissue 3D code and creation of the simple tissue models. In cooperation with Pawel Krupinsky, who has written a C++ version of FEM, we were able to detect otherwise difficult to observe bugs in previous implementation. The bugs have been found and removed. Careful study of the results of Mathematica processing of original source code as well as multiple performance measurements for different implementations resulted to multi-fold increase in performance of Mathematica implementation. The gain was especially noticeable on complex tissue when performance reached up to 100-fold improvement. The main technique was the reuse of the previously calculated data, which resulted in smaller memory footprint as well as in better performance. The gain on complex systems could be explained by more efficient use of CPU cache and smaller amount of page faults for virtual memory when program uses less memory. Another approach was development of algorithms that are more functional programming oriented and less imperative programming oriented, though in some cases performance analysis shows an advantage for imperative programming implementations. The main models that were simulated on Mathematica Tissue 3D software were models tissues that were subject to homogeneous turgor pressure. One hypothesis was that tissues with different 3D shape would experience larger stress in the direction of minimal cross-

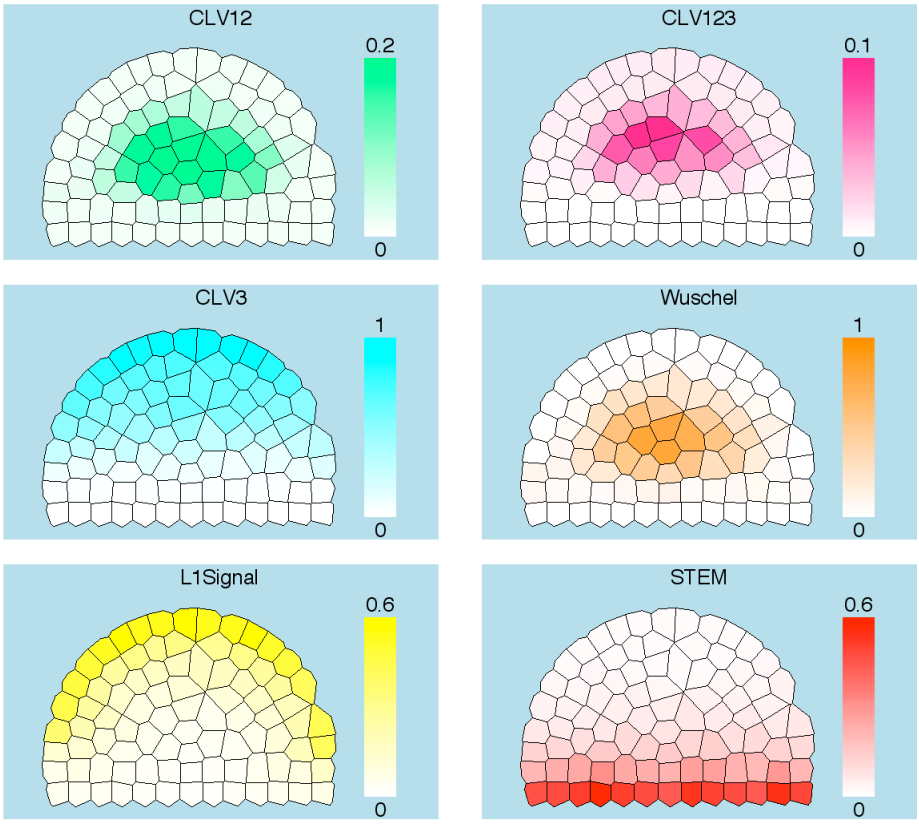
section. This was found to be true for plant cell models because plant cell rigidity is achieved mostly by higher stiffness in the cell walls. Our experiments both in Mathematica and C++ implementations demonstrated that for such systems the largest stress is across the minimal cross-section. That could mean that plants could build new division walls in the direction of main stress, which results in effective relaxation of existing stresses in cell walls and improves mechanical rigidity of the tissue in the most efficient way.

4.2.3 "Cellerator" (Computer algebra) derived modeling tools (Bruce Shapiro)

Cellerator is a biological model-generation package built on a computer algebra system, allowing for sophisticated model analysis. We created Cellzilla, a simple but surprisingly useful extension to the latest Cellerator version (xCellerator) which replicates intra- and inter-cellular regulatory networks by processing a cell index (eg. the integer "i" in "kinase[i]") which is added each network reactant, thereby creating model multicellular tissues (see http://www.xcellerator.info/usersguide/cellzilla.html).

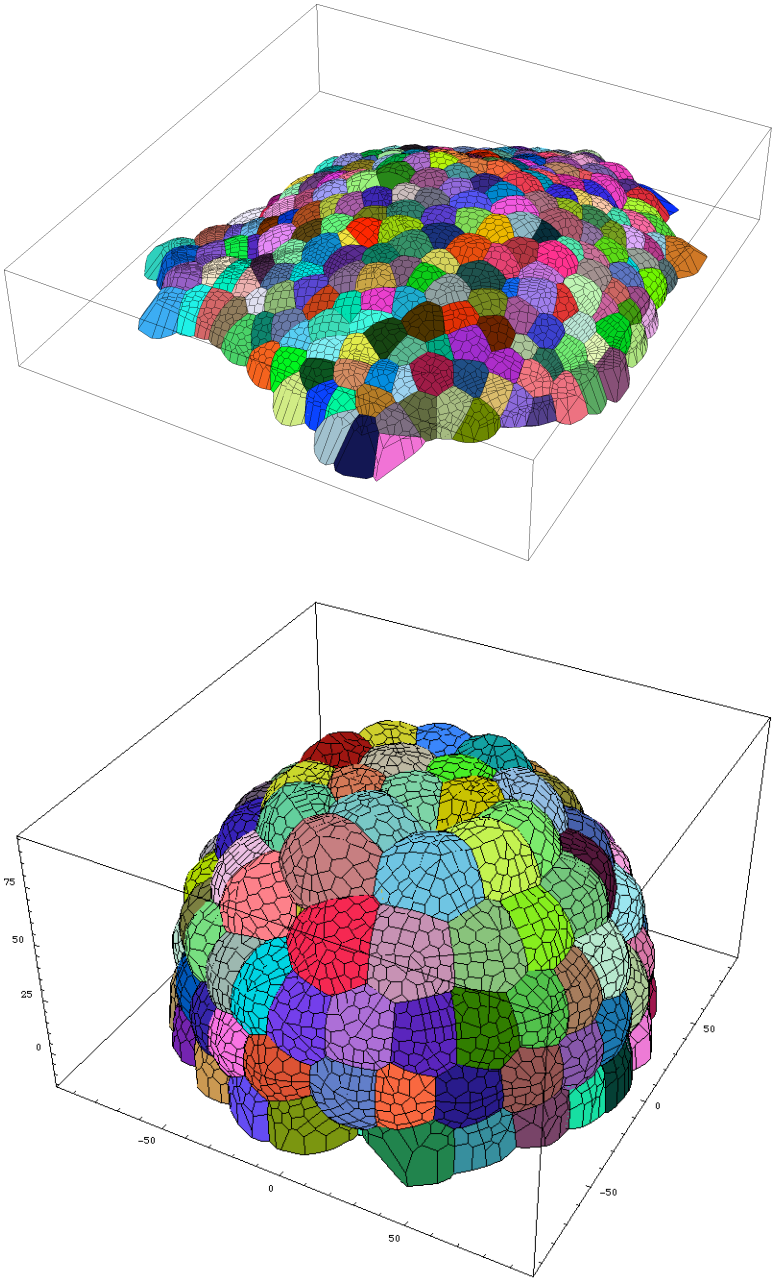
We examined several variants of CLV1/2 models and simulated them in Cellzilla. Illustrated: typical model; typical steady state concentrations for a second model; and typical Cellzilla implementation for a third model.



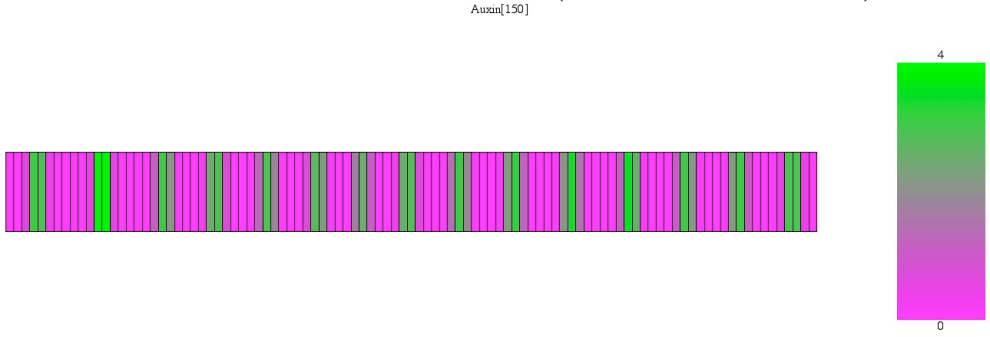

CLV12
0.2
0
CLV123
0.1
0
CLV3
1
0
Wuschel
1
0
L1Signal
0.6
0
STEM
0.6
0

```
internal[i_] := {

   (* Maintenance of L1 Layer *)
   {Z[i] ↦ Z[i], GRN[r_Z, T_{Z,Z}, 1, h_Z]},
   {Z[i] → ∅, k_Z},
   {{Z[i], L1[i], STEM[i]} ↦ L1[i], GRN[r_L1, {T_{Z,L1}, T_{L1,L1}, T_{STEM,L1}}, 1, h_L1]},
   {L1[i] → ∅, k_L1},

   (* Maintenance of StemCell Layer *)

   {ZZ[i] ↦ ZZ[i], GRN[r_ZZ, T_{ZZ,ZZ}, 1, h_ZZ]},
   {ZZ[i] → ∅, k_ZZ},
   {{StemCell[i], ZZ[i]} ↦ StemCell[i], GRN[r_SC, {T_{SC,SC}, T_{ZZ,SC}}, 1, h_SC]},
   {StemCell[i] → ∅, k_SC},

   (* Generation of STEM Signal *)

   {StemCell[i] → StemCell[i] + STEM[i], k_{STEM,f}},
   {STEM[i] → ∅, k_{STEM,r}},

   (* Generation of L1 Signal *)

   {L1[i] → L1[i] + L1Signal[i], k_{L1Signal,f}},
   {L1Signal[i] → ∅, k_{L1Signal,r}},

   (* Wuschel Model *)

   {{L1Signal[i], STEM[i], rho[i]} ↦ Wuschel[i], GRN[r_Wuschel, {T_{L1,W}, T_{Stem,W}, T_{rho,W}}, 1, h_W]},
   {Wuschel[i] → ∅, k_Wuschel},

   (* X=Unknown Wuschel Induced Diffusible Signal  *)

   {Wuschel[i] ↦ X[i], GRN[r_X, T_{W,X}, 1, h_X]},
   {X[i] → ∅, k_X},

   (* CLV3 Model *)

   {{L1Signal[i], X[i], STEM[i]} ↦ CLV3[i], GRN[r_CLV3, {T_{L1,CLV3}, T_{X,CLV3}, T_{Stem,CLV3}}, 1, h_CLV3]},
   {CLV3[i] → ∅, k_CLV3},

   (* CLV12 Model *)

   {X[i] → X[i] + CLV12[i], k_{CLV12,f}},
   {CLV12[i] → ∅, k_{CLV12,r}},

   {CLV12[i] + CLV3[i] ⇄ CLV123[i], k_{CLV123,f}, k_{CLV123,r}},

   (* CLV123 inactivation of Wuschel via rho-signal *)

   {CLV123[i] → CLV123[i] + rho[i], k_{rho,f}},
   {rho[i] → ∅, k_{rho,r}}
  };

external[i_, j_] := {
   {Z[i] → Z[j], D_Z},
   {ZZ[i] → ZZ[j], D_ZZ},
   {STEM[i] → STEM[j], D_STEM},
   {L1Signal[i] → L1Signal[j], D_L1Signal},
   {X[i] → X[j], D_X}
  };
```

Visualization algorithm for 3D meristem based on Voronoi diagrams. Also used to generate simulated data for M. Burl's image analysis. Shown: visualization of real meristem based on 3D voronoi of cell centers (top); simulated meristem (bottom)



There is a new website for released Computable Plant models (http://computableplant.caltech/edu/models - which can be reached from the main website by clicking on models). SBML & Cellerator versions of models as well as movies are posted: (1) Activator model from Bioinformatics 21:i232; (2) One dimensional Auxin model from PNAS 103:1633 (visualization illustrated).



Software infrastructure progress:

- Tissue3D: conversion to package compatible with Cellerator.
- Cellzilla: Cellzilla generates simulated layouts of cells on standardized geometric templates and uses mPower (qhull) to simulate cell boundaries and connectivity. Added conversion of data points to Tissue3D data structure; add functionality for simple spring model to be integrated with signaling model.
- xCellerator: optional compatibility with the MathSBML simulator so that events can be eventually included. Input/Output of SBML models. Automated layout of SBML models. This was done in preparation of automated layout of cellerator models.
- X20: Development of a Mathematica interface to generate *organism* model files, and ability to run simulations in organism from within mathematica. This was done in preparation of automated conversion of Cellerator models to H. Jönsson's *organism* simulator.
- SSA: new program that uses Cellerator mass-action arrow notation to generate stochastic models using Gillespie algorithm.

5. Selected Activities and Meetings

Weekly group meetings (Photo 5.1). An essential element of team science, even e-science, is periodic physical co-location. Nearly every week, one or more UCI team members attend the Caltech weekly group meeting. Work pairs have repeatedly emerged from this process.

Annual project meeting, Feb 3, 2007. Photos 5.2-5.5 are from the annual Computable Plant project meeting held at Caltech's Kerckhoff Marine Lab in Corona del Mar, California, near the UC Irvine campus. The Novosibirsk and Lund collaborators were in attendance. A thorough review of the year's progress was conducted and new interactions were initiated in mechanical modeling and comparison between shoot, root, sepal, leaf and other tissues.

NSF HQ 2007: "The Computable Plant: Modeling Plants and Plants as Models". This outreach activity at the NSF open house is discussed in Section 6.

Novosibirsk collaborators' annual visit February 2007. Previous years' visits have resulted in a large number of relevant papers, now starting to enter journal publication (Section 7). We expect the same will be true of this years' very fruitful visit.

University of Nottingham Center for Plant Integrative Biology visit, March 2007: Mjolsness is a member of the advisory board for this new United Kingdom systems biology center. He visited it, along with two more of the six UK systems biology centers, as part of a mini-sabbatical in March. Auxin signal transduction pathway, root growth, seed germination, and root image analysis were among the areas discussed and identified as of mutual interest.

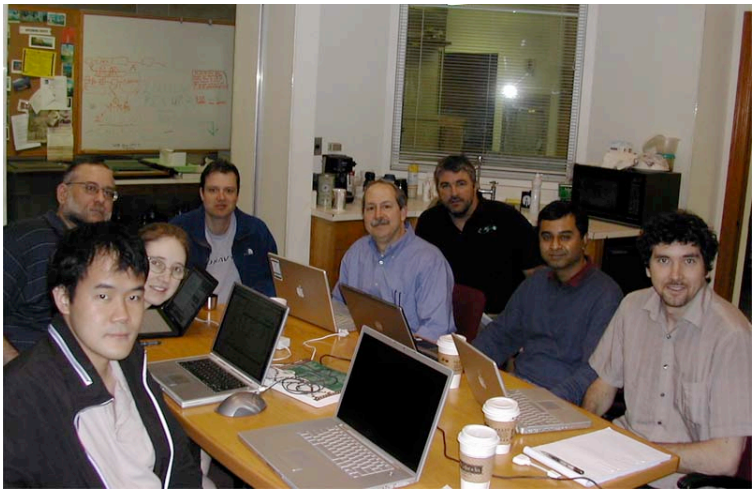


Photo 5.1: A CP weekly group meeting at Caltech. Clockwise around the table from front left: Patrick Hung, Adrienne Roeder, Bruce Shapiro, Marcus Heisler, Elliot Meyerowitz, Mike Burl, Vijay Chickarmane, Henrik Jönsson.



Photos 5.2-5.5: Annual CP meeting at Caltech's Kerckhoff Marine Lab in Corona del Mar, California.

6. K-12 Outreach

Grounding in Botany at the Huntington Botanical Gardens has completed its third full year. This year, the *Grounding in Botany* program combined forces with another high school teacher professional development course at the Huntington Gardens that is supported by the Arthur Vining Davis Foundations. Pooling our resources and expertise allowed us to extend the course from a one-week to a five-week format and expand and strengthen our content material. The program year began with a very successful summer course (three days a week) for 2006 and was followed by five workshops scheduled through the 2006-2007 academic year.

We continued to expand recruitment efforts this year, increasing the number of contacts for advertising the summer program. Again the course was approved by the Los Angeles Unified School District for salary point credit, and LAUSD advertised it on their web site of professional development opportunities. In addition to email announcements to various list-serves, we also sent personal letters to over 120 department science chairs, covering a large portion of the LA basin. The 19 participants included teachers from as far as Long Beach and Santa Ana. The teachers represented a variety of academic backgrounds and classroom levels, including continuation schools and Advance Placement biology.

The summer institute (Photos 6.1-6.4) included lectures and lab work on topics including: genetics; plant physiology; the scientific process; current botanical research; mathematical modeling; growing Wisconsin Fast Plants and using them in the classroom; diffusion and osmosis; sexual and asexual reproduction; plant hormones; and plant morphology. The class even took a field trip to the Los Angeles Zoo to learn about plant/animal interactions and adaptations. Lectures and labs were lead and facilitated by Huntington staff with guest lectures from

- Dr. Elliot Meyerowitz, George W. Beadle Professor of Biology and Chair of the Division of Biology at the California Institute of Technology.
- Dr. Eric Mjolsness, Associate Professor, Department of Information and Computer Science at the University of California at Irvine
- Dr. Jose Luis Reichmann, Director, Gene Expression Center at Caltech
- Elaine Wong, Graduate student at the University of California at Irvine
- Sean Gordon, Graduate student at the California Institute of Technology

Our follow up workshops have provided additional labs and lectures on a variety of topics that help strengthen and expand the use of plants in the classroom. The workshops in the 2006-2007 series were:

- **October 28th, 2006: "Lesson Sharing and Discussions with Program Graduates."** Participants shared the lesson plans that they designed as part of the course with each other and received valuable input from their peers.
- **November 18th, 2006: "I'm Your Venus: Carnivorous Plants in the Classroom."** Ecology and evolution standards where addressed with an engaging look at the peculiar world of carnivorous plants. Participants experimented with (and took home) meat-eating flora, including the ever-famous Venus' fly trap.

- **February 10th, 2007: "Hormones in the Harvest."** Dr. Deb Folsom of the Huntington and Pasadena City College gave a guest lecture about how people manipulate plant hormones so that we have "better" consumable goods. This fascinating talk ended with a trip to see the Camellia Festival, where there where beautiful and interesting examples of what can happen when these hormones are manipulated.
- **March 10th, 2007: "Composters Make It From The Ground-Up."** Decomposers are an integral but often hidden part of the food web. In this workshop, participants looked closely (even microscopically) at the decomposition process and learned how to bring it into the classroom as a fascinating illustration of the carbon and nitrogen cycles.
- **April 14th, 2007: "The Joy of (Plant) Sex".** In this workshop, teachers observed normally hidden aspects of plant reproduction. For instance, teachers germinate pollen on onion skins and look at pollen tube formation.

We are extremely pleased with the reactions from our participants. Comments such as "*[Grounding in Botany]* completely exceeded my expectations" and "I feel like I got great ideas for my classroom and learned a lot myself" were common in our evaluations, and we continued to hear praise for the course as the teachers were supported through workshops. At our most recent workshop, for example, one teacher took aside an instructor to let her know just how many lessons and activities from the course she has incorporated into her classroom already and how, most importantly, she now has the confidence to teach about plants where she hadn't before. Some participants have even brought family members to attend follow-up workshops because they where so excited about the material. Another extremely important outcome of the *Grounding in Botany* course is the camaraderie and sharing of ideas and resources among participants. At each follow-up workshop, participants compare labs completed and activities planned, share successes and discuss challenges, trade lesson plans, and share stories about student achievements.

On our front-end and summative evaluation of participants to assess the success of the program, biology content scores raised an average of 21 percent after completion of the institute. Additionally, teachers' intent to make botanical sciences and botanical lab work a part of their classroom curriculum increases substantially, as does their level of confidence in teaching about plant biology. "What I like best about this workshop was the emphasis on plants in meeting biology standards, the hands-on activities, and the authenticity of information" said one participant. Another added, "I truly enjoyed all the content, hands-on experiments, research and field work in the Huntington, and the degree of organization and knowledge of content that was brought to the workshop. I would *love* to do this workshop again!" These comments are backed by our year-end evaluation in which teachers reported a significant increase in the number of plant based labs they where using in their classroom (an average of ten plant labs).

Not only do participants gain more content knowledge in botany, but evaluation has revealed that they also gain the skills to translate that knowledge to their students in meaningful ways. The 19 teachers we worked with this year together reach a total of

1,500 students in the classroom—and evidence shows that the performance of those students will improve. For example, after all the high school science teachers in the Pasadena Unified School District (PUSD) attended Huntington workshops based on GIB materials, the scores of PUSD students (where 65% students are eligible for federal free-reduced lunch and 30% are English language learners) on the 2005–2006 California Standards Test in biology rose by 10 percent.

This February we were invited to participate in the first NSF open house. In our booth (Photo 6.5), we highlighted some of the teacher's work and had several hands-on activities based on materials from the workshop. Additionally, we had articles about the program accepted at *Dimensions* the Journal of the Association of Science and Technology Centers (May/June 2007) and at a Huntington distributed journal called *Frontiers* (Fall 2006). We presented materials from the course at the annual meeting of California Agriculture in the Classroom (October 2006). We are also working in conjunction with the San Francisco Exploratorium to put together a joint program for our teachers targeted for February of 2008 at the Huntington Gardens.

We are in the process of preparing for the 2007 summer academy. This summer's course, which will again be co-sponsored by Arthur Vining Davis Foundations, will be a four-week academy (July 10th-August 3rd, four-days a week) and will have five follow-up workshops spaced throughout the academic year.

For the 2007-2008 year, we have further expanded our recruitment efforts by adding the following groups to our contacts: the local AP list serve, directly mailing 152 Southern California teachers on the California Agriculture in the Classroom database, the California School Garden Network online calendar and newsletter, the California Science Teachers Association online calendar and the National Science Teachers Association online calendar. We expect to be reviewing applications in the next couple weeks.

Photo 6.1

Photo 6.2

Photo 6.3

Photo 6.4

Photo 6.5. Mike Kerkman and Elliot Meyerowitz at NSF open house, Computable Plant booth, including Meyerowitz's ABC model for floral organ determination (foreground) and the new phyllotaxis model (video monitor, background) as well as a microscope (off image to right).

7. Research Dissemination

NSF Highlight

E. Mjolsness, E. Meyerowitz, M. Heisler, and H. Jönsson, "National Science Foundation Highlight: The Computable Plant." January 31, 2007. *Appended to this report*.

Journal Publications, 6/2006-5/2007.

Martha Kirouac. "Experience, Confidence, and Tools: The 'Grounding in Botany' Program". ASTC (Association of Science-Technology Centers) Dimensions, May/June 2007. http://www.astc.org/pubs/dimensions.htm .

Eric Mjolsness, "Towards a Calculus of Biomolecular Complexes at Equilibrium". Briefings in Bioinformatics, in press, 2007.

Michniewicz, M., Zago, M.K., Abas, L., Weijers, D., Schweighofer, A., Meskiene, I., Heisler, M.G., Ohno, C., Zhang, J., Huang, F., Schwab, R., Weigel, D., Meyerowitz, E.M., Luschnig, C., Offringa, R. and Friml, J. Phosphorylation-dependent apical-basal targeting of PIN regulated by antagonistic activities of Phosphatase 2A and PINOID kinase. Cell, in press, 2007.

A. Sadovsky, P. Baldi, and F. Wan. "A Theoretical Study of the In Vivo Mechanical Properties of Angiosperm Roots: Constitutive Theories and Methods of Parameter Estimation". Journal of Engineering Materials and Technology, in press 2007.

Eric Mjolsness, "On Cooperative Quasi-Equilibrium Models of Transcriptional Regulation". Journal of Bioinformatics and Computational Biology, **5**(4) in press, 2007.

N. Komarova, L. Wu, and P. Baldi. On the Luria-Delbruck Model with a Nonzero Death Rate. Mathematical Biosciences, in press (2007).

Reddy, G.V., Gordon, S.P. and Meyerowitz, E.M. Unravelling developmental dynamics: transient intervention and live imaging in plants. Nature Reviews Molecular Cell Biology **8**, 491-501, 2007.

M. Heisler and H. Jönsson, "Modelling meristem development in plants". Current Opinion in Plant Biology 10, 92-97, February 2007.

Eric Mjolsness and Guy Yosiphon. "Stochastic Process Semantics for Dynamical Grammars", Annals of Mathematics and Artificial Intelligence, **47**(3-4) January 2007.

Heisler, M.G., and Jonsson, H.. Modeling auxin transport and plant development. Journal of Plant Growth Regulation **25**(4), 302-312, December 2006.

Eric Mjolsness. "The Growth and Development of Some Recent Plant Models: A Viewpoint". Journal of Plant Growth Regulation **25**(4), 270-277, December 2006.

Ashish Bhan and Eric Mjolsness, "Static and dynamic models of biological networks". Complexity **11**(6), 2006. (Listed as "in press" in the 2005-6 Annual Report.)

S. J. Swamidass and P. Baldi. "Bounds and Algorithms for Exact Searches of Chemical Fingerprints in Linear and Sub-Linear Time". Journal of Chemical Information and Modeling, **47**(2), 302-317, 2007.

S.I. Fadeev, S.V. Nikolaev, V.V. Kogay, E. Mjolsness , N.A. Kolchanov, "Analysis of a one-dimensional model for the regulation of the size of the renewable zone in biological tissue". (In Russian.) Computational Technologies, http://www.ict.nsc.ru/mathpub/comp-tech/eng/, **11**(2), 2006. (Listed as "in press" in the 2005-6 Annual Report. English translation newly provided at www.computableplant.org, this year.)

Vitaly Likhoshvai and Alexander Ratushny "Generalized Hill function method for modeling molecular processes". Journal of Bioinformatics and Computational Biology, in press, V5, N4 2007.

Ilya Akberdin, Evgeniy Ozonov, Victoria Mironova, Nadezda Omelyanchuk, Vitaly Likhoshvai, Dmytry Gorpinchenko, Nikolay Kolchanov "A cellular automation to model the development of primary shoot meristems of Arabidopsis thaliana". Journal of Bioinformatics and Computational Biology, in press , V.5, N 4 2007.

Vitaly Likhoshvai, Nadezda Omelianchuk, Victoria Mironova, Stanislav Fadeev, Eric Mjolsness, Nikolay Kolchanov "Mathematical model of auxin distribution in the plant roots", Russian Journal of Developmental Biology in press 2007.

S.V. Nikolaev, A.V. Penenko, V.V. Lavreha, E.D. Mjolsness, N.A. Kolchanov "A modeling of CLV1, CLV2, CLV3 and WUS interactions in the shoot apical meristem structure control", Russian Journal of Developmental Biology in press 2007 .

N.A. Omelianchuk, V.V. Mironova, E.M. Zalevsky, I.S. Shamov, A.S. Poplavsky, N.L. Podkolodny, D. K. Ponomaryov, S.V. Nikolaev, E.D. Mjolsness, E.M. Meyerowitz, N.A. Kolchanov "Towards a systemic level approach to morphogenesis in Arabidopsis thaliana: I. AGNS database ", Russian Journal of Biophysics in press 2007.

S.V. Nikolaev, S.I. Fadeev, A.V. Penenko, V.V. Lavreha, V.V. Mironova, .N.A. Omelianchuk, , E.D. Mjolsness, N.A. Kolchanov "Towards a systemic level approach to morphogenesis in Arabidopsis thaliana: II. Modeling of the shoot apical meristem structure control", Russian Journal of Biophysics in press 2007.

Ilya Akberdin, Evgeniy Ozonov, Victoria Mironova, Dmytry Gorpinchenko, Nadezda Omelyanchuk, Vitaly Likhoshvai, Nikolay Kolchanov "Modeling morphogenesis of

Arabidopsis thaliana in terms of cellular automaton", Russian Journal of Biophysics in press 2007 .

Conference Publications

Eric Mjolsness, "New Mathematical Methods for Systems Biology". Tutorial (oral presentation and written notes), International Conference on Systems Biology, October 8 2006.

Tigran Bacarian, Marcus Heisler, Eva-Maria Schoetz, and Eric Mjolsness, "Calculating Derivative Displacement Fields from Confocal Fluorescence Microscopy Data". Proceedings of the 2006 Workshop on Multiscale Biological Imaging, Data Mining and Bioinformatics. University of California, Santa Barbara, CA, USA, Sept 7-8, 2006. http://www.bioimageinformatics.org/2006/program.html .

Michael Burl, Adrienne Roeder, Carolyn Ohno, Eric Mjolsness, and Elliot Meyerowitz, "Automatic Extraction of 3D Nuclear Bounding Surfaces from CLSM Imagery of Developing Arabidopsis Flowers". Proceedings of the 2006 Workshop on Multiscale Biological Imaging, Data Mining and Bioinformatics. University of California, Santa Barbara, CA, USA, Sept 7-8, 2006.
http://www.bioimageinformatics.org/2006/program.html .

Mjolsness E., "Modeling transcriptional regulation with equilibrium molecular complex composition". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 1, pp. 118-121. July 2006.

Nikolaev SV, Fadeev SI, Kogai VV, Mjolsness E, Kolchanov NA, "A one-dimensional model for the regulation of the size of the renewable zone in biological tissue". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 2, pp. 213-217. July 2006.

Nikolaev SV, Penenko AV, Belavskaya VV, Mjolsness E, Kolchanov NA, "A system for simulation of 2D plant tissue growth and development". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 2, pp. 218-22. July 2006.

Omelianchuk NA, Mironova VV, Poplavsky AS, Pavlov KS, Savinskaya SA, Podkolodny NL, Mjolsness ED, Meyerowitz EM, Kolchanov NA, "AGNS (*Arabidopsis* GenNet Supplementary Database), release 3.0". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 2, pp. 223-226. July 2006.

Ponomaryov D, Omelianchuk N, Kolchanov N, Mjolsness E, Meyerowitz E.,"Semantically rich ontology of anatomical structure and development for *Arabidopsis thaliana*". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 2, pp. 227-230. July 2006.

Ponomaryov D, Omelianchuk N, Mironova V, Kolchanov N, Mjolsness E, Meyerowitz E., "A program method of constructing ontology of phenotypic abnormalities for *Arabidopsis thaliana*". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 2, pp. 231-234. July 2006.

Podkolodny NL, Podkolodnaya NN, Miginsky DS, Poplavsky AS, Likhoshvai VA, Compani B, Mjolsness E., "An integration of the descriptions of gene networks and their models presented in Sigmoid (Cellerator) and GeneNet". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 3, pp. 86-90. July 2006.

Mironova V.V., Poplavsky A.S., Ponomaryov D.K., Omelianchuk N.A. "Ontology of Arabidopsis GenNet Supplementary Database AGNS), cross database references to TAIR ontology. 5th International Conference on Bioinformatics of Genome Regulatioin and Structure(BGRS'2006). Volume. 2, pp. 209-212. July 2006.

Likhoshvai V.A., Rudneva D.S., Fadeev S.I." Oscillations of chaotic type in symmetric gene networks of small dimension". 5th International Conference on the Bioinformatics of Genome Regulation and Structure (BGRS 2006), Volume 3, pp. 74-77. July 2006

Poster presentations

"Systems Biology Software Support in Mathematica: New Developments in Cellerator", B. E. Shapiro, A. Vorobyov, J. G. Murakami, E. D. Mjolsness. Poster presentation, International Conference on Systems Biology, 9-10 October 2006.

"Simplified models of growth for cells and tissues", Eric Mjolsness, Sergey Nikolaev, Przemek Prusinkiewicz, Alex Sadovsky, S. Fadeev, and Nikolay Kolchanov, Poster presentation, International Conference on Systems Biology, October 9-10 2006.

"An auxin transport model for regulation of plant organ initiation", Henrik Jönsson, Marcus Heisler, Bruce E. Shapiro, Elliot M. Meyerowitz, and Eric Mjolsness, Poster presentation, International Conference on Systems Biology, October 9-10 2006.

Talks featuring the Computable Plant Project

Keynote presentation, Systems Biology Workshop: From Nucleotides to Ecosystems, "Computational modeling of plant development" , Melbourne, Australia, May 21 - June 1, 2007. (Jönsson)

U.C. Irvine, Institute for Genomics and Bioinformatics Distinguished Speaker, "How Plants Compute: Cellular Interactions in the Shoot Apical Meristem and Patterns of Plant Growth", May 18, 2007 (Meyerowitz)

Workshop INTAS – SB RAS 2006 Scientific Cooperation and Collaborative Call, "System-level analysis of functional modules in Arabidopsis developmental gene networks". Novosibirsk, Russia. 10-12 May 2006 http://www.intas.be/content/news/workshop/Novosibirsk/Documents/Book_of_Abstracts.pdf (Omelyanchuk)

Institute for Systems Biology Annual Symposium, Seattle, WA, April 23, 2007 (Meyerowitz)

ETH Zürich, "Variable-Structure Dynamical Systems: Recent Work", invited talk, April 18, 2007. (Mjolsness)

Nottingham University Center for Plant Integrative Biology, "Progress and Techniques from the Computable Plant Project", invited talk, Nottingham University Sutton Bonington Campus, UK April 5, 2007. (Mjolsness)

Plenary Lecture, British Society for Developmental Biology, Edinburgh, UK, March 30, 2007 (Meyerowitz)

Parameter Estimation In Systems Biology (PESB) Pascal Workshop, invited talk "Model Reduction for Parameter Estimation", Manchester, UK March 28, 2007. http://www.cs.manchester.ac.uk/ai/pesb07/ . (Mjolsness)

University of Edinburgh, "An algebra of stochastic processes as the formal semantics for a biological modeling language", invited talk, March 20 2007. (Mjolsness)

Second Workshop on Mathematical Aspects of Systems Biology, "Computational models of plant shoot development", Gothenburg, Sweden, March 21-24, 2007. (Jönsson)

Oral presentation at the Basel Computational Biology Conference (USGEB07), H. Jönsson, M. Heisler, P. Melke, E.M. Meyerowitz, E. Mjolsness, and B. S. Shapiro, "Computational modelling and live imaging of plant development", Basel, Switzerland, March 13-14, 2007. (Jönsson)

University of Minnesota, February 27, 2007 (Meyerowitz)

Gordon Conference on Quantitative Genetics, Ventura, CA, February 20, 2007 (Meyerowitz)

Washington University, St. Louis MO, January 23, 2007 (Meyerowitz)

University of Missouri, Columbia, MO, January 22, 2007 (Meyerowitz)

Department of Energy-Joint Genome Initiative, Walnut Creek, CA, January 18, 2007 (Meyerowitz)

SIAM Minisymposium on Phyllotaxis, "Mathematical models of likely mechanisms for phyllotaxis: Polarized auxin transport, cell growth, and dynamic connectivity", invited talk, Joint Mathematics Meetings, New Orleans Louisiana January 5 2007. (Mjolsness)

Plenary Lecture, American Society for Cell Biology, San Diego, CA December 12, 2006 (Meyerowitz)

Neural Information Processing Systems (NIPS) 2006 Workshop: Revealing Hidden Elements of Dynamical Systems, December 8 2006. "Formulating inference problems for variable-structure dynamical Systems", invited talk. Vancouver, Canada. http://www.haifa.il.ibm.com/Workshops/nips2006/ . (Mjolsness)

Kavli Institute for Theoretical Physics, Santa Barbara. "Physical Methods for Modeling Biological Development", invited seminar. November 14, 2006. http://online.kitp.ucsb.edu/online/bio99/mjolsness/ . (Mjolsness)

Banbury Center Conference on Integration of Hormonal and Genetic Regulation in Plant Development, Cold Spring Harbor Laboratories. "Integrative mathematical modeling frameworks for plant development", invited talk. November 8 2006. (Mjolsness)

Department of Systems Biology, Harvard Medical School. "Building multiscale mathematical models of development in Arabidopsis and Drosophila", invited talk. November 3 2006. http://vcp.med.harvard.edu/abstracts/mjolsness.html. (Mjolsness)

VII All Russian conference on mathematical modeling and information technologies, "Modeling of morphogenesis in *Arabidopsis thaliana* in terms of cellular automaton", Krasnoyarsk, Russia, November 1-3, 2006 http://www.ict.nsc.ru/ws/show_abstract.dhtml?en+154+10583 http://www-sbras.nsc.ru/HBC/hbc.phtml?12+398+1 (Akberdin)

The Eleventh Workshop on Software Platforms for Systems Biology, "Structured and dynamic collections: SBML Level 3 support?", Tokyo Japan October 13 2006. http://www.sbml.org/workshops/eleventh/presentations/mjolsness/Mjolsness-arrays.pdf (Mjolsness)

The Eleventh Workshop on Software Platforms for Systems Biology, "Developmental modeling in SBML", Tokyo Japan October 12 2006. (Mjolsness) http://www.sbml.org/workshops/eleventh/presentations/mjolsness/Mjolsness-Developmental.pdf .

Tutorial (3 hours, 40 attendees), "New Mathematical Methods for Systems Biology", International Conference on Systems Biology, Yokohama Japan October 8 2006. http://www.icsb-2006.org/tutorials/tutorials.htm . (Mjolsness)

Department of Theoretical Physics, Lund University, Sweden, October 2, 2006 (Meyerowitz)

Keynote Lecture, Opening of the Mendel Institute, Vienna, Austria, September 29, 2006 (Meyerowitz)

Peking University, Beijing, China, August 18, 2006 (Meyerowitz)

Computable Plant workshop for high school science teachers, "The Computable Plant: How Differential Gene Expression Leads to Pattern Formation in Plants", Huntington Botanical Gardens teaching resource center, August 9 2006. (Mjolsness)

FASEB Conference on Plant Development, Saxton's River, VT, August 6, 2006 (Meyerowitz)

Plenary Lecture, Federation of European Societies of Plant Biology, Lyon, France, July 18, 2006 (Meyerowitz)

St. Petersburg Polytechnic University, "Computational modeling and image analysis approaches to understanding the dynamics of the *Arabidopsis thaliana* shoot apical meristem", St. Petersburg Russia, July 12 2006. (Mjolsness)

Exploratorium, San Francisco, CA, July 7, 2006 (Meyerowitz)

Plenary Lecture, Society for Developmental Biology Annual Meeting, Ann Arbor, MI, June 19, 2006 (Meyerowitz)

NKS 2006 Wolfram Science Conference, "Towards a searchable space of dynamical systems models", Washington DC, June 15 2006. (Mjolsness) http://wolframscience.typepad.com/wolfram_science/2006/06/eric_mjolsness_.html

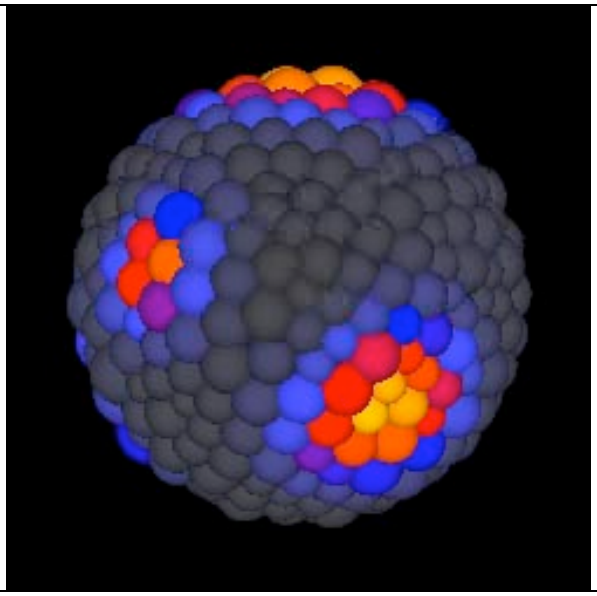
Principal Investigators' meeting, Frontiers in Biological Research Program, "The Computable Plant: An Experimental and Computational Framework for Developmental Modeling in Plants", National Science Foundation Headquarters, June 1 2006. (Mjolsness and Heisler)

Web site distributed software (at www.computableplant.org)

segtrack Cell segmentation and tracking software in matlab and C/C++
http://computableplant.ics.uci.edu/sw/segtrack/index.html
sassign multiple cell-tracking software based on softassign matching algorithm
http://computableplant.ics.uci.edu/sw/sassign/index.htm
Mathematica packages:
(access from http://computableplant.ics.uci.edu/sw.html)
xCellerator Modeling and Simulation software
mPower wrapper for qhull, regtet, pwrvtx
SSA stochastic simulation

from www.xcellerator.info: Cellzilla
phazeplot example of doing phase portrait
tissue3D finite element modeling

National Science Foundation Highlight : The Computable Plant

Award No(s): #030786	
Project Title: The Computable Plant (FIBR)	
Investigator(s): **E. Mjolsness (UCI), E. Meyerowitz (Caltech), J. Folsom (Huntington)**	
Institution(s): **University of California Irvine, California Institute of Technology, Huntington Botanical Gardens**	
Website: www.computableplant.org	**3D Model of floral pattern formation** Top view of a computer simulation of phyllotactic pattern formation leading to a spiral pattern of floral buds in plant shoot growth. Future buds are indicated by the emergence of regions of high auxin (red and yellow). Cell growth and division displace older auxin peaks outwards, making room for new ones. H. Jönnson, M. Heisler, B. Shapiro, E. Meyerowitz, E. Mjolsness - *Proc. Nat'l Acad. Sci.* 1/06.

Project and Outcomes

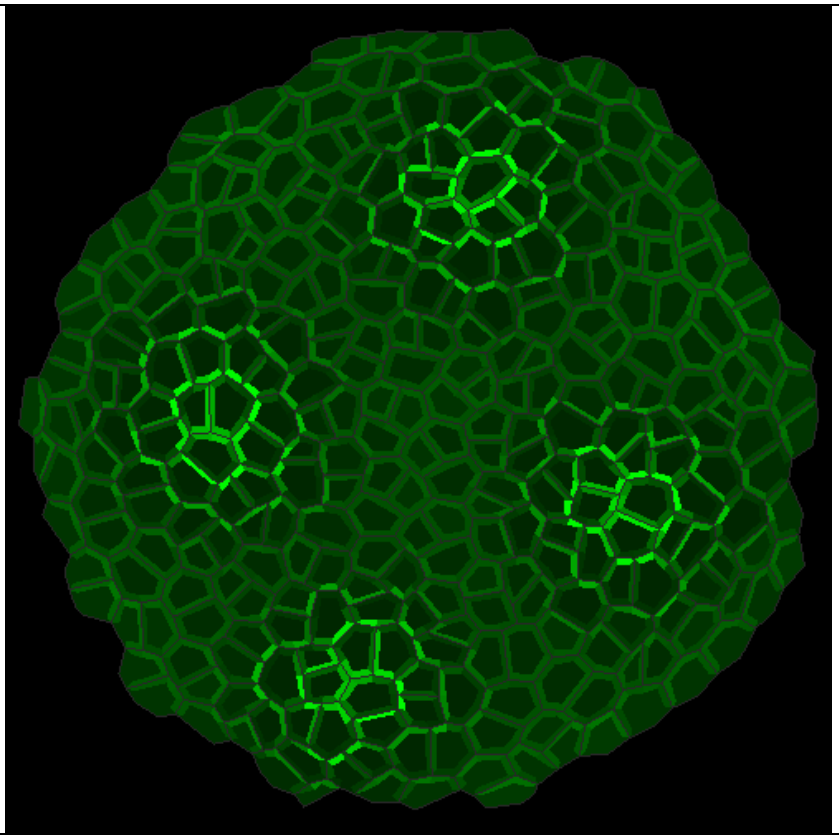
Why do many plants have a spiral pattern of flowers, leaves and branches? How can this pattern continue stably for the lifetime of the plant? A classic scientific problem, and one of the first scientific problems ever simulated with digital computers, is now yielding to a new combination of computing, microscopy, and molecular biology. In the NSF-funded Computable Plant project, essential mechanisms of cell growth, cell communication, and molecular regulation are represented in mathematical models. The computed behavior of the models is compared with time-lapse microscope movies of real plant development. The results provide new insight into fundamental plant biology and could ultimately impact biotechnology and engineering.

One new insight is about communication between cells. The spatial patterning of plant shoots, roots and leaves are all deeply influenced by the plant growth hormone auxin and its movement between cells. A new model of the shoot suggests that auxin can influence the direction of its own movement. In the model, it does this by regulating which cell membranes contain the proteins (such as PIN1) that direct auxin from one cell to another. If confirmed experimentally, this "autoregulated transport" of auxin would represent an entirely new mechanism for communication between cells in biological development.

When combined with models of cell and tissue growth, the auxin transport model can provide a molecular explanation for Hofmeister's 1868 observation that new leaves at the shoot tip occur as far as possible from old ones. This rule can explain spiral and other "phyllotaxis" patterns of leaves, but it in turn needs a more fundamental molecular explanation. In the Computable Plant project models, new floral buds form when and where tissue growth makes room for them by moving the older primordia, which compete for auxin, out of the way. This explains Hofmeister's rule, using very different mechanisms from those of computational pioneer Alan Turing in his 1952 simulations of phyllotaxis. Another Computable Plant project model addresses the problem of the long-term stability of gene expression patterns in the meristem, even against destructive experimental interventions with a laser.

Potential applications of a fundamental understanding of spatial patterning in plants are manifold. The shoot and root constitute stem cell "niches" in the plant: regions of the adult organism that preserve all-purpose cells that can multiply and specialize as needed. These niches may be a relevant model system for animal stem cell niches, and may also demonstrate new principles by which communication between units leads to dynamic patterns – which could lead to new types of machines. Also the ability to reengineer the architecture of plants, by controlling their basic spatial patterning mechanisms, could be important in redesigning plants for energy, food, or growth in altered environments.

Simulated PIN1 localization



Computer simulation of “autoregulated transport” of the plant growth hormone auxin, in phyllotaxis. The plant protein PIN1 (green) may accumulate at particular cell boundaries (small green rectangle-like areas) so as to direct the movement of auxin from one cell (larger polygons with black centers in the image) to the next. If auxin can in turn influence the localization of PIN1 within a cell, as in this simulated model, then peak regions of both auxin and PIN1 can arise. These will eventually become new floral buds in a spiral pattern.