The Computable Plant: Annual Report, 6/2005-5/2006

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1. Introduction

The problems of phyllotaxis and shoot meristem maintenance were the primary arenas of scientific progress for the Computable Plant project this year, with additional progress in image analysis, root meristem dynamics, models of tissue growth, network statistics, biological modeling languages, and high-level software implementations.

To explain recent live imaging observations of phyllotaxis by our project [Heisler et al. 2005] and others, a fundamental alternative to the standard reaction-diffusion modeling paradigm was developed based on polarized transport of growth hormone (auxin) and dynamic geometry due to cell growth and proliferation [Jönsson et al. 2006]. The testable prediction of PIN1 polarity reversal was confirmed. New versions of the model that incorporate AUX1, which facilitates auxin uptake, along with PIN1, the auxin efflux facilitator, are under development.

In meristem maintenance, the model of WUSCHEL expression published in [Jönsson et al. 2005] has been reimplemented in Cellerator format. A one-dimensional version of this model has been analyzed [Fadeev et al. 2006]. Numerous new Cellerator facilities, and a fundamental new modeling language [Mjolsness 2006] that generalizes the concept of dynamical grammars, were implemented to support future developmental modeling work. Image analysis has been further advanced and applied to root meristem imagery to quantify mitoses and cell growth, as input to a new one-dimensional model of the stele [Sadovsky et al. 2005]. Further developments in image analysis have included Voronoi and power diagrams, generative statistical models, and the augmentation of the JPL team with several new members. A new mechanical model based on power diagrams has been formulated, and a Finite Element Method implementation of elastic and plastic dynamics has been created for future integration with Cellerator. Regulatory network statistics [Bhan and Mjolsness 2006] and inference methods have been developed.

The project's work has been communicated in five journal papers and numerous conference presentations, submitted manuscripts, a well-reviewed high school teacher training program, and on the project web site (www.computableplant.org).

Setting of the Research

Major Activities, 2005-2006

Research was managed through twice weekly meetings, augmented with special occasions, as follows.

Weekly meetings – Caltech
> Usual attendees: Heisler, Jönsson (biweekly videoconference), Meyerowitz, Mjolsness, Roeder, Shapiro, Gordon
> Occasional guests: Bacarian, Bhan, Sadovsky, Burl

Weekly meetings – UCI
> Usual attendees: Bacarian, Bhan, Krupinsky, Liang, Yosiphon, Mjolsness

Computable Plant teachers' workshop: "The ABCs of Developmental Botany: Integrating Plants into the High School Classroom", July 11-15 and 28-29 2005.
http://computableplant.ics.uci.edu/outreach.html

Computable Plant FIBR Project retreat, Kerckhoff Marine Laboratory, Corona del Mar, CA February 11, 2006

Visit of ICG collaborators February 2006 (three weeks).

FIBR PI meeting, NSF Headquarters, 6/1/06.

Numerous papers and presentations (see Dissemination, below).

Personnel

A strong group of researchers are involved either as project employees, part time or full time, or as collaborating scientists whose research is synergistic with the project. In addition to the PI's (Mjolsness, Meyerowitz) and co-I's (Baldi, Folsom) the cast includes:

Postdocs: Marcus Heisler, Adrienne Roeder (Caltech Biology), Tigran Bacarian, Ashish Bhan, Pawel Krupinski (UCI Bioinformatics).

Staff: Martha Kirouac (Huntington); Alexey Vorobyov (1/4 time programmer, UCI); Michael Burl, Bruce Shapiro, Michael Turmon (Caltech Jet Propulsion Laboratory).

Graduate Students: Elaine Wong (UCI Math), Guy Yosiphon (UCI Computer Science).

Collaborators: Henrik Jönsson, research scientist, Lund University, Sweden (former Caltech and UCI postdoc); Sean Gordon, Caltech graduate student; Alex Sadovsky, postdoc, UCI; Gang Liang, UCI statistics faculty; collaborators from the Institute for

Cytology and Genetics, Novosibirsk, Russia (Nikolay Kolchanov, Nadezda Omelianchuk, Vitali Likoshvai, Nikolay Podkolodny, Sergey Nikolaev).

Space. New space at UCI was occupied in May 2005 at the UCI branch of the California Institute for Telecommunications and Information Technology http://www.calit2.net/ .

Image analysis

Activities in image processing for the computable plant project in 2005-06 by Tigran Bacarian, UCI Postdoctoral Scholar.

- Scanning microscope 2D or 3D stack + time data were successfully segmented by combination of code implemented in series of Matlab subroutines/C-based mex-files based on morphological reconstruction, pyramidal hierarchical segmentation, watershed transform algorithms, and level set methods with shape analyzing post-processing.

- The resulting segmentation showed >98% correct segmentation for nuclei-marked data in the area with signal/noise ratio >~2, which was applicable for the apical shoot meristem data (M. Heisler), except central regions of large cell conglomerates.

- Current model assumes a point of view on cell growth as on combination of "elastic" stretch (i.e. growth itself), and fine-tuning deformation not containing significant volumetric change. The first part of cell structure deformation within this model, was described via a sequence of Thin Plate Spline (TPS) transformations, found using previously developed software for cell tracking [CVPR2005].

- Incentive for such an approach comes from the fact that even at far from ideal segmentation, correctly identifying only half or less of all cells, the found cells used as landmarks still correctly describe growth properties within the accuracy of several cell lengths. Velocity, and derivative maps produced by this method showed excellent results in the case of root growth data from Ben Scheres, Utrecht.

- For separation of the second part, each timeframe is transformed through a series of solved TPS transformations up to the last frame in the time series, thereby producing a new series of frames describing cell structure changes with growth essentially removed, but with a preserved map of all cell divisions, as well as relative local geometry changes.

- While in the case of polyhedron cells, Voronoi diagrams from nuclear positions found after segmentation describes the cell geometry relatively well, for large cells with strongly varying shape and size like sepal giant cells, using the cell wall data channel is important. In this case, the commonly used method of active contours alone, or a watershed transform based method, does not produce satisfactory results due to the fact that wall images are typically very scattered, and are much less resolved in one of the directions (Z-axis) compared to the other directions. In this case using Voronoi diagrams from the nuclear channel, which is typically better segmented and, therefore, better preserves the distribution of the cell locations, provides a good first approximation for consequent use of an active contour method with wall channel data.

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- Similar methods were used for image processing of Zebrafish embryo development data (E-M. Schotz). Velocity field evolution found for the not yet cell-type-separated cell conglomerate showed distinct active development of two groups of cells right before appearance of ecto- and mesodermal layers in the conglomerate, especially for in vivo movies.

- A computational model was built to describe cell motility of two groups of cells, based on surface tension differentiation, biologically corresponding to interaction of specific groups of cells on the cell surface.

- With this background, analysis of the more difficult SAM imagery may proceed as planned.

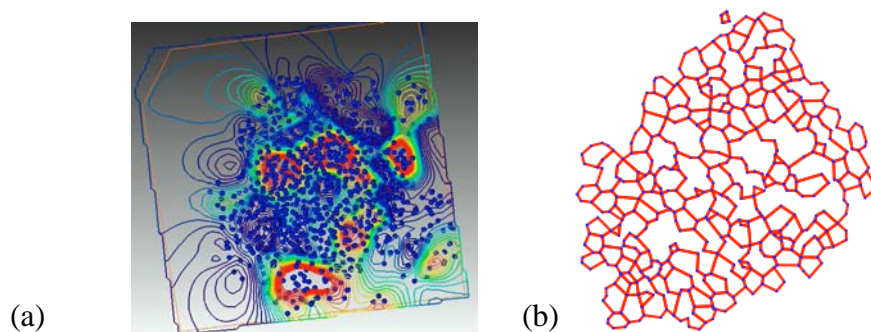(a)   (b)

Figure 1: (a) 2D slice and contour map through 3D interpolated growth field for SAM. (b) 2D detected cell boundaries from imagery by Bayesian method [G. Liang, unpublished].

Recent live imaging observations of phyllotaxis formation by our project [Heisler et al. 2005] have established the basis for the cell-cell communication sector of the phyllotactic model described in the next section, in terms of polarized transport of auxin by PIN1.
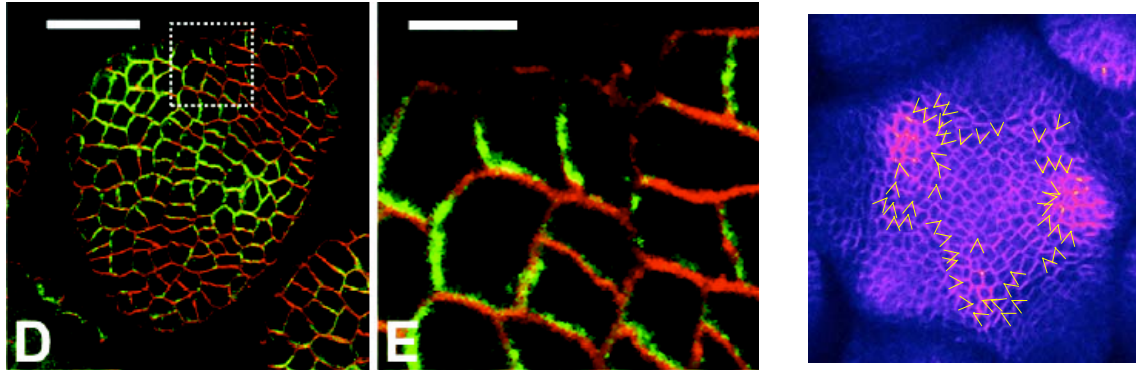

Figure 2: (a-c) Confocal projections of PIN1-GFP signal in the shoot Magnified view of box shown in (b) with both (a) and (b) showing polar localization of PIN1-GFP signal in green in a shoot meristem counterstained with the red membrane stain FM4-64. (c) PIN1-GFP signal in a meristem at lower resolution with signal intensities colorized blue (weak) to pink (strong). Yellow arrows indicate presumed direction of auxin transport.

Image analysis has been further advanced and applied to root meristem imagery to quantify mitoses and cell growth, as input to a new one-dimensional model of the stele [Sadovsky et al. 2005]. Further developments in image analysis have included Voronoi and power diagrams, generative statistical models, and the augmentation of the JPL team with several new members.

Biological modeling

A fundamental alternative to the standard reaction-diffusion modeling paradigm was developed based on polarized transport of growth hormone (auxin) and dynamic geometry due to cell growth and proliferation. The testable prediction of polarity reversal was confirmed. New versions of the model that incorporate AUX1, which facilitates auxin uptake, along with PIN1 are under development. This development was lead by a collaboration between postdoctoral scholars Marcus Heisler and Henrik Jönsson.

Recent studies show that plant organ positioning may be mediated by localized concentrations of the plant hormone auxin. Auxin patterning in the shoot apical meristem is in turn brought about by the subcellular polar distribution of the putative auxin efflux mediator, PIN1. However, the question of what signals determine PIN1 polarization and how this gives rise to regular patterns of auxin concentration remains unknown. We addressed these questions by using mathematical modeling combined with confocal imaging. We propose a model that is based on the assumption that auxin influences the polarization of its own efflux within the meristem epidermis. We show that such a model is sufficient to create regular spatial patterns of auxin concentration on systems with static and dynamic cellular

connectivities, the latter governed by a mechanical model. We also optimize parameter values for the PIN1 dynamics by using a detailed auxin transport model, for which parameter values are taken from experimental estimates, together with a template consisting of cell and wall compartments as well as PIN1 concentrations quantitatively extracted from confocal data. The model shows how polarized transport can drive the formation of regular patterns. [Jönsson et al. 2006].
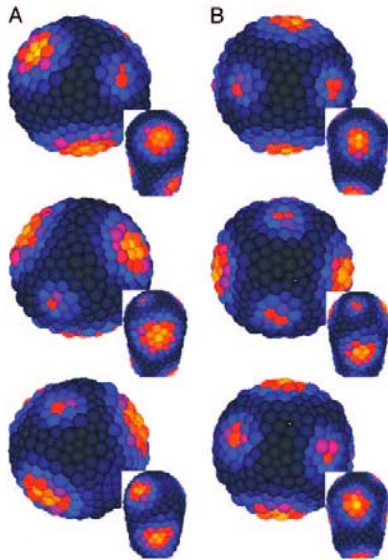

Fig. 5. Simulation of the phyllotaxis model on a half-sphere cylinder surface including cellular growth and proliferation. The main images show a top view (with the insets showing a side view), and time is increasing from top to bottom. The two simulations have different values for the size of the defined central zone. (A) Peaks formed in a spiral pattern. (B) Peaks formed in a whorled (decussate) pattern.
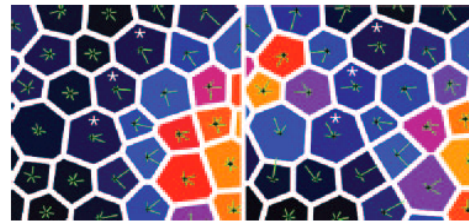

Fig. 6. Simulation of the phyllotaxis model on a two-dimensional plane. Shown is the PIN1 polarization in cells as a new peak is formed. PIN1 polarization (P_{ij}) is shown as bars, with lengths corresponding to a measure of its value, and the color coding shows the auxin concentration. Cells reversing polarity are marked with an asterisk.

Figure 3. Two figures excerpted from [Jönsson et al. 2006].

In meristem maintenance, the model of WUSCHEL expression published in [Jönsson et al. 2005] has been reimplemented in Cellerator format (see http://computableplant.caltech.edu/models/Activator/index.html). A one-dimensional version of the WUSCHEL model has been analyzed [Fadeev et al 2006]. In this work, a "cell-oriented" model for the structural-functional organization of the renewable zone is suggested. The shoot apical meristem (SAM) is provided as an example. The model is cell-oriented because its purpose is to describe observed cell behavior within the framework of a minimal model .

We are testing a new promoter sequence for driving GFP in a more uniform pattern than the previously used 35S promoter. Hopefully this will improve the nucleus tracking significantly. These plants are growing and will also be stained with the plasma membrane stain to generate some new nucleus plus membrane pictures for image processing attempts.

Further work is in progress to add new elements (from experimental data) that should stabilize the phyllotaxis model (such as AUX1 the auxin influx carrier). Experimentally

we are trying to test two of the core assumptions in the model. 1: PIN1 polarization is influenced by auxin and 2: that there is a short range signal activated by auxin that tells neighboring cells to polarize PIN1 accordingly.

The AUX1 addition is to bring the model closer to reality, and to incorporate a known feature of the growing shoot apical meristem. Our models to date are essentially two-dimensional, with the epidermis of the shoot apical meristem the tissue being modeled. This is an acceptable simplification, as the microscopic imaging work has shown that PIN1, the auxin efflux facilitator, is largely confined to epidermal cells, and that auxin, the morphogen in the model, is also largely found only in the meristem surface (as indicated by use of fluorescent reporter constructs in the plants). However, a real meristem is three-dimensional, and therefore an explanation is necessary for the concentration of auxin in the surface layer of cells. It is known that the cells of the meristem epidermis express an auxin influx carrier, AUX1. By modeling on a three-dimensional template, and having AUX1 expressed in epidermal cells, we can reproduce the in vivo concentration of auxin in the surface cells. The next steps are to test a variety of parameters to assess the robustness of the model, and to test the model experimentally by observing the effects of changes (due to mutation) in the activity of AUX1 and PIN1 proteins, which act oppositely in the respect that, in the model, higher AUX1 leads to greater epidermal concentration of auxin, and higher PIN1 reduces the gradient of auxin toward the surface.

Two additional and key parts of the computational model for phyllotaxis are that the polarization of PIN1 in epidermal cells, which is responsible for the vectorial movement of auxin, and therefore for the eventual phyllotactic pattern of flowers, is organized locally and that these local signals are in turn controlled by auxin levels. Tests of whether auxin can influence polarization of PIN1 are just starting. As the auxin transport mechanism is highly robust, simply adding auxin to the meristem surface doesn't necessarily lead to any effects – the added auxin, though added asymmetrically, could be rapidly incorporated in normal auxin flow, and thus only provide a highly transient stimulus. We thus need to use mutant plants, in which the repolarization of PIN1 is compromised (but not eliminated), so that asymmetric applications of auxin can provide longer-term auxin gradients. The genotypes being developed are various alleles and allelic combinations of mutations in the PINOID (PID) gene, which encodes a protein kinase that controls PIN1 localization in the apical and basal directions. In the *pid* mutant primordia fail to form. However this defect can be rescued by micro-application of auxin, which leads to the formation of primordia in regular patterns. Critically, this regular patterning of primordia formation depends on PIN1 function and so this mutant background provides an ideal test system for monitoring the dynamics of PIN1 response to local auxin treatments starting from a neutral symmetric starting point. Preliminary results indicate that PIN1 can respond to auxin in a directional manner and these experiments are being repeated and examined in more detail.

To test whether auxin has its effect on PIN1 via local cell-cell signals we plan to use a laser micro-beam to ablate individual cells, or groups of cells, on the meristem surface, while observing the PIN1 subcellular location by use of PIN1-GFP fluorescent reporter

genes. The laser ablation protocol has been established, and the experiments started. So far, very preliminary results indicate that ablation of a small group of cells toward which PIN1 was initially polarized leads to a rapid relocalization of PIN1 to the opposite sides of the cells adjacent to those that were laser ablated. This strongly supports the local interaction hypothesis, but additional experiments, and dynamic timecourse measurements of PIN1 relocalization will be necessary to prove the point, and to compare the parameters of PIN1 localization with those used to date in the computational models.

Mathematical and Software tools

Stochastic Process Semantics for Dynamical Grammar Syntax

We define a class of probabilistic models in terms of an operator algebra of stochastic processes, and a representation for this class in terms of stochastic parameterized grammars. A syntactic specification of a grammar is mapped to semantics given in terms of a ring of operators, so that grammatical composition corresponds to operator addition or multiplication. The operators are generators for the time-evolution of stochastic processes. Within this modeling framework one can express data clustering models, logic programs, ordinary and stochastic differential equations, graph grammars, and stochastic chemical reaction kinetics. This mathematical formulation connects these apparently distant fields to one another and to mathematical methods from quantum field theory and operator algebra. [Mjolsness 2006]

Graduate student Guy Yosiphon has developed a *Mathematica* notebook implementation of a Stochastic Parameterized Grammar interpreter, called "Plenum". A new algorithm allowed this to be generalized to Dynamical Grammars, which incoporatate differential equations. With this tool, it has been possible to replicate results in Prusinkiewicz's model of cellular growth of the filamentous cyanobacteria *Anabaena catenula*, to replicate Shapiro and Mjolsness's weak spring model of cell growth and division, and create new models of cell division and growth of the root of *Arabidopsis*.

Numerous new Cellerator facilities, and a fundamental new modeling language [Mjolsness 2006] that generalizes the concept of dynamical grammars, were implemented to support future developmental modeling work. A new mechanical model based on power diagrams has been formulated, and a Finite Element Method implementation of elastic and plastic dynamics has been created for future integration with Cellerator.

Regulatory network statistics [Bhan and Mjolsness 2006] and inference methods also have been developed:postdoctoral scholar Ashish Bhan is currently developing these network inference optimization algorithms. He has implemented a Levenberg-Marquardt optimization routine and tested it on small metabolic networks (about 5 variables and unknowns) successfully, and is currently testing the algorithm on systems of intermediate size (20 variables and unknowns).

Bhan has also performed topological analysis of *C. elegans* protein-interaction data. We showed that the degree distribution followed a power-law with exponent consistent with other protein-interaction datasets. We also analyzed other properties of this network and showed that it is a small-world network. We are currently investigating the graphlet frequency count for this network and attempting to reproduce these results using a stochastic parameterized grammar. These computations are quite expensive but can be parallelized and we are setting up the ability to implement these calculations on a local cluster.
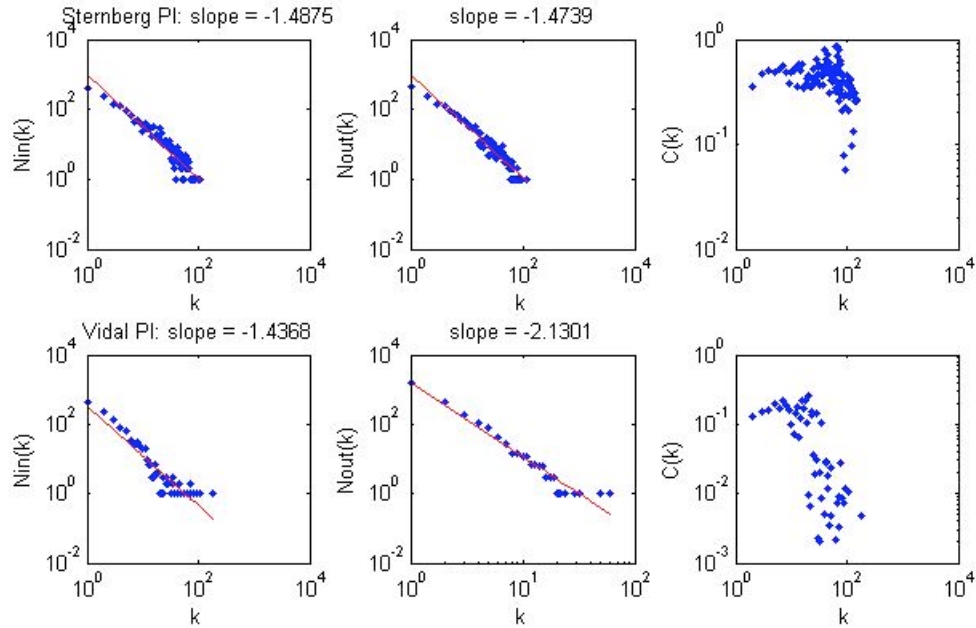
Computational Geometry Algorithms

Dr. Bruce Shapiro implemented wrappers for qHull and regtet to calculate Voronoi diagrams, Delaunay triangulations, and power diagrams in mathematica, including 2D and 3D visualizations. These algorithms significantly improve computation time compared to native Mathematica functions that only handle 2D. There were used in the simulations described below.
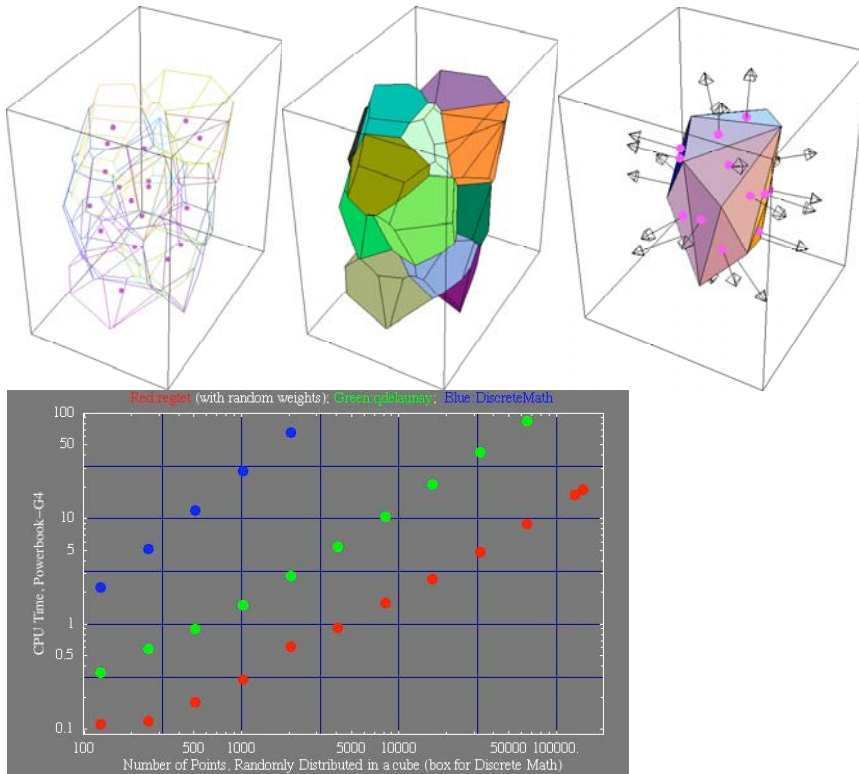
Cellzilla algorithms to generate models on a palette of cells

Shapiro has implemented in Cellzilla code to generate a Cellerator model on a palette of cells given by the xy-coordinates of the cell centers. Connectivity is determined using the Vornoi/Delaunay tessellation as discussed in the following section. The advantage of this implementation is that one only needs to specify the reactions in a single cell and the diffusion reactions, and the rest of the reaction network is calculated automatically. For example, the following Cellzilla commands will generate a 6002 reaction-network between 253 cells illustrated in the following section.

```
internal[i_] := {
    {Y[i] ↦ W[i], GRN[1 / tauw, Twy, 1, hw, sigma]},
    {A[i] ↦ W[i], GRN[1 / tauw, Twa, 1, hw, sigma]},
    {W[i] → ∅, dw},
    {∅ ⇌ Y[i], ky * L1[i], dy},
    {∅ ⇌ A[i], a, beta + d * Y[i][t]},
    {2 A[i] + B[i] → 3 A[i], c},
    {A[i] → B[i], b}
  };
external[i_, j_] := { {Y[i] → Y[j], Dy}, {A[i] → A[j], Da},
    {B[i] → B[j], Db}};
stn = createNetwork[xy, internalNetwork → internal,
    interactionNetwork → external, connectionList → "PrunedDelaunay"
  ];
```

Otherwise it would be necessary to type in all 6002 reactions manually. Generating the reactions automatically from the above code takes less than 1 second of CPU time (1.8 MHz Powerbook G4) and running a simulation to reproduce the published results 42 seconds on the same laptop.

We have also automated visualization functions that will generate the results of the simulation on the palette showing the value of a particular species as a color. The user specifies the range of colors in RGB format and the value is interpolated linearly in RGB space between minimum and maximum values selected by the user. A sequence of such images could then be used to generate a movie (see figure).
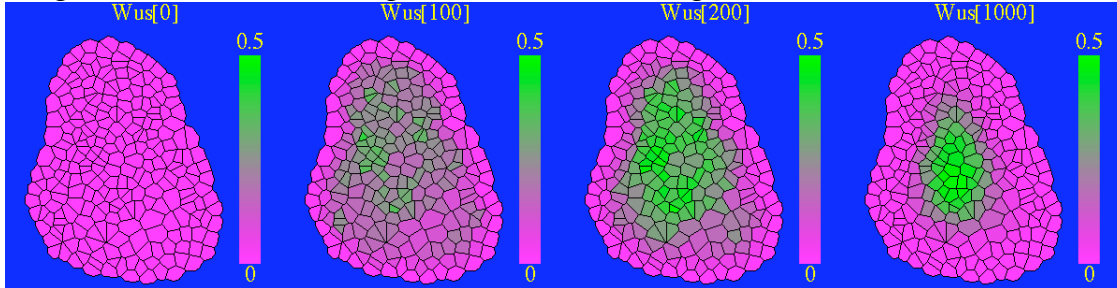

Implementation of Cellzilla Algorithm for Detection of L1 Layer

Shapiro also implemented an algorithm to identify the L1 layer as well as the complete connection matrix from a set of cell center coordinates based on Voronoi tessellations and Delaunay triangulations. The usual problem with the Voronoi tessellation is that the cells on the edge extend to infinity and this does not correspond to the true edge of the tissue (see figure 1a). We have fixed this problem by generating an artificial cell layer along the convex hull (Figure 1b); recalculating the Voronoi Diagram and then removing the artificial cells (figure 1c). The L1 layer corresponds to any cell that shared a border with the artificial cell layer. The connection matrix is then found by first calculating the Delaunay triangulation and then eliminating any connections between cells that do not actually share a Voronoi border (figure 1d).
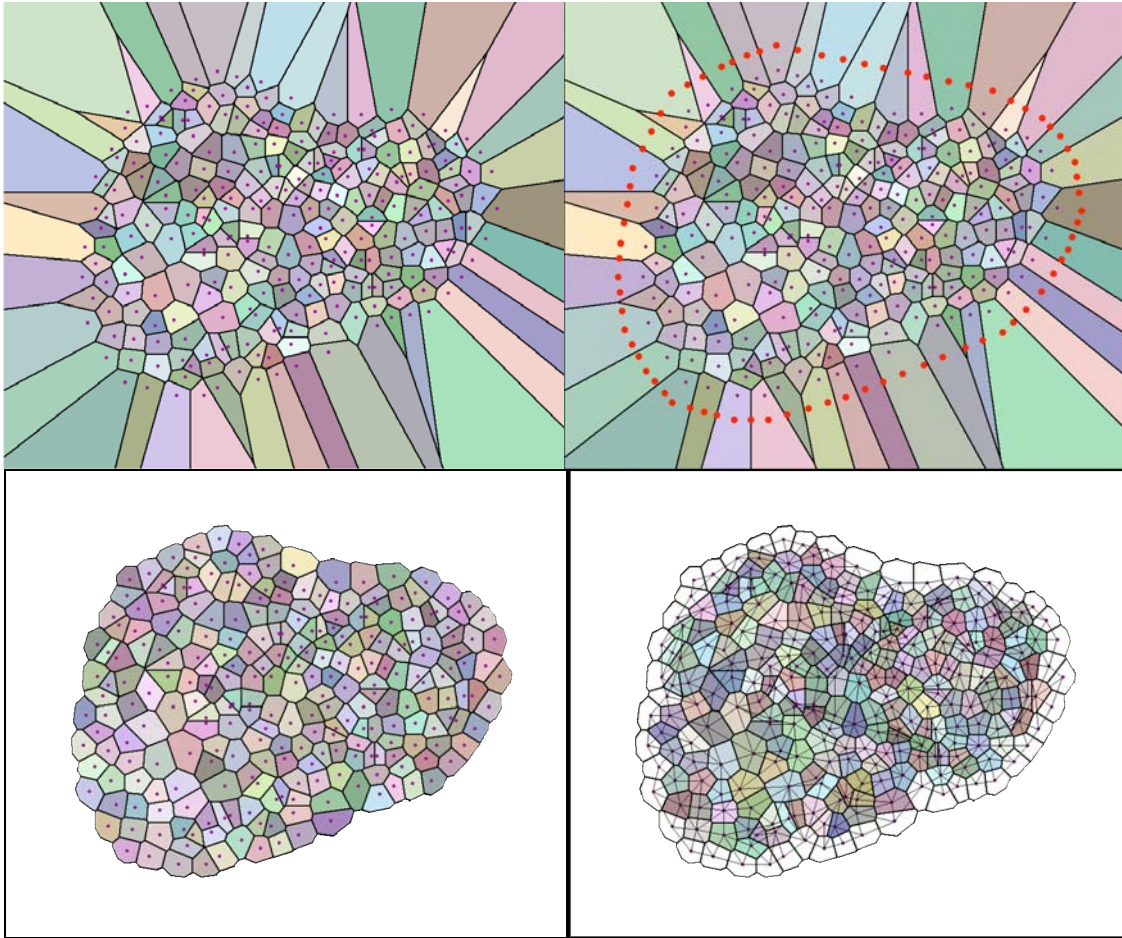
Models Studied

Using the foregoing technology we reproduced our WUSCHEL model of last year within Cellerator, simulating again the laser ablation experiment of Reinhardt et al.
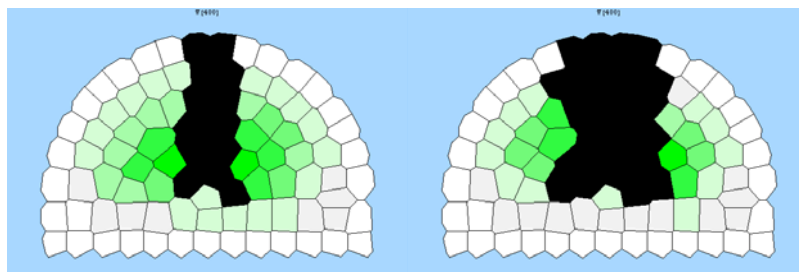
A more detailed model of Auxin/IAA regulation was implemented, as follows.

ArfP = Arf Protein

FreePromoter = Aux/IAA promoter that does not have any TF bound

ActiveGene = Aux/IAA gene that is actively producing RNA

InactiveGene = Aux/IAA gene with bound ArfP-Aux/IAA dimer

AuxIAARNA = AUX/IAA RNA

AuxIAA = Aux/IAA Protein

Auxin_AuxIAA = Auxin bound to Aux/IAA Protein

```
model = {
    {∅ ⇄ ArfP, k12, k13},
    {ArfP + FreePromoter ⇄ ActiveGene, k10, k11},
    {ActiveGene → ActiveGene + AuxIAARNA, k1},
    {AuxIAARNA → ∅, k2},
    {AuxIAARNA → AuxIAA + AuxIAARNA, k3},
    {AuxIAA + ActiveGene ⇄ InactiveGene, k4, k5},
    { AuxIAA ⇄ Auxin_AuxIAA, k6 * Auxin, k7},
    {Auxin_AuxIAA → ∅, k8},
    {AuxIAA → ∅, k9}
}
```
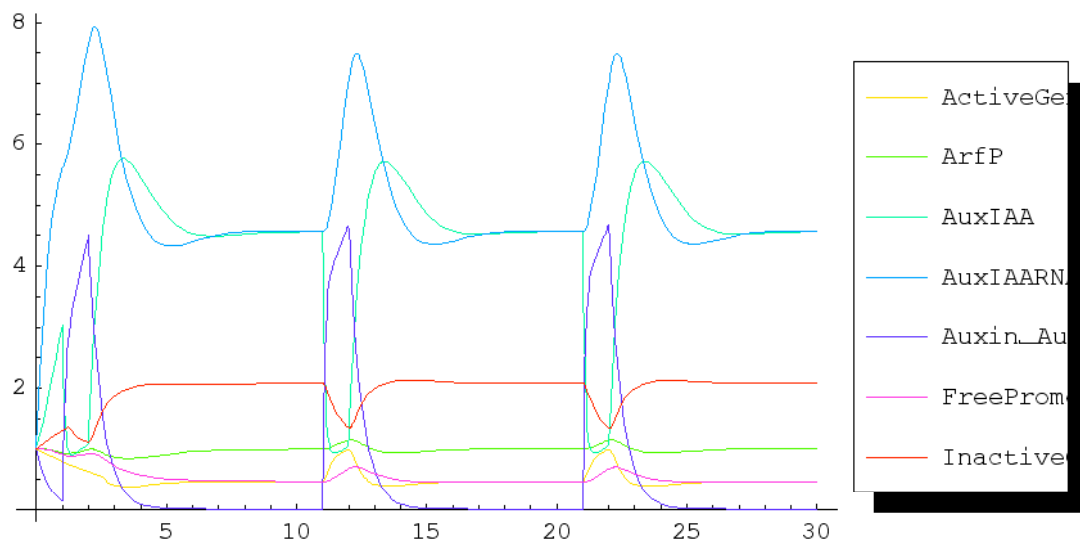

4. CLV1/2/3 Model Generated by Jennifer Paek (high school student at Marlborough High School in Los Angeles) reproduced the results of the Activator Model qualitatively:

　　1.　WUS + CLV3Gene __ Activated CLV3Gene

　　2.　ActivatedCLV3Gene _ ActivatedCLV3Gene + CLV3-RNA

　　3.　CLV3-RNA _ 0 (CLV3-RNA is decayed at a constant rate)

4. CLV3-RNA _ CLV3-RNA + CLV3 (the RNA is translated to protein)

5. CLV3 + CLV12 __ CLV123

6. CLV123 + X _ CLV123X (X is an unknown protein representing a cascade

   in the signal transduction pathway)

7. CLV123X + WUS __ CLV123 + Inactive WUS (WUS is unable to produce

   RNA when the unknown X is bound to it)

8. WUS --> 0 (WUS is decayed at a constant rate)

(4) Three dimensional extension of Wuschel model (Dana Mohamed, student at Harvey Mudd College). Wuschel concentration:
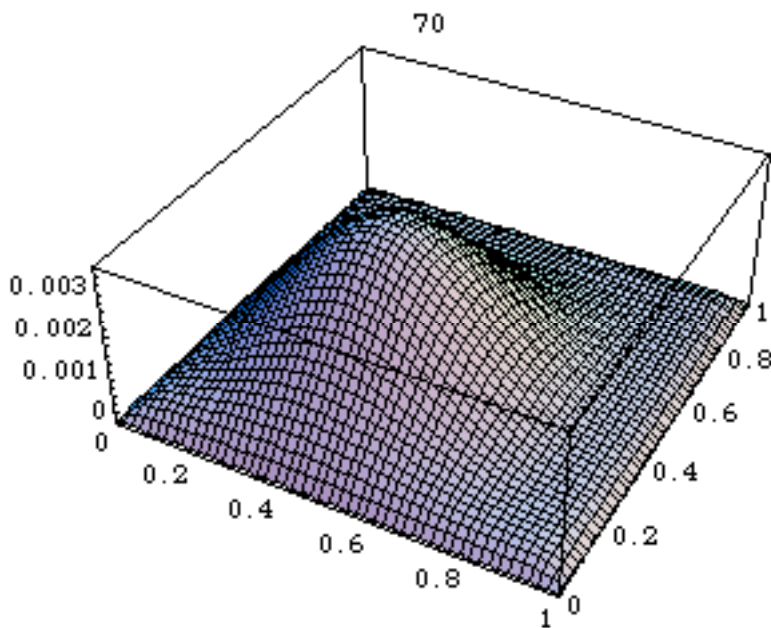
Mechanical models for plant development

Beveled fractured polyhedral geometry for cells.

The approximately polyhedral cells of the SAM allow for simplifications of the usual geometry for applying the Finite Element Method to spatial simulation. We construct radial lines from a center of the cell (for example a time-averaged nucleus center position) to the vertices of the approximating polyhedron. Moving inward a fixed fraction epsilon (a few per cent) along these radials from the vertices, we define new vertices for the inner edge of the cell membrane/wall compartment. These thin volumes are beveled and enclose the cytoplasmic volumes with which they are in 1:1 correspondence. Likewise we can define a time-averaged nuclear geometry by moving outward a variable fraction of each radial from the nuclear center, to define the corners of a nuclear polyhedron. There are now two options for introducing elementary FEM volumes: to create tetrahedral or hexahedra. For tetrahedra, simply triangulate each polyhedral face, and create the corresponding radial tetrahedra joining at the nuclear center. For hexahedra, choose new vertices near the face centers and edge centers. Join the face centers to the nuclear center by new radials, and the edge centers to the face centers. The result is a set of hexahedra, one per vertex of the original approximating polyhedral cell. The face subdivision rules must be applied consistently to pairs of cells that share a face, but that is easy to do. Cell division is possible within the hexahedral alternative by adjusting the arbitrarily chosen center vertices to conform roughly to a division plane through the center point, performing the division, and creating new face-centered radials as before. In the tetrahedral alternative, cell division along a plane requires bisecting and retriangulating the affected polyhedral faces. In both cases some faces of the dividing cells retain their previous subdivision, and neighboring cells fracture further to a modest extent, but the fracture doesn't propagate beyond the nearest neighbor cells.

Tissue3D package

The hexahedral alternative above has been implemented in Tissue3D, as has much of the machinery required for the tetrahedral alternative. Tissue3D is a Mathematica package for exploring and defining FEM methods and models of relevance to developmental modeling, implemented by Alexey Vorobyov in consulation with Mjolsness. Also in Tissue3D, anisotropic material properties were introduced by defining an appropriate modulus and by tracking the deformation of the preferred directions under strain. Support for plasticity was added. Viscous dynamics is supported by calculating derivatives of mechanical potential energy with respect to vertex positions. Power diagrams are now supported through input from our "mpower" package for power diagram calculation using a mathematica interface. A preliminary version of cell division was implemented in the hexahedral alternative.

Project meetings

Caltech Kerckhoff Marine Laboratory (KML), Corona del Mar, CA February 11, 2006. Site reserved at no cost to the project.

KML meeting agenda 2/11/06

8:30-9:30 Coffee and tea with ocean view
9:30am Eric Mjolsness: Welcome; adjusting the agenda
Elliot Meyerowitz: Introduction & biology/modeling progress report
Adrienne Roeder (Caltech): New plant biology image analysis problems
Tigran Bacarian (UCI): Image analysis
Coffee break
Nadya Omelianchuk, Sergei Nikolaev, Nikolay Podkolodny,
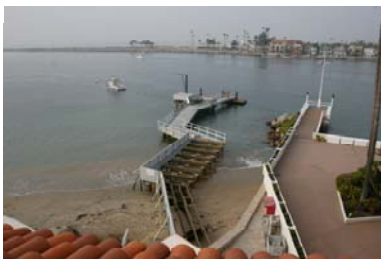   Vitali Likoshvai, (ICG): Progress reports for the year
Lunch break
Bruce Shapiro (Caltech): Software and methods for modeling
Alex Sadovsky (UCI): Root modeling
Ashish Bhan: network inference
Eric Mjolsness (UCI): "New Tropisms for the Computable Plant"
3:30pm Adjourn

Computable Plant FIBR Project retreat, Kerckhoff Marine Laboratory, Corona del Mar, CA February 11, 2006.

K-12 Outreach

Workshop

FIBR outreach September 2005- May 2006

- We have just finished four half-day follow-up workshops (December 10th, February 4th, March 11th, and April 1st) open to all participants from the summer 2004 and 2005 Academies, as well as teachers from another high school teacher professional development program at the Huntington. Cadres of teachers from both Academies choose to participate in the workshops. On average each workshop had 12 participants. Topics for these standards based workshops included: invasive plants to see how humans can alter their environment with a modeling simulation and field work; composting to study the carbon, nitrogen and water cycles; carnivorous plants to look at proteins and carbohydrates as well as plant adaptations; and using *Agrobacterium* to induce tumors in sunflowers to study excessive cell division and cancer.

- For the 2006 summer program, we have combined funding with an Arthur Vining Davis grant to allow for an extended 5-week Academy for the teachers. This will enable us to go into greater depth, with more in-class projects and will help prevent teacher burn out.

- We are calling the course "Grounding in Botany: Integrating Plants into the High School Science Classroom". The course will take place Wednesdays- Fridays, July 12th- August 11th, 9 am-3:30 pm. This course includes mandatory participation in six follow-up workshops through out the 2006-2007 academic year.

- We have 20 spots available for high school biology teachers. To advertise the academy we have: sent out individualized letters to 124 high school science department chairs in the Los Angeles Basin; e-mailed 319 high school teachers on our mailing list; and listed the course on the Los Angeles Unified School District's professional development website. Additionally, we contacted several list-serves for teachers including the California Science Teachers Association (CSTA), the Greater Los Angeles Science Teacher Association (GLASTA), and our regional chapter of the National Association of Biology Teachers (NABT).

- We are in the process of sending out our first round of acceptance letters, although we expect more applications over the next couple weeks. We have approximately 23 applicants as of May 9th.

- This year we set up a pilot partnership with Pasadena Unified School District to provide professional development outreach to all of their high school biology teachers. Over the course of the 2005-2006 academic calendar we have had six full-day workshops. Once every other month, all 20 biology teachers attended a

workshop to prepare for the upcoming instructional period. We were able to provide them hands-on inquiry based labs that use plants as a model organism to explore the California Science Standards relevant to that instructional period. This series of workshops was well attended and well received. In addition to providing the community with a valuable service, this also allowed us to pilot units for use in the summer academy.

- We have initiated talks with Pacific Oaks College in an effort to offer teachers college credit for the summer academy. While this may not be in place for the 2006 Academy, we believe it will prove useful in future recruitment efforts. In addition, LAUSD will be offering 5 Salary point credits for LAUSD teachers that are accepted into the 2006 summer program.

- We have attended several Computable Plant weekly meetings to work on developing relevant programming in the summer academy and to initiate discussions on the development of a kiosk in the Huntington's Conservatory, which has a hands-on plant lab room geared toward a middle school audience, and would be an optimal location for an exhibit on plant development and modeling.

- We presented our summer program and evaluation findings at the Western Museum Association Meeting, "A Rose by Any other Name: Integrity, Mission, Authenticity" in Pasadena on September 29th, 2005. Panel discussion titled, "Make it Useful, Please! Successful Collaborations Among Teachers and Museums"

Computable Plant teachers' workshop: "The ABCs of Developmental Botany: Integrating Plants into the Classroom", July 11-15 and 28-29 2005.

Standards-based Modeling units in preparation for 2006:

Invasive plants (graduate student Elaine Wong, UCI math)

Expression domains (Eric Mjolsness)

Other education

1. Dana Mohamed, a senior at Harvey Mudd, did a summer project studying the three dimensional extensions of the Wuschel Activator Model.

Dissemination of the work

Web site maintained and updated: www.computableplant.org . (Shapiro, et al.)

Selected models: http://www.computableplant.org/#models

Deposited in model databases: CLV/Wus --> Sigmoid, Biomodels

Software: (http://www.computableplant.org/#software)
Cell tracking for SAM, bacterial colonies, zebrafish embryo, root (segtrack) [Gor et al 2005].
Cellerator spatial extensions (cellzilla, mpower)

Publications:

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

[Jönsson et al 2005] "Modeling the Organization of the WUSCHEL Expression Domain in the Shoot Apical Meristem", Henrik Jönsson, Marcus Heisler, G. Venugopala Reddy, Vikas Agrawal, Victoria Gor, Bruce E. Shapiro, Eric Mjolsness, Elliot M. Meyerowitz. Bioinformatics 21(Suppl. 1):i232-i240 June 2005.

[Fadeev et al 2006] "Analysis of a one-dimensional model for the regulation of the size of the renewable zone in biological tissue", S.I. Fadeev*, S.V. Nikolaev*, V.V. Kogay*, E. Mjolsness, N.A. Kolchanov. (In Russian.) Computational Technologies, http://www.ict.nsc.ru/mathpub/comp-tech/eng/, to appear 2006.

[Bhan and Mjolsness 2006] "Static and dynamic models of biological networks", Ashish Bhan and Eric Mjolsness, accepted for Complexity, 2006.

[Heisler et al. 2005] "Patterns of Auxin Transport and Gene Expression during Primordium Development Revealed by Live Imaging of the Arabidopsis Inflorescence Meristem", Heisler M.G., Ohno, C., Das, P., Sieber, P., Reddy, G.V., Long, J.A., and Meyerowitz, E.M. Curr. Biol. 15:1899-1911.

[Mjolsness 2006] "Stochastic Process Semantics for Dynamical Grammar Syntax: An Overview", Eric Mjolsness. On-line proceedings of the Ninth International Symposium on Artificial Intelligence and Mathematics, January 2006.

[Sadovsky et al 2005] Sadovsky A, Bacarian T, Campilho A, Heisler MG, Meyerowitz EM, Scheres B, Mjolsness E, Baldi PF. Statistical Biodynamics of Arabidopsis thaliana: 1-Dimensional Mathematical Models of the Growing Root. poster presentation at ICSB 2005.

Demidenko GV, Likhoshvai VA, Khropova Yu.E. On one class of systems of differential equations and on retarded systems, Siberian Mathematical Journal, 47(1):58-68.

Demidenko GV, Likhoshvai VA. On Differential Equations with Retarded Argument, Siberian Mathematical Journal , 46(3):417-430.

Gor V, Shapiro BE, Jönsson H, Heisler M, Reddy GV,Meyerowitz EM, Mjolsness E A Software Architecture for Developmental Modeling in Plants: The Computable Plant Project. In: Bioinformatics of Genome Regulation and Structure II,(Eds. N.Kolchanov, R. Hofestaedt, L. Milanesi) Springer, pp. 345-354.

Omelyanchuk N, Mironova V, Poplavsky A, Podkoldny N, Kolchanov N, Mjolsness E, Meyerowitz E AGNS-A Database on expression of Arabidopsis Genes. In: Bioinformatics of Genome Regulation and Structure II (Eds. N.Kolchanov, R. Hofestaedt, L. Milanesi) Springer.

Venugopala Reddy G, Meyerowitz EM. Stem-Cell Homeostasis Growth Dynamics can be Uncoupled in the Arabidopsis Shoot Apex. Science 310(5748):663-667.

Conference papers

"Modeling Transcriptional Regulation with Equilibrium Molecular Complex Composition", Eric Mjolsness, accepted May 2006 for Proceedings of Bioinformatics of Genome Regulation and Structure (BGRS) July 2006.

"AGNS (Arabidopsis GeneNet Supplementary Database) Release 3.0" Omelianchuk N.A.[1]*, Mironova V.V.[1], Poplavsky A.S., Pavlov K.S., Savinskaya S.A., Podkolodny N.L., Mjolsness E.D., Meyerowitz E.M., Kolchanov N.A. To appear in Proceedings of Bioinformatics of Genome Regulation and Structure (BGRS) July 2006.

"A Program Method for Inferring Relationships Between Phenotypic Abnormalities of Arabidopsis" Ponomaryov D., Omelianchuk N.[2], Mironova V., Kolchanov N., Mjolsness E., Meyerowitz E. To appear in Proceedings of Bioinformatics of Genome Regulation and Structure (BGRS) July 2006.

"Cellular-level modelling of plant tissue growth and morphogenesis", Nikolaev S.V., Fadeev S.I., Penenko A.V., Belavskaya V.V., Kogay V.V., Mjolsness E., Kolchanov N.A. To appear in Proceedings of Bioinformatics of Genome Regulation and Structure (BGRS) July 2006.

Posters

Sadovsky AV, Heisler MG, Meyerowitz EM, Campilho A, Mjolsness E, Baldi PF. Biostatistics of Arabidopsis thaliana: 1-dimensional Mathematical Models of the Growing Root. International Conference on Systems Biology (ICSB-2005), Boston, MA, USA, Oct. 19-24, 2005.

(2005) Shapiro BE, Agrawal V, Gor V, Heisler M, Jönsson H, Meyerowitz EM, Mjolsness E, Reddy GV, A Computational Modeling Framework for the Arabidopsis Shoot Apical Meristem. Plant Biology 2005, Annual Meeting of the American Society of Plant Biologists, Seattle, WA USA, 16-20 July 2005.

Talks at which NSF-FIBR results were featured:
2005:
Invited seminar Center for Theoretical Biological Physics (CTBP) in San Diego, a joint effort between research groups at UCSD, the Salk Institute, the Scripps Research Institute and the San Diego Supercomputer Center http://ctbp.ucsd.edu/seminars.html . May 20, 2005 (Mjolsness)
Iowa State University Symposium on Temporal and Spatial Dynamics of Gene Expression, June 2-5, 2005 (Heisler)
Department of Energy-British Petroleum meeting on Biofuels, Washington, DC, June 13 (Meyerowitz)
University of California, Riverside, June 30 (Meyerowitz)

American Society of Plant Biologists, July, Seattle (Shapiro)

International Congress of Botany, Vienna, Austria, July 21 (Meyerowitz and Mjolsness, session co-organizers and speakers)

32nd Annual Conference of the Plant Growth Regulation Society of America, Newport Beach, CA July 24-27, 2005 (Heisler)

Society for Developmental Biology Annual Meeting, San Francisco, July 30 (Meyerowitz and Reddy)

International Society for Developmental Biology Congress, Sydney, Australia, September 6 (Meyerowitz)

Wolfram Technology Conference, Urbana-Champaign Illinois October 6 2005 (Mjolsness).

University of Freiburg International Imaging Symposium November 4-5, 2005 (Heisler)

NSF Plant Science Cyberinfrastructure Workshop, NSF HQ, Washington DC October 17-18 2005 (Mjolsness).

Crop Science Society Annual Meeting, Salt Lake City, November 7 (Meyerowitz)

University of Nebraska, Lincoln distance education seminar series "Plant organization and crop simulation modeling: Integrating interdisciplinary perspectives", invited by Albert Weiss, P. Stephen Baenziger and D. Namuth. Narration-recorded slides online November 2005 (Mjolsness).

2006:

Phi Beta Kappa Lectures, College of Mary Washington, Virginia January 23-24 (Meyerowitz)

Phi Beta Kappa Lectures, Bucknell University, Lewisburg, Pennsylvania January 26-27 (Meyerowitz)

Caltech Biological Network Modeling Center, Biological Image Analysis workshop. February 2, 2006 (Mjolsness and Bacarian).

Salk Institute, February 17, 2006 (Mjolsness).

Phi Beta Kappa Lectures, Colorado State University, March 5-7 (Meyerowitz)

Phi Beta Kappa Lectures, Willamette College, March 8-9 (Meyerowitz)

Physics Research Conference, Caltech Department of Physics. March 9, 2006 (Mjolsness)

Physics and Astronomy Department Colloquium, California State University Los Angeles. April 30, 2006 (Mjolsness)