iPlant Grand Challenge Workshop in Computational Approaches to Plant Development: Computational Morphodynamics of Plants

Organizers

Primary Contact: Eric Mjolsness, University of California, Irvine, Institute for Genomics and Bioinformatics (IGB), and Departments of Computer Science and Mathematics
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Eric Mjolsness is an Associate Professor in the Department of Computer Science, with a joint appointment in Mathematics, and is program leader for systems biology in the Institute for Genomics and Bioinformatics at the University of California, Irvine. By means of the Computable Plant collaboration co-organized with Meyerowitz, he has initiated a wave of successful plant development modeling at the level of cells and tissues. He has developed numerous mathematical modeling methods for systems biology.

Elliot Meyerowitz, California Institute of Technology, Division of Biology
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Meyerowitz is an Arabidopsis developmental geneticist, with experience in plant genetics, genomics, and molecular biology whose lab is currently pioneering methods for live imaging and live image analysis of growing plants at the cellular and subcellular level. He has started, with others, three outreach programs - one an NIH-funded program connecting Caltech graduate students, postdocs, and faculty with national teacher-training efforts organized at the Exploratorium in San Francisco, and the other an NSF-FIBR and Arthur Vining Davis Foundation-funded summer teacher training program, and an American Society of Plant Biologists-funded school-term teacher training program.

Potential Participants:

The following people are interested in attending the proposed workshop.

Image Analysis: Edgar Spalding, Univ. Wisconsin, Botany & Biomedical Engineering, spalding@wisc.edu; B.S. Manjunath, UCSB, manj@ece.ucsb.edu; Robert Murphy, Carnegie Mellon University, <murphy@cmu.edu>; Andrew Bangham, Univ. East Anglia, A.Bangham@uea.ac.uk; Charless Fowlkes, U.C. Irvine, Computer Science, fowlkes@ics.uci.edu; Ronald Michaels, Phenotype Screening Corporation, Tennessee, ron@phenotypescreening.com; Marisa Otegui, Univ. Wisconsin, Botany, otegui@wisc.edu; Dan Szymanski, Purdue, dszyman@purdue.edu; Alan L. Yuille, UCLA, yuille@stat.ucla.edu

Biochemical/Developmental Models: Siobhan Brady, U.C. Davis, chevybra@duke.edu; Jianlin Cheng, Univ. Missouri, Computer Science, chengji@missouri.edu; Vijay S. Chickarmane vchickar@its.caltech.edu; Christophe Godin, INRIA Montpellier, christophe.godin@inria.fr; Henrik Jonsson, Lund University (Biological Physics) henrik@thep.lu.se; Eric Kramer, Simon's Rock College, Physics, ekramer@simons-rock.edu; Jingdong Liu, Monsanto, jingdong.liu@monsanto.com; Przemek Prusinkiewicz, Univ. Calgary, Computer Science, pwp@cpsc.ucalgary.ca; Kristen Shepard, Barnard, kshepard@barnard.edu; Patrick Shipman, Colorado State, shipman@math.umd.edu; V. Sundaresan, UC Davis, sundar@ucdavis.edu; David Jackson, Cold Spring Harbor Labs, jacksond@cshl.edu; Andrew Bangham, Univ. East Anglia, A.Bangham@uea.ac.uk;

Mechanical Models: Marcus Heisler, Caltech, mheisler@caltech.edu; Alan Newell, Univ. Arizona, anewell@math.arizona.edu; Bruce Shapiro, Caltech, bshapiro@caltech.edu; Patrick Shipman, Colorado State, shipman@math.umd.edu;

Education: Martha Kirouac mkirouac@huntington.org

Summary of the Proposed Workshop:

A grand challenge facing the plant biology community is to understand how plants develop and grow - that is, how genomic and environmental information combine to produce a three-dimensional and highly dynamic plant consisting of intercommunicating cells and tissues. The proposed workshop will develop plans to create a novel computational approach that will bridge existing gaps between biochemical, cellular, and organismal levels of understanding. Central to the approach is the notion that much of the necessary bridging information can be computationally extracted from images and used to inform computational models that reveal the causal relationships between biochemical and genetic activities of cells and cellular activities in development on one hand, and between cellular activities in development and the structure and function of tissues at the organismal level, on the other.

There are three specific areas of need: acquisition and analysis of images of cells, tissues, and organ systems actively undergoing morphogenesis; computational modeling, to represent and test specific hypotheses for the mechanisms by which cellular activities and cell-cell communication and coordinated growth result in defined and dynamic cellular patterns; and mechanical modeling, to provide computer representations of plant tissues in which each cell, its mechanical influence on its tissue, and the results of mechanical force on its enlargement and division combine to provide a realistic and testable substrate for developmental models. The grand challenge will be greatly served by a cyberinfrastructure that facilitates the flow of information about growth and development from image acquisition devices to interoperable databases to modeling functions.

The 1½ day workshop is expected to involve approximately 30 participants. (A followup day of strictly optional technical discussions may also be scheduled.) The opportunities and present barriers to progress in the three different areas of need will be assessed. Participants will create a strategic plan for developing cyberinfrastructure required for image acquisition and analysis at the subcellular, cellular and organ levels; computational modeling of pattern formation in developing plant tissues; and mechanical models of plant tissues using finite element models at the cellular and tissue level. An expected outcome is that close and well-defined links between the iPlant central organization and the individual laboratories that have already developed tools and/or data sets will emerge as a key element of a feasible Grand Challenge project. Workshop time will also be dedicated to exploring educational opportunities, with emphasis on plant and computation lessons for middle and high school biology classes, and on the possibilities for the products of the project to influence undergraduate research and pedagogy.

Biographical Sketches:
Dr. Eric Mjolsness

(a) Professional Preparation

School	Major	Degree/Year
Washington University	Physics and Mathematics	A.B/1980
California Institute of Technology	Physics and Computer Science	Ph.D/1986

(b) Appointments

2002 – present	Associate Professor, Dept of Information & Computer Science, UC Irvine
2000 – present	Visiting Faculty in Biology, Caltech
2000 – present	Principal, Jet Propulsion Laboratory, Caltech
1998 - 2000	Computer Scientist – Principal/Senior, Jet Propulsion Laboratory, Caltech
1995 - 1998	Research Scientist, Department of Computer Science and Engineering, University of California, San Diego
1994 - 1998	Faculty member of the Institute for Neural Computation, UCSD
1990 - 1994	Associate Professor, Department of Computer Science, Yale University, New Haven
1985 - 1990	Assistant Professor, Yale University, New Haven
1980 - 1985	Graduate Research Assistant and Teaching Assistant, Caltech

Honors and Awards

Action Editor, Neural Computation (1995 to present), Board Member, Neural Information Processing Systems Foundation (1995 to 2000), NASA Summer Faculty Fellowship in Aeronautics and Space Research, at the Jet Propulsion Laboratory (1996), Senior Member of Sigma Xi (May 1999), Assoc. Editor, IEEE Transactions on Neural Networks, (1991-92; 1998)

(c) 5 Significant Publications

1. "Stochastic Process Semantics for Dynamical Grammars", Eric Mjolsness and Guy Yosiphon. Annals of Mathematics and Artificial Intelligence, 47(3-4) January 2007.
2. "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.
3. "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.
4. "Cellerator: extending a computer algebra system to include biochemical arrows for signal transduction simulations." Bruce E. Shapiro, Andre Levchenko, Elliot M. Meyerowitz, Barbara J. Wold and Eric D. Mjolsness. Bioinformatics, 19(5):677-678, 2003.
5. "Tracking Cell Signals in Fluorescent Images", Victoria Gor, Tigran Bacarian, Michael Elowitz, Eric Mjolsness. Computer Vision Methods for Bioinformatics (CVMB) workshop at Computer Vision and Pattern Recognition (CVPR). June 2005.

5 Other Significant Publications:

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

7. “Sigmoid: Towards an Intelligent, Scalable, Software Infrastructure for Pathway Bioinformatics and Systems Biology”, Jianlin Cheng, Lucas Scharenbroich, Pierre Baldi, Eric Mjolsness, IEEE Intelligent Systems, May/June 2005.

8. “A Mathematical Model for the Branched Chain Amino Acid Biosynthetic Pathways of Escherichia coli K12”, Chin-Ran Yang, Bruce E. Shapiro, She-pin Hung, Eric D. Mjolsness, and G. Wesley Hatfield, Journal of Biological Chemistry, Mar 25; 280(12):11224-32 2005.

9. “Visual Grammars and Their Neural Nets”, Eric Mjolsness, Advances in Neural Information Processing Systems 4, editors Moody, Hanson and Lippmann, pp. 428-435, Morgan-Kaufman 1992.

10. “A Connectionist Model of Development", Eric Mjolsness, David H. Sharp, and John Reinitz, *Journal of Theoretical Biology,* vol 152 no 4, pp 429-454 , 1991.

(d) Synergistic Activities

International Advisory Board, Center for Plant Integrative Biology, Nottingham UK. Computable Plant project outreach program to high school science teachers (PI, supervisor of grad student curriculum developer, lecturer). ICSB 2006 (Yokohama) tutorial on mathematical methods for systems biology (to occur October 2006). Conference co-organizer, ICSB 2007 in Southern California under the auspices of UC Irvine and the California Institute of Technology. Cellerator cell simulation research tool. Sigmoid pathway modeling database research tool.

(e) Collaborators and Co-Editors.

Anelia Angelova (NASA Jet Propulsion Laboratory, Caltech), Vikas Agrawal, Lee Bardwell (UCI, Pierre Baldi (UCI), Ashish Bhan (UCI), B. Bornstein (JPL), Ann Calof (UCI), Jianlin Cheng (UCI), G. Wesley Hatfield (UCI), Chris Hart (Yale), Andrew Howard (JPL), Andre Levchenko (Johns Hopkins), S.I. Fadeev (Institute for Cytology and Genetics, Novosibirsk), James Folsom (Huntington Botanical Gardens), Victoria Gor (JPL), Marcus Heisler (California Institute of Technology), She-pin Hung (UCI), Henrik Jonsson (Lund University), Brandon King (Caltech), V.V. Kogay (ICG Novosibirsk), Nikolay Kolchanov (ICG, Novosibirsk), Arthur Lander (UCI), Vitali Likohshvai (ICG, Novosibirsk), Larry Matthies (JPL), Elliot Meyerowitz (Caltech), Tarek S. Najdi (UCI), Nadezhda Omelyanchuk (ICG Novosibisk), Nikolay Podkoldny(ICG, Novosibirsk), Bruce Shapiro (JPL), S.V. Nikolaev (ICG, Novosibirsk), G. Venugopala Reddy (UC Riverside), Sharenbroich(UCI), Barbara Wold (Caltech), Benyang Tang (JPL), Diane Trout (Caltech), Michael Turmon (JPL), Chin-Ran Yang (U. Texas)

Graduate Advisor: John Hopfield, PhD Supervisor (Princeton).

Phd Thesis Advisees:

Steven Gold (Ph.D., Yale University, 1996), Chien-Ping Lu (Ph.D., Yale University, 1996), Dimitris Tsioutsias (Ph.D., Yale University, 1997), Georgios Marnellos (Ph.D., Yale University, 1997), Todd Johnson (current UCI Ph.D. Student, UC Irvine), David Orendorff (current UCI Ph.D. Student, UC Irvine), Yuanfeng Wang (current UCI Ph.D. Student, UC Irvine), Guy Yoshiphon (current UCI Ph.D. Student, UC Irvine), Li Zhang (current UCI Ph.D. Student, UC Irvine)

Postdoctoral Scholars:

Tigran Bacarian (Sep 04-present), Ashish Bhan (Jul 04-Jul 06), Alex Sadovsky (Sep 04-Jul 06), Pawel Krupinski (Jun 06-Oct 07), Michael Duff (at UCI 2005-2006, now at U. Mass)

BIOGRAPHICAL SKETCH

Elliot M. Meyerowitz
George W. Beadle Professor of Biology and Chair, Division of Biology
Division of Biology 156-29, California Institute of Technology, Pasadena, California, USA

(a) Professional Preparation:

1973 A.B. in Biology *summa cum laude,* Columbia University, New York, New York
1975 M. Phil. in Biology, Yale University, New Haven, Connecticut
1977 Ph.D. in Biology, Yale University (with D.R. Kankel)
1977-9 Postdoctoral Fellow, Stanford University School of Medicine (with D.R. Hogness)

(b) Appointments:

2002- G.W. Beadle Professor of Biology, California Institute of Technology
2000- Chair, Division of Biology, California Institute of Technology
1989-2002 Professor of Biology, California Institute of Technology
1985-1989 Associate Professor of Biology, California Institute of Technology
1980-1985 Assistant Professor of Biology, California Institute of Technology

(c i) 5 Publications Most Closely Related to the Proposed Project:

Ito, T., Wellmer, F., Yu, H., Das, P., Ito, N., Alves-Ferreira, M., Riechmann, J.L. and Meyerowitz, E.M. (2004) The homeotic protein *AGAMOUS* controls microsporogenesis by regulation of *SPOROCYTELESS*. Nature **430**, 356-360.

Reddy, G.V. and Meyerowitz, E.M. (2005) Stem cell homeostasis and growth dynamics can be uncoupled in the *Arabidopsis* shoot apex. Science **310**, 663-667.

Jönsson, H., Heisler, M., Shapiro, B.E., Meyerowitz, E.M. and Mjolsness, E. (2006) An auxin-driven polarized transport model for phyllotaxis. Proc. Natl. Acad. Sci. USA **103**, 1633-1638.

Long, J.A., Ohno, C., Smith, Z.R. and Meyerowitz, E.M. (2006) *TOPLESS* regulates apical embryonic fate in Arabidopsis. Science **312**, 1520-1523.

Gordon, S.P., Heisler, M.G., Reddy, G.V., Ohno, C., Das, P. and Meyerowitz, E. M. (2007) Pattern formation during *de novo* assembly of the *Arabidopsis* shoot meristem. Development **134**, 3539-3548.

(c ii) 5 Other Significant Publications:

Shapiro, B.E., Levchenko, A., Meyerowitz, E.M. Wold, B.J., and Mjolsness, E.D. (2003) Cellerator: Extending a computer algebra system to include biochemical arrows for signal transduction. Bioinformatics **19**, 677-678.

Yu, H., Ito, T., Wellmer, F. and Meyerowitz, E.M. (2004) Repression of AGAMOUS-LIKE 24 is a crucial step in promoting flower development. Nature Genetics **36**, 157-161.

Heisler, M.G., Ohno, C., Das, P., Sieber, P., Reddy, G.V., Long, J.A. and Meyerowitz, E.M. (2005) Patterns of auxin transport and gene expression during primordium development revealed by live imaging of the *Arabidopsis* inflorescence meristem. Curr. Biol. **15**, 1899-1911.

Wellmer, F., Alves-Ferreira, M., Dubois, A., Riechmann, J.L. and Meyerowitz, E.M. (2006) Genome-Wide Analysis of Gene Expression during Early *Arabidopsis* Flower Development. PLoS Genetics **7**, 1012-1024.

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

(d) Synergistic Activities:

1. Web Resource: The Arabidopsis Book, coedited with Chris Somerville, a large-scale compendium of Arabidopsis review articles sponsored by the American Society of Plant Biologists and available free of charge at http://www.bioone.org/bioone/?request=get-toc&issn=1543-8120
2. Selected Concurrent Professional Positions:
   President, International Society for Plant Molecular Biology (1995-1997)
   President, Genetics Society of America (1999)
   Head, Plant Biology Faculty, Faculty of 1000 (2000 -)
   President, Society for Developmental Biology (2005-6)

3. <u>Selected Recent Honors:</u>
   1995 Member, U.S. National Academy of Sciences
   1997 International Prize for Biology (Japan)
   1999 Richard Lounsbery Award, National Academy of Sciences
   2002 Foreign Associate, Académie des Sciences, France
   2004 Foreign Member, Royal Society, U.K.
   2005 Ross G. Harrison Prize, International Society of Developmental Biologists
   2006 Balzan Prize (shared with Christopher Somerville)
   2007 Docteur *Honoris Causa*, École Normale Supérieure, Lyon, France
4. <u>Current Editorial Boards:</u> Cell (1991-); Current Biology (1993-); Trends in Genetics (1993-); Development (1994-); BioEssays (1996-); Curr. Opin. Plant Biol. (1997-); Genome Biology (1999-); J. Biology (2001 -); Phil. Trans. Roy. Soc. B (2006 -)

(e) List of Collaborators (Other than those in Lists of Students and Postdoctoral Fellows), Last 48 Months

Alvarez-Buylla, E., U. Mexico
Barton, M. Kathryn, Carnegie Institution
Bowman, J., Monash Uni., Australia
Erhardt, David, Stanford Univ.
Fletcher, Jennifer, PGEC and UC Berkeley
Ferreira, Marcio Alves, Fed. Univ. Rio, Brazil
Friml, Jiri, University of Ghent
Gasser, C., U.C. Davis
Glimelius, Kristina, Swedish U Ag. Sci.
Gor, V., Jet Propulsion Lab
Jönsson, H. U. Lund, Sweden
Kolchanov, N., Russ. Acad. Sci, Novosibersk
Kumar, Prakash, Natl. Univ. Singapore
Levchenko, A., Johns Hopkins U.
Mjolsness, E., U.C, Irvine
Omelianchuk, N., Russ. Acad. Sci
Peng, Jinrong, IMCB, Singapore
Ponomaryov, D., Russ. Acad. Sci,
Sakai, H., Dupont and Co.
Shapiro, B., Jet Propulsion Lab
Somerville, C.R., U.C. Berkeley
Wagner, Doris, U. Pennsylvania
Weigel, Detlef, MPI Tübingen

Graduate and Postdoc Advisors: Douglas R. Kankel, Yale; David S. Hogness, Stanford
Students and Postdocs Trained in the Past 5 Years:

<u>Graduate Students, Past 5 Years:</u>	<u>Year Ph.D. Granted</u>	<u>Present Location</u>
Catherine Baker	2003	Stanford University

<u>Present Graduate Students:</u> Sean Gordon

<u>Former Postdocs, Past 5 Years</u>	<u>Years in Lab</u>	<u>Present Faculty Position</u>
Long, Jeffrey	1999 – 2003	Salk Institute, La Jolla, California
Yu, Hao	2002 – 2003	National University of Singapore
Dubois, Annick	2003 – 2005	INRA, Lyons, France
Kubat, Nicole	2004 – 2005	Univ. Paris, France
Agrawal, Vikas	2004 – 2005	Intel Corp.
Das, Pradeep	2002 – 2005	INRA, Lyons, France
Ito, Toshiro	1997 – 2005	Temasek Life Sci. Lab, Singapore
Sieber, Patrick	2003 – 2006	University of Zürich
Reddy, G. Venugopala	1999 – 2006	U.C. Riverside
Wellmer, Frank	1999 – 2006	Trinity College, Dublin, Eire
Haswell, Elizabeth	2000 – 2007	Washington Univ., St. Louis

<u>Present Postdocs</u>: Vijay Chickarmane, Yuling Jiao, Wuxing Li, Carolyn Ohno, Xiang Qu, Marcus Heisler, Zack Nimchuk, Adrienne Roeder, Kaoru Sugimoto, Xiaolan Zhang
<u>Total Graduate Students Advised</u>: 15 (14 former, 1 present)
<u>Total Postdoctoral Fellows Sponsored</u>: 59 (49 former, 10 present)

Grand Challenge Workshop Description

We will convene a workshop directed to the grand challenge of *discovering how plant morphology arises from and feeds back on cellular, biochemical and informational processes*. This fundamental question of developmental biology when applied to plants necessarily includes the novel aspect of information flowing not only from cellular to morphological levels via developmental and growth processes, but also from morphology to cellular and biochemical process through cytoskeletal and hormonal responses to mechanical force, which conditions differential cell growth, cellular anisotropy via cellulose deposition, and cell division planes. We believe that cyberinfrastructure deficiencies presently impede the image analysis and modeling activities required for understanding in a unified way the two-way flow of developmentally relevant information between the biochemical, cellular, morphological, and organismal levels of organization. The workshop will result in a plan to address the key deficiencies.

Proposed Workshop

The workshop will address three interrelated cyberinfrastructure areas: image analysis, modeling of gene and cell-cell communication networks, and modeling of the mechanical properties of plant cells and tissues; and also how progress in these areas can contribute to outreach and educational opportunity. New cyberinfrastructure is required for image analysis, from the point of image acquisition through the extraction of machine-usable information. The principle has been proved – useful information can be automatically extracted from images of roots, shoots, leaves, flowers, and embryos, sometimes even as they grow and with high spatiotemporal resolution, resulting in high resolution on growth patterns and growth rates. It has also been demonstrated that biochemical/developmental modeling employing systems of differential or stochastic equations can describe cellular and tissue activities such as enzymatic pathways, gene regulatory networks, and networks of cell-cell communication that define growth and differentiation. Realities of plant development further require modeling that accounts for cellular level mechanics reflective of plant-unique turgor pressures and cell wall properties, and large-scale tissue movements (such as buckling) that feed back into cellular activities. What is needed is a robust cyberinfrastructure that supports and links each of these areas of activity.

The workshop will bring together biologists and computational scientists with experience, interests, and/or data related to the three main scientific areas, each of which will be the subject of a specific session. Sessions will consist of plenary level lectures followed by parallel breakout groups. Discussions will be focused on identifying the most critical cyberinfrastructure deficiencies impeding specific avenues of research. Each session will have the goal of outlining the type of data to be used and the eventual computational product to be produced. Each group will also be asked to supply names of others who should be informed and invited to participate.

Each session will feature teams of participants with different expertise and experience. The image analysis discussions will address whole plant imaging (led by Edgar Spalding), analysis of confocal microscope images, and image databases (to be covered by Robert Murphy and B.S. Manjunath) . Computational modeling of development at the cellular level will be led by Eric Mjolsness, and will include discussions of models of pattern formation in the shoot apical meristem, root apical meristem, leaf, and flower. Mechanical models will be led by Marcus Heisler, and will include discussions of finite element models (FEM) of plant tissues at the cellular level, and mechanical models of plant tissues at the organismal level. A session on outreach and educational opportunities and strategies will be led by Martha Kirouac.

Datasets:

The datasets that currently exist, or that are expected in the next couple of years include large sets of live imaging data of a variety of reporter genes and proteins in shoot apical meristems (see Heisler et al., 2005; Gordon et al., 2007 for examples); live imaging data at the cellular level of root growth in a variety of conditions (e.g. Grieneisen et al., 2007) and http://www.plantsci.cam.ac.uk/Haseloff/); thousands of time-lapse image series of seedling roots and hypocotyls responding to gravity and light (see Miller et al., 2007 and http://phytomorph.wisc.edu/phytomorph.htm); large number of electron tomographs with ultrahigh subcellular resolution obtained by Marisa Otegui. In addition to these Arabidopsis data sets, we expect to use live images of growth of the alga Coleochaete (http://www.plantsci.cam.ac.uk/Haseloff/). Confocal microscope imagery of the shoot apex will be made available to the iPlant project from at least the laboratories of Jan Traas (Lyon), Chris Kuhlemeier (Bern), and Elliot Meyerowitz. Sepal imagery will be provided by Adrienne Roeder, currently in Meyerowitz's laboratory. Furthermore, a major consortium of UK laboratories is developing live imaging data for root development, and they have agreed to the eventual release of all imagery. This project is the CPIB (Centre for Plant Integrative Biology) at the University of Nottingham - http://www.cpib.info/. Each of these is sufficient for the development of the image analysis infrastructure. For computational modeling, the existing datasets are relevant to specific problems. Phyllotaxis is represented by the literature on auxin transport and response of shoot apical meristem cells to auxin, as summarized in Heisler et al., 2005. Root cell type specification has its own literature and data sets, on gene expression in specific cell types it is (Birnbaum et al., 2003), for auxin gradient control (Grieneisen et al. 2007) and the references therein, and for responses to gravity (http://phytomorph.wisc.edu/phytomorph.htm). Input information for development of modeling infrastructure also includes early attempts at modeling environments, for example Cellerator (Shapiro et al., 2003).

Current State of Computational Thinking in the Field

Computational thinking is beginning to seep into the field of plant development, although the tools are far too difficult to use to engage most of the plant biologists whose research could benefit. Substantial hardware resources are virtually unused, though there is clearly a need for them in both large-scale tissue simulation and in automated parameter optimization/model selection computations. The Workshop will discuss the means by which these existing tools can suited to use by plant scientists.

Leading computational technologies in the field of plant developmental modeling include those generated by the Computable Plant project (Mjolsness, Meyerowitz, and collaborators) outlined below, as well as L-Systems simulation and virtual laboratory software as long developed by P. Prusinkiewicz and collaborators, C. Godin's OpenAlea software platform for virtual plants, and Cellular Potts Models (Grieneisen et al. 2007), among others. The Computable Plant project approaches include the simple Cellzilla extension of Cellerator to generate fixed-template tissue models from reaction network arrows, weak spring models, the Organism/FEM C++ program for simulating weak spring and FEM mechanics combined with ODE regulatory models, and the fundamental Dynamical Grammars (DG) framework for variable-structure systems such as arise in development, along with its "Plenum" prototype implementation. DG's are fundamental because they combine time-evolution operators in the mathematically simplest way: addition. A potentially related project is the Sigmoid web-accessible GUI and model database wrapped around Cellerator, which currently however is limited to fixed-structure models.

Other developmental modeling approaches used in biological development generally include noncellular reaction-diffusion partial differential equations, membrane energy functions accounting for stretch and adhesion, P-systems and "membrane computing", κ-calculus (Danos and Laveve 2004), level set methods, the MGS simulator with dynamical topology by Giavitto, dynamic topological cell complexes (Brisson 1993), polygonal vertex models (Hufnagel et al. 2007), and spatial stochastic modeling using the R-leap algorithm (Auger et al. 2006). Mathematical objects of interest that may be captured in such models include emergent symmetries, instabilities, and patterns of deformation.

A botanically universal modeling environment must simulate heterogeneous dynamics, which is possible using shallow, black-box style integration of disparate solvers (for example via second-order operator splitting methods) or much more efficiently by less general but deeper integration of numerical methods. Examples of the latter include the combination of stochastic discrete events and continuously operating ODE's in Plenum and (less accurately for the ODE's) L-system software, and many other solution algorithms (some yet to be invented) that require full access to the solution algorithm source code. Model exchange formats such as SBML with suitable future extensions, or CellML+FieldML, may be able to usefully represent developmental models.

Thus, there is a wealth of useful starting points for developmental modeling cyberinfrastructure. But taken individually, none of these methods is fully scalable to the Cyberinfrastructure challenge. Problems of inadequate use of standard mathematics, such as for stochastic processes and their integration with accurate ODE solvers in continuous time, are widespread. It is by a synthesis of the best that the developmental modeling community has to offer, that a useful cyberinfrastructure will be delivered.

Barriers that currently prevent effective utilization of available data:

Image analysis

Barrier: Absence of image analysis tools sufficient for segmentation of plant images at the cellular and subcellular level, and absence of ability to correspond features in time-series images in cellular and whole-plant images. The variety of image formats, not necessarily compatible with all tools, is a problem being addressed by the Open Microscopy Environment (http://www.openmicroscopy.org/). The need for distributed or high throughput computing and workflow tools to manage the analysis of many images generated by automated acquisition platforms is unmet.

Finite element mechanical modeling

Barrier: The lack of any FEM elastic dynamics code that can incorporate continual cell growth and frequent cell division. Cell division requires frequent remeshing of the dividing cells and often their neighbors. The usual assumption is for infrequent global remeshing, which is inadequate. Very strong 3D data structures and algorithms will be required to support these operations especially on large, organism-sized simulations that may have to be parallelized even within a single run. Multiple commercial engineering codes have been tried (at Caltech CACR and at CPIB) and found lacking in these areas.

Barrier: The lack of available-source and open-source FEM code that does the foregoing. Source availability is essential for deep integration, beyond the low-order accuracy available through operator splitting (via interleaved execution), of simulation engines for mechanical processes, (possibly stochastic) biochemical processes, and growth processes. This combination is virtually the definition of Computational Morphodynamics, and the key to plant developmental modeling. Open-source code is a key facilitating factor for continued progress in these areas.

Developmental modeling

Barrier: The lack of a mathematically and physically well-founded, computationally well-engineered plant development modeling system.

Barrier: The lack of parallel computing in either single-run simulations of large 3D tissue models, or even in parameter searches.

Barrier: The lack of a standardized systems biology model exchange format (such as SBML) that can be used to model large, developing tissues. SBML has a disastrous built-in deficiency from this point of view: the lack of array and dynamical array constructs. This implies that as a modeler increases the number of cells in a tissue model, the size of the SBML file must increase proportionately, and that an arbitrary-sized growing tissue cannot be represented at all. This is a barrier to developmental modeling to at least the extent that a standardized model exchange language is useful for coordinating or combining many modeling efforts. We have made a formal SBML proposal for dynamical arrays (Shapiro et al. 2004), but no-one admits to having the resources to pursue it.

Barriers that can be addressed with additional datasets:

These can only be identified after the development of the cyberinfrastructure using the existing datasets described above - once knowledge has been generated from the existing data, it should become clear if there is a need for any different amount of type of data to gain full understanding of plant growth and development.

Plan for diverse participation:

Our plan is to have broad geographical representation, including international participation; and attendance of scientists from different types of institution of higher education, from large state universities (e.g. Mjolsness, University of California; Spalding, University of Wisconsin), large private universities (e.g. Szymanski, Purdue and Murphy, Carnegie Mellon), small private research universities (e.g. Meyerowitz, Caltech), small liberal arts colleges (e.g. Kramer, Simon's Rock College) and in addition research institutes (e.g. Jackson, Cold Spring Harbor labs); and industry, both large (e.g. Liu, Monsanto) and small (e.g. Michaels, Phenotype Screening Inc.). We will also have representatives of private educational institutions that are not universities, e.g. Kirouac, Huntington Botanical Gardens). As the list of potential participants makes clear, gender diversity is also accounted for, including representation from women's colleges (e.g. Shepard, Barnard).

Assessment of Education, Outreach and Training opportunities that derive from potential GC questions in this field.

There is an opportunity to engage students in the life sciences through dissemination of web-accessible and visually appealing interactive simulations of plant development. Once available, software to measure plant growth or root curvature could form the basis for new student laboratories at the high school or college level. The methods developed could also be part of teacher education programs (such as the Grounding in Botany program at the Huntington Botanical Garden) in which the teachers develop new lesson plans and high school laboratories that would use computational approaches equally with standard laboratory procedures. Thus, new and existing outreach efforts could be greatly bolstered by appropriate use of such cyberinfrastructure.

Collateral activities

We will submit a proposal to the Kavli Institute of Theoretical Physics, UC Santa Barbara, as we have been invited to convene the best physics-based plant developmental modeling minds and directions as a followup to the Spring 2008 Morphogenesis workshop at this prominent theoretical physics institute.

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