Design a Better Leaf

Organizers:

Steve Long: Professor. Institute of Genomic Biology, University of Illinois at Urbana Champaign, 217 333 2487 (phone), email: slong@uiuc.edu; leaf and canopy photosynthesis, global change, energy crops.

Xinguang Zhu: Faculty Fellow, National Center for Supercomputing Applications at Urbana Champaign, Department of Plant Biology, Institute of Genomic Biology, University of Illinois at Urbana Champaign; 217 244 6317 (phone); email: zhu3@uiuc.edu; photosynthesis modeling, plant primary metabolism modeling, systems analysis.

Keith Mott: Professor, Department of Biology, Utah State University, Phone: (435) 797-3563 Fax: (435) 797-1575. kmott@biology.usu.edu, control of stomata conductance.

Oliver Fiehn: Associate Professor, Metabolomics Laboratory, Genome Center, UC Davis. (530) 754 8258 ofiehn@ucdavis.edu

Eric DeSturler: Associate Professor, Department of Mathematics, Virginia Tech. (217) 721-7422 sturler@vt.edu

Proposed Participants

David Kramer, Plant Biology, WSU
Wim Vermaas, School of Life Sciences, ASU
John Tyson, Computational Cell Biology, VT
Ferran Garcia-Pichel, School of Life Sciences, ASU
David Peak, Physics, USU
Jorg Schwender, Biology, Brookhaven National Lab
Alistair Rogers, Environmental Science, Brookhaven National Lab.
Sue Rhee, Plant Biology, Carnegie Institution, Stanford
Mark Stitt, Max-Planck Institute of Molecular Plant Physiology, Golm
Susanne von Caemmerer, Australian National University, Canberra
Irv Forseth, University of Maryland, College Park (Modeling of leaf microclimates)
Andreas Dress, Mathematics, PICB, Max Planck Institute/Chinese Academy of Sciences
John Evans: RSBS. Australian National University, Canberra.
Christine Foyer: Molecular agriculture, Newcastle University
Wolfram Weckwerth: Metabolomics. Max Planck Institute of Molecular Plant Physiology, Golm.
Yair Shachar-Hill: Plant Biology, Michigan State University
Bard Ermentrout: Mathematics, University of Pittsburgh
Oliver Ebenhöh: Computational biology. Max Planck Institute of Molecular Plant Physiology
Owen Atkin: RSBS, Australian National University, Canberra.
Tom Buckley: Biology, University of New South Wales
Petro Mendes, Systems Biology, Virginia Tech
James Myers, Database and algorithm integration, National Center for Supercomputing Applications.

Summary

Society faces the grand challenge of providing enough food, feed and fuel for the growing population, while at the same time preserving our fragile ecosystems in a changing climate. Increasing the productivity of plants and crops is the ideal solution, since this would maximize use of existing agricultural land and minimize or avoid conflicts of food vs. feed vs. fuel. Both theoretical and experimental evidence show, despite early doubts around sink limitation, which increase in photosynthetic efficiency does increase yield. Although conventional plant breeding has failed to select for increased photosynthetic efficiency, transgenic over-expression of a limiting Calvin cycle enzyme has been shown repeatedly and independently to result in a substantial increase in photosynthetic rate and yield. Elevation of CO_2 in the field, causing a direct increase in leaf photosynthesis, has similarly increased grain yield. Selecting for decreased dark respiration in herbage grasses has also resulted in increased yield. Therefore increasing photosynthesis or/and decreasing respiration provides a route to solve the challenge of increasing crop and plant productivity at a time when the routes of the Green Revolution, increased light interception and harvest index have become exhausted. But, how can we engineer higher photosynthesis and lower respiration?

This question is clearly challenging. First, photosynthesis and respiration involve over 200 proteins, coded both in the organelles and nucleus, and many coded for by gene families in turn influenced by multiple transcription factors. Second, photosynthesis and respiration interact with almost all other aspects of metabolism in the mesophyll cells, in particular nitrogen metabolism. Third, water loss through the stomata is tightly linked and clearly integrated at the leaf level with water loss through stomata. With all the complexities of photosynthesis, respiration and related metabolism, how can we identify the traits for the ideal leaf? We propose to develop an *in silico* leaf (i-Leaf), a detailed description not only of the biophysical, biochemical reactions involved in the plant central metabolism, but also the control of stomata, leaf mass and energy balance, and spatial distribution of resources between cells of the leaf. This will be interconnected with the underlying patterns of gene and protein expression. In a collaboration between math, computer and plant scientists we have shown that a complete and quantitatively realistic dynamic simulation of photosynthesis can be achieved, and used with a genetic algorithm to guide improved photosynthetic efficiency, the next challenge is to incorporate this into the other primary metabolism, stochastic properties, and environmental physiology.

The key to the success of this proposed research is close collaboration among the plant biologists, mathematicians and computer scientists. The organizers have already collaborated with one or more of the invitees on computational biology projects; this workshop will build on that record. The workshop will include about 25 participants over three days. It will start with speaker presentations from experts in our group and from iPlant, with generous discussion time and completion of each session by a rapporteur relating the session to our objectives (below). It will conclude with breakout discussions, focused around realizing the different parts of the proposed GC. The objectives are:

1) An understanding of what is, and what is not, achievable within the time-scale of i-Plant.
2) A framework for developing an integrated GC proposal.
3) Definition of the databases, visualizations and computational math needed to achieve 2.
4) Definition of how this i-Plant GC proposal can complement and integrate with parallel work being conducted by the MPI, CAS Institute for Computational Biology, ANU and any other major activities outside the USA.
5) Plan a paper for publication in a leading journal (Plant, Cell & Environment is proposed) explaining the opportunity for "designing a better leaf", to be completed with 90 days of the workshop, which will form the introduction and blueprint for a GC proposal. (Proposed title: "Toward the *in silico* leaf – A tool for improving productive efficiency, environmental relations, education and outreach."

BIOGRAPHICAL SKETCH STEPHEN PATRICK LONG

(i) Professional Preparation

UndergraduateInstitution(s)	**Major Degree & Year**
University of Reading, UK.	Agricultural Botany, B.Sc. (Honors, 1st Class, University Prize), 1972
Graduate Institution(s)	**Major Degree & Year**
University of Leeds, UK.	Environmental Physiology, Ph.D. (University Scholarship), 1976
University of Lancaster, UK	Environemntal Sciences, D.Sc. (Honoris Causa), 2007.

(ii) Appointments

Deputy Director, UCB-UIUC-BP Energy Biosciences Institute (07-present)
Faculty Fellow, National Center for Supercomputer Applications (NCSA)
Robert Emerson Professor, Department of Plant Biology, University of Illinois, Champaign-Urbana. 99-present. Also: Faculty Fellow, National Center for Supercomputer Applications (01-02);

Full Professor, Department of Biological Sciences, University of Essex, UK. 90-98 (also Director of Photosynthesis Research 93-96; Director of Biology Undergraduate Schemes96-98)
Reader, Department of Biological Sciences, University of Essex 87-89
Lecturer/Senior Lecturer (tenured) = Assoc. Prof., Dept. Biol. Sci., University of Essex, 78-87
Lecturer (tenure track) = Asst. Prof. Department of Biological Sciences, University of Essex 75-78
Other appointments/fellowships
Chief and Founding Editor, Global Change Biology (94 – present)
Associate Editor, Photosynthesis Research (81-84; 00 – 03)
Associate Editor, Proceedings of the Royal Society B (07-)
Section Editor, Plant, Cell & Environment (90 – present)
Visiting Scientist, Brookhaven National Laboratory, NY 92-99
Visiting Professor, Chemistry Department, Arizona State University, Tempe. 93.
Gästprofessor, Institute of Plant Physiology, University of Vienna, Austria. 89-90
Smithsonian Institution Fellowship, SERC, Edgewater MD. 89
Assessor UNEP/UNDP/FAO-IAEA programs (83, 86, 89, 91, 95)

(iii) Publications (201 peer-reviewed journal publications)

(i) up to 5 publications most closely related to the proposed project;

1. Long S.P., Ainsworth E.A., Leakey A.D.B., Ort D.R., Nosberger J. & Schimel D. (2007) Crop models, CO2, and climate change - Response. *Science*, **315**, 460-460.
2. Long S.P., Ainsworth E.A., Leakey A.D.B., Nosberger J. & Ort D.R. (2006) Food for thought: Lower-than-expected crop yield stimulation with rising CO2 concentrations. *Science*, **312**, 1918-1921.
3. Long S.P., Zhu X.G., Naidu S.L. & Ort D.R. (2006) Can improvement in photosynthesis increase crop yields? *Plant Cell and Environment*, **29**, 315-330.
4. Zhu X.G., de Sturler E. & Long S.P. (2007) Optimizing the distribution of resources between enzymes of carbon metabolism can dramatically increase photosynthetic rate: A numerical simulation using an evolutionary algorithm. *Plant Physiology*, **145**, 513-526.
5. Zhu X.G., Govindjee, Baker N.R., deSturler E., Ort D.R. & Long S.P. (2005) Chlorophyll a fluorescence induction kinetics in leaves predicted from a model describing each discrete step of excitation energy and electron transfer associated with photosystem II. *Planta*, **223**, 114-133.

(ii) up to 5 other significant publications.

1. Humphries S.W. & Long S.P. (1995) Wimovac - a Software Package for Modeling the Dynamics of Plant Leaf and Canopy Photosynthesis. *Computer Applications in the Biosciences*, **11**, 361-371.
2. Martin M.J., Stirling C.M., Humphries S.W. & Long S.P. (2000) A process-based model to predict the effects of climatic change on leaf isoprene emission rates. *Ecological Modelling*, **131**, 161-174.
3. Ainsworth E.A. & Long S.P. (2005) What have we learned from 15 years of free-air CO_2 enrichment (FACE)? A meta-analytic review. *New Phytologist*, **165**, 351-371.
4. Bernacchi C.J., Singsaas E.L., Pimentel C., Portis A.R. & Long S.P. (2001) Improved temperature response functions for models of photosynthesis. *Plant Cell and Environment*, **24**, 253-259.
5. Zhu X.G., Ort D.R., Whitmarsh J. & Long S.P. (2004) The slow reversibility of photosystem II thermal energy dissipation on transfer from high to low light may cause large losses in carbon gain by crop canopies: a theoretical analysis. *Journal of Experimental Botany*, **55**, 1167-1175.

(iv) Synergistic Activities
1) Fellow of the American Association for the Advancement of Science (elected 2007); Listed among the 250 "Most Highly Cited" authors of Animal and Plant Biology by the authors of Science Citation Indix (http://isihighlycited.com/) and "Top 20 most cited Authors Overall" on the topic of Global Warming (www.esi-topics.com/index)
2) Teaching initiatives: McNair Minority Undergraduate Research Program Award for partner support (2005), Author to American Society of Plant Biology undergraduate text "Plants, Genes & Agriculture"; initiated and directed access program for mature student entry to Biology via the local community college at the University of Essex a model now broadly adapted in the UK; initiated a link and summer Undergraduate Research Experience for students from Central State University OH (an HBCU) at UIUC.
3) Public Awareness of Science: 2005-7 activities include Whitehouse Briefing to the President on developments in biofuel feedstocks; Congressional briefing on biofuels and global change; interviewed and research included in programs of Science-Discovery Channel, BBC One Planet, BBC The Material World, BBC World Service; CBC and ABC News, reporter articles about my groups work in The Times of London, Washington Post, New York Times, Nature News and Views, Science Now (Science Magazine); talks to a Rotary Club, an Exchange Club, 3 UIUC Extension Groups, and 1 Alumni group; 3 conducted tours of research in progress and field experiments at UIUC (23- 125 participants; ranging from Junior High to Agribusiness groups) .
4) Invited plenary lecturer (last 5 years): Woolhouse Lecture, Society of Experimental Biology (Marseilles, 08); Heilborn Lecturer, Northwestern Univ. (Chicago, 08); 2nd Porter Lecture, Imperial College (London, 07); 23rd Blackman Lecture (Oxford, UK 07); ComBio (Brisbane, Australia 06; Canberra 08); MercoSoja (Rosario, Argentina 06), 100th Annual Meeting of the Italtian Botanical Society (Rome, 05), British Association Festival of Science (Dublin 05), International Botanical Congress (Vienna, 05), Society for Experimental Biology (Sheffield, 05), International Conference on Atmospheric Pollution and Change (Tsukuba, 04), Nottingham Easter School (Nottingham, UK, 04); National Biology Conference (Kuala Lumpur, 03); ABC Conference (Tokyo, 03); American Society of Plant Biologists (Boston, 06, Merida, 08), International Photosynthesis Congress (Glasgow 07);
5) Member – Natural Environment Research Council (UK) and Biotechnology and Biological Sciences. Research Council (UK) various Training Grant Committees and Review Groups (1989-1998). USDA-NRI Award Panels (2000, 2003) and Panel Manager (2004,5); NSF Award Advisory Panels (2003,04,05). Also: Program Leader: Terrestrial Initiative Global Environmental Research (TIGER IVa) for the Natural Environment Research Council, UK (1991-8), Terrestrial Ecosystems Research & Training Facilities Planning Committee. US Department of Energy (2000-4). Co-chair Stategic Planning Workshop on the National Phytotron at Duke (2001); EU Biomass Energy and Miscanthus Networks (88-99), UK BBSRC Global Change Staregy Group (2007-8), European Science Foundation Review of Global Change Plant/Ecosystem Research Needs (2007-8).
(v) Conflicts (Former Graduate Students/Post-Docs and collaborators during last 5 years).
Patrick Morgan, LI-COR Inc., Lincoln, NB, Emily A. Heaton, CERES Inc., Thousand Oaks, CA, Elizabeth A. Ainsworth, USDA-ARS, Champaign, IL, Andrew Leakey, University of Illinois, Urbana, IL, Carl Bernacchi, Illinois State Water Survey, Champaign, IL, Shawna Naidu, University of Illinois, Urbana, IL, Abdul Al Shoabi, King Abdul Aziz University, Saudi Arabia, Stephen Humphries, ADAS, Birmingham, UK., Alistair Rogers, Brookhaven National Laboratory, NY, Graham Hymus, Mendel Biotechnology, Hayward, CA, Colin Osborne, University of Sheffield, UK., Marion Martin, University of Lund, Sweden, Anne Gravett, Imperical College, UK, Amiro Perez, EU Environment Program, Brussels, Belgium; Elizabeth Ireland, British Petroleum plc, London; Sarath Wanigasuriya, Rice Research Station, Government of Sri Lanka; Asoka Nugawela Rubber Research Institute, Sri Lanka; Joseph Macharia, Egerton University, Kenya; Peter Farage, University of Essex, UK. Michael John Roberts, Department of the Environment, London; Andrew Weber. Department of Plant Biology, Arizona State University, Tempe; Saberi bin Othman, Pertanian University of Malaysia.Bert Drake, Smithsonian Institution, DC; Eric Davidson, Woods Hole, MA; Neil Baker, University of Essex, UK; Christine Raines, University of Essex, UK; Christopher Somerville, UC Berkeley, CA; Joseph Noesberger, ETH Zurich, Switzerland; Sarah Assmann, Penn State Univ., PA; Keith Mott, Utah State Univ., UT; David Schimel, National Center for Atmospheric Research, CO; Susanne von Caemmerer, Australian National Univ., Canberra

BIOGRAPHICAL SKETCH XINGUANG ZHU

(i) Professional Preparation

• Shandong Normal University, China.	Biology	B.Sc., 1996
• Institute of Botany, Chinese Academy of Sciences, China.	Plant Physiology	M.Sc., 1999
• University of Illinois at Urbana Champaign	Physiology and Molecular Plant Biology	Ph.D., 2004

(ii) Appointments

- Research scientist, Department of Plant Biology, Institute of Genomic Biology, University of Illinois at Urbana Champaign, 03/06 – current
- Postdoc research scientist Plant Biology/UIUC 08/04-03/06

(iii) Publications

(i) up to 5 publications most closely related to the proposal project:

1. **Zhu X-G,** Long SP, Ort DR (2008) What is the maximum efficiency with which photosynthesis can convert solar energy into biomass? *Current Opinion in Biotechnology* 19: 153-159.
2. **Zhu X-G**, Govindjee, Baker, N.R., deSturler, E., and Long, S.P. (2005) Fluorescence *in silico*: Simulations of chlorophyll a fluorescence induction kinetics of green plants via representation of the complete sequence of excitation energy and electron transport events around photosystem II. *Planta* 223, 114-133
3. **Zhu, X-G** , deSturler, E. and Long, S.P. (2007) Optimized distribution of carbon metabolism enzymes can dramatically increase photosynthetic CO_2 uptake rate. - Theoretical explorations using a complete model of photosynthetic carbon metabolism, *Plant Physiology*, 145: 513-526.
4. **Zhu, X-G**, Whitmarsh, J., Ort, D.R. and Long, S.P. (2004) Study of the effects of photoinhibition on dynamics of carbon uptake using reverse ray-tracing algorithm. *Journal of Experimental Botany* 55: 1167-1175.
5. Long SP**, Zhu X-G,** Naidu SL, Ort DR (2006) Can improvement in photosynthesis increase crop yields? *Plant Cell and Environment* 29: 315-330.

(ii) up to 5 other significant publications

1. **Zhu, X-G**, Portis, A.R. and Long, S.P. (2004) Would transformation of C3 crop plants with foreign Rubisco increase productivity? A computational analysis extrapolating from kinetic properties to canopy photosynthesis. *Plant Cell and Environment* 27, 155-165.
2. Wang Z, **Zhu X-G**, Chen YZ, Yang J, Li YY, Li YX, Liu L (2006) Exploring photosynthesis evolution by comparative analysis of metabolic network between chloroplast and cyanobacteria. *BMC Genomics* 7: 100.
3. Wittig, W., Bernacchi, C.J., **Zhu, X.-G.**, Gielen, B., Miglietta, F., Angelis, P.D., Ceulemans, R. and Long, S.P. (2005) Modeling gross primary production for Populus spp grown under free-air CO_2 enrichment. *Global Change Biology*, 11, 644-656.
4. **Zhu X-G**, de Sturler E, Alba R (2008) A simple model of the Calvin cycle has only one physiologically feasible steady state under the same external conditions, Nonlinear Analysis (In press).
5. Wang SW and **Zhu X-G**(2008). Coupling cyberinfrastructure and GIS to empower ecological and environmental research. *Bioscience.*

(iv) Synergistic Activities

1) Education and Training. Development of lecture series to train graduate students on metabolism and agro-ecosystem modeling. Development of online education material for teaching systems biology (http://ilabs.inquiry.uiuc.edu).
2) Development of the e-photosynthesis web portal (http://www.e-photosynthesis.net). This portal supports online simulation of detailed photosynthesis process. This portal is freely accessible to academic research community, students, and general public for testing hypothesis related to photosynthesis. In addition, I helped construct the National Center for Design of Biomimetic Nanoconductors headed by Prof. Eric Jakobsson (http://www.nanoconductor.org/).
3) Involvement of woman and underrepresented groups in my research. Train woman undergraduates to conduct research in computational biology via PACI REU program (http://www.npaci.edu/Outreach/PACI-REU/). Involvement of minority students in my research via McNair Scholar Program (http://www.omsa.uiuc.edu/McNair/).
4) Reviewer for *Plant, Cell & Environment, Tree Physiology, Global Change Biology, Photosynthesis Research, Functional Plant Biology, Plant Physiology, New Phytologist, Journal of Photochemistry and Photobiology, Biochimica et Biophysica Acta*

(v) Research Grants

a. Pending support

Developing a three-dimensional hydromechanical and biochemical leaf model to bridge anatomy and photosynthesis (James S. McDonnell Foundation). This is a collaborative grant between UIUC and Virginia Tech. I am the PI from UIUC. Professor Eric de Sturler is the PI from Virginia Tech, request: 455, 200$, funding period: 8/16/2008-8/15/2013.

b. Ongoing research support

1) QEIB 0417126 Long and deSturler (PI) 9/1/2004-4/30/2008. NSF QEIB: unifying and mechanistic mathematical models of stomata behavior and photosynthesis. Role: Research scientist
2) National Center for the Design of Biomimetic Nanoconductors (NIH), Co-PI (total 16 investigators from 12 US and UK universities and national labs, PI: Prof. Eric Jacobson in Biophysics, UIUC), $6,476,476. 9/20/2005 –9/9/2010.
3) National Center for Supercomputing Applications (NSF), PI, $ 25000, 8/15/2008-8/15/2009

c. Completed Research Support

NCSA Faculty Fellow Award Long and Whitmarsh (PI) 8/15/2001-8/15/2002
NCSA/UIUC. e-Photosynthesis: Towards the photosynthesis workbench -'e-Photosynthesis'. Role: Research assistant

(vi) Collaborators & Other Affiliations

Collaborator:

Baker, N.R. (Essex Univ., UK), Bernacchi, C.J. (Water Survey, IL), Cornic, G. (Uni. Paris), DeLucia, E.H. (Univ. Illinois), de Sturler, E. (Virginia Tech), Govindjee (Univ. Illinois), Kramer, D. (Washington State Univ.), Li, Y.X. (Shanghai Center for Bioinformatics Tech), Liu, L. (Univ. Illinois), Long, S.P. (Univ. Illinois), Mott, K. (Utah State Univ.), Ort, D.R. (Univ. Illinois), Portis, A.R. (Univ. Illinois), Rogers, A. (Brookhaven National Laboratory, NY), Sheng, Z. (Univ. Illinois), Wang, S (Univ. Illinois)

Graduate and Postdoctoral Advisors:

Long, S. P. (Univ. Illinois), Zhang, Q.D. (Institute of Botany, Chinese Academy of Sciences, Retired).

Graduate students advised: Chieh-Chun Chen, Zhuo Wang

Biographical Sketch
Keith A. Mott

Professional Preparation

Union College, Schenectady, NY	Biology	B.S., 1977
University of Arizona, Tucson, AZ	Cell. & Dev. Biology	Ph.D., 1982
University of Arizona, Tucson, AZ	photosynthesis biochemistry	1982-1983
Carnegie Institution of Washington Stanford, CA	photosynthesis biochemistry	1983-1984

Appointments

July 1, 1994 to current	Professor of Biology, Utah State University, Logan, UT
July 1, 1990 to June 30 1994	Associate Professor of Biology, Utah State University, Logan, UT
Sept 1, 1984 to June 30, 1990	Assistant Professor of Biology, Utah State University, Logan, UT

Publications (5 most closely related)

Mott KA, Sibbernsen ED, Shope JC (2008) The role of the mesophyll in stomatal responses to light and CO_2. Plant, Cell and Environment (in press)

Shope JC, Peak D, Mott KA (2008) Stomatal responses to humidity in isolated epidermes. Plant, Cell and Environment (in press)

Messinger SM, Buckley TN, Mott KA (2006) Evidence for involvement of photosynthetic processes in the stomatal response to CO_2. Plant Physiology 140: 771-778

Peak D, West JD, Messinger SM, Mott KA (2004) Evidence for complex, collective dynamics and emergent, distributed computation in plants. Proceedings of the National Academy of Sciences 101: 918-922

Buckley TN, Mott KA, Farquhar GD (2003) A hydromechanical and biochemical model of stomatal conductance. Plant, Cell and Environment 26: 1767-1782

Publications (5 other significant)

Messinger SM, Mott KA and Peak D (2007) Task-performing dynamics in irregular, biomimetic networks. Complexity 12: 14-21.

Shope JC and Mott KA (2006) Membrane trafficking and osmotically induced volume changes in guard cells. Journal of Experimental Botany 57: 4123-4131

West JD, Peak D, Peterson JQ, Mott KA (2005) Dynamics of stomatal patches for a single surface of *Xanthium strumarium* L. leaves observed with fluorescence and thermal images. Plant, Cell and Environment 28:633-641.

Shope JC, DeWald, DB, and Mott KA (2003) Changes in surface area of intact guard cells are correlated with membrane internalization. Plant Physiology 133: 1314-1321.

Buckley TN and Mott KA (2002) Dynamics of stomatal water relations during the humidity response: implications of two hypothetical mechanisms. Plant, Cell and Environment 25: 407-419.

Synergistic Activities

Editor-in-Chief: *Plant, Cell and Environment*. 2002—current

Associate Editor: *Plant, Cell and Environment*. 2000—2002

Monitoring Editor, *Plant Physiology.* 1996—2000

Voluntarily assumed responsibility for the team-taught Introductory Biology course for majors at USU (enrollment >700). Spearheaded the conversion of this class to electronic presentations (PowerPoint) and advanced web-based features such as 'streaming' technology for delivering audio and video recordings of lectures.

Involvement of undergraduates in research. Approximately 8 students over the past three years.

Collaborators (last 5 years)

Peter Franks, James Cook University, Australia
Graham Farquhar, ANU, Australia
James Powell, Utah State University
James Haefner, Utah State University
Ian Woodrow, University of Melbourne, Australia
John Andrews, ANU, Australia
Tom Buckley, ANU, Australia
Joseph Shope, Utah State University
Steve Long, University of Illinois
Xinguang Zhu, University of Illinois

Co-Editors of Plant, Cell and Environment

Tom Sharkey	Mark Stitt
Steve Long	Rick Amasino
Neil Baker	Hans Bohnert
John Grace	Dirk Inze
Christine Foyer	Werner Kaiser
Mark Tester	Dan Yakir

Graduate and Post-Doctoral Advisors

James O'Leary – Graduate Advisor
Richard Jensen – Postdoctoral Advisor
Joseph Berry – Postdoctoral Advisor

Graduate Students

Thomas Buckley	Joseph Shope
Yun Lan	Freya Denne
Jerriann Ernstsen	Jevin West
Susanna Messinger	

Eric de Sturler
http://www.math.vt.edu/people/sturler/index.html

Professional Preparation:
- Delft University of Technology, Computer Science, M.Sc. cum laude (highest level), 1990,
- Delft University of Technology, Applied Sciences/Mathematics, Ph.D., 1994.

Appointments:
- Associate Professor of Mathematics, Virginia Tech, December 2005 – present,
- Adjunct Associate Professor of Computer Science, University of Illinois at Urbana-Champaign, 2005 – present,
- Assistant Professor of Computer Science, University of Illinois at Urbana-Champaign, 1999–2005,
- Senior research scientist, Center for Simulation of Advanced Rockets, UIUC, 1998-1999,
- Research scientist, Swiss Center for Scientific Computing, ETH Zurich, 1993-1998.

Affiliated Faculty:
- Interdisciplinary Center for Applied Mathematics (VT),
- Materials Computation Center (UIUC),
- Institute for Genomic Biology (UIUC),

Honors and Awards:
- Second Prize awarded at the Leslie Fox Prize Meeting 1997 (worldwide biennial award in Numerical Analysis) for my paper 'Truncation Strategies for Optimal Krylov Subspace Methods',
- Best Paper (1 of 15) 'Parallel Solution of Irregular, Sparse Matrix Problems Using High Performance Fortran', International Conference on High Performance Computing & Networking Europe 1997,
- Best Paper (1 of 10) 'Surface Parameterization for Meshing by Triangulation Flattening', 9th International Meshing Round Table Conference 2000,
- M.Sc. Computer Science awarded 'cum laude' (highest level), Delft University of Technology.

Professional associations:
1. Society for Industrial and Applied Mathematics, Philadelphia, PA, USA. Editor SIAM J. on Numerical Analysis (since 2003), Member of the Activity Groups on Linear Algebra, Supercomputing (<u>Program Director 2003-06</u>), and Computational Science and Engineering (<u>chair of 3rd SIAM Conference on CS&E 2005</u>),
2. Koninklijk Instituut van Ingenieurs (Royal Institute of Engineers), The Hague, The Netherlands, Member of the departments of Information Technology, Electrical Engineering, and Mechanical Engineering,
3. IEEE Computer Society,
4. Werkgemeenschap Numerieke Wiskunde (Dutch Community of Numerical Mathematicians).

Publications related to the project: (copies are available from my home page, above)
1. Xin-Guang Zhu, Eric de Sturler, Stephen P. Long, *Optimizing the distribution of resources between enzymes of carbon metabolism can dramatically increase photosynthetic rate. A numerical simulation using an evolutionary algorithm*, Plant Physiology, October 2007, Vol. 145, pp. 513—526, 2007
2. Xin-Guang Zhu, Govindjee, Neil Baker, Eric de Sturler, Donald R. Ort, Stephen P. Long, *Chlorophyll a fluorescence induction kinetics in leaves predicted from a model describing each discrete step of excitation energy and electron transfer associated with Photosystem II*, Planta 223(1), pages 114-133, 2005
3. Xin-Guang Zhu, Eric de Sturler, Rafael Alba, and Stephen P. Long, *A Simple Model of the Calvin Cycle Has Only One Physiologically Feasible Steady State under the Same External Conditions*, Nonlinear Analysis Series B: Real World Applications, in press,
4. Shun Wang, Eric de Sturler, and Glaucio Paulino, *Large-scale topology optimization using preconditioned Krylov subspace methods with recycling*, Int. J. Numer. Meth. Engng Vol. 69 (2007) , pp. 2441—2461,
5. Mike Parks, Eric de Sturler, Greg Mackey, Duane D. Johnson, and Spandan Maiti, *Recycling Krylov Subspaces for Sequences of Linear Systems*, SIAM Journal on Scientific Computing, Vol. 28 (2006), pp. 1651--1674,

Other significant publications: (copies are available from my home page, above)
1. Misha Kilmer and Eric de Sturler, *Recycling Subspace Information for Diffuse Optical Tomography*, SIAM Journal on Scientific Computing Vol. 28 (2006), pp. 1651—1674,
2. Chris Siefert and Eric de Sturler, *Preconditioners for Generalized Saddle-Point Problems*, SIAM Journal on Numerical Analysis, Vol. 44, No. 3, pp. 1275—1296, 2006,

3. Chris Siefert and Eric de Sturler, *Probing Methods for Saddle-Point Problems*, Electronic Transactions on Numerical Analysis Vol. 22, pp. 163—183, 2006,
4. Eric de Sturler and Jörg Liesen, *Block-Diagonal and Constraint Preconditioners for Nonsymmetric Indefinite Linear Systems. Part I: Theory*, SIAM Journal on Scientific Computing 26 (2005), pp. 1598-1619,
5. Eric de Sturler, *Truncation Strategies for Optimal Krylov Subspace Methods*, SIAM Journal on Numerical Analysis Vol. 36 (1999), pp. 864-889.

Synergistic Activities:

- Editor SIAM Journal on Numerical Analysis (since 2003),
- Editor Applied Numerical Mathematics (since 2005),
- Editor International Journal on Computational Science and Engineering (since 2004),
- Editor Open Applied Mathematics Journal (since 2007),
- Guest Editor special issue on "Saddle Point Problems: Numerical Solution and Applications", Electronic Transactions on Numerical Analysis (ETNA), Vol. 22, 2006,
- Program Director SIAM Activity Group on Supercomputing (2003-06),
- Co-Chair of the 3rd SIAM Conference on Computational Science and Engineering, February 12-15, 2005,
- Recent Program Committees: IASTED-Intl Conf. Parallel Distributed Computing and Networks (PDCN) 2007, 2006, 2005, 2004, Innsbruck, Austria. 10th Intl Conf. on High Performance Computing (HiPC'03), Hyderabad, India. High Performance Fortran User's group conference 2000 and 2001, Parallel and Distributed Processing Techniques and Applications 1999.
- Online lectures, short courses, and other educational material: Lectures on Iterative (Krylov) methods, multigrid, and eigenvalue solvers for two summerschools on computationsl materials and nanoscale science and engineering at UIUC: (1) Tools for multiple length and time scales (2001) and (2) Introduction to Computational Nanotechnology (2004). Lecture notes available from http://www.mcc.uiuc.edu/summerschool. Seminars on Krylov subspace methods, parallel iterative methods, parallel computing, and High Performance Fortran at various institutions in Europe: Cath. Univ. Leuven (multiple times), Univ. of Basel, EPFL, Delft Univ. of Technology, ETH Zurich; see http://www-faculty.cs.uiu.edu/~sturler.
- Extended Visits: ERCOFTAC visitor, ETH Zurich CEE (Peter Rutschmann), summer 1999; Visitor SCCM-program Stanford University (Gene Golub), summer '97; Visiting Fellowship in the CS Lab. of the RSISE, Australian National University (Markus Hegland and Mike Osborne), November 1997. Utrecht University, Netherlands (Henk van der Vorst), December 2001-January 2002.

Graduate students: PhD: Chris Siefert (CS'06), Shun Wang (CS'07), Mike Parks (CS'05); MS: Zhen Cheng (CS'05), Greg Mackey (CS MS'03); MCS Naomi Caldwell (MCS'04);, Anoush Najarian (MCS'01), Jie Zheng (MCS'01), Robert Zhang (MCS'01), Bertrand Sagnet (MCS'99).

Undergraduate students: Mark Hoemmen (CS'02), Hormozd Gahvari (CS'03), Ben Kaap (CS'04).

Postdoctoral students: Joerg Liesen (TU Berlin), Alla Sheffer (UBC), Xinguang Zhu (UIUC).

Collaborators and Co-Editors (past 48 months): UIUC: P. Bellon, D. Ceperley, K. Dahmen, D. Goldberg, R. Haber, D. Johnson, J. Kim, S. Long, R. Martin, T. Martinez, G. Paulino, X. Zhu; **VT:** C. Beattie, S. Gugercin, L. Li (VT); **Other**: M. Benzi (Emory), K. Bartschat (Drake), R. Cohen (CIW), R. Henning (Ohio), M. Kilmer (Tufts), R. Lehoucq (Sandia), J. Liesen (TU Berlin), G. Mackey (Sandia), S. Maiti (MTU), B. Militzer (CIW), L. Mitas (NC State), K. Mott (USU), M. Parks (Sandia), B. Schneider (NSF), C. Umrigar (Cornell), Q. Ye (Kentucky).

Editorial boards: SIAM Numerical Analysis: http://www.siam.org/journals/sinum/edboard.htm, Appl. Numer. Math: http://www.elsevier.com/wps/find/journaleditorialboard.cws_home/505602/editorialboard#editorialboard, Intl J. on Comp. Science and Eng.**:** https://www.inderscience.com/browse/index.php?journalID=125, Open Appl. Math: http://www.bentham.org/open/toamj/EBM.htm

Thesis advisors: Henk van der Vorst (Utrecht University, Netherlands), Piet Wesseling (Delft University, Netherlands).

OLIVER FIEHN
Associate Professor, Department of Molecular and Cellular Biology
Faculty Lead, UCD Genome Center Metabolomics Core

University of California, Davis

451 Health Sci. Dr., Davis, CA 95616
530-754-8258 / 538-754-9658 (fax) / ofiehn@ucdavis.edu

(a) Education

Berlin Free University	Chemistry	diploma, 1994
Berlin Technical University	Analytical Chemistry	Ph.D., 1997
Max-Planck Inst. Mol. Plant Phys.	Plant biochemistry	Post-doc - 1998-1999

(b) Appointments

2004-present	Assoc. Professor, Genome Center, UC Davis
2000-2004	Group Leader, MPI Mol Plant Physiol., Potsdam, Germany
1998-1999	Postdoctoral Research Scientist, MPI Mol Plant Physiol., Potsdam, Germany
1994-1997	Research Scientist, Inst. Environmental Protection, TU Berlin, Germany

(c) Publications

Fiehn O, Wohlgemuth G, Scholz M, Kind T, Lee DY, Lu Y, Moon S, Nikolau BJ (2008) Quality control for plant metabolomics: Reporting MSI-compliant studies. Plant Journal 53, 691-704

Fiehn O (2008) Extending the breadth of metabolite profiling by gas chromatography/mass spectrometry. TrAC - Trends Anal. Chem. 27, 261-269

Kind T, **Fiehn** O (2007) Seven golden rules for heuristic filtering of molecular formulas obtained by accurate mass spectrometry. BMC Bioinformatics 8: 115

Horie K, Ikegami T, Hosoya K, Saad N, **Fiehn** O, Tanaka N (2007) Highly efficient monolithic silica capillary columns modified with poly(acrylic acid) for hydrophilic interaction chromatography. J. Chromatogr. A 1164, 198-205

Fiehn O, Sumner LW, Rhee SY, Ward J, Dickerson J, Lange BM, Lane G, Roessner U, Last R, Nikolau B (2007) Minimum reporting standards for plant biology context information in metabolomic studies. Metabolomics 3, 195-201

Meyer RC, Steinfath M, Lisec J, Becher M, Witucka-Wall H, Toerjek O, **Fiehn** O, Eckardt A, Willmitzer L, Selbig J, Altmann T (2007) The metabolic signature related to high plant growth rate in Arabidopsis thaliana. Proc. Natl. Acad. Sci. USA 104, 4759-4764

Scholz M, **Fiehn** O (2007) SetupX - A Public Study Design Database for Metabolomic Projects. Pacific Symp. Biocomp. 12, 169-180

Fiehn O (2007) Cellular Metabolomics: The Quest for Pathway Structure. In: The Handbook of Metabonomics and Metabolomics, Chapter 2. Eds. Lindon JC, Nicholson JK, Holmes E. Elsevier BV, Amsterdam and Oxford, ISBN-13: 978-0-44-452841-4, pp. 35-54

Fiehn O (2006) Study of metabolic control in plants by metabolomics. In: Control of Primary Metabolism in Plants. Eds. Plaxton WC and McManus MT. Blackwell, Annual Plant Reviews 22, 60-84

Kind T, **Fiehn** O (2006) Metabolomic database annotations via query of elemental compositions: Mass accuracy is insufficient even at less than 1 ppm. BMC Bioinformatics 7:234

Fiehn O, Wohlgemuth G, Scholz M (2005) Setup and Annotation of Metabolomic Experiments by Integrating Biological and Mass Spectrometric Metadata. Proc. Lect. Notes Bioinformatics 3615, 224-239

Boelling C, **Fiehn** O (2005) Metabolite profiling of Chlamydomonas reinhardtii under nutrient deprivation. Plant Physiol. 139, 1995-2005

Cook D, Fowler S, **Fiehn** O, Tomashow M (2004) Role of the CBF cold response pathway in configuring the low temperature metabolome of Arabidopsis. Proc. Natl. Acad Sci. USA 101, 15243-15248

Weckwerth W, Loureiro ME, Wenzel K, **Fiehn** O (2004) Metabolic networks unravel the effects of silent plant phenotypes. Proc. Natl. Acad. Sci. USA 101, 7809-7814

Weckwerth W, Wenzel K, **Fiehn** O (2004) Process for the integrated extraction, identification and quantification of metabolites, proteins and RNA to reveal their co-regulation in biochemical networks. Proteomics 4, 78-83

Fiehn O (2003) Metabolic networks of Cucurbita maxima phloem. Phytochemistry 62, 875-886

Steuer R, Kurth J, **Fiehn** O, Weckwerth W (2003) Observing and interpreting correlations in metabolic networks. Bioinformatics 19, 1019-1026

Tolstikov VV, **Fiehn** O (2002) Analysis of highly polar compounds of plant origin: combination of hydrophilic interaction chromatography and electrospray ion trap mass spectrometry. Anal Biochem 301, 298-307

Fiehn O (2002) Metabolomics – the link between genotype and phenotype. Plant Mol. Biol. 48, 155-171

Roessner U, Luedemann A, Brust D, **Fiehn** O, Linke T, Willmitzer L, Fernie AR (2001) Metabolic profiling allows comprehensive phenotyping of genetically or environmentally modified plant systems. Plant Cell 13, 11-29

Fiehn O, Kopka J, Dörmann P, Altmann T, Trethewey RN, Willmitzer L (2000) Metabolite profiling for plant functional genomics. Nat. Biotechnol. 18, 1157-1161

Fiehn O, Kopka J, Trethewey RN, Willmitzer L (2000) Identification of uncommon plant metabolites based on calculation of elemental compositions using gas chromatography and quadrupole mass spectrometry. Anal. Chem. 72, 3573-3580

(d) Synergistic Activities

1. Editorial Board Member *Journal of Biological Chemistry* (2006-present), *Plant Methods* and *Metabolomics* (2004-present)
2. Board of Directors, the Metabolomics Society (2004 – present)
3. International Advisory Board member for the 2nd, 3rd and 4th International Congress on Plant Metabolomics, held 2003, 2004 and 2006.
4. Organizer of the 2nd International Conference on Plant Metabolomics, held in Potsdam, Germany, June, 2003

(e) Collaborators & Other Affiliations

Collaborators and Co-Editors (past 48 months)

Kaddurah-Daouk, R.	Duke University
Kristal, B.	Harvard Medical Center
Griffin, J.	Cambridge University, UK
Denkert, C., M.D.	Charite Berlin, Germany
Oresic, M.	VTT, Finland

Graduate and Postdoctoral Advisors

Martin Jekel	Technical University, Berlin, Germany
Lothar Willmitzer	Max-Planck Institute of Molecular Plant Physiology, Potsdam, Germany
Richard Trethewey	Metanomics, Berlin, Germany

Thesis Advisor and Postgraduate-Scholar Sponsor (past 48 months)

Dr. Wolfram Weckwerth	Max-Planck Institute of Molecular Plant Physiology, Potsdam, Germany
Dr. Tobias Kind	UC Davis
Dr. Nabil Saad	UC Davis
Dr. Baichen Zhang	Danforth Plant Sci. Center
Mungur, R.	UC Berkeley
Gatzeck, S.	Novartis, Basil, Switzerland
	16 = Total number of graduate students advised and postdocs sponsored

Scientific questions

The leaf, in terms of function and behavior is arguably the best known plant organ, and the one which sets the upper limit on productivity. As the point of light interception, energy transduction and carbon assimilation, the vegetative sink for most nitrogen and the site of transpiration it is key to determining plant production and plant resource use efficiency. It is therefore the logical starting point for developing an *in silico* plant. Unlike the whole plant and plant community though, developing a model based on dynamic model of primary metabolism appears an achievable GC within the initial timeframe of the iPlant initiative, and given the evolutionarily conserved nature of photosynthesis and respiration, one that would have wide applicability. The goal is to develop an *in silico* leaf (*iLeaf*) which mimics the environmental responses of the leaf *in vivo,* which may be used as a platform to test complex hypotheses and to explore, for example through the use of evolutionary (genetic) algorithms changes in organization and allocation that may improve production and resource use efficiency. Simultaneously it would provide a unique teaching tool for exploring how leaf processes respond to the environment, and in particular climate change. This workshop will address the broad question of the extent to which a complete picture of primary metabolism, cellular and inter-cellular compartmentation, and integration with leaf and environmental physiology can be achieved. In parallel, it will determine the database, visualization and computational math tools that need to be developed to achieve a functioning *in silico* leaf.

Photosynthesis is ultimately the source of energy for all ecosystems, our food, fibre and fuel. With the explosive increase in global population, demand for food and energy has been dramatically increased. Engineering photosynthesis for higher nitrogen and light use efficiency is one of the major routes, still potentially available, to realized dramatic increases in crop yields for now and for the future(Long et al., 2006). In contrast to the first Green Revolution, which used classical plant breeding, today and for the first time we have the blueprint (DNA sequence) of model species and some of our major crops. Modern biotechnology now has the power to engineer every gene in photosynthesis. However, improvement in photosynthesis has not played an important role in improving crop yield. Theoretical analysis however suggest that there is substantial room for us to further increase photosynthetic efficiency(Zhu et al., 2008). The critical challenge is to identify what specific targets for genetic engineering to achieve higher photosynthetic efficiency for crops grown under different conditions. This is a very significant challenge for the following reasons. Photosynthesis and respiration involve more than 200 proteins, which are dependent on and interact with each other. As the source of carbon and energy in leaf mesophyll cell, photosynthesis has extensive feedback and feedforward interactions with various metabolisms related to sink activities, e.g. the synthesis of starch, export of sucrose, glycolysis, TCA cycle, the nitrogen assimilation, even the synthesis of macromolecules such as lipid and protein (Smith and Stitt, 2007). In addition, CO_2, the key substrate used in photosynthesis, must diffuse through stomata, intercellular space, mesophyll cell wall, cytosol, before entering chloroplast to be fixed through Rubisco. Stomata conductance in turn is influenced by various environmental factors, such as CO_2, temperature, humidity, light, drought (Farquhar and Sharkey, 1982; Buckley et al., 2003) and signals from the mesophyll. These factors are constantly varying in nature and with climate change. As a result, the optimal leaf for any crop species will vary under different conditions, and will be a compromise to deal with this variability. With such complexity, what is the most efficient way to identify the optimal properties for given environments, including those of the future?

It is possible to transgenically up-regulate or down-regulate almost every protein involved in photosynthesis and respiration. Even if manipulation is limited to simply altering the amount of protein, rather than its properties, the potential permuations will run into the millions. Clearly it would be experimentally inefficient, even with pipeline transformations to find the optimal solution this way. However, if the metabolic pathways are faithfully represented in the *in silico* leaf, then an evolutionary algorithm provides an efficient way to solve this challenge. We propose to develop an integrated leaf central metabolism model, the *iLeaf*. This model will extend the dynamic model of photosynthesis, that has been developed over the past 6 years(Zhu, 2004; Zhu et al., 2005; Zhu et al., 2007; Zhu et al., 2008; Zhu et al., In prep) to include other plant primary metabolisms, and also the control of stomata conductance. The future *iLeaf* model will include the basic biophysical and biochemical reactions involved in the light reactions, the Calvin cycle, the starch and sucrose synthesis, photorespiratory pathway, the glycolysis, pentose phosphate pathway, and also the TCA cycle. In addition, it will include the key reactions involved in nitrogen assimilation, and the key entry fluxes into major sinks, such as the flux from key metabolites in the carbon metabolism to different groups of amino acid and lipid synthesis.

The *iLeaf* model, once developed, offers tremendous research opportunities in both basic and applied research. First, it provides a direct link of genomic data to phenotypic data. The input of the model is the enzyme activity or protein content, which can be obtained from either literature survey or proteomics. An output is the metabolomics and fluxomics. Therefore, we can use the model to generate hypotheses regarding potential mechanisms behind certain phenotype under genetic or environmental perturbations. This can be achieved through replacing the activity data one by one, and then check the simulated phenotypic changes. The one enzyme or parameter, when modified, show the experimentally observed phenotypic changes will possibly be the enzyme responsible for certain phenotype. Secondly, the *iLeaf* model can be used to study the adaptive significance of changes at molecular level on photosynthesis and plant productivity. Current leaf properties are the results of billions of years of evolution and at concentrations of CO_2 that for 25 M years have been about 60% of those today and where selection has been for survival and fecundity, and not productivity. How optimal are current leaf properties for photosynthetic CO_2 uptake? Zhu et al (2007) has demonstrated that the current investment to photorespiratory pathway might reflect a protective mechanism of plant to survive under extremely hot, drought and low CO_2 conditions. Since extinctions is forever, wild plants must survive a 1 in 10000 year event, whereas for crops such rare events are a risk that agriculture can contend with. Use of evolutionary or genetic algorithms is one approach to designing a more efficient leaf. With *iLeaf* model, we can explore the adaptive significance of various changes in leaf mesophyll cell metabolism under different conditions. Similarly, *iLeaf* also offers a venue where we can study the possible driving force responsible for the changes in photosynthetic properties. Thirdly, the *iLeaf* model offers an unprecedented opportunity to test hypotheses regarding mechanisms controlling dynamic changes in plant primary metabolism. For example, it can be used to study the impact of the theoredoxin on the homeostasis of plant primary metabolism; it can be used to study the potential mechanisms behind the stomatal conductance. Fourthly, the *iLeaf* model provides a framework to identify where we can engineer the system for yet higher efficiency. Finally, *iLeaf* will provide a unique teaching tool to allow class-room discovery of the factors affecting photosynthesis, transpiration and respiration, and at a higher level conducting numerical experiments as individual projects.

Computational Challenges

The existing off-the-shelf research methodologies and computational power are not sufficient to tackle the proposed research. First, the reactions occur in the plant primary metabolism occur on timescales of dynamics that vary over 10 orders of magnitude. For example, the photosynthetic charge separation has a time constant of about 2.5×10^{10} s^{-1} (Roelofs et al., 1993); while Rubisco has a rate constant about 2.5 s^{-1} (Spreitzer and Salvucci, 2002). These drastically different rate constants in the same system make the differential equations describing the integrated plant metabolism extremely “stiff”. In another words, novel numerical algorithm will be needed in order to solve the system both accurately and efficiently. Secondly, as a complex system, the plant primary metabolism will inevitably operate in different states under different conditions. For example, photosynthesis operates under either sink limited conditions or with unlimited sink strength. The efficiency of photosynthesis under these two different states are drastically different (Sharkey, 1985; Zhu et al., 2007). The transition between states of the plant primary metabolism will correspond to major shifts in leaf physiological processes. Now, we are lack of one efficient method to study the number of potential states that a Leaf will operate in and study the transition between different states under various conditions. Although there are a few software packages for dynamic systems analysis available in the mathematical literature, e.g. XPPAUT(Marray, 1993), POLYSYS_PLP(Wise et al., 2000), they have only been tested with smaller systems. The *iLeaf* model will have more than 100 ordinary differential equations, which requires advanced packages to study the transition of states. In addition, the existing software packages for analyzing dynamic system properties are not as user intuitive as desirable. Thirdly, to identify the best plant primary metabolism for optimal photosynthetic efficiency, millions of simulations will be done with each simulation taking about 10 minutes to an hour. Apparently, this number of computations exceed the computational power of any desktop computers. Access of modern power of the supercomputers through the infrastructure that iPlant will provide will be absolutely critical for the success of this approach. Fourthly, the current dynamic models are limited by consistent data set for any leaf grown under well defined conditions. In literature, there are however a large number of relatively incomplete data set, which contains partial information and still be valuable for model parameterization. To effectively use those data sets, novel algorithms are needed in order to effectively extract high quality parameters from these relatively incomplete data.

The key datasets required to develop the proposed *iLeaf* model are mostly available. The *iLeaf* model requires both enzyme kinetics information and enzyme activities. The enzyme activities for all reactions involved in the plant primary metabolism can be collected through literature search. Previously, when we were working on developing the dynamic photosynthesis model, the enzyme activities and also the concentrations of proteins in the electron transfer chain were obtained through literature search and a cross-reference normalization method (Zhu et al., 2007). We will take this same approach in the beginning phase of the model development to collect the protein and metabolite amounts, enzyme and electron transport protein kinetic data, cell and organelle volumes. The ideal data required for the *iLeaf* model will be quality proteomic and metabolomic datasets from leaves killed under carefully defined microclimatic conditions with defined *in vivo* photosynthetic CO_2 assimilation and electron transport rates. Though such data is still not available, integrated measurement of enzyme activities and metabolite concentrations for leaf central metabolisms are emerging (Osuna et al., 2007). The data needed to validate the *iLeaf* model will be metabolomics data and also in vivo physiological and biophysical measurements. The large number of in vivo probes (CO_2 uptake, O_2 evolution, fluorescence, spectroscopy *etc*) will also be used to validate the model of the *iLeaf* model. The control of stomata conductance will be a key component of the integrated *iLeaf* model. Though the mechanism behind the control of stomata conductance is still not completely understood, there are large amount of empirical evidence showing the intrinsic interaction between photosynthesis and stomata conductance (Wong et al., 1979; Farquhar and Sharkey, 1982; Messinger et al., 2006). We will implement various potential mechanisms to link the stomata conductance with photosynthesis. In the beginning, we will incorporate the biochemical and hydromechanical model of stomata conductance(Buckley et al., 2003) in the *iLeaf* model.

Education and Outreach

To educate the next generation of computational biologist, and also to bring broad participation of plant biologists in systems biology research, it is highly valuable to have a plant metabolism workbench, which can simulate metabolic pathways, accessible for the web, and usable for numerical experiments where users can vary kinetic properties, protein amounts, alternative pathways. iPlant, with its expertise in software engineering and the computational resources available, will provide an excellent opportunity to realize this. Furthermore, we will explicitly involve the minority and woman students in our research program. We have established collaboration with the McNair program to recruit minority students to work in the proposed research. Four black American and two Hispanic American undergraduates worked on *e-Photosynthesis* through the McNair program, over the past 3 years. Three have continued into graduate research in plant sciences.

Workshop

The major expected output of the proposed research is to develop the computational tools to study the molecular, biochemical, stomatal and whole leaf properties that characterize a productive leaf both *in vivo* and evolved *in silico.* In addition, we will deliver an *in silico* modeling platform of leaf primary metabolism, which the community may use to investigate engineering. The goal of the workshop is to bring together plant biologists, particularly working in the field of plant primary metabolism and stomata conductance, and computer scientist and mathematician, particularly those in the field of numerical analysis, to discuss the major challenges to these two goals. Photosynthesis, being the key plant physiological process underlines productivity, are also modeled in other GCW proposals as well. The current proposal will complement, not compete with, any other proposal. In fact, the integrated *iLeaf* model, once developed, can be easily integrated into the modeling work at canopy and ecosystem models, which other groups are possibly working on, to study processes at higher organizational levels. In addition, the *iLeaf* model can serve as a base model to which the control over expression of the plant primary metabolism can be exerted to create a model which can be used to study diurnal changes in leaf metabolism under changing environmental conditions.

The format of the workshop will include both presentations (from the group and iPlant) and also discussions.

Proposed Agenda

<u>Day 1</u>

- I. Keynotes
  - A. Introduction to iPlant Collaborative: iPlant Staff
  - B. Define the issue: food and energy and human society: Steve Long
  - C. Interaction of stomata conductance with photosynthesis: Keith Mott
  - D. Interaction between nitrogen and carbon metabolism: Mark Stit
  - E. Interaction between photosynthesis and respiration: Owen Atkin
  - F. The grand challenge discussion and formalize vision of *iLeaf* model
- II. Modeling efforts related to plant primary metabolism and stomata conductance
  - A. Photosynthesis model: Xinguang Zhu
  - B. Stomata conductance model: Tom Buckley
  - C. Network and flux control analysis: Oliver Ebenhöh
  - D. Discussion about model integration and new model development
- III. Existing software packages for systems biology research
  - A. Parameter estimation: Eric de Sturler
  - B. Bifurcation analysis and phase diagram: Bard Ermentrout
  - C. Systems modeling tools: Petro Mendes
  - D. Database and software integration: James Myers
  - E. Discussion of algorithm and infrastructure needs

<u>Day 2</u>

- IV. Data sets and genome resources available
  - A. Plant metabolism database: Sue Rhee

B. Integrated enzyme activity data and metabolite: Mark Stitt
C. Plant metabolomics: Oliver Fiehn
D. Flux analysis in plant primary metabolism: Jorg Schwender
E. Discussion about the dataset needs

V. Education and Outreach
A. Online simulation platform for systems and synthetic biology research for researchers
B. Getting the simulation into university and high school classroom

VI. Discussion
A. Breakout group discussion on model integration, method development, and data integration
B. Report of the discussion result from each group
C. Joint discussion about the model, algorithm, and data integration
D. Assignment of writing groups

Day 3. Break out groups.

A. Database needs. (e.g. complete databases of all prior leaf proteomics and metabolomics, defining the necessary meta-data).
B. Computational math and visualization needs (e.g. more efficient numerical integration, routines to extract kinetic constants from *in vivo* data, dealing with the stochastic nature of resource and response within the leaf, bifurcation analysis, phase diagram for large systems ….).
C. Representing metabolism. (What primary metabolism beyond photosynthesis and respiration can be represented? How do we deal with partitioning and cross-linkage between pathways).
D. Linking genomics, proteomics and metabolomics to leaf behavior and function.
E. Environmental physiology. What are the key environmental responses, how are environmental response, acclimation and adaptation linked into the model.
F. EOT. What are the opporunites for using A-E in EOT, what are the visualization, workbench and Web tools that will be needed?

Suggested reviewers:

Christine Raines, Plant Biology, University of Essex, tel. +44 (0)1206 873310, email: rainc@essex.ac.uk

Maarten Chrispeels: Biology, UCSD, tel: (858)534-2571. Email: mchrispeels@ucsd.edu

Lothar Willmitzer: Plant Systems Biology, Max Planck Institute of Molecular Plant Physiology, tel: +49 (331) 567 – 8200, email: willmitzer@mpimp-golm.mpg.de

Dirk Inze: Plant Systems Biology, University of Gent, tel: + 32 (0)9 33 13 806, email: diinz@psb.ugent.be

References

Buckley TN, Mott KA, Farquhar GD (2003) A hydromechanical and biochemical model of stomatal conductance. Plant Cell and Environment **26:** 1767-1785

Farquhar GD, Sharkey TD (1982) Stomata conductance and photosynthesis. Annual Review of Plant Physiology **33:** 317-345

Long SP, Zhu XG, Naidu SL, Ort DR (2006) Can improvement in photosynthesis increase crop yields? Plant Cell And Environment **29:** 315-330

Marray JD (1993) Mathematical biology, 2nd corrected ed., Springer 1993, ISBN 3-540-57204-X.

Messinger SM, Buckley TN, Mott KA (2006) Evidence for involvement of photosynthetic processes in the stomatal response to CO_2. Plant Physiology **140:** 771-778

Osuna D, Usadel B, Morcuende R, Gibon Y, Blasing O, Hohne M, Gunter M, Kamlage B, Trethewey R, Scheible WR, Stitt M (2007) Temporal responses of transcripts, enzyme activities and metabolites after adding sucrose to carbon-deprived Arabidopsis seedlings. Plant J **49:** 463 - 491

Roelofs TA, Kwa SLS, Vangrondelle R, Dekker JP, Holzwarth AR (1993) Primary processes and structure of the photosystem-II reaction center.2. Low temperature picosecond fluorescence kinetics of a D1-D2 Cyt B559 reaction center complex isolated by short triton exposure. Biochimica et Biophysica Acta **1143:** 147-157

Sharkey TD (1985) O_2 insensitive photosynthesis in C_3 plants. Plant Physiology **78:** 71-75

Smith AM, Stitt M (2007) Coordination of carbon supply and plant growth. Plant, Cell & Environment **30:** 1126-1149

Spreitzer RJ, Salvucci ME (2002) RUBISCO: structure, regulatory interactions, and possibilities for a better enzyme. Annual Review of Plant Biology **53:** 449-475

Wise SM, Sommese AJ, Watson LT (2000) Algorithm 801: POLSYS_PLP: a partitioned linear product homotopy code for solving polynomial systems of equations. ACM Transactions on mathematical software **26:** 176-2000

Wong S-C, Cowan IR, Farquhar GD (1979) Stomatal conductance correlates with photosynthetic capacity. Nature **282:** 424-426

Zhu X-G, de Sturler E, Long SP (2007) Optimizing the distribution of resources between enzymes of carbon metabolism can dramatically increase photosynthetic rate: A numerical simulation using an evolutionary algorithm. Plant Physiology **145:** 513-526

Zhu X-G, Govindjee, Baker NR, deSturler E, Ort DR, Long SP (2005) Chlorophyll *a* fluorescence induction kinetics in leaves predicted from a model describing each discrete set of excitation energy and electron transfer associated with photosystem II. Planta **223:** 114-133

Zhu XG (2004) Computational Approaches to Guiding Biotechnological Improvement of Crop Photosynthetic Efficiency. Ph. D. thesis, the University of Illinois. Urbana, IL.

Zhu XG, Long SP, Ort DR (2008) What is the maximum efficiency with which photosynthesis can convert solar energy into biomass? Trends in Biotechnology **19:** 153-159

Zhu XG, Ort DR, Long SP (In prep) Systems study of the global optimization of nitrogen investment in photosynthetic apparatus under different light levels.