Multiscale Metabolic Modelling (MMM): an Integrative Crop Systems Biology Approach for Biomass Research

Johannes Müller¹, Andre Eschenröder¹, Mohammad-Reza Ghaffari², Mohammad-Reza Hajirezaei², Thomas Herter³, Astrid Junker², Björn Junker², Michael Leps⁴, Katrin Lotz⁴, Björn Usadel³, Falk Schreiber⁵

¹Martin-Luther-University Halle-Wittenberg, Crop and Ecological Physiology/Plant Systems Modeling, Betty-Heimann-Str. 5, D-06120 Halle (Saale), Germany
²Leibniz-Institute of Plant Genetics and Crop Plant Research (IPK), Corrensstr. 3, D-06466 Gatersleben, Germany
³Max Planck Institute of Molecular Plant Physiology, Integrative Carbon Biology. Am Muehlenberg 1, D-14476 Potsdam-Golm, Germany
⁴SunGene GmbH, a BASF Plant Science Company, Corrensstr. 3, D-06466 Gatersleben, Germany
⁵Martin-Luther-University Halle-Wittenberg, Institute of Computer Science, Von-Seckendorff-Platz 1, D-06120 Halle (Saale), Germany
Contents

- Background, goals, concepts
- Some general problems to cope with
- Plant material
- Main questions of the research
- Introduce project groups and specific goals
- Conclusions
Background

Cereals – The World’s Principal Food Resource
Background

Cereals – The World‘s Principal Food + Energy Resource?
Background

An important goal of climate and energy policy of the Federal Republic of Germany is a significant increase in the production of biomass crops for energy purposes.

The project network ‘MMM’ is part of an initiative of the Federal Ministry of Education and Research, funding systems biology approaches for optimizing bio-energy crops.

Actually, the ‘MMM’ project is just running for some month.

(Thus, originally I planed only a short poster information, but I was asked to give an overview on the project by an oral presentation. However, since we are just at the beginning, this overview will be mainly give conceptual information.)
Overall Goals and General Concept

Better understanding of existing bottle-necks and future prospects for increasing plant biomass formation

- Establishing a combined experimental and model based systems biology approach
- Studying function, regulation, integration, and interaction of metabolic/physiological processes of biomass formation
- Covering different hierarchical scales of the plant
General Concept – Core Models

The approach will integrate:

• A comprehensiv **model of whole plant C, N and dry matter dynamics**

• **Stoichiometric models** for the metabolism of specific organs/processes

• **Detailed kinetic models** for specific pathways of central metabolism
Problems: Complexity

- Biological systems are very complex
- Calculation time and parameter number increase rapidly with complexity

→ Special approaches are needed to get a computable model
Problems: Gradient in Model Comprehensiveness and Degree of Abstraction

Fig. 1. The Multiscale Metabolic Modelling approach will integrate comprehensive models of whole plant C, N and dry matter dynamics, stoichiometric models of the metabolism of specific organs, quantitative flux models of the central metabolism and detailed kinetic models for specific pathways.
Problems: ‘Classical‘ Crop Models

Use mixed ‘mechanistic‘ and empirical equations, lumped processes, lumped parameters

→ No direct relations to basic processes (and specific organs)

→ Parameter values cannot not be derived directly from basic (metabolic) knowledge

→ Empirical calibration (parameterisation)

Generic character of these models and portability between different crops may be restricted
Problems: Metabolic Models

• Key points for using kinetic modeling are...
  – ...the data coverage (are variables and/or kinetic parameters known?)

Usually lack of information!
Problems: Metabolic Models

Solution 1: use parameters from different sources/objects
- take from another organ
- take from another plant from same family
- take from another dicot plant
- take from monocot, but still a plant
- take from another multi-cellular eukaryote
- take from another eukaryote
- take from *Escherichia coli*
  (well, at least you don't estimate)

Solution 2: parameter estimation

Necessary condition:
quantitative experimental data of the according model variables (subcellular)
Problems

Solution 3: Combine hierarchically nested models

More detail only for selected components!

Architectural frame
Plant Material

Test of two small barley populations for their genomic variation in metabolites and enzyme activities

IL's Hord. vul. x Hord. spont.    Genebank accessions (IPK)

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Schmalenbach & Pillen 2006  Prof. Graner, Dr. Börner
Schmalenbach et al. 2009
Main Questions

Is there any considerable genomic variation in metabolite patterns in different cultivars?

Is there any correlation between agromonomical important traits and metabolic patterns?

Will it be possible to identify optimum metabolic patterns by model-based analysis?
Project groups and specific goals

1. Process model network LEAFC3N-ProNetCN: Coupling of radiation interception, photosynthesis, dynamics and balances of main functional carbon and nitrogen compounds and its allocation between interacting source and sink organs, up-scaling to biomass formation.

Martin-Luther-University Halle-Wittenberg
Project leader, scientist: J. Müller, A. Eschenröder.
Project groups and specific goals

2. Metabolic flux analysis:
Estimation of C-Fluxes in carbohydrate production based on $^{13}$C steady state labeling experiments in leafs, in generation of cell wall compounds from nucleotide sugars, and in production of storage compounds in developing seeds.

Biochemical data will be integrated into a modelled flux map to refine balance models (→1), to validate stoichiometric models (→3a) and to estimate parameters of kinetic models (→3b).

IPK Gatersleben
Project leader, scientist: B. Junker, A. Junker.
3. Metabolic network modelling:
   a) **Stoichiometric (structural) models of the primary metabolism** of various plant organs (source/sink leaf, stem and grain)
   b) **Kinetic models** of selected metabolic pathways
   c) **Integration of a) and b) into the MetaCrop information system** for detailed representation of metabolic networks (navigation between related networks, convenient network creation, linking of different model hierarchies)

IPK Gatersleben
Project groups and specific goals

4. Biochemical analyses of primary metabolism:
Main enzymes of relevant pathways (sucrose cleavage and synthesis, glycolysis, pentose phosphate pathway, TCA cycle, amino acid biosynthesis and nitrate and ammonium assimilation);
All relevant metabolites (soluble and insoluble sugars, organic acids, amino acids and phosphorylated metabolites, flux experiments using labelled sugars such as $^{14}$C-sucrose).

IPK Gatersleben
Project leader, scientist: M.-R. Hajirezaei, M.-R. Ghaffari.
5. Metabolism and regulation of cell wall biosynthesis:

Enzyme activities in the nucleotide sugar interconversion pathway

Composition and amount of important cell wall constituents (cellulose, individual sugar monosaccharide components of polymeric components).

MPI Potsdam-Golm, Germany
Project leader, scientist: B. Usadel, T. Herter.
Project groups and specific goals

6. Application of results from barley to stoichiometric and kinetic modelling in rice:
Integrative stoichiometric model about primary metabolism in rice (source-leaf and grain)
Kinetic models from selected pathways that will be constructed and adapted for rice.

SUNGENE™ Gatersleben (BASF Plant Sciences)
Project leader, scientist: M. Leps, K. Lotz.
Main conclusion (Opinion)

Classical Crop Growth Modelling
+ Crop Systems Biology Approaches
+ Plant Architectural Modelling?

should be combined!

Strong interdisciplinary collaborative engagement is required!
Outlook:
Outlook: a ‘win-win-win’ Scenario!
Outlook: a ‘win-win-win’ Scenario! ...

Thanks For Your Attention!
Thanks to the MMM Consortium for contributions to the presentation!

Prof. Dr. Falk Schreiber (speaker)

Stoichiometric and kinetic models of metabolic pathways
IPK Gaterleben and University Halle-Wittenberg

Dr. Mohammad-Reza Hajirezaei
Biochemical analysis of primary metabolism
IPK Gaterleben

Model network
LEAFC3N-ProNetCN
University Halle-Wittenberg

Dr. Johannes Müller

Metabolic flux analysis
IPK Gaterleben

Dr. Björn Junker

Cell wall analysis
MPI, Potsdam-Golm

Dr. Björn Usadel

Model validation in rice
Sungene GmbH Gatersleben

Dr. Michael Leps

AGRO 2010 Montpellier