SynthSys
SYNTHETIC & SYSTEMS BIOLOGY

THE UNIVERSITY OF EDINBURGH

Systems for Biological Timing in the Green Lineage

EPSRC
Engineering and Physical Sciences Research Council

BBSRC
bioscience for the future

Andrew Millar
SynthSys-Plants

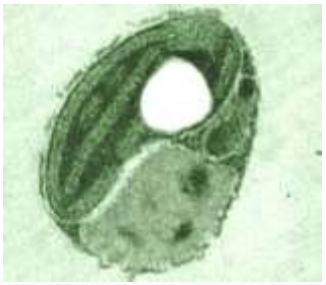
Multiscale models – plant biology

Genomics

Phenomics

- ‘Crop-style’ growth model for *A.t*.

- A tool to reconcile and understand pleiotropic (dynamic, quantitative) phenotypes.



- How can a community build such a tool?
- What about its impact on Food Security?

Biological clocks in theory and experiments

www.amillar.org @A_J_Millar

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Current:

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Laszlo Kozma-Bognar
Kieron Edwards
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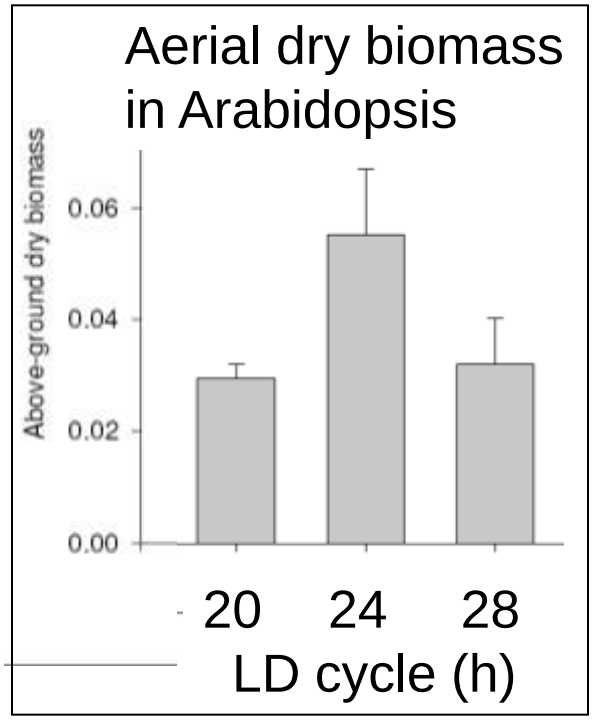
TiMet

ROBuST

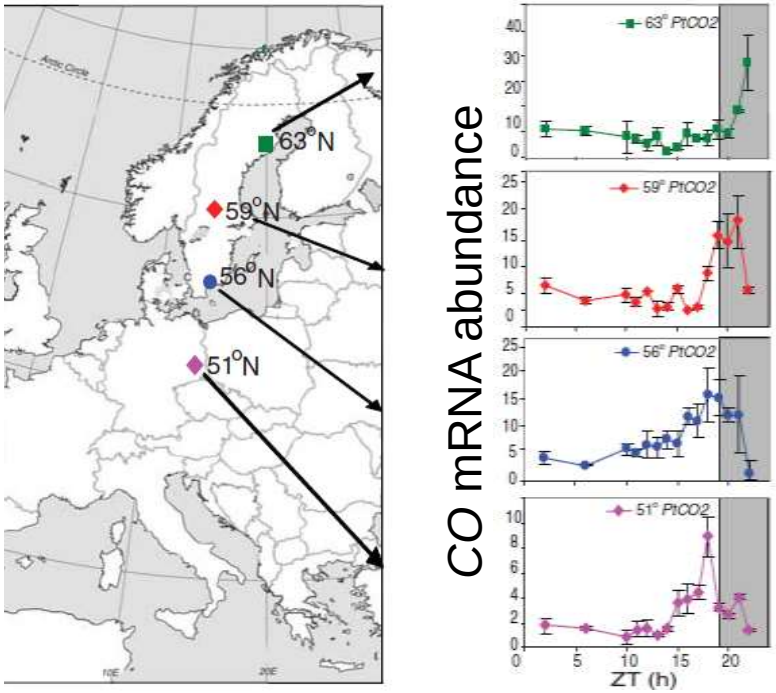
Funding: BBSRC, EU, EPSRC, HFSP

Phase matters



Dodd *et al.*
Science 2005

Critical day length in aspen trees

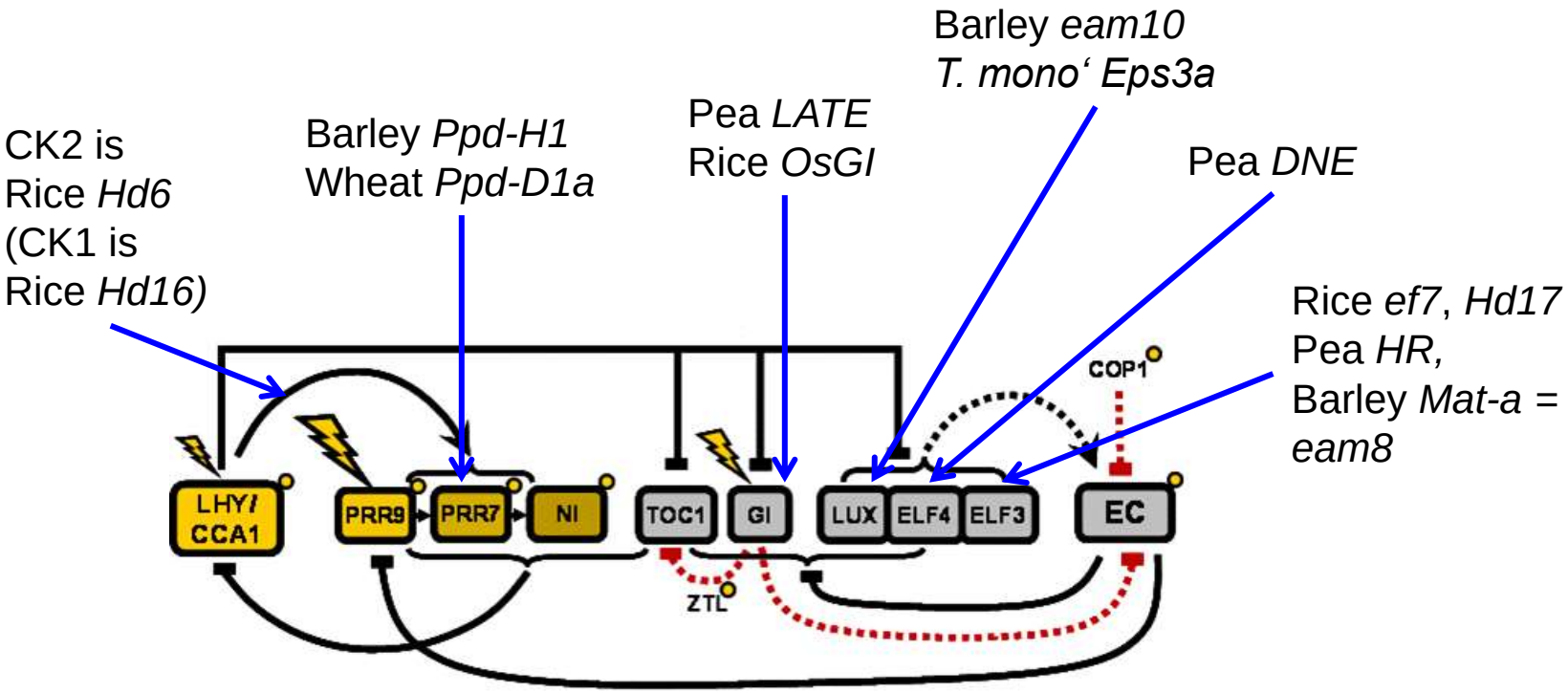


Bohlenius *et al.* Science 2006

- Altering the day/night cycle changes the peak times = *phase*
- Correct phase optimises growth and seasonal development

A.t. Clock Genes in Crops

- Regulation of photoperiodic flowering

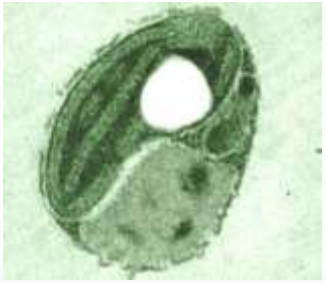


- Also many flowering-specific genes, like *Arabidopsis CO, FT.*

Schema from Pokhilko et al., Molecular Systems Biology 8:574 (2012)

Multiscale models – plant biology

- ‘Crop-style’ growth model for *A.t*.
- A tool to reconcile and understand *conditional,* pleiotropic (dynamic, quantitative) phenotypes.



Genomics

Phenomics

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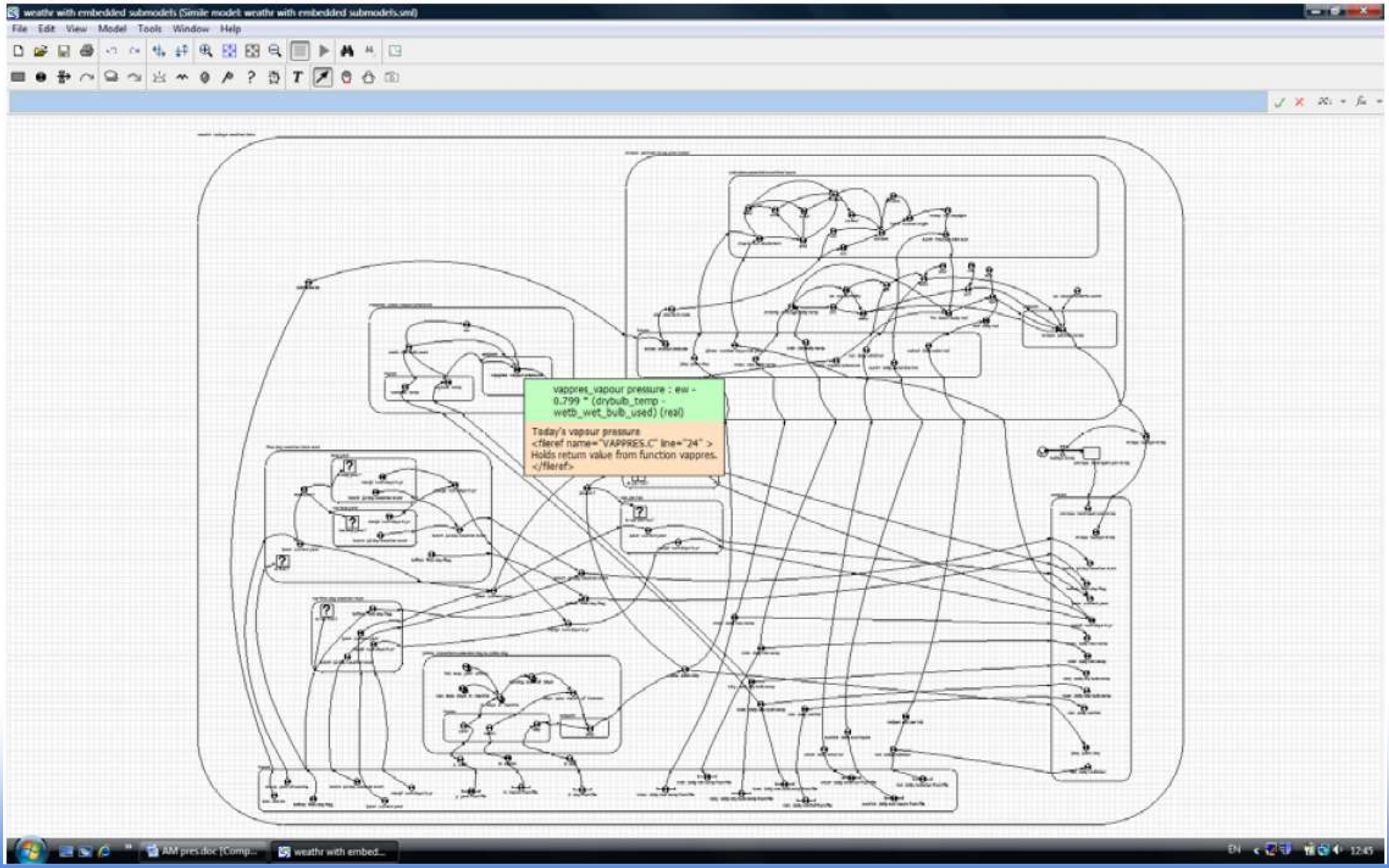
Collate models, in Simile software



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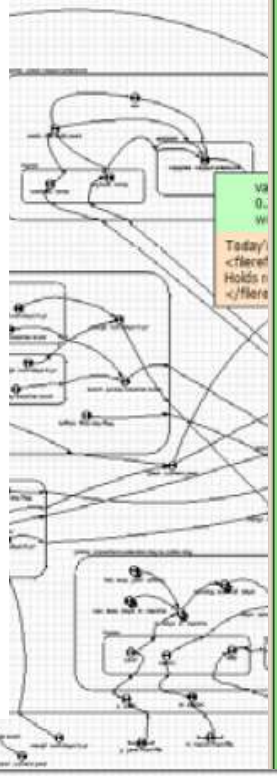
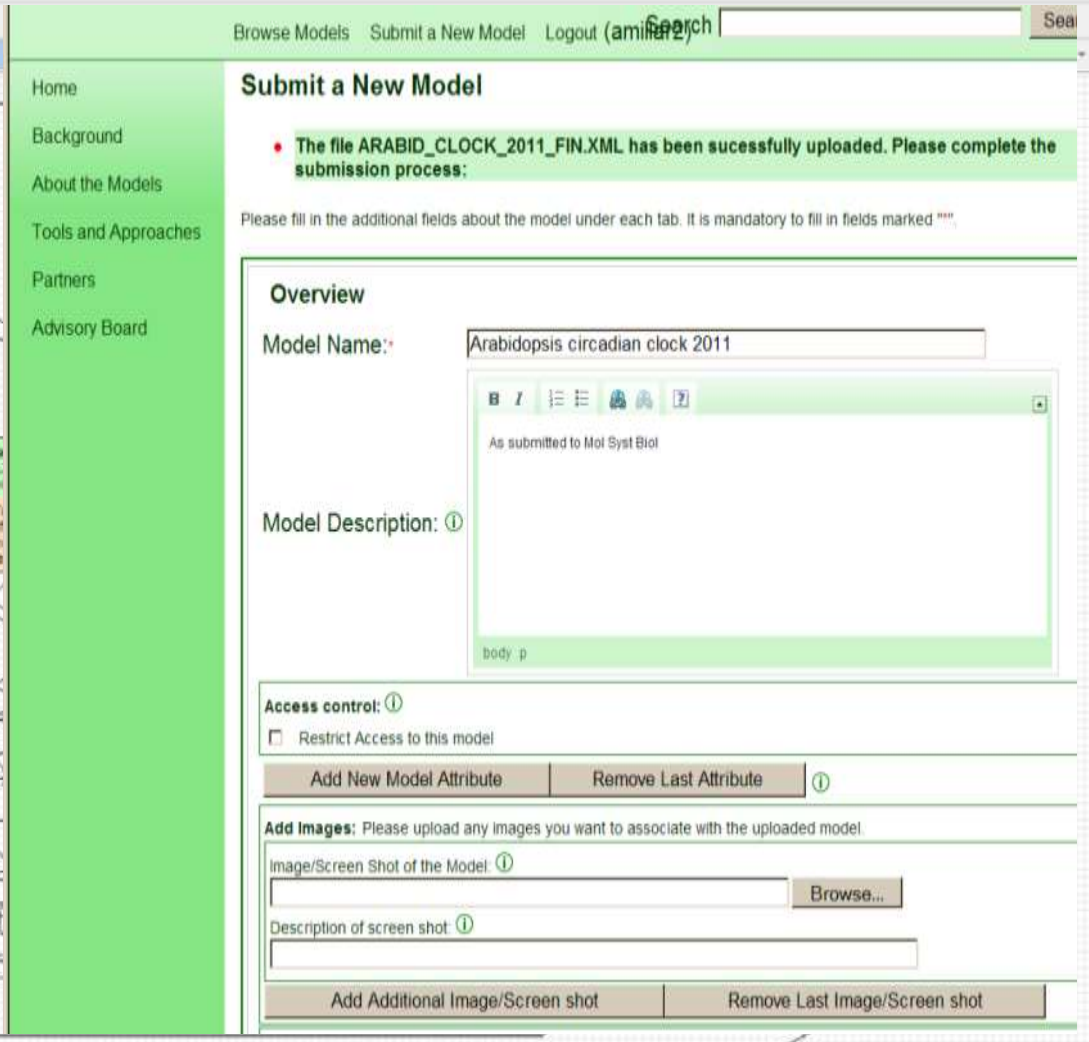
www.plasmo.ed.ac.uk

(Private) model database

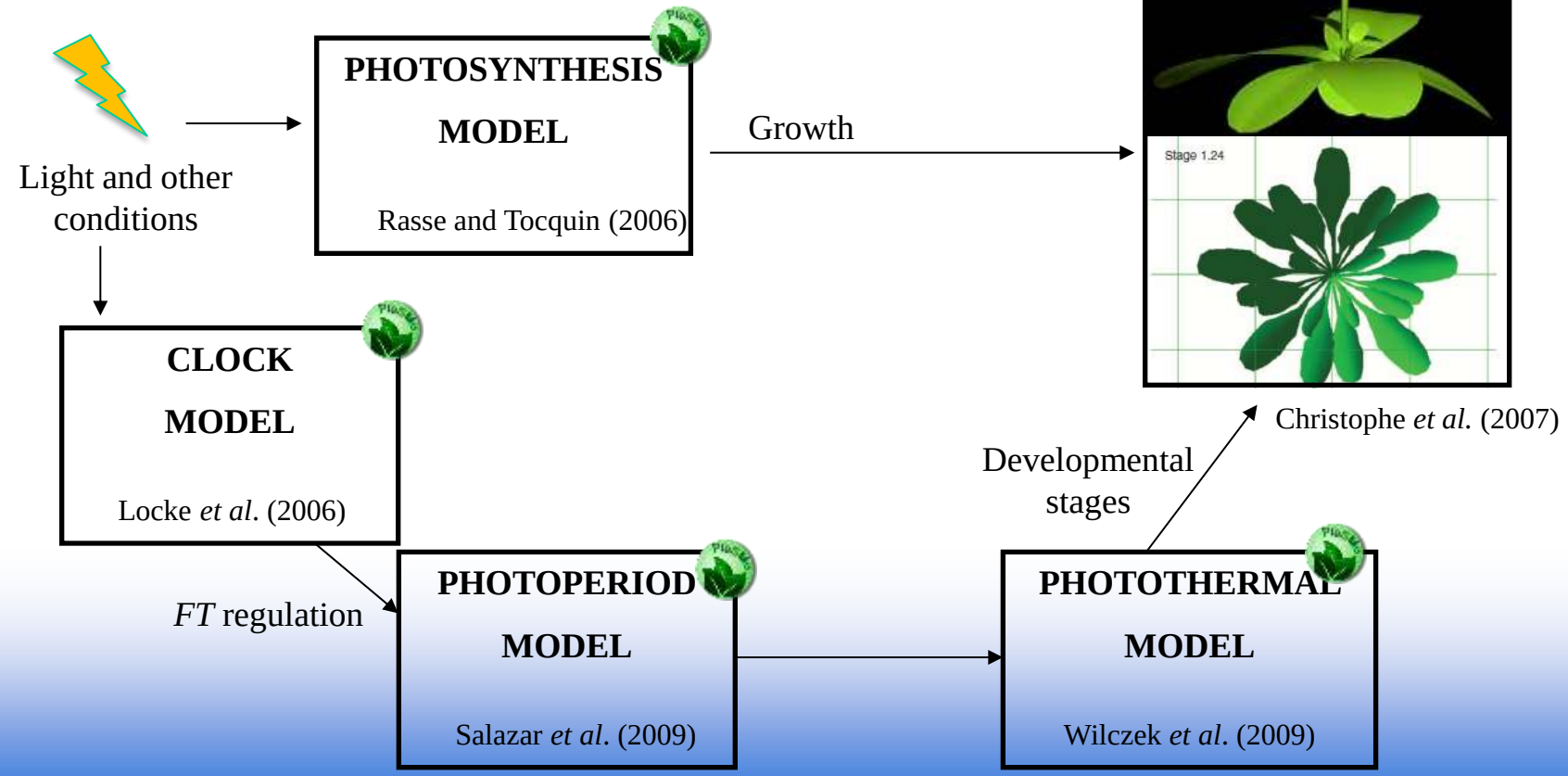
SBML
SimileXML
XGMML
(Cytoscape)
SBGN-ML
…





Modular models?

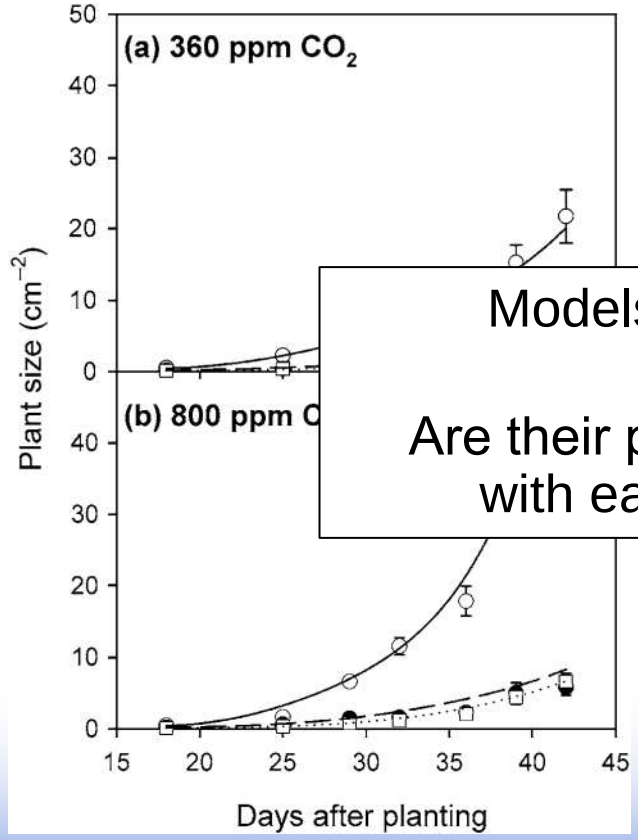
- 'Crop-style' growth model for Arabidopsis
- Q: can we build from existing models?
  - ➢ simple at first; experts (you) can add detail
- A: only if they are comparable!



Comparing models

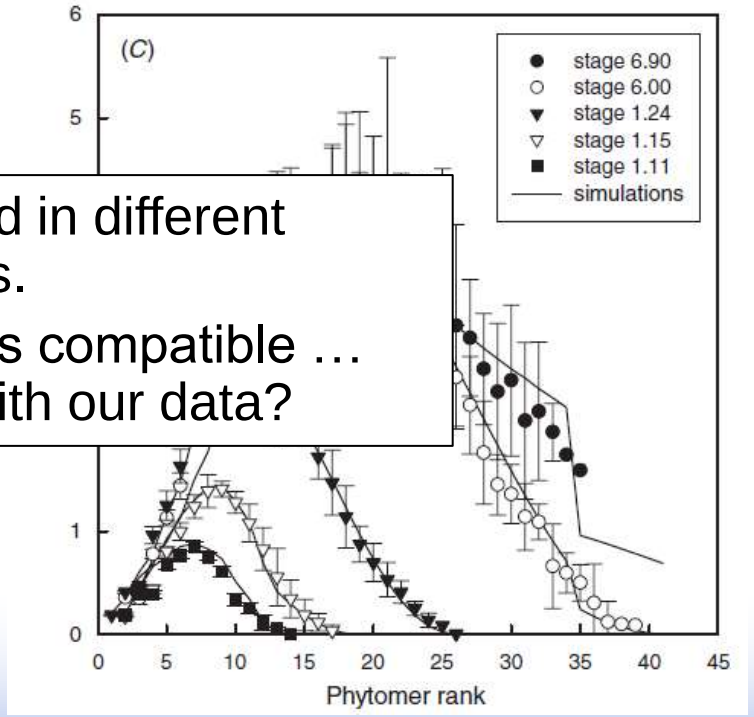
- Total leaf area from Rasse & Tocquin
- Predicts carbon biomass.
- Model runs in time.

- Individual leaf areas from Greenlab
- Predicts total biomass.
- Model runs in developmental stages.



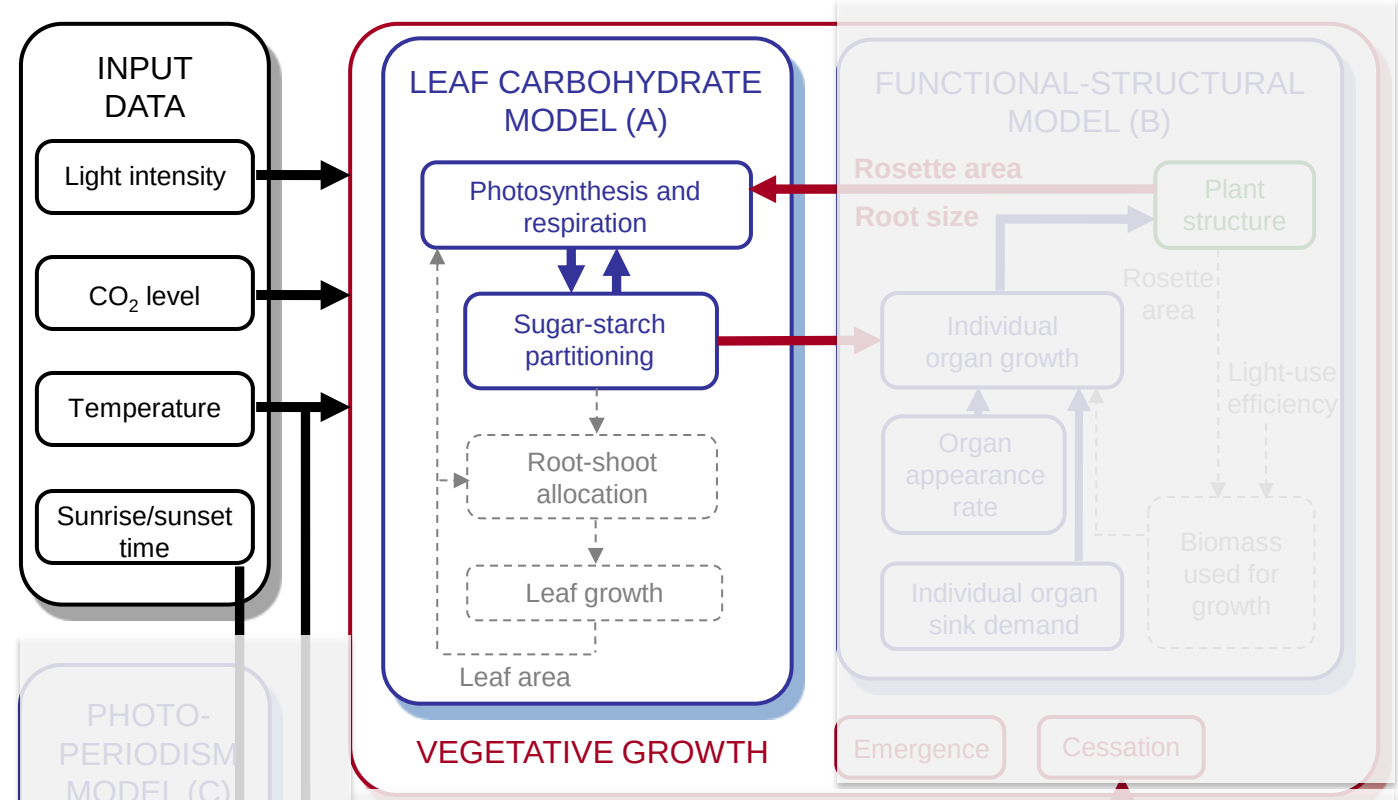
Models were calibrated in different laboratories.

Are their parameter values compatible … with each other, and with our data?



Yin-Hoon Chew *et al.* PNAS 2014

Framework Model



Blue – original
Red – new links
Grey – replaced

Research

New Phytologist

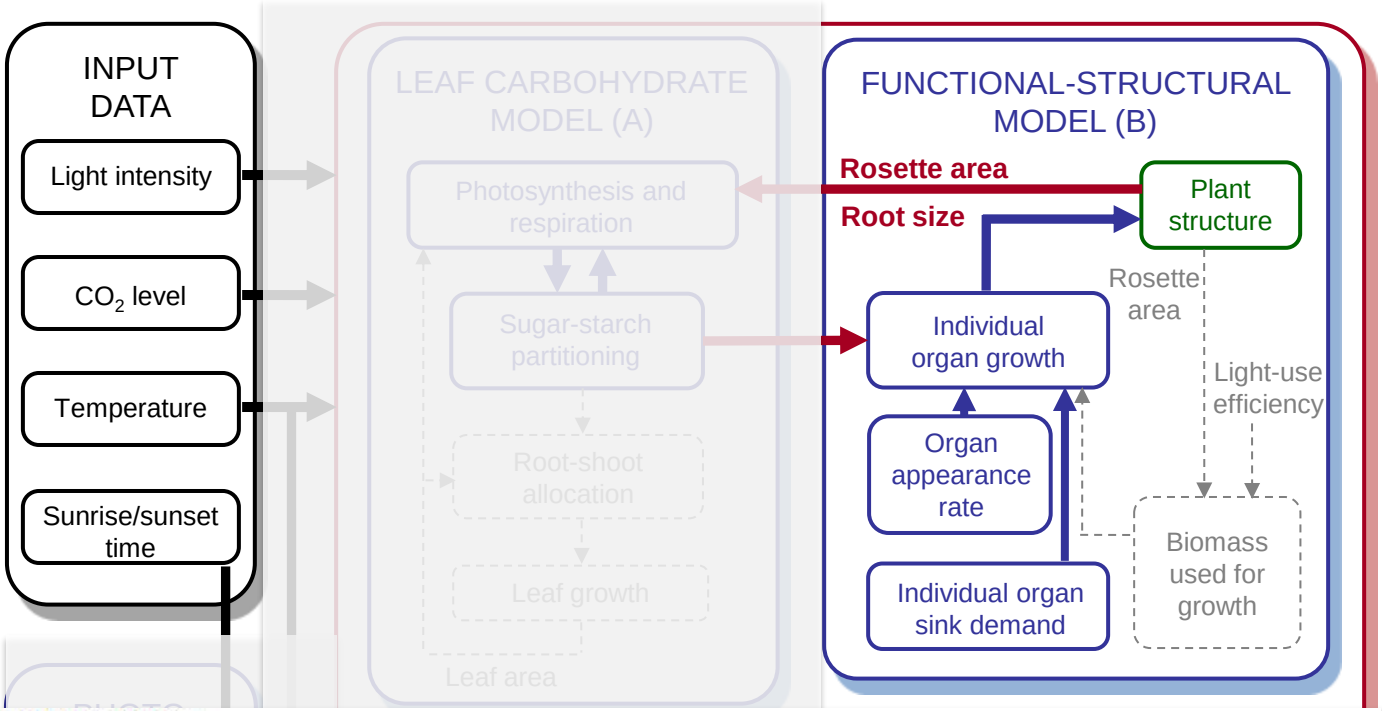
Leaf carbohydrate controls over *Arabidopsis* growth and response to elevated CO_2: an experimentally based model

Daniel P. Rasse[1,2] and Pierre Tocquin[3]

Matlab and Simile software.

Chew *et al.*
PNAS 2014

Framework Model



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CSIRO PUBLISHING
www.publish.csiro.au/journals/fpb
Functional Plant Biology, 2008,

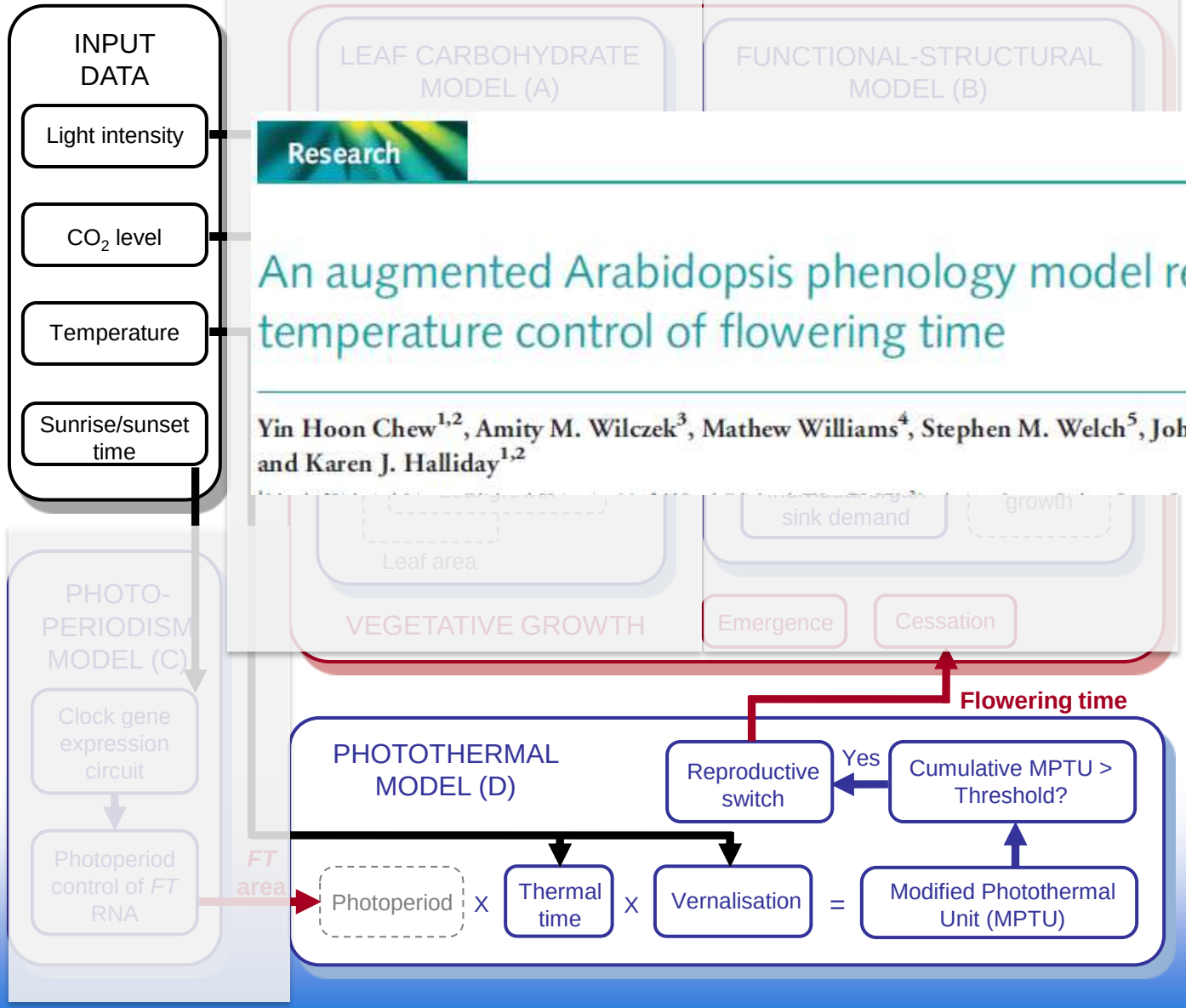
A model-based analysis of the dynamics of carbon balance at the whole-plant level in *Arabidopsis thaliana*

Angélique Christophe[A,E], *Véronique Letort*[B], *Irène Hummel*[A], *Paul-Henry Cournède*[B], *Philippe de Reffye*[C] and *Jérémie Lecœur*[D]

Matlab and Simile software.

Chew *et al.*
PNAS 2014

Framework Model



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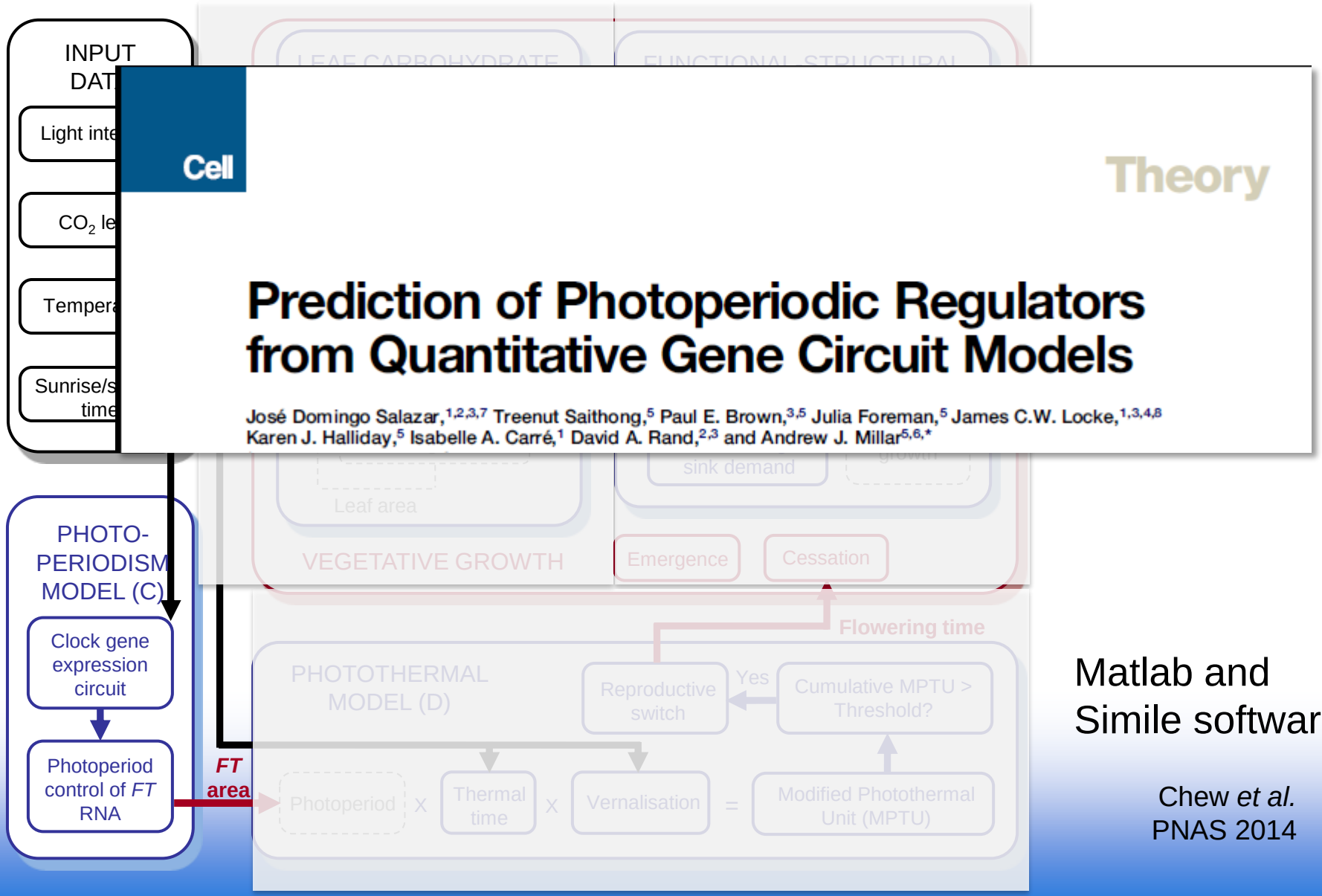
Chew *et al.* PNAS 2014

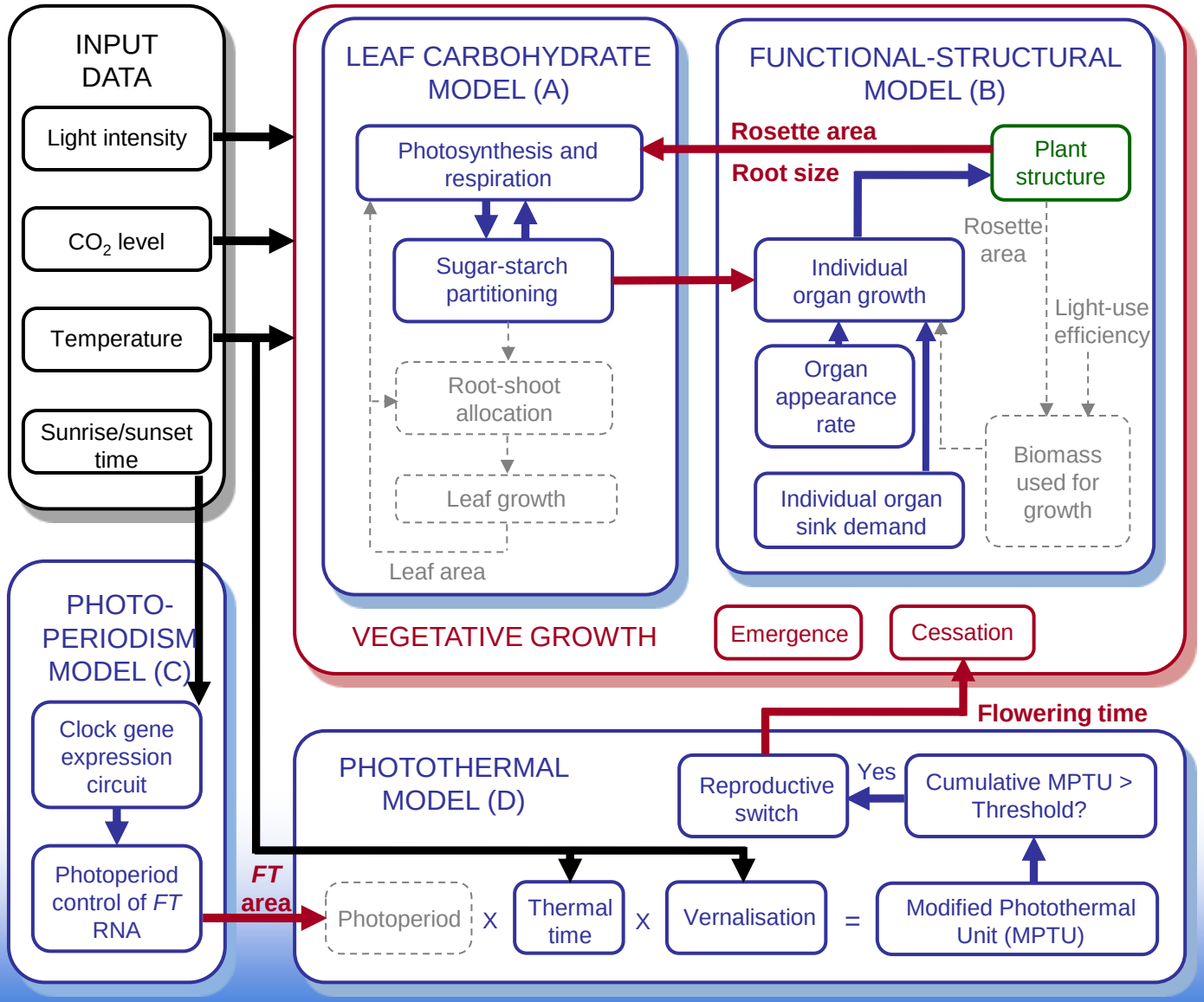
Framework Model



Matlab and Simile software.

Chew *et al.*
PNAS 2014

Framework Model



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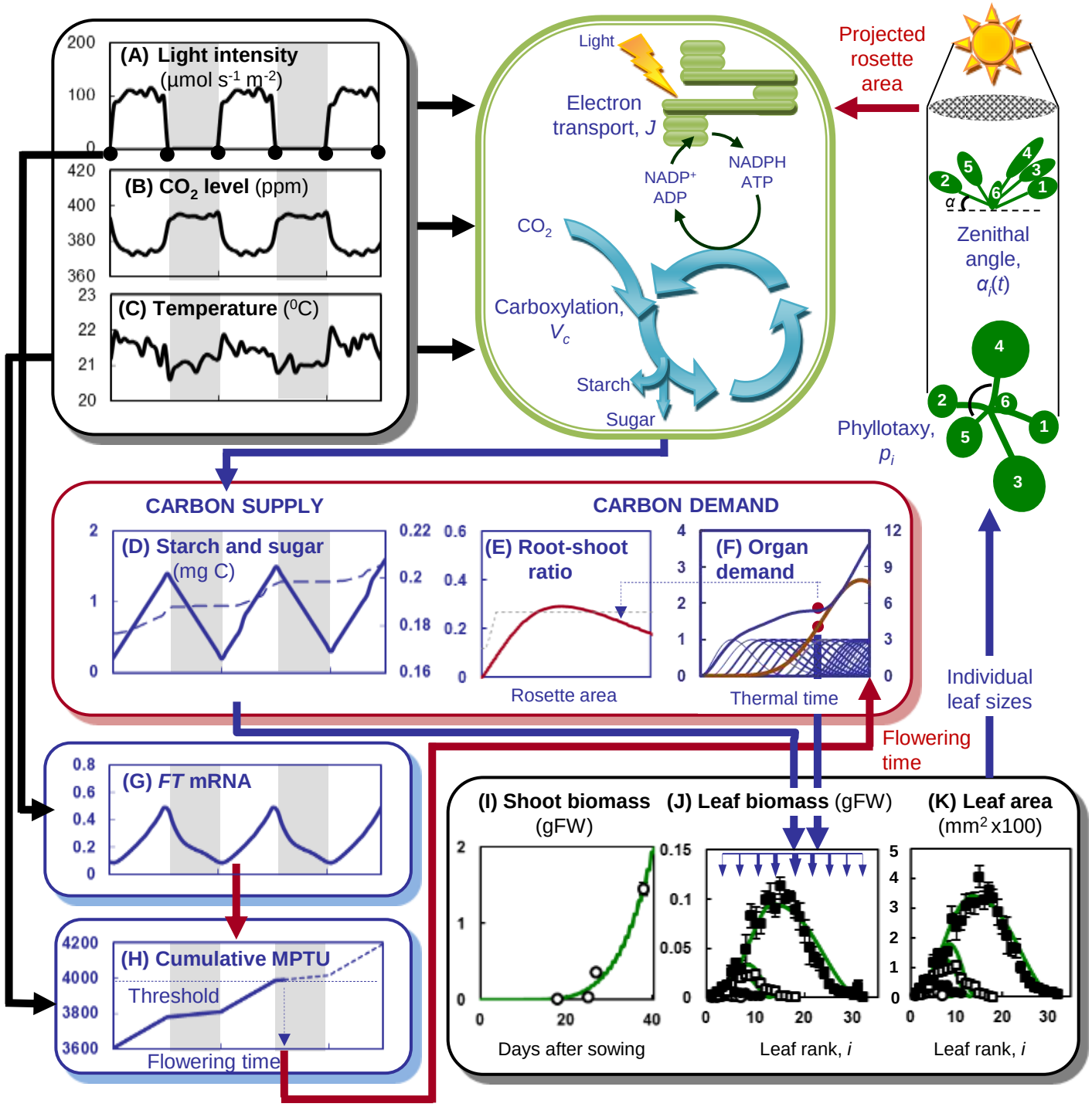
Matlab and Simile software.



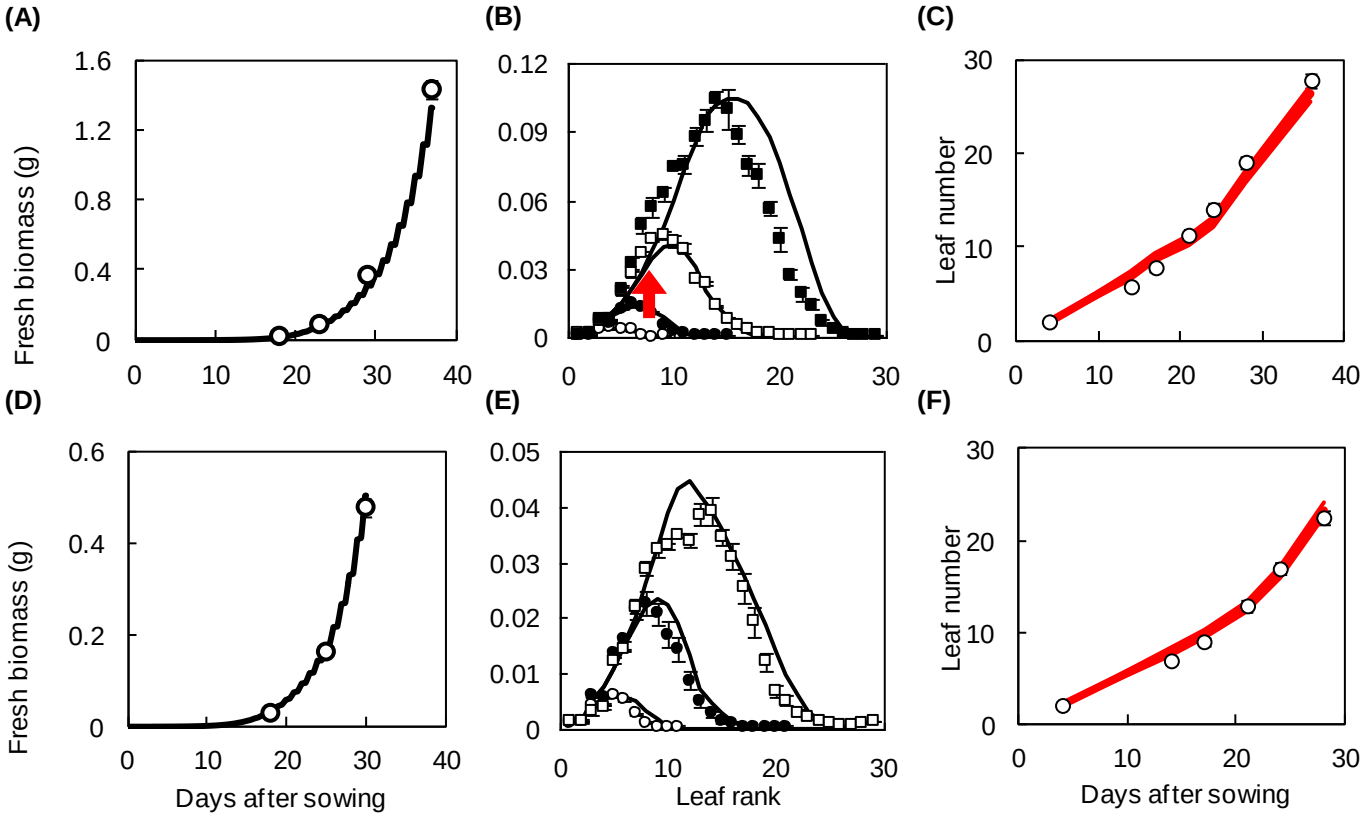
- Minimal changes to link models

(units; flowering)

- Compatible!

- Validation: Col rosette, 12L:12D.

Testing on other accessions



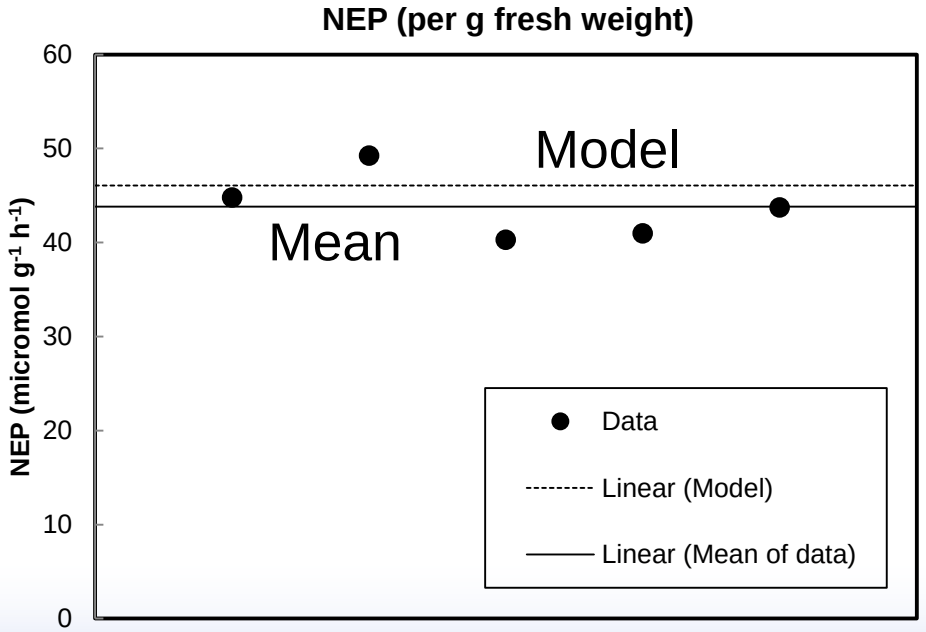
- La(*er*) leaves 5-9 grow for longer (red arrow)
- Good performance without re-calibration, also other labs? Median R^2 0.94, nRMSE 17% (as good as Col).

Key processes match well

- Parameter sensitivity analysis: what controls biomass?

126 parameters in total; 8 of the 12 most sensitive parameters are in photosynthesis model.

- Gas exchange measures for photosynthesis
- Good match *in reference conditions.*



Col WT on Day 38

Testing: altered leaf initiation

Col

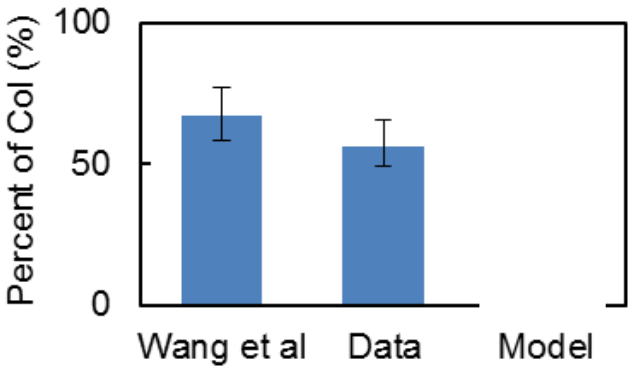
Pro35S:MIR156

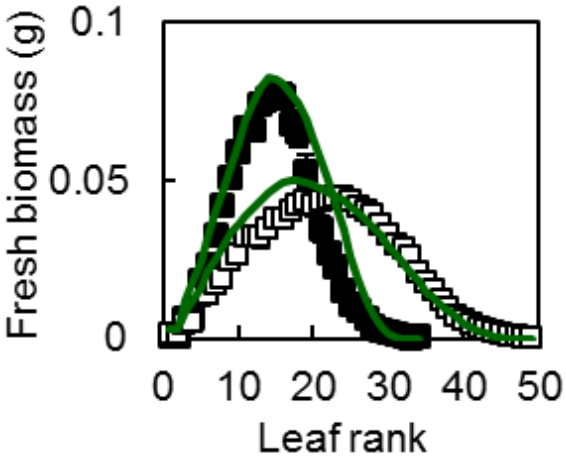
The Plant Cell, Vol. 20: 1231–1243, May 2008, www.plantcell.org © 2008 American Society of Plant Biologists

Dual Effects of miR156-Targeted *SPL* Genes and *CYP78A5/KLUH* on Plastochron Length and Organ Size in *Arabidopsis thaliana* W OA

Jia-Wei Wang, Rebecca Schwab,[1] Benjamin Czech,[1] Erica Mica,[2] and Detlef Weigel[3]
Department of Molecular Biology, Max Planck Institute for Developmental Biology, D-72076 Tübingen, Germany

- Increased leaf initiation rate and small leaves
  - One causal effect + 'compensatory regulation" or two separate mechanisms ?
- Change *only* initiation, test simulated area...





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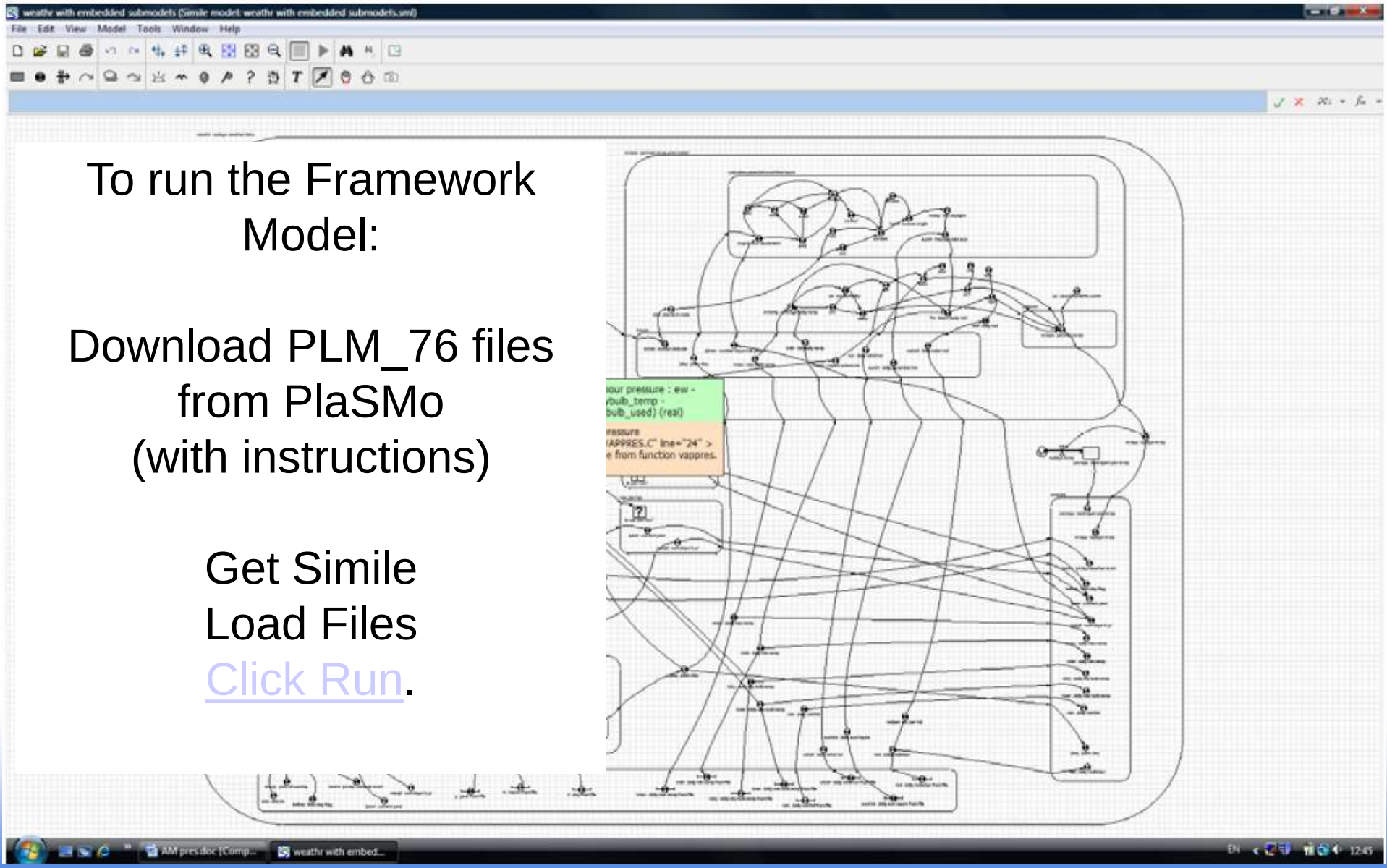
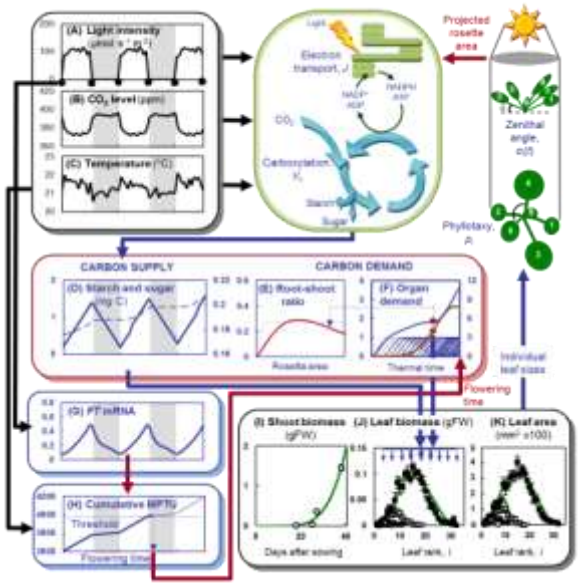


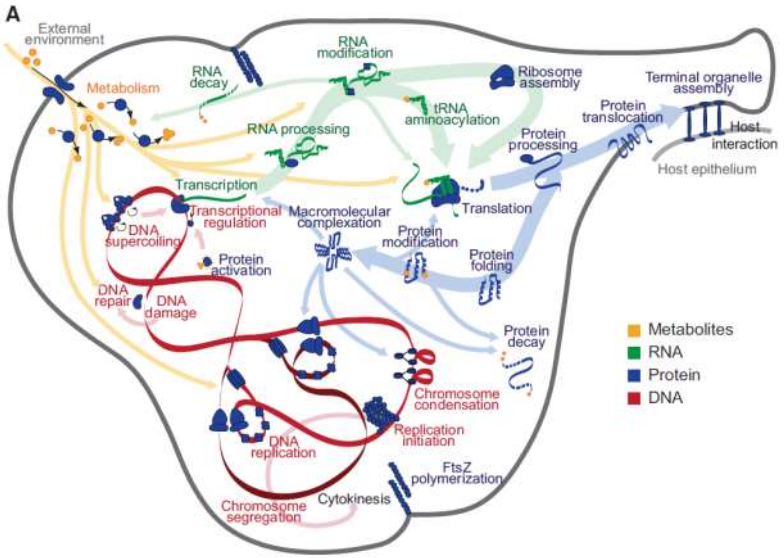
To run the Framework Model:

Download PLM_76 files from PlaSMo (with instructions)

Get Simile
Load Files
Click Run.

A Framework around the Clock





- Multiple clock effects, interacting, to give whole-plant phenotype: links to multiple research fields.
  - Quantitative molecular detail, linked to genome: ☑
  - Effective concepts, linked to physiology: ☑
- “Digital Organism” technology to link models
  - e.g. Karr et al. Cell 2012, ‘whole-cell’ Mycoplasma model.

Summary

- Systems Biology aims to understand (explain and predict) complex processes
  - All components; Across scales.
- Framework model predicts Arabidopsis growth
  - combination of existing models: only in *A.t.* ?
  - disparate data (and derived models) were compatible for biomass, less so for flowering.
  - now integrating multiple clock effects on growth.
- A primitive “Digital Organism”, to be extended.
  - How should we do this, as a community?