Plantes numériques : accélérer la sélection variétale et le développement de biosolutions

- Peyraud Rémi -

iMEAN
Life engineering using digital organisms

The team

Baudoin Delépine

iMEAN

Life engineering using digital organisms

Founded in 2018

INRAE

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www.imean-biotech.com

CONTEXT

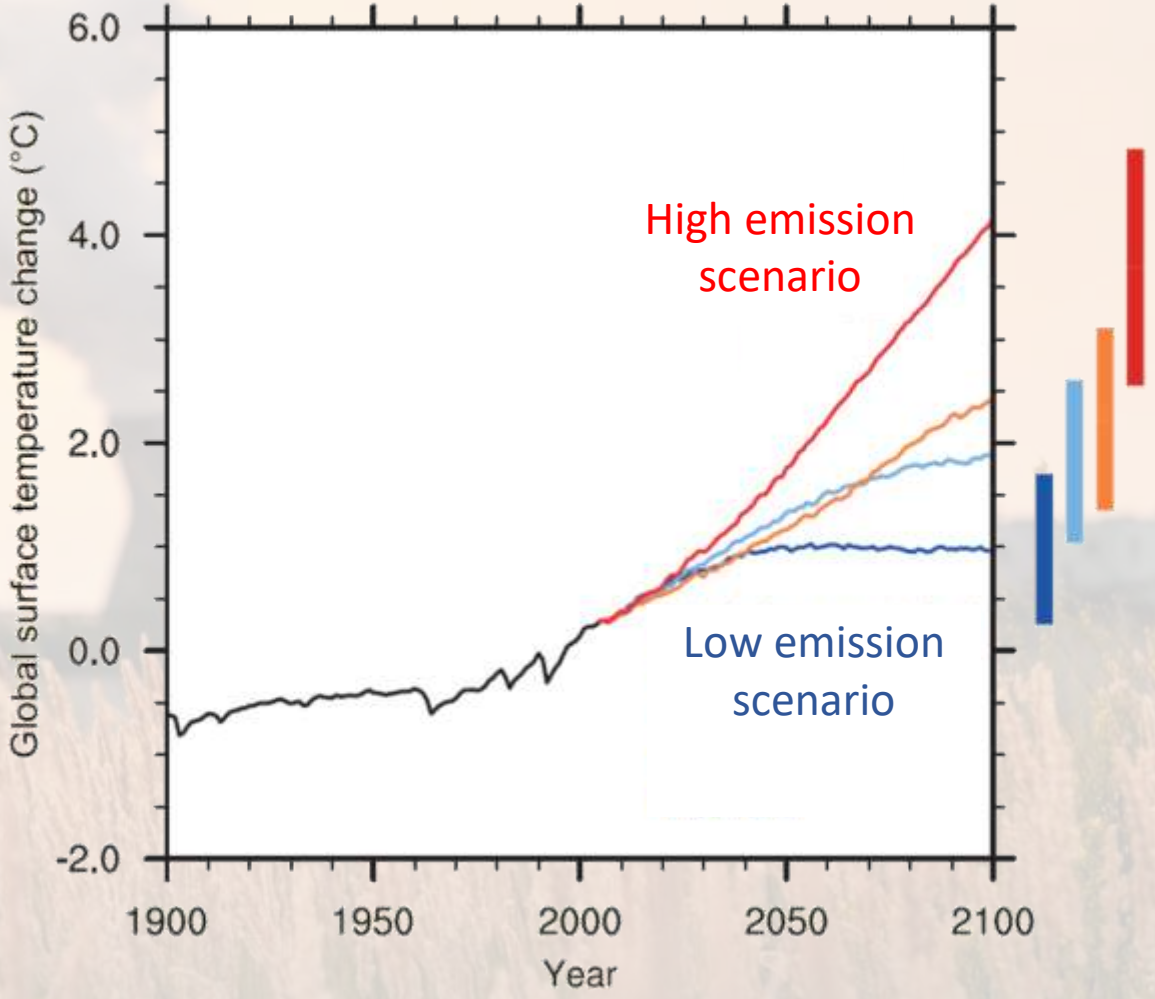
WHY MODELING PLANT

PLANT AND MICROBES MODELING

DESIGN CROP BREEDING

DESIGN MICROBIAL COMMUNITIES

GLOBAL WARMING



IPCC report

Food productivity

Sustainable agriculture

increasing food productivity, the most impactful option for mitigation, adaptation, combating desertification and land degradation, and enhancing food security.

IPCC

«**540 billion $ per year** if spread of **invasive pests and pathogens** is not stopped »

State of the World’s Plants

How to find solutions, NOW?

Scenario 1. We accelerate game breaking discoveries?

Scenario 2. We mobilize all the knowledge we already have?

Knowledge

Mathematical predictor of plant performance

Accelerate discovery

Engineering agroecosystems

Wise decision making

CONTEXT

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DESIGN CROP BREEDING

DESIGN MICROBIAL COMMUNITIES

NATURE

Ressources

R&D Process

Industrial
Microbiology

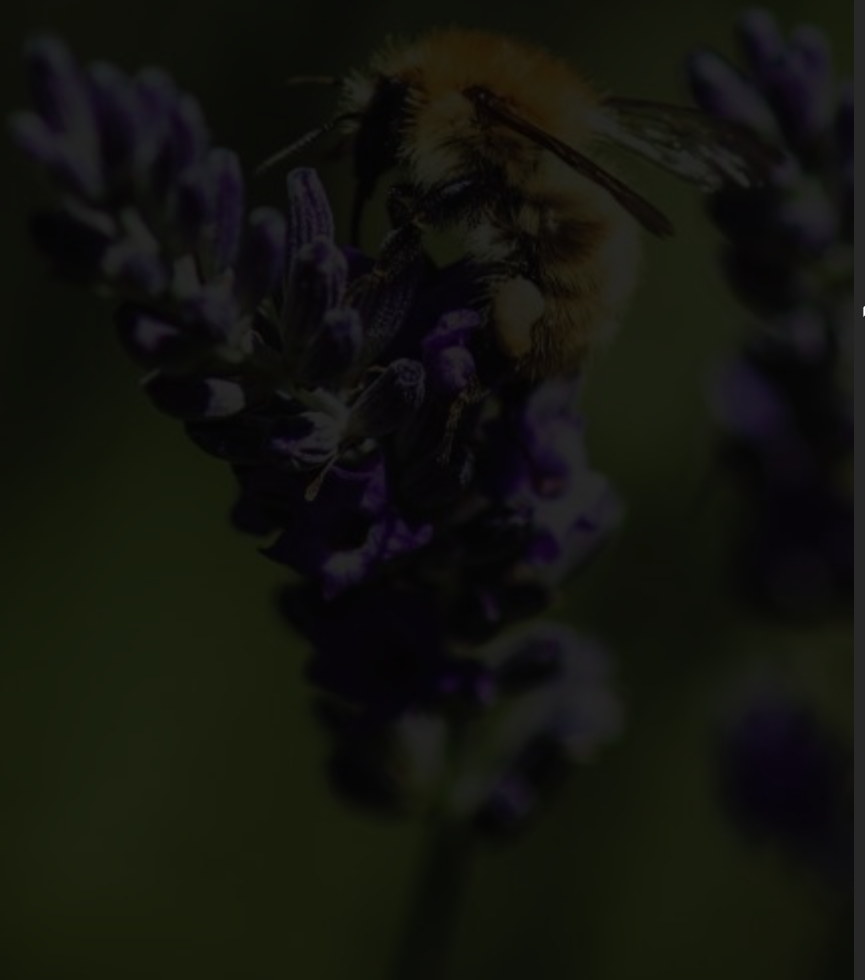
Crops

NEEDS

Chemicals
Food
Biotransformation

NATURE

Ressources



R&D Process

Time to market

~10 years

Industrial Microbiology

Investment cost

~ 5M €/4Y -> up to 100M€

Failure rate

up to 85%

Crops

NEEDS

Chemicals
Food
Biotransformation

Life is complex

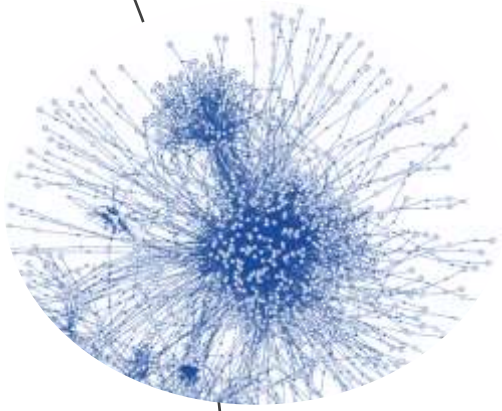
Living organisms functioning is a black box

Source of failure
Pain to find solutions

Life modelling

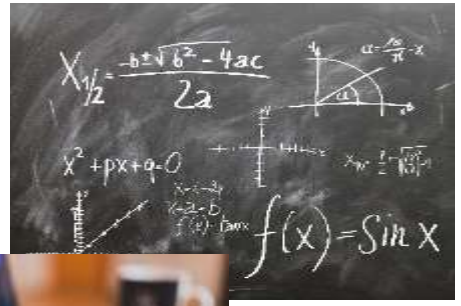
gene

Complex molecular networks



Phenotype

Mathematical modelling



Digital organism

Understanding

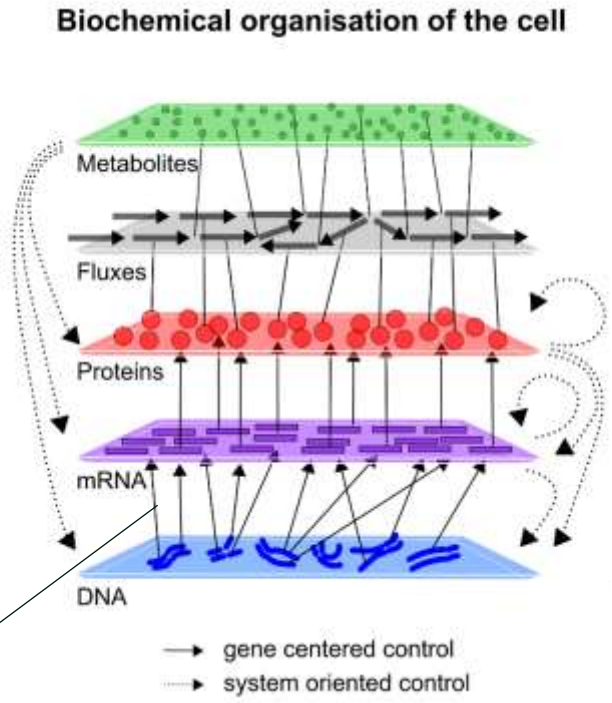
Engineering

Innovation

Life modelling

Inside the cell

Environment

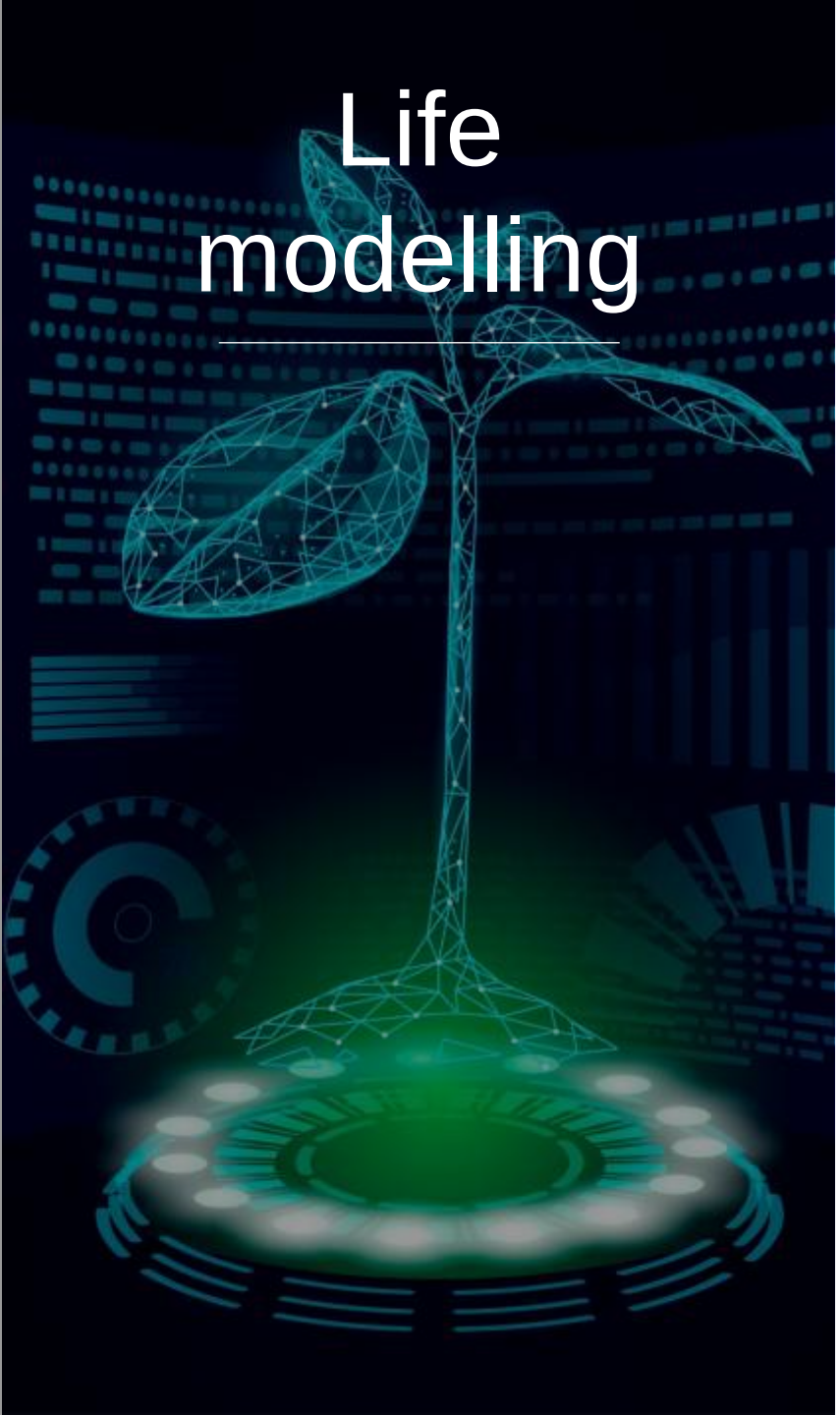


Phenotype

Causal relationship

Genotype

Peyraud *et al.* PlantJ 2017



Life modelling

Models based on causal mechanisms

- Physics laws
- Molecular makeup
- Biochemistry
- Cellular physiology
- Enzymology

State of the art scientific knowledge

High prediction capacity

Predict plant traits

Robustness to environmental changes

Yield

Resistance to pathogens

Predict interactions

Crops
Horticultures

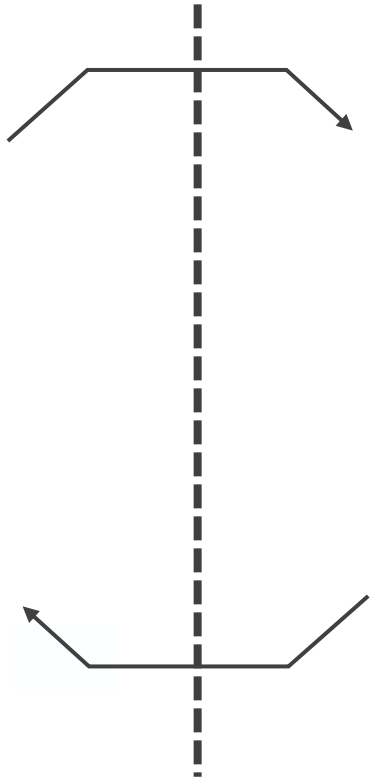
Environmental
microbes

Pathogens

In sillico experiments

Mathematical model reconstruction

Real organism



Digital organism

Complex molecular network

Prediction validation

Simulations

CONTEXT

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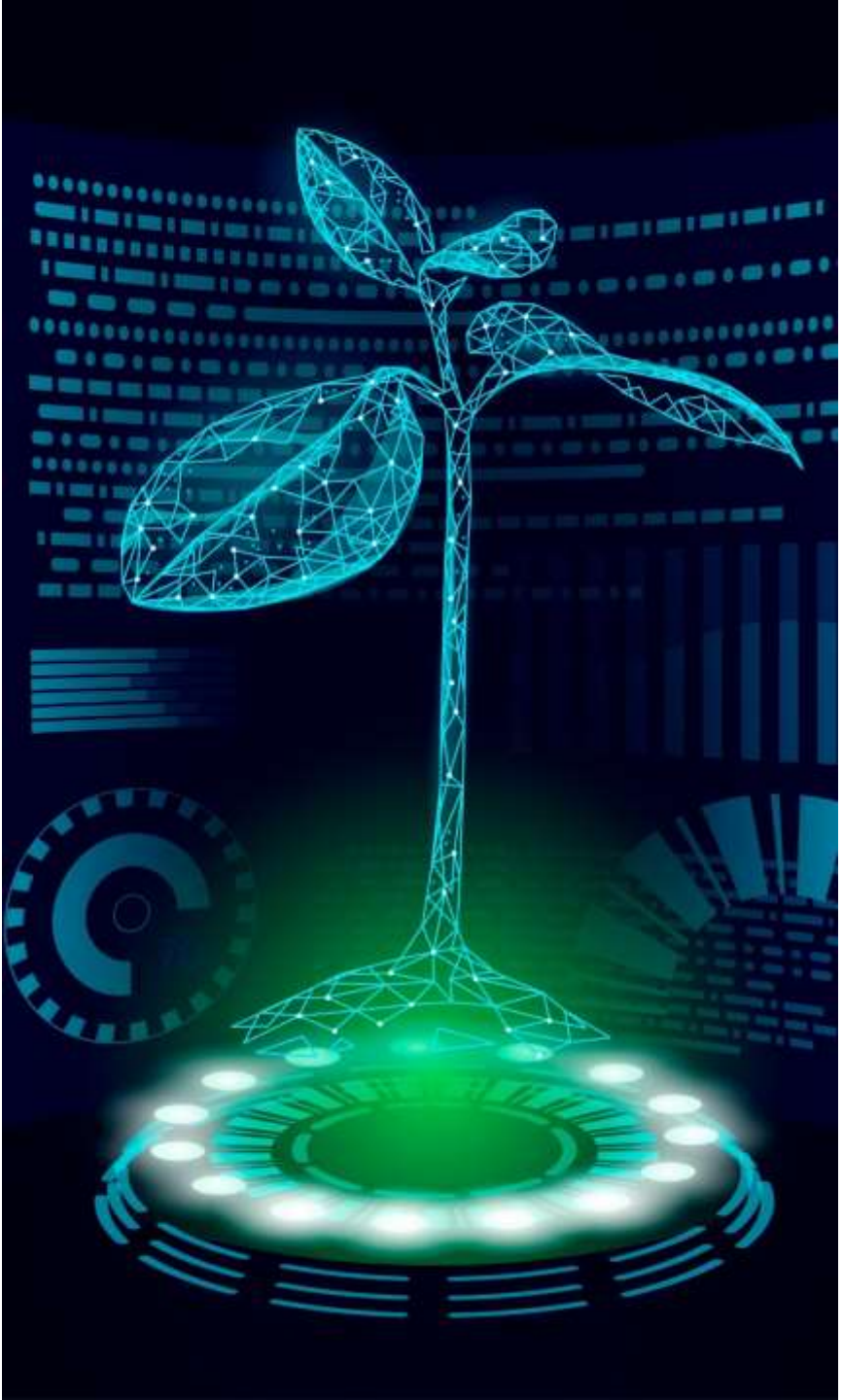
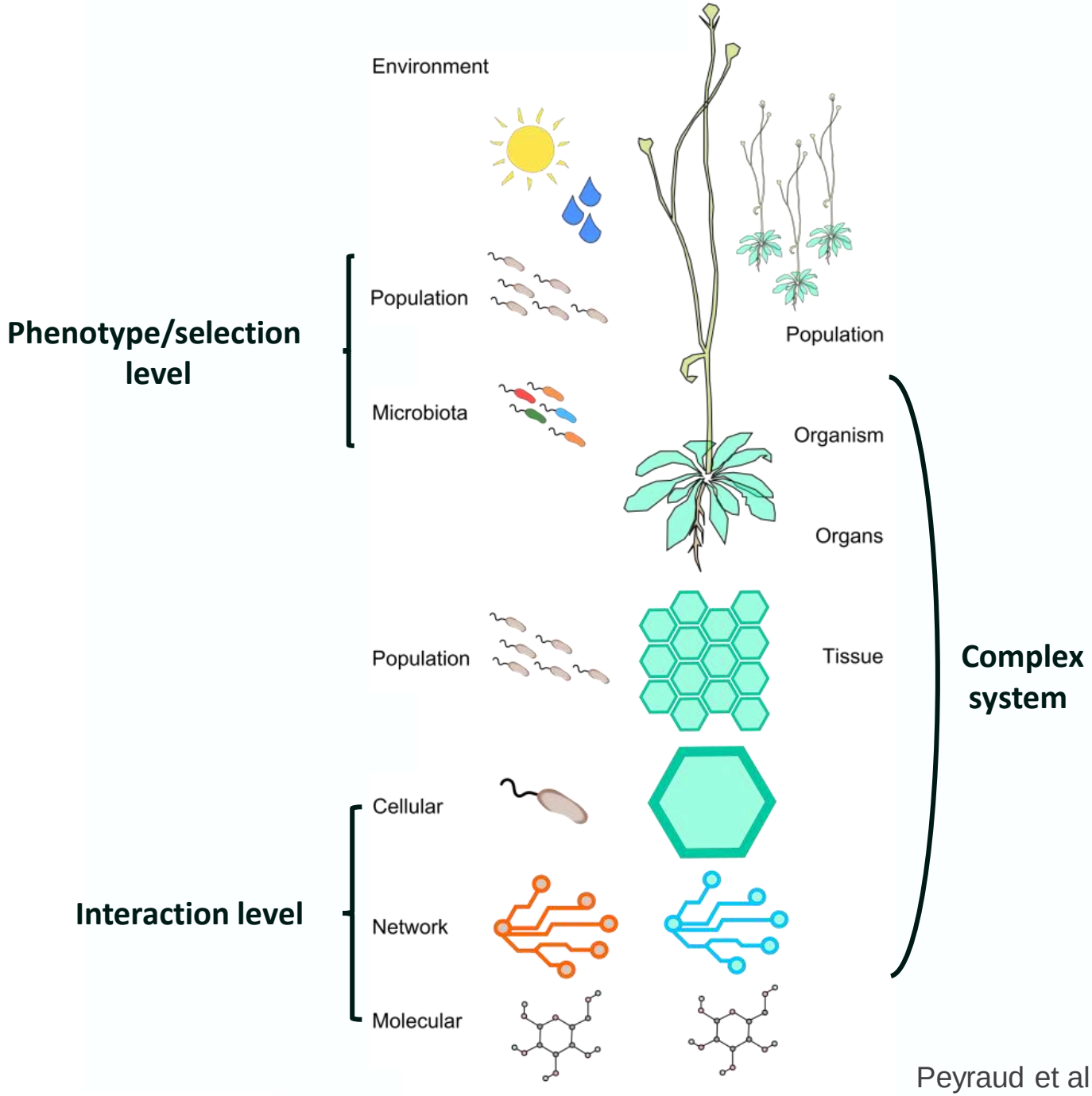
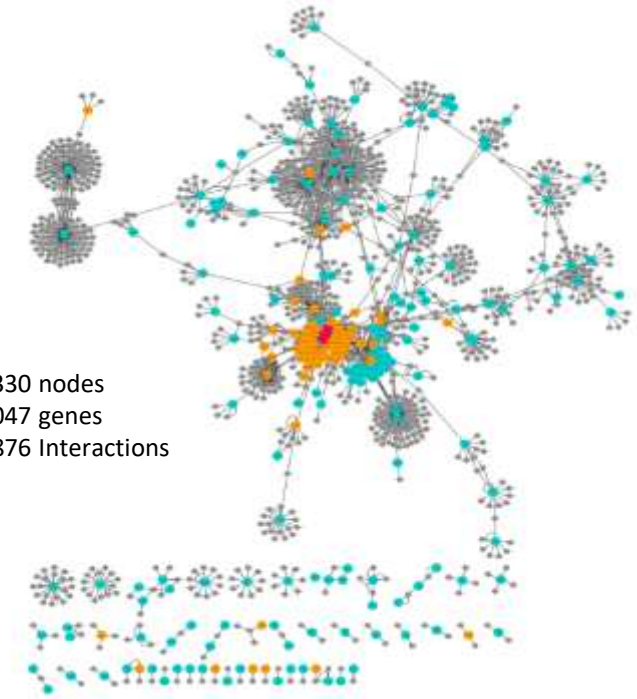




Peyraud et al. PlantJ 2017

The molecular level

Arabidopsis thaliana quantitative resistance



1330 nodes
1047 genes
1876 Interactions

Immune system network

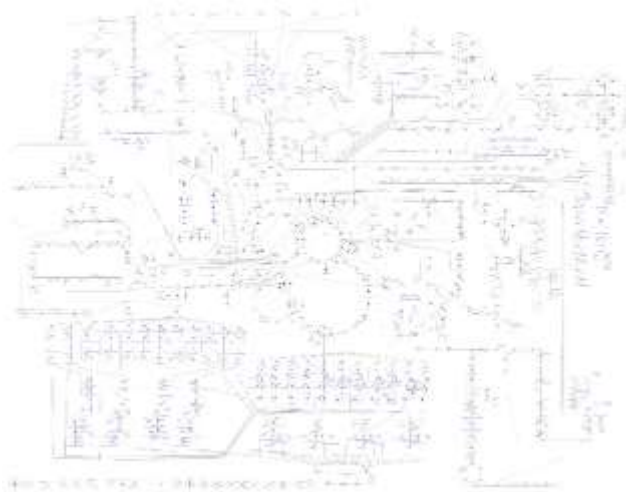
Delplace et al. in press PNAS 2020

Crops
Horticultures

Environmental microbes

Pathogens

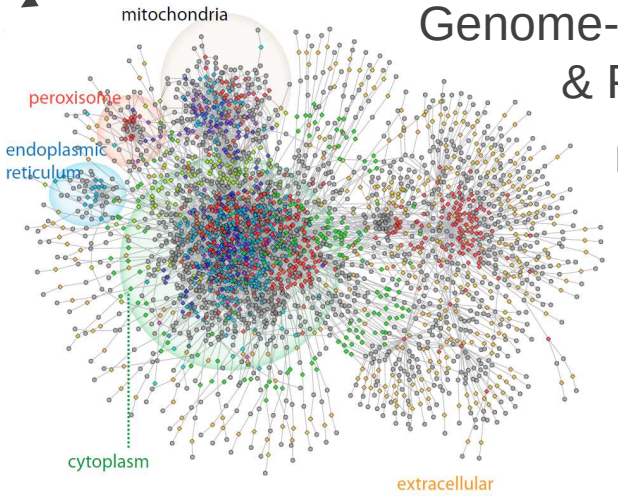
Methylobacterium extorquens



Genome-scale metabolic network

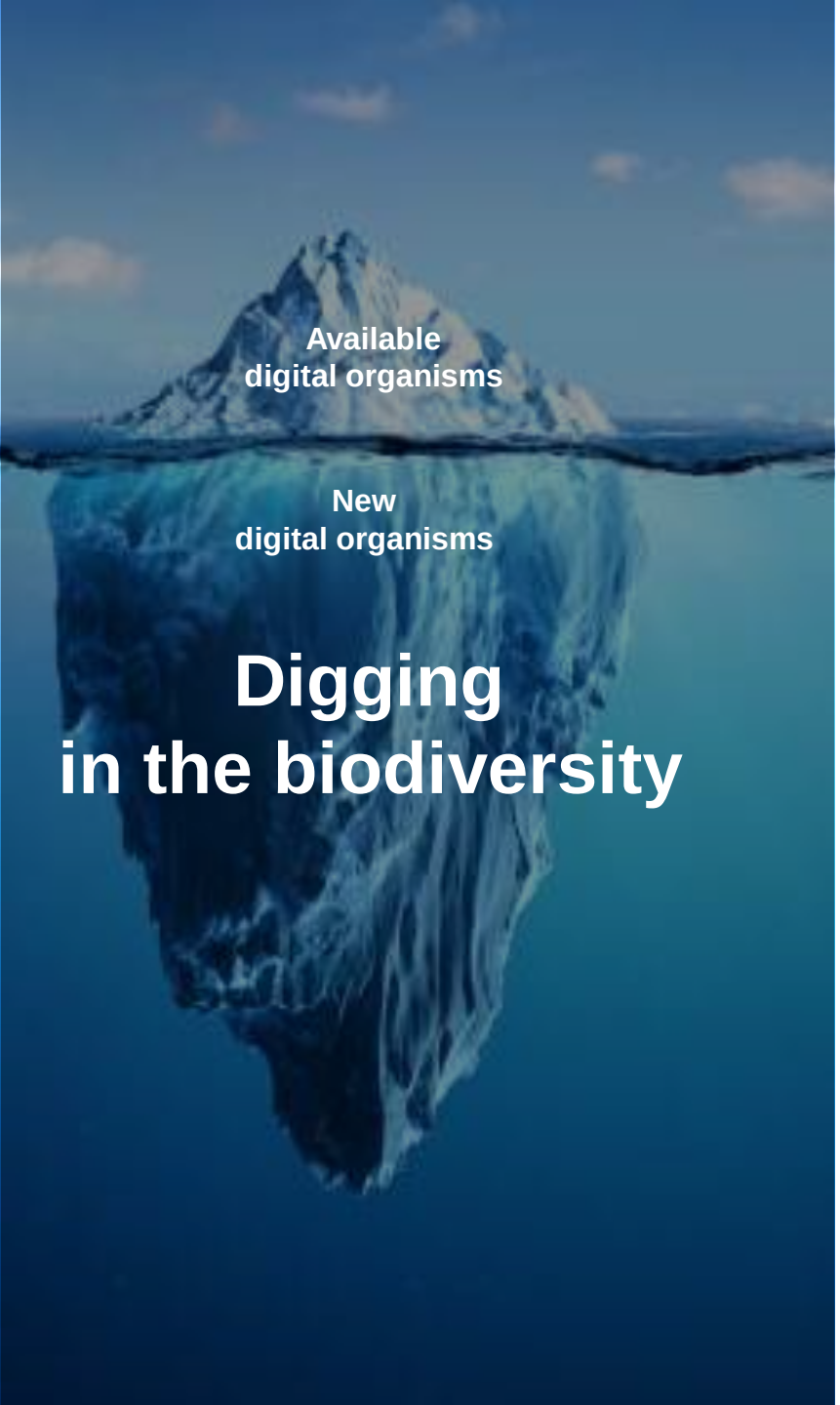
Peyraud *et al.* PNAS 2009
Peyraud et al. BMCsystbiol 2011

Sclerotinia sclerotiorum

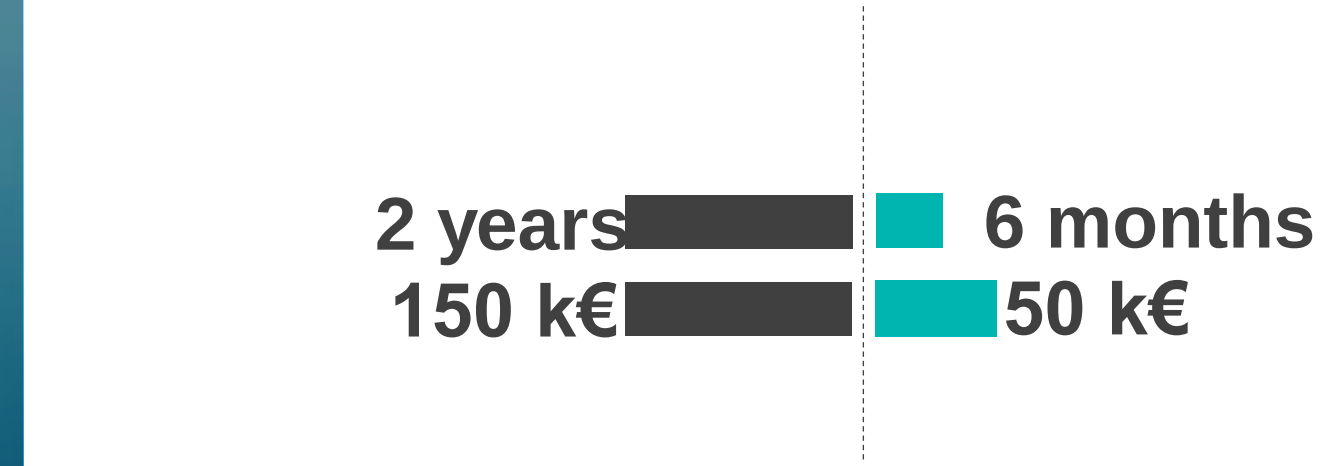


Genome-scale metabolic network & PCW degradation

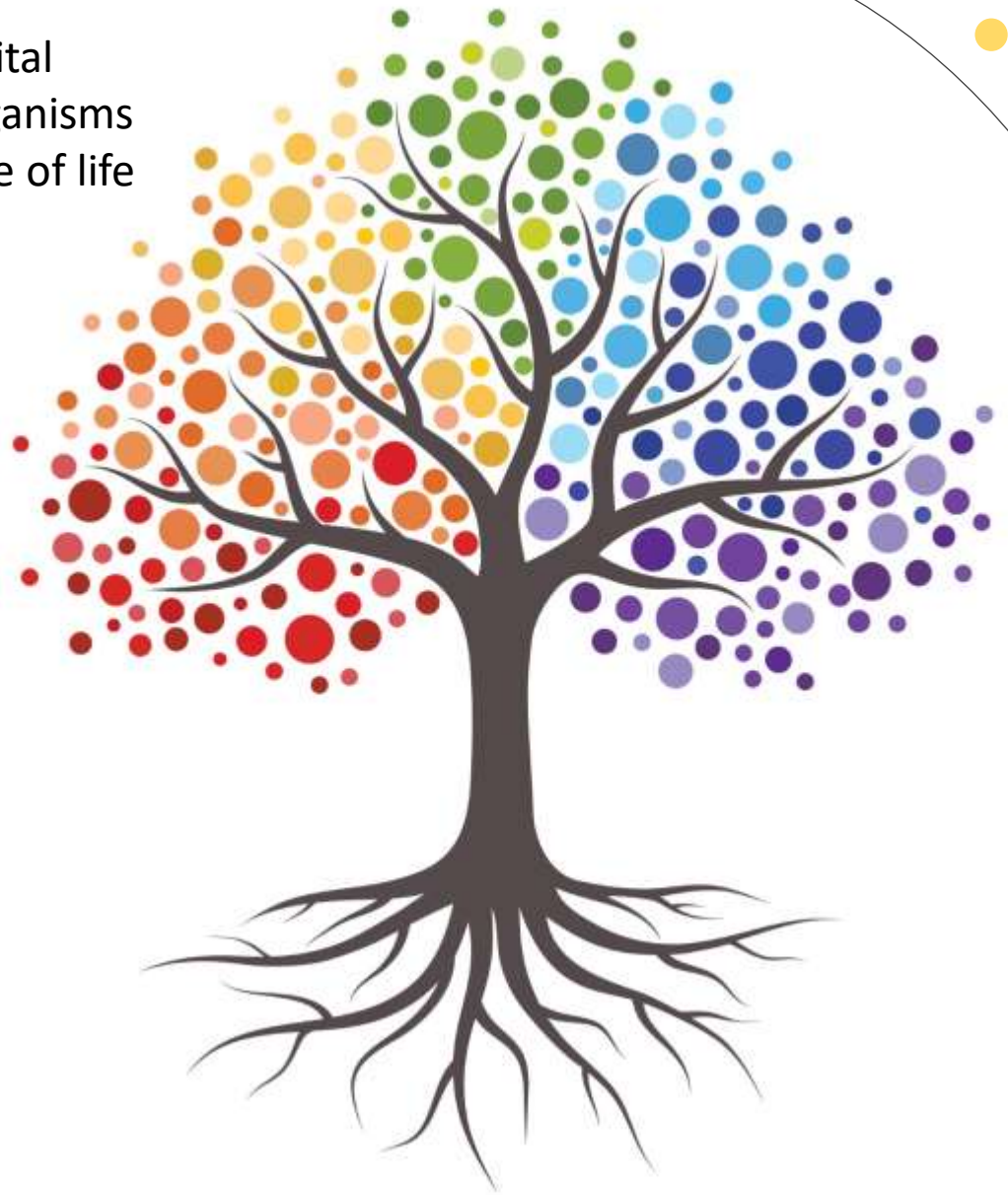
Peyraud *et al.* PNAS 2019



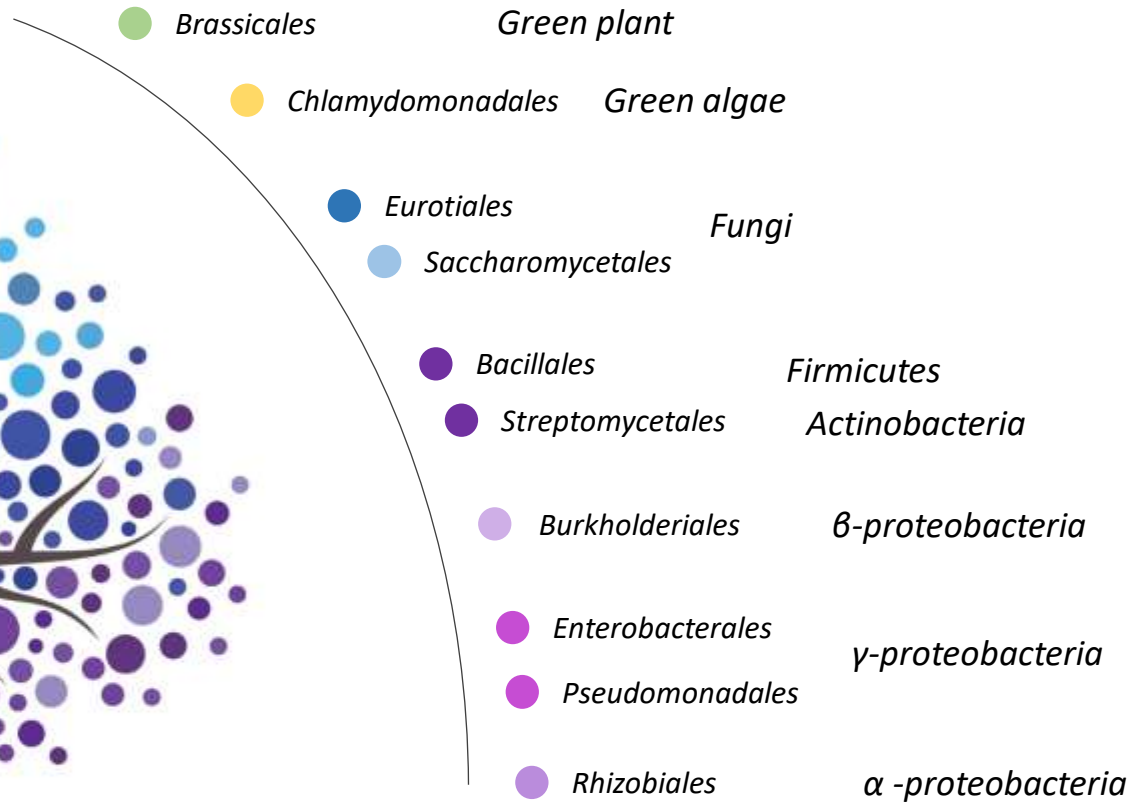
Cutting access price to the technology



Digital
Organisms
Tree of life



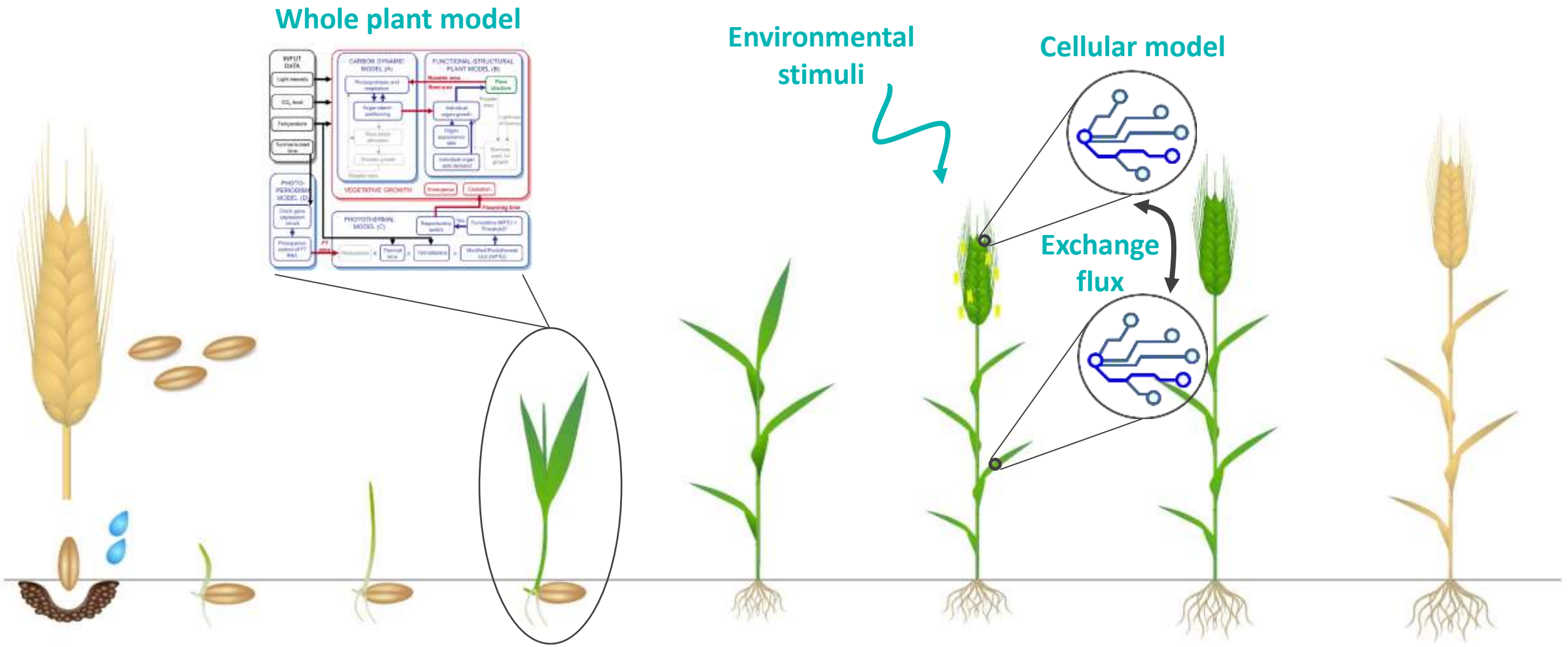
Gaïa - iMEAN database

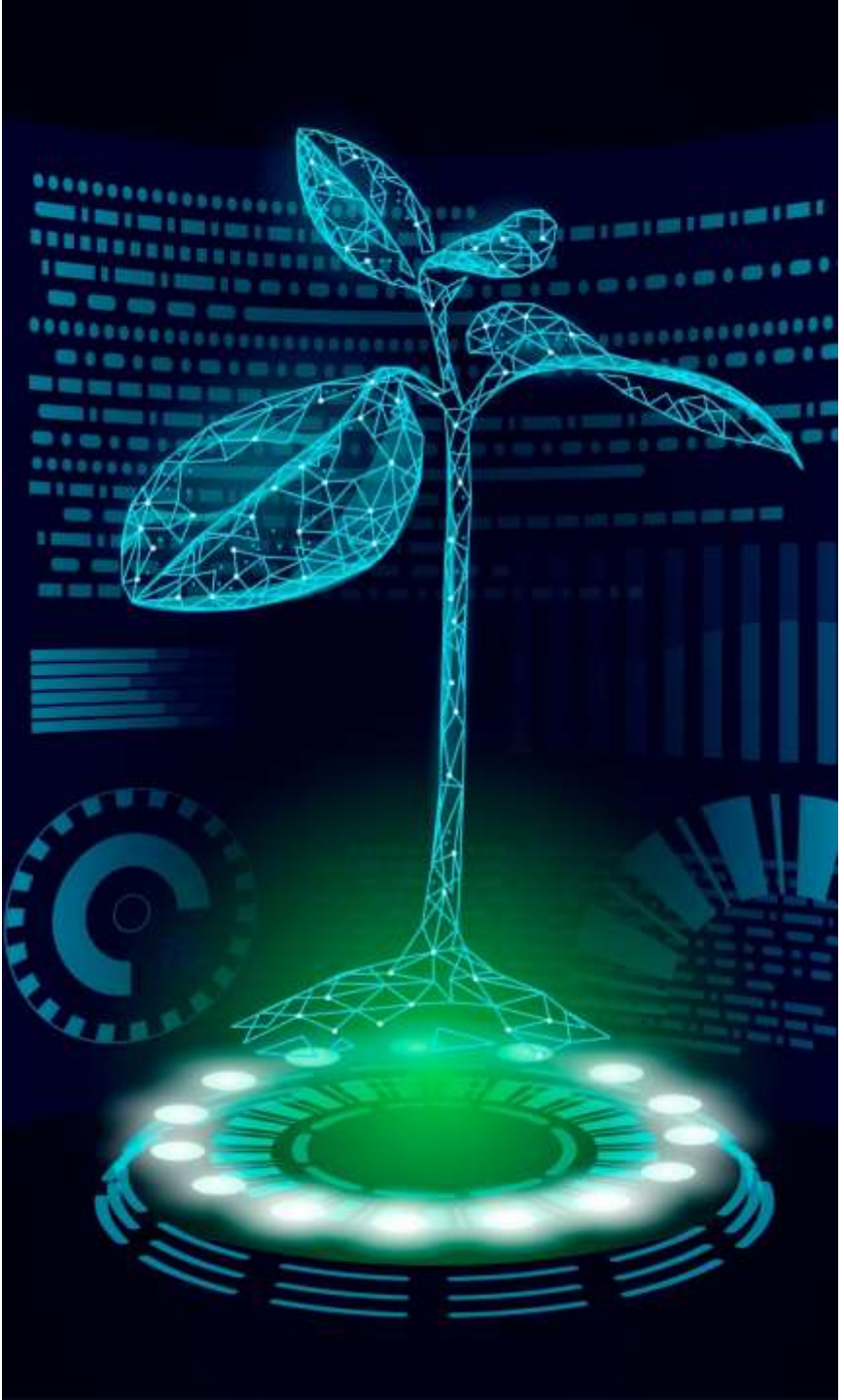


Models delivered in 2019

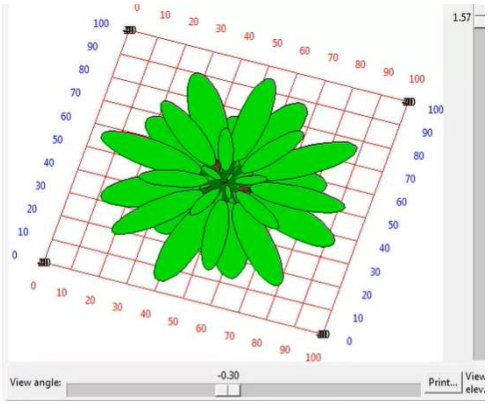
8 industrial organisms
6 environmental organisms

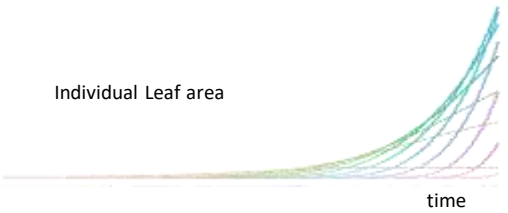
The whole plant level



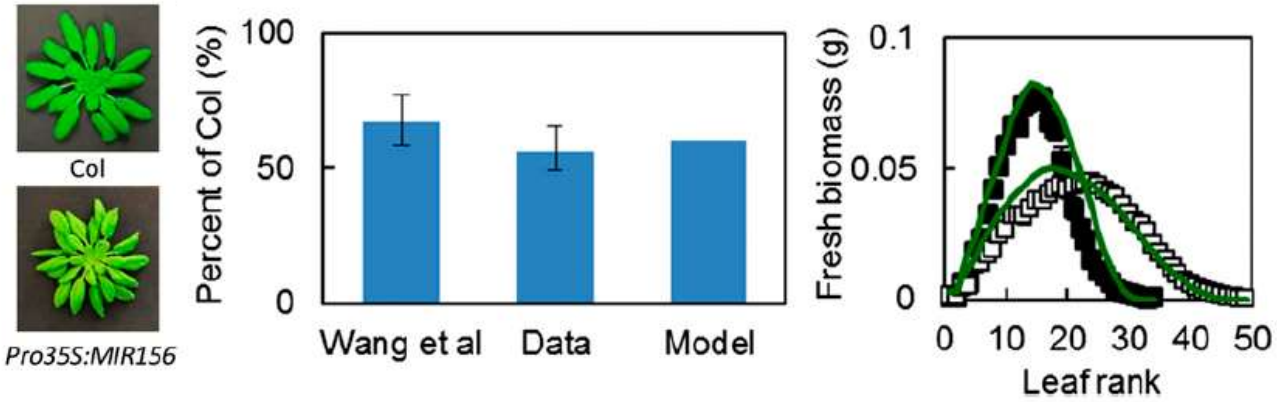


The whole plant level





- ✓ Predicting plant growth
- ✓ Predicting resources allocation
- ✓ Predicting plant architecture



Chew et al. PNAS 2014

CONTEXT

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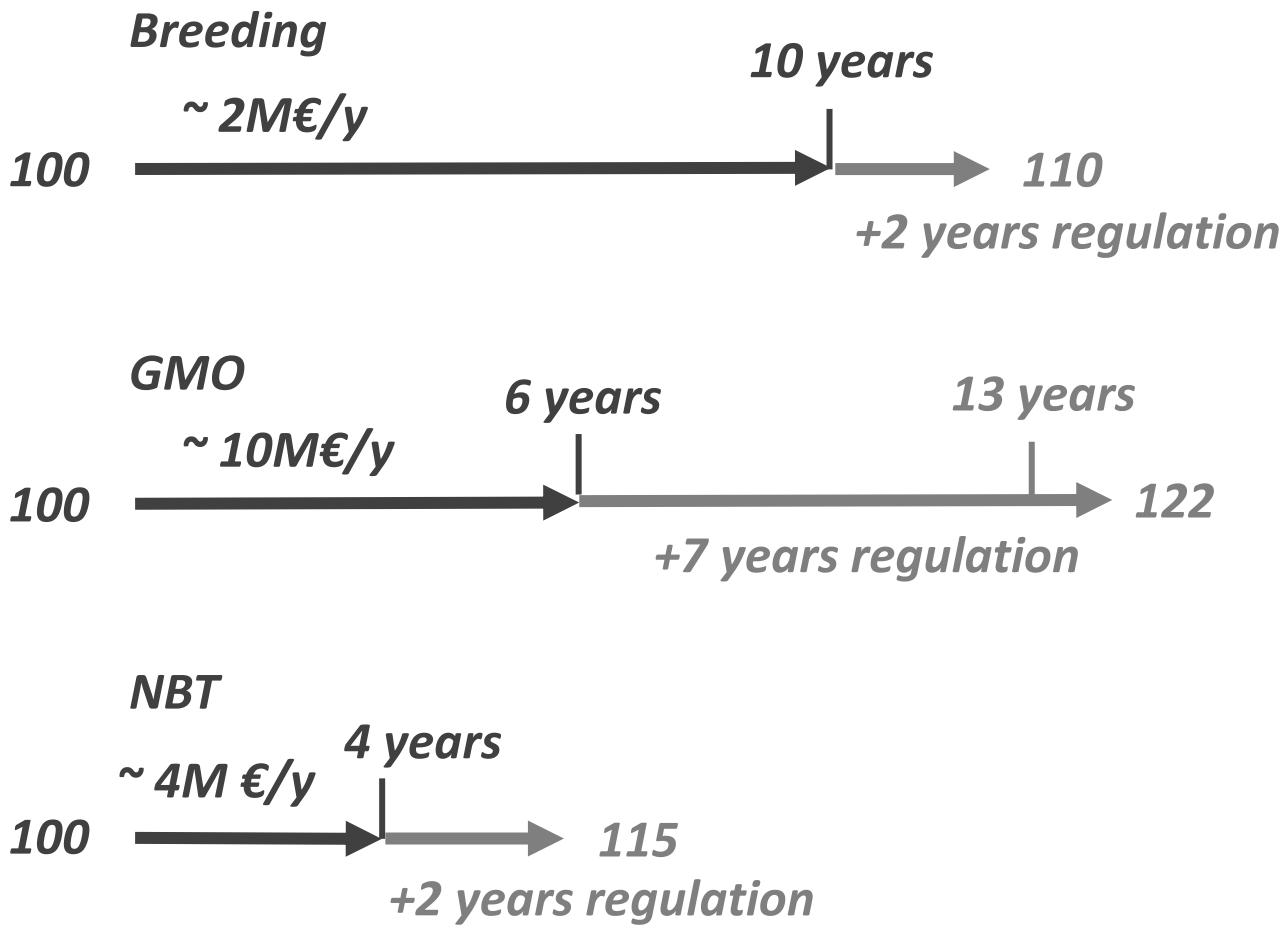
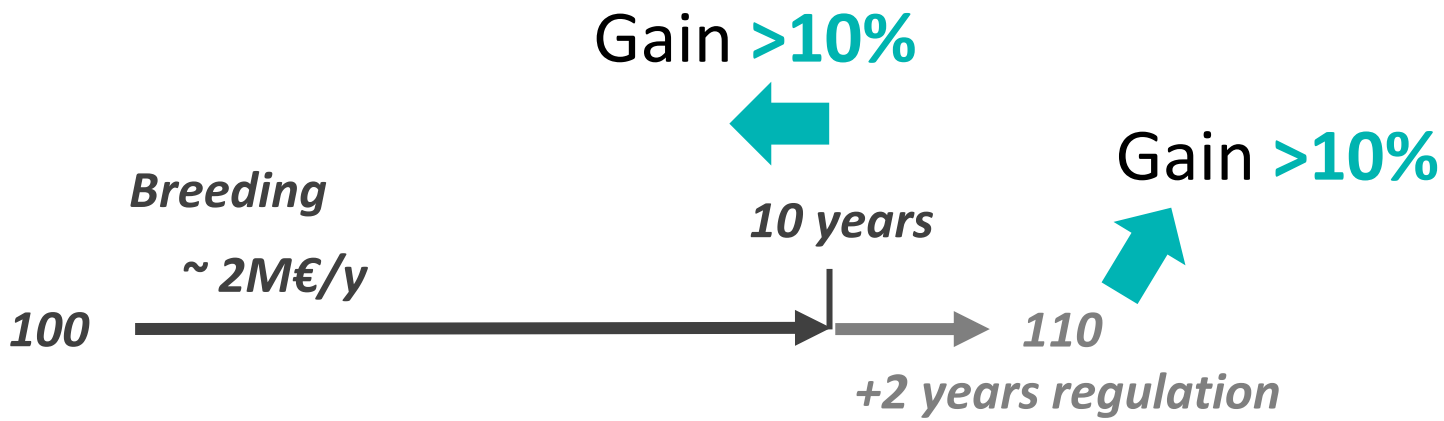
Seed R&D cost & benefits

Yield, base 100



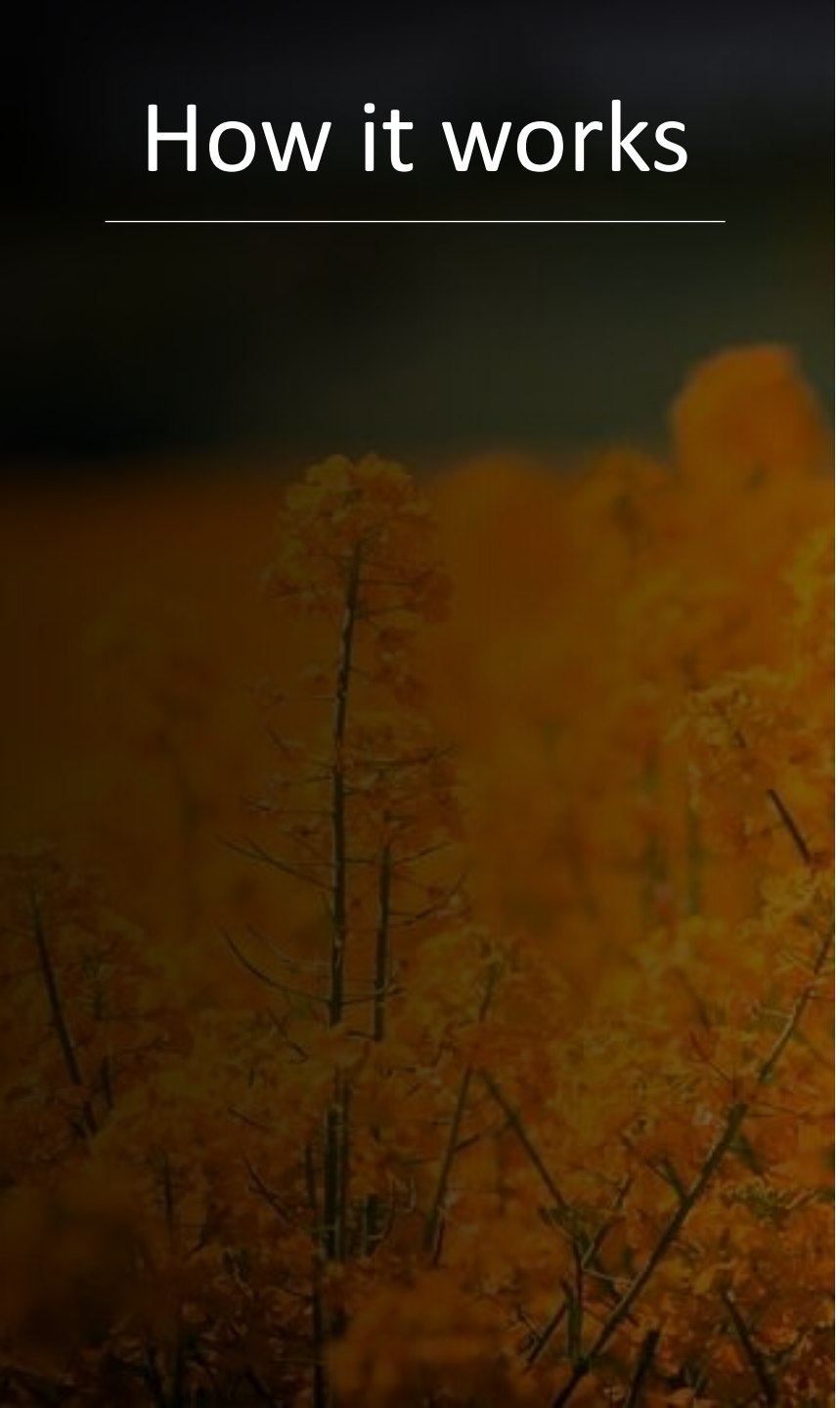
Seed Design

New traits
New varieties
New process



Crop breeding
assisted by systems biology

How it works



Selected trait

Digital organism

Complex molecular network

Identification of the network controlling the trait of interest

Genomic selection model

Increase prediction accuracy

PLANT SYS

Arabidopsis thaliana

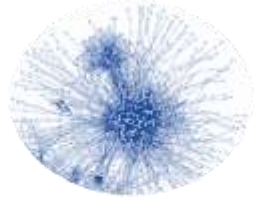
Predicting plant phenotype by systems biology

Dr Fabrice Roux

Dr Ludovic Cottret

Genotypic data

Quantitative genetics



Systems biology

Phenotypic data

Arabidopsis thaliana

Experimental setup

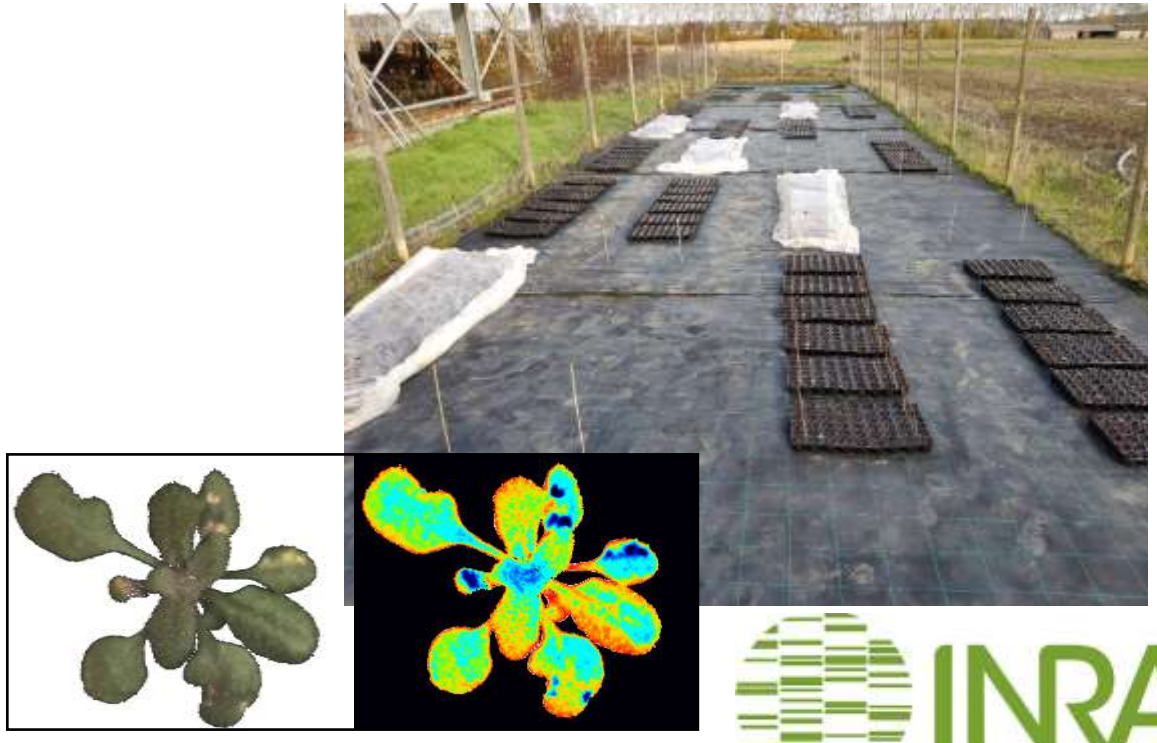
Genotypic data

Mapping population of **305** natural lines
~1.9 million SNPs

Phenotyping platform

Toulouse Plant-Microbe Phenotyping Platform

Field experiment

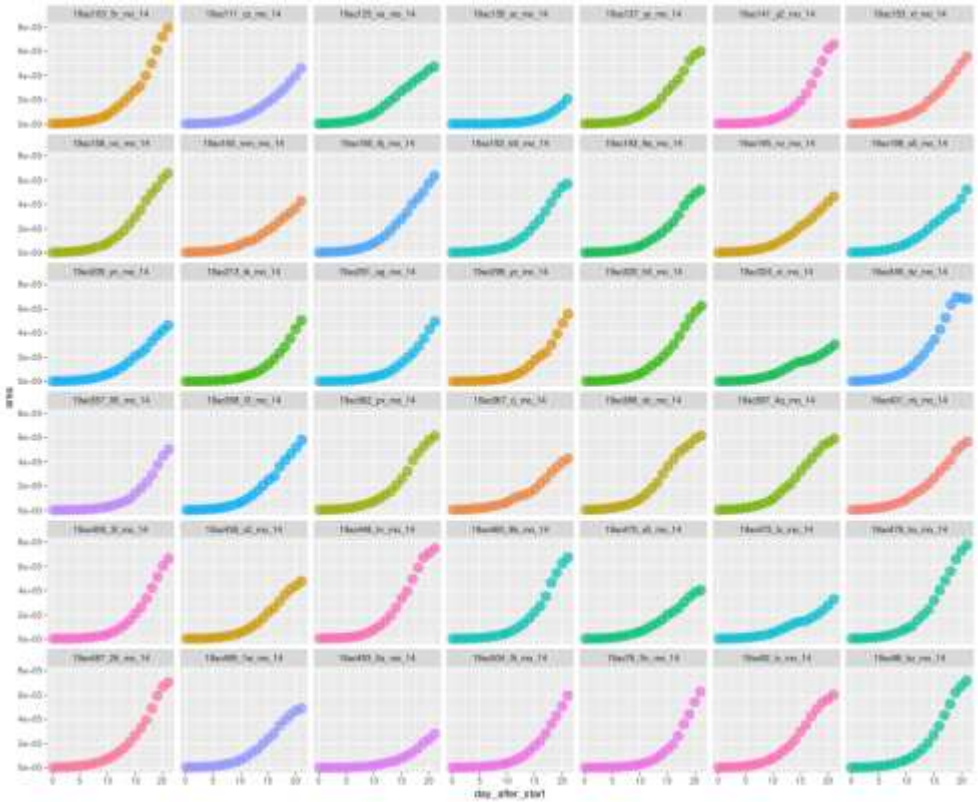


Experimental setup

Experimental data

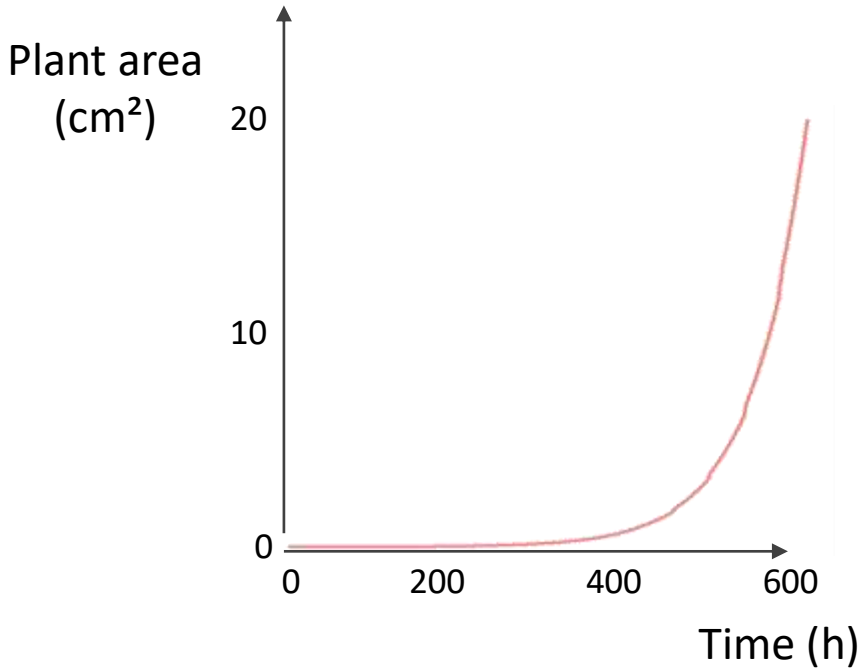
Genotypes

Plant area



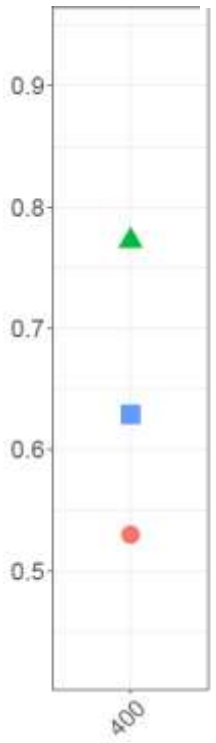
time

Simulated data



Results

Accuracy
h2=0.6 , 400 individuals, 10000 SNPs

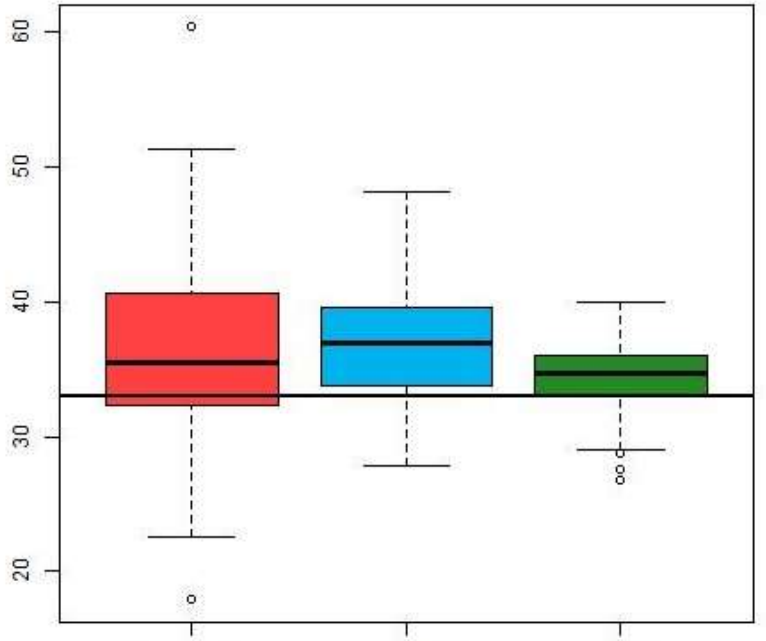


With a priory information (total population)

With a priory information (training population)

Classical model

Variability of genetic values predicted on 100 samples for one individual



Phenotype

DESIGN CROP BREEDING

The technology is soon validated with model plant in field condition

Need to be demonstrated on crop

CONTEXT

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DESIGN MICROBIAL COMMUNITIES

Synthetic microbial community Design

Efficient biopesticides
Robust products

MICROBIOTA

Improving plant health & productivity thanks to microbial communities

Low robustness in front of variation in field conditions

Fastidious empirical testing
Data based on diversity

Synthetic microbial community Design

DNA
Sampling & sequencing

Community identification

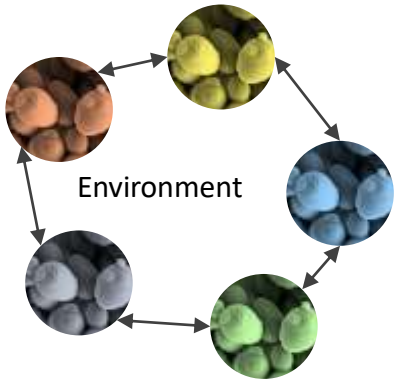
OTU 1
OTU 2
OTU 3
OTU 4

Data

Digital microbes reconstruction

Model 1
Model 2
Model 3
Model 4

In silico community



Data

Community model Validation

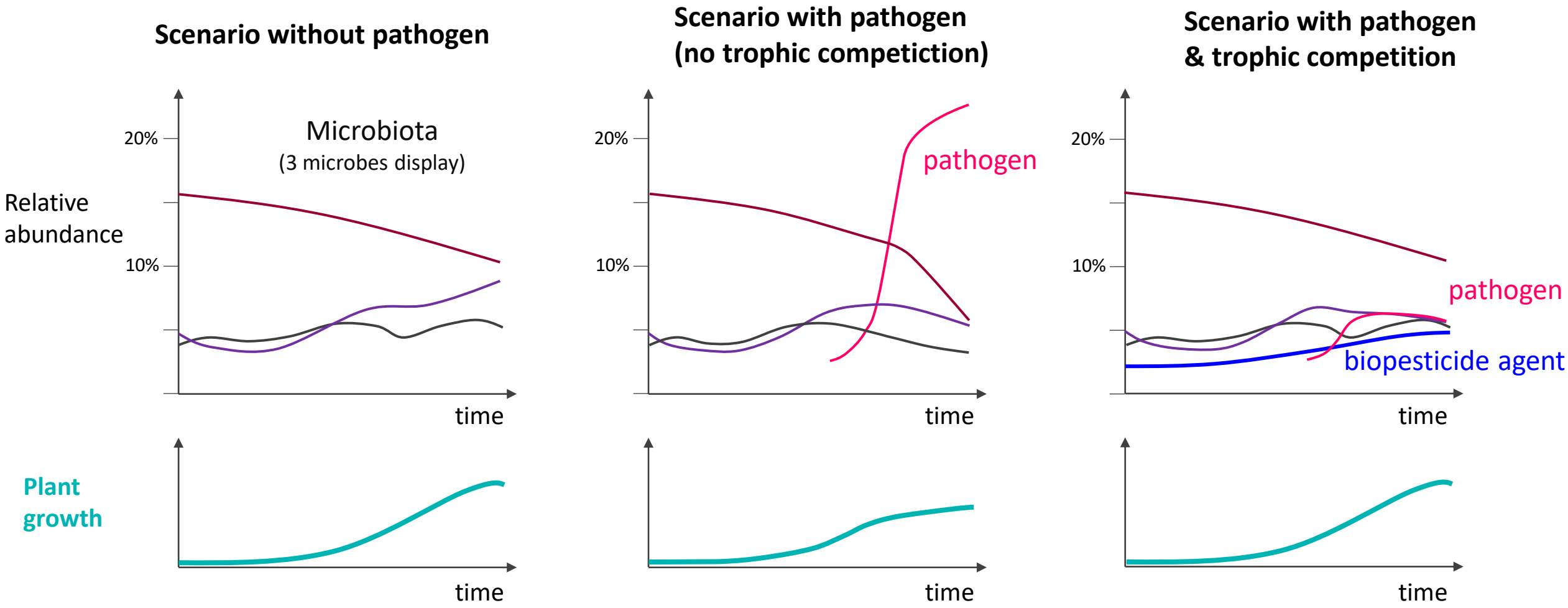
Microbiota & Environment Design

Optimisation
Increase performance
Increase robustness

Synthetic community or environmental changes

In silico screening of biopesticides

Rational design based on population dynamics



MICROBIAL COMMUNITY MODELING

The technology is ready for rational design of microbiome

The time to build models is the key limitation factor

The technology can be plugged with plant breeding programs

Thank you

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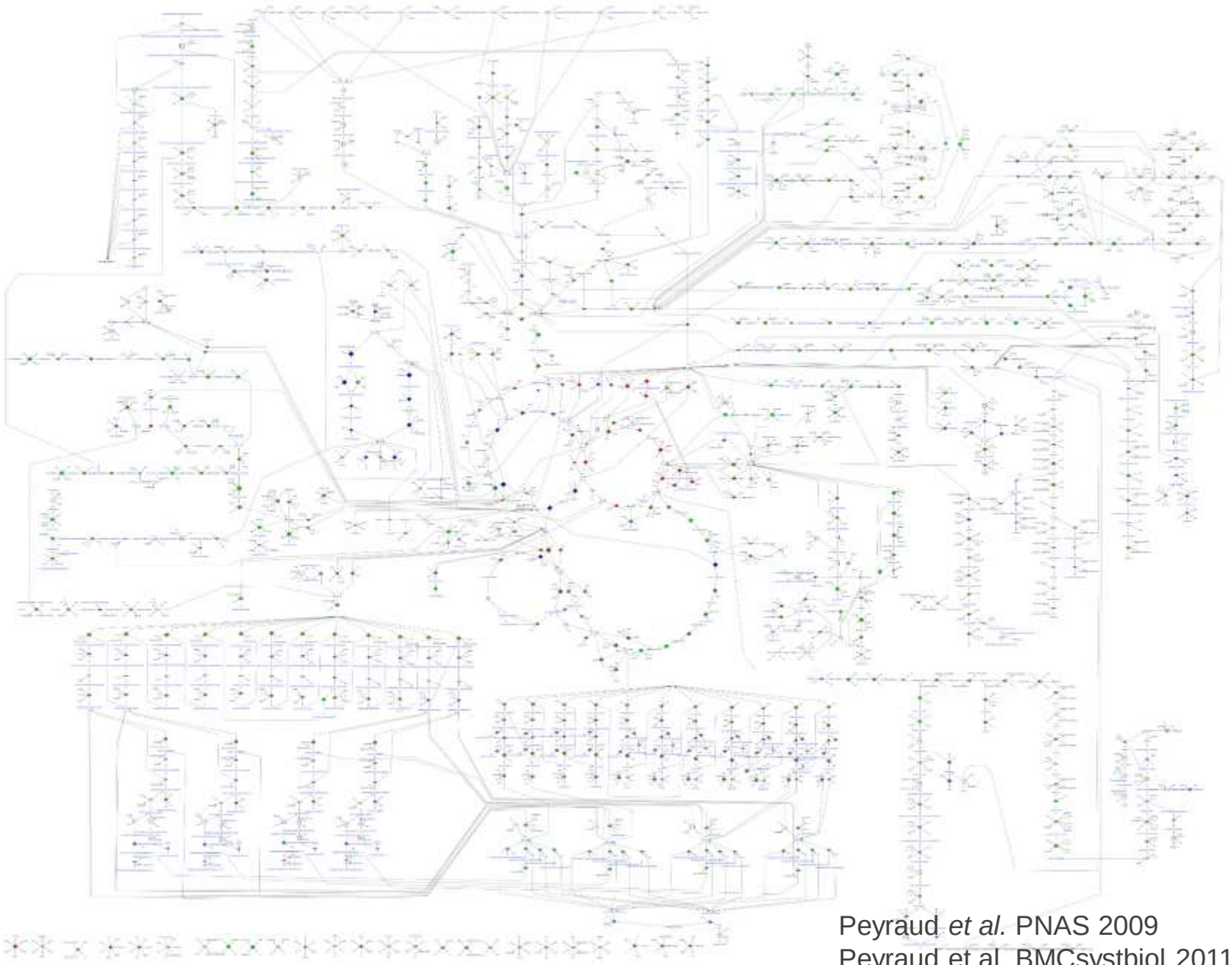
Genome-scale metabolic network

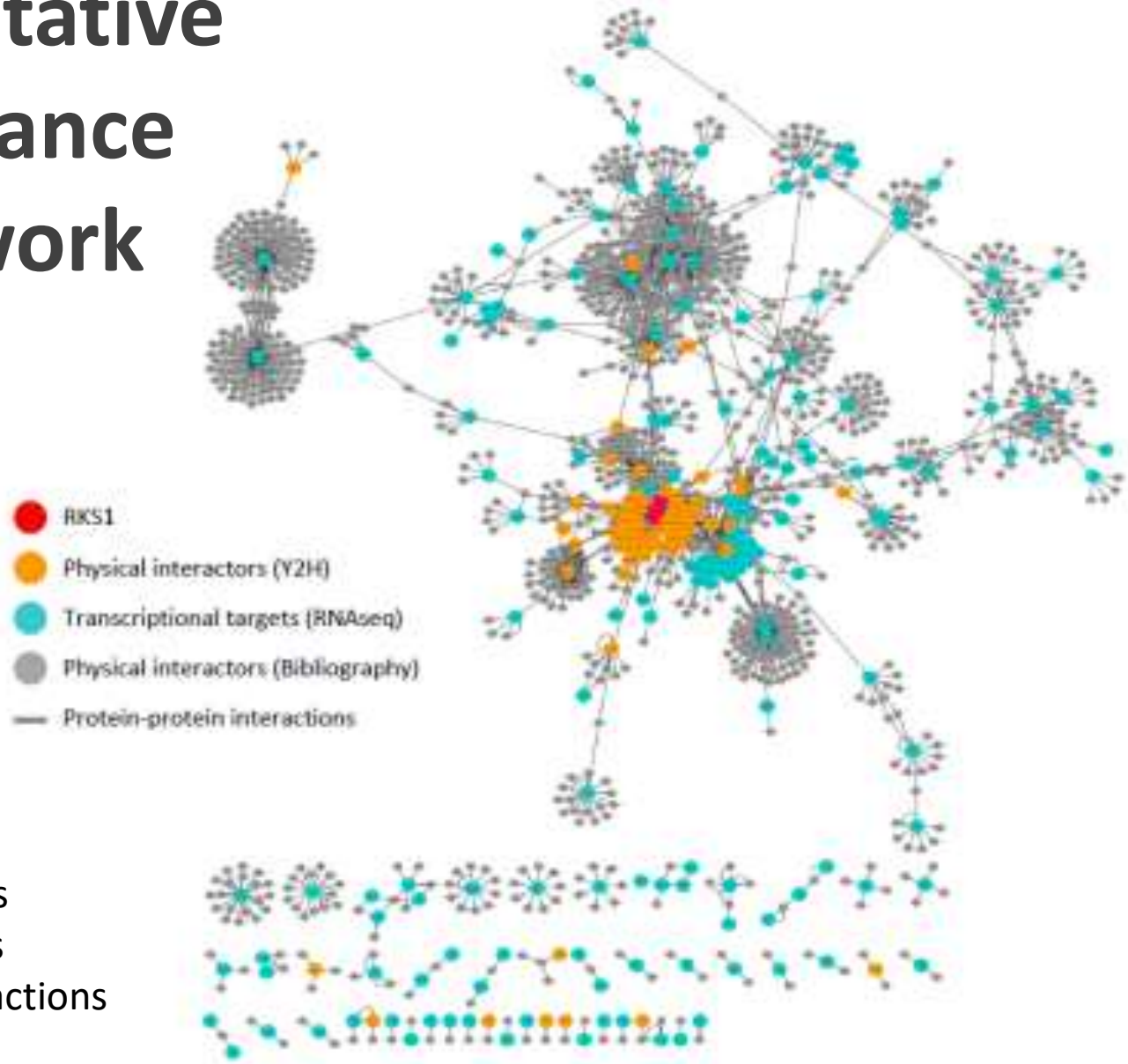
Methylobacterium extorquens



Peyraud *et al.* PNAS 2009
Peyraud et al. BMCsystbiol 2011

Immune system network

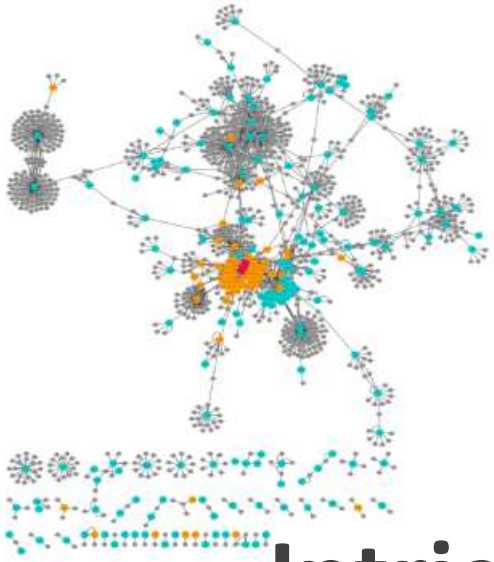
Quantitative resistance network



1330 nodes
1047 genes
1876 Interactions

Delplace et al. in press PNAS

Immune system network



Intricated protein-protein interaction network

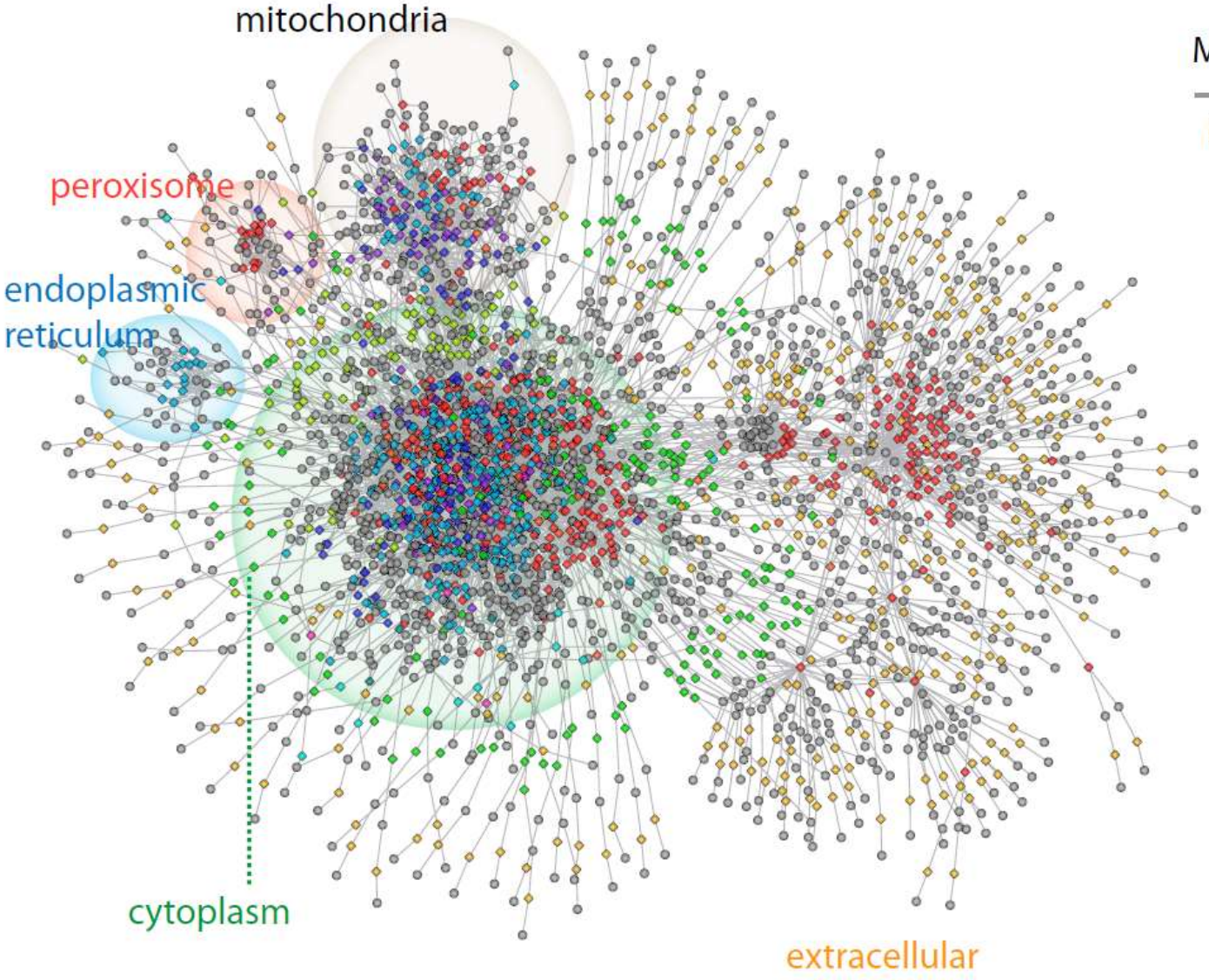
Decentralised structure

Various biological functions

Robustness to pathogen evolution

Delplace et al. in press PNAS

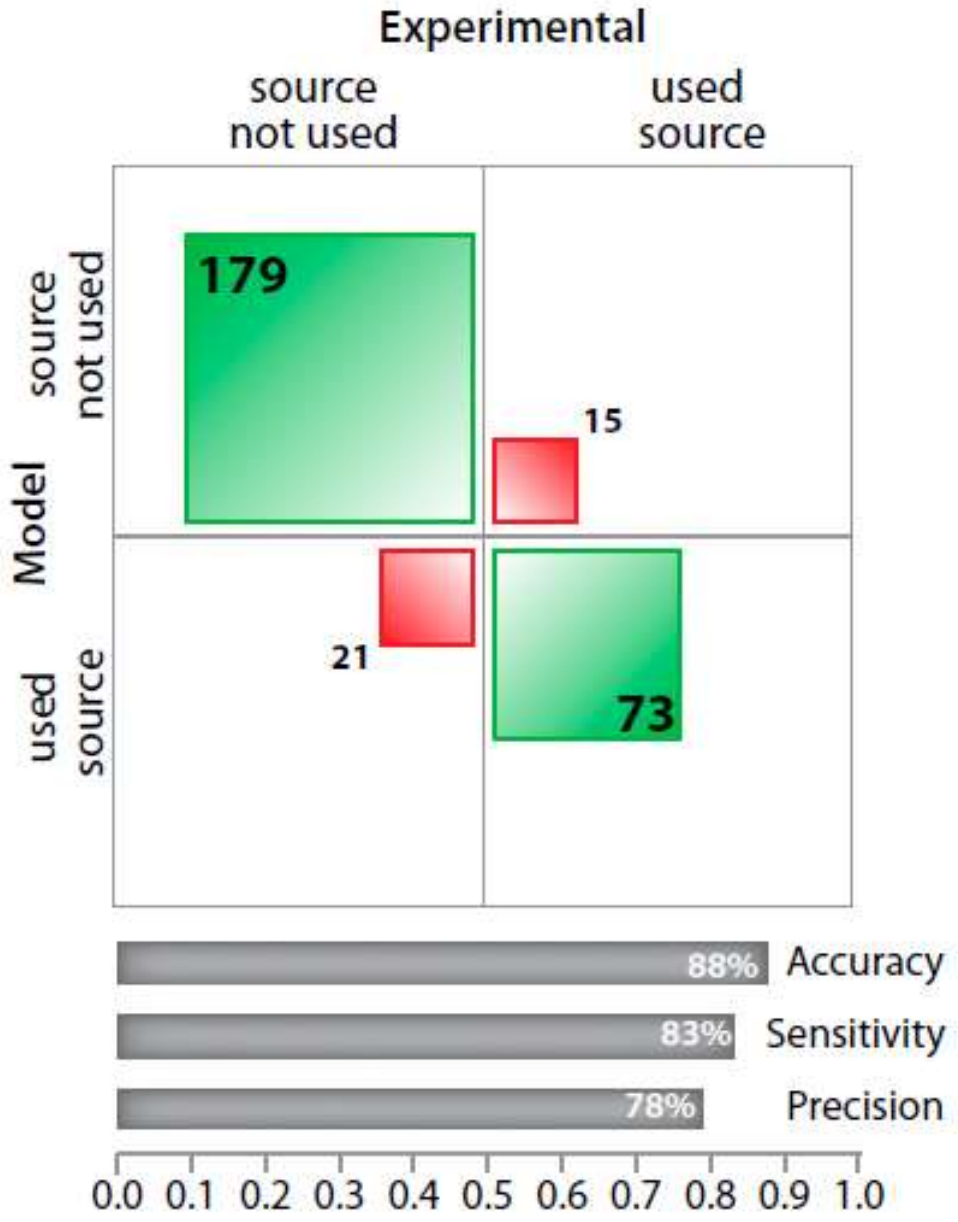
Genome-scale metabolic network of *Sclerotinia sclerotiorum*



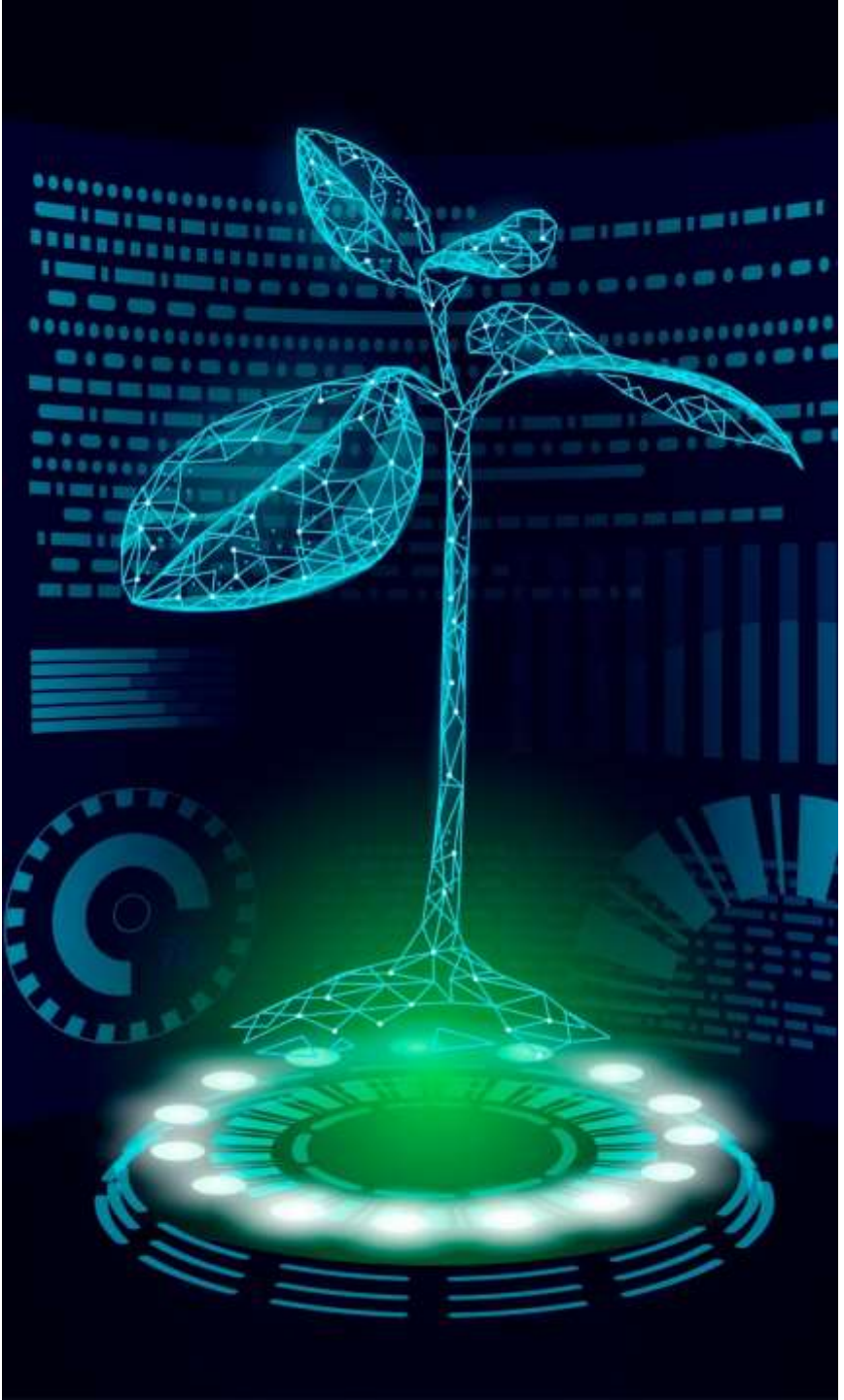
Model features	Metabolic module	PCW deg. module
Reactions		
Biomass biosynthesis	291	0
Central metabolism	89	0
Cofactor biosynthesis	77	0
Degradation pathway	280	83
Exchange	213	135
Regulation	6	0
Salvage pathway	9	0
Secondary metabolism	33	0
Sink	14	0
Transport, external	183	0
Transport, internal	82	0
Total	**1277**	**218**
Metabolites	**1185**	**340**
Genes	919	120

Peyraud *et al.* PNAS 2019

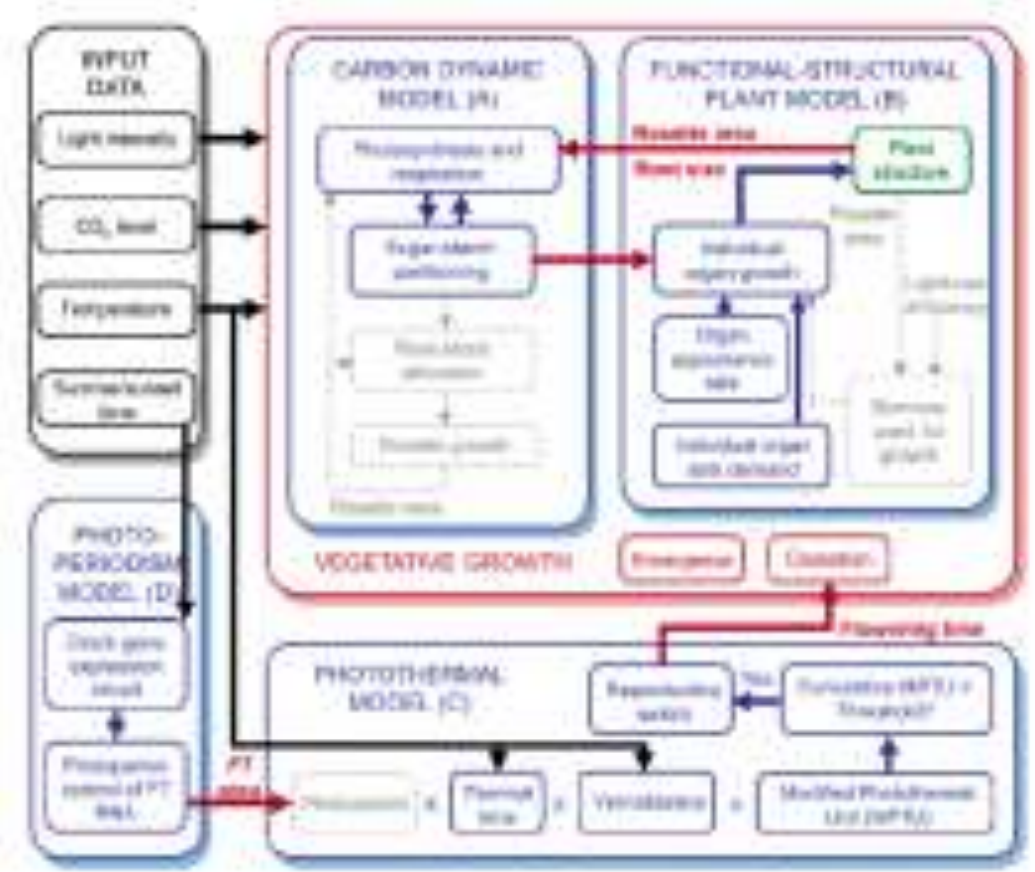
Sclerotinia sclerotiorum substrate usage



Peyraud *et al.* PNAS 2019



Whole digital plant



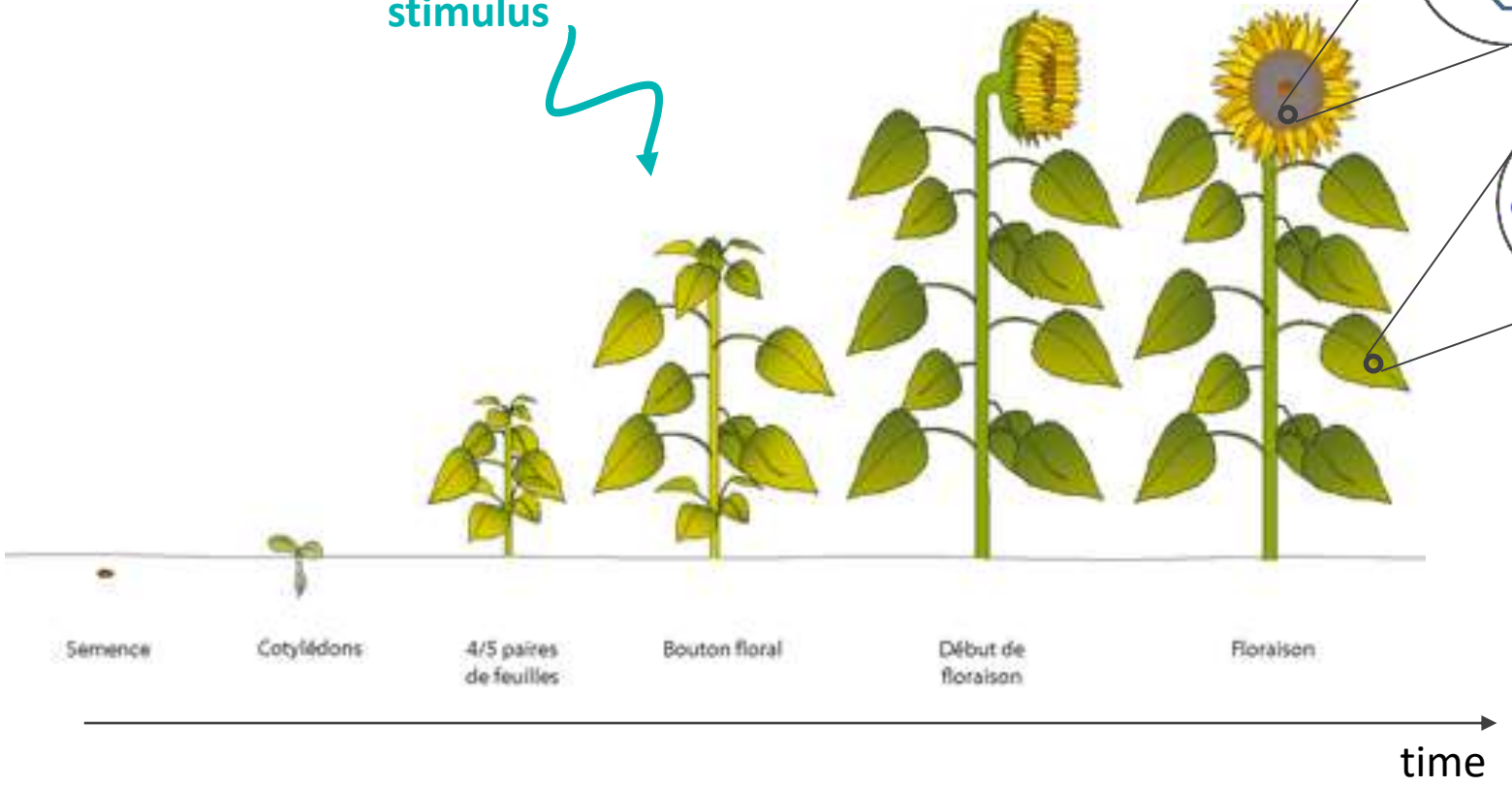
Chew *et al.* PNAS 2014

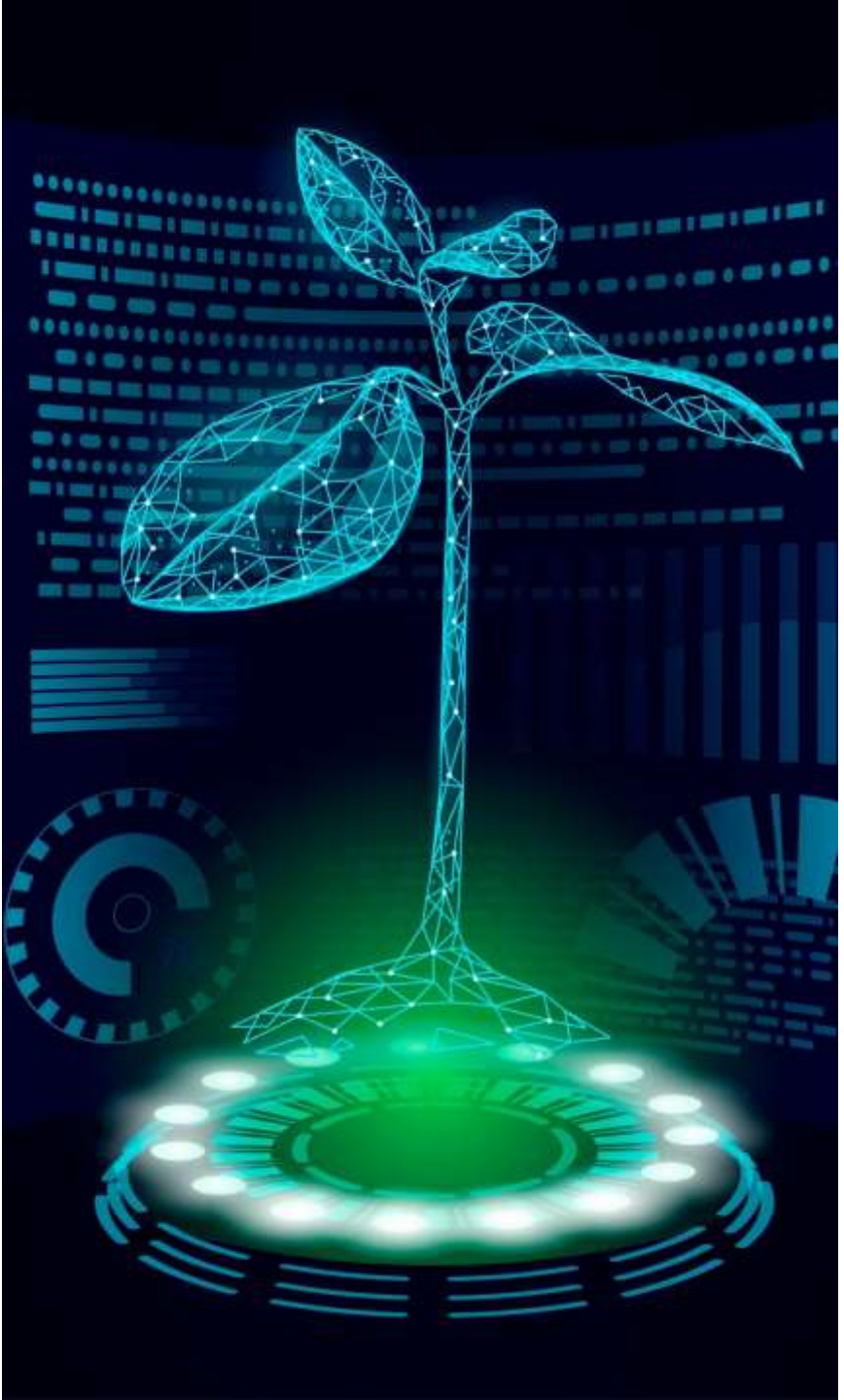
Plant life cycle modeling

Cellular model with their own behaviour

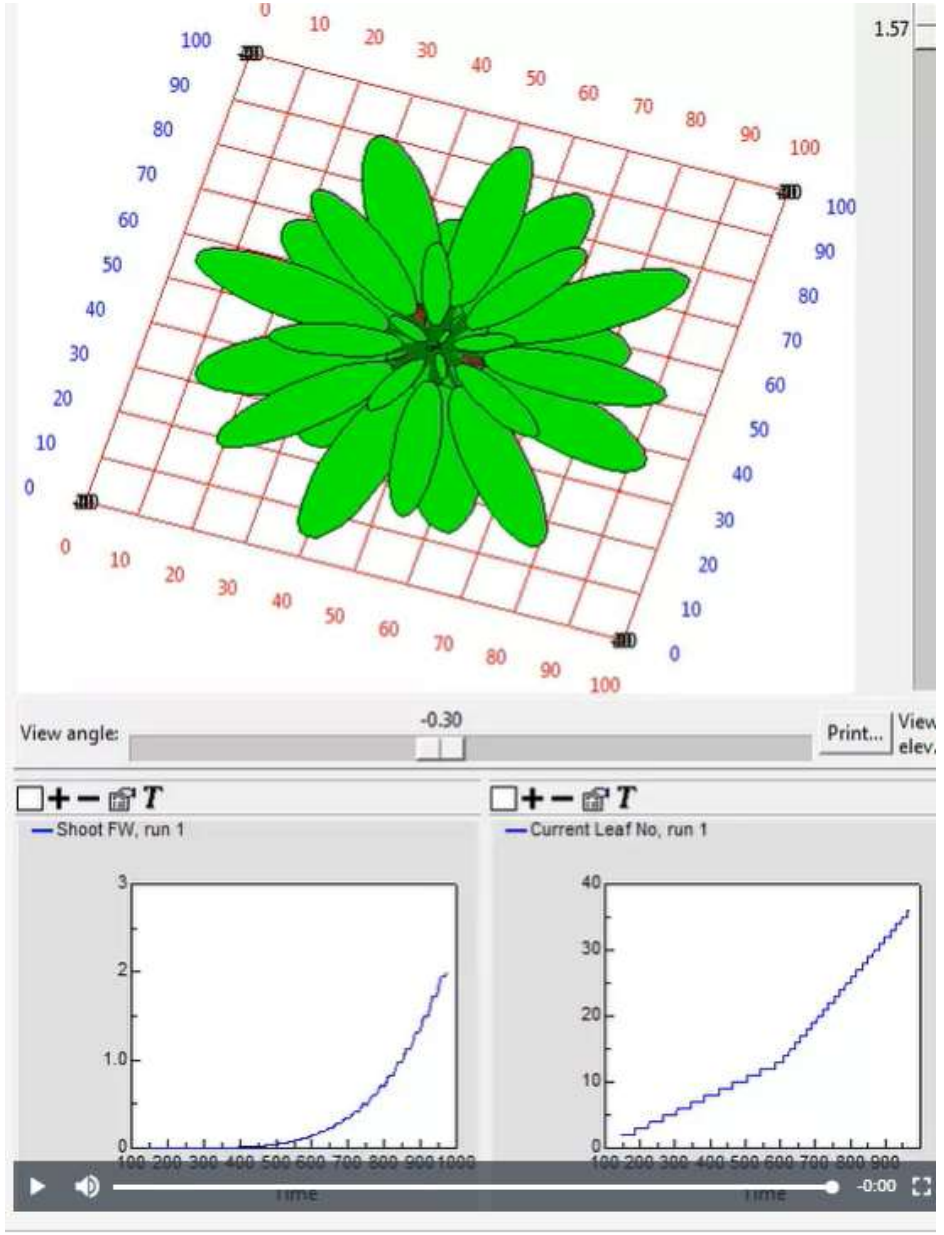
Environnemental stimulus

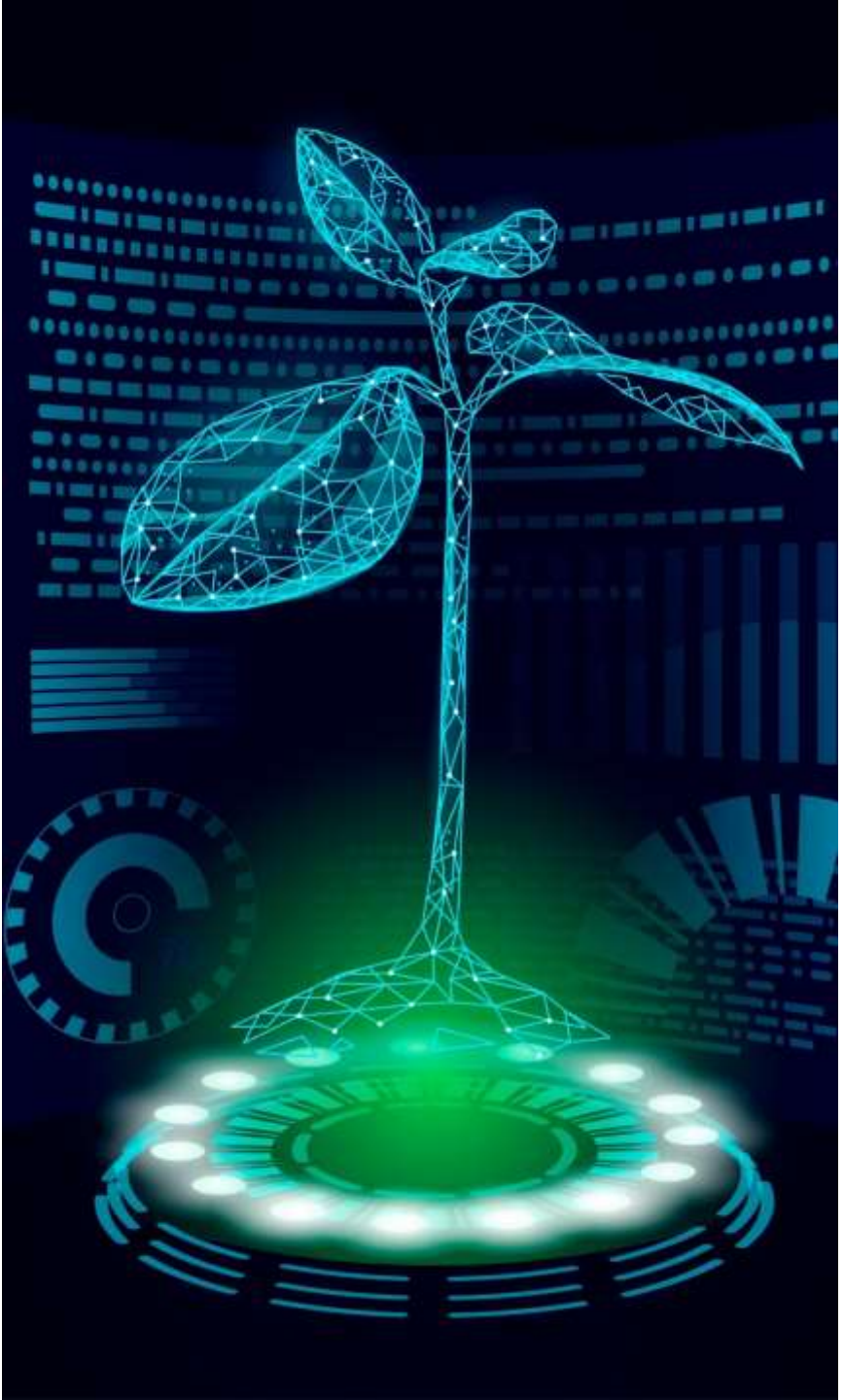
Exchange flux

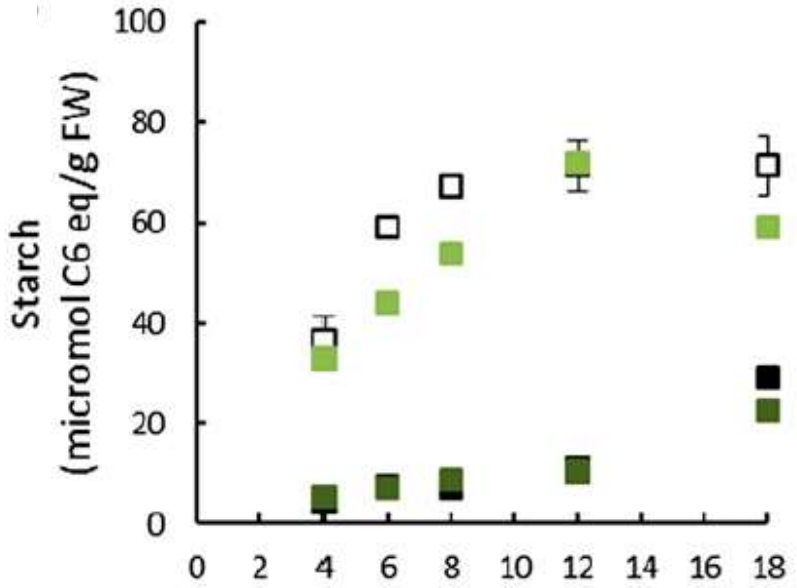


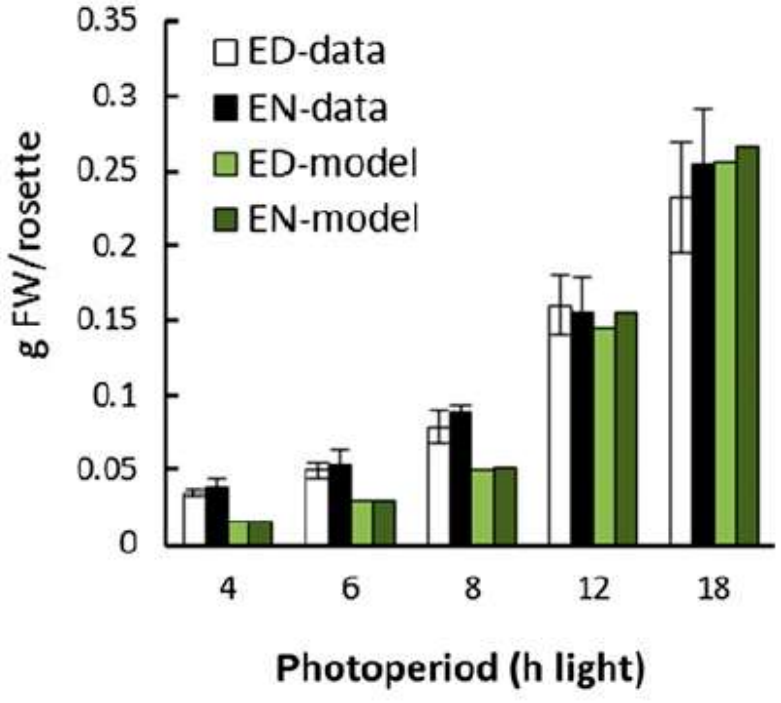


Predicting plant growth



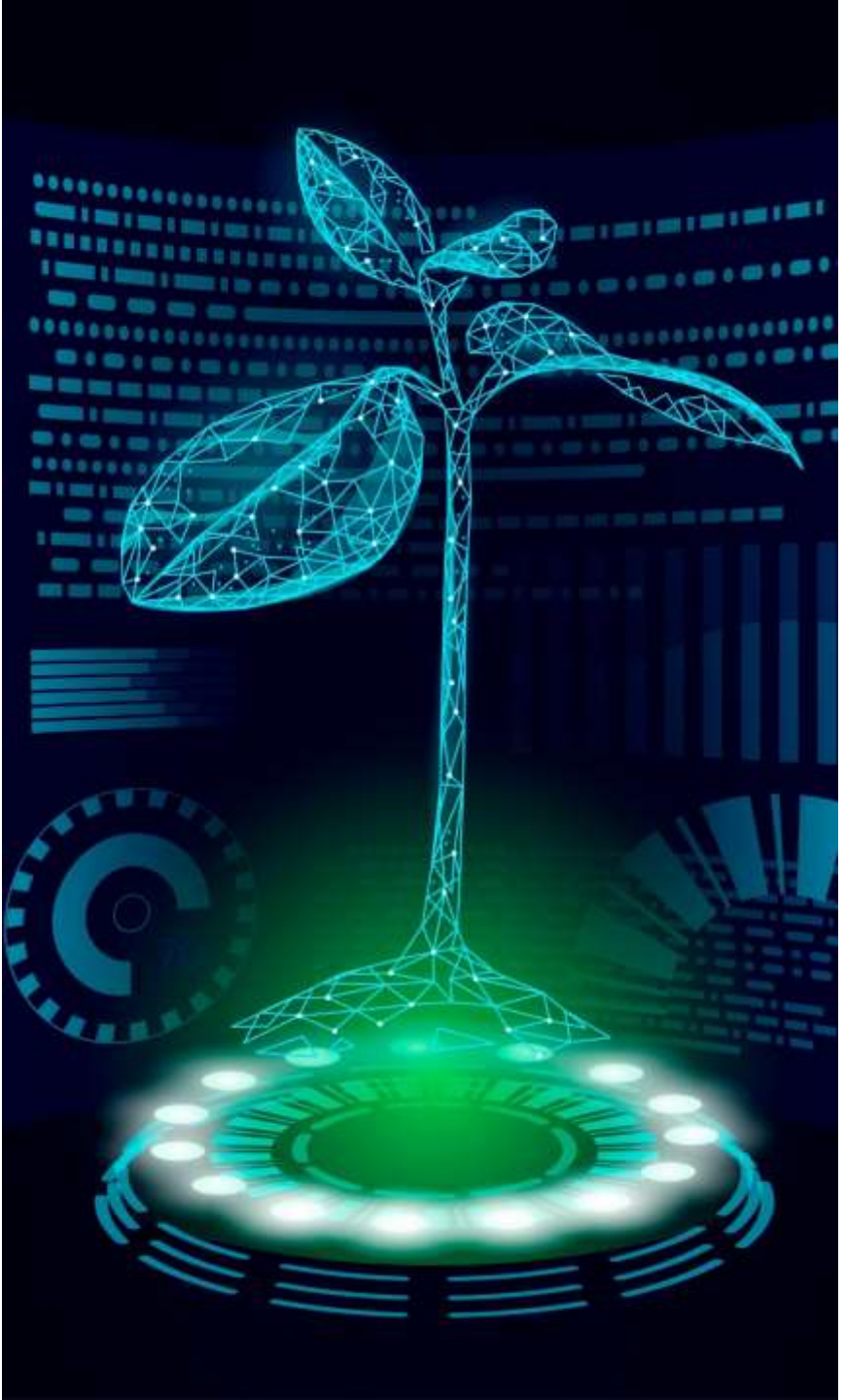






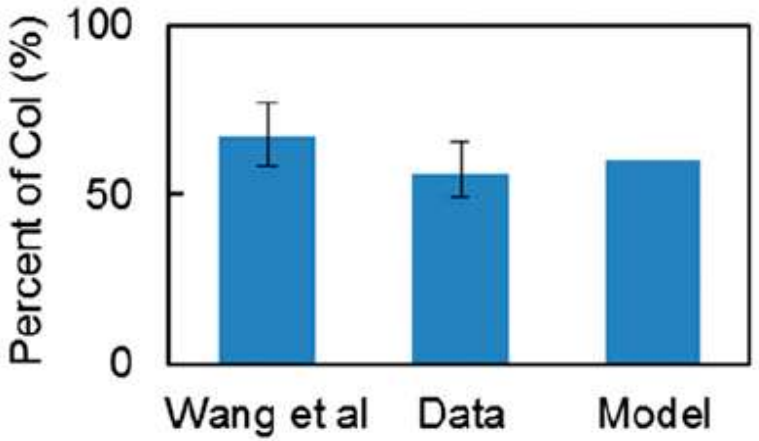
Predicting resources allocation

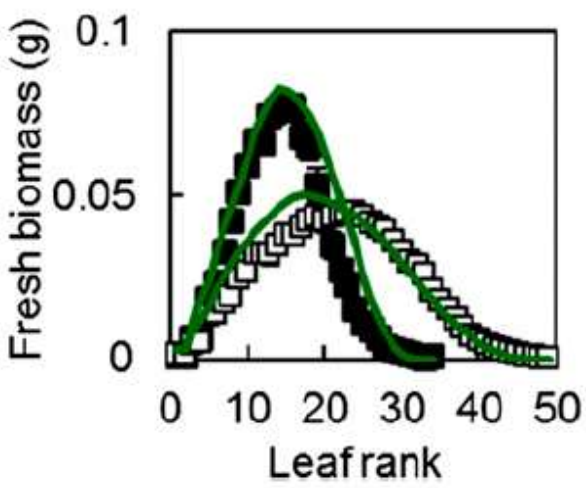
Chew *et al.* PNAS 2014



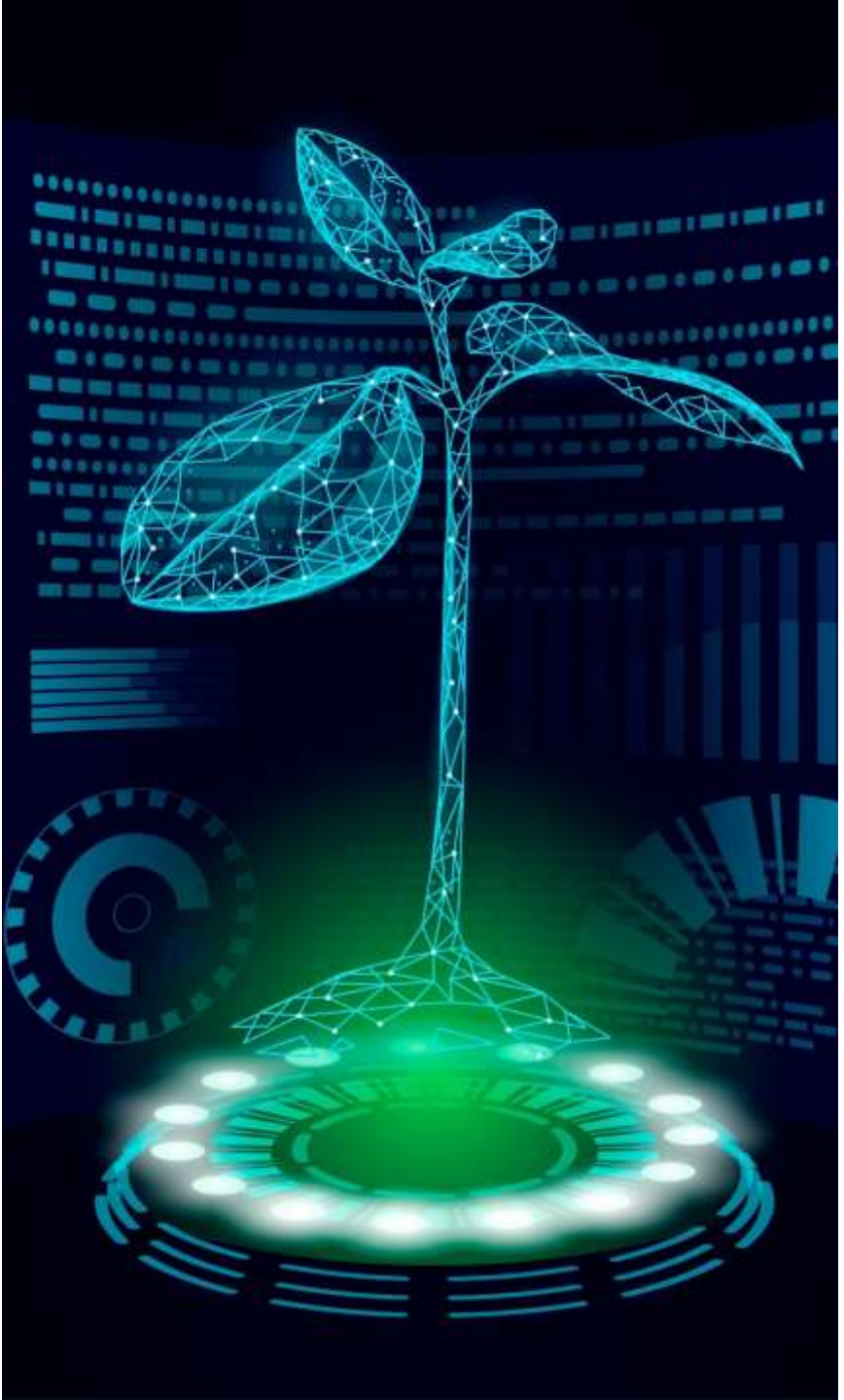
Predicting plant architecture

Pro35S:MIR156

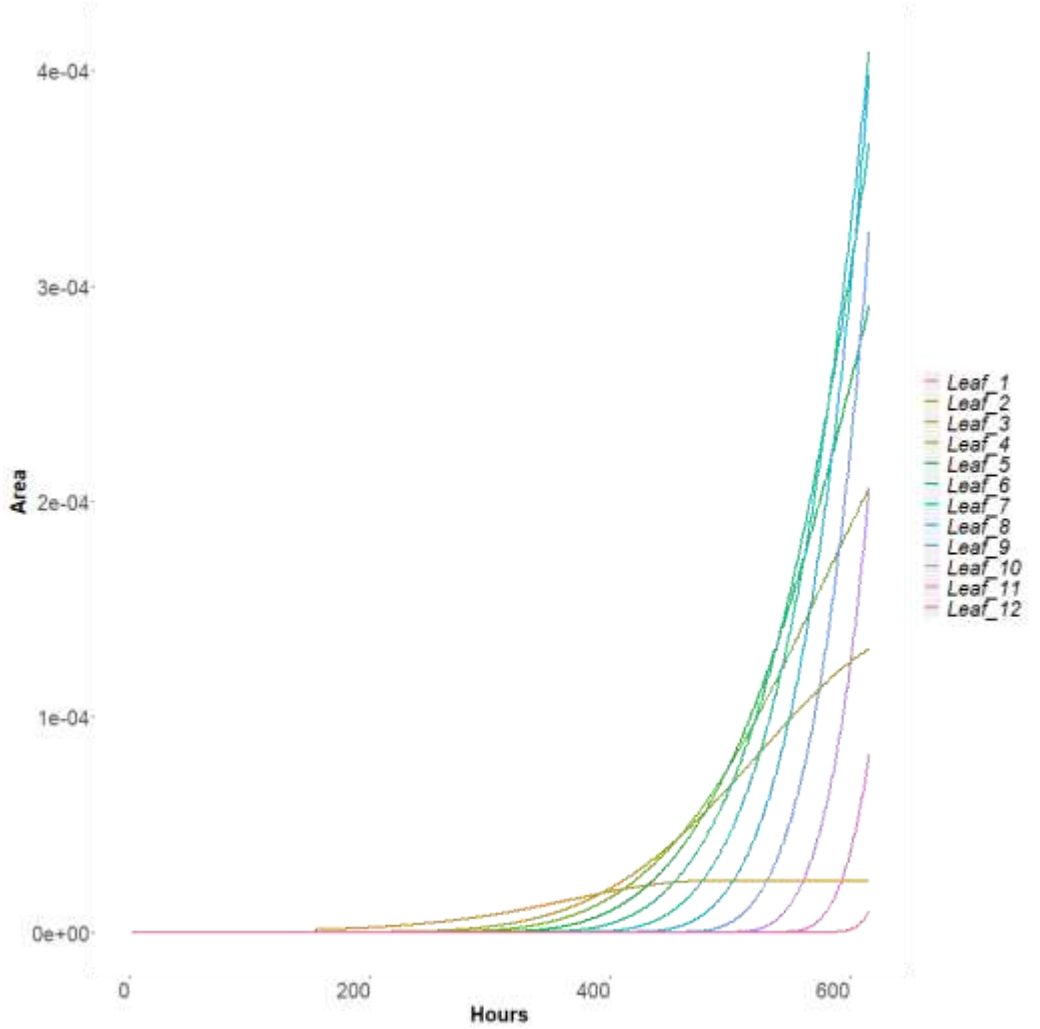




Chew *et al.* PNAS 2014



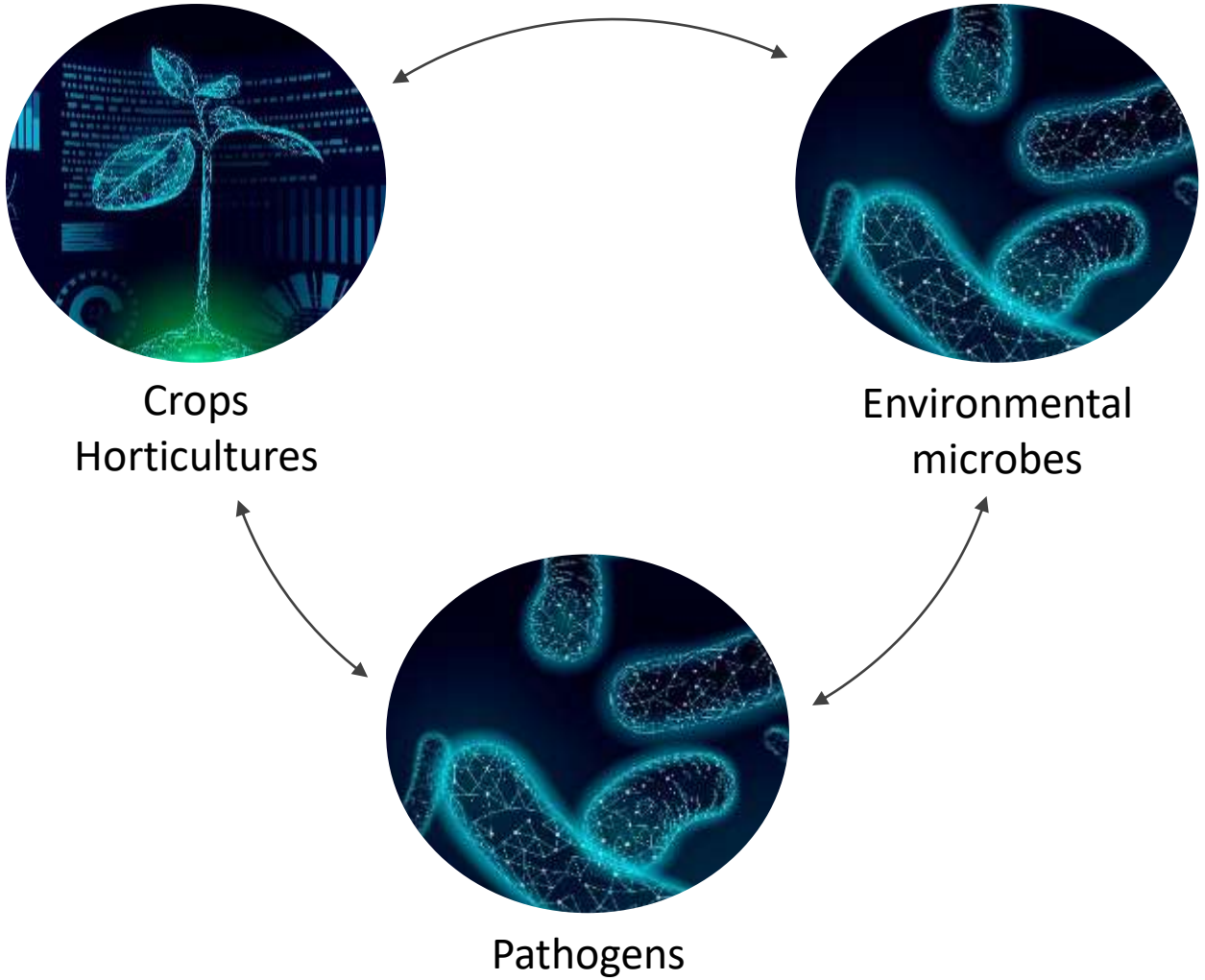
Predicting leaf growth from genome-scale metabolic network



Duplan & Bonnafous *et al.* unpublished

Predict interactions

Trophic interaction
Secondary metabolites exchanges



Engineering network (epistasis “domestication”)

Design novel traits

Increase robustness of the crops

Genomic selection

Most advance solution

Statistical analysis

Genotypic diversity

& Phenotypic diversity

Learning correlations

Systems biology

Tomorrow technology

Complex molecular network

Scientific knowledge

& environmental constraints

Causal relationship

How it works

Genotypic diversity

***in silico* diversity**

Environmental constraints

Phenotypic diversity prediction

Experimental setup - Robotized phenotyping platform

Genotypic data

- Mapping population of **216** natural lines

~1.9 million SNPs

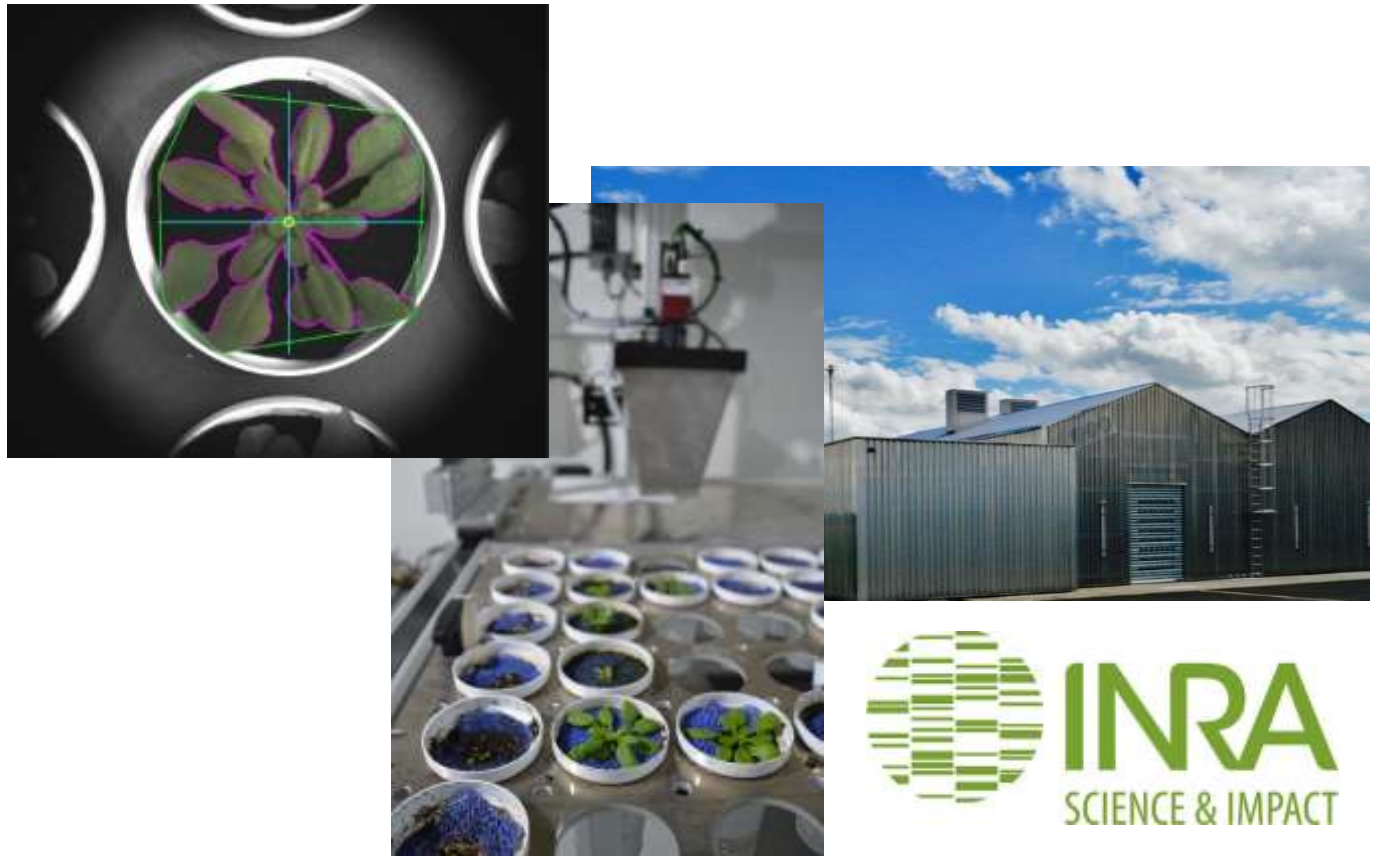
Phenotypes & stresses

- Biomass growth
- Pathogen attack (collected in Midi-Pyrénées)
- Photoperiod

Imaging

High definition imaging

- Multispectral imaging
- Chlorophyll Fluorescence imaging



Toulouse Plant-Microbe Phenotyping Platform

Experimental setup - Field experiment

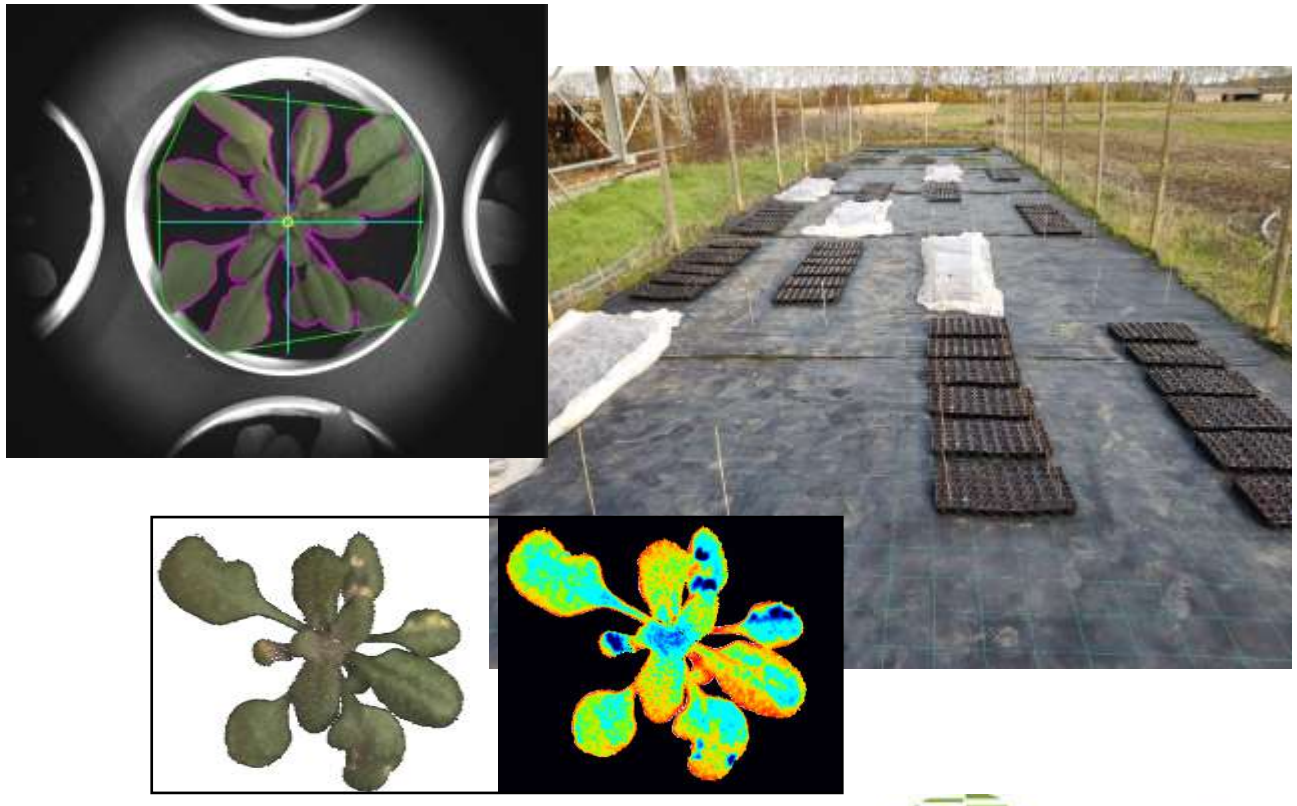
Genotypic data

- Mapping population of **305** natural lines

~1.9 million SNPs

Phenotypes & stresses

- Biomass growth and seed production (Yield)
- Flowering time
- Pathogen attack (collected in Midi-Pyrénées)
- Photoperiod



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