

# Welcome !

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- Education and Training in 'Omics' Sciences
- Demonstration of on-line 'Omics' resources
- Lab and demonstration of modern Proteomics

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## Outline

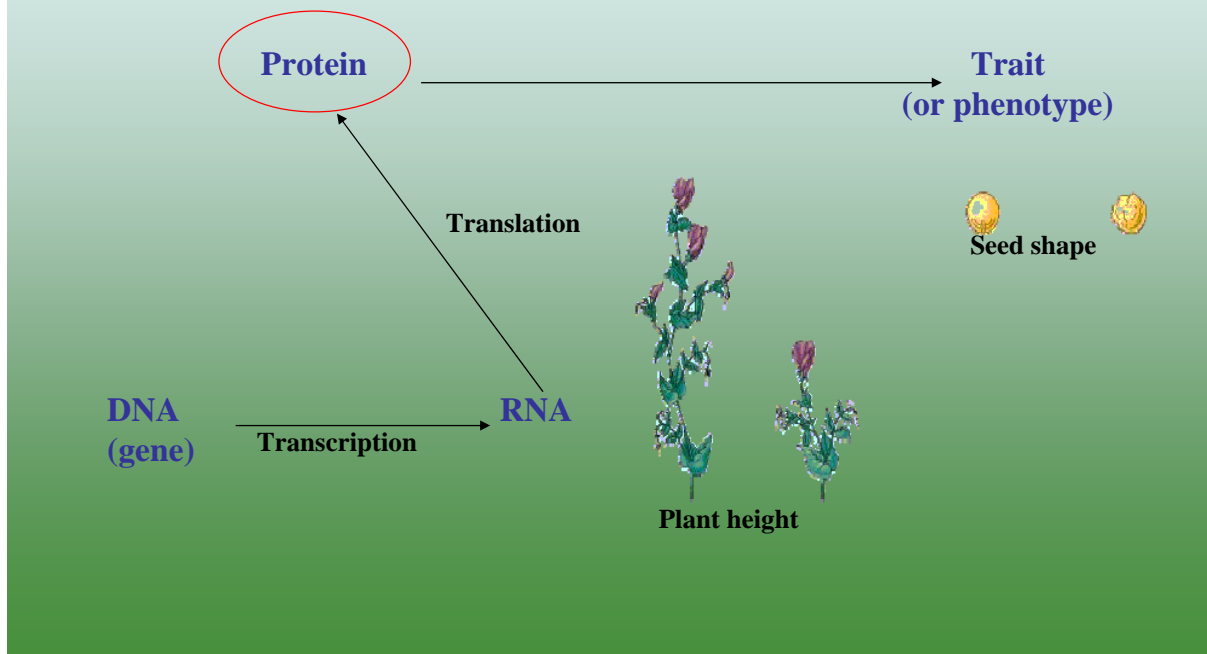
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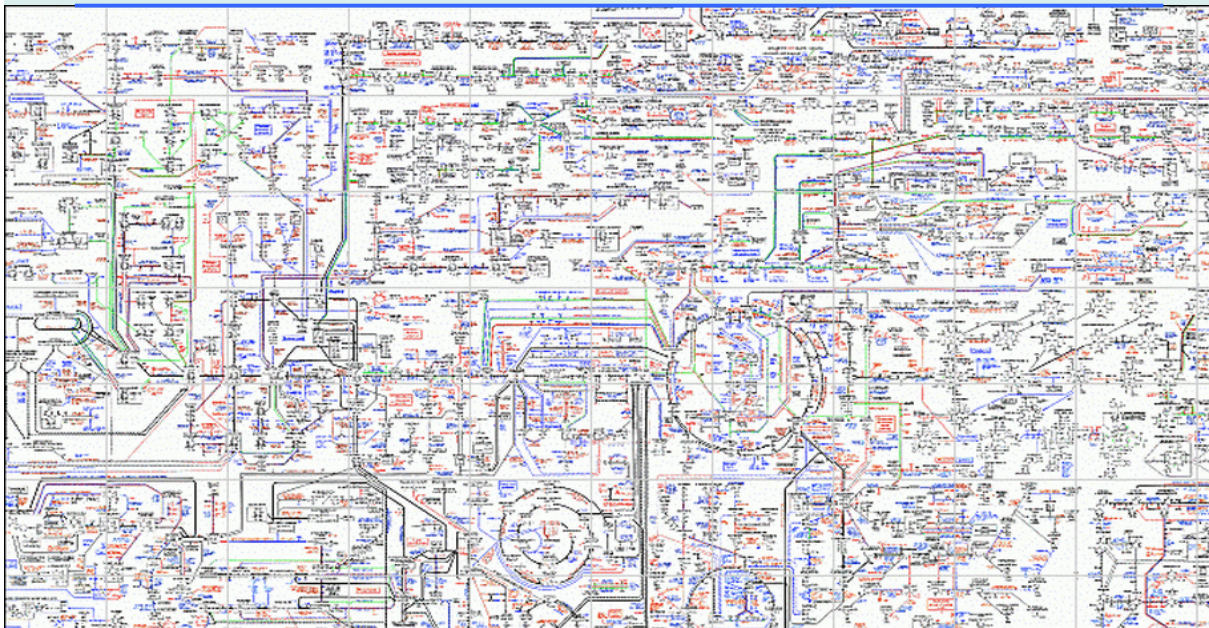
- **What is modern and future biological sciences ?**
- Large scale biology – 'Omics': revolution in screening important traits and creation of 'in silico' organisms
- 'Omics' modules – example of proteomics in addressing the differences in control and virus infected peanut leaves

# Central Dogma of Molecular Genetics

(The guiding principle that controls trait expression)



## Traits and Phenotypes are Controlled by Molecular Networks



Trying to understand life without knowledge of biochemical network would be like trying to understand Shakespeare without knowledge of English grammar.

## Our Problems

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- That one gene encodes one protein, which catalyzes one reaction and determines one phenotype is no longer the case.
- Manipulating one gene can cause pleiotropic effects ?
- How to capture all molecules and their interactions, dynamics, regulations and turnover ... ?
- How to determine the rate-limiting molecule and step ? How to predict ?
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## Outline

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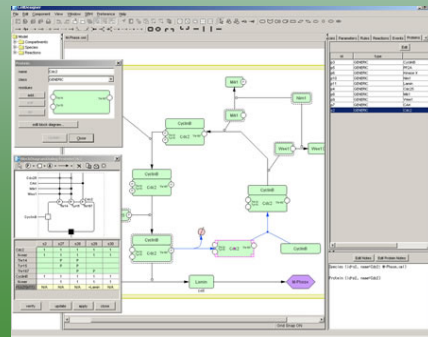


- What is modern and future biological sciences ?
- **Large scale biology – ‘Omics’: revolution in screening important traits and creation of ‘in silico’ organisms**
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## 'Omics' and Systems Biology

- "Omics"
  - Genomics – the comprehensive study of whole sets of genes & their interactions (DNA microarrays)
  - Proteomics - the study of the full set of proteins encoded by a genome
  - Metabolomics - the comprehensive study of the small molecules or metabolites
  - Bioinformatics - the application of computer & statistical techniques to the management of biological information

Systems Biology-  
"An interdisciplinary approach for integrating experimental data with mathematical modeling tools to analyze & predict the behavior of biological systems." (Henson, 2005)



## Starvation: Importance of Cassava

Cassava (*Manihot esculenta*) - yucca, manihot, tapioca

- cultivated in tropics and sub-tropics for its edible storage root
- a major source of dietary energy for more than 700 million people
- source for a variety of food stuffs, animal feed and industrial products
- major component in micro-economies of more than 150 countries





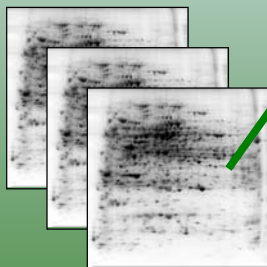
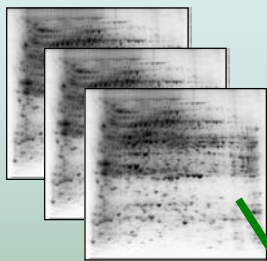
# Cassava tuberous roots developed from fibrous roots

- Tuberous roots develop from fibrous roots through massive cell division and differentiation of parenchyma cells of the secondary xylem
- Not all fibrous roots are designated for tuberous root formation



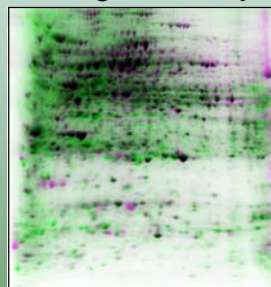
## Proteomics is the approach

Fibrous Root

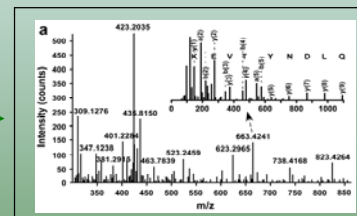


Tuberous Root

2D gel overlay



Protein Identification

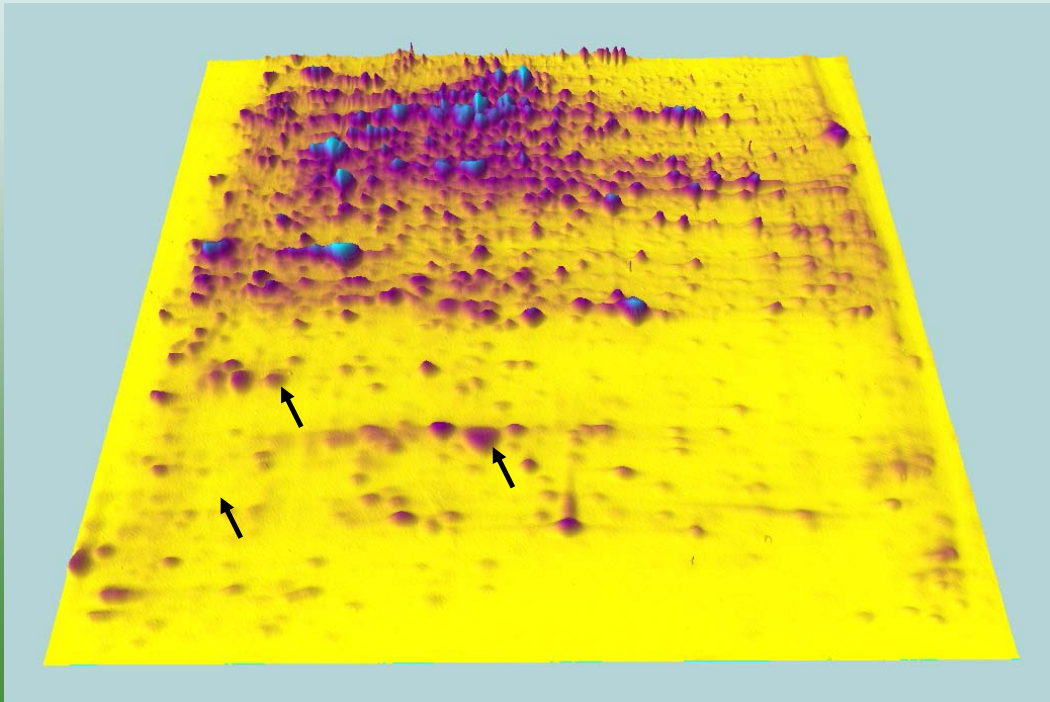


Compare physiological functions of the two types of roots

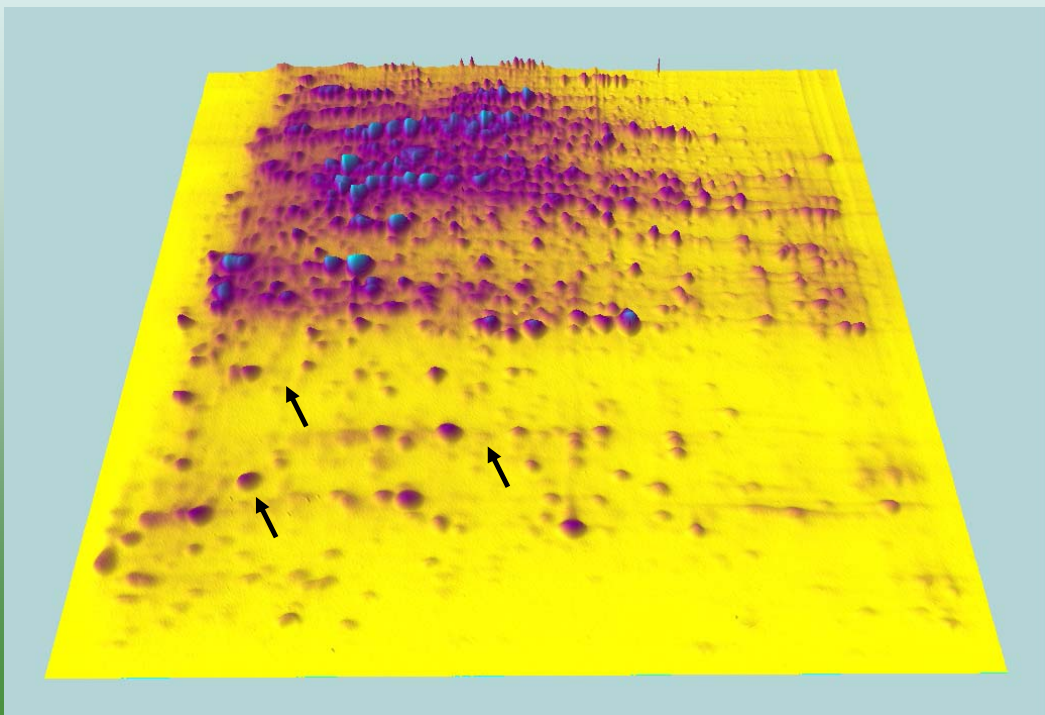
Identify targets for engineering

Protein map for comparison with other cultivars or tissue types

## 3D view of Fibrous Gel



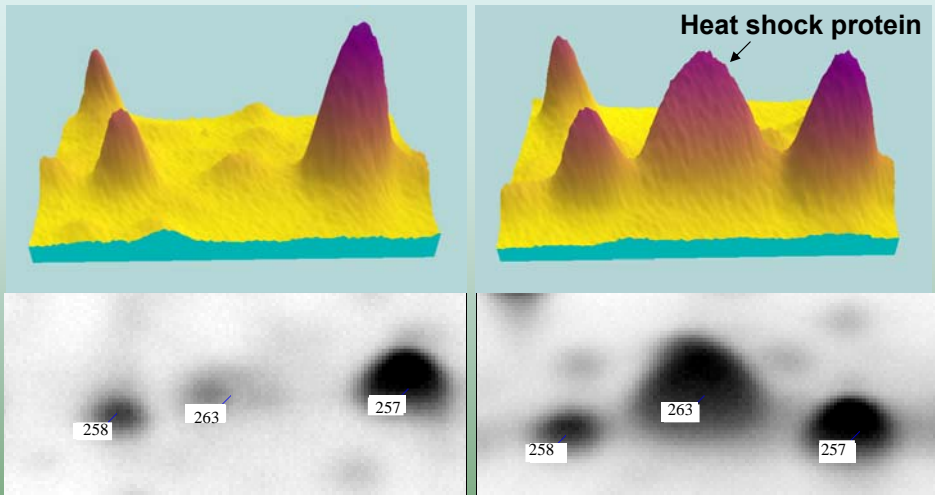
## 3D view of Tuberos Gel



HPLC coupled online with 4000 QTRAP Mass Spectrometer



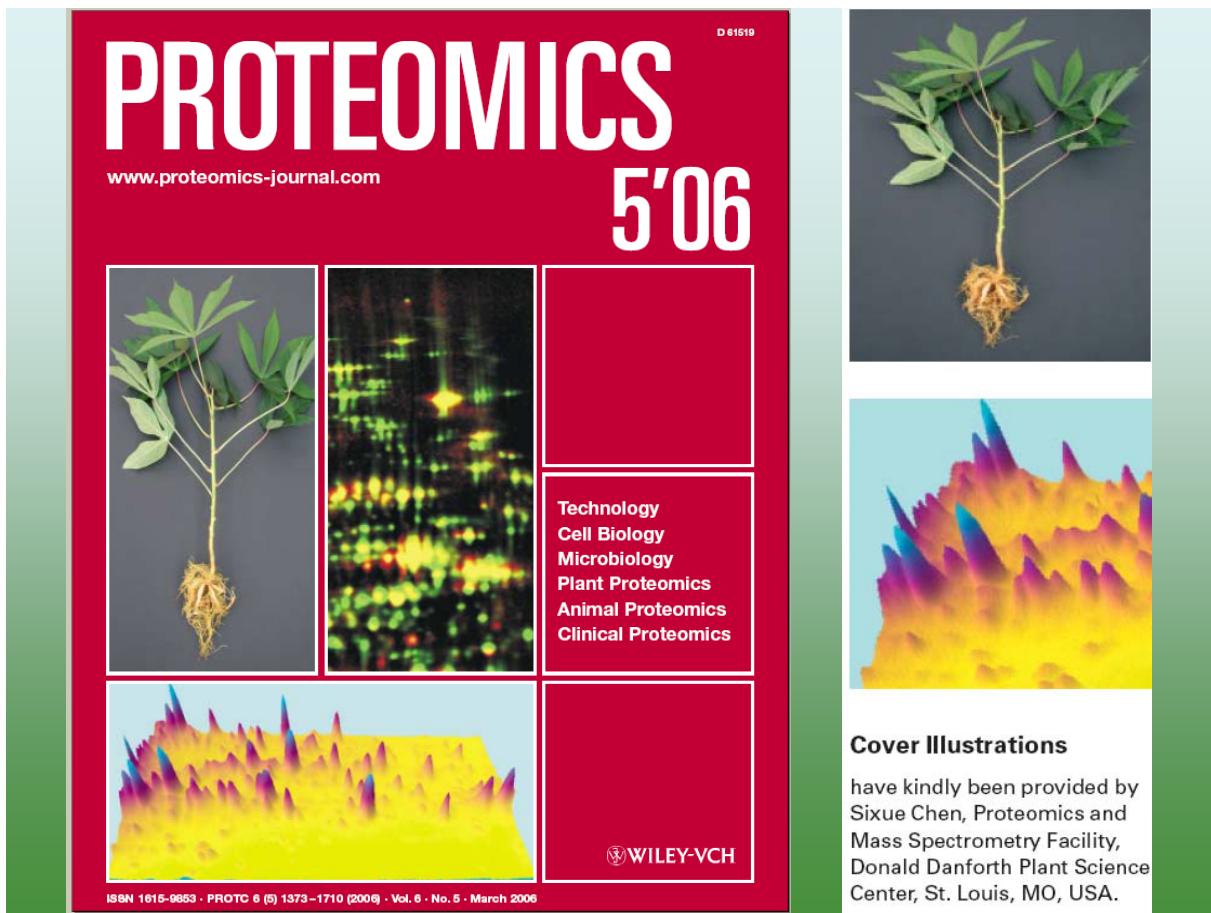
## Novel Targets for Biotechnological Application



BioCassava Plus project: it is proposed to **increase the yield and protein content** of cassava storage roots **by four-fold**







**Cover Illustrations**

have kindly been provided by Sixue Chen, Proteomics and Mass Spectrometry Facility, Donald Danforth Plant Science Center, St. Louis, MO, USA.

# Galactose utilization in yeast

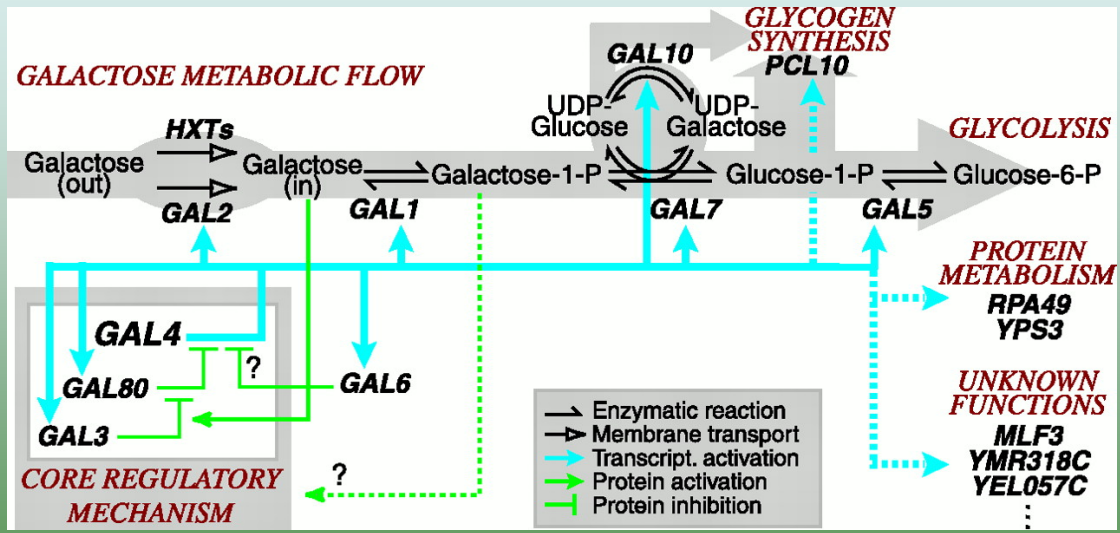
**Strategy**

- For each gene or condition change (i.e. delete the gene) and measure the global effect on both mRNA and protein levels.
- Integrate mRNA and protein responses with the pathway model and with global network of protein interactions.
- Formulate new hypotheses to explain novel observations and refine models.

- Science 292: 929-934 (galactose utilization)  
Combines: literature knowledge, microarray, proteomics, visualization, and network techniques to refine what is known about galactose utilization in yeast.
- Genome Res. 13: 244-253 (Genome scale network reconstruction)

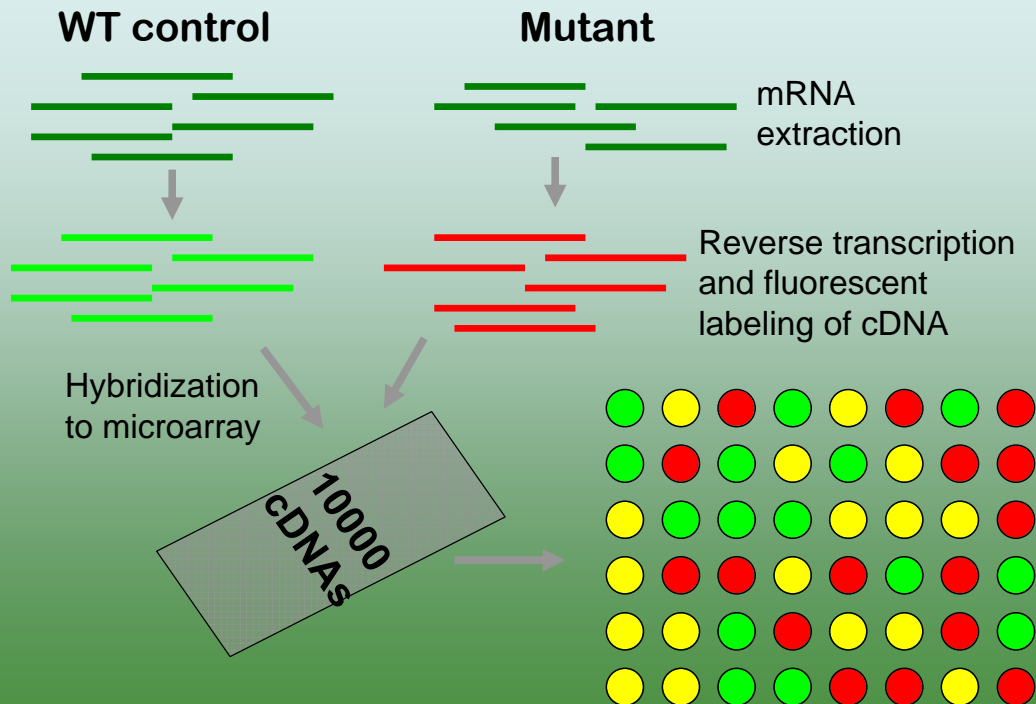


# Galactose metabolism



- Science 292: 929-934

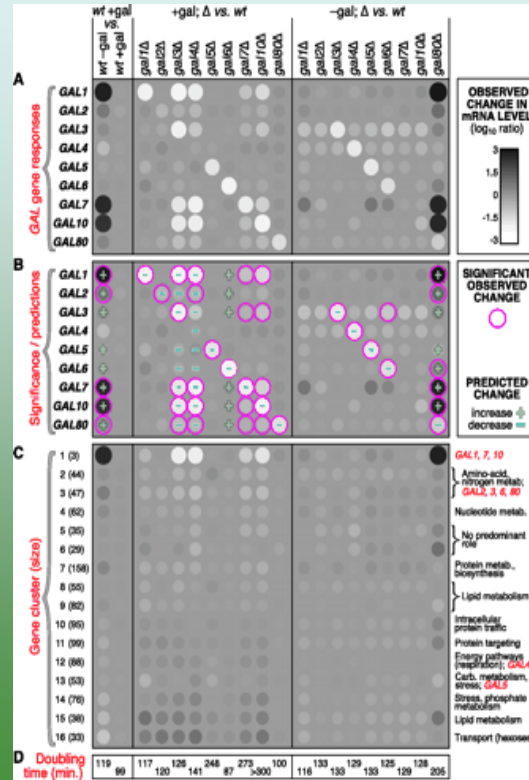
# Expression measurements



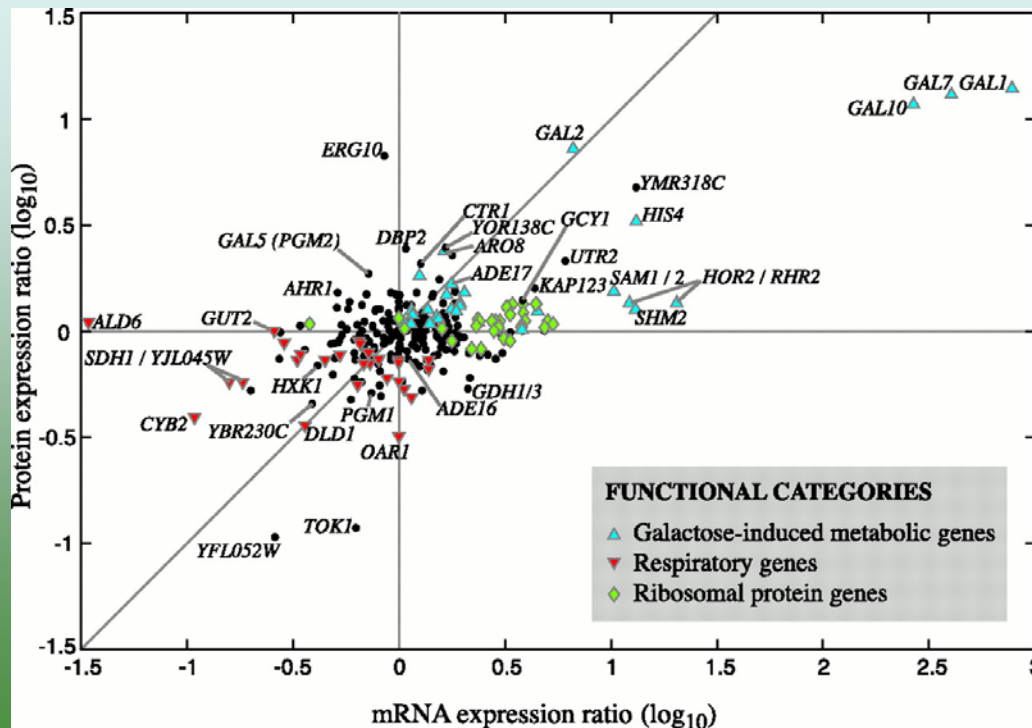
# Expression measurements

## Microarray:

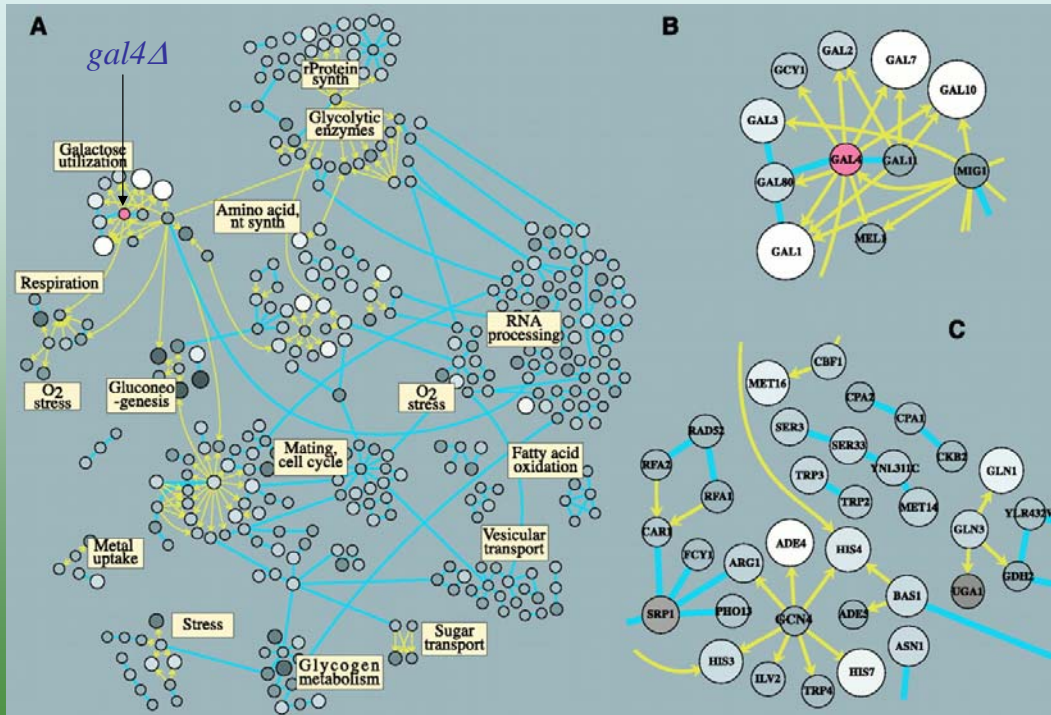
- a perturbed strain vs. wt + gal, 4 replicates
- statistics: maximum-likelihood estimation → 997 significant genes → 16 clusters by self-organizing maps, each cluster contains genes with similar responses over all perturbations.



# Expression measurements



# Visualizing the data



- Blue line (p-p); Yellow line (p-d); node diameter scales with the magnitude of cha

## More Systems Biology to follow...



**Multiple High-Throughput Analyses Monitor the Response of *E. coli* to Perturbations**  
 Nobuyoshi Ishii, *et al.*  
*Science* **316**, 593 (2007);  
 DOI: 10.1126/science.1132067

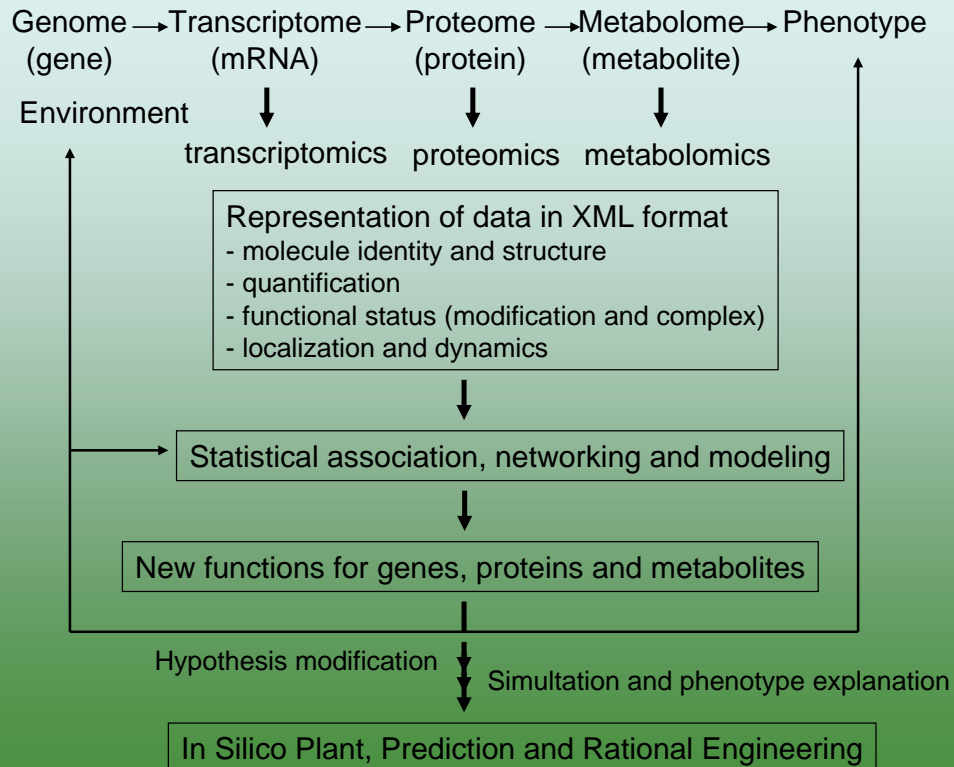
### Multiple High-Throughput Analyses Monitor the Response of *E. coli* to Perturbations

Nobuyoshi Ishii,<sup>1,2\*</sup> Kenji Nakahigashi,<sup>1,2\*</sup> Tomoya Baba,<sup>1,2,3\*</sup> Martin Robert,<sup>1,2\*</sup> Tomoyoshi Soga,<sup>1,2,6\*</sup> Akio Kanai,<sup>1,2\*</sup> Takashi Hirasawa,<sup>1,2\*</sup> Miki Naba,<sup>1</sup> Kenta Hirai,<sup>1</sup> Aminul Hoque,<sup>1,2</sup> Pei Yee Ho,<sup>5</sup> Yuji Kakazu,<sup>1</sup> Kaori Sugawara,<sup>1</sup> Saori Igarashi,<sup>1</sup> Satoshi Harada,<sup>1</sup> Takeshi Masuda,<sup>1,2</sup> Naoyuki Sugiyama,<sup>6</sup> Takashi Togashi,<sup>1</sup> Miki Hasegawa,<sup>1</sup> Yuki Takai,<sup>1</sup> Katsuyuki Yugi,<sup>1,2</sup> Kazuharu Arakawa,<sup>1</sup> Nayuta Iwata,<sup>1,2</sup> Yoshihiro Toya,<sup>1,2</sup> Yoichi Nakayama,<sup>1,2</sup> Takaaki Nishioka,<sup>1,2,4</sup> Kazuyuki Shimizu,<sup>1,2,5</sup> Hirotada Mori,<sup>1,2,3</sup> Masaru Tomita<sup>1,2,6†</sup>

Analysis of cellular components at multiple levels of biological information can provide valuable functional insights. We performed multiple high-throughput measurements to study the response of *Escherichia coli* cells to genetic and environmental perturbations. Analysis of metabolic enzyme gene disruptants revealed unexpectedly small changes in messenger RNA and proteins for most disruptants. Overall, metabolite levels were also stable, reflecting the rerouting of fluxes in the metabolic network. In contrast, *E. coli* actively regulated enzyme levels to maintain a stable metabolic state in response to changes in growth rate. *E. coli* thus seems to use complementary strategies that result in a metabolic network robust against perturbations.



# Systems Biology Scheme



## “Golden Rice”

Over 120 million children worldwide are deficient in vitamin A. Rice has been engineered to accumulate  $\beta$ -carotene, Incorporation of this trait into rice cultivars and widespread distribution could prevent 1 to 2 million deaths each year.

- Vitamin A deficiency is a serious problem
- Causes blindness
  - Influences severity of diarrhea, measles



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Thank you !

