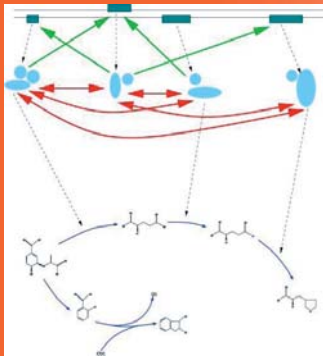


Molecular Interaction Networks

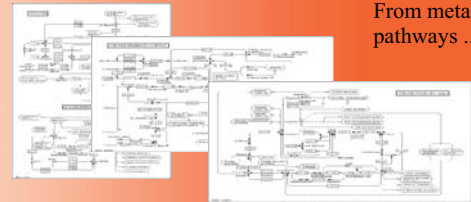


Gene regulation network

Protein Interaction Network

Metabolic Network

Introduction



From metabolic pathways ...

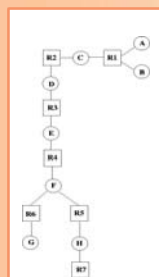
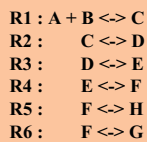
...to metabolic networks



Are there regularities in these networks ?
Are some parts functionally equivalent ?
Do they share common ancestry ?

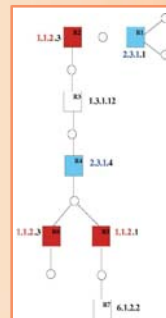
Modelling

Metabolic network is modeled as a graph



Metabolic graph

motif = { }



Regularities are modeled as sets of enzymatic functions
 (no constraint on the order not on topology)

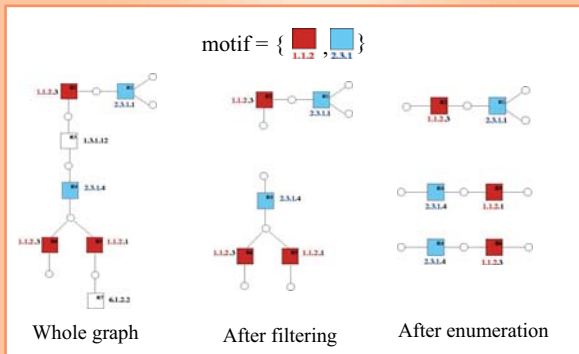
Color definition

- The "EC" classification : enzyme \leftrightarrow code with 4 numbers expressing the chemistry of the reaction
- Ex : 1.1.2.3
- Two enzymes are considered similar if their codes are identical down to a given depth
- Ex : 1.1.2.3 is similar to 1.1.2.1 (for threshold 3)

Algorithm

The search is performed in two steps:

- **filtering** step (straightforward)
- **enumeration** step (NP-hard problem but solved with an exact algorithm)

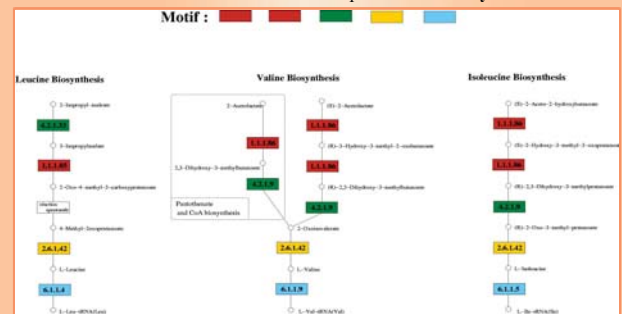


running time :- 8 μ s for motifs of size 3

Applications

Evolutionary hypotheses: an example based on Valine biosynthesis

Motif defined with the 5 last steps of Valine biosynthesis



Motif is found 4 times:

- => Leucine biosynthesis and Isoleucine biosynthesis might share common ancestry with Valine biosynthesis
- => Reactions classically involved in another pathway (Pantothenate and CoA biosynthesis) might be used as an alternative pathway for Valine biosynthesis

Short-time perspectives

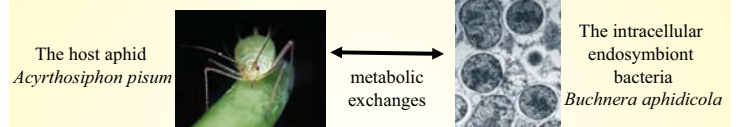
A model to integrate metabolic and genetic data

Biological applications we are interested in lead to build models that integrate simultaneously metabolic and genetic knowledges. Our goal is to better understand the relations between genetic and metabolic components.
 We shall start our modelling work with the case study of the **diauxic shift in yeast** (shift from anaerobic growth to aerobic respiration) that leads to the activation of different metabolic pathways, depending of environmental conditions (glucose depletions).

From a static to a dynamic analysis of networks

A further purpose concerns the development and adaptations of mathematical tools to capture, for example, the steady-state characteristics of the model. Our goal is to carry out comparisons between networks of species or networks under different environmental conditions with the idea to extract knowledges and to provide bases for the definition and understanding of modularity in biological networks.

Metabolic study of a symbiotic association



The intracellular endosymbiont bacteria *Buchnera aphidicola* has essentially a nutritional role in its association with the aphid *Acyrthosiphon pisum*. A new project between Baobab and the BF21, specialist of this association, will first concern the modelling of the metabolic network of the bacterium. This study will focus on two complementary aspects :

- The functional characterization of the metabolic network of *Buchnera*
- The evolutionary history of this metabolic network.

This project will integrate both methodological work and experimental validation.