

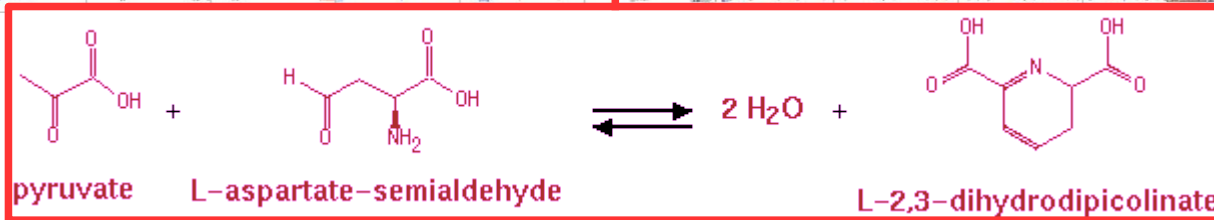
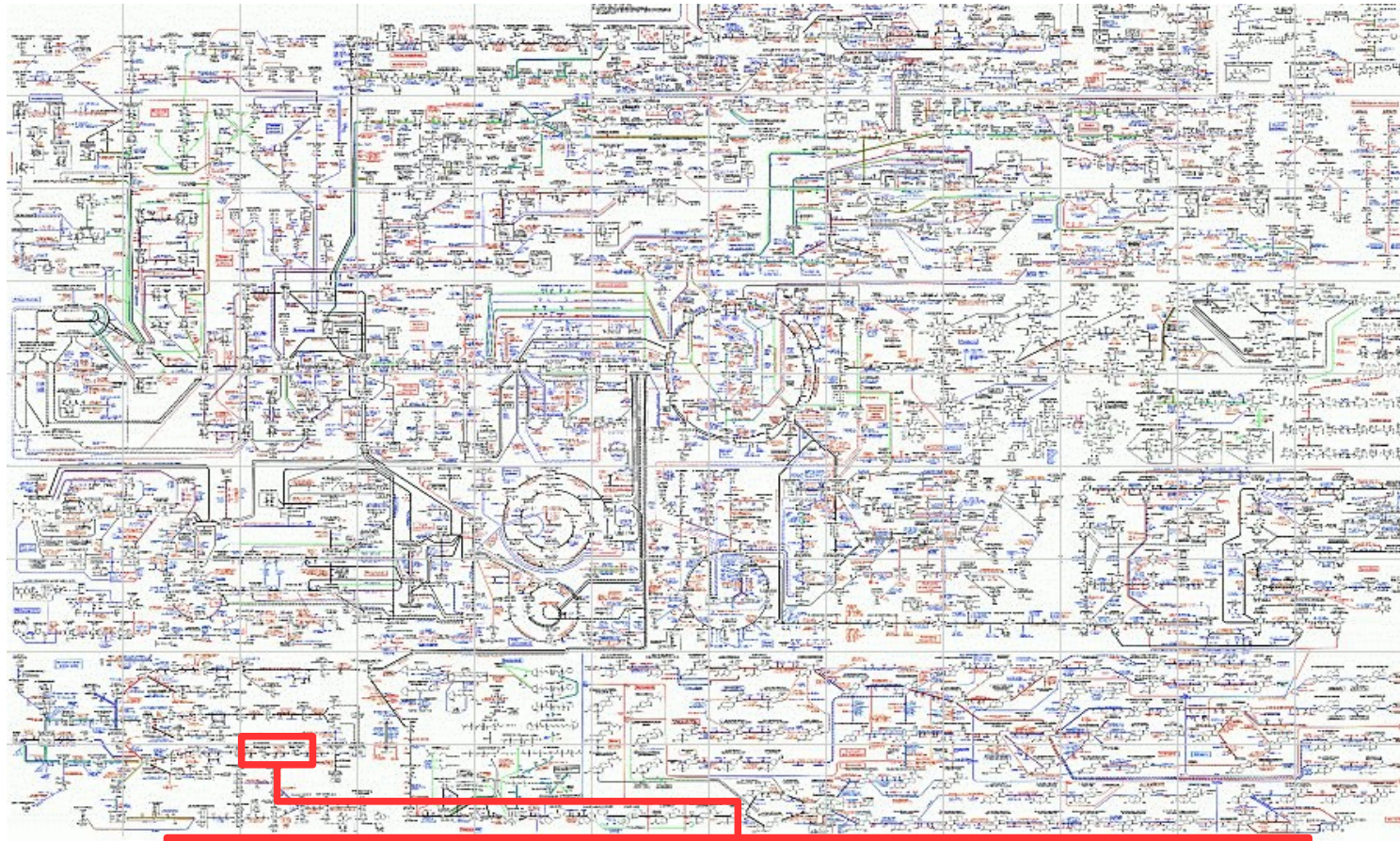
Metabolic network visualisation

Ludovic Cottret
LIPM
CATI BBRIC

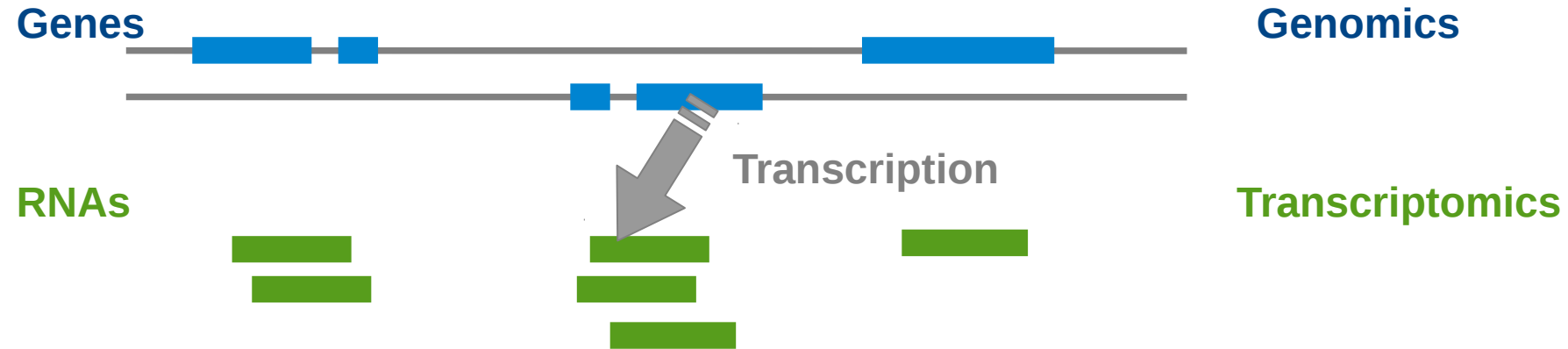
Séminaire Méthodes et outils pour l'Open Data
Notre-Dame de Londres

18 décembre 2014

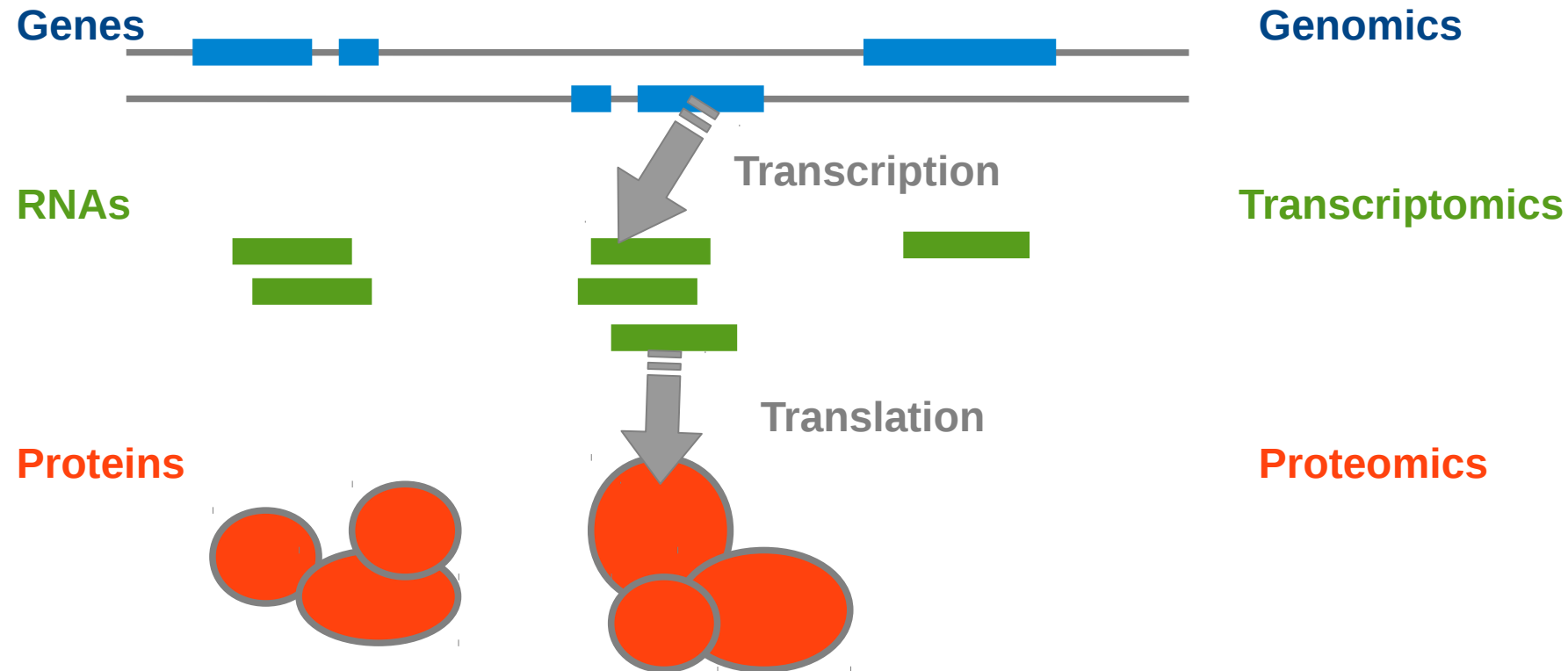
What is a metabolic network?



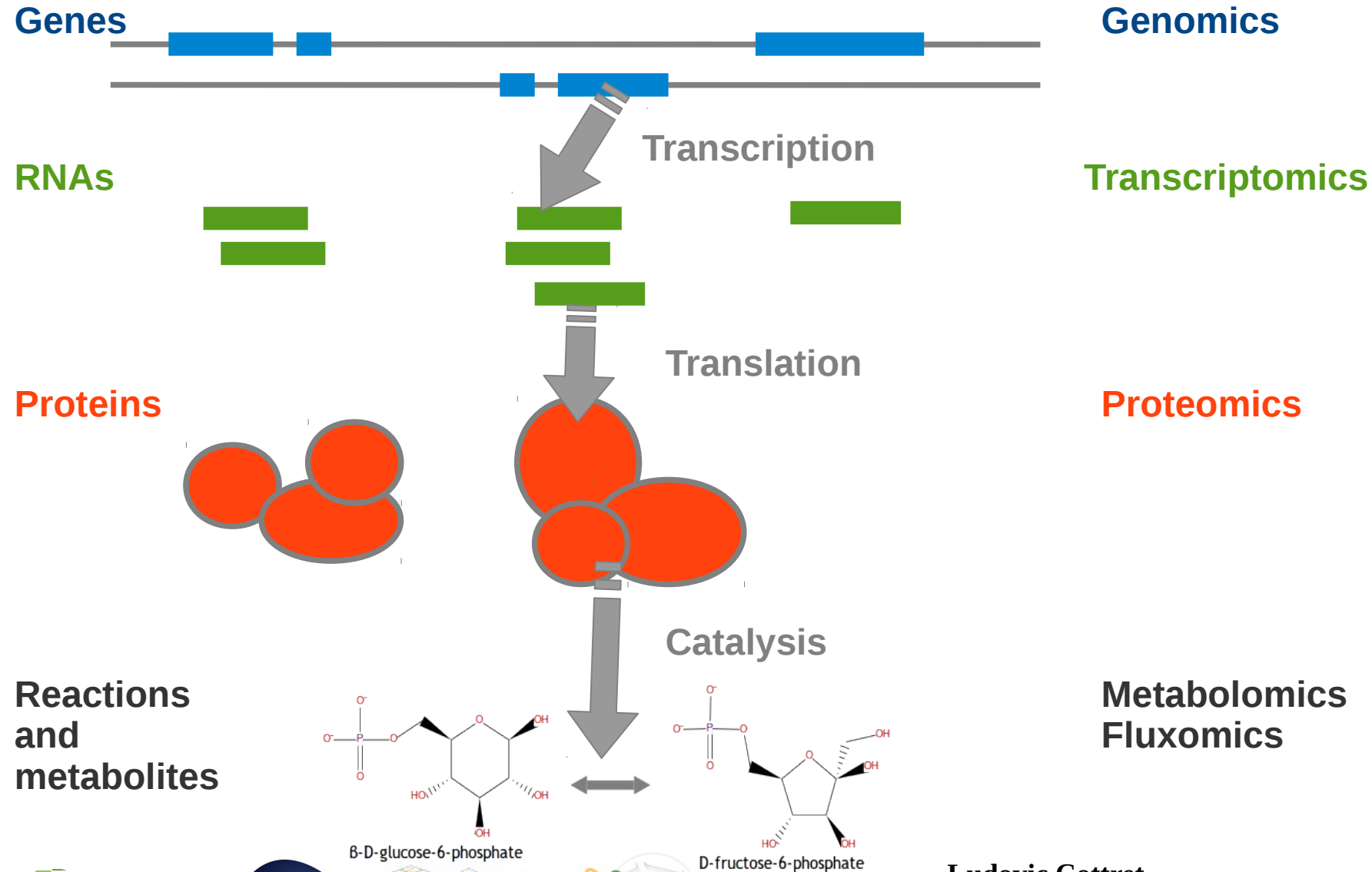
From genes to reactions



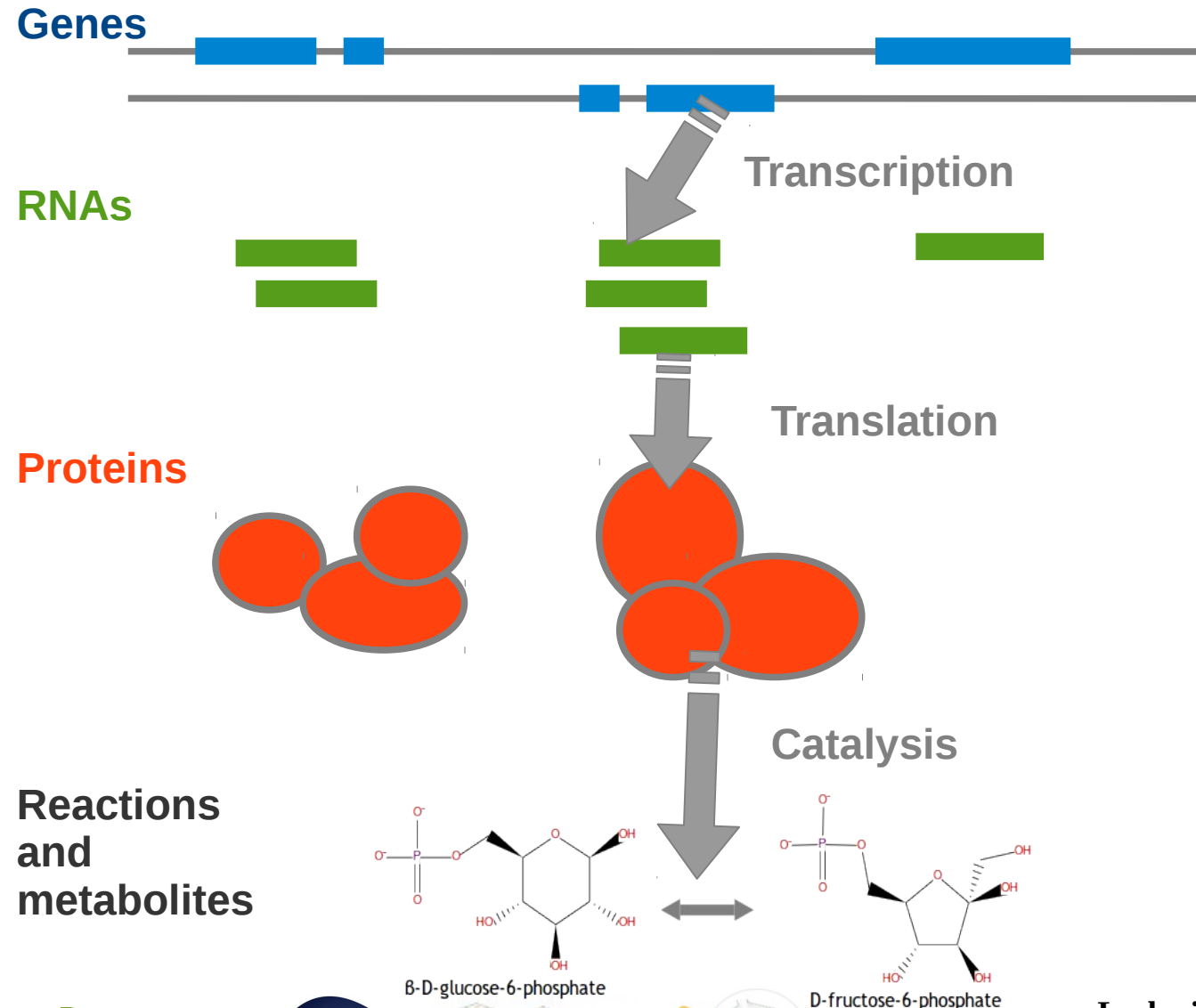
From genes to reactions



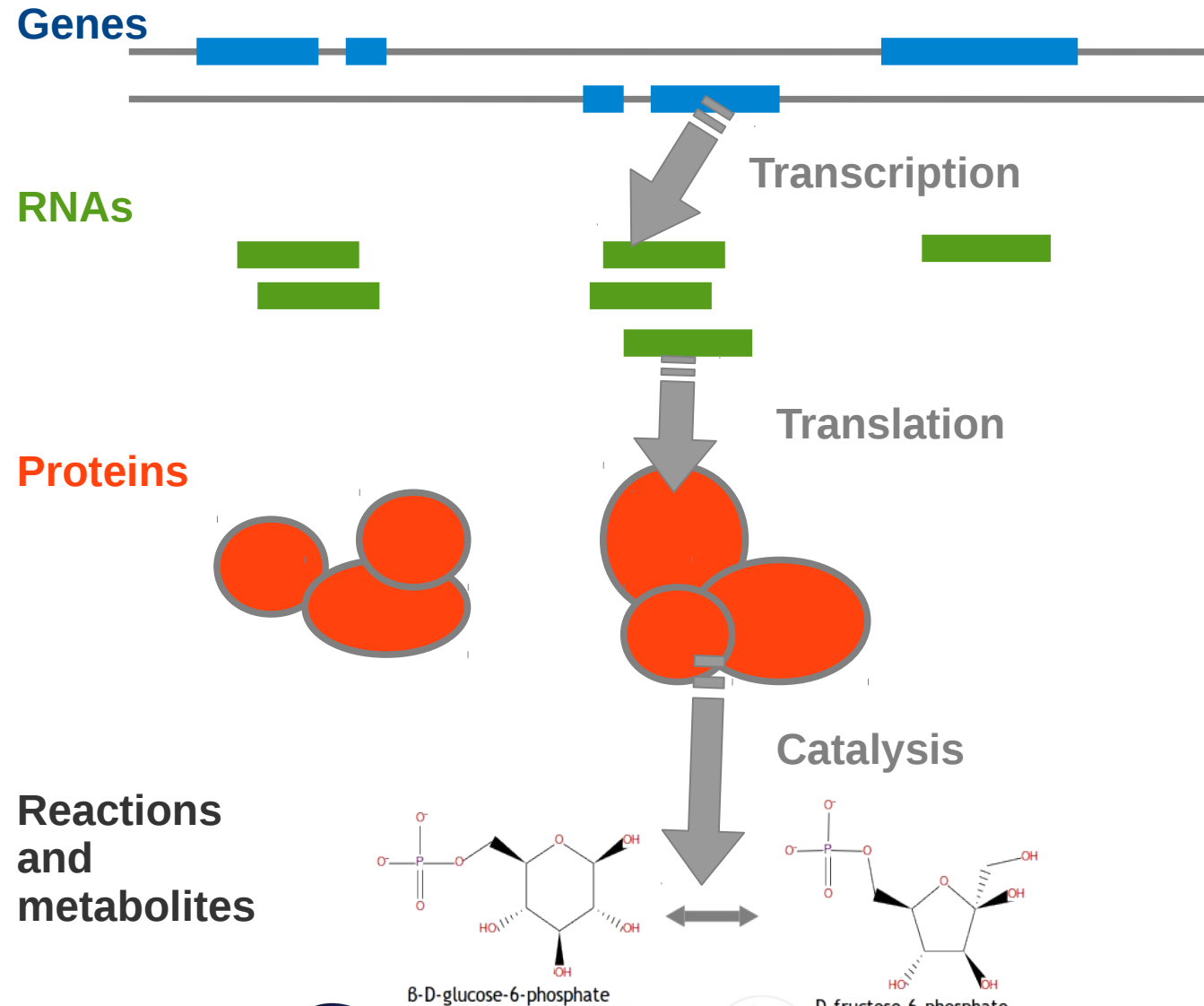
From genes to reactions



From genes to reactions



From genes to reactions

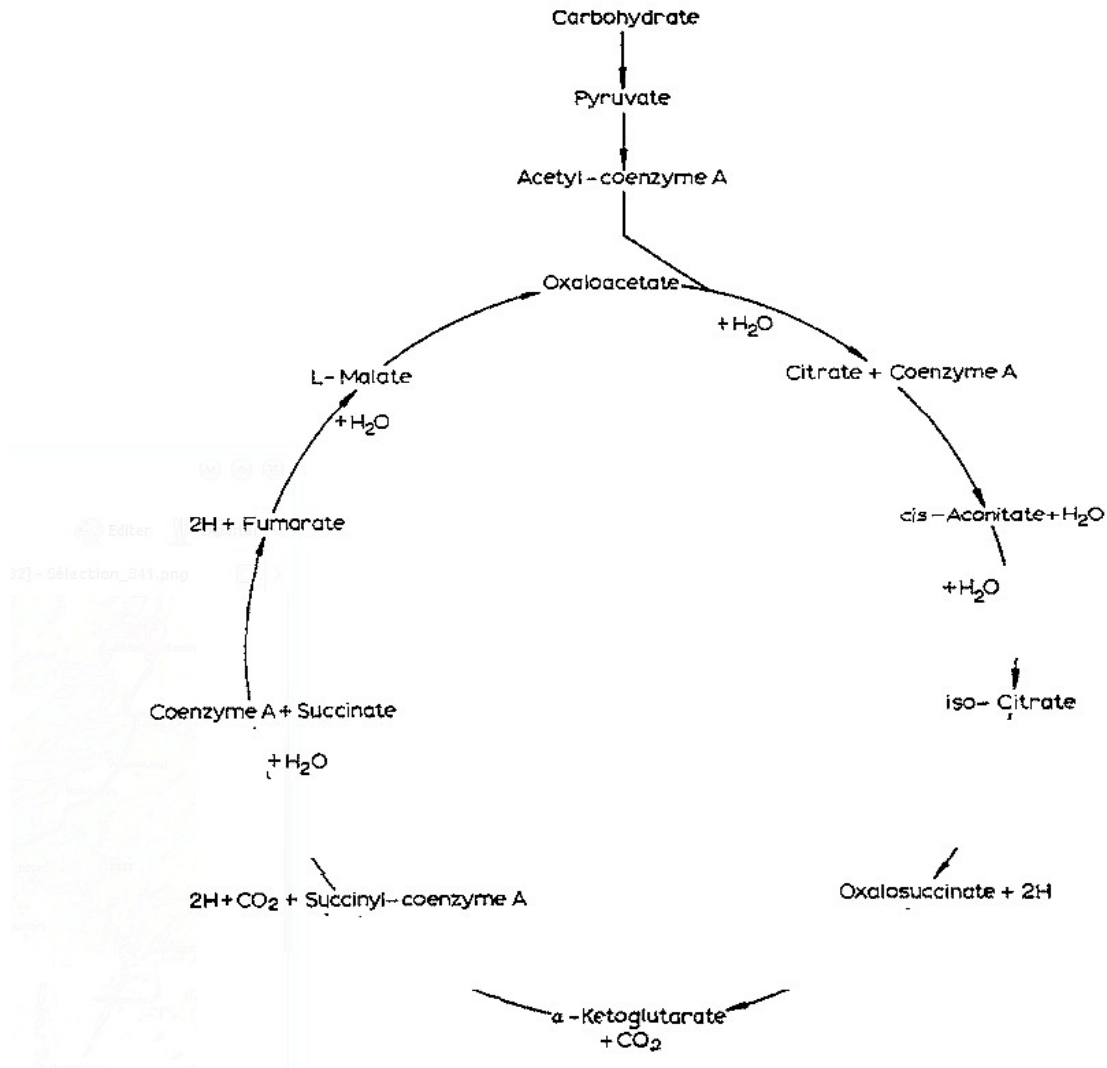


Metabolic network is a useful context for omics data interpretation...

... and visualisation facilitates this interpretation!

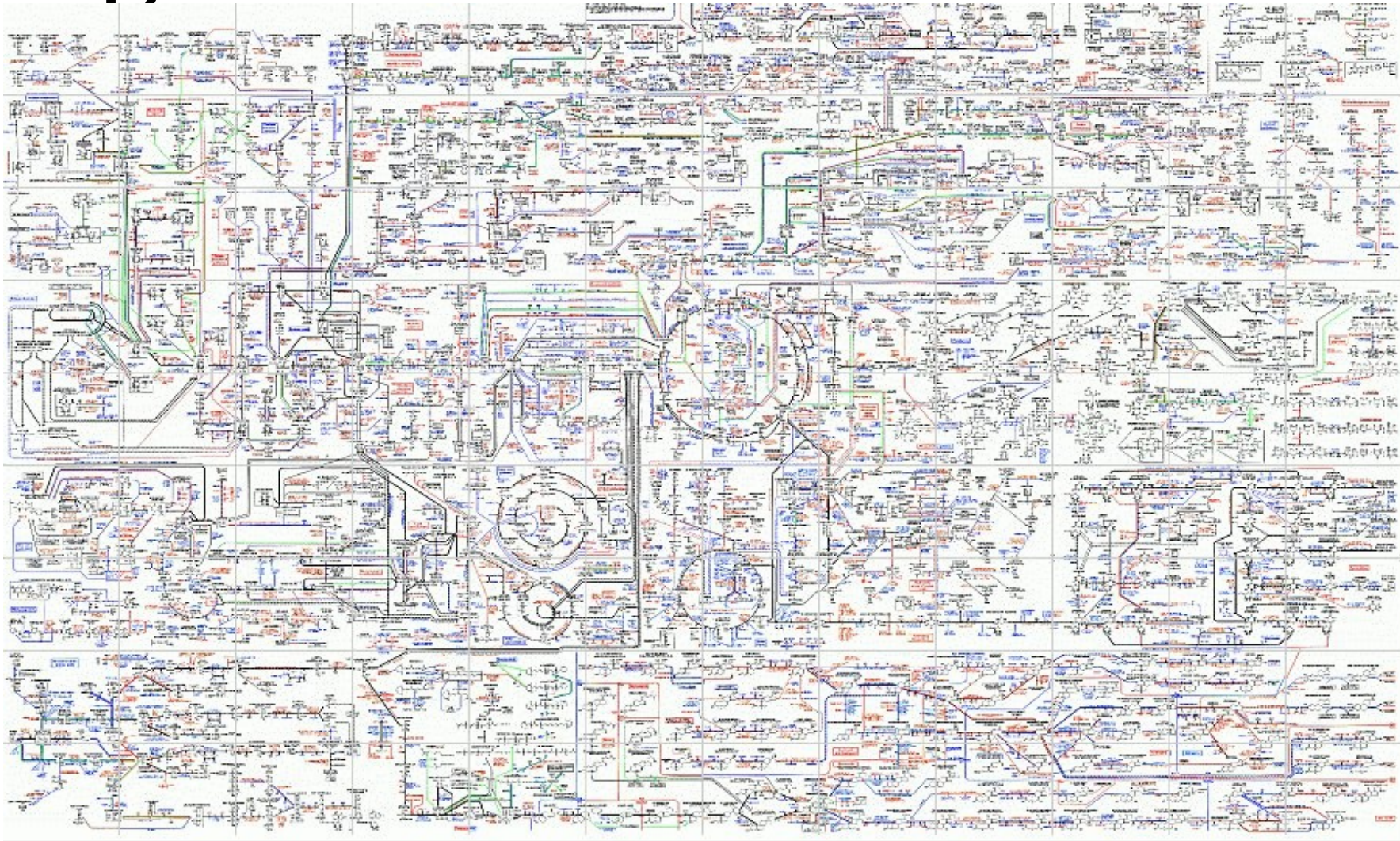
Metabolic network static visualisation

Before computers...



HANS A. KREBS
 The citric acid cycle
 Nobel Lecture, December 11, 1953

Roche BioChemical Pathways (Boehringer map)



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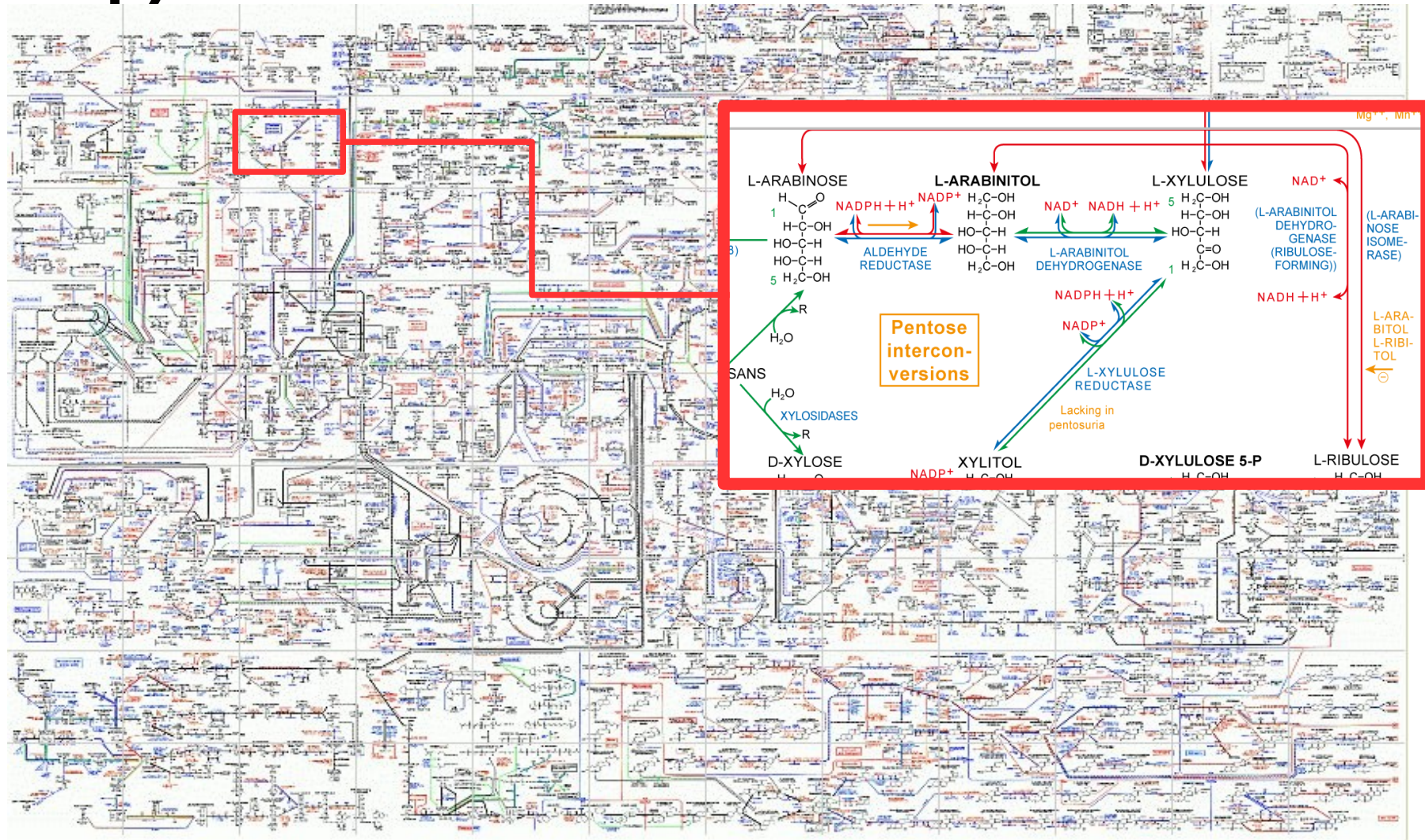
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Biodiversité
Représentation
& Intégration
des Connaissances



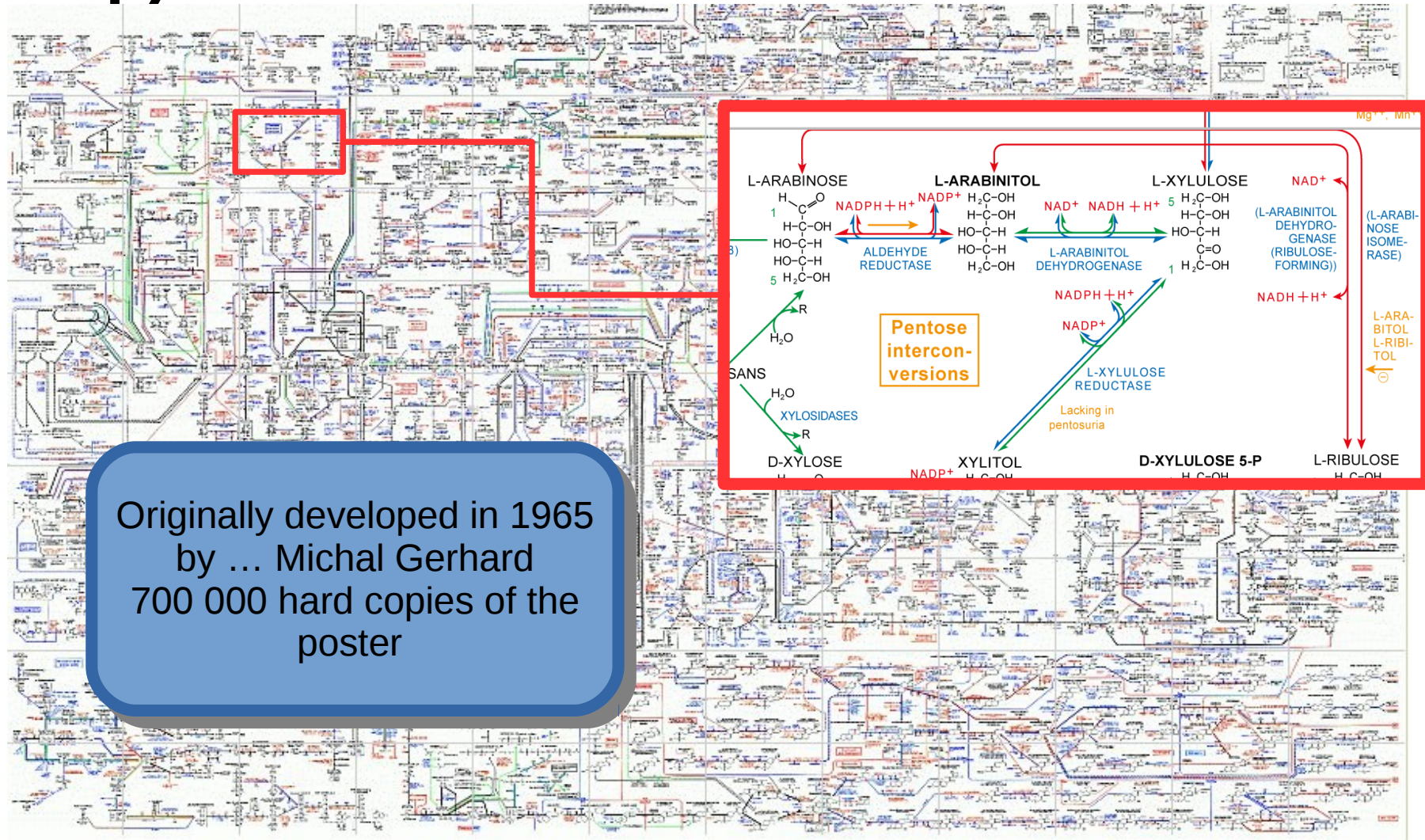
Laboratoire Interactions Plantes Micro-organismes

Ludovic Cottret
Séminaire “Méthodes et outils pour l'Open Data”
Saint-Martin de Londres, 18 décembre 2014

Roche BioChemical Pathways (Boehringer map)



Roche BioChemical Pathways (Boehringer map)



Originally developed in 1965
by ... Michal Gerhard
700 000 hard copies of the
poster

Interactive Boehringer map

Biochemical Pathways Roche.com Contact Share

Part 1: Metabolic Pathways Part 2: Cellular and Molecular Processes

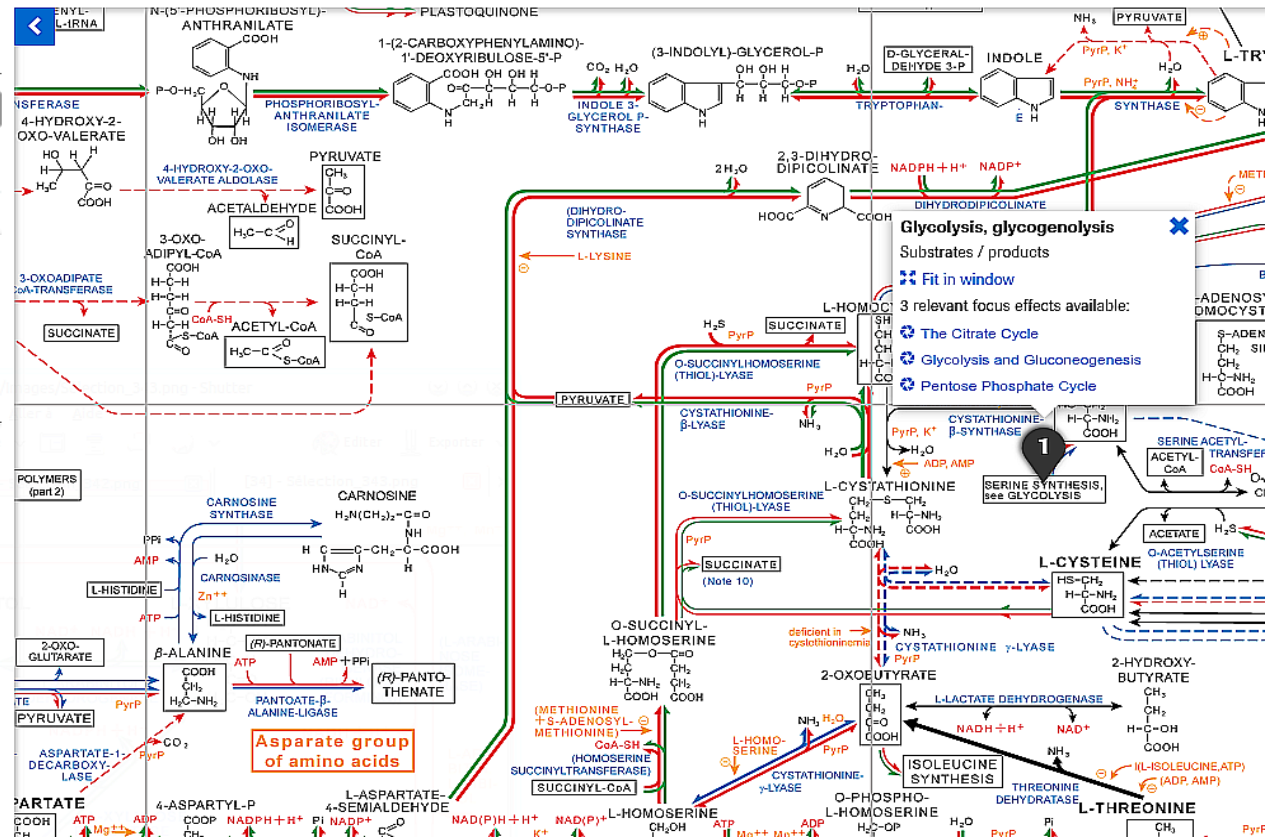
Search Filter Focus Legend

glycolysis

Show 1 matches in Part 2

1 matches in Part 1

- Glycolysis, glycogenolysis**
Substrates / products
3 relevant focus effects available:
 - The Citrate Cycle
 - Glycolysis and Gluconeogenesis
 - Pentose Phosphate Cycle



<http://biochemical-pathways.com/>



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Metabolic pathways in KEGG



Lysine biosynthesis - Reference pathway

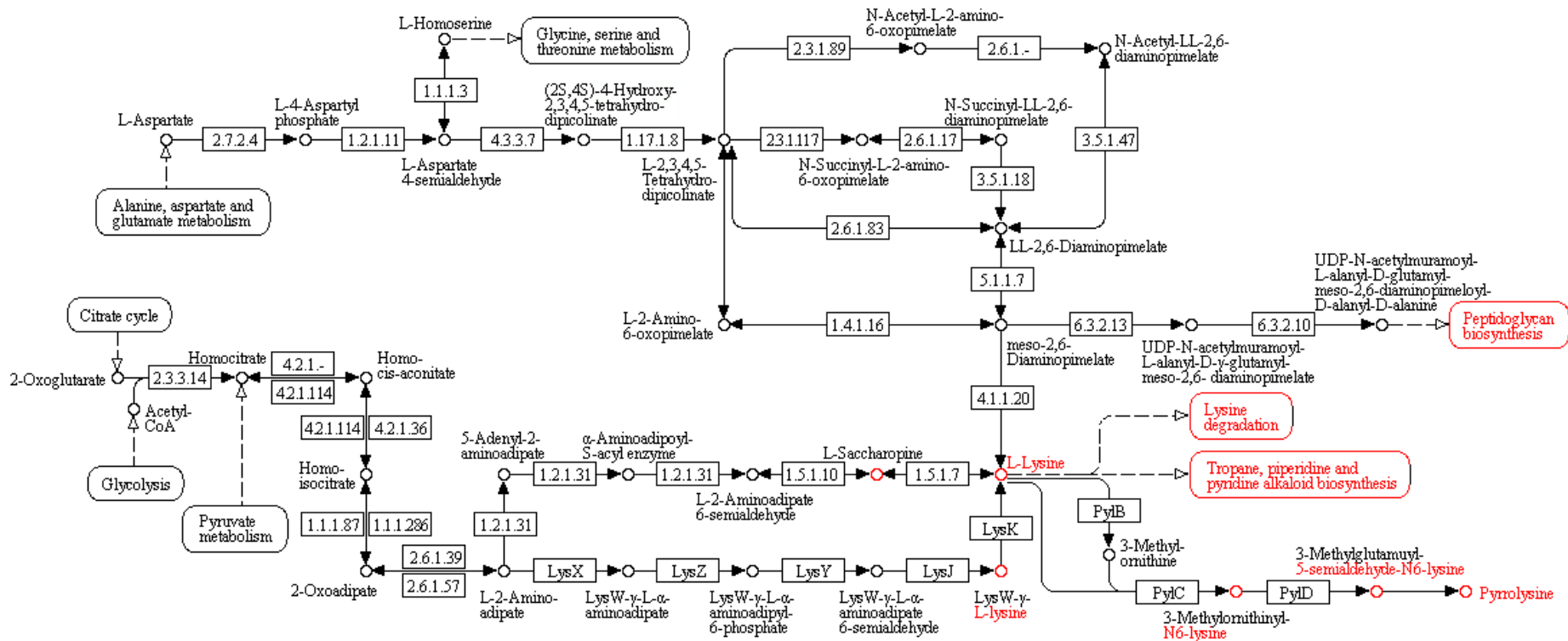
[Pathway menu | Organism menu | Pathway entry | User data mapping]

Reference pathway

Go

100%

LYSINE BIOSYNTHESIS



00300 11/19/13
(c) Kanehisa Laboratories

Metabolic pathways in KEGG

KEGG Lysine biosynthesis - *Saccharomyces cerevisiae* (budding yeast)

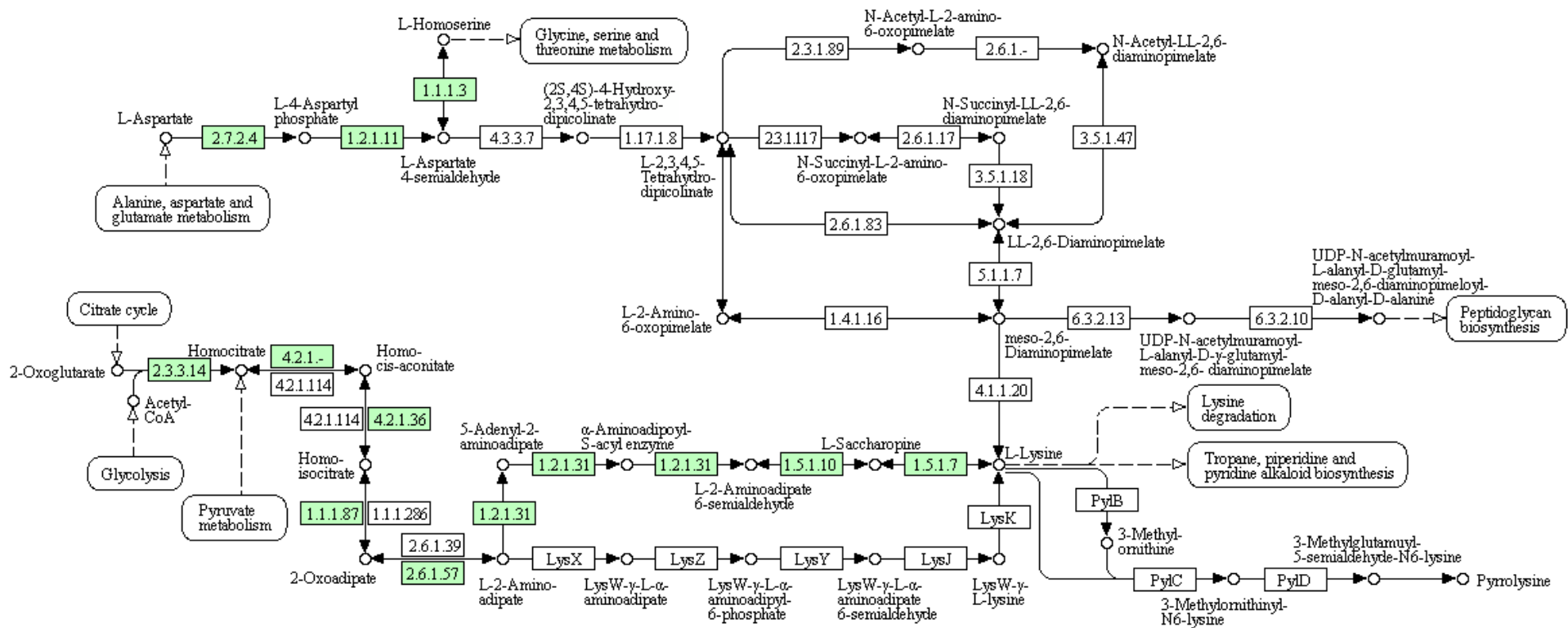
[Pathway menu | Organism menu | Pathway entry | Download KGML | User data mapping]

Saccharomyces cerevisiae (budding yeast)

Go

100%

LYSINE BIOSYNTHESIS



00300 11/19/13
(c) Kanehisa Laboratories



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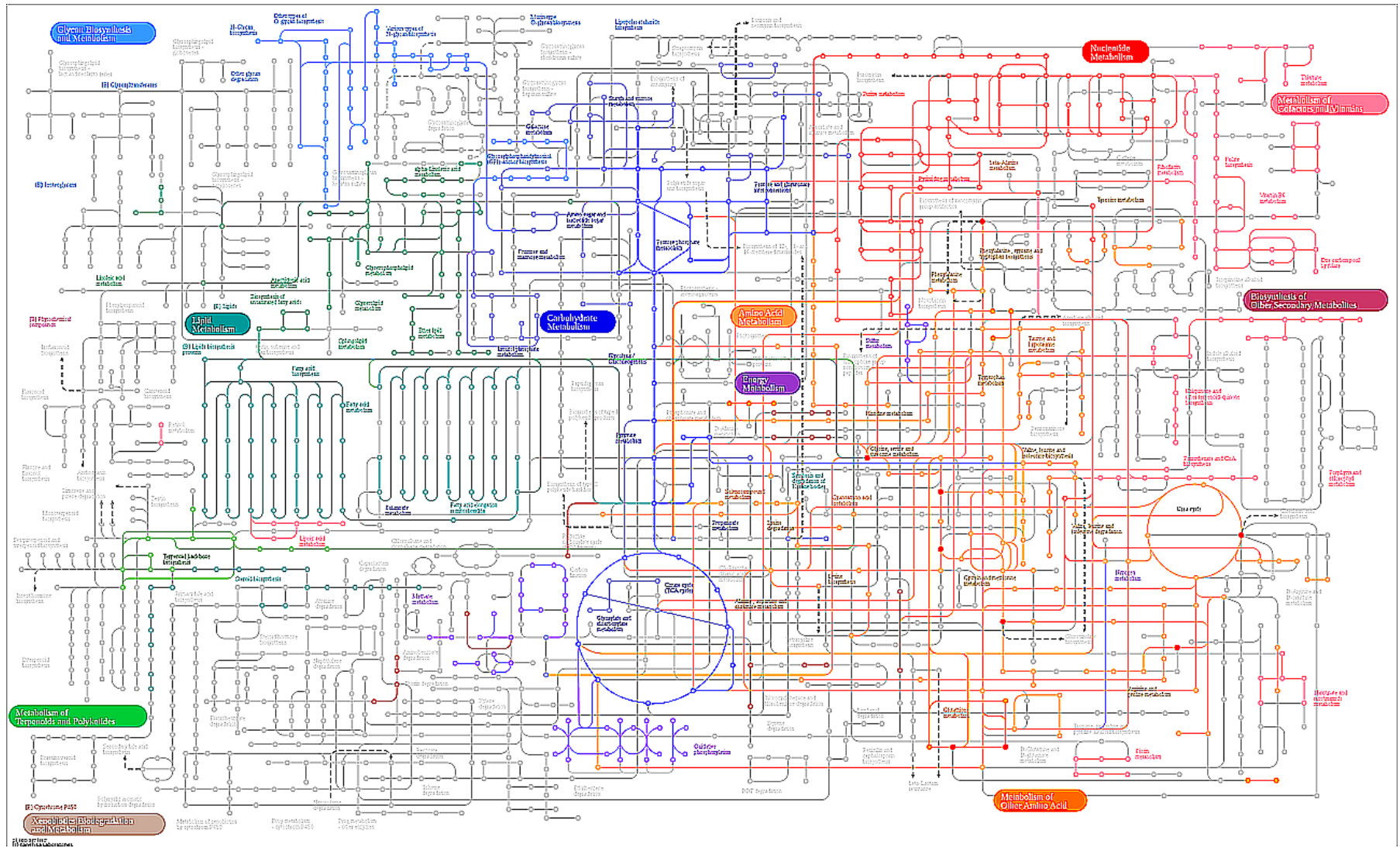
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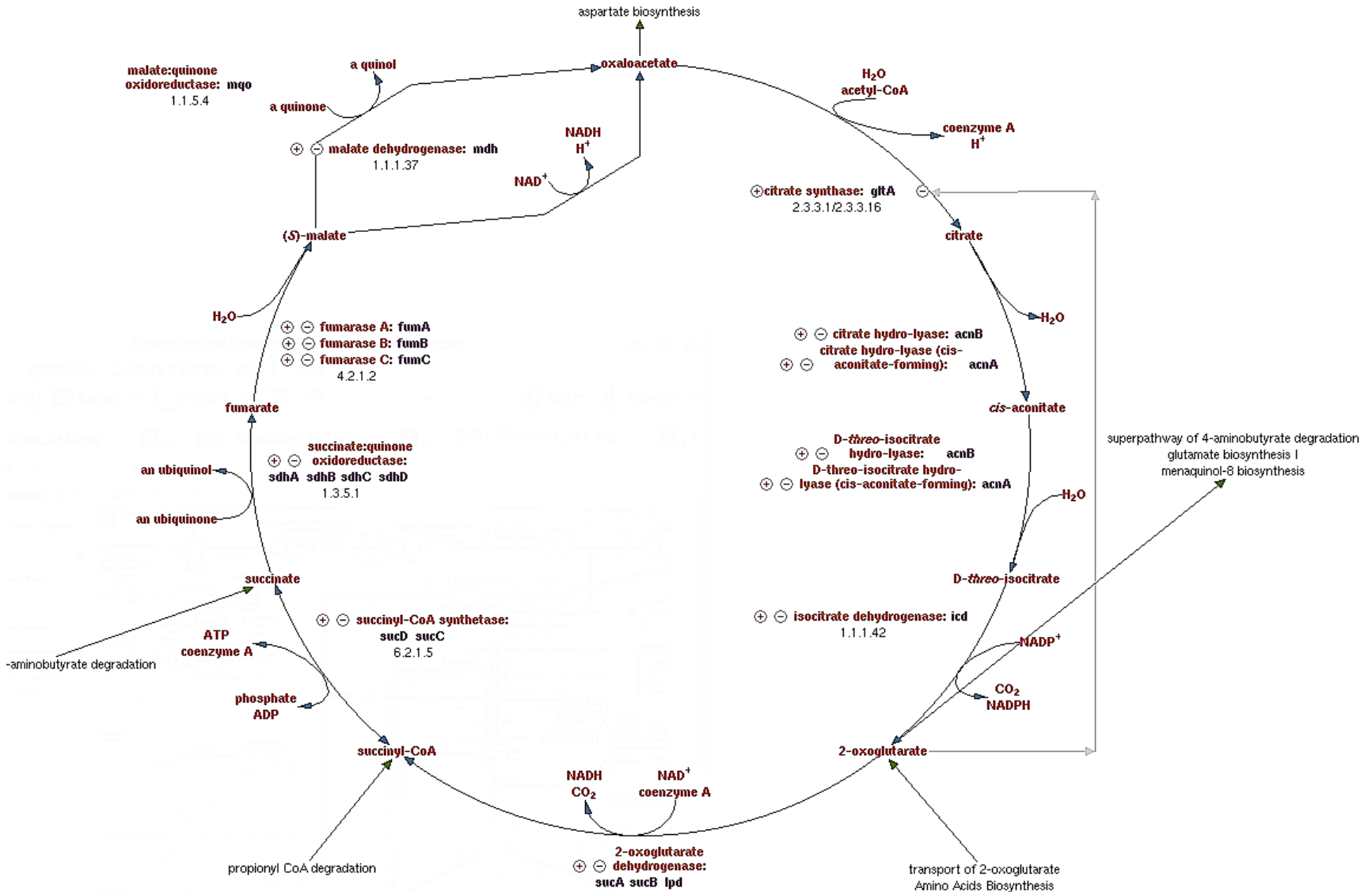
Ludovic Cottret
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Metabolic pathways in KEGG



Metabolic pathways in BioCyc

More Detail Less Detail

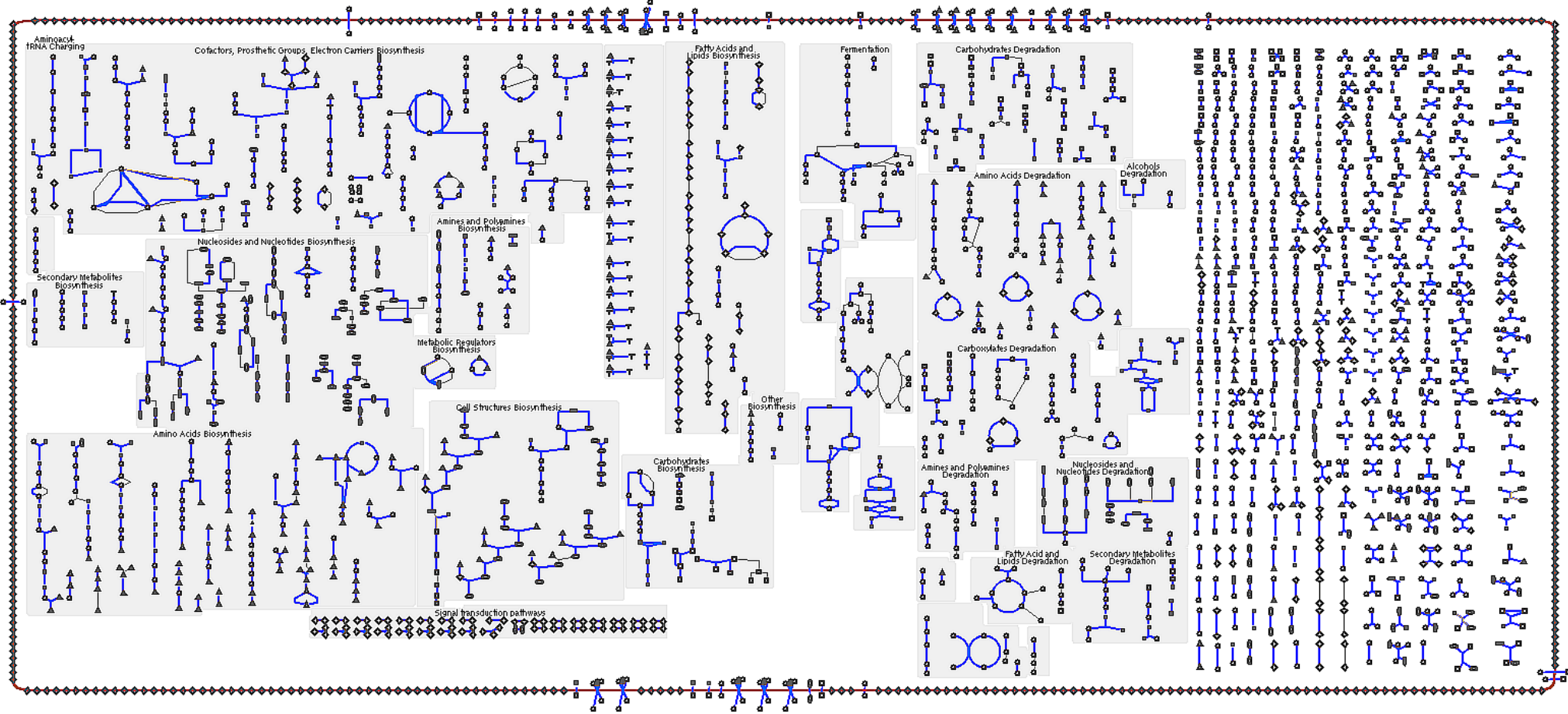


Metabolic pathways in BioCyc

Cellular Overview of *Bacillus subtilis subtilis* 168

Pan left/right/up/down the entire diagram by holding the left mouse button, click on an object for more info, right-click (ctrl-click for Mac) for menu

Cellular Overview



Creation and edition of metabolic pathways

Pathway editor in the pathway-tools (BioCyc)

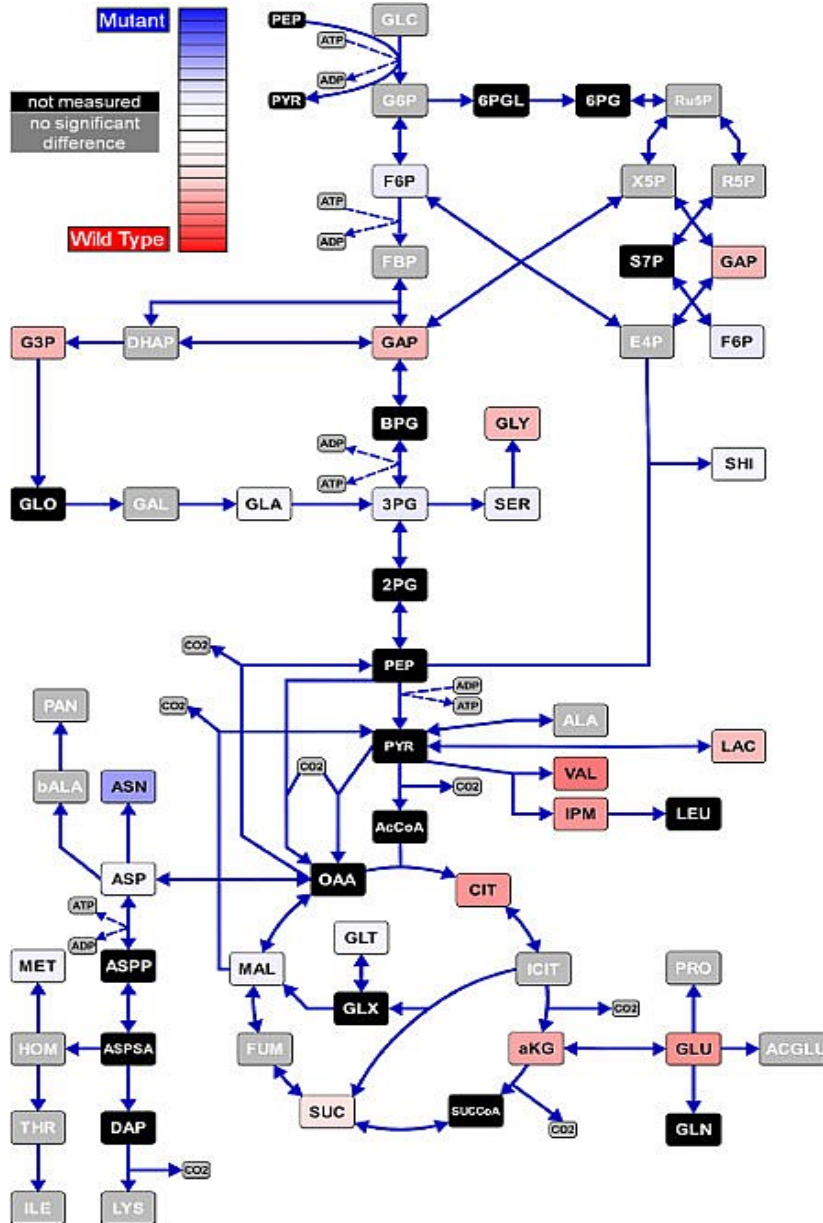
The screenshot displays the BioCyc pathway editor interface. The top menu bar includes "Exit", "Reaction", and "Pathway". Below it, the title bar reads "Editing Pathway test".

The left panel contains a text box with the following reaction details:

```
AMINEPHEN-RXN  
1.4.3.21  
phenylethylamine + oxygen +  
H2O -> phenylacetaldehyde +  
ammonia + hydrogen peroxide + H+
```

The right panel shows a pathway diagram. At the top, "phenylacetaldehyde" is written in red. Two green arrows branch downwards from this molecule. The left arrow points to "phenylacetate" and is associated with the conversion of NAD^+ and H_2O to 2H^+ and NADH . The right arrow points to "2-phenylethanol" and is associated with the conversion of NADH and H^+ to NAD^+ .

Omix



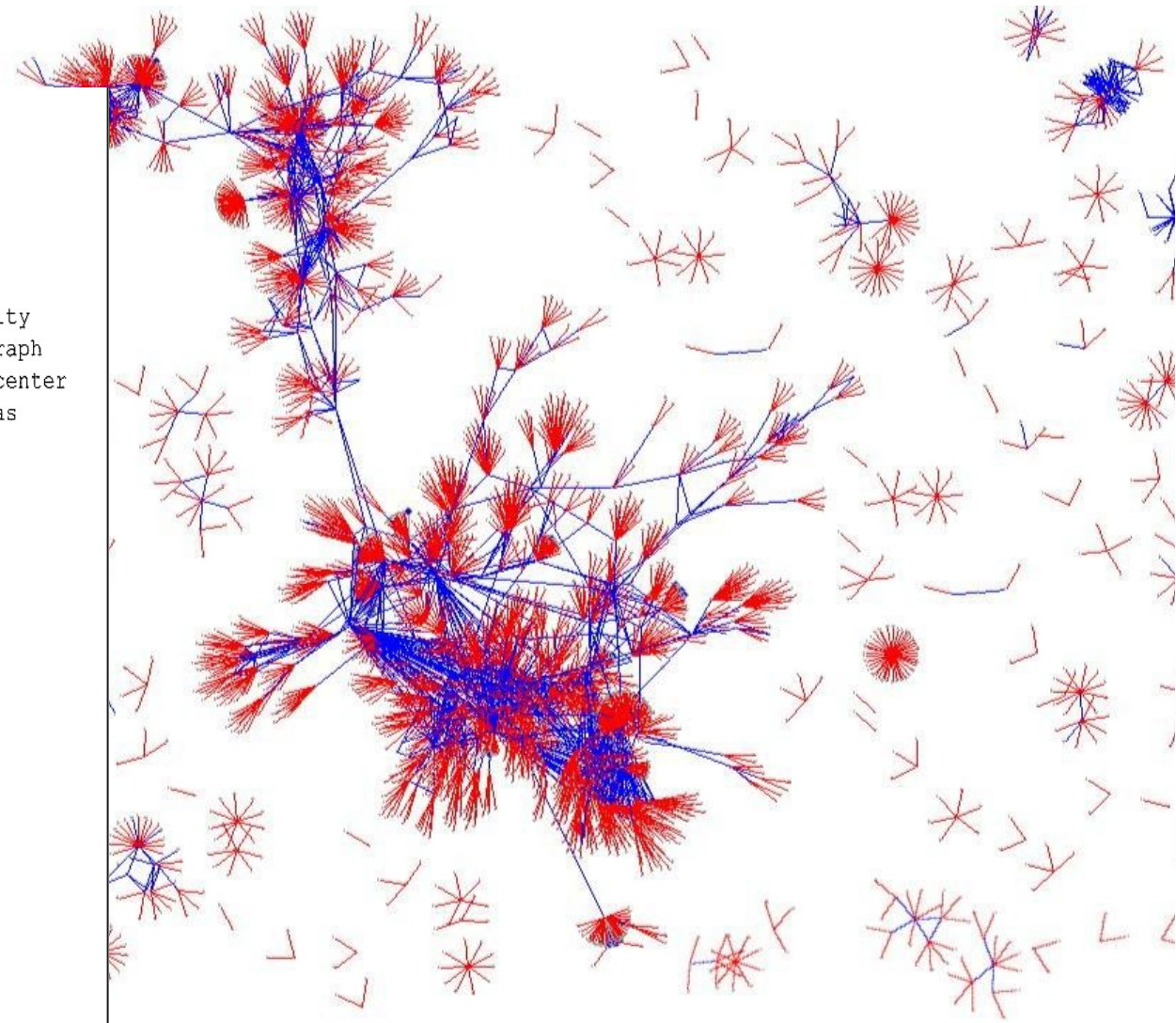
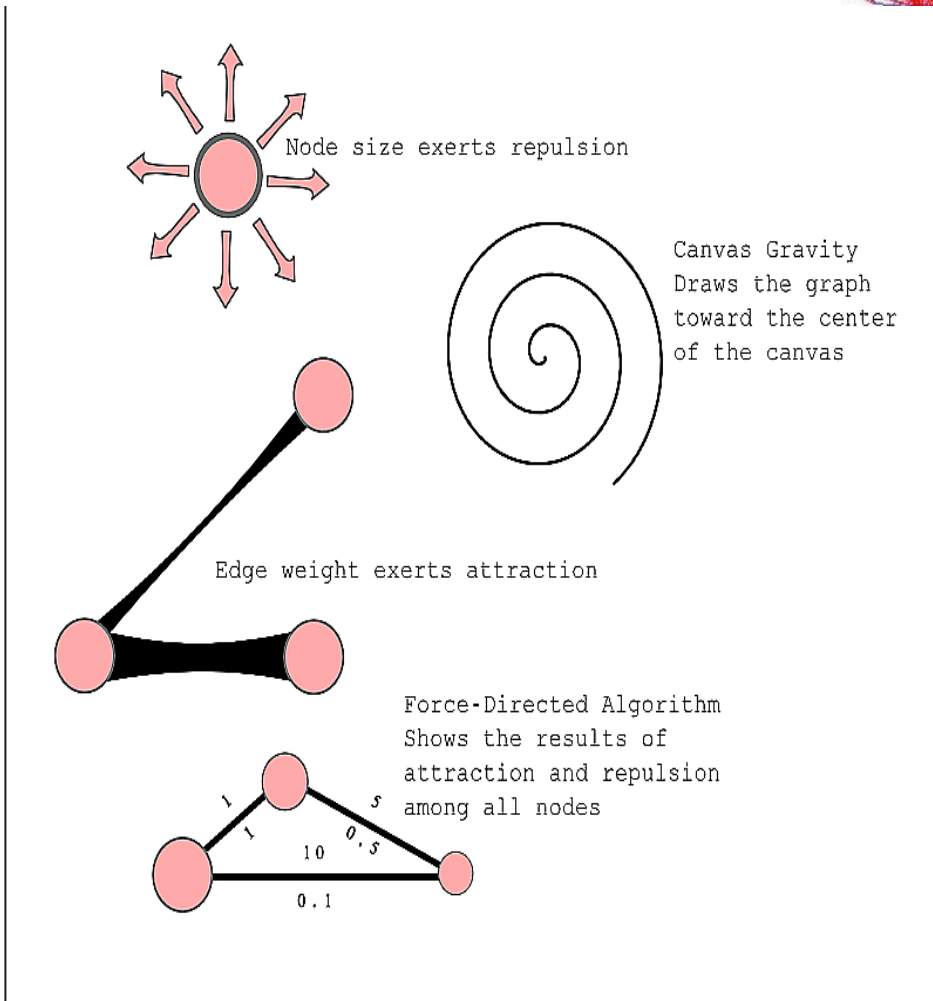
<http://www.omix-visualization.com/>

Metabolic graph visualisation

Principles

- One entity (reaction or metabolite) = one node
- Nodes are linked by interactions (edges)
- Layout algorithms for optimising the visualisation

Force-directed layout



<https://dhs.stanford.edu/visualization/more-networks/>



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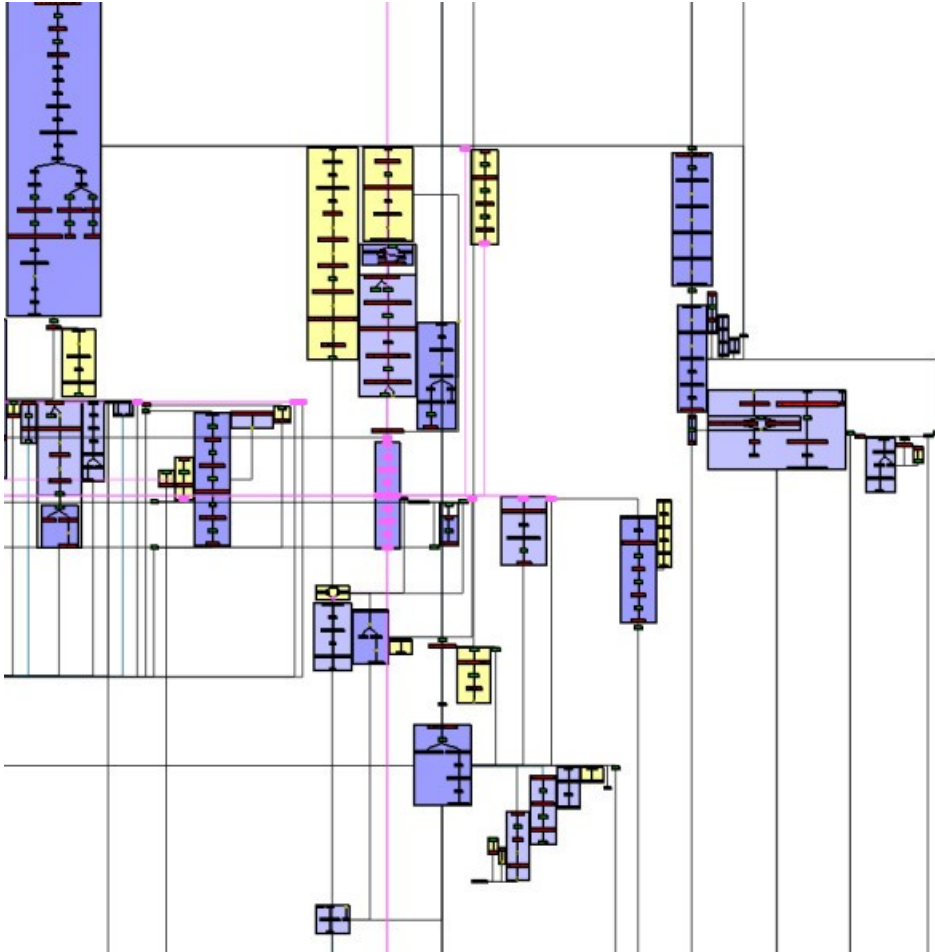
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Layout designed for metabolic networks

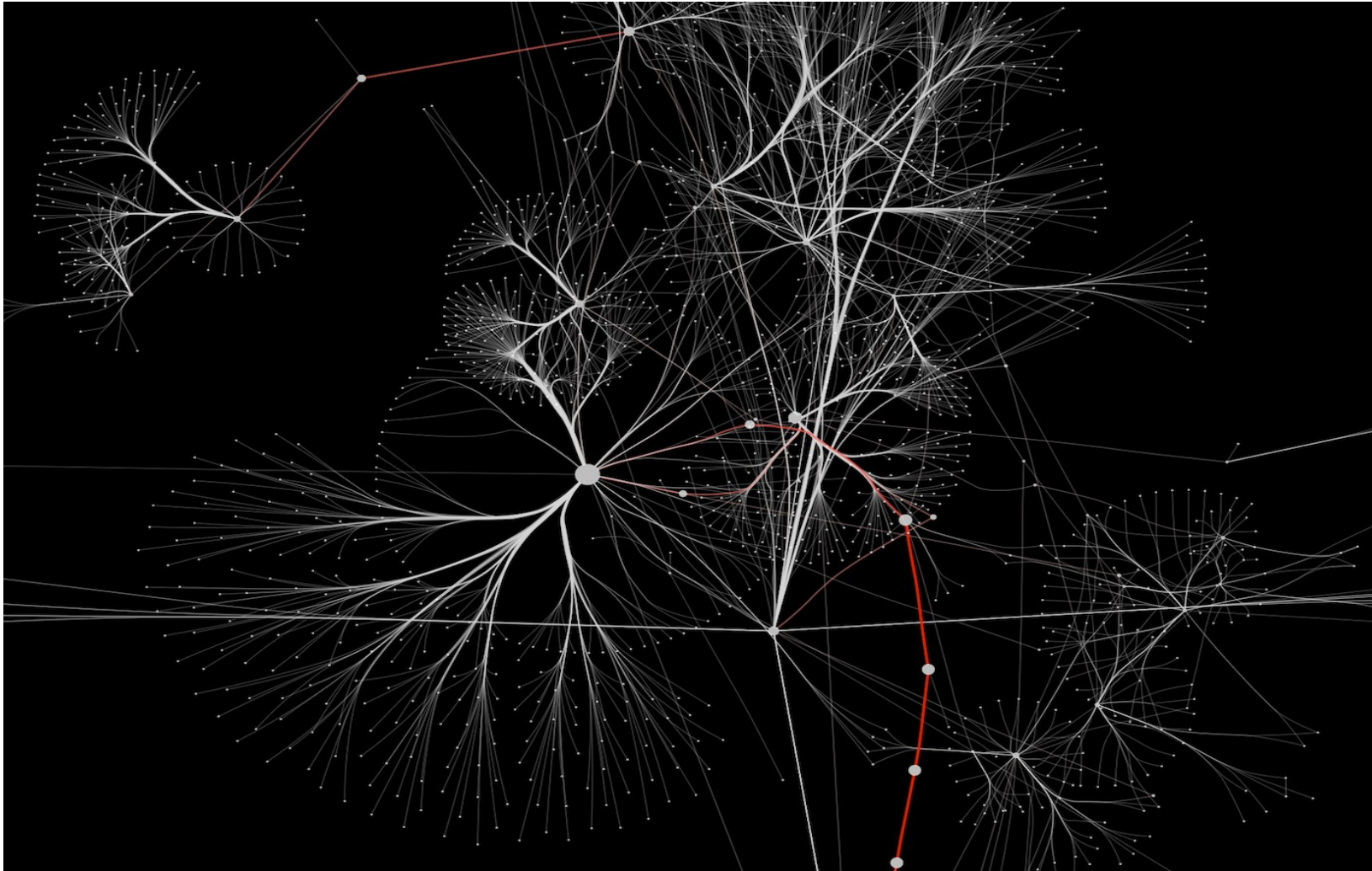


Objectives

- when possible, preserves the classification of the reactions in metabolic pathways
- takes into account the metabolic pathway drawing conventions

Bourqui R, Cottret L, Lacroix V, et al. Metabolic network visualization eliminating node redundancy and preserving metabolic pathways. BMC Systems Biology 2007;1:29.

Cytoscape Java



Cytoscape JAVA

- user friendly
 - visual styles
 - a lot of plugins
 - may be linked to Web pages by Java Web start
- Version 3.0 :
 - V2 plugins can not be used
 - Web start not possible?



Tulip / Systrip

<http://tulip.labri.fr/TulipDrupal/?q=systrip>

The screenshot displays the Tulip software interface for analyzing metabolic networks. The main window shows a complex network of nodes and edges for *Trypanosoma brucei*. The interface is divided into several panels:

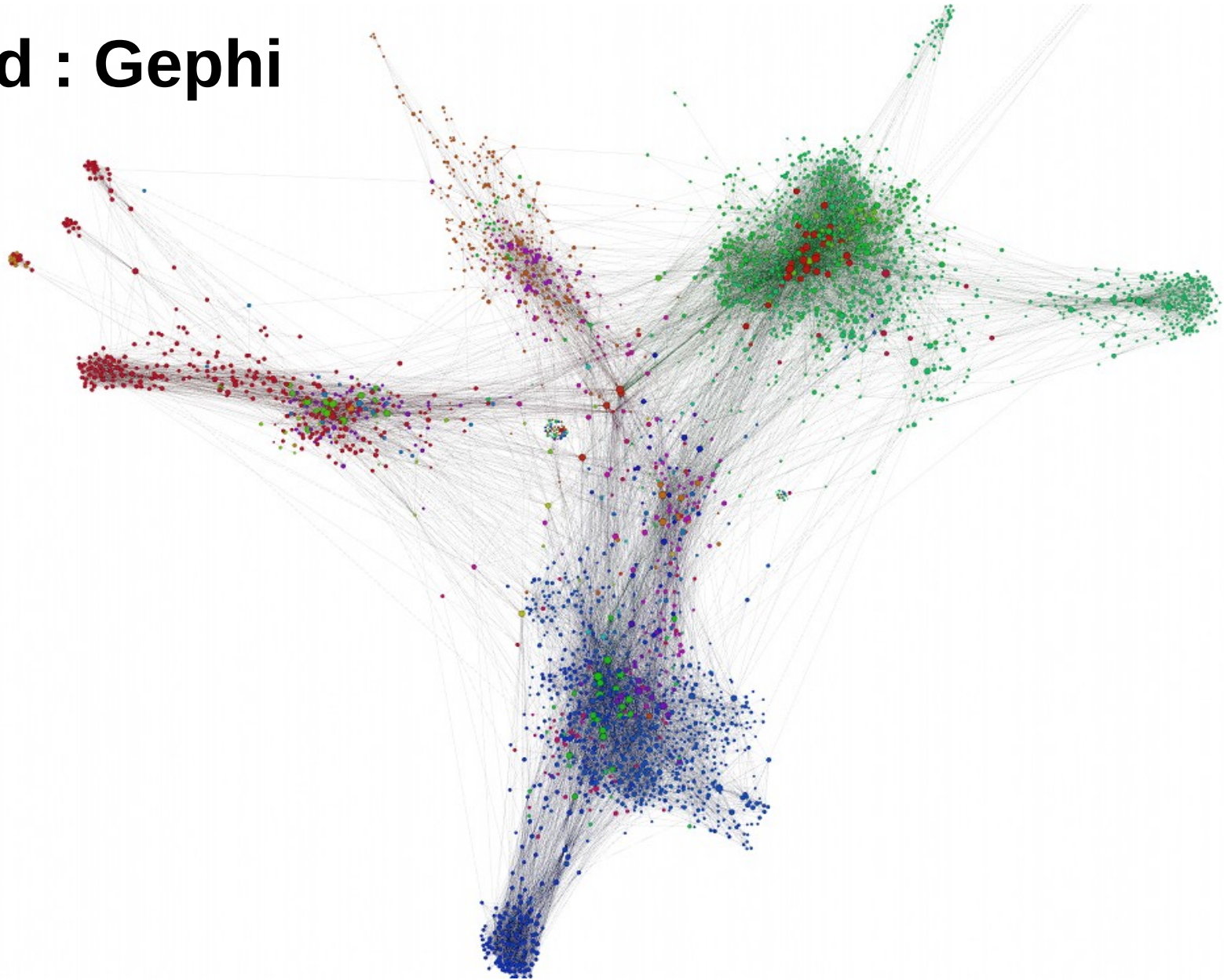
- Info Editor:** Lists nodes and reactions with columns for ID, Name, Type, Nodes, and Select. It includes a legend for node types (e.g., UTP, UDP, NAC, N-AC, D-GLT, L-GL, D-GL, UDP).
- Views:** A tree view showing the current sub-view: "Sub-view" > "threonine degradation I".
- Network View:** A dense network of nodes and edges, with a "Sub-view" window showing a zoomed-in section of the network.
- Histogram View:** A bar chart showing the distribution of node counts, with a y-axis labeled "number of nodes" and x-axis labels "-sd", "m", "+sd".
- Parallel Coordinates View:** A visualization of the network data using parallel lines.
- Information View:** Details for reaction R06417, including its name, definition, equation, and RPair information. The reaction is: $(-)\text{-cis-isopulegone} + \text{NADPH} + \text{H}^+ \rightleftharpoons (+)\text{-cis-isopulegone} + \text{NADP}^+$.
- 3D Model:** A ball-and-stick model of a pyruvate molecule.

Tulip et Systryp

- Powerful (OpenGL)
- Many graph measures
- Not very user friendly
- Nobody to maintain !!!

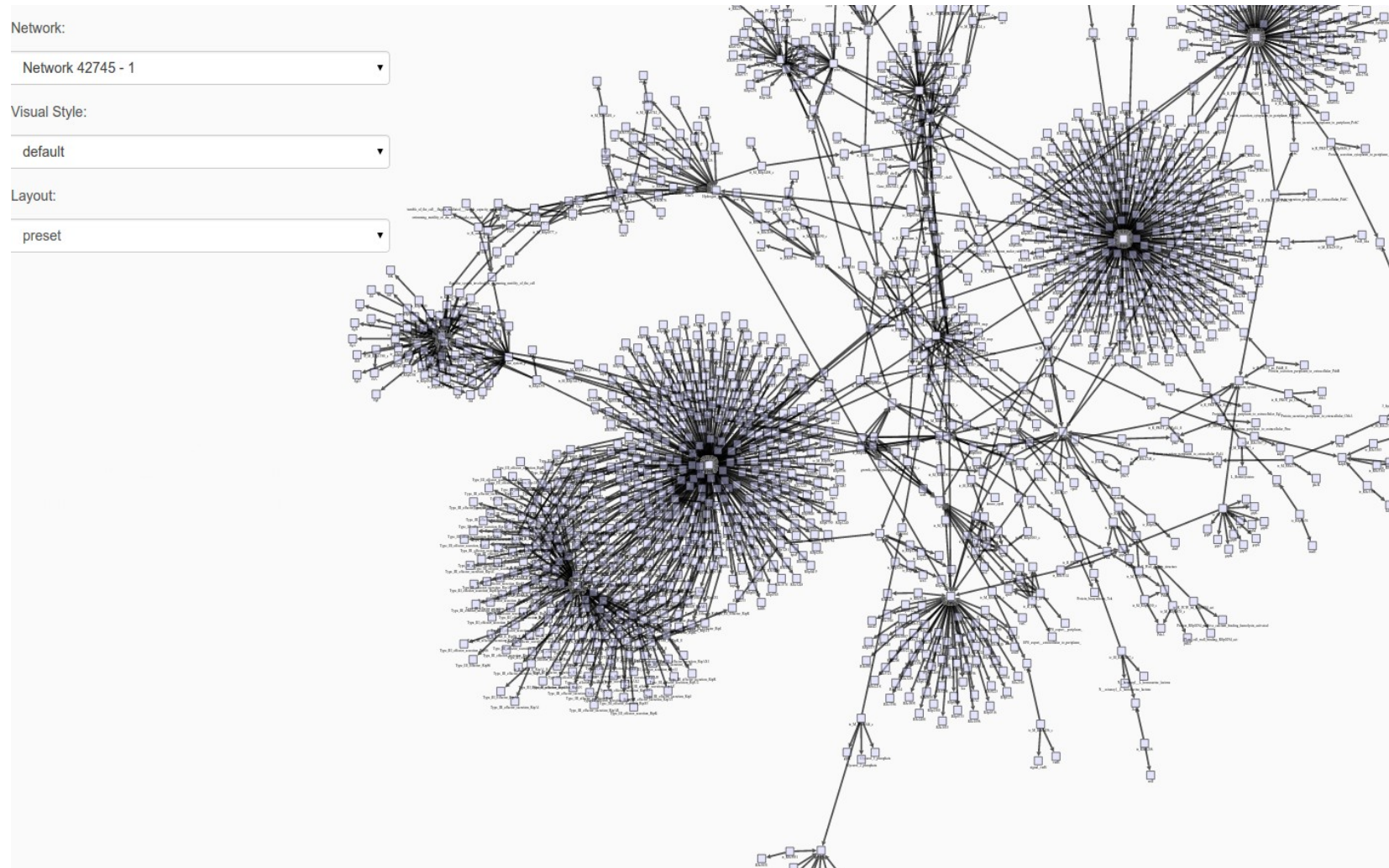


Trend : Gephi



Metabolic network web visualisation

Cytoscape.js



Cytoscape.js

- Large community
- Links with Cytoscape Java
- Lags with large networks



d3.js



d3.js

- Powerful
 - More generic
 - Large community
- Interactions more difficult to handle (→ SVG)



Future : Network visualisation with WebGL ?

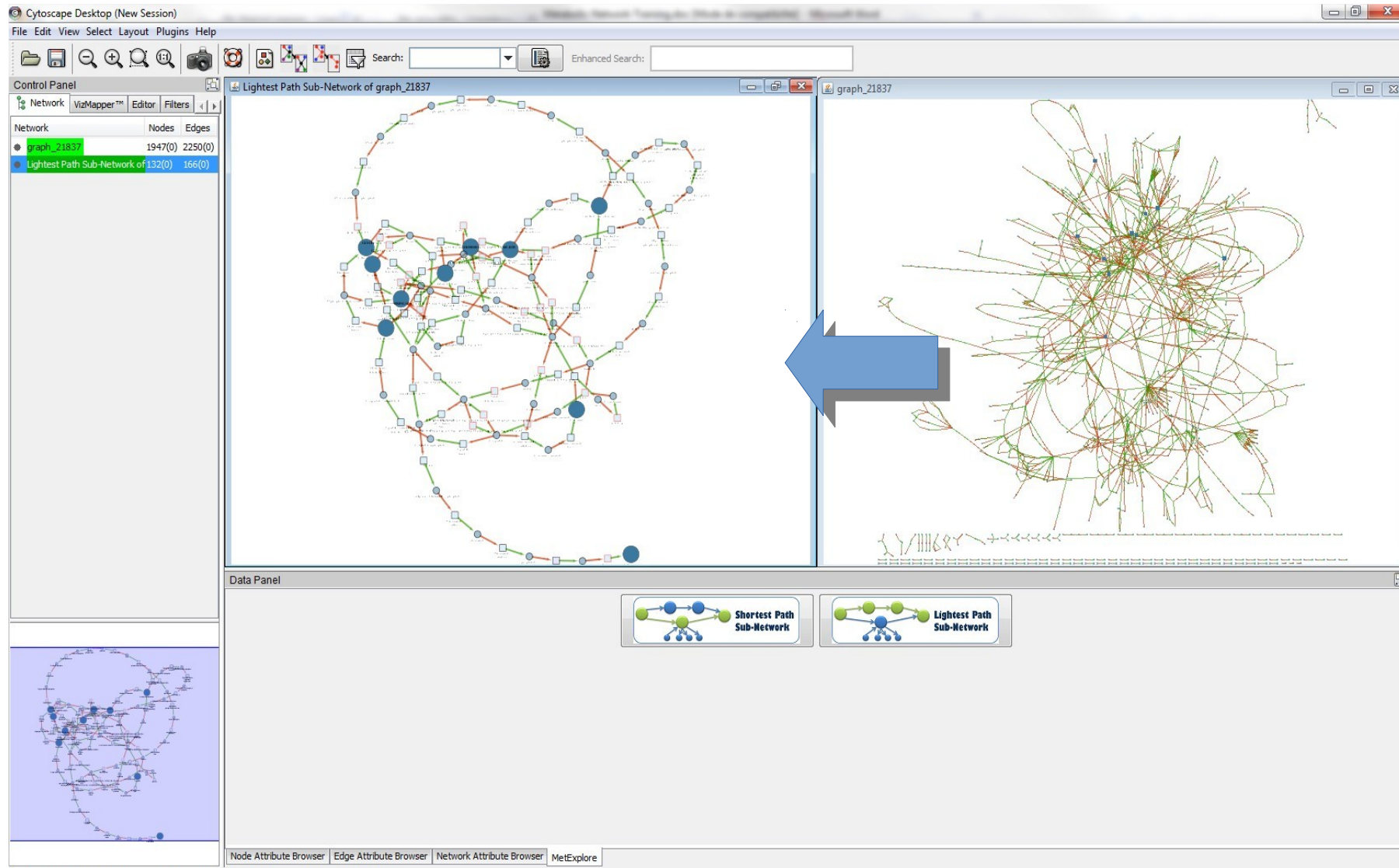
Ex: sigmaajs

- Uses the graphic cards

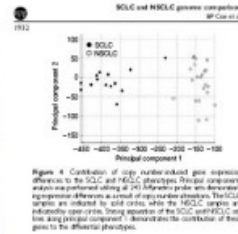
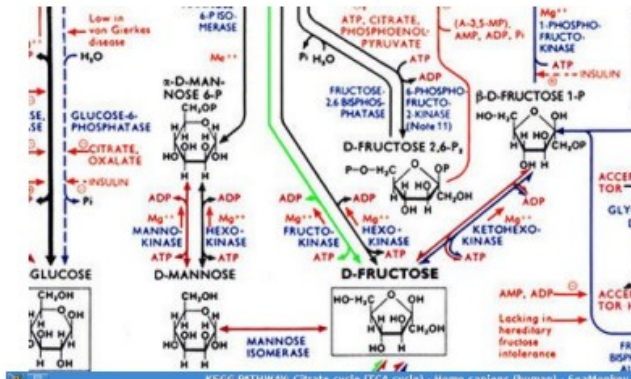


<http://sigmaajs.org/>

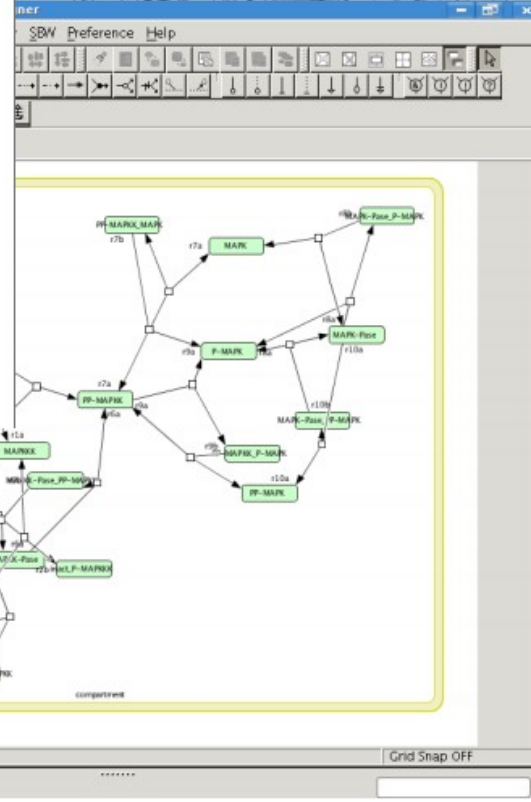
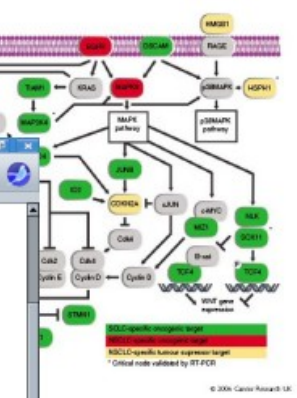
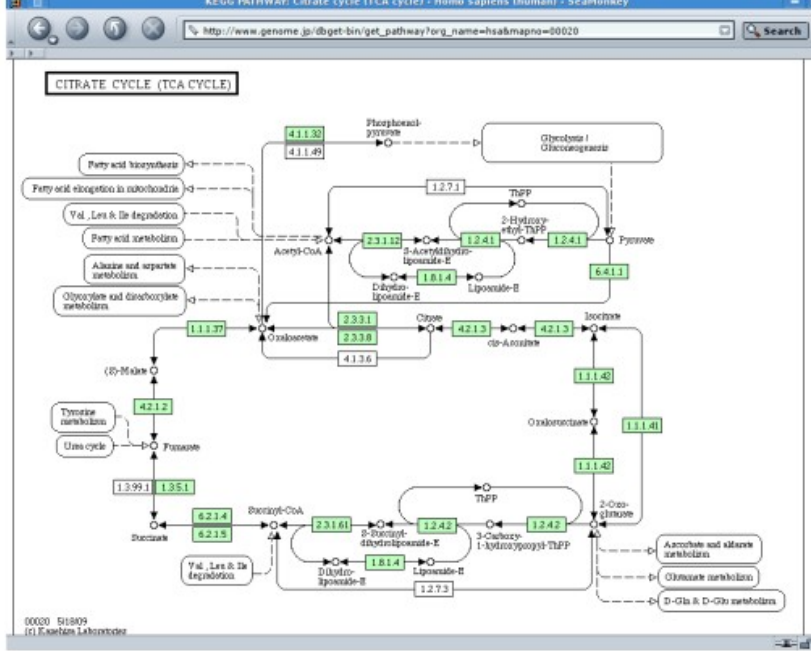
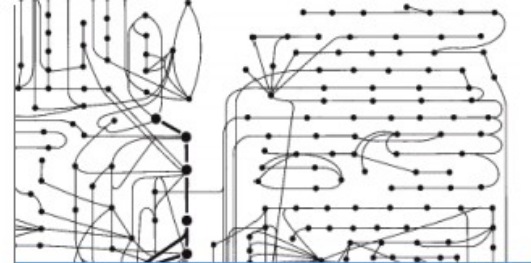
Sub network identification helps the visualisation



How to share network views?



implication in the SGLC complex as well suggests that this gene may play an essential role in the development of long neurons (Santoni et al. 2006).
 It is noteworthy that a subset of the genomic alterations between the SGLC and HSLC cell lines could be the result of adaptation to in vitro conditions. Testing this hypothesis into the biology of the clinical disease will be valuable through analysis of different tissues than that cultivated in genetic alternatives and gene regulation.
 Regions of difference
 Through our analysis, numerous regions throughout the genome were identified to be differentially altered between the SGLC and HSLC samples. This difference-based approach compares the regions of copy number variants and identifies the regions that are strongly linked to clinical disease. These regions might be used from whole genome approaches (Chromosomes 21) to identify genetic alterations in the HSLC cell lines. Using our analysis, we identified several regions that differ strongly in their alternative status between the cell lines, we refer to these as phenotype-specific copy number alterations (PSCNAs). These included 19q13.31-q13.41.



From N. Lenovère's slides

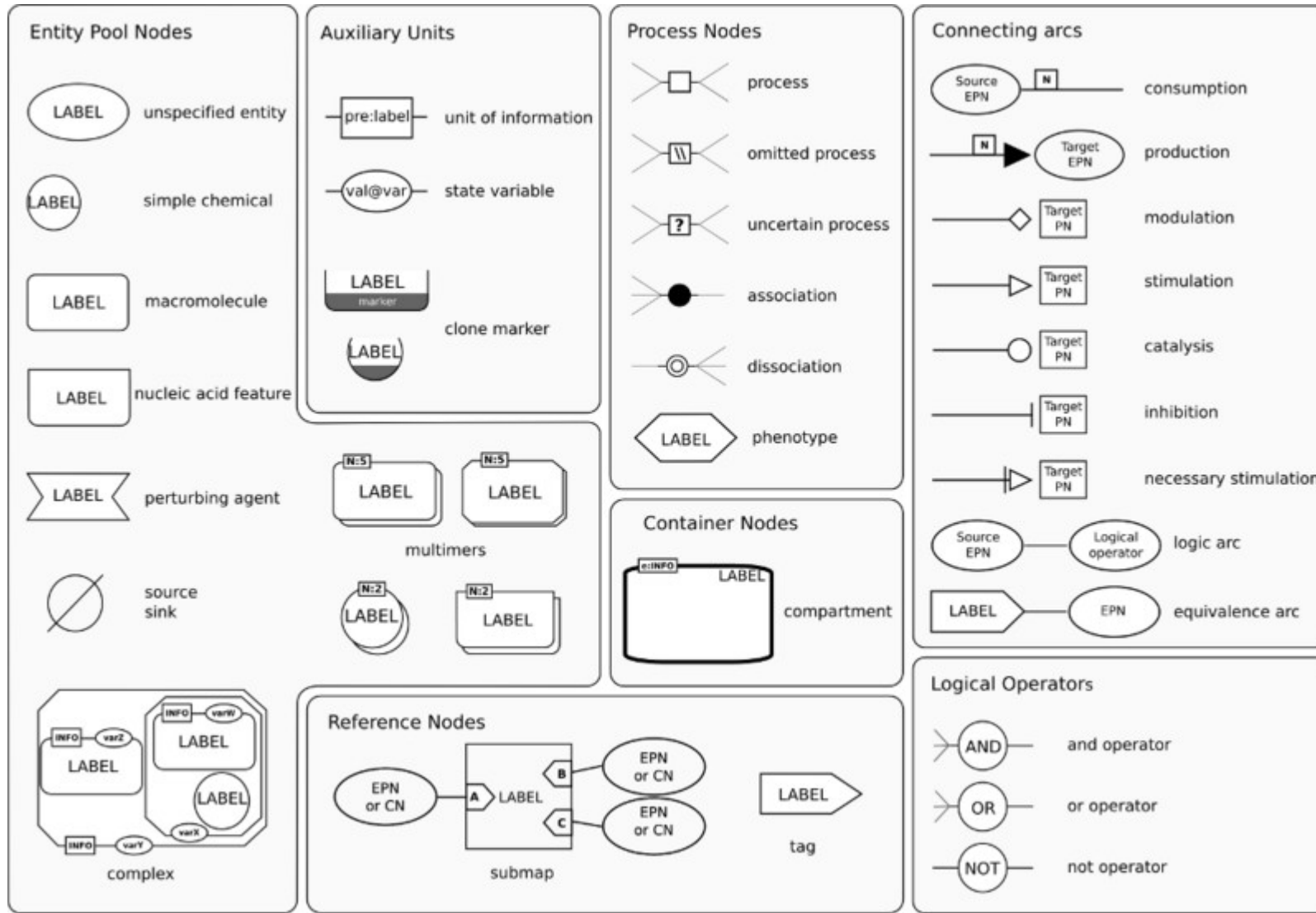
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Challenges

- Numerous visual styles
- Layouts not always deterministic

Systems Biology Graphical Notation (SBGN)



<http://www.sbgn.org/>

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Take home messages

- Network visualisation is now interactive
- Large network visualisation is still a challenge
- Sub network identification helps the interpretation
- Network visualisation in web is now possible
- Standardisation initiatives allows sharing biological network views



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