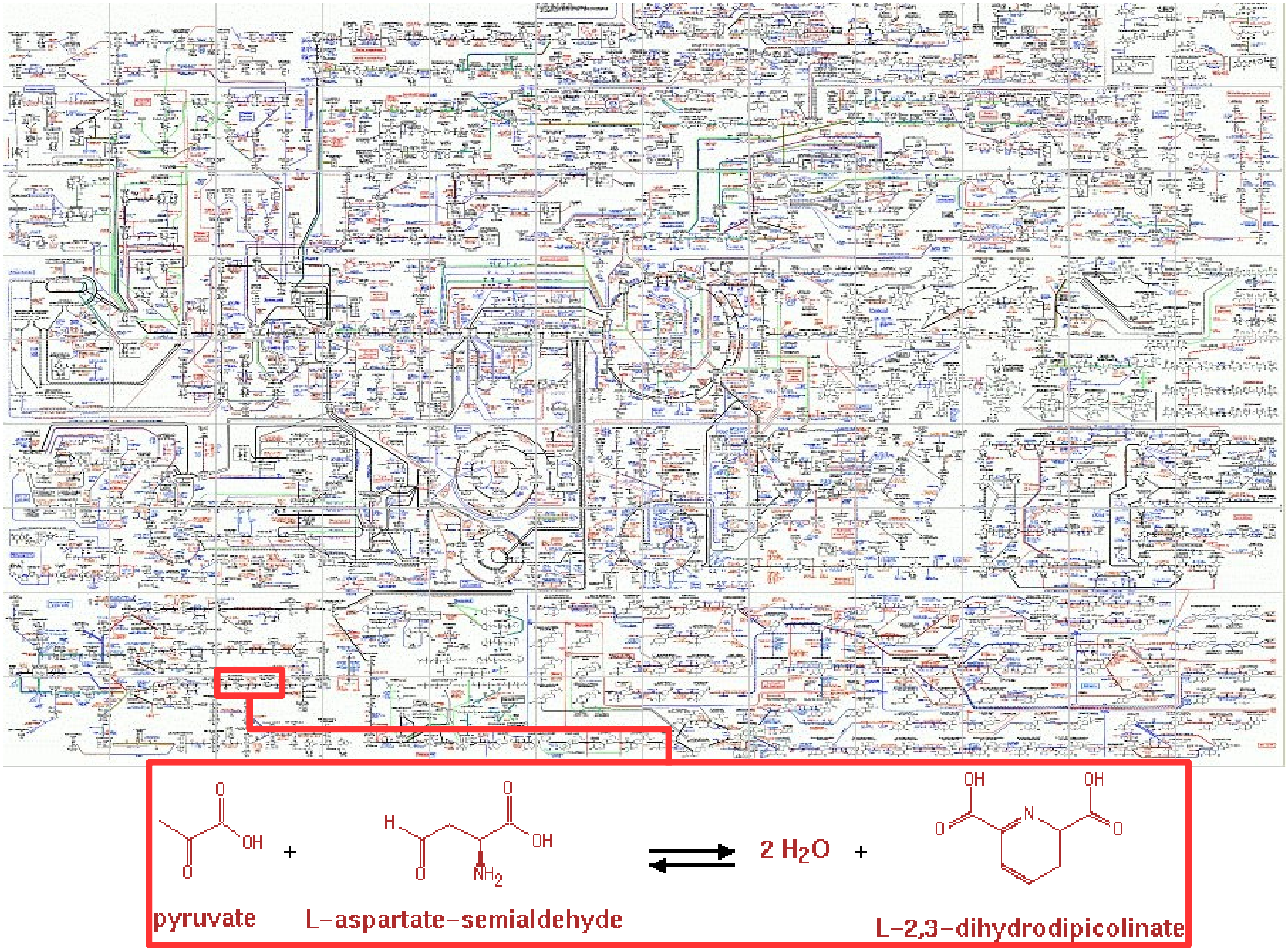
Metabolic network visualisation

Ludovic Cottret
LIPM
CATI BBRIC

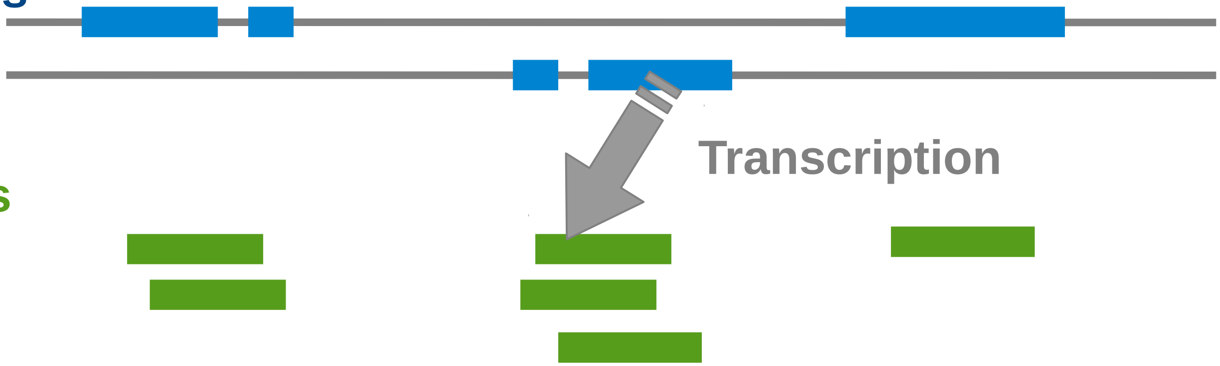
Séminaire Méthodes et outils pour l'Open Data
Notre-Dame de Londres

18 décembre 2014

What is a metabolic network?



From genes to reactions



Genes

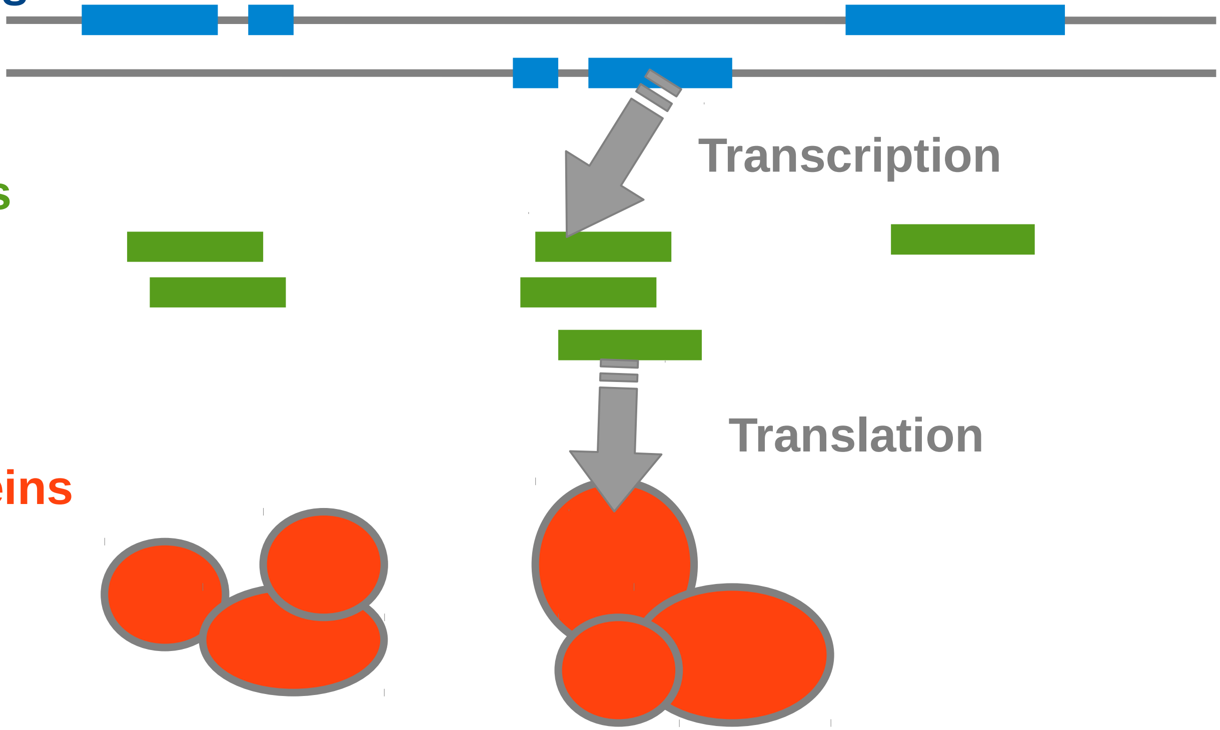
Genomics

Transcription

RNAs

Transcriptomics

From genes to reactions



Genes **Genomics**

RNAs **Transcriptomics**

Proteins **Proteomics**

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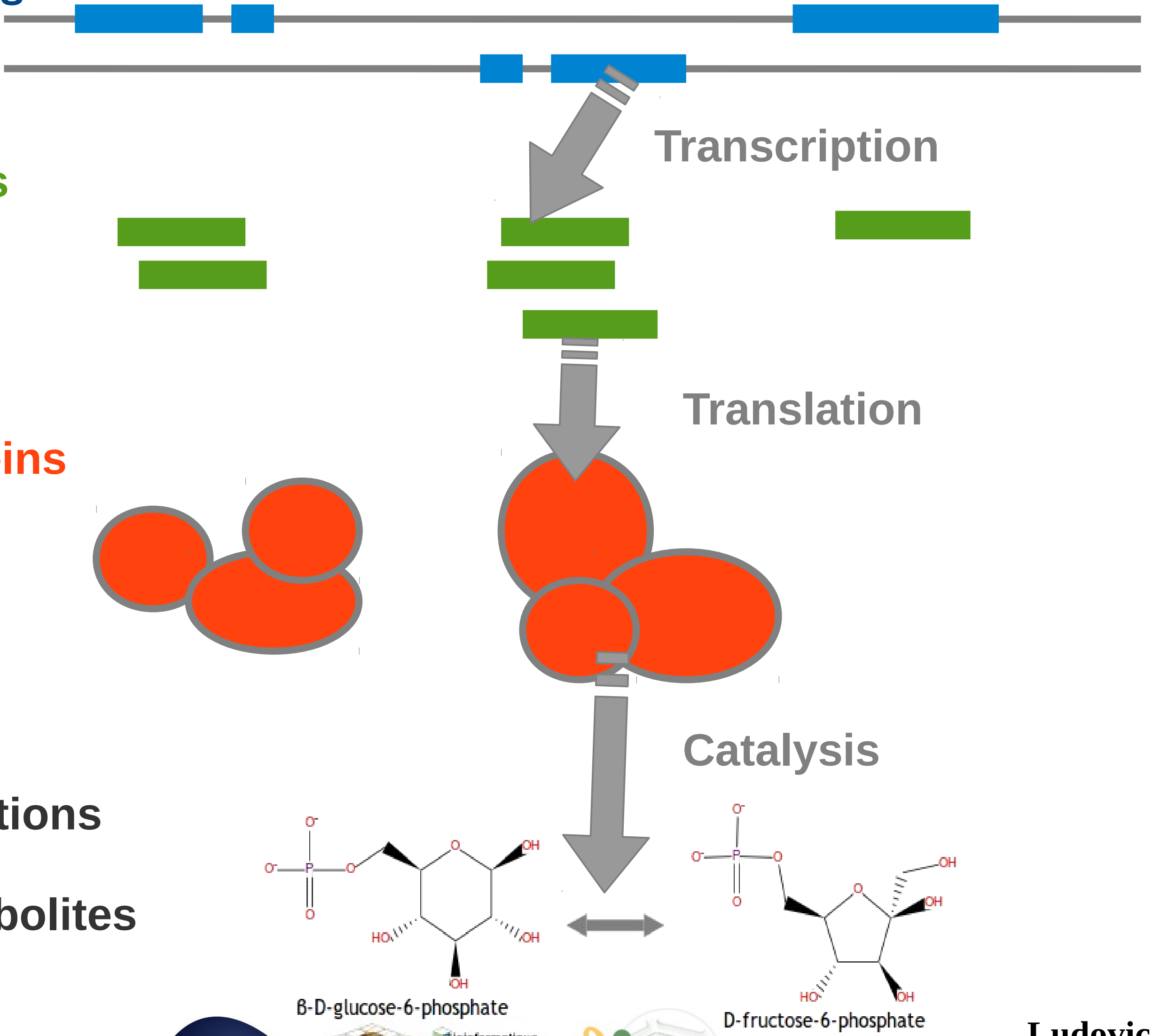
From genes to reactions



Genes — **Genomics**

RNAs — **Transcriptomics**

Proteins — **Proteomics**

Reactions and metabolites — **Metabolomics Fluxomics**

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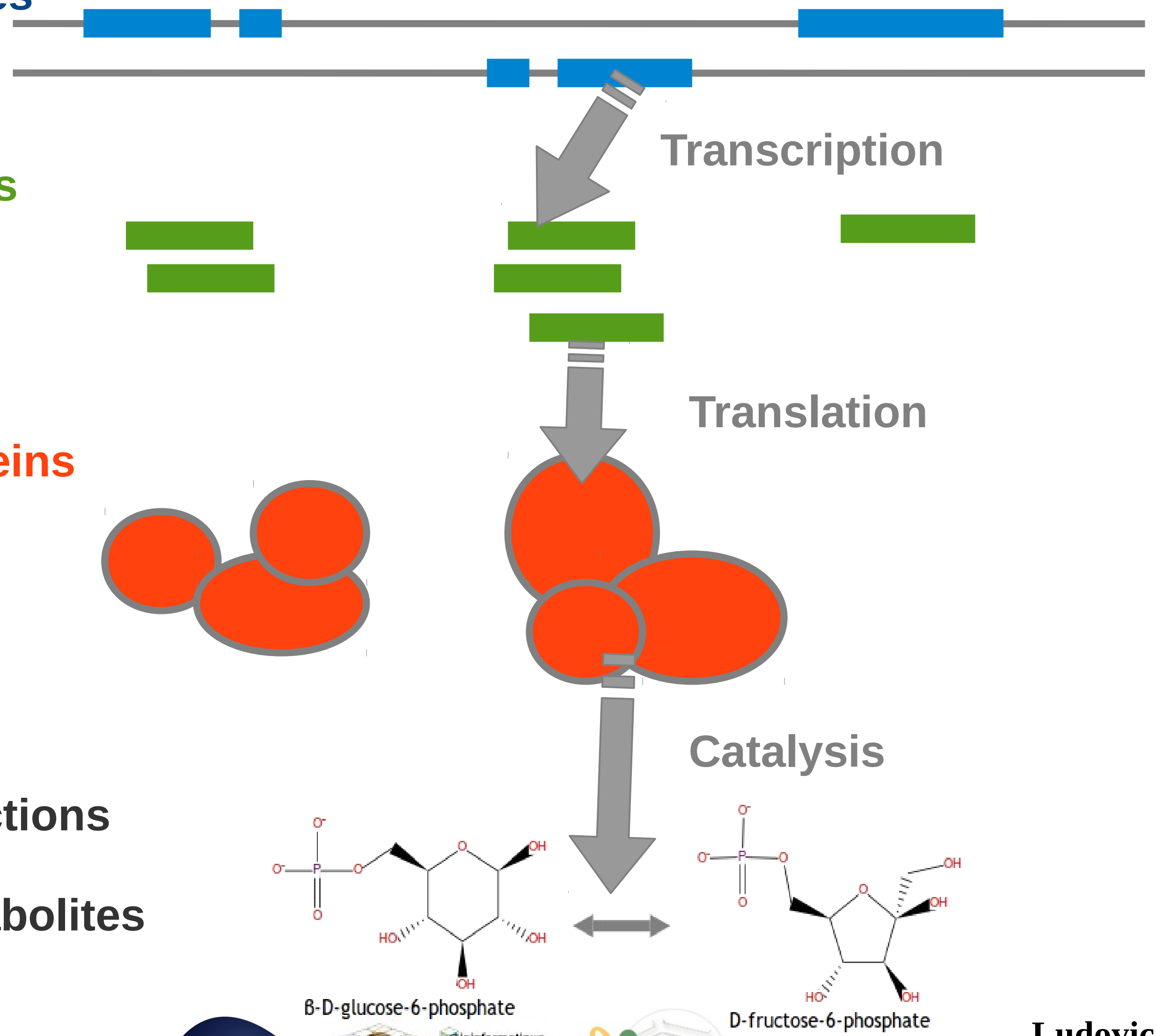
From genes to reactions



Genes

RNAs

Transcription

Proteins

Translation

Reactions and metabolites

Catalysis

β-D-glucose-6-phosphate

D-fructose-6-phosphate

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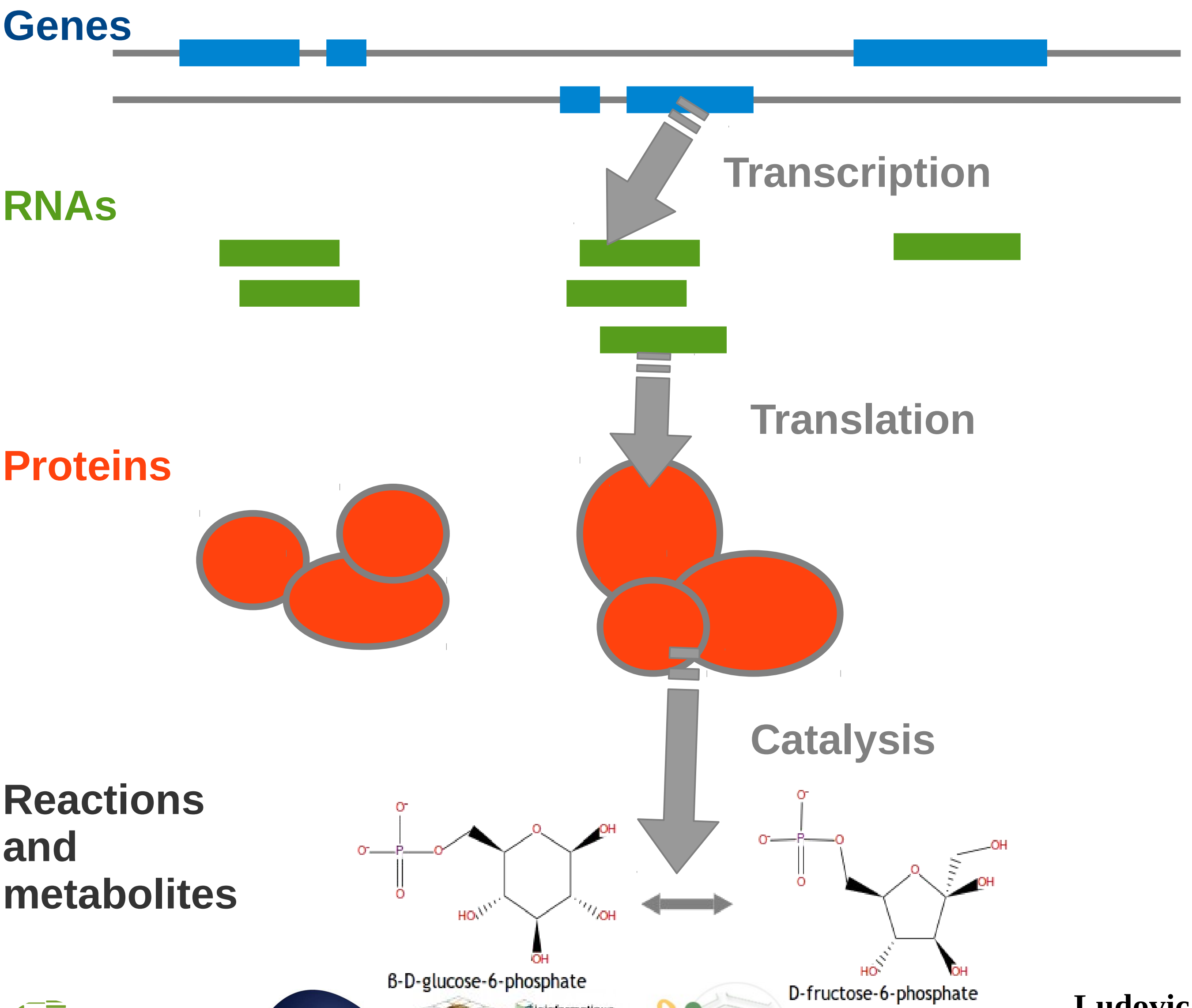
Séminaire “Mé
Saint-Martin d

PHENOTYPE

From genes to reactions



Genes

RNAs

Proteins

Reactions and metabolites

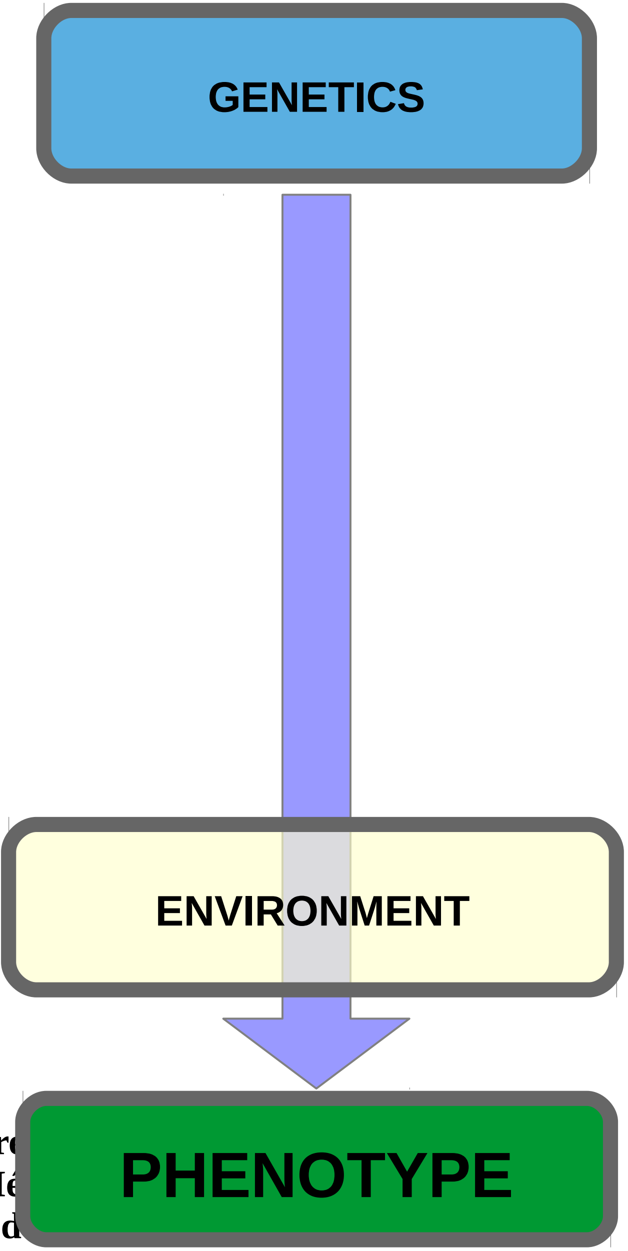
Transcription

Translation

Catalysis

ß-D-glucose-6-phosphate

D-fructose-6-phosphate



GENETICS

ENVIRONMENT

PHENOTYPE

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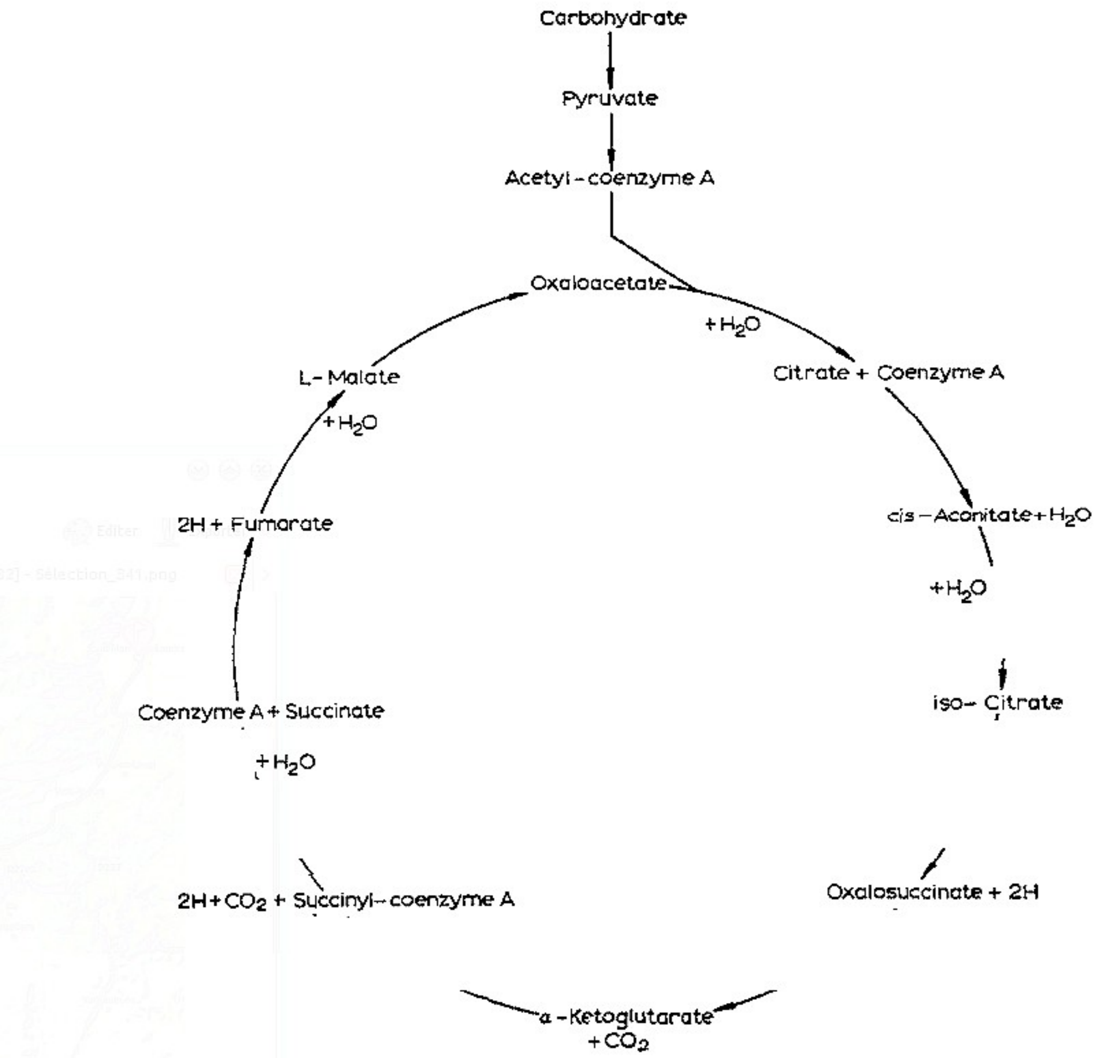
Saint-Martin d

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

… and visualisation facilitates this interpretation!

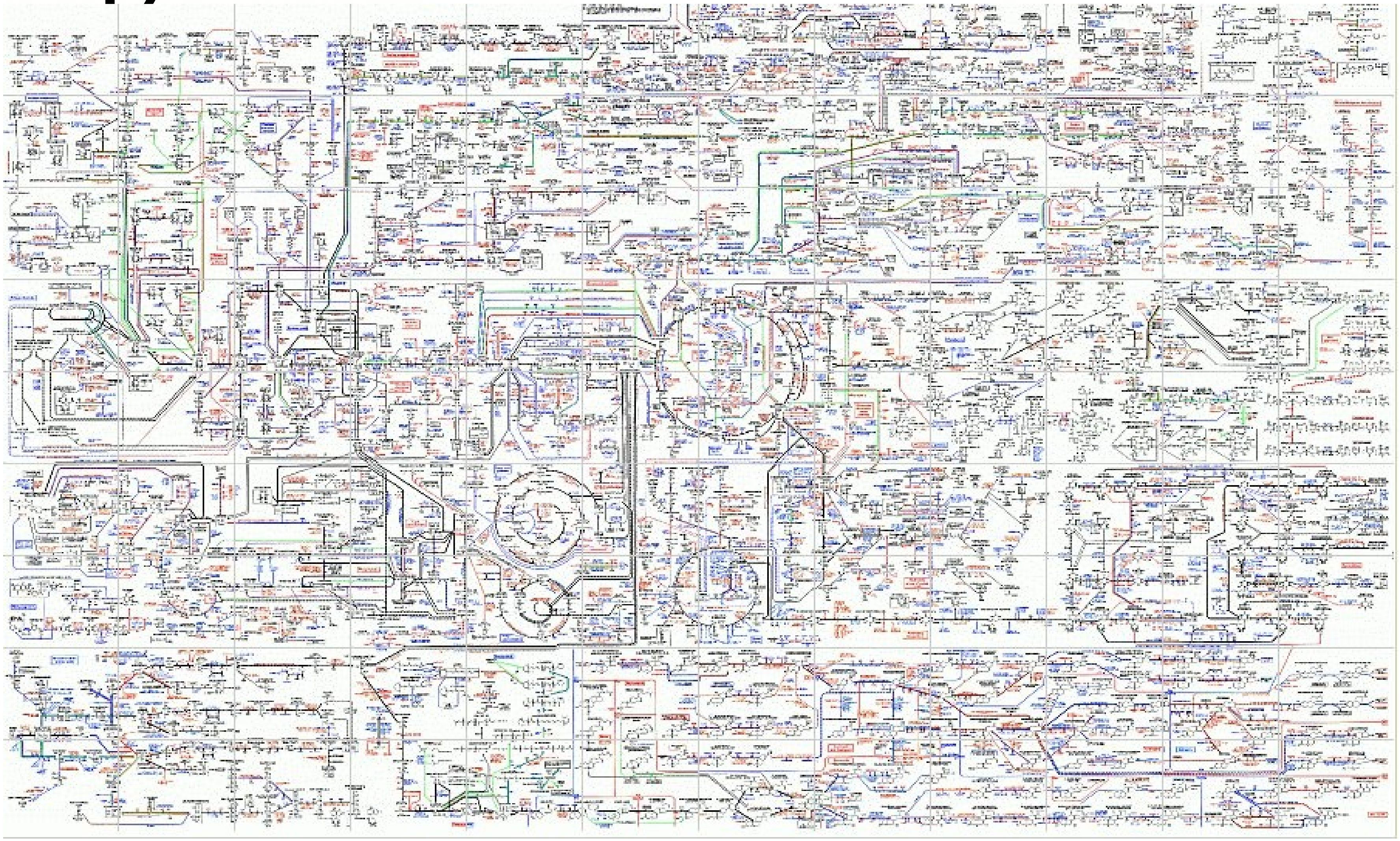
Metabolic network static visualisation

Before computers...

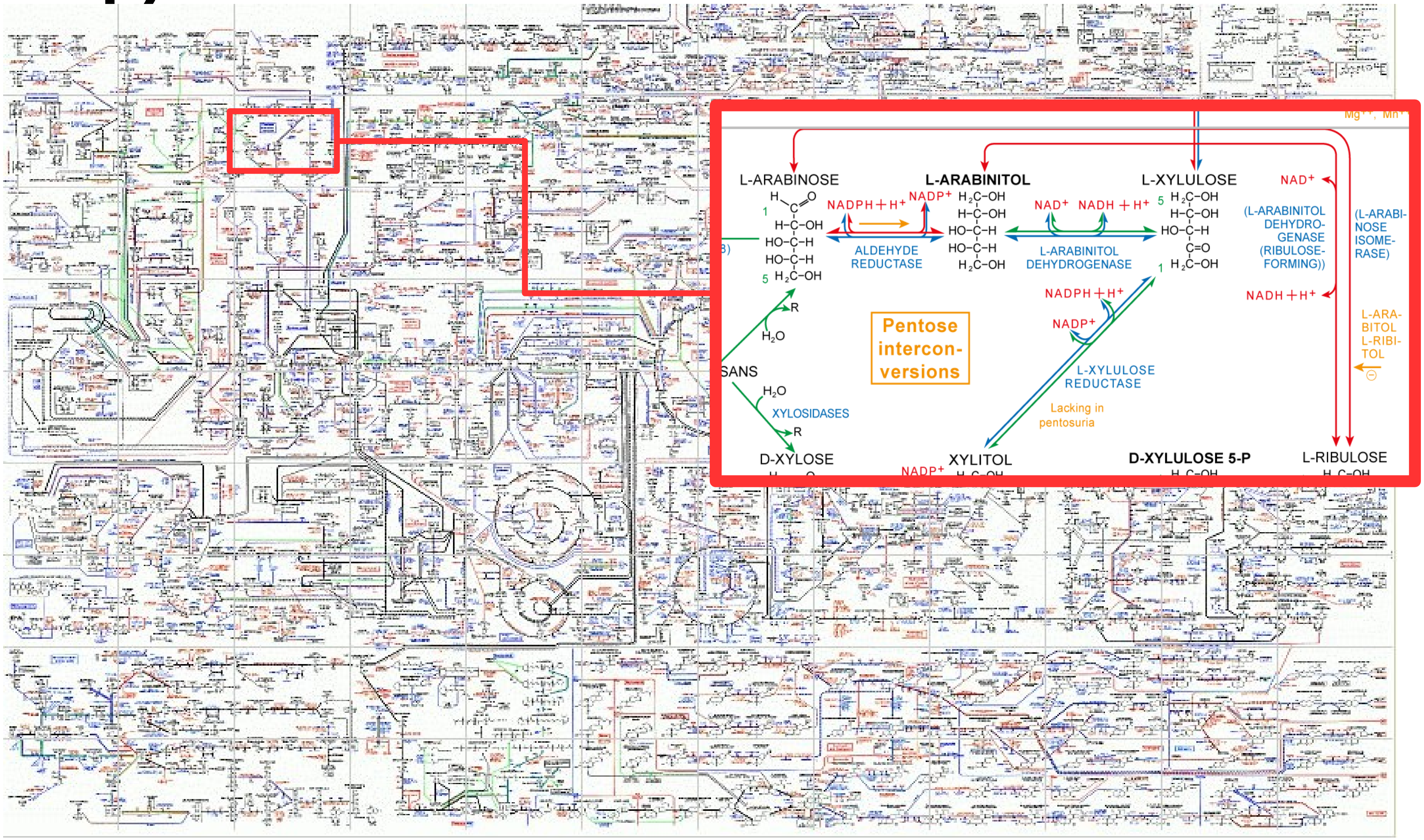


H ANS A. KREB S
The citric acid cycle
Nobel Lecture, December 11, 1953

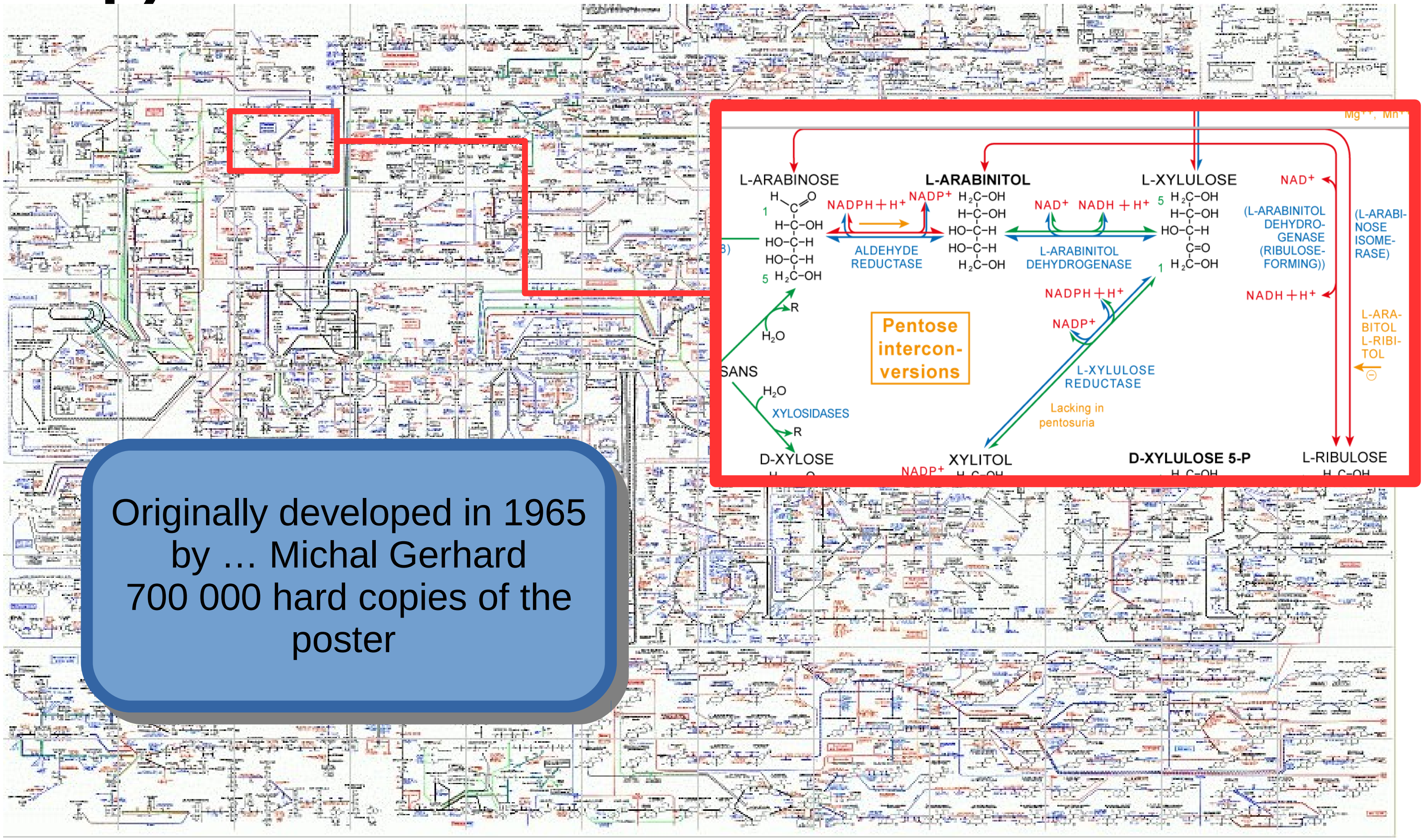
Roche BioChemical Pathways (Boehringer map)



Roche BioChemical Pathways (Boehringer map)

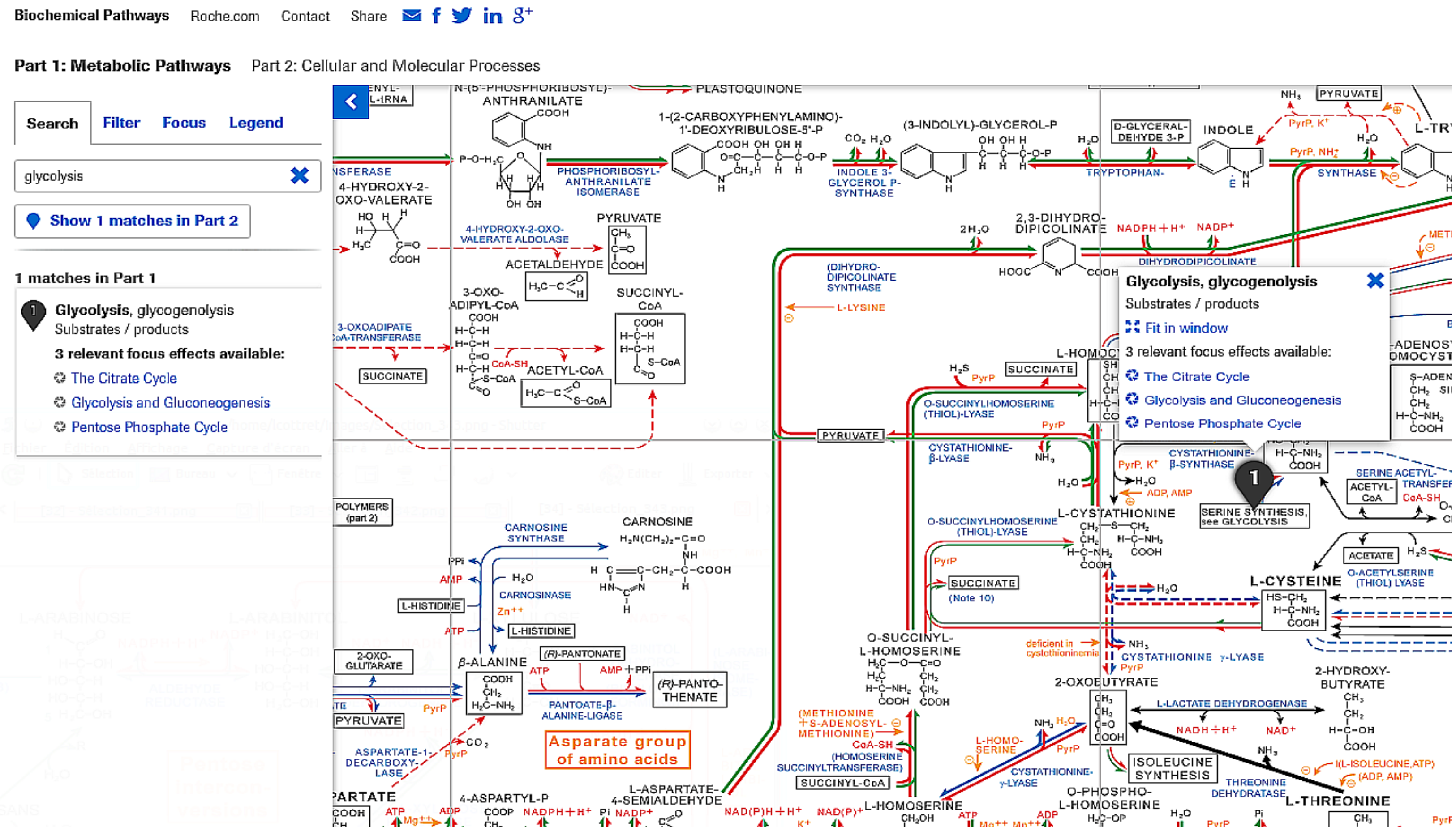


Roche BioChemical Pathways (Boehringer map)



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

Interactive Boehringer map



glycolysis

1 matches in Part 1

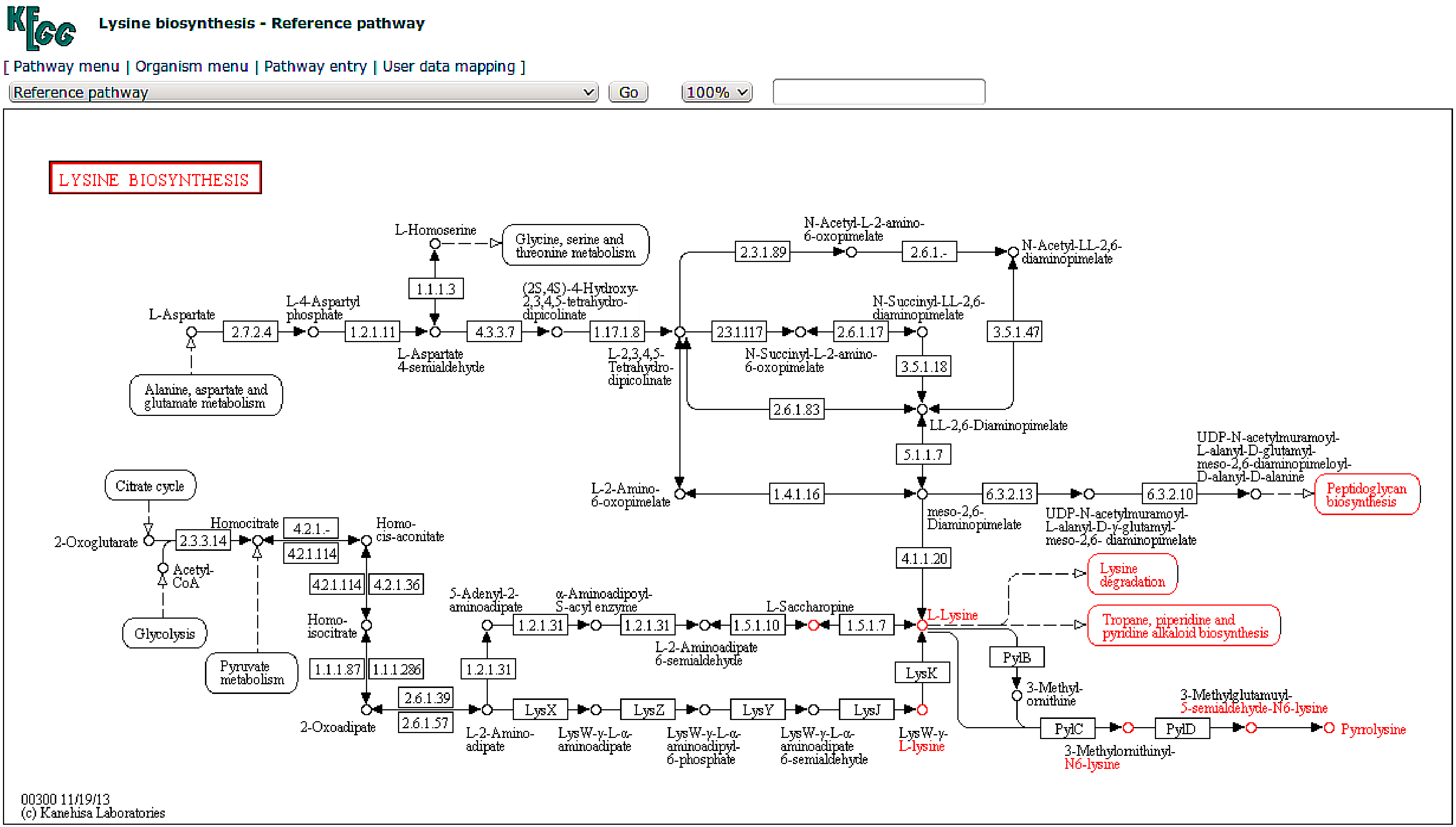
Glycolysis, glycogenolysis
Substrates / products

3 relevant focus effects available:
- The Citrate Cycle
- Glycolysis and Gluconeogenesis
- Pentose Phosphate Cycle

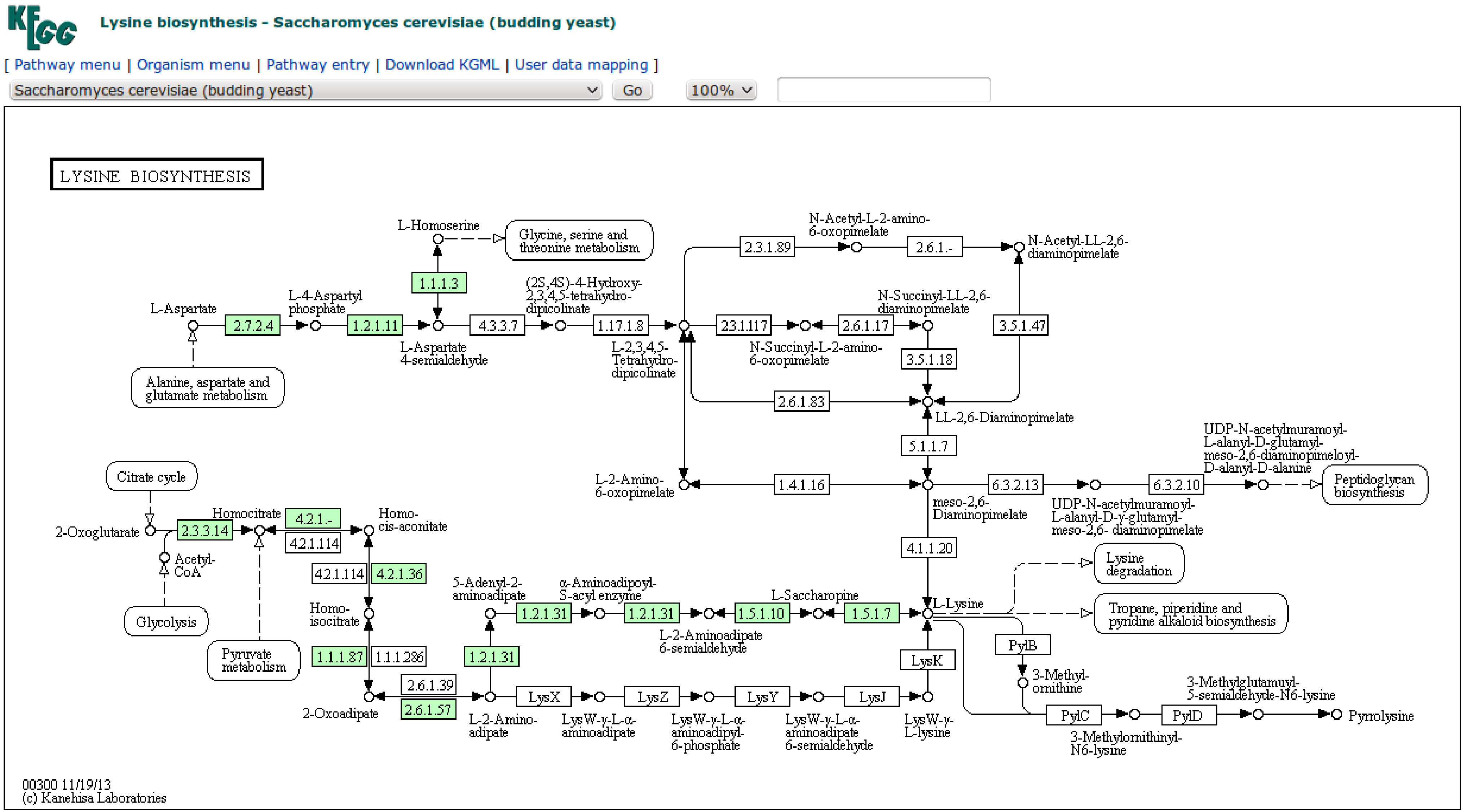
Glycolysis, glycogenolysis
Substrates / products
Fit in window
3 relevant focus effects available:
- The Citrate Cycle
- Glycolysis and Gluconeogenesis
- Pentose Phosphate Cycle

http://biochemical-pathways.com/

Metabolic pathways in KEGG



Metabolic pathways in KEGG



Lysine biosynthesis - Saccharomyces cerevisiae (budding yeast)

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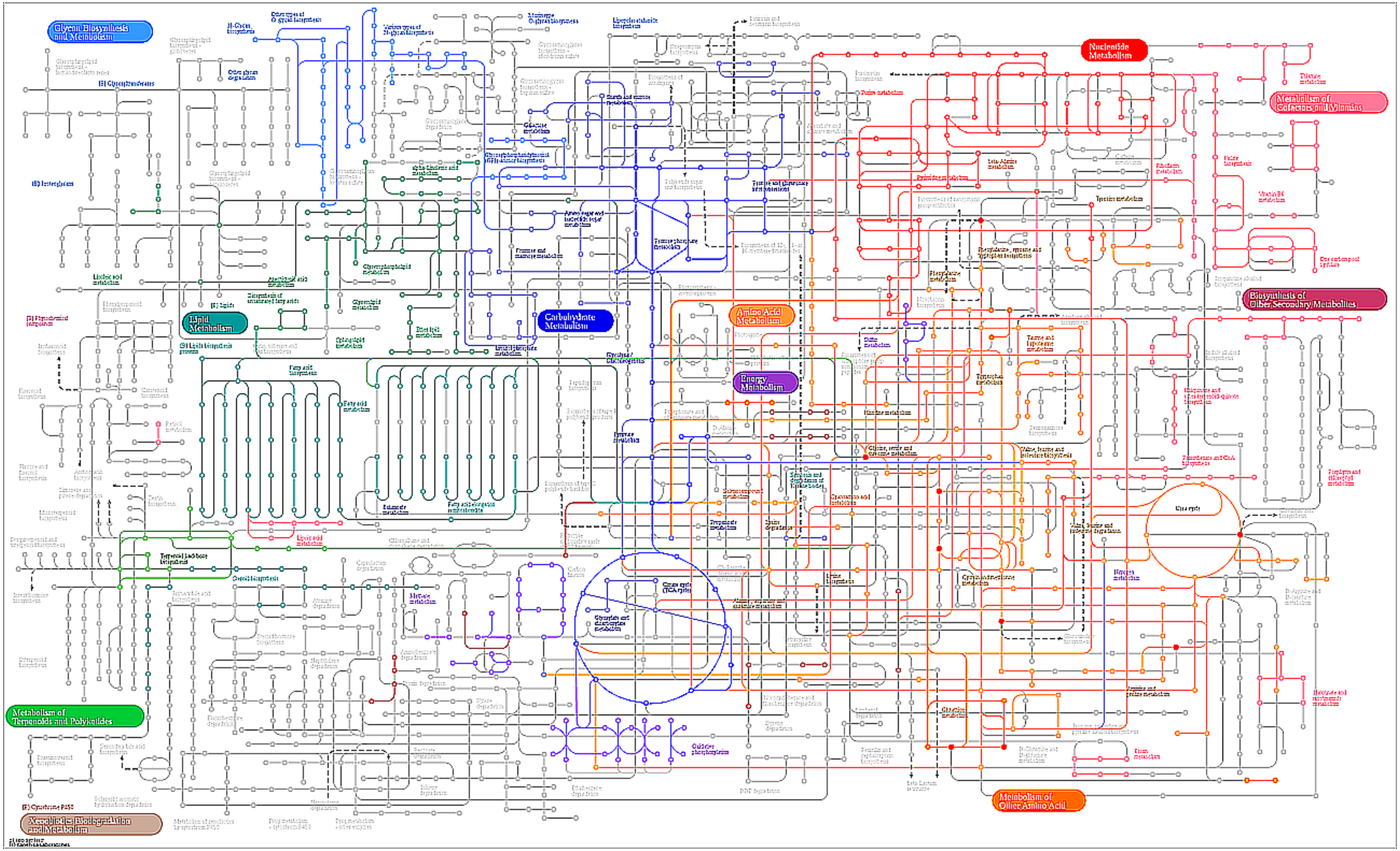
Metabolic pathways in KEGG



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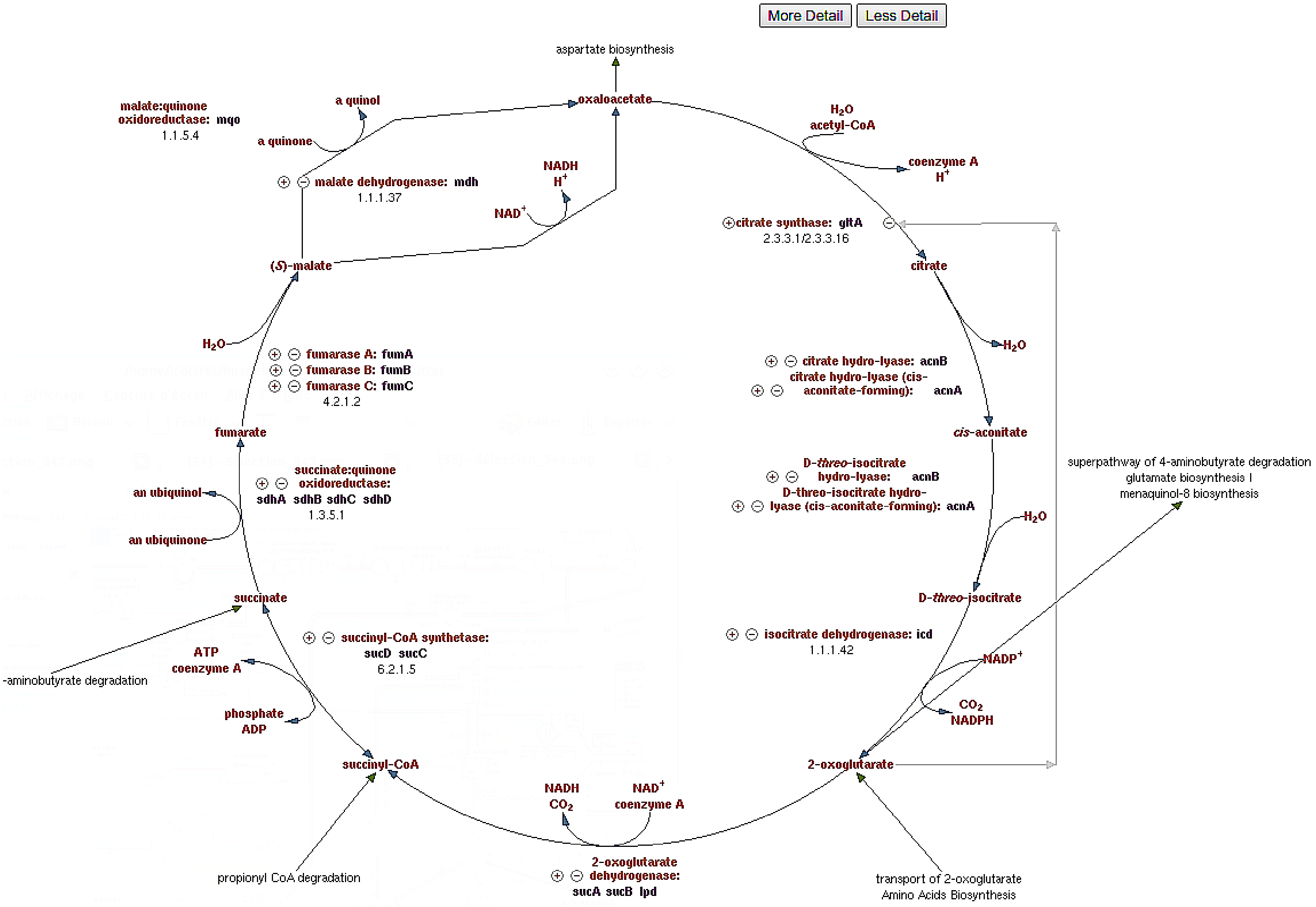
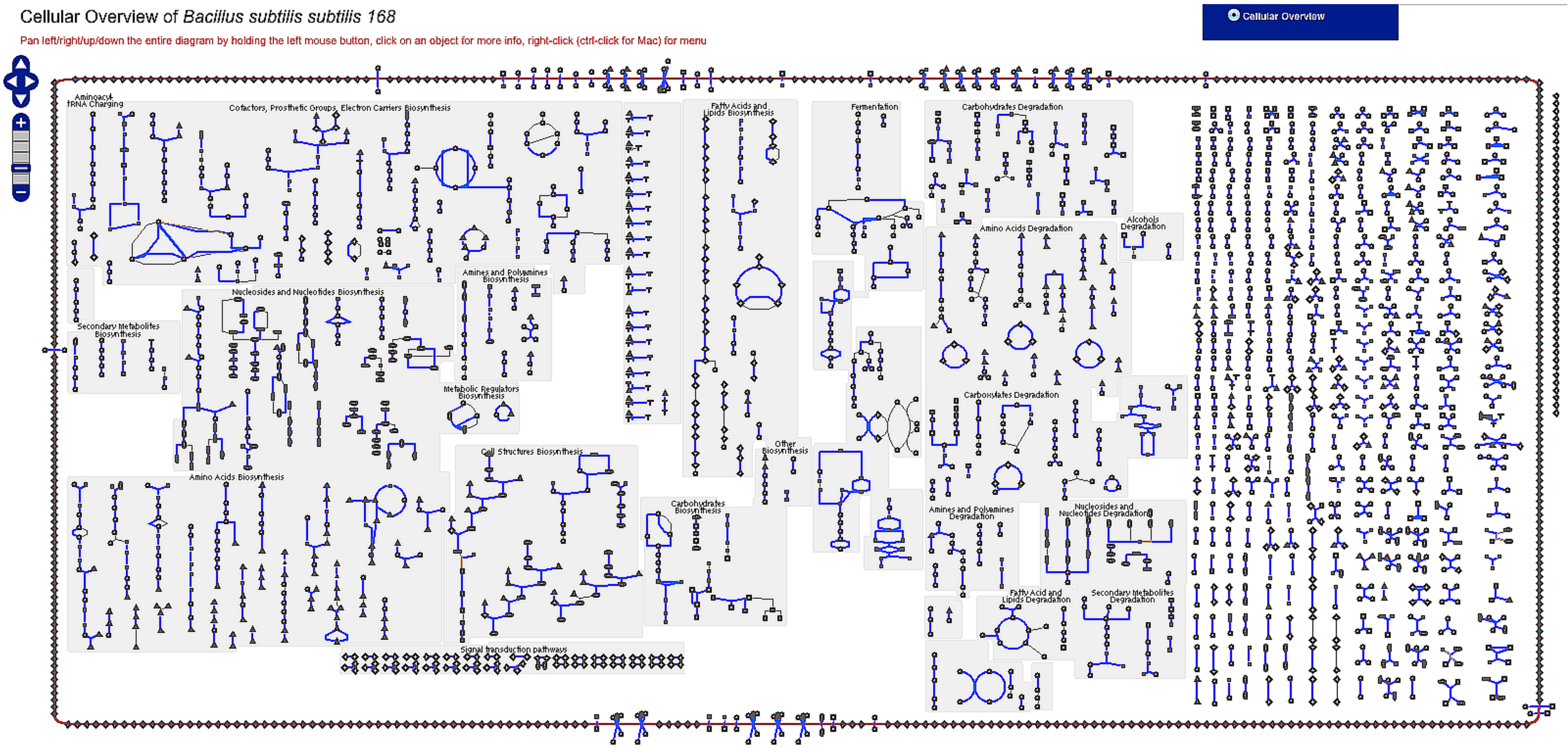
Metabolic pathways in BioCyc



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

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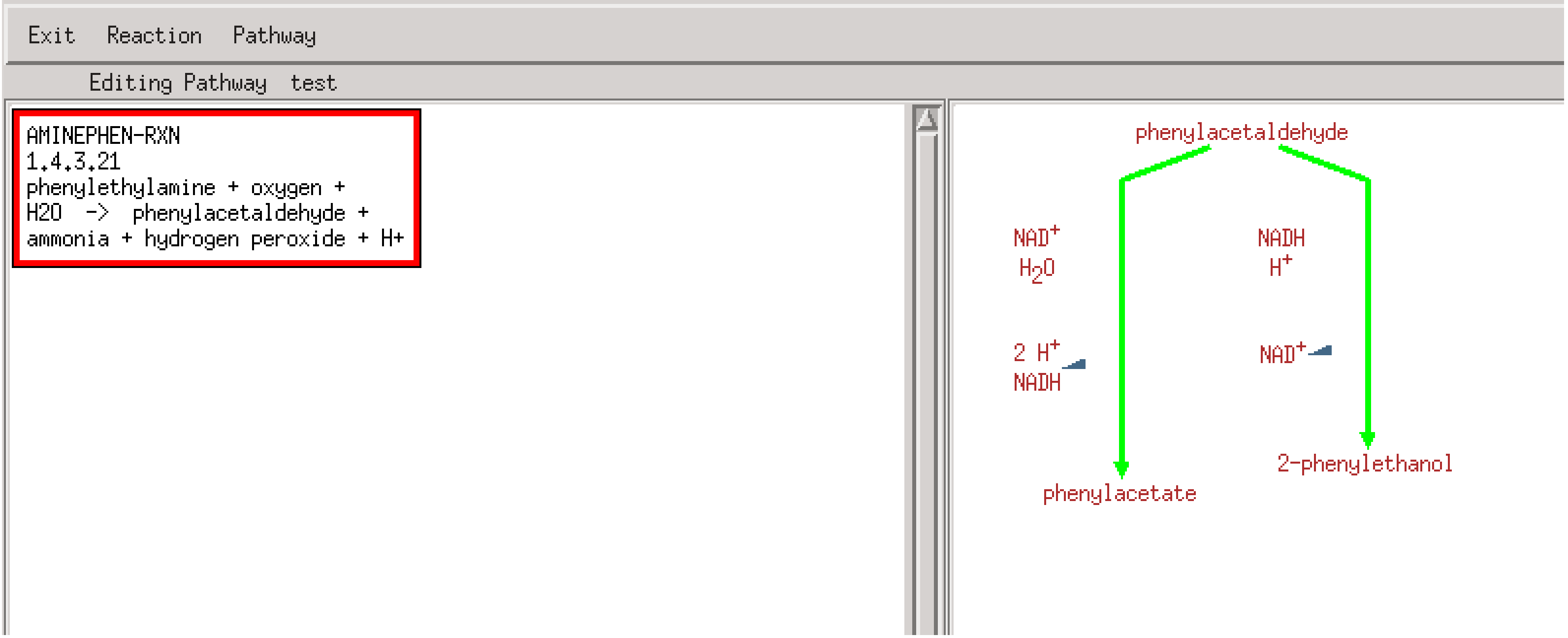
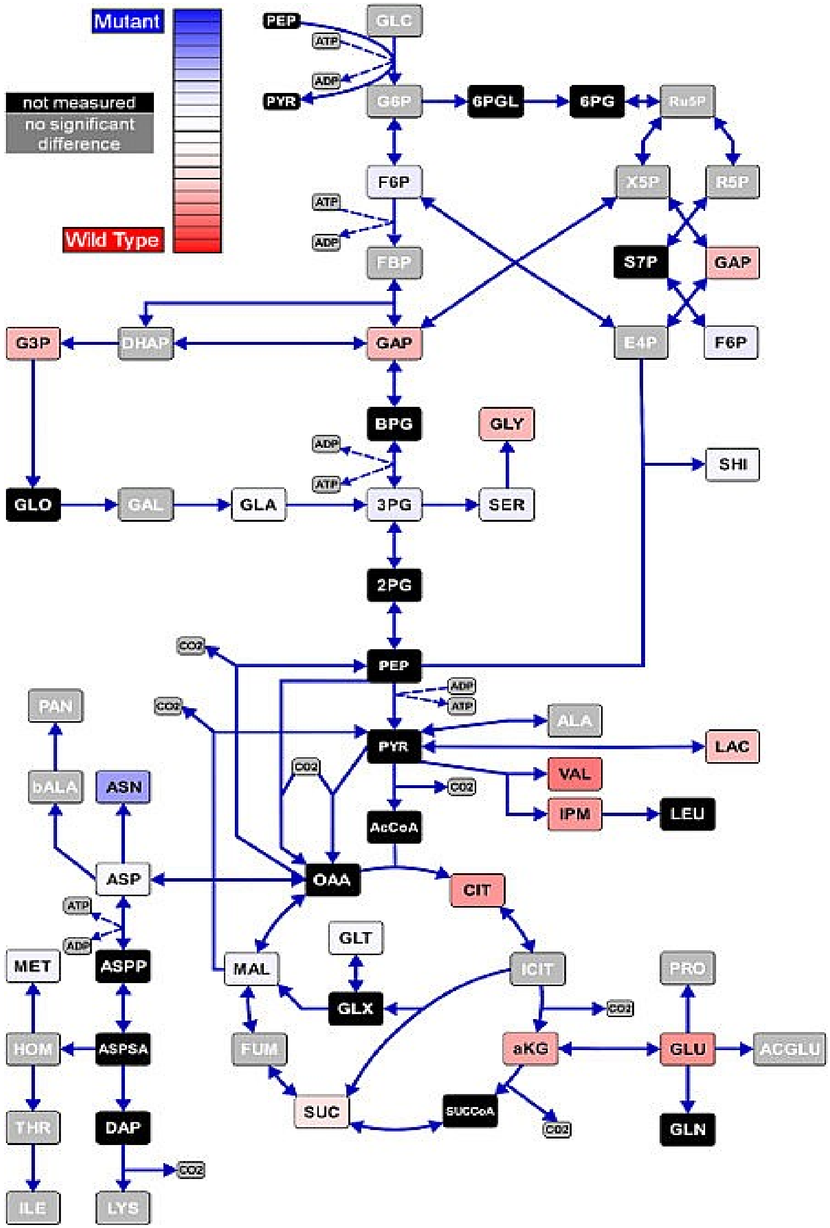
Creation and edition of metabolic pathways

Pathway editor in the pathway-tools (BioCyc)



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

Omix



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

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Metabolic graph visualisation

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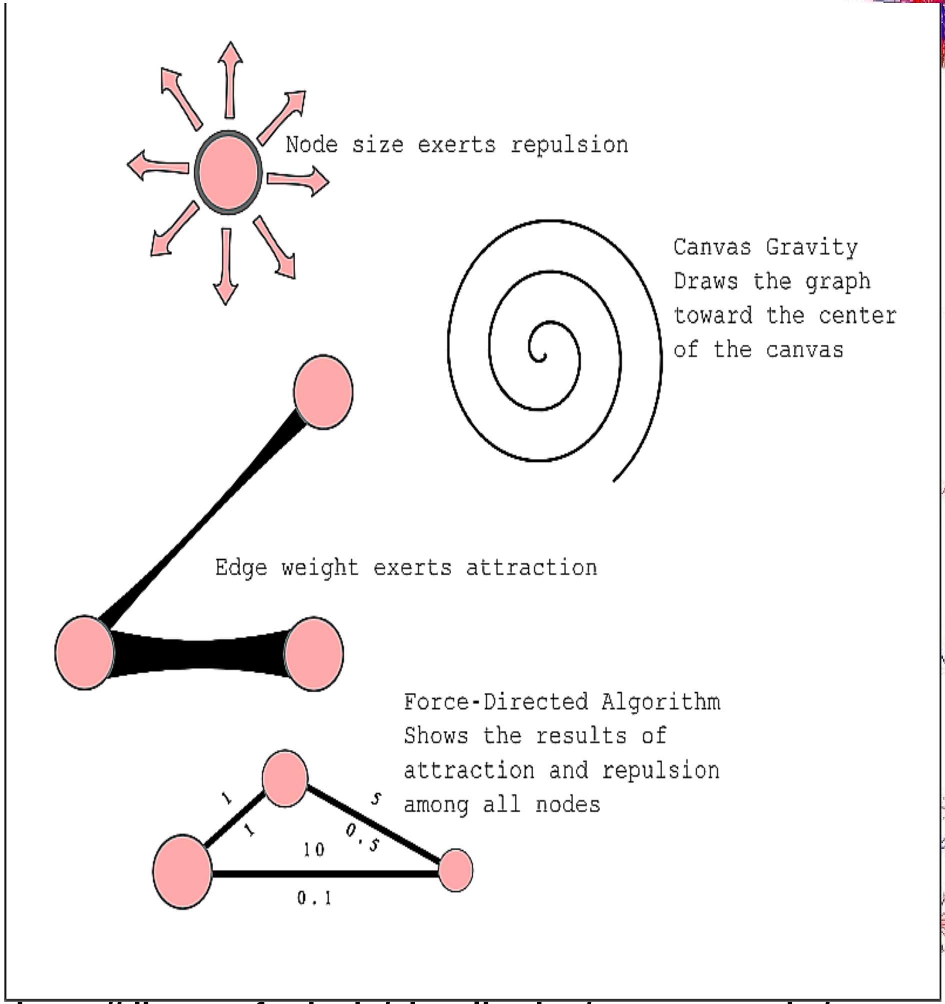
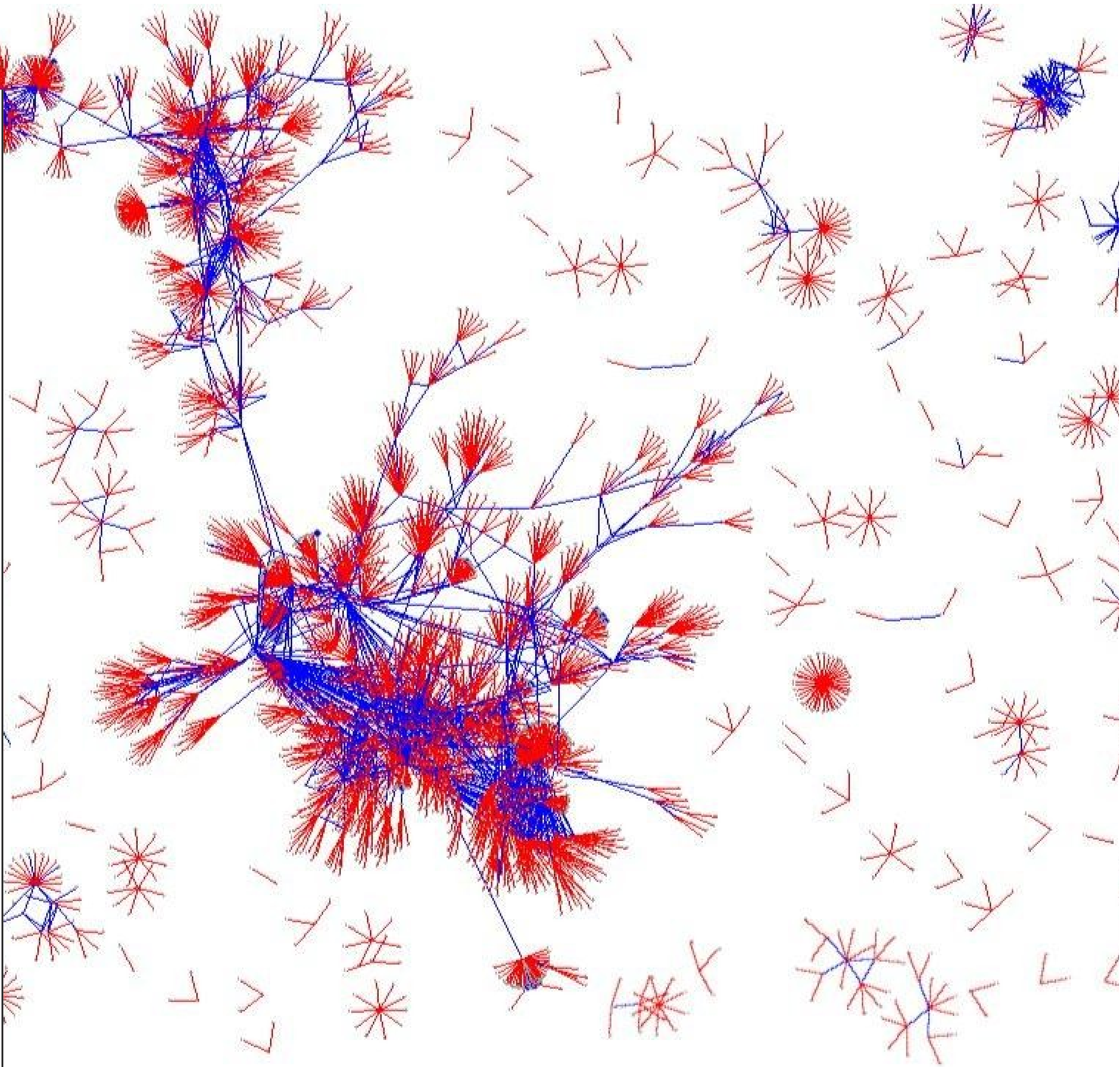
Principles

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

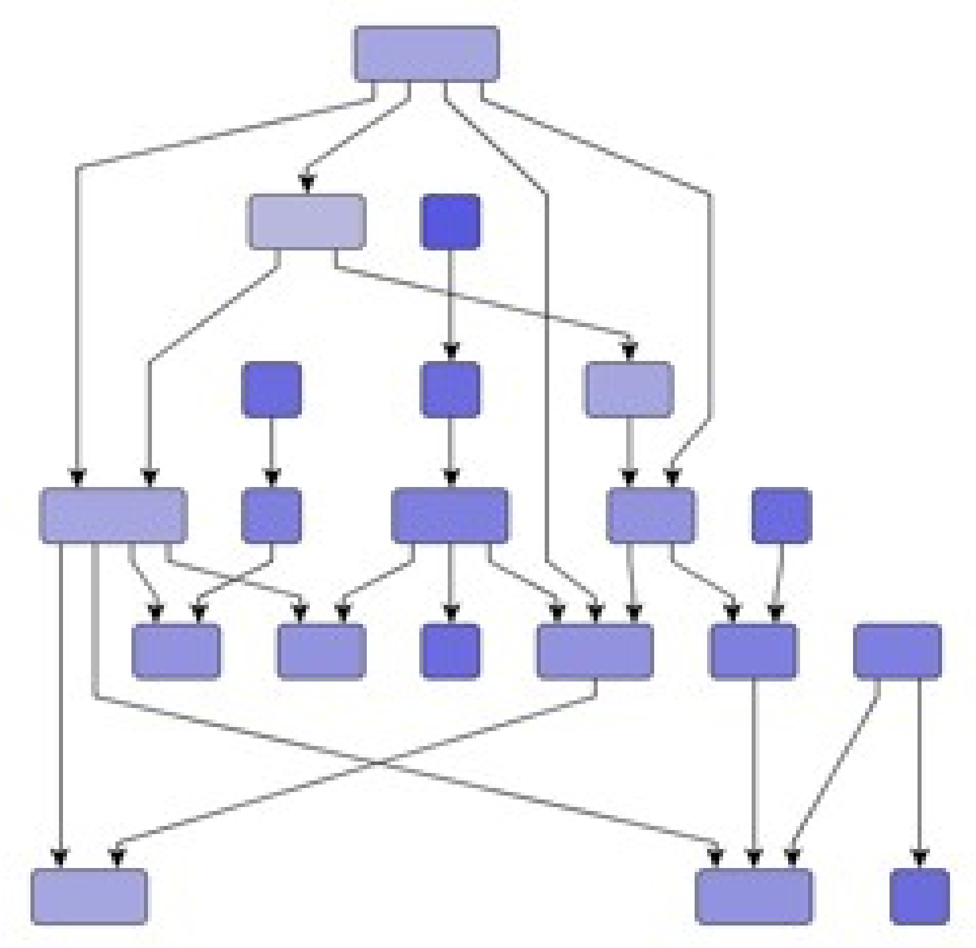
Force-directed layout



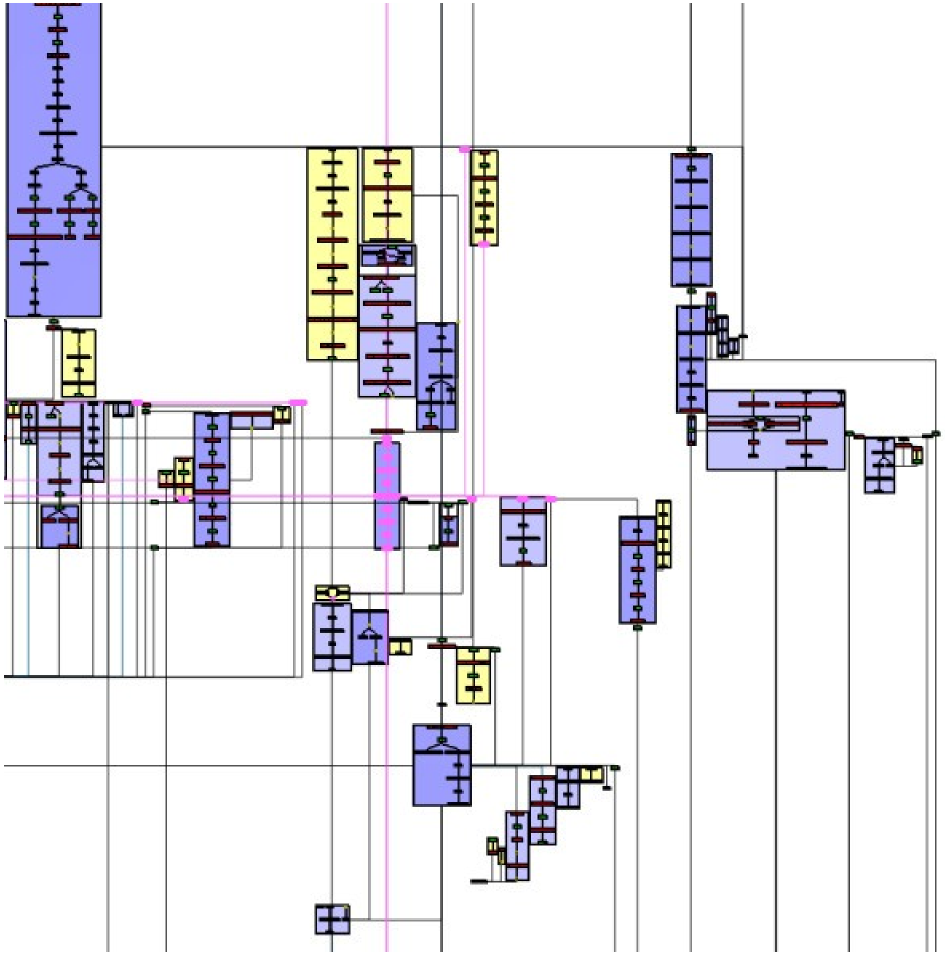


https://dhs.stanford.edu/visualization/more-networks/

Hierarchical layout



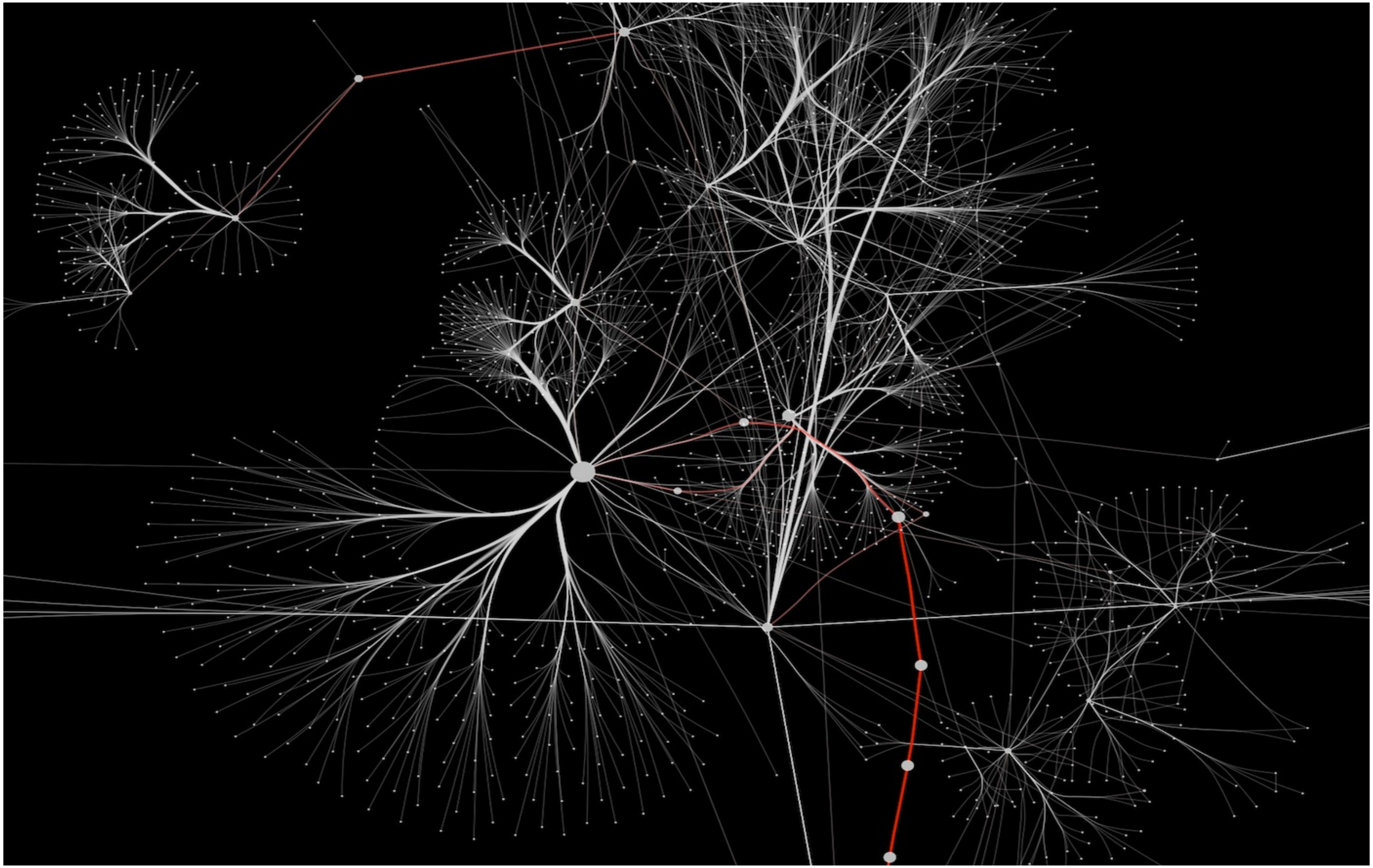
Layout designed for metabolic networks



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 redundance and preserving metabolic pathways. BMC Systems Biology 2007;1:29.

Cytoscape Java



Cytoscape JAVA

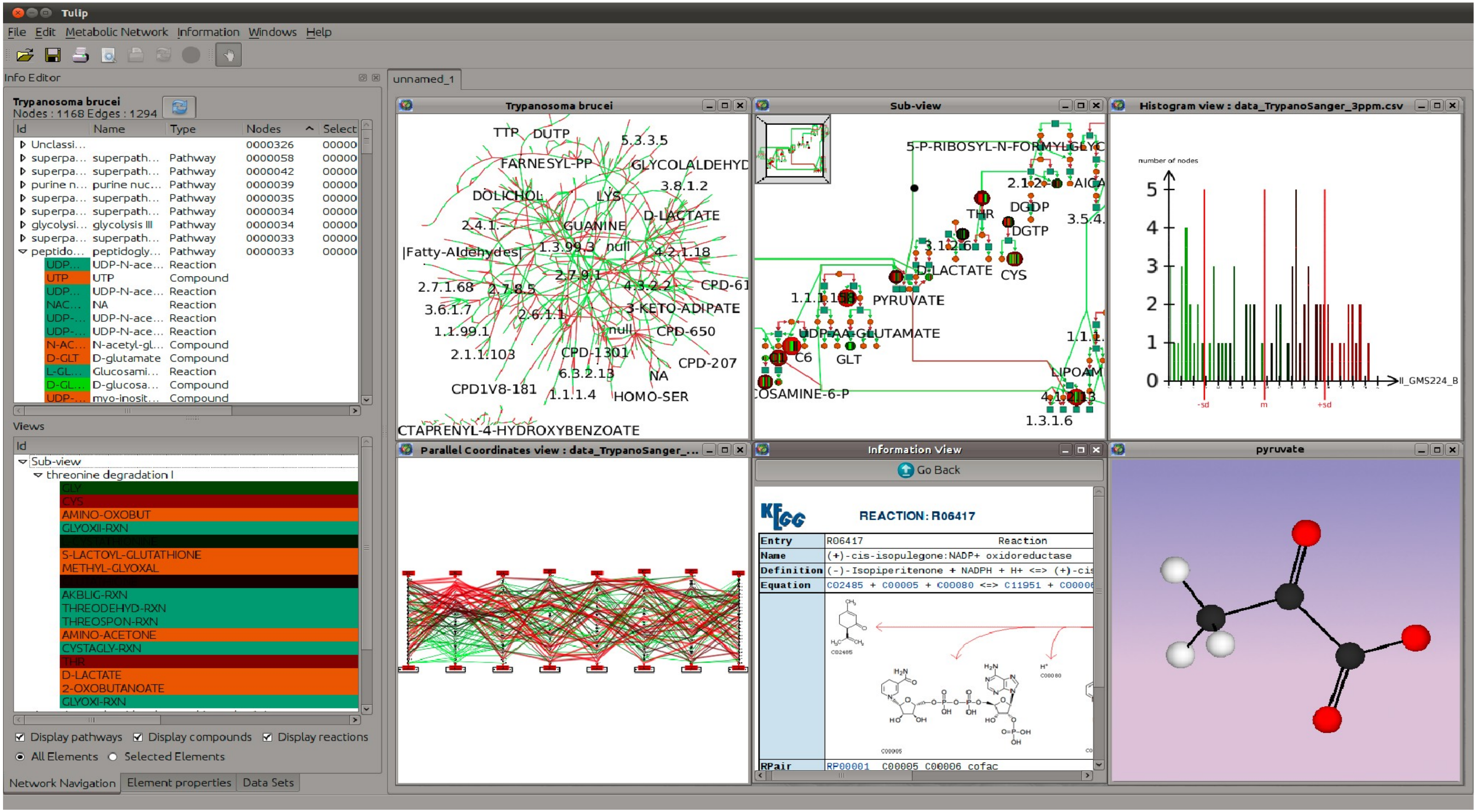
- user friendly
- visual styles
- a lot of plugins
- may be linked to Web pages by Java Web start

👍

- Version 3.0 :
  - V2 plugins can not be used
  - Web start not possible?

👎

Tulip / Systrip
http://tulip.labri.fr/TulipDrupal/?q=systrip



Trypanosoma brucei
Nodes : 1168 Edges : 1294

Id	Name	Type	Nodes	Select
Unclassi…			0000326	00000
superpa…	superpath…	Pathway	0000058	00000
superpa…	superpath…	Pathway	0000042	00000
purine n…	purine nuc…	Pathway	0000039	00000
superpa…	superpath…	Pathway	0000035	00000
superpa…	superpath…	Pathway	0000034	00000
glycolysi…	glycolysis III	Pathway	0000034	00000
superpa…	superpath…	Pathway	0000033	00000
peptido…	peptidogly…	Pathway	0000033	00000
UDP…	UDP-N-ace…	Reaction		
UTP	UTP	Compound		
UDP…	UDP-N-ace…	Reaction		
NAC…	NA	Reaction		
UDP-…	UDP-N-ace…	Reaction		
UDP-…	UDP-N-ace…	Reaction		
N-AC…	N-acetyl-gl…	Compound		
D-GLT	D-glutamate	Compound		
L-GL…	Glucosami…	Reaction		
D-GL…	D-glucosa…	Compound		
UDP-…	myo-inosit…	Compound		

Id
- Sub-view
  - threonine degradation I
    - GLY
    - CYS
    - AMINO-OXOBUT
    - GLYOXII-RXN
    - S-LACTOYL-GLUTATHIONE
    - METHYL-GLYOXAL
    - AKBLIG-RXN
    - THREODEHYD-RXN
    - THREOSPON-RXN
    - AMINO-ACETONE
    - CYSTAGLY-RXN
    - THR
    - D-LACTATE
    - 2-OXOBUTANOATE
    - GLYOXI-RXN

☑ Display pathways ☑ Display compounds ☑ Display reactions
● All Elements ○ Selected Elements

KEGG REACTION: R06417

Entry	R06417	Reaction
Name	(+)-cis-isopulegone:NADP+ oxidoreductase	
Definition	(-)-Isopiperitenone + NADPH + H+ <=> (+)-cis	
Equation	C02485 + C00005 + C00080 <=> C11951 + C0000	
RPair	RP00001 C00005 C00006 cofac	

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Tulip et Systryp

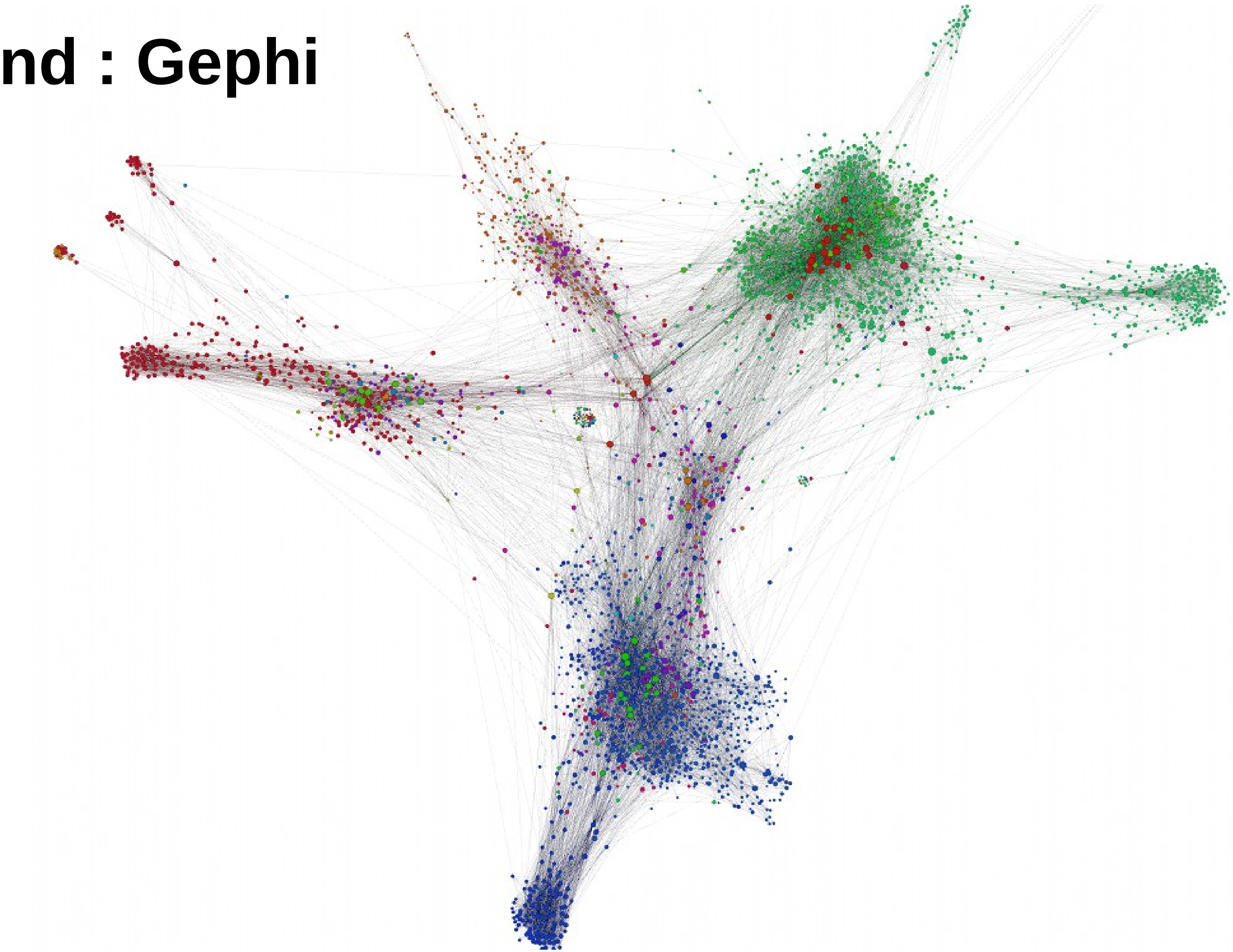
- Powerful (OpenGL)
- Many graph measures

👍

- Not very user friendly
- Nobody to maintain !!!

👎

Trend : Gephi



Metabolic network web visualisation

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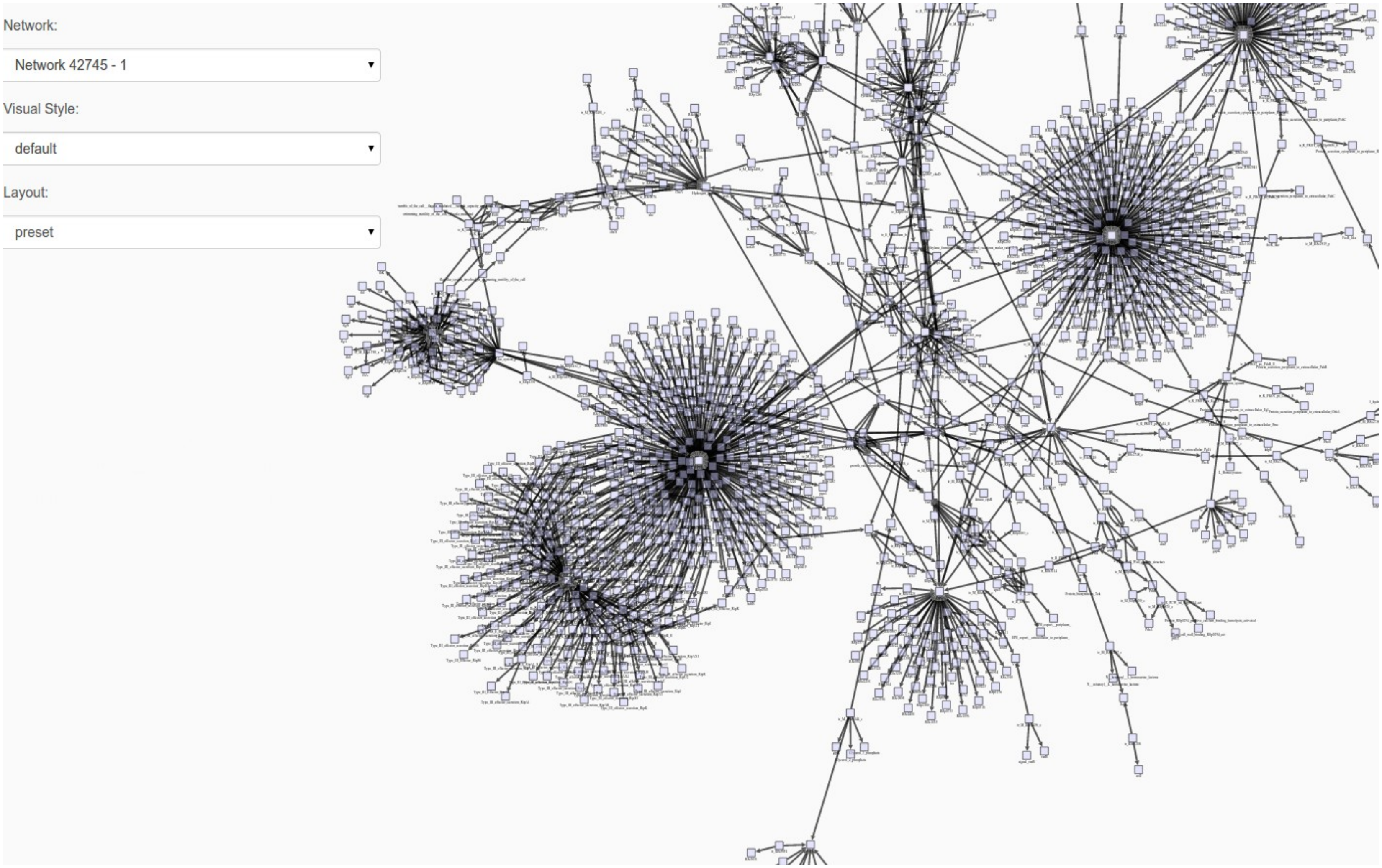
Cytoscape.js



Network:

Network 42745 - 1

Visual Style:

default

Layout:

preset

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Cytoscape.js

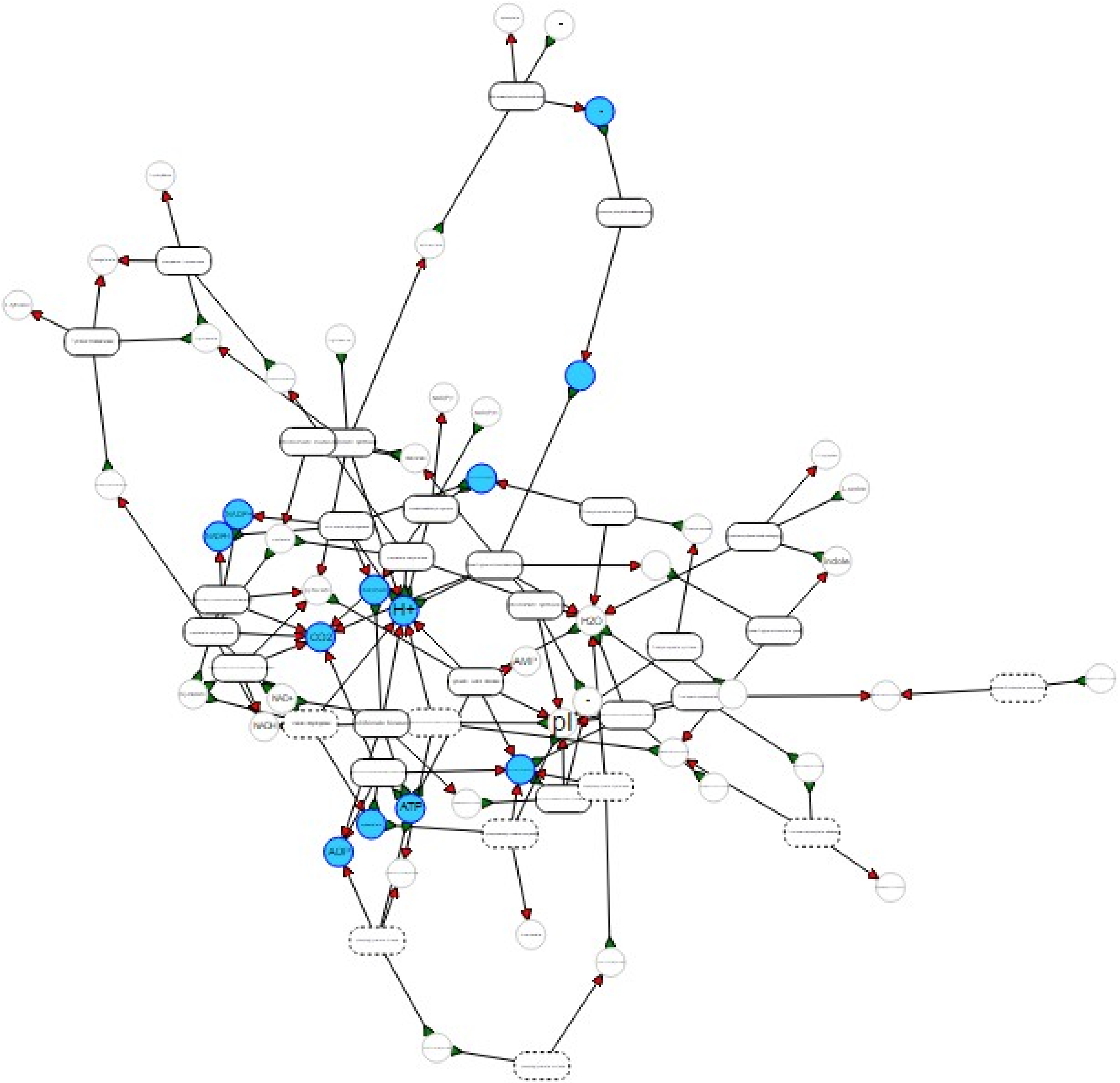
- Large community
- Links with Cytoscape Java

👍

- Lags with large networks

👎

d3.js



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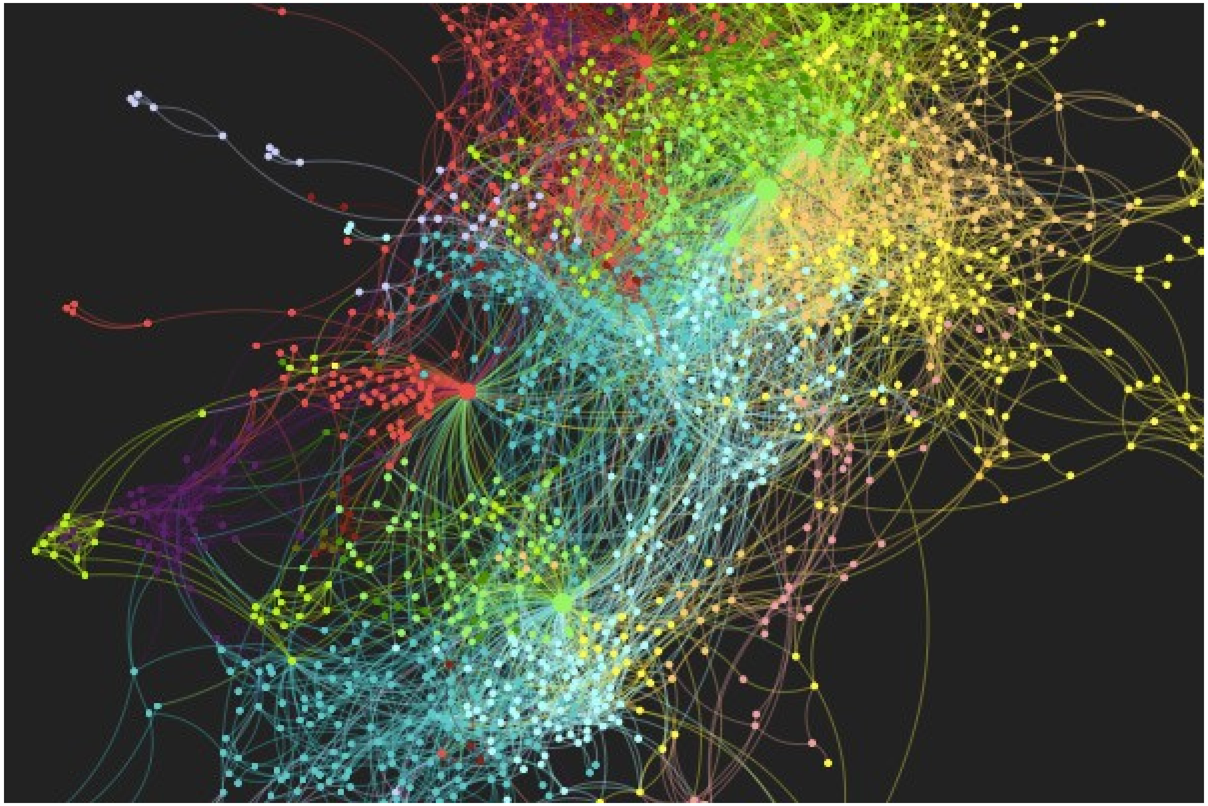
d3. js

- Powerful
- More generic
- Large communauty

- Interactions more difficult to handle (→ SVG)

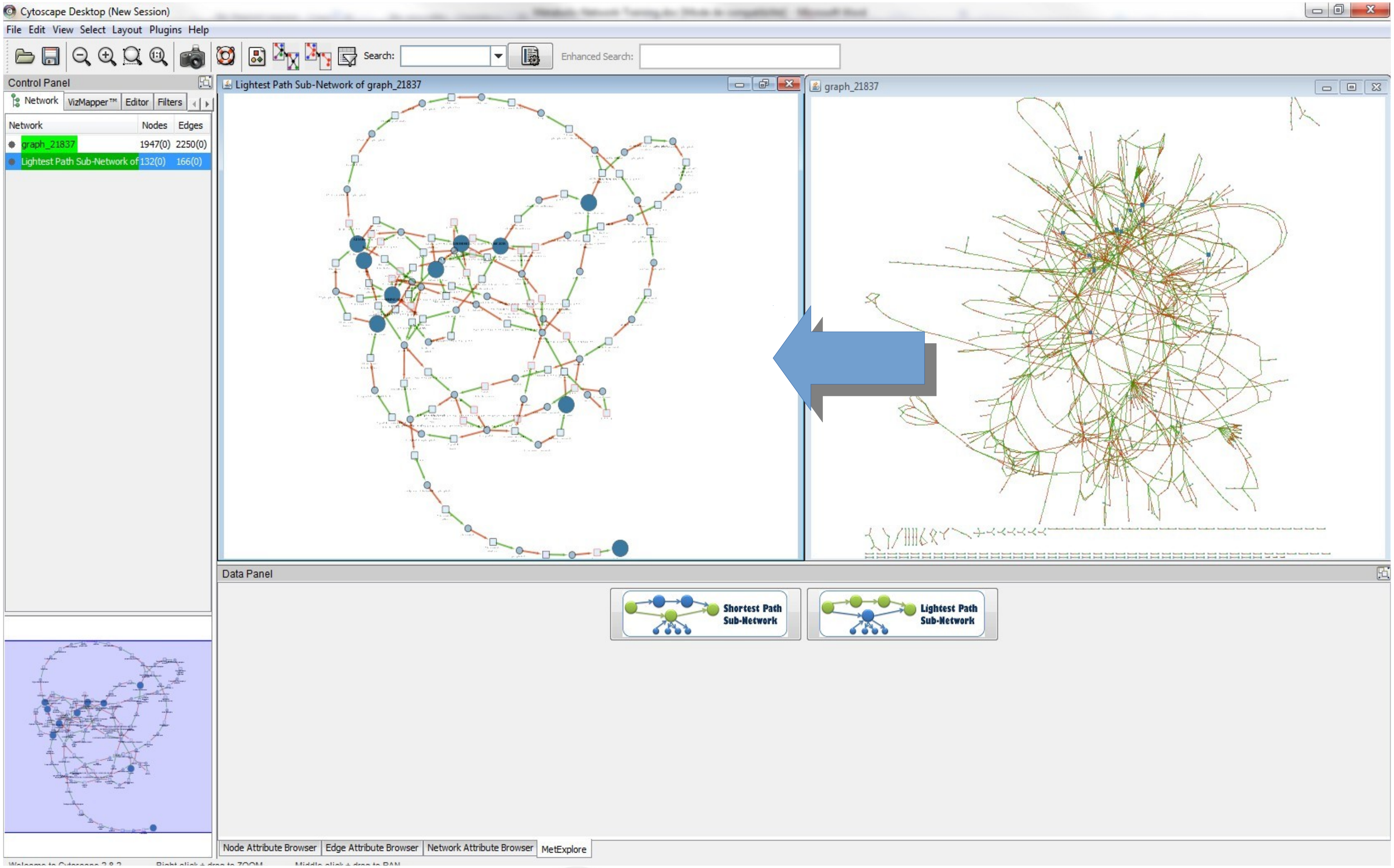
Future : Network visualisation with Webgl ?
Ex: sigmajs

- Uses the graphic cards



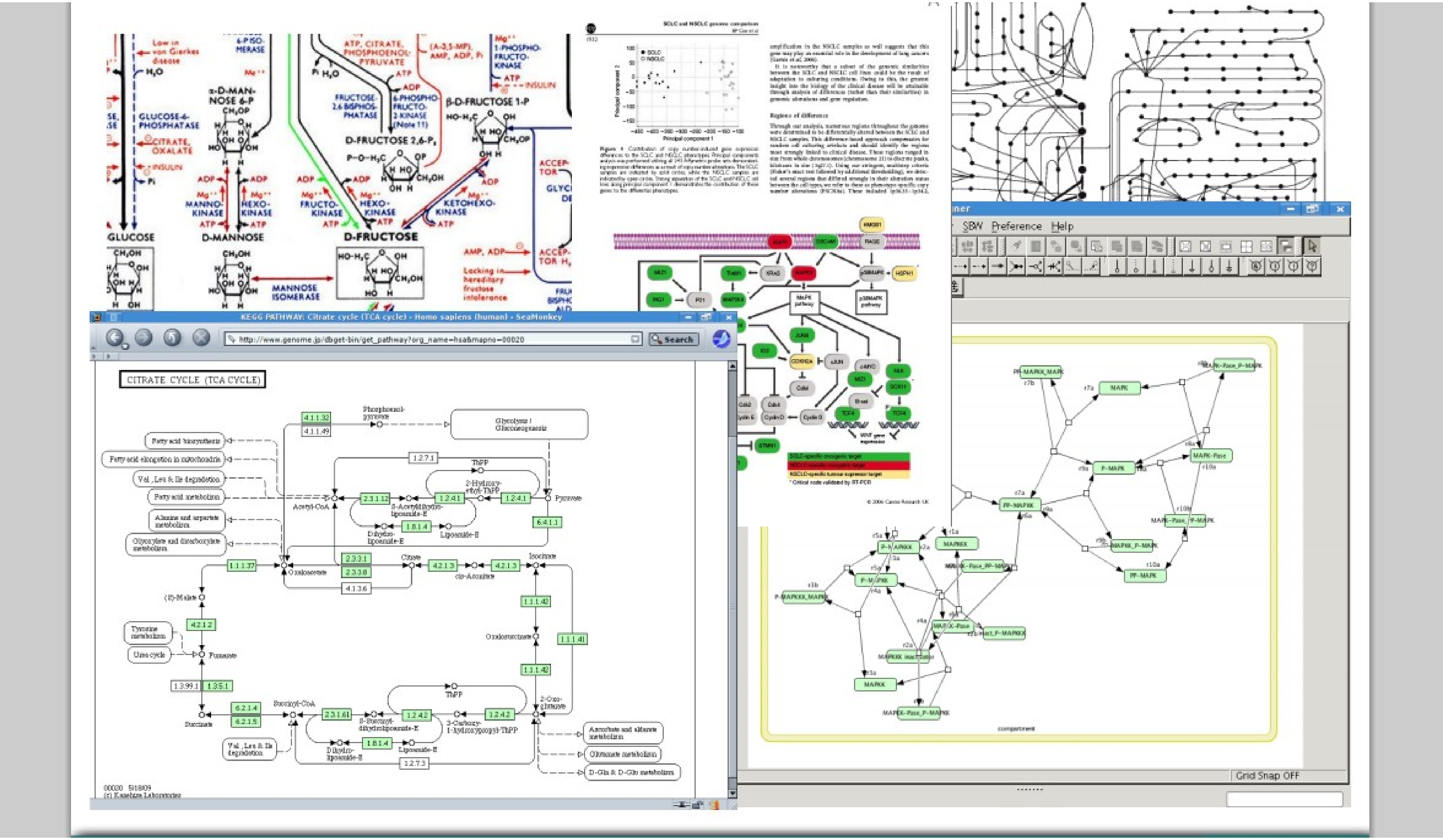
http://sigmajs.org/

Sub network identification helps the visualisation



Network	Nodes	Edges
graph_21837	1947(0)	2250(0)
Lightest Path Sub-Network of	132(0)	166(0)

How to share network views?

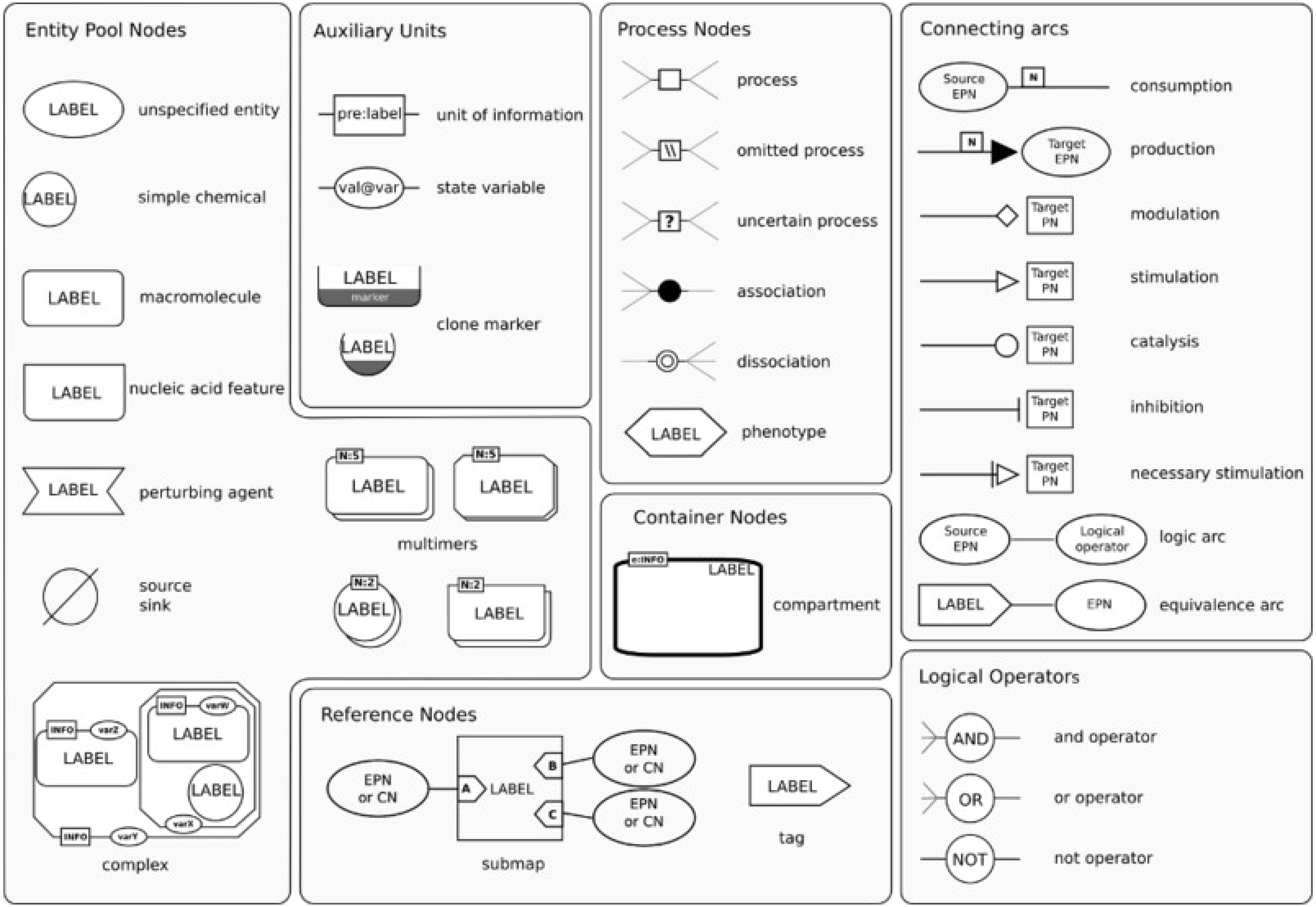


From N. Lenovère's slides

Challenges

- Numerous visual styles
- Layouts not always deterministic

Systems Biology Graphical Notation (SBGN)



http://www.sbgn.org/

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