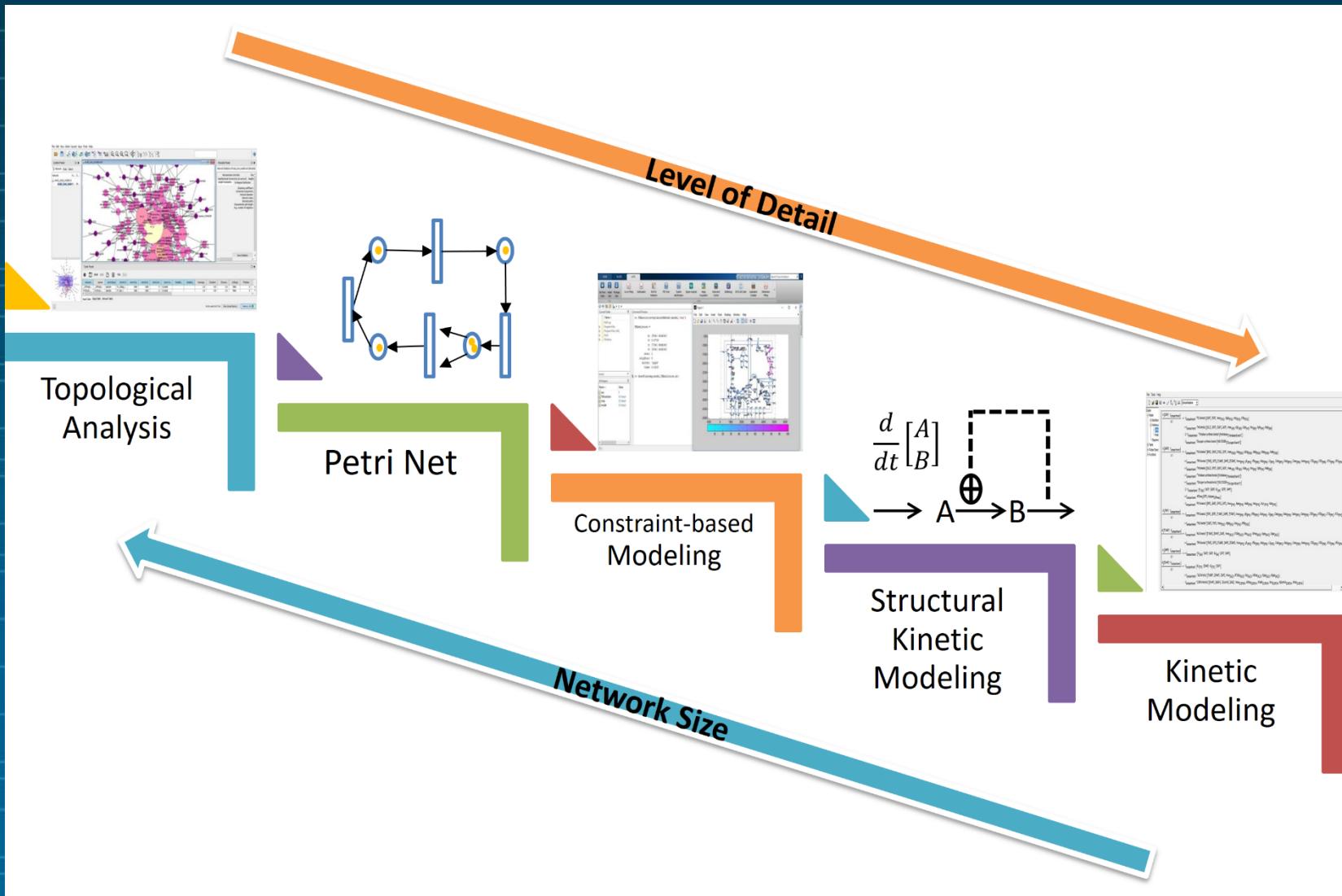


Computational
&
Systems Biology

Metabolic Network Reconstruction

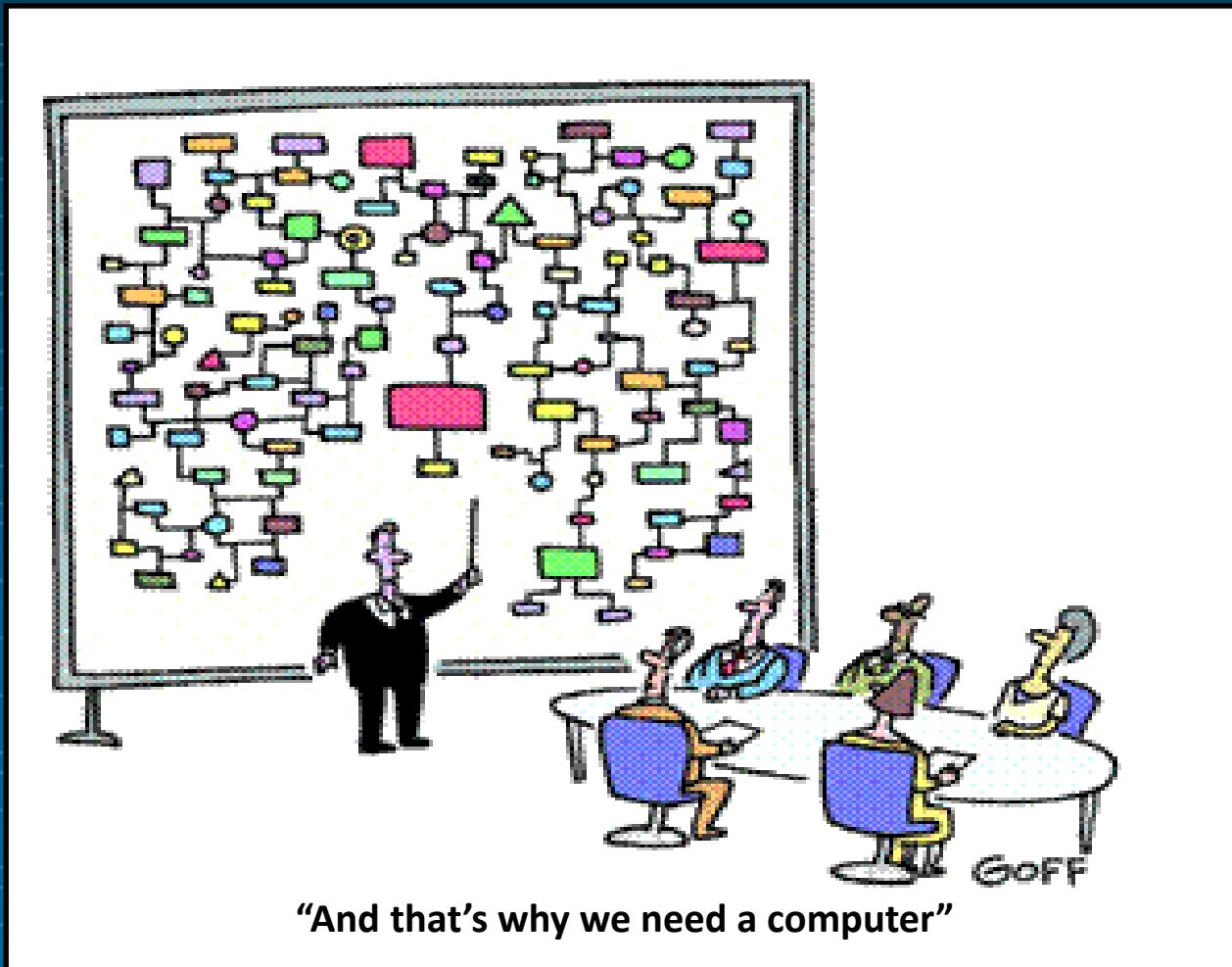
Yazdan Asgari
2020

Metabolic Modeling

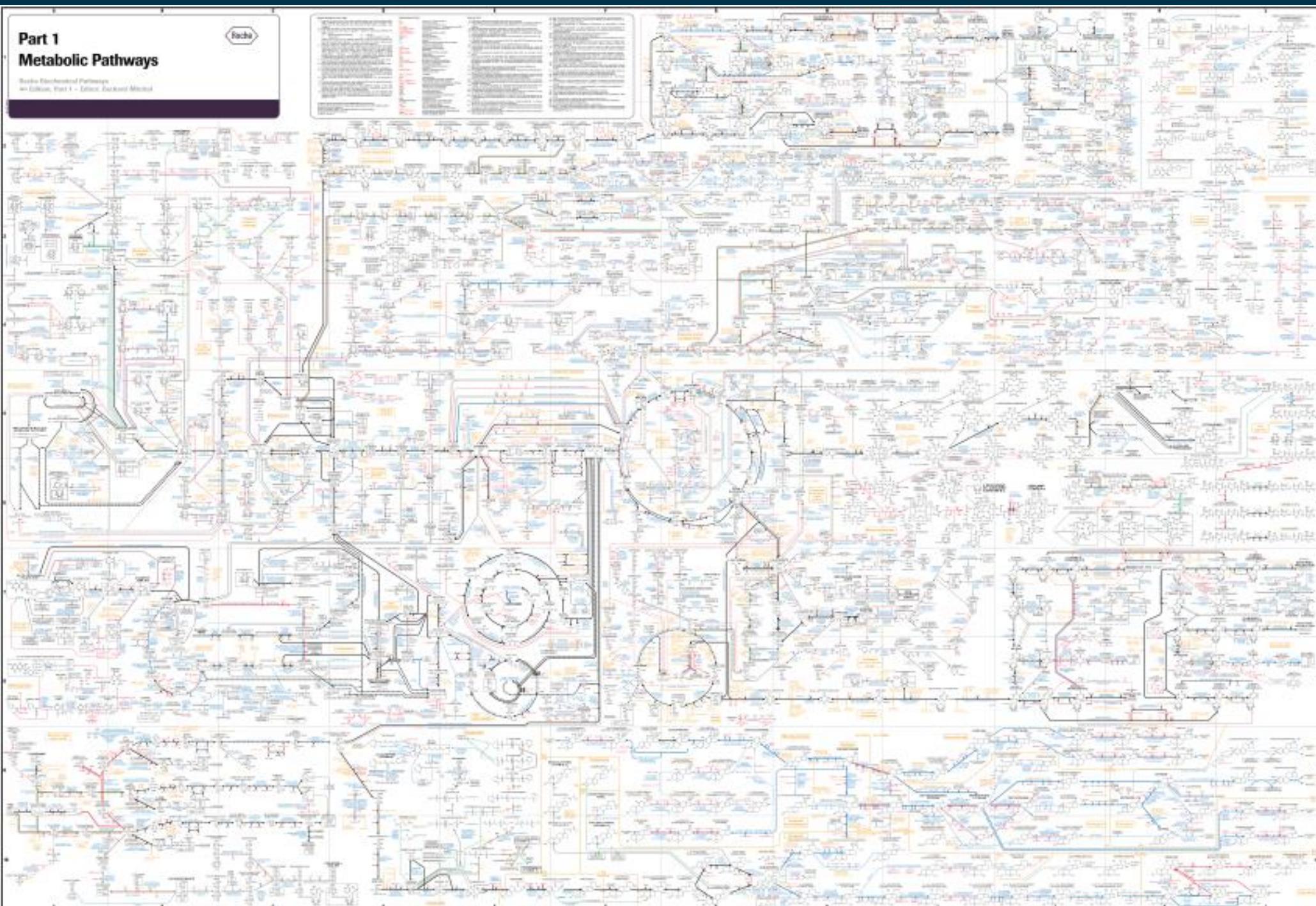


After this session, one could

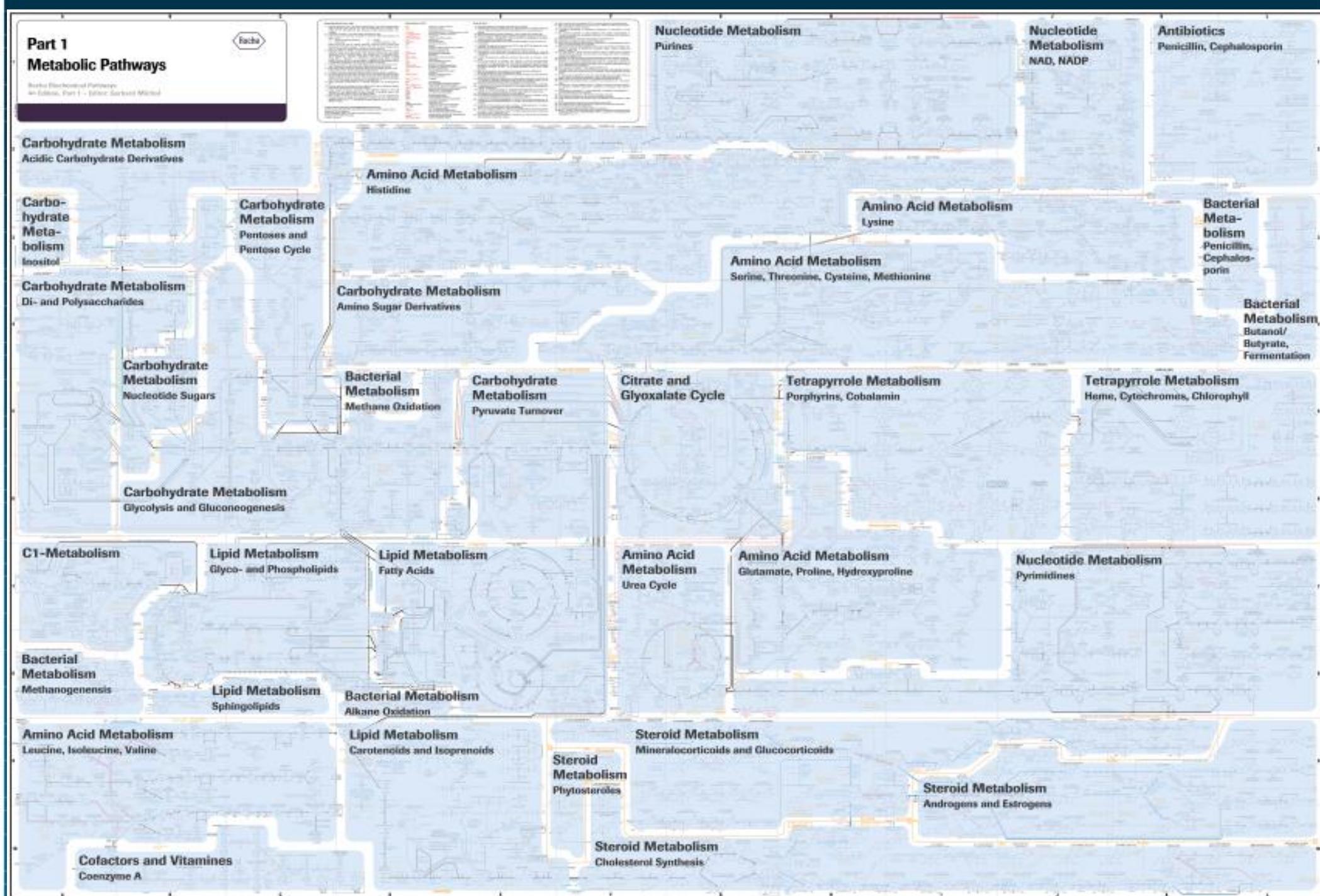
- ❖ *Find how Metabolic models have been constructed*
- ❖ *Understand and modify existing reconstructed models*



Metabolic Modeling: The Dream



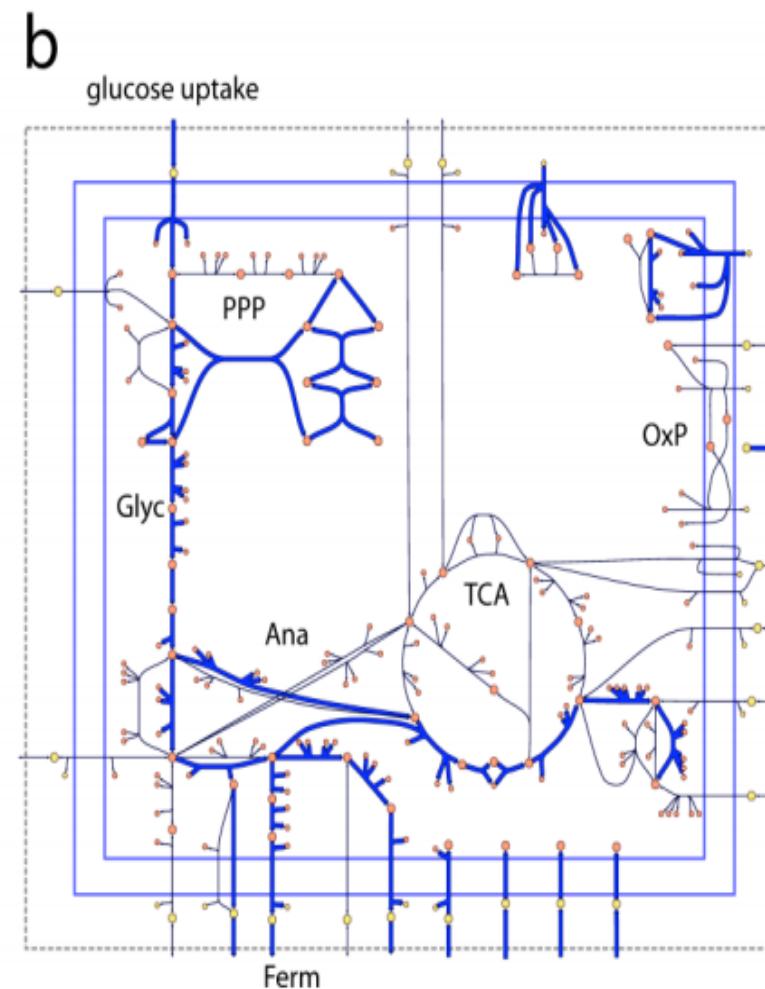
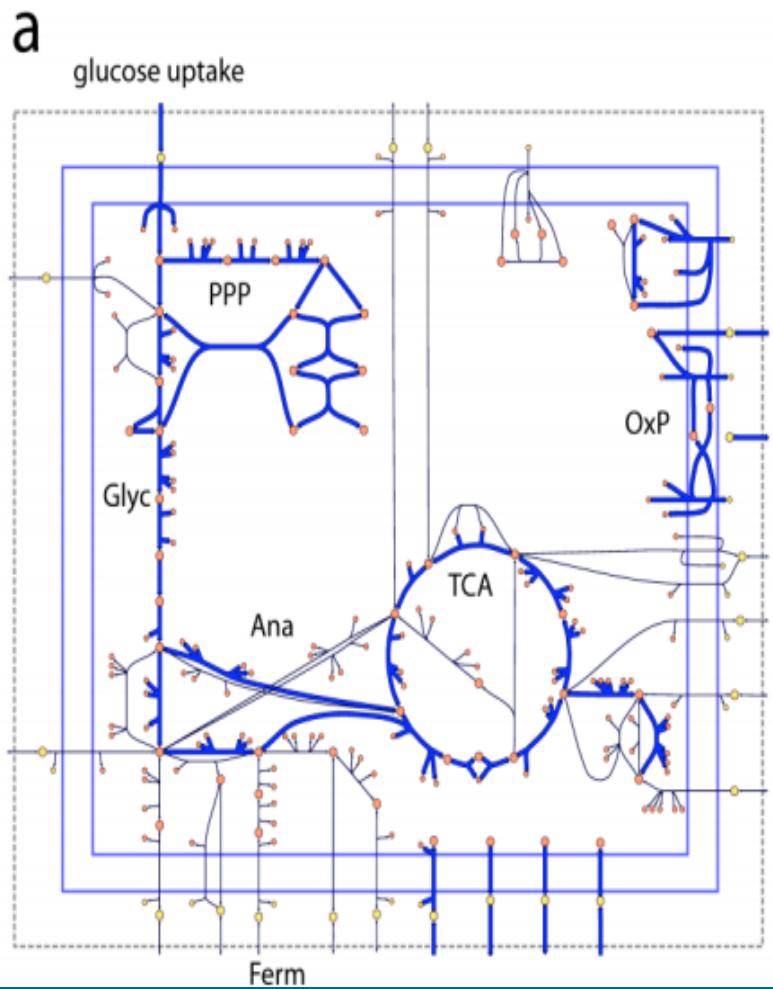
Metabolic Modeling: The Dream



Example

aerobic

anaerobic



How are metabolic networks reconstructed?

Genome Annotation

- by homology, location

Biochemical Data

- protein characterized

Physiological Data

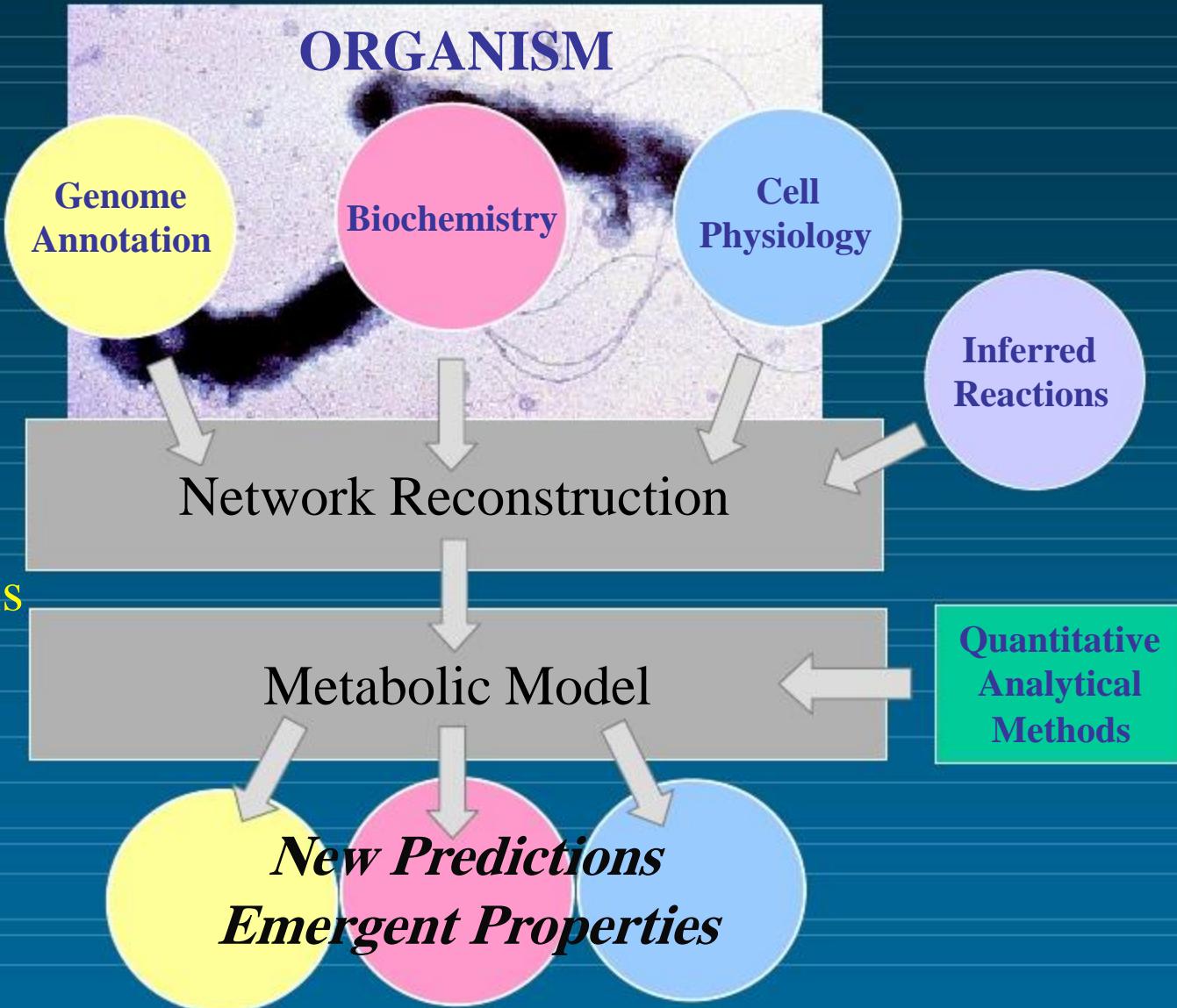
- indirect, pathway known

Inferred Reactions

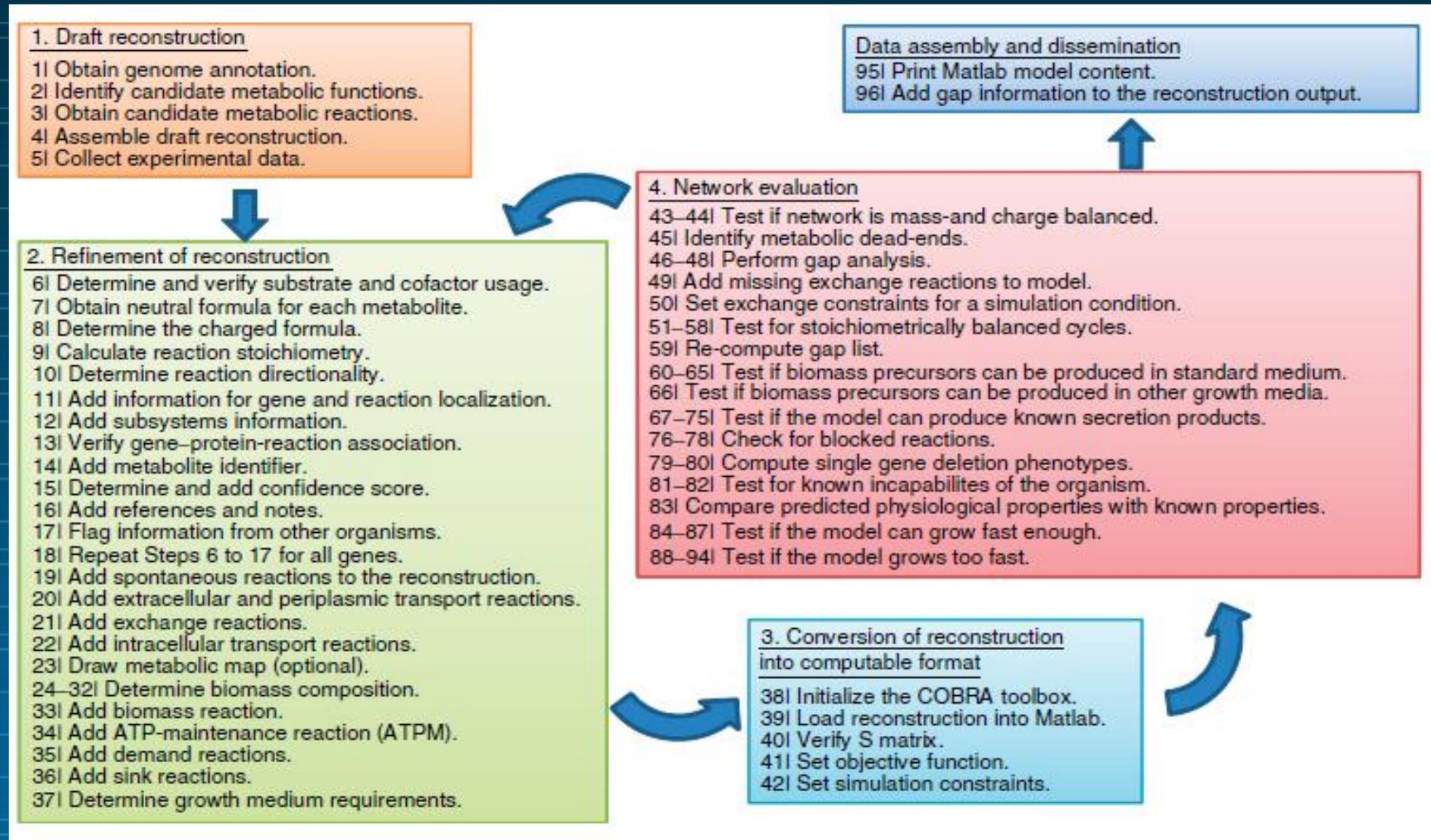
- indirect, inferred from
biomass requirements

Quantitative Analysis

- simulate cell behavior
- drive experimental studies



Reconstruction: Full steps



PROTOCOL

A protocol for generating a high-quality genome-scale metabolic reconstruction

Ines Thiele^{1,2} & Bernhard Ø Palsson¹

Draft Reconstruction (in summary)

- Finding genome of an organism
- Exploring its proteins
- Extracting proteins with known metabolic functions (using available annotations such as GO and KO)
- Adding
 - Corresponded reaction
 - Directionality
 - GPR
 - Compartment
 - Transport and Exchanges
- Gap filling

Draft Reconstruction: Example: *E. coli* K12 MG1655

NCBI Resources How To Sign in to NCBI

Gene Gene txid511145[Organism:noexp] AND metab* Search Create alert Advanced Help

Gene sources Tabular ▾ 20 per page ▾ Sort by Relevance ▾ Send to: ▾ Hide sidebar >>

Genomic

Categories Annotated genes Filters: [Manage Filters](#)

Annotated genes Non-coding Protein-coding Pseudogene

Non-coding Protein-coding Pseudogene

Sequence content RefSeq

Status clear

Current

Chromosomes

Search results

Items: 1 to 20 of 860

<< First < Prev Page 1 of 43 Next > Last >>

i Showing Current items.

x Wildcard search for 'metab*' used only the first 600 variations. Lengthen the root word to search for all endings.

Name/Gene ID	Description	Location	Aliases
fadR ID: 948652	fatty acid metabolism regulon transcriptional regulator [<i>Escherichia coli</i> str. K-12 substr. MG1655]	NC_000913.3 (1234938..1235657)	b1187, ECK1175, JW1176, dec, ole, oleR, thdB
glpK ID: 948423	glycerol kinase [<i>Escherichia coli</i> str. K-12 substr. MG1655]	complement)	NC_000913.3 (4115714..411722, JW3897 complement)

Find related data Database: Select Find items

txid511145[Organism:noexp] AND (metab[All Fields] OR metabasis[All Fields])

Draft Reconstruction: Example: *E. coli* K12 MG1655

NCBI Resources How To

Gene Gene Advanced

Full Report Send to:

glpK glycerol kinase [*Escherichia coli* str. K-12 substr. MG1655]

Gene ID: 948423, updated on 31-Oct-2015

Summary

Gene symbol glpK
Gene description glycerol kinase
Primary source EcoGene:EG10398
Locus tag b3926
Gene type protein coding
RefSeq status PROVISIONAL
Organism *Escherichia coli* str. K-12 substr. MG1655 (strain: K-12, substrain: MG1655)
Lineage Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales; Enterobacteriaceae; Escherichia
Also known as ECK3918; JW3897
Summary The enzyme can undergo a reversible subunit dissociation between tetramer and dimer . [More information is available at EcoCyc: EG10398].

Gene Symbol	Locus Name	EntrezGene Function	EC Number
glpk	b3926	Can undergo a reversible subunit dissociation between tetramer and dimer	

Draft Reconstruction: Example: *E. coli* K12 MG1655

NCBI Resources How To

Gene Gene Advanced

Full Report Send to:

glpK glycerol kinase [*Escherichia coli* str. K-12 substr. MG1655]

Gene ID: 948423, updated on 31-Oct-2015

Summary

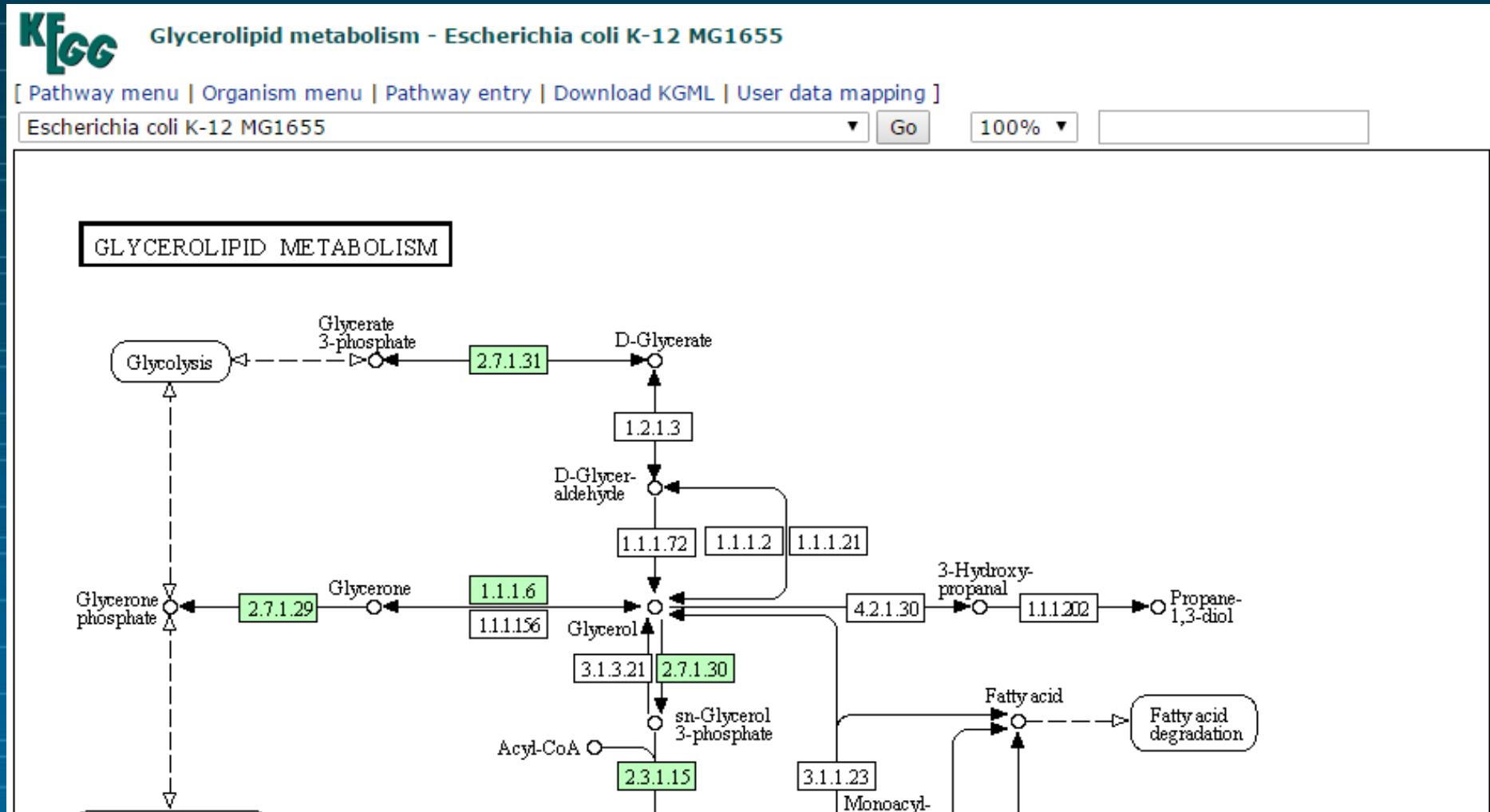
Gene symbol glpK
Gene description glycerol kinase
Primary source EcoGene:EG10398
Locus tag b3926
Gene type protein coding
RefSeq status PROVISIONAL
Organism [Escherichia coli str. K-12 substr. MG1655 \(strain: K-12, substrate: MG1655\)](#)
Lineage Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales; Enterobacteriaceae; Escherichia
Also known as ECK3918; JW3897
Summary The enzyme can undergo a reversible subunit dissociation between tetramer and dimer . [More information is available at EcoCyc: EG10398].

Pathways from BioSystems

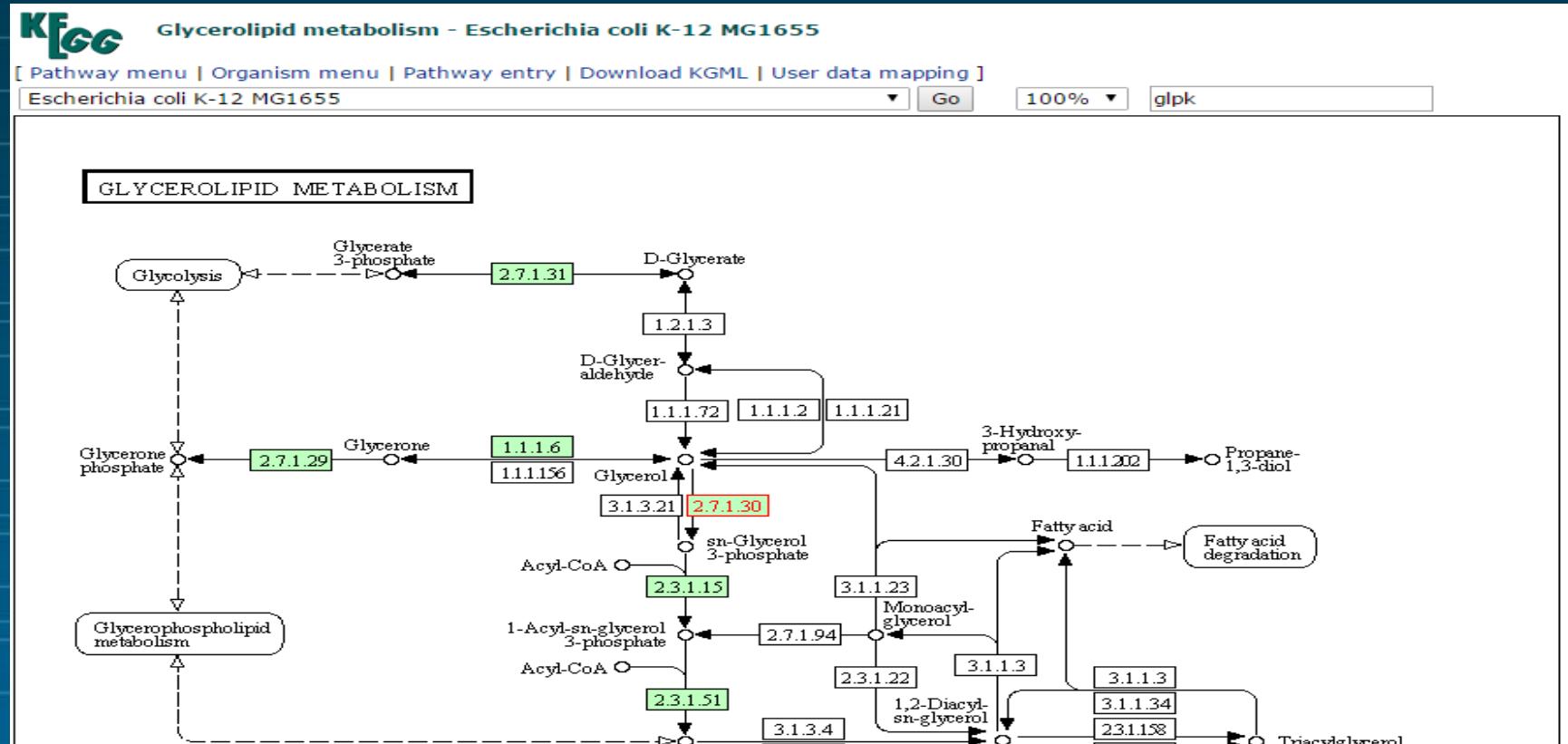
[Glycerolipid metabolism, organism-specific biosystem \(from KEGG\)](#)
[Glycerolipid metabolism, conserved biosystem \(from KEGG\)](#)
[Metabolic pathways, organism-specific biosystem \(from KEGG\)](#)
[glycerol and glycerophosphodiester degradation, organism-specific biosystem \(from BIOCYC\)](#)
[glycerol and glycerophosphodiester degradation, conserved biosystem \(from BIOCYC\)](#)
[glycerol degradation I, organism-specific biosystem \(from BIOCYC\)](#)
[glycerol degradation I, conserved biosystem \(from BIOCYC\)](#)

Draft Reconstruction: Example: *E. coli* K12 MG1655

Draft Reconstruction: Example: *E. coli* K12 MG1655

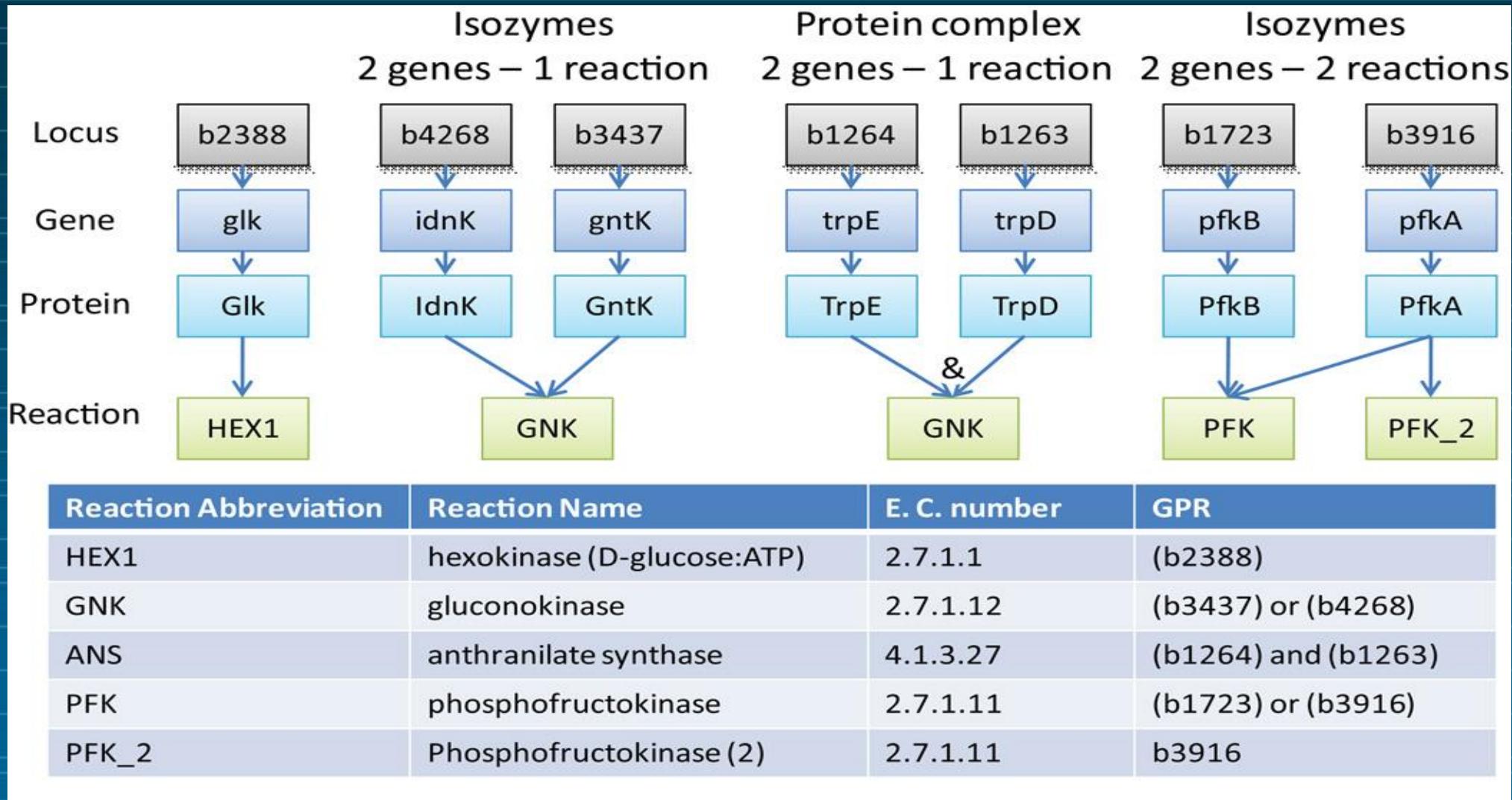


Draft Reconstruction: Example: *E. coli* K12 MG1655



Gene Symbol	Locus Name	EntrezGene Function	EC Number
glpk	b3926	Can undergo a reversible subunit dissociation between tetramer and dimer	2.7.1.30

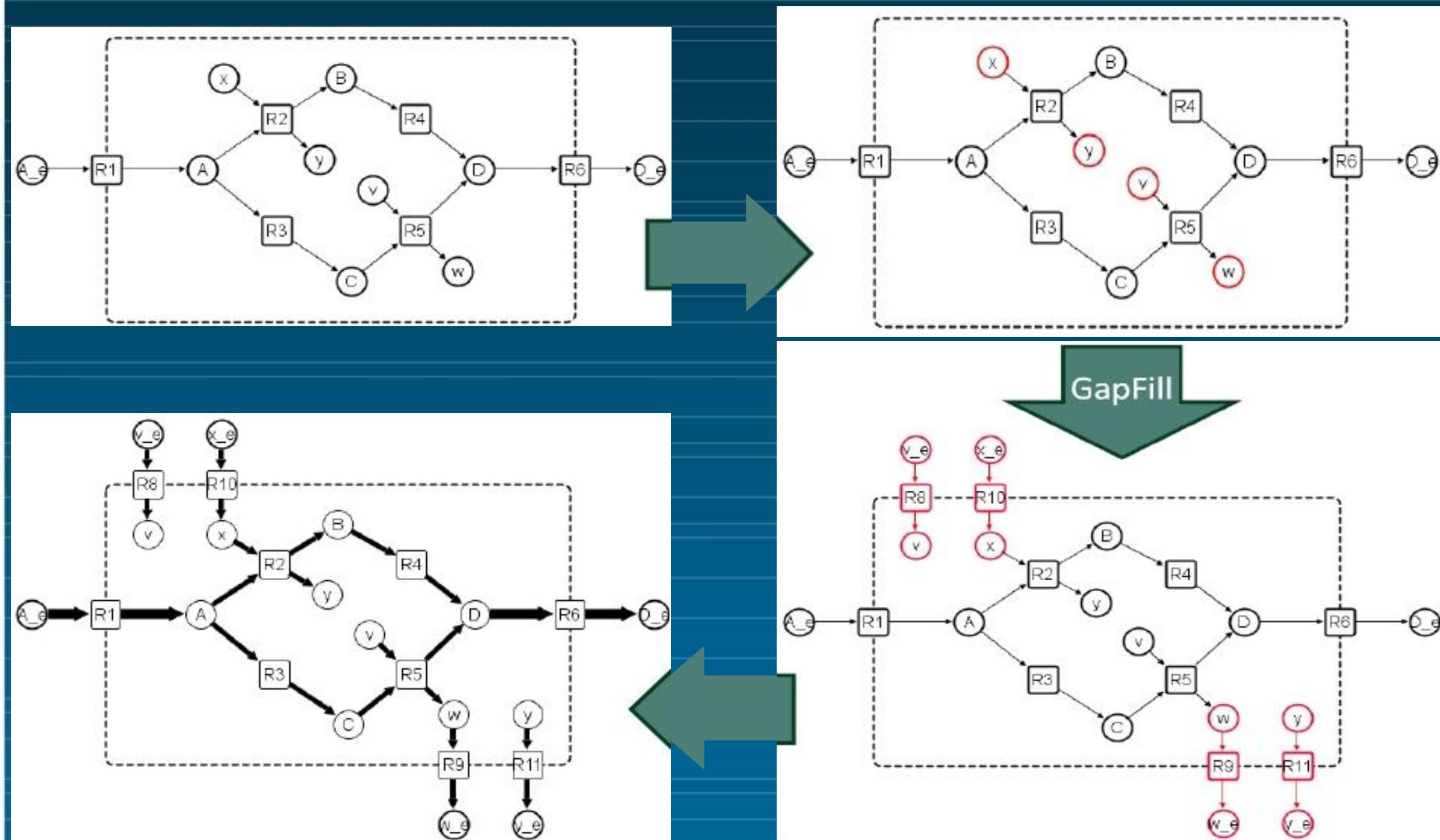
GPR rules



Metabolite Compartment

Compartment	Commonly used symbol [#]	Achaea	Bacteria	Eukaryotic pathogens ^a	Fungi ^b	Photosynthetic eukarya ^c	Baker's yeast	Human
Extracellular space	[e]							
Periplasm	[p]							
Cytoplasm	[c]							
Nucleus	[n]							
Mitochondrion	[m]							
Chloroplast	[h]							
Lysosome*	[l]							
Vacuole	[v]							
Golgi apparatus	[g]							
Endoplasmatic	[r]							

Gap Finding and Gap Filling



Convert information into a software

1. Adding metabolites and reactions information in Excel
2. Specify parameter values
3. Convert information to a computer-based format
4. Ready to simulate

Example – Recon1

recon1.xls [Compatibility Mode] - Excel

	A	B	C	D	E	G	H	I	J	K	L	M
1	Rxn name	Rxn description	Formula	(Genes	Subsystem	Reversible	(EC Number	Notes		
2	AGTim	alanine-glyoxylate transaminas	ala-L[m] + glx[m] -> gly[m] + pyr[m]	(64850.1 64902.1	Alanine and Aspartate Me	0	2.6.1.44	NCD			
3	AGTix	alanine-glyoxylate transaminas	ala-L[x] + glx[x] -> gly[x] + pyr[x]		189.1	Alanine and Aspartate Me	0	2.6.1.44	NCD			
4	ALAR	alanine racemase	ala-L[c] <=> ala-D[c]		11212.1	Alanine and Aspartate Me	1	5.1.1.1	LOCUS:_11212#TRANSCRIPT:1#ABBREVIATION:PROSC#			
5	ARGSL	argininosuccinate lyase	argsuc[c] <=> arg-L[c] + fum[c]		435.1	Alanine and Aspartate Me	1	4.3.2.1	LOCUS:_435#TRANSCRIPT:1#ABBREVIATION:ASL#ECNUMB			
6	ARGSS	argininosuccinate synthase	asp-L[c] + atp[c] + citr-L[c] -> amp[c] + argsuc[c] + h[c]	(445.1 445.2	Alanine and Aspartate Me	0	6.3.4.5	LOCUS:_445#TRANSCRIPT:2#ABBREVIATION:ASS#			
												PMID: 11984834 (denotes it as potentially mitochondrial)
7	ASNNm	L-asparaginase (mitochondrial)	asn-L[m] + h2o[m] -> asp-L[m] + nh4[m]		80150.1	Alanine and Aspartate Me	0	3.5.1.1	mm			
8	ASNS1	asparagine synthetase (glutamine	asp-L[c] + atp[c] + gln-L[c] + h2o[c] -> amp[c] + asn-L[c]	(440.1 440.2 440.3	Alanine and Aspartate Me	0	6.3.5.4	LOCUS:_440#TRANSCRIPT:3#ABBREVIATION:ASNS#ECNUM			
9	ASPNTAm	aspartate N-acetyltransferase, n	accoa[m] + asp-L[m] -> Nacasp[m] + coa[m] + h[m]			Alanine and Aspartate Me	0	2.3.1.17	MM			
10	ASPTA	aspartate transaminase	akg[c] + asp-L[c] <=> glu-L[c] + oaa[c]		2805.1	Alanine and Aspartate Me	1	2.6.1.1	LOCUS:_2805#TRANSCRIPT:1#ABBREVIATION:GOT1#ECNU			
11	ASPTAm	aspartate transaminase	akg[m] + asp-L[m] <=> glu-L[m] + oaa[m]		2806.1	Alanine and Aspartate Me	1	2.6.1.1	NCD			
12	DASPO1p	D-aspartate oxidase, peroxisom	asp-D[x] + h2o[x] + o2[x] -> h2o2[x] + nh4[x] + oaa[x]	(8528.1 8528.2	Alanine and Aspartate Me	0	1.4.3.1	MM			
13	NACASPAH	N-Acetyl-L-aspartate amidohyd	Nacasp[c] + h2o[c] -> ac[c] + asp-L[c]	(443.1 91703.1	Alanine and Aspartate Me	0	3.5.1.15	SAB			
14	COKECBESr	Carboxylesterase (cocaine) (er)	coke[r] + h2o[r] -> bz[r] + egme[r] + h[r]		8824.1	Alkaloid biosynthesis II	0	3.1.1.1	SAB			
												SAB
15	ECGISOr	Ecgonine isomerase (ER)	ecgon[r] <=> pecgon[r]			Alkaloid biosynthesis II	1		reaction name uncertain			
												SAB
16	EGMESTr	ecgonine methyl esterase (ER)	egme[r] + h2o[r] -> ecgon[r] + h[r] + meoh[r]		13.1	Alkaloid biosynthesis II	0		EC 3.1.1.-			
17	NMPTRCOX	N-Methylputrescine:oxygen oxid	nmptrc[c] + o2[c] -> 1mpyr[c] + h2o2[c] + nh4[c]	(26.1 314.1 314.2 8	Alkaloid biosynthesis II	0	1.4.3.6	SAB			
												SAB
18	PECGONCOATr	Pseudoecgonine CoA transferase	atp[r] + coa[r] + h[r] + pecgon[r] -> amp[r] + pecgoncoa[r] + ppi[r]			Alkaloid biosynthesis II	0		EC 6.2.1.-			
									name uncertain			
									NCD			

SBML: a standard file format for metabolic modeling

BIOINFORMATICS

Vol. 19 no. 4 2003, pages 524–531
DOI: 10.1093/bioinformatics/btg015



The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models

biochemical network models

SBML structure

```
1  <?xml version="1.0" encoding="UTF-8"?>
2  <sbml xmlns="http://www.sbml.org/sbml/level1"
3      level="1" version="2">
4      <model name="gene_network_model">
5          <listOfUnitDefinitions>
6              ...
7          </listOfUnitDefinitions>
8          <listOfCompartments>
9              ...
10         </listOfCompartments>
11         <listOfSpecies>
12             ...
13         </listOfSpecies>
14         <listOfParameters>
15             ...
16         </listOfParameters>
17         <listOfRules>
18             ...
19         </listOfRules>
20         <listOfReactions>
21             ...
22         </listOfReactions>
23     </model>
24 </sbml>
```

Fig. 1. The skeleton of a model definition expressed in SBML, showing all possible top-level elements.

Level 1

- Tags
 1. sbml
 2. model
 3. Unit Definition
 4. Compartments
 5. Species
 6. Parameters
 7. Rules
 8. Reactions

Level 2

- Tags
 1. sbml
 2. Model
 3. Function Definitions
 4. Unit Definition
 5. Compartments types
 6. Species types
 7. Compartments
 8. Species
 9. Parameters
 10. Initial Assignments
 11. Rules
 12. Constraints
 13. Reactions
 14. Events

Level 3

- Tags
 1. sbml
 2. Model
 3. Function Definitions
 4. Unit Definition
 5. Compartments
 6. Species
 7. Parameters
 8. Initial Assignments
 9. Rules
 10. Constraints
 11. Reactions
 12. Events

Convert an Excel file into a SBML file

1. Using a perl/java script to convert the excel data into a SBML file.
2. Using tools such as MetaNetX to convert the excel data into SBML.

Example

The screenshot shows a Microsoft Excel spreadsheet with the following data:

	A	B	C	D	E	F	G
1	r1	$s_1 + 2s_2 \rightarrow 2p_1 + 3p_2$					
2	r2	$s_3 + s_4 \leftrightarrow p_3 + p_4$					
3							
4							
5							

The formula $s_1 + 2s_2 \rightarrow 2p_1 + 3p_2$ is selected in cell B1. The formula $s_3 + s_4 \leftrightarrow p_3 + p_4$ is selected in cell B2. The cell B3 is currently active, indicated by a green border.

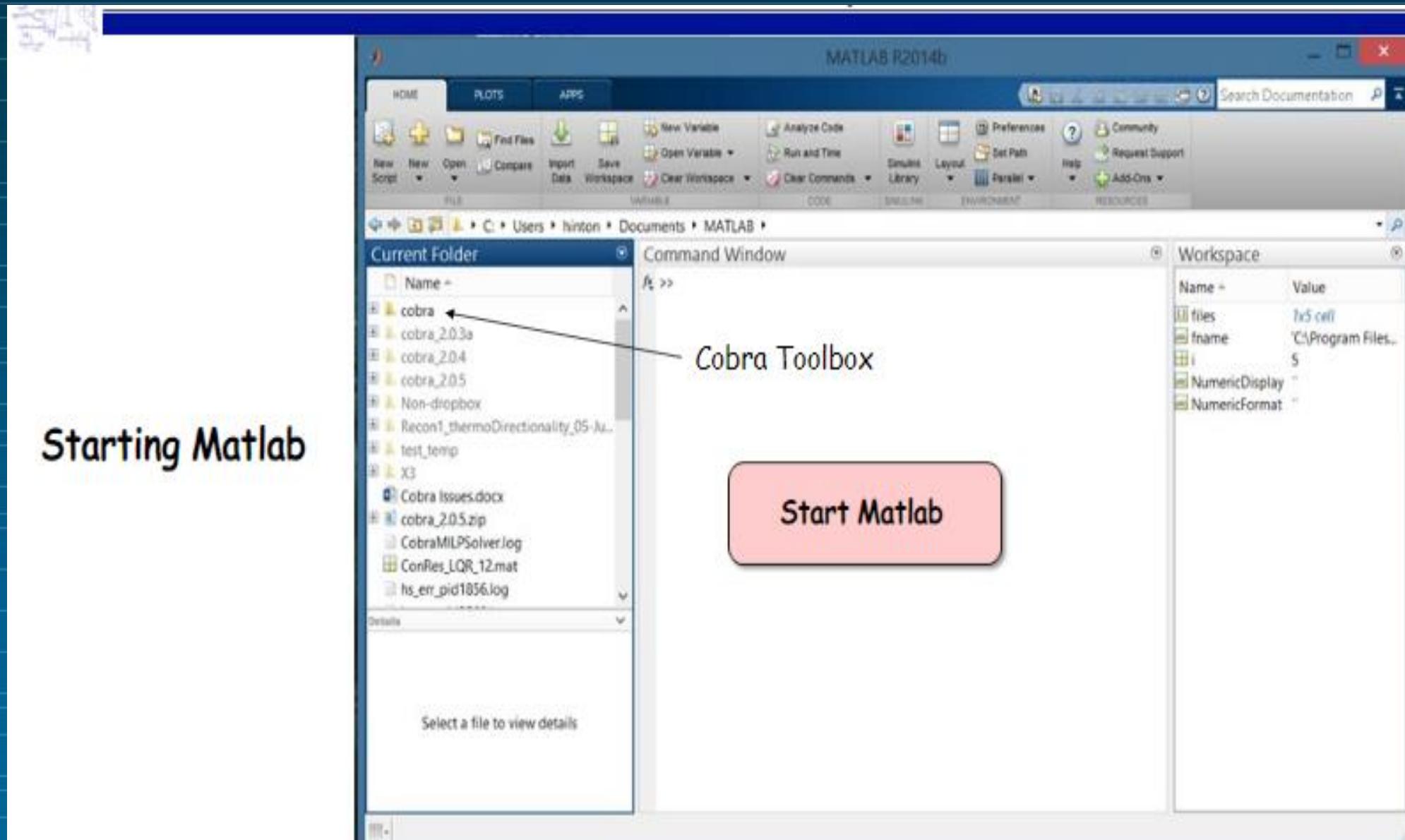
```
>java -jar convert2sbml.jar -kind excel -in newinfile.xls -sheet Sheet2 -headers 0 -rcol 2 -rncol 1 -xt  
"external_.*" -out outfile.xml -name outtest
```

```
<?xml version="1.0" encoding="UTF-8"?>  
- <sbml version="1" level="2" xmlns="http://www.sbml.org/sbml/level2">  
  - <model name="outtest">  
    - <listOfCompartments>  
      <compartment name="default" size="0.0" id="default"/>  
      <compartment name="external" size="0.0" id="external"/>  
    </listOfCompartments>  
    - <listOfSpecies>  
      <species name="s1" id="s1" initialConcentration="1.0" compartment="default"/>  
      <species name="s2" id="s2" initialConcentration="1.0" compartment="default"/>  
      <species name="p1" id="p1" initialConcentration="1.0" compartment="default"/>  
      <species name="p2" id="p2" initialConcentration="1.0" compartment="default"/>  
    </listOfSpecies>  
    - <listOfReactions>  
      - <reaction name="r1" id="r1" reversible="false">  
        - <listOfReactants>  
          <speciesReference stoichiometry="1.0" species="s1"/>  
          <speciesReference stoichiometry="2.0" species="s2"/>  
        </listOfReactants>  
        - <listOfProducts>  
          <speciesReference stoichiometry="2.0" species="p1"/>  
          <speciesReference stoichiometry="3.0" species="p2"/>  
        </listOfProducts>  
      </reaction>  
      - <reaction name="r2" id="r2" reversible="true">  
        - <listOfReactants>  
          <speciesReference stoichiometry="1.0" species="s1"/>  
          <speciesReference stoichiometry="2.0" species="s2"/>  
        </listOfReactants>  
        - <listOfProducts>  
          <speciesReference stoichiometry="2.0" species="p1"/>  
          <speciesReference stoichiometry="3.0" species="p2"/>  
        </listOfProducts>  
      </reaction>  
    </listOfReactions>  
  </model>  
</sbml>
```

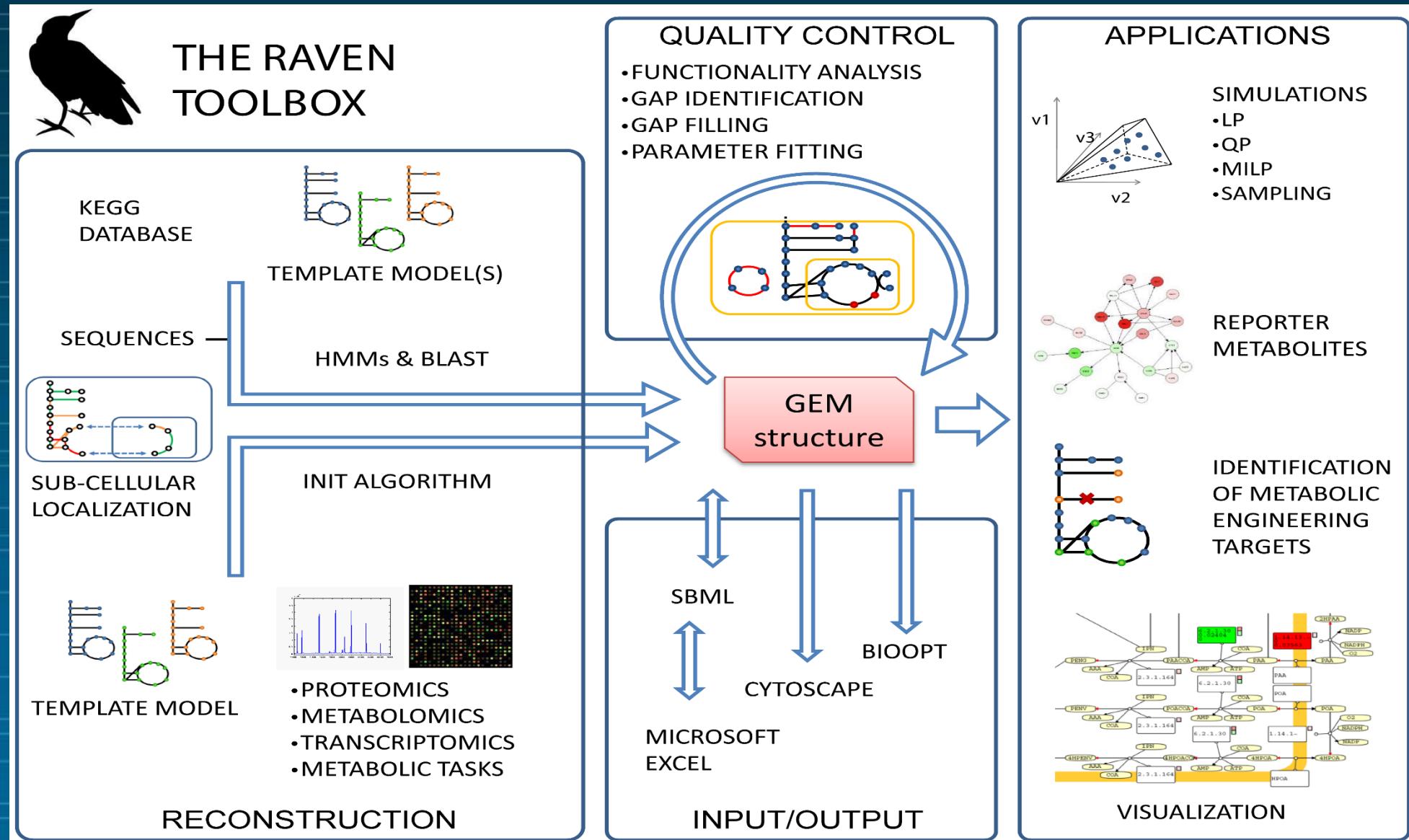
Reconstruction Softwares

- COBRA toolbox
- RAVEN toolbox
- Pathway tools
- MetNetMaker
- SuBliMinaL
- VANTED

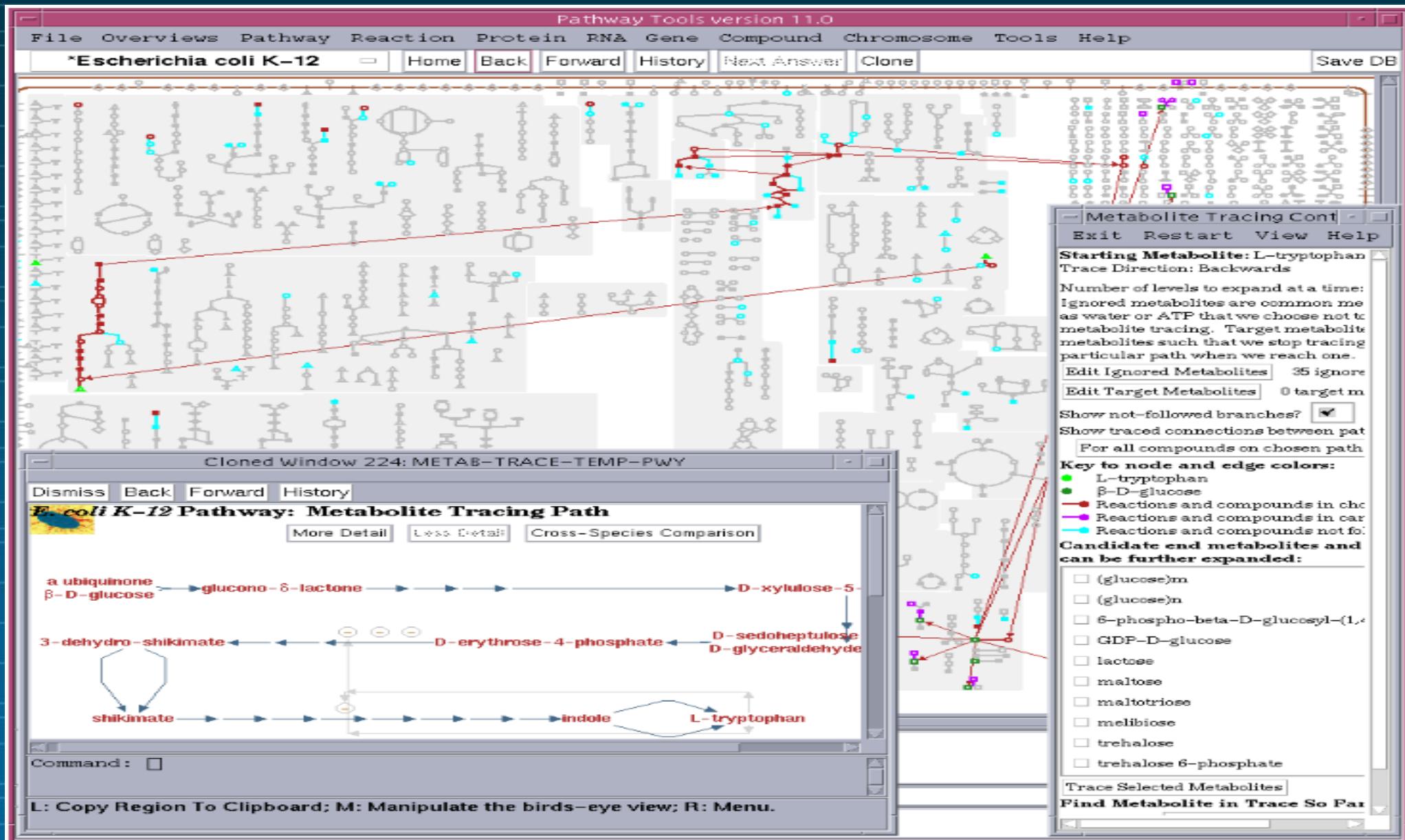
COBRA toolbox



RAVEN toolbox



Pathway tools



MetNetMaker

MetNetMaker Ribbon Acrobat

Import Export Export Export Selected Reactions
Excel SBML (L2V1) SBML (L2V4) Visualise in Show Dead-End Cytoscape Compounds

Reaction Picker
Reaction Creator
Selected Reactions (pop-up)
Application Components

Download and Parse KEGG LIGAND
Populate Database
Backup User
Reactions
Restore User
Reactions

Clear Database
Merge .xgml Visualisations
Advanced Visualisation

Reaction Picker

Reaction Filters

Reaction Compound Pathway

Reaction ID:
Reaction Name:
EC number:

Clear Filters Filter!

Reaction Chooser

Reaction ID	Preferred Name
R00016	D-glucose-1-phosphate:D-glucose-1-phosphate 6-phosphotrans
R00017	ferrocytochrome-c:hydrogen-peroxide oxidoreductase
R00018	putrescine:putrescine 4-aminobutyltransferase (ammonia-form
R00019	hydrogen:ferredoxin oxidoreductase
R00021	L-glutamate:ferredoxin oxidoreductase (transaminating)
R00022	chitobiase N-acetylglucosaminohydrolase
R00023	hydroxylamine:NAD ⁺ oxidoreductase;
R00024	D-ribulose-1,5-bisphosphate-forming)
R00025	ethylnitronate:oxygen 2-oxidoreductase (nitrite-forming)
R00026	cellobiose glucohydrolase
R00027	2-hydroxy-1,2-diphenylethanone benzaldehyde-lyase(benzalde
R00028	maltose glucohydrolase
R00029	thiosulfate:ferricytochrome-c oxidoreductase
R00031	1,2-Benzenediol:oxygen oxidoreductase

Delete Reaction Edit Reaction Create New Reaction

Selected Reactions Open in a Separate Window

Currently Loaded:

Reaction ID	Compartment	EC Number	Max +ve Flux	Max -ve Flux
R00001	Cytosol	3.6.1.10	500	-50
*				

Record: 1 2 of 2 3 No Filter Search

Reaction Viewer

Reaction ID: R00001 Preferred Name: Polyphosphate polyphosphohydrolase

Pathways:

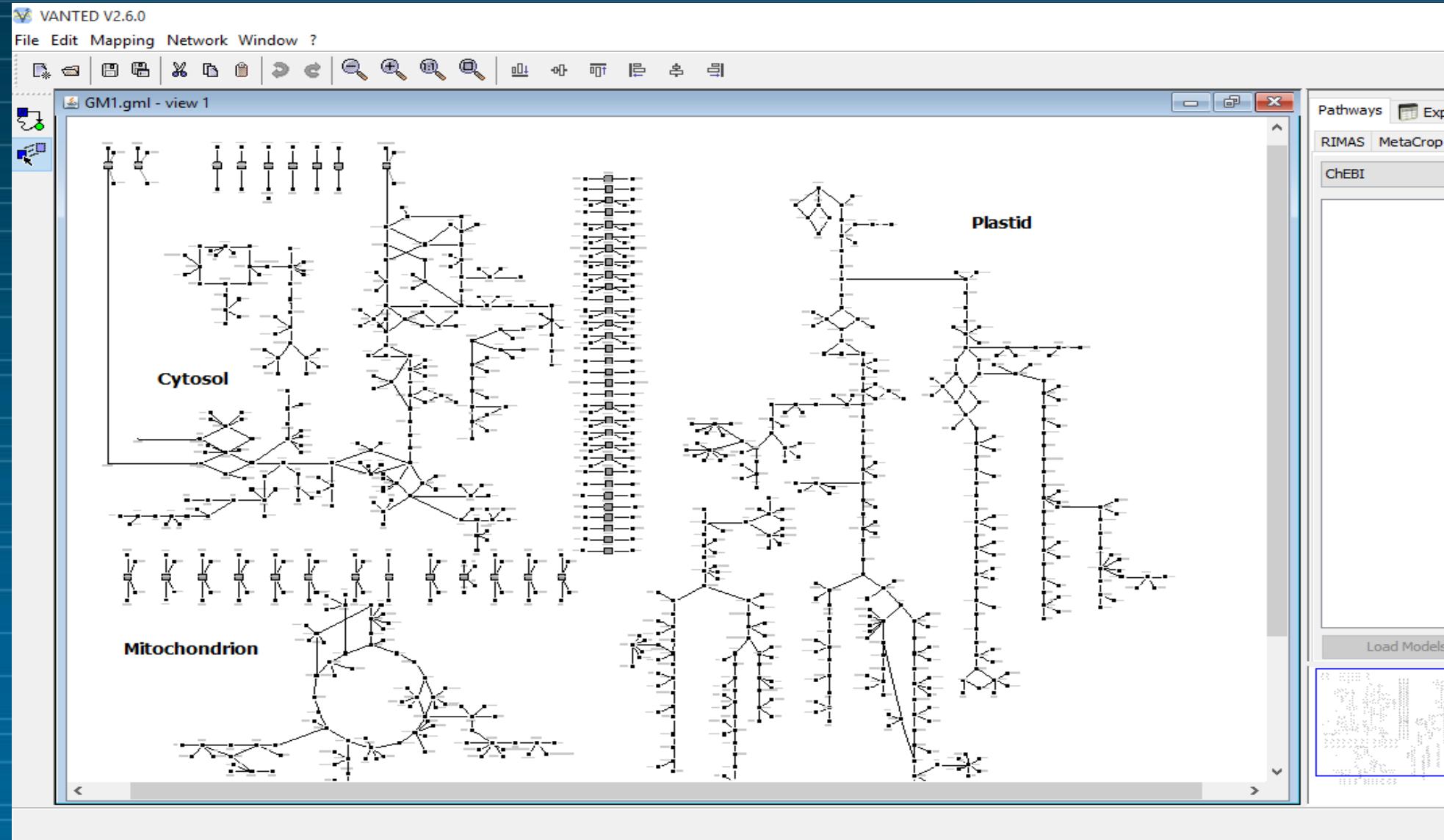
Record: 1 2 of 8135 Unfiltered Search

Form View Num Lock Powered by Microsoft Office Access

SubliMinal

A	B	C	D	E	F	G	
Rxn ID	Rxn Name	Gene Locus/ Loci	EC No	Rxn Description	Rxn Description (detailed)	Pathway/Subsystem	
1	R00004[c]	diphosphate phospho	GRMZM2G026470 or G	3.6.1.1	[c] : C00013 + C00001 --> 2 C00009	[c]: Pyrophosphate + H2O --> 2 Orthophosphate	
2	R00006[c]	pyruvate:pyruvate ad	GRMZM2G143357	2.2.1.6	[c] : 2 C00022 --> C00900 + C00011	[c]:2 Pyruvate --> 2-Acetylactate + CO2	PATH: rn00770 Pantothenate and CoA biosynthesis
4	R00009[x]	hydrogen-peroxide:h	GRMZM2G088212 or G	1.11.1.6	[x] : 2 C00027 --> 1 C00007 + 2 C00001	[x]:2 H2O2 --> Oxygen + 2 H2O	
5	R00010[c]	alpha,alpha-trehalose	GRMZM2G162690	3.2.1.28	[c] : 1 C01083 + 1 C00001 --> 2 C00031	[c]: alpha,alpha-Trehalose + H2O --> 2 D-	PATH: rn00500 Starch and sucrose metabolism
6	R00014[c]	pyruvate:thiamin diph	(GRMZM2G033894 and	1.2.4.1 or 4.1.1.1	[c] : 1 C00022 + 1 C00068 + 1 C00008 -->	[c]: Thiamin diphosphate + Pyruvate -->	PATH: rn00010 Glycolysis / Gluconeogenesis , P
7	R00021[p]	L-glutamate:ferredox	GRMZM2G036609 or G	1.4.7.1	[p] : 10 C00064 + 10 C00026 + 7 C00138 -	[p]: 10 L-Glutamine + 10 2-Oxoglutarate +	PATH: rn00910 Nitrogen metabolism
8	R00022[c]	chitobiose N-acetylglu	GRMZM2G134251 or G	3.2.1.52	[c] : 1 C01674 + 1 C00001 --> 2 C00140	[c]: Chitobiose + H2O --> 2 N-Acetyl-D-glu	PATH: rn00520 Amino sugar and nucleotide sugar
9	R00024[p]	3-phospho-D-glyceral	GRMZM2G113033 and	4.1.1.39	[p] : C01182 + C00011 + C00001 --> 2 C00	[p]: D-Ribulose 1,5-bisphosphate + CO2 +	PATH: rn00710 Carbon fixation in photosynthetic
10	R00026[c]	cellobiose glucohydro	GRMZM2G146192 or G	3.2.1.21	[c] : 1 C00185 + 1 C00001 --> 2 C00221	[c]: Cellobiose + H2O --> 2 beta-D-Glucos	PATH: rn00500 Starch and sucrose metabolism
11	R00028[c]	maltose glucohydrola	GRMZM2G428518 or G	3.2.1.20	[c] : 1 C00208 + 1 C00001 --> 2 C00267	[c]: Maltose + H2O --> 2 alpha-D-Glucose	PATH: rn00500 Starch and sucrose metabolism ,
12	R00028[p]	maltose glucohydrola	GRMZM2G428518 or G	3.2.1.20	[p] : 1 C00208 + 1 C00001 --> 2 C00267	[p]: Maltose + H2O --> 2 alpha-D-Glucose	PATH: rn00500 Starch and sucrose metabolism ,
13	R00036[c]	5-aminolevulinic hyd	GRMZM2G397247 or G	4.2.1.24	[c] : 2 C00430 --> C00931 + 2 C00001	[c]:2 5-Aminolevulinate --> Porphobilinogen	PATH: rn00860 Porphyrin and chlorophyll metabo
14	R00047[c]	6-hydroxynicotinate,h	GRMZM2G410515	1.14.99.-	[c] : C00007 + 2 C01020 --> 2 C01059 + 2	[c]: Oxygen + 2 6-Hydroxynicotinate --> 2	PATH: rn00760 Nicotinate and nicotinamide meta
15	R00066[c]	6,7-Dimethyl-8-(1-D-	GRMZM2G009196	2.5.1.9	[c] : 2 C04332 + 1 C00008 --> 1 C00255 +	[c]:2 6,7-Dimethyl-8-(1-D-ribityl)umazine -	PATH: rn00740 Riboflavin metabolism , PATH: rn
16	R00068[c]	L-ascorbate:oxygen c	GRMZM2G157929 or G	1.10.3.3	[c] : 1 C00007 + 1 C00072 + 2 C00008 -->	[c]: Oxygen + 2 Ascorbate --> 2 L-Dehydr	PATH: rn00053 Ascorbate and aldarate metabolis
17	R00084[c]	porphobilinogen:(4-[2	GRMZM2G026117	2.5.1.61	[c] : 4 C00931 + C00001 --> C01024 + 4 C	[c]:4 Porphobilinogen + H2O --> Hydroxy	PATH: rn00860 Porphyrin and chlorophyll metabo
18	R00086[c]	ATP phosphohydrolas	(GRMZM2G027860 or G	3.6.3.1 or 3.6.3.	[c] : 1 C00002 + 1 C00001 <=> 1 C00008	[c]:ATP + H2O <=> ADP + Orthophosph	PATH: rn00230 Purine metabolism
19	R00095[c]	NADH:monodehydroa	GRMZM2G134708 or G	1.6.5.4	[c] : 1 C00003 + 1 C00072 <=> 1 C00004	[c]:NAD+ + 2 Ascorbate <=> NADH + 2	PATH: rn00053 Ascorbate and aldarate metabolis
20	R00100[c]	NADH:ferricytochrom	GRMZM2G157263	1.6.2.2	[c] : C00004 + 2 C00996 + C00080 --> C00	[c]: NADH + 2 Ferricytochrome b5 + H+ --	PATH: rn00520 Amino sugar and nucleotide sugar
21	R00115[c]	glutathione:NADP+ o	GRMZM2G172322	1.8.1.7	[c] : 2 C00051 + 1 C00006 <=> 1 C00127	[c]:NADP+ + 2 Glutathione <=> Oxidized	PATH: rn00480 Glutathione metabolism
22	R00122[c]	ADP phosphohydrolas	GRMZM2G124209 or G	3.6.1.15	[c] : 1 C00008 + 1 C00001 --> 1 C00020 +	[c]: ADP + H2O --> AMP + Orthophosph	PATH: rn00230 Purine metabolism
23	R00124[c]	ATP:ADP phosphatraf	GRMZM2G106099 or G	2.7.4.6	[c] : 1 C00002 + 1 C00008 <=> 1 C00008	[c]:ATP + ADP <=> ADP + ATP	PATH: rn00230 Purine metabolism , PATH: rn01
24	R00124[p]	ATP:ADP phosphatraf	GRMZM2G106099 or G	2.7.4.6	[p] : 1 C00002 + 1 C00008 <=> 1 C00008	[p]:ATP + ADP <=> ADP + ATP	PATH: rn00230 Purine metabolism , PATH: rn01
25	R00127[c]	ATP:AMP phosphotraf	GRMZM2G030628 or G	2.7.4.3	[c] : 1 C00002 + 1 C00020 <=> 2 C00008	[c]:ATP + AMP <=> 2 ADP	PATH: rn00230 Purine metabolism , PATH: rn01
26	R00127[p]	ATP:AMP phosphotraf	GRMZM2G030628 or G	2.7.4.3	[p] : 1 C00002 + 1 C00020 <=> 2 C00008	[p]:ATP + AMP <=> 2 ADP	PATH: rn00230 Purine metabolism , PATH: rn01
27	R00130[c]	ATP:dephospho-CoA	GRMZM2G043819	2.7.1.24	[c] : 1 C00002 + 1 C00082 --> 1 C00008 +	[c]: ATP + Dephospho-CoA --> ADP + C	PATH: rn00770 Pantothenate and CoA biosynthe
28	R00131[c]	Urea amidohydrolase	GRMZM2G461569	3.5.1.5	[c] : 2 C00086 + 2 C00001 --> 2 C00011 +	[c]:2 Urea + 2 H2O --> 2 CO2 + 3 NH3	PATH: rn00230 Purine metabolism , PATH: rn00
29	R00132[c]	carbonate hydro-lyas	(GRMZM2G113191 or G	4.2.1.1	[c] : C00001 + C00011 --> C00080 + C002	[c]: H2O + CO2 --> H+ + HCO3-	PATH: rn00910 Nitrogen metabolism
30	R00132[m]	carbonate hydro-lyas	(GRMZM2G113191 or G	4.2.1.1	[m] : C00001 + C00011 --> C00080 + C002	[m]: H2O + CO2 --> H+ + HCO3-	PATH: rn00910 Nitrogen metabolism
31	R00132[p]	carbonate hydro-lyas	(GRMZM2G113191 or G	4.2.1.1	[p] : C00001 + C00011 --> C00080 + C002	[p]: H2O + CO2 --> H+ + HCO3-	PATH: rn00910 Nitrogen metabolism
32	R00149[c]	Carbon-dioxide:amm	GRMZM2G061990	6.3.4.16	[c] : 2 C00002 + 1 C00014 + 1 C00011 + 1	[c]:2 ATP + NH3 + CO2 + H2O <=> 2 A	PATH: rn00250 Alanine, aspartate and glutamate
33	R00149[p]	Carbon-dioxide:amm	GRMZM2G061990	6.3.4.16	[p] : 2 C00002 + 1 C00014 + 1 C00011 + 1	[p]:2 ATP + NH3 + CO2 + H2O <=> 2 A	PATH: rn00250 Alanine, aspartate and glutamate
34	R00156[c]	ATP:UDP phosphotraf	GRMZM2G106099 or G	2.7.4.6	[c] : 1 C00002 + 1 C00015 <=> 1 C00008	[c]:ATP + UDP <=> ADP + UTP	PATH: rn00240 Pyrimidine metabolism , PATH: r
35	R00156[p]	ATP:UDP phosphotraf	GRMZM2G106099 or G	2.7.4.6	[p] : 1 C00002 + 1 C00015 <=> 1 C00008	[p]:ATP + UDP <=> ADP + UTP	PATH: rn00240 Pyrimidine metabolism , PATH: r
36	R00158[c]	ATP:UMP phosphotraf	GRMZM2G149535 or G	2.7.4.22	[c] : 1 C00002 + 1 C00105 <=> 1 C00008	[c]:ATP + UMP <=> ADP + UDP	PATH: rn00240 Pyrimidine metabolism , PATH: r
37	R00174[c]	ATP:pyridoxal 5'-pho	GRMZM2G069758	2.7.1.35	[c] : 1 C00002 + 1 C00250 --> 1 C00008 +	[c]: ATP + Pyridoxal --> ADP + Pyridoxal	PATH: rn00750 Vitamin B6 metabolism , PATH: i
38	R00177[c]	ATP:L-methionine S-a	GRMZM2G061135 or G	2.5.1.6	[c] : 1 C00009 + 1 C00013 + 1 C00019 + 1	[c]: ATP + L-Methionine + H2O --> Ortho	PATH: rn00270 Cysteine and methionine metabo
39	R00178[c]	S-adenosyl-L-methion	GRMZM2G060369 or G	4.1.1.50	[c] : 1 C00019 --> 1 C01137 + 1 C00011	[c]: S-Adenosyl-L-methionine --> S-Adeno	PATH: rn00270 Cysteine and methionine metabo

VANTED



Example



ARTICLE

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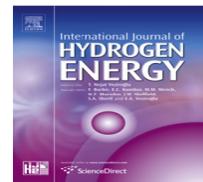
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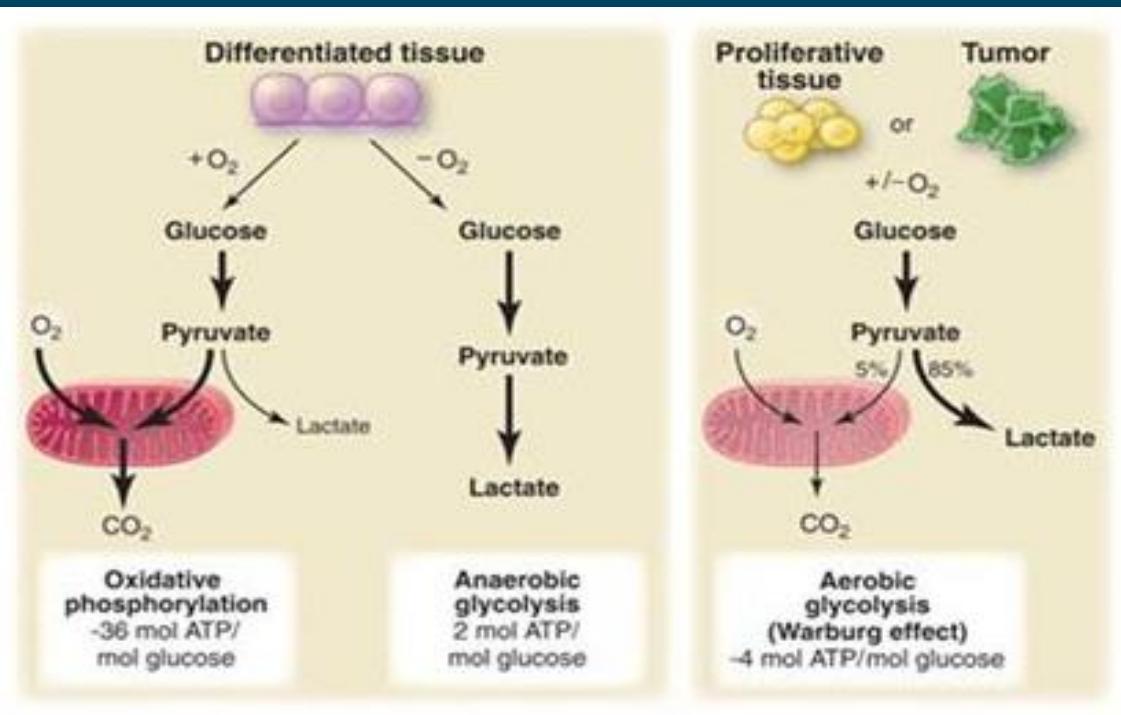
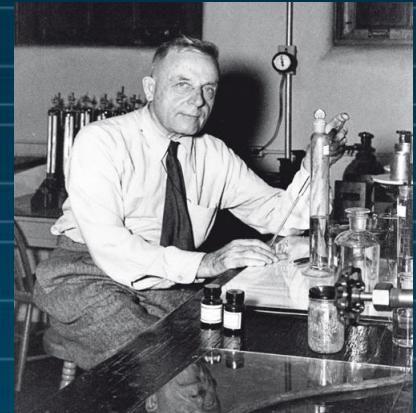


Genome based metabolic flux analysis of *Ethanoligenens harbinense* for enhanced hydrogen production

Example

Otto Heinrich Warburg

1883-1970 / Nobel prize in Physiology and Medicine for his Warburg effect in 1931

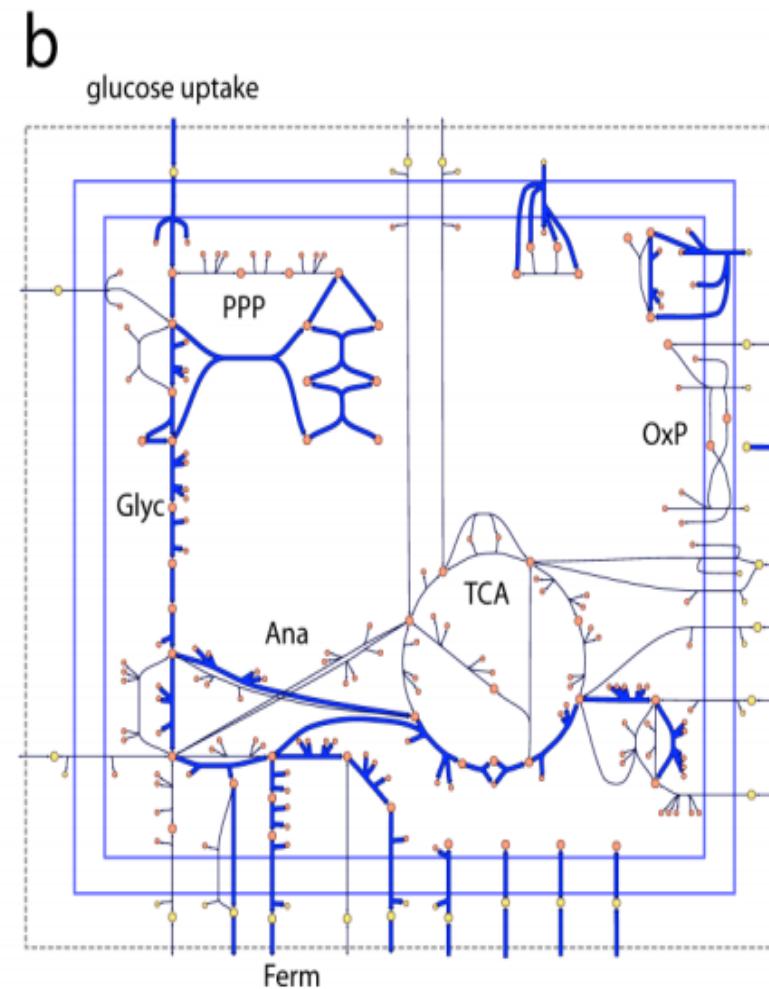
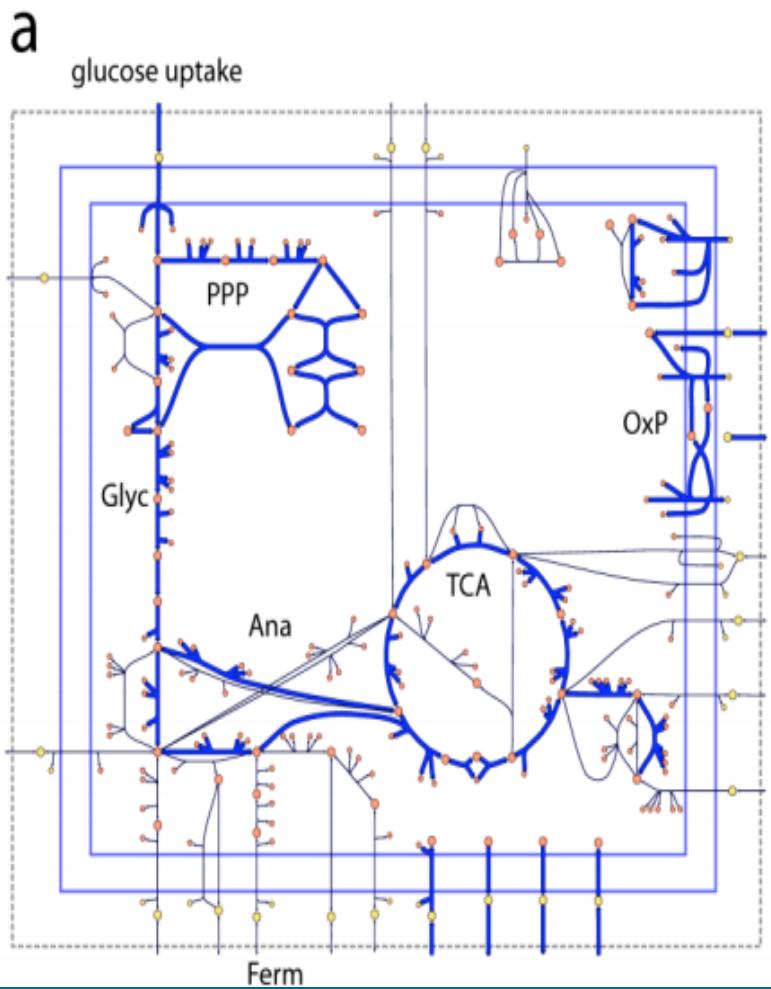


The "Warburg effect" asserts that even when oxygen is plentiful, cancer cells continue to use glycolysis followed by lactic acid fermentation, rather than through oxidative phosphorylation in the mitochondria.

Example

aerobic

anaerobic



Example

Subsystems/Cancer type	Adrenal	Breast-d	Breast-l	Cervix	Colon	Head and neck	Leukemia	Lung-n	Lung-p	Liver-ve	Liver-e	Liver-a	Liver-va	Ovary	Pancreas	Prostate	Stomach	Thyroid
Ala & Asp m	↑	↓	—	—	—	—	—	—	—	—	↑	—	↑	—	—	↑	↑	—
Arg & Pro m	—	↑↓	—	↑	↑↓	—	—	—	↑↓	↑	↑	↑	—	—	—	↑	↑↓	↑
β-Ala m	↓	↓	↓	↑↓	↑↓	↑	—	—	↑↓	↑	↑	—	—	↑	—	↑	—	↑
Cys m	—	↑↓	↑↓	↑↓	↑↓	↑	—	—	—	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—
D-Ala m	↑	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Glu m	↑↓	↓	↑↓	↑↓	↑↓	↑	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑	↑↓
Gly, Ser & Thr m	↑	↑↓	↑↓	↑↓	↓	↑	—	—	—	—	—	—	—	—	—	—	↑	↑
Lys m	—	↑↓	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	↑
Met m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Tyr m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Val, Leu & Ile m	—	↑↓	↑	—	↑↓	—	↑↓	—	↑↓	↑↓	↑↓	↑	—	↑↓	—	↑↓	↑	↑↓
Amino group m	↑	↑↓	↓	↑↓	↑↓	↑↓	—	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑	—	↑	↑↓	↑↓
Aminosugar m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ascorbate & Aldarate m	—	↓	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Biotin m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Carnitine shuttle	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Cholesterol m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Fatty acid Elongation	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	↑↓
Fatty acid m	—	↑↓	↓	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Fatty acid oxidation	↑	↓	↑	—	—	—	—	—	—	—	—	—	—	—	—	—	↑	—
Folate m	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
Thiamine m	—	↓	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Vitamin A m	↑↓	—	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
Vitamin B6 m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Fructose & Mannose m	↑↓	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Galactose m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Glutathione m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Glycerophospholipid m	—	—	—	↑	↑↓	—	↑↓	—	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	—	↑	↑↓
Glyoxylate & Dicarboxylate m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
IMP biosynthesis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Inositol Phosphate m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
N-Glycan biosynthesis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Nucleotides	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
Triacylglycerol synthesis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Glycolysis & Gluconeogenesis	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
Oxidative Phosphorylation	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Pentose & Glucuronate interconversion	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Pentose Phosphate Pathway	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
TCA	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
Propanoate m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Purine catabolism	—	↑↓	↑↓	↑↓	↑↓	—	↑	—	—	—	—	—	—	—	—	—	↑↓	—
Pyrimidine biosynthesis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Pyrimidine catabolism	—	↑	↓	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Pyruvate m	↑	↑↓	↑↓	↑↓	↑↓	↑↓	—	—	—	—	—	—	—	—	—	—	—	—
Sphingolipid m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Starch & Sucrose m	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
T, Endoplasmic Reticular	↑↓	↑↓	↑↓	↑↓	↑↓	↑	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
T, Extracellular	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
T, Lysosomal	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
T, Mitochondrial	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
T, Nuclear	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓
T, Peroxisomal	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	—	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓	↑↓

“What I cannot create, I do not understand”

Richard Feynman

