

## **MetExplore: collaborative edition and exploration of metabolic networks**

Cottret et al.

Supplementary Material

User Profile
Network Data
Network Curation
Network Viz
Import SBML

**Warning**  
If you are unfamiliar on how SBML files are structured, please use the default Advanced parameters

☒ Import the FBC Package Elements

The Flux Balance Constraint (FBC) Importer allows the Import process to read the SBML package FBC (version 2) contained in the SBML file (specifications [here](#)).  
**If you do not know whether your SBML uses the FBC version 2 package, keep this enabled as it will not cause any errors if the package is not present in the file.**

☒ Import the Annotation Elements

The Annotation Importer allows the main Import process to read the annotations present in your Network file

☐ Use default Parameters for importing Annotations Elements

The annotation Importer is based on the MIRIAM annotations scheme. You can find more information on MIRIAM annotations [here](#). Annotations are used to create a logical link between an object of the model (reaction, metabolite,...) and a piece of biological knowledge.

MIRIAM annotations consist of the triplet {collection-namespace, identifier, qualifier}, they combine the collection's namespace with the identifier to create an unambiguous link to the piece of knowledge. This link can be enriched by an optional but unique descriptor, the qualifier (e.g. "is", "isDescribedBy", "isEncodedBy", ...) that refines that meaning of that link.

MIRIAM can use two types of pattern to create its links, URIs or URN.

MIRIAM Pattern:

Choose which annotation pattern is used in your model. MIRIAM compliant annotations use URIs:  
`http://identifiers.org/{collection-namespace}/{identifier}`  
or URNs:  
`urn:miriam:{collection-namespace}:{identifier}`

☒ Import the SBML Note Elements

The Note Importer allows the main Import process to read the "notes" elements present in your SBML File. In most SBML files, this is where the metabolic pathways occurring in the network are specified.

☐ Use default Parameters for importing Notes Elements

SBML notes are user defined information that can be joined to any model constituent. In most genome scale metabolic network, these notes are COBRA-compliant SBML note structure ([J. Schellenberger et al., \(2011\)](#)). Notes in this format consist in Key/Value(s) pairs that allow the addition of informations that cannot be stored in other SBML constituents.

The customization of the Notes plugin allows you to modify which key/value pairs are associated with your data.

— Notes for Reactions —

Pathway Key:

This key defines in which pathway(s) the given reaction is. e.g.:  
SUBSYSTEM: Glycolysis/Gluconeogenesis

Pathway Separator:

In the case in which a reaction is in multiple pathways, this defines how the pathways are separated. e.g.:  
SUBSYSTEM: Glycolysis/Gluconeogenesis || Citrate cycle


EC Number Key:

This key defines the EC Number associated with the given reaction. e.g.:  
EC Number: 2.3.3.8

Gene Association:

This key defines the Gene-Reaction Association of the given reaction. e.g.:

**Supplementary Figure 1.** MetExplore provides a very complete import tool for SBML files. It is able to import the latest SBML formats with the FBC package as well as the SBML files in the format specific to certain tools such as the Cobra Toolbox. Depending on the format of the information stored in the SBML file, different options will be selected in the MetExplore import form. Each option is documented directly in the form.



Access Level	Description
<u>Owner</u>	Can manage <i>Projects</i> and their <i>Users</i> .
<u>Read/Write</u>	Can edit the Network.
<u>Annotator</u>	Can comment and give their opinion about the Network.
<u>Read only</u>	Can view all components of the Network.
<u>Access denied</u>	Has no access to the Network.

**Supplementary Figure 2.** Access levels for a project.

User profileProject DetailsNetwork DataNetwork VizNetwork Curation

Project Agrobacterium

Created 2015-05-12Edit project

TODO list

Description	User	Limit date	Status
Cure reactions of pathways with completeness less than 100%	agromics	2015-06-03	Not started
Remove pathways with no reactions in KEGG BioSource	Floréal Cabanettes	2015-06-01	Not started
Cure reactions of pathways with completeness less than 60%	agromics	2015-06-01	Not started
Cure reactions of pathways with completeness less than 30%	Cottret Ludovic	2015-05-29	In progress
Check proteins of BioCyc BioSource	agromics	2015-05-25	Done

Personal

All

BioSourcesCommentsHistoryDescriptionUsers

	Id	Name	Organism	Strain	Source Database	Database Type	Publication
1	2000	AGTSA	Agrobacterium tumefaciens	5A	Agromics	biocyc	
1	2001	AGRTSA	Agrobacterium tumefaciens	5A v2	Agromics	biocyc	
1	2595	Agrobacterium fabrum KEGG Genes Data...	Agrobacterium tumefaciens	C58	Kegg	Kegg	
1	3008	Whole Genome Metabolism - Agrobacteri...	Agrobacterium tumefaciens	C58	Subliminal...	SBML	<a href="#">Swainston...</a>

Add BioSource to the project

**Supplementary Figure 3.** MetExplore Project Panel.

My projects		My BioSources		History	
Date	User	Project	BioSource	Action	
2015-05-27	agromics	Agrobacterium tumefaciens	Agrobacterium fabrum KEGG ...	Update pathway "atu02010"	...
2015-05-27	agromics	Agrobacterium tumefaciens	Agrobacterium fabrum KEGG ...	Add reaction R00136	...
2015-05-27	agromics	Agrobacterium tumefaciens	Agrobacterium fabrum KEGG ...	Update reaction R00135	...
2015-05-27	Floréal Cabanettes	Agrobacterium tumefaciens	Whole Genome Metabolism - ...	Update reaction R_bigg_quin_kt_out	...

From: 2015-05-12
To: 2015-05-27

 Personal
 All

**Supplementary Figure 4.** The MetExplore History Panel lists all the modifications performed on the projects where the user is involved.

### Votes for this reaction (6)

My opinion   All votes

I think that this reaction:

- ☒ Exists in this organism
- ☒ **Exists but contains some errors**
- ☒ Does not exist in this organism
- ☒ I have no idea

### Votes for this reaction (6)

My opinion   All votes

6 persons vote for this reaction:

- ☒ 1 (17%) Exists
- ☒ 3 (50%) Has errors
- ☒ 2 (33%) Not exists

Details

BioSources	Compartments (3/3)	Pathways (19/19)	Reactions (109/109)	Metabolites (113/113)	Enzymatic Complexes (874/874)	Gene Products (284/284)	Ger
<div style="display: flex; justify-content: space-between;"> <span>⊕ Add</span> <span>✎ Edit</span> <span>✕ Delete</span> <span>💾 Save</span> <span>⚙ Multiple affectation</span> <span>📊 Curation Statistics</span> <span>🗳 Curation Votes</span> <span>🔍 Equations</span> </div>							
Name	Identifier	E.C.	GPR	Reversible	Flux Low...	Flux Up...	Votes summary
1 <b>R_ACCOAC</b>	R_ACCOAC	NA	(32.1 and 31.4) or (31.5) or (32.1 ...	<input type="checkbox"/>	0	1000	<b>1</b>
2 <b>R_ACITL</b>	R_ACITL	NA	(47.2) or (47.1)	<input type="checkbox"/>	0	1000	No votes
3 <b>R_ACONT</b>	R_ACONT			<input type="checkbox"/>	0	1000	No votes
4 <b>R_ACONTm</b>	R_ACONTm			<input type="checkbox"/>	-1000	1000	No votes
5 <b>R_ADK1</b>	R_ADK1			<input type="checkbox"/>	0	1000	<b>1</b>
6 <b>R_AKGDM</b>	R_AKGDM			<input type="checkbox"/>	0	1000	No votes
7 <b>R_AKGMALtm</b>	R_AKGMALtm			<input type="checkbox"/>	-1000	0	No votes
8 <b>R_ALAGLNexR</b>	R_ALAGLNexR			<input type="checkbox"/>	-1000	1000	No votes
9 <b>R_ALATA_L</b>	R_ALATA_L			<input type="checkbox"/>	-1000	0	No votes
10 <b>R_ALCD21_L</b>	R_ALCD21_L			<input type="checkbox"/>	0	1000	No votes
11 <b>R_ALR2</b>	R_ALR2			<input type="checkbox"/>	0	1000	No votes
12 <b>R_ALR3</b>	R_ALR3			<input type="checkbox"/>	0	1000	No votes
13 <b>R_ATPS4m</b>	R_ATPS4m			<input type="checkbox"/>	0	1000	No votes
14 <b>R_ATPtm</b>	R_ATPtm			<input type="checkbox"/>	0	1000	No votes
15 <b>R_CATm</b>	R_CATm			<input type="checkbox"/>	0	1000	No votes
16 <b>R_CITtm</b>	R_CITtm			<input type="checkbox"/>	0	1000	No votes
17 <b>R_CO2t</b>	R_CO2t			<input type="checkbox"/>	-1000	0	No votes
18 <b>R_CO2tm</b>	R_CO2tm			<input type="checkbox"/>	-1000	1000	No votes
19 <b>R_CSm</b>	R_CSm			<input type="checkbox"/>	0	1000	No votes
20 <b>R_CYOom3</b>	R_CYOom3			<input type="checkbox"/>	0	1000	No votes
21 <b>R_CYOR_u10m</b>	R_CYOR_u10m			<input type="checkbox"/>	0	1000	No votes
22 <b>R_DPGase</b>	R_DPGase			<input type="checkbox"/>	0	1000	No votes
23 <b>R_DPGM</b>	R_DPGM			<input type="checkbox"/>	0	1000	No votes
24 <b>R_ENO</b>	R_ENO			<input type="checkbox"/>	0	1000	No votes
25 <b>R_EX_ala_L_LPAREN_e_RPAREN_</b>	R_EX_ala_L_LPAREN_e_RPAREN_			<input type="checkbox"/>	0	1000	No votes
26 <b>R_EX_co2_LPAREN_e_RPAREN_</b>	R_EX_co2_LPAREN_e_RPAREN_			<input type="checkbox"/>	0	1000	No votes
27 <b>R_EX_fru_LPAREN_e_RPAREN_</b>	R_EX_fru_LPAREN_e_RPAREN_	NA		<input type="checkbox"/>	-1	0	No votes
28 <b>R_EX_glc_LPAREN_e_RPAREN_</b>	R_EX_glc_LPAREN_e_RPAREN_	NA		<input type="checkbox"/>	-1000	0	No votes
29 <b>R_EX_gln_L_LPAREN_e_RPAREN_</b>	R_EX_gln_L_LPAREN_e_RPAREN_	NA		<input type="checkbox"/>	-1000	0	No votes

#### R\_ACCOAC [R\_ACCOAC]

Equations of the reaction

GPR association viz

This reaction exists in 1 Pathways

This reaction involves 6 Genes

This reaction has 0 Comment

#### Votes for this reaction (1)

My opinion   All votes

I think that this reaction:

- ☒ **Exists in this organism**
- ☒ Exists but contains some errors
- ☒ Does not exist in this organism
- ☒ I have no idea

Close

Supplementary Figure 5. Vote panel for a reaction.

BioSources		Compartments (1/1)		Pathways (377/377)		Reactions (1740/1740)					
⊕ Add		Edit		✕ Delete		☁ Commit Changes		☰ Multiple affectation		🗳 Curation Votes	
			Name	Identifier	E.C.	Votes summary ▼					
1	📘	🔗	2-oxoglutarate dehydrogenase...	2OXOGLUTARATE...	NA	1	3	2			
2	📘	🔗	α-N-arabinofuranosidase	3.2.1.55-RXN	3.2.1.55	1					
3	📘	🔗	α-galactosidase	ALPHAGALACTOSI...	3.2.1.22	1					
4	📘	🔗	α-amylase	ALPHA-AMYL-RXN	3.2.1.1	1					
5	📘	🔗	DEOXYADENPHOSPHOR-RXN	DEOXYADENPHOS...	2.4.2.1	No votes					
6	📘	🔗	β-N-acetylhexosaminidase	3.2.1.52-RXN	3.2.1.52	No votes					

Supplementary Figure 6. Reaction grid with *column resuming the votes of the annotators*.



+

 Create Biosource

+

 Add Element

Add a new Element

Metabolite

Create/update Metabolite

Metabolite Identifier\*:

Name \*:

H2O

Formula:

H2O

Charge:

Molecular Weight:

18.0153

Compartment \*:

-- Select Compartment --

Create New Compartment

☐ Generic Compound

External DataBase Identifiers

KEGG Id:

C00001

Auto-Complete

ChEBI:

15377

Auto-Complete

Inchi:

InChIKey:

SMILES:

CAS:

7732-18-5

✕

PubChem:

3303

✕

ChEMBL:

CHEMBL1098659

✕

PDB-CCD:

HOH O

✕

3DMET:

B01124

✕

NIKAJI:

J43.587B

✕

Modellisation Parameters (Optional)

☐ Constant Metabolite
 ☐ Set Boundary Condition to True
 ☐ Side Compound

☐ Metabolite has no concentration
 Associated Unit Definition:

Initialisation type:

☒ Amount

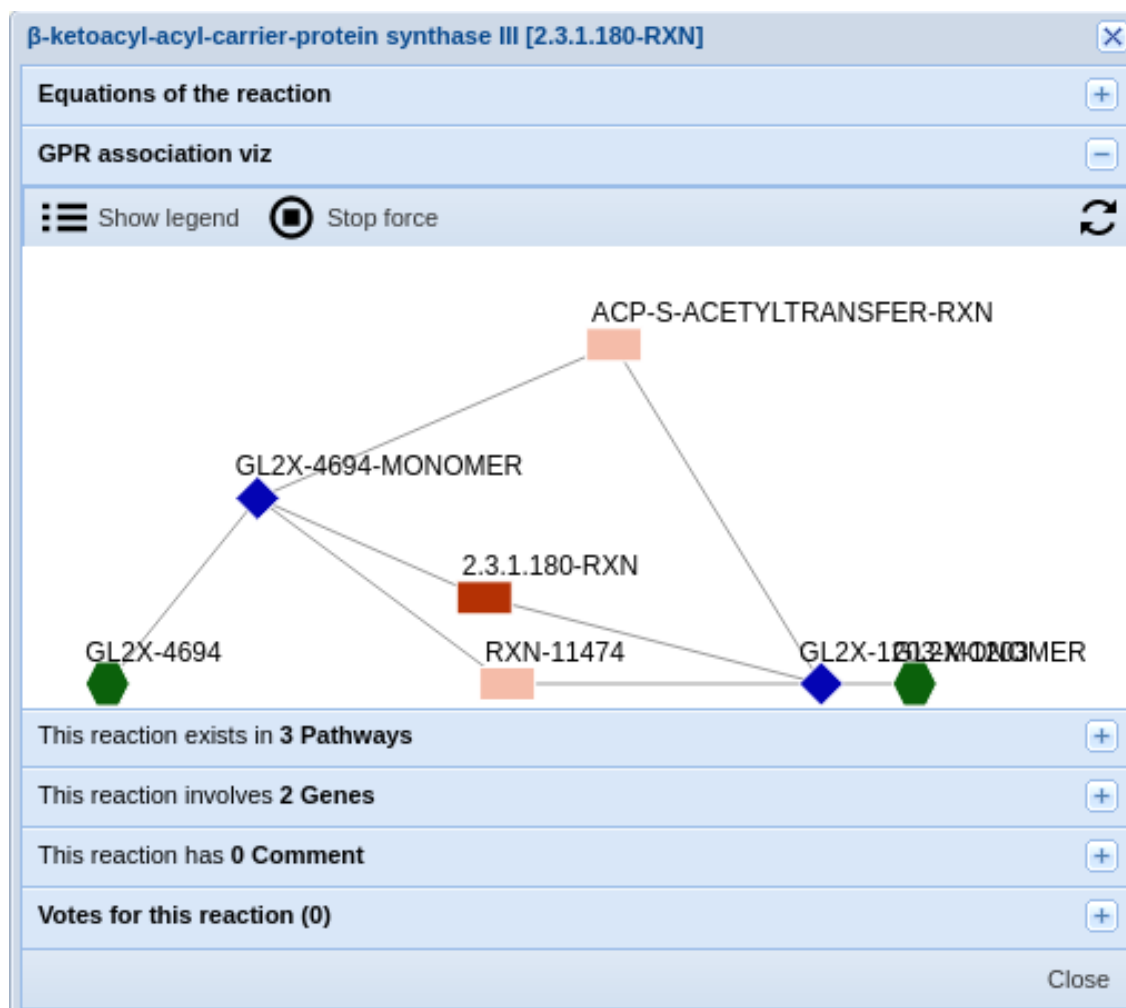
Initial Value:

Save

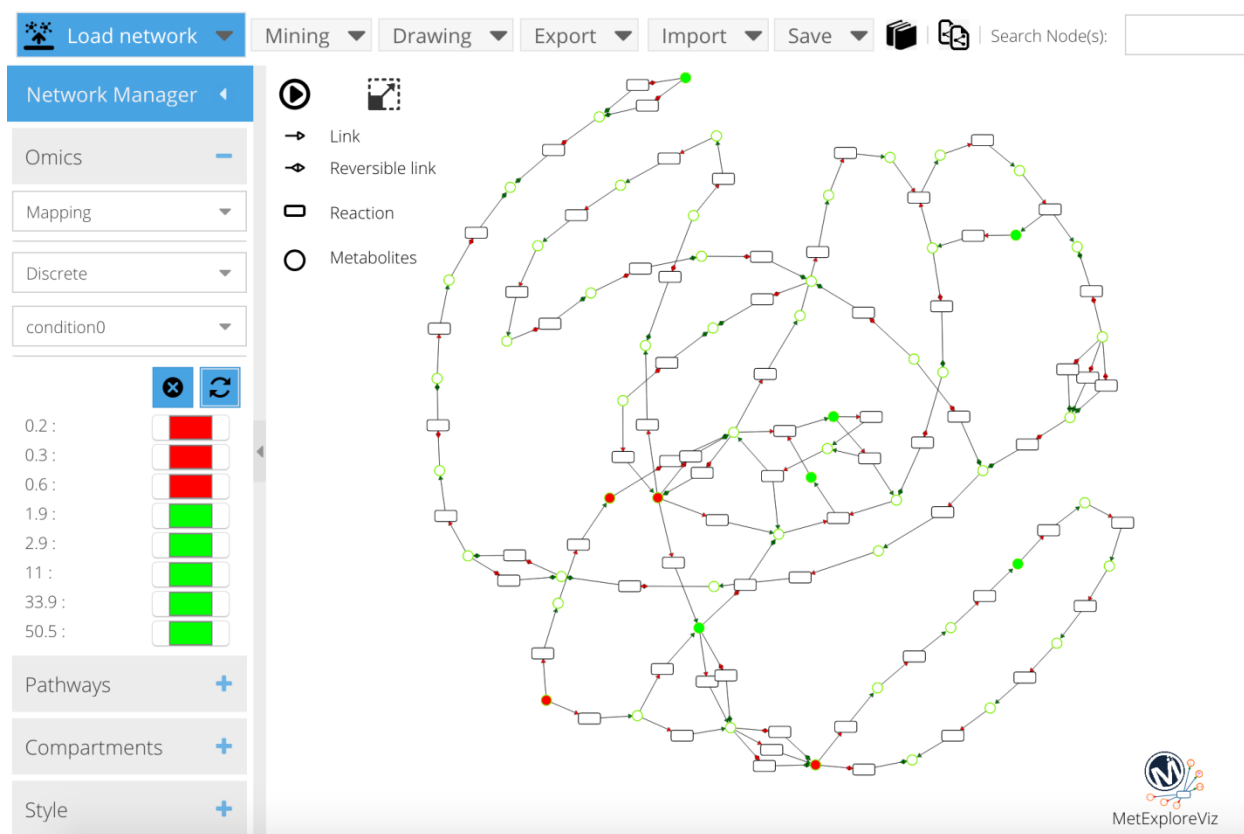
Save, and go back to table

**Supplementary Figure 7.** MetExplore form to add or edit a metabolite. Here the fields have been automatically completed from the KEGG identifier C00001 (water).





**Supplementary Figure 8.** Visualisation of the Gene Protein Reaction links in a reaction info window.



**Supplementary Figure 9.** Sub-network corresponding to the union of all lightest paths between each pair of metabolites in the metabolic fingerprint of Yeast exposed to Cadmium.