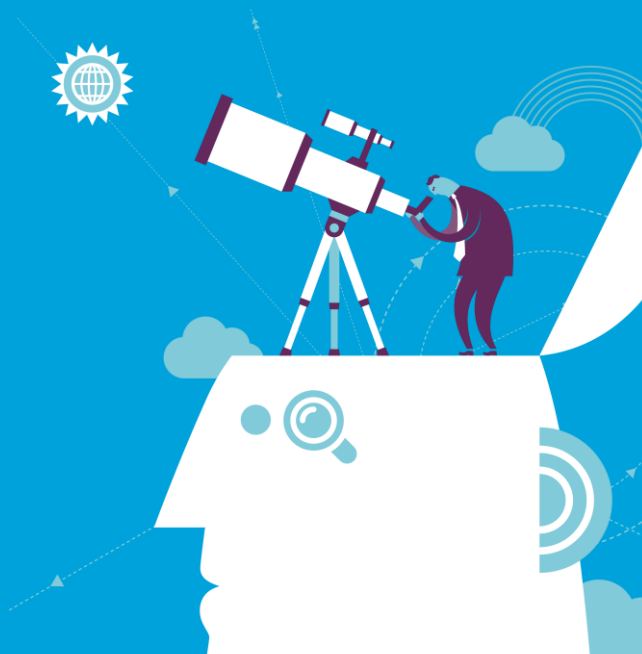
Increasing the understanding of Metabolomics data with network approaches

Denise Slenter, Chris Evelo, Egon Willighagen

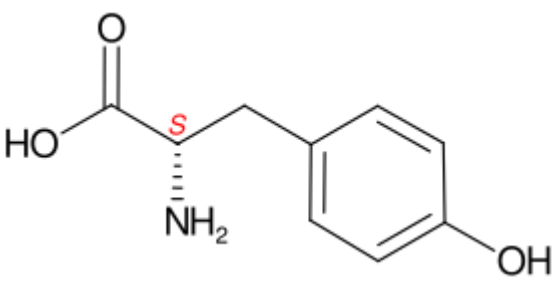
Twitter: @SMaLLCaT4Sci and @BiGCaT_UM
Blog: http://smallcats4science.blogspot.nl
ORCID: 0000-0001-8449-1318

2018-11-29 Metabolomics in Maastricht

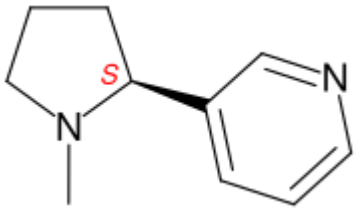


Maastricht University

Linking metabolomics data to pathways…

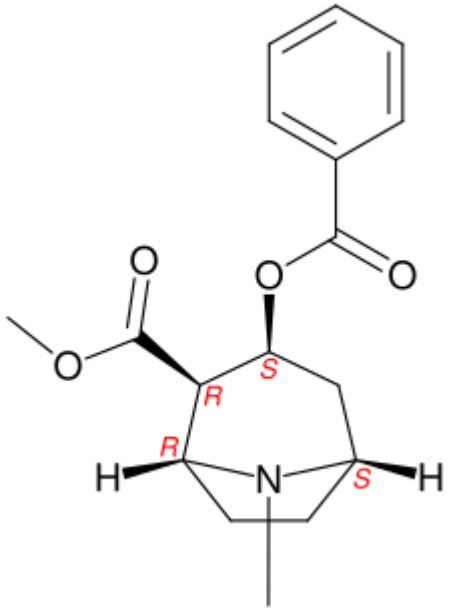


L-tyrosine



Nicotine

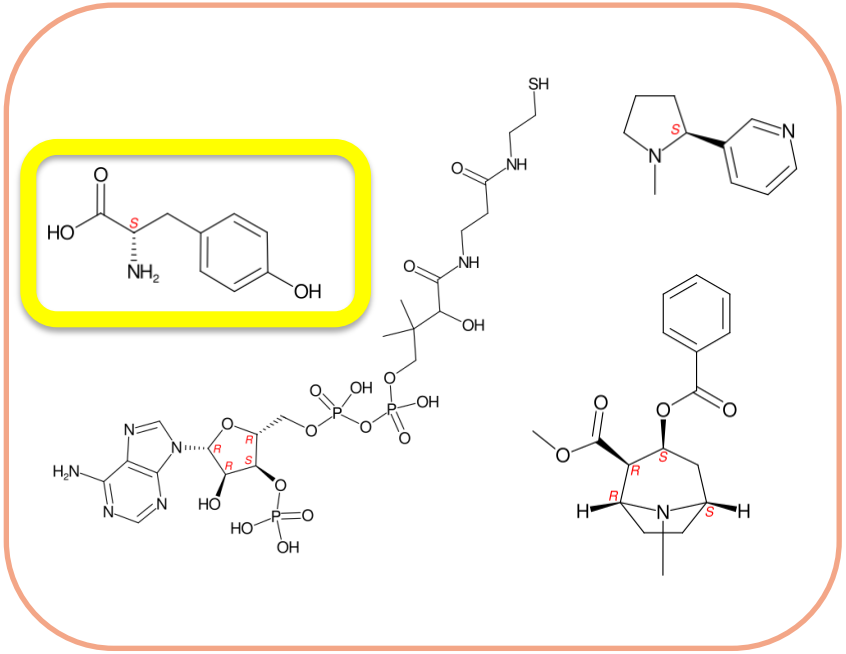
Co-A

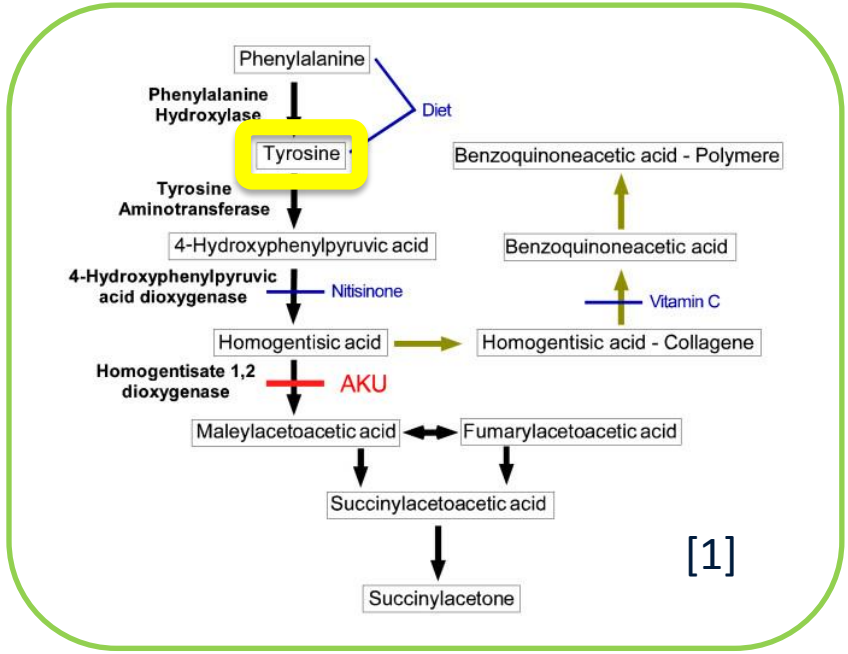


Cocaine

Structures obtained from Wikidata [2018-11-01]

Linking metabolomics data to pathways…





[1]

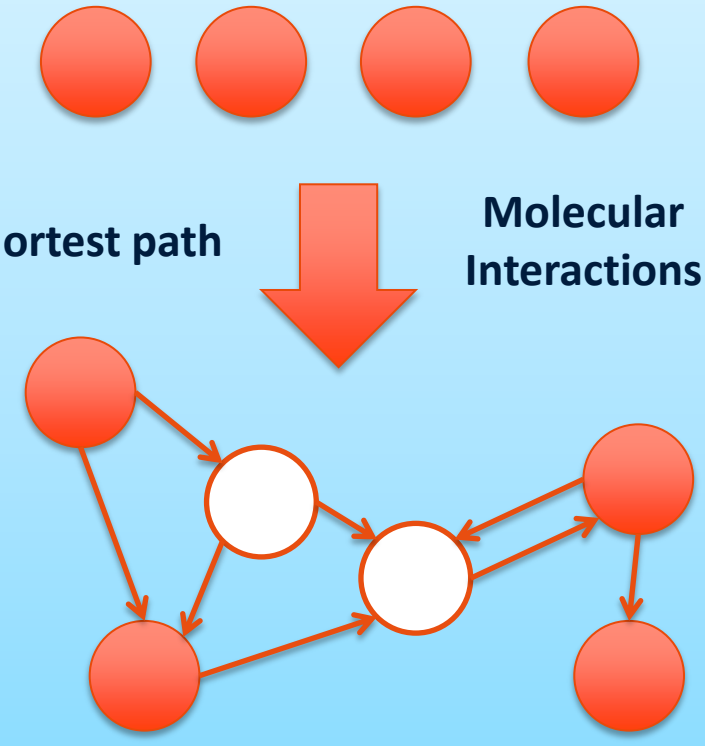
Sparseness of Data

Maastricht University

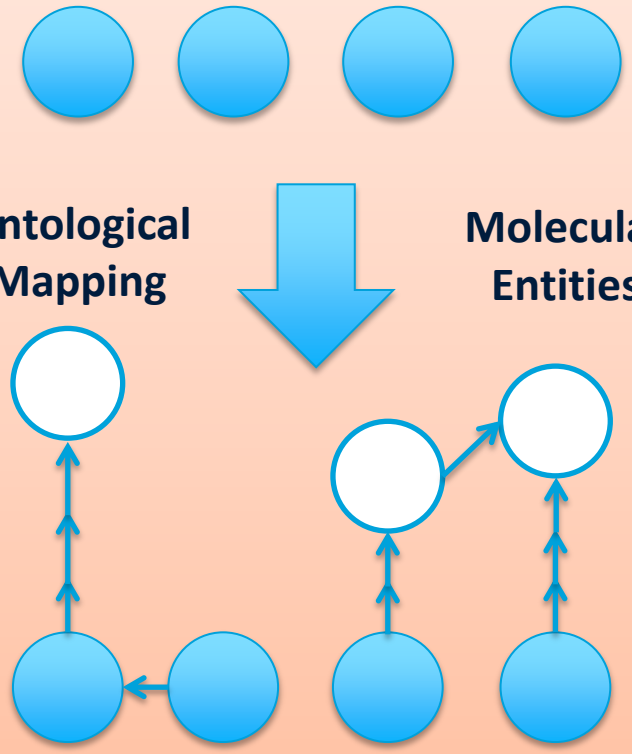
[1] Lindner, et al. BMC ophthalmology (2014)

Two approaches:

Network approach [1]



Ontological approach [2]

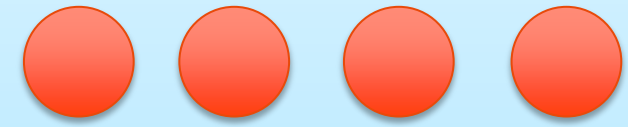


Maastricht University

[1] DOI: 10.6084/m9.figshare.5234851.v1
[2] DOI: 10.6084/m9.figshare.6368921.v1

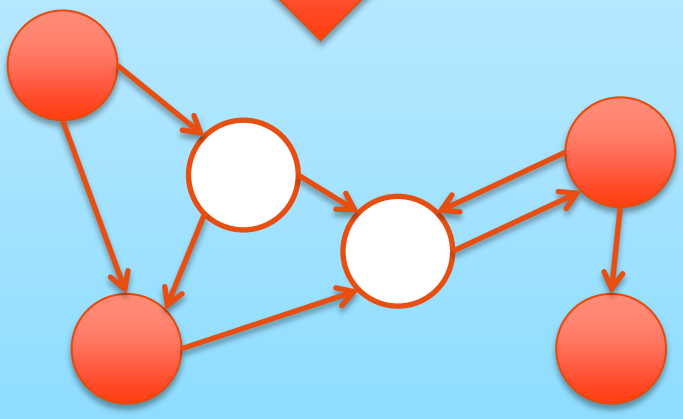
Two approaches:

Network approach [1]



Shortest path

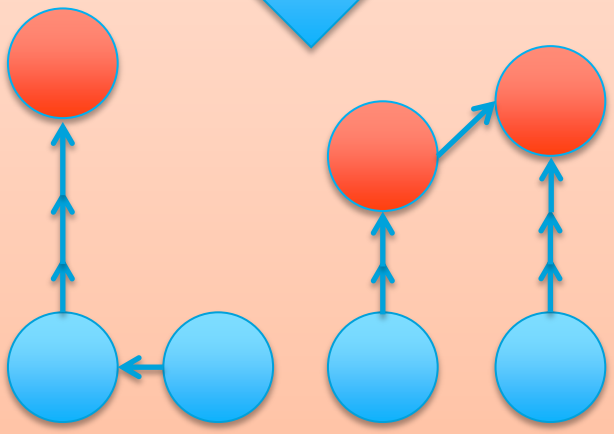
Molecular Interactions



Ontological approach [2]

Ontological Mapping

Molecular Entities



Maastricht University

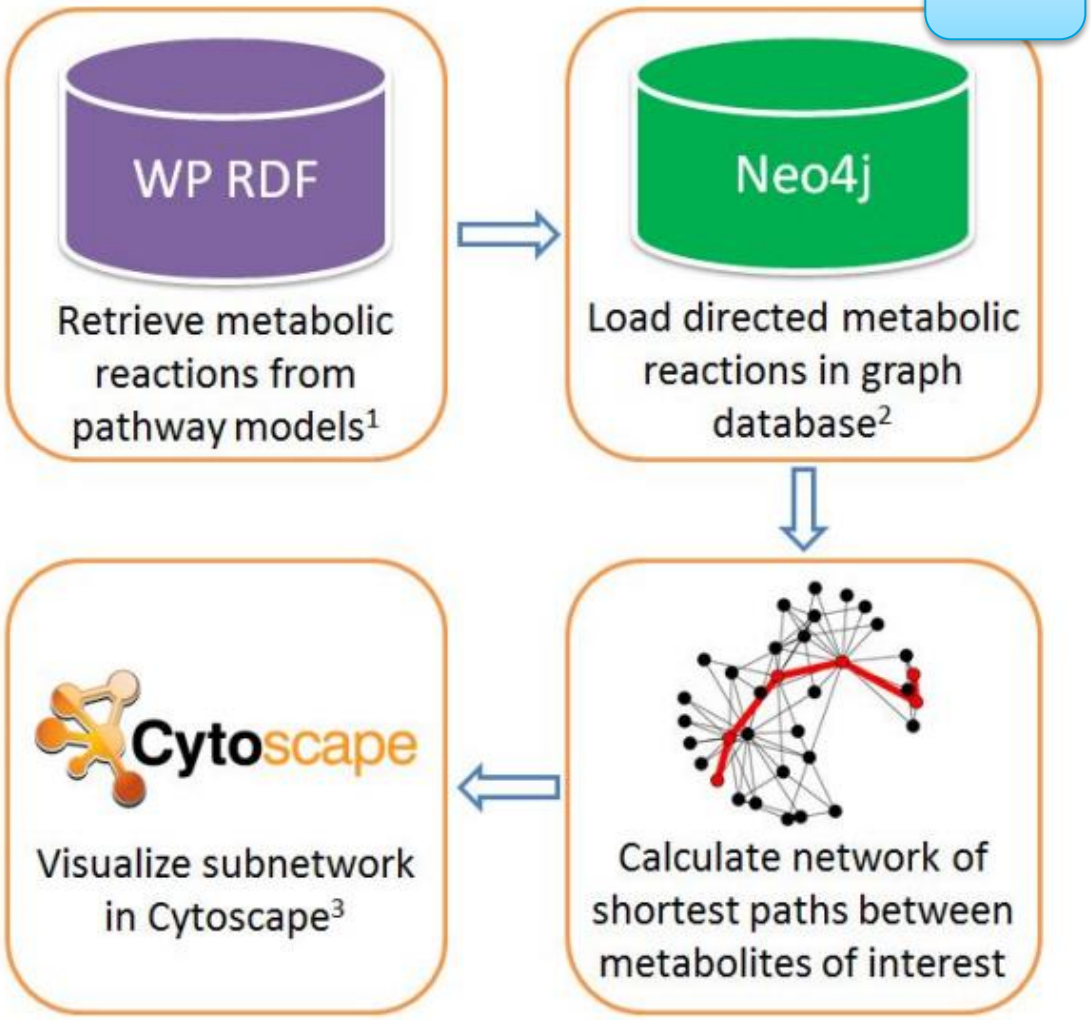
[1] DOI: 10.6084/m9.figshare.5234851.v1
[2] DOI: 10.6084/m9.figshare.6368921.v1

Network approach: AIM

- Directed network of metabolites from pathway knowledge bases
- Calculate sub-network between active metabolites
- Visualise directed paths
- Interpret metabolomics datasets

Workflow

1. Directed metabolic reactions in human pathway models are retrieved from the WikiPathways RDF[1].
2. Those interactions are stored in the graph database Neo4j[2].
3. Using the Cypher query language the shortest paths between metabolites of interests are calculated.
4. Finally, the resulting subnetwork is visualized in Cytoscape[3].



Maastricht University

[1] **WikiPathways RDF:** http://sparql.wikipathways.org (released July 10, 2017)
Kutmon *et al* (2016) doi:10.1093/nar/gkv1024, Waagmeester *et al.* (2016) doi: 10.1371/journal.pcbi.1004989

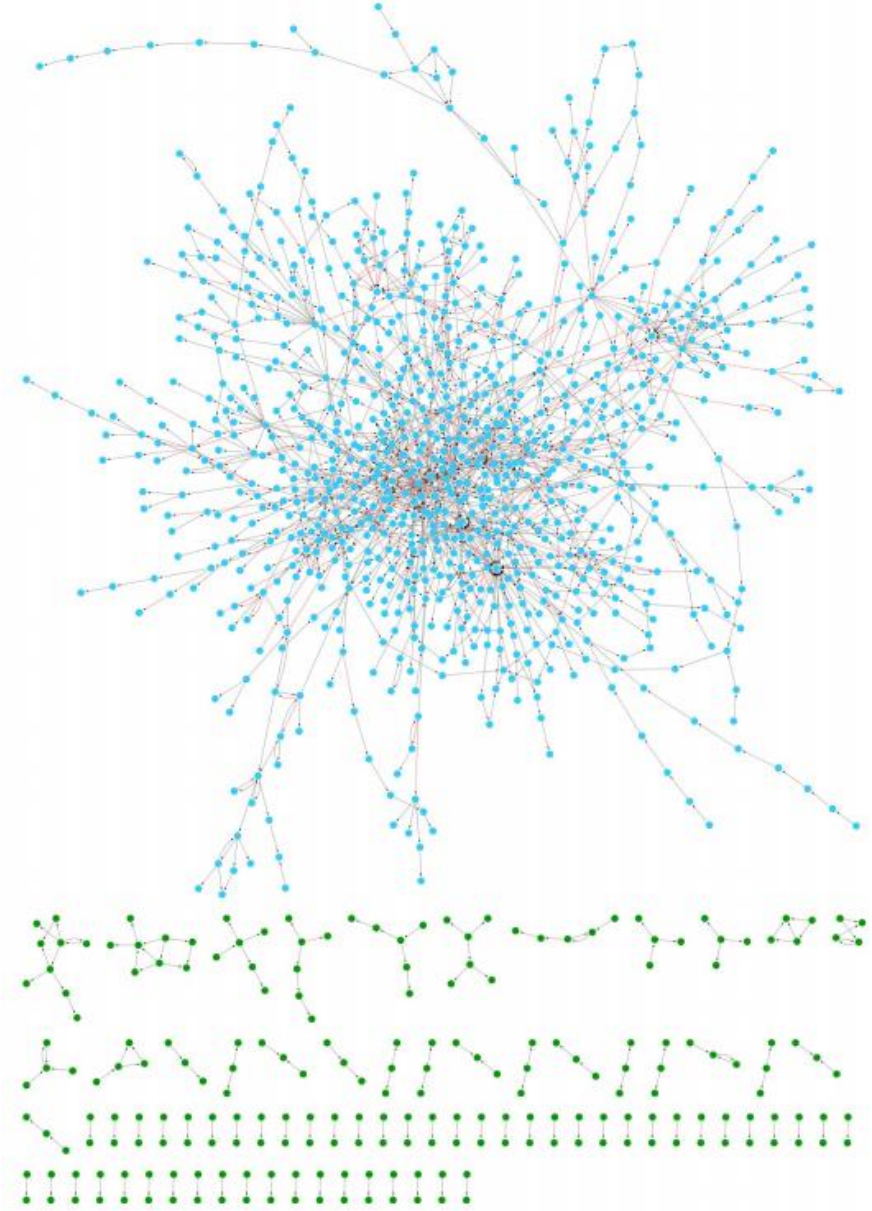
[2] **Neo4j**: https://neo4j.com/

[3] **Cytoscape**: http://cytoscape.org/
Shannon *et al.* (2003) doi: 10.1101/gr.1239303

Biological role					
Electron donor/receiver.		Energy donor/receiver.		Miscellaneous, relevant for various metabolic reactions.	
Identifier	**Name**	**Identifier**	**Name**	**Identifier**	**Name**
Q5203615	O2	Q80863	ATP	Q307434	S-adenosyl-L-homocysteine
Q506710	H+	Q185253	ADP	Q201312	S-adenosyl-L-methioninate
Q20856948	Na+ (redirected to Q3154110)	Q318369	AMP	Q407635	Coenzyme-A
Q3154110	Na+	Q422582	GDP	Q715317	Acetyl coenzyme a
Q283	H2O	Q392227	GTP		
Q1997	CO2	Q26987754	NADP+		
Q177811	PO4 3-	Q26841327	NADPH		
Q411092	Pyrophos-phoric acid	Q26987253	NAD+		
Q190901	ammonium cation	Q26987453	NADH		
		Q27102690	FADH2		

Side metabolites

DIRECTED NETWORK VISUALISATION

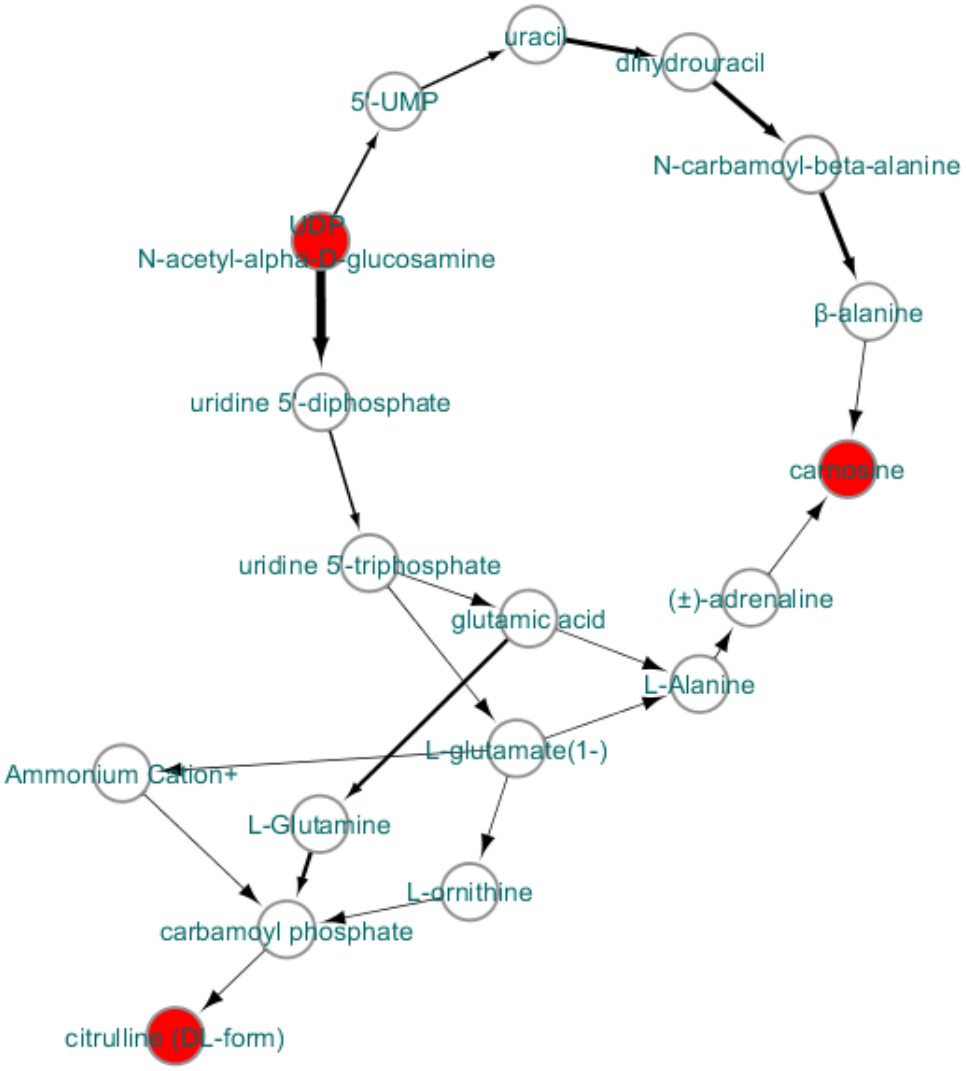


Dataset 1:

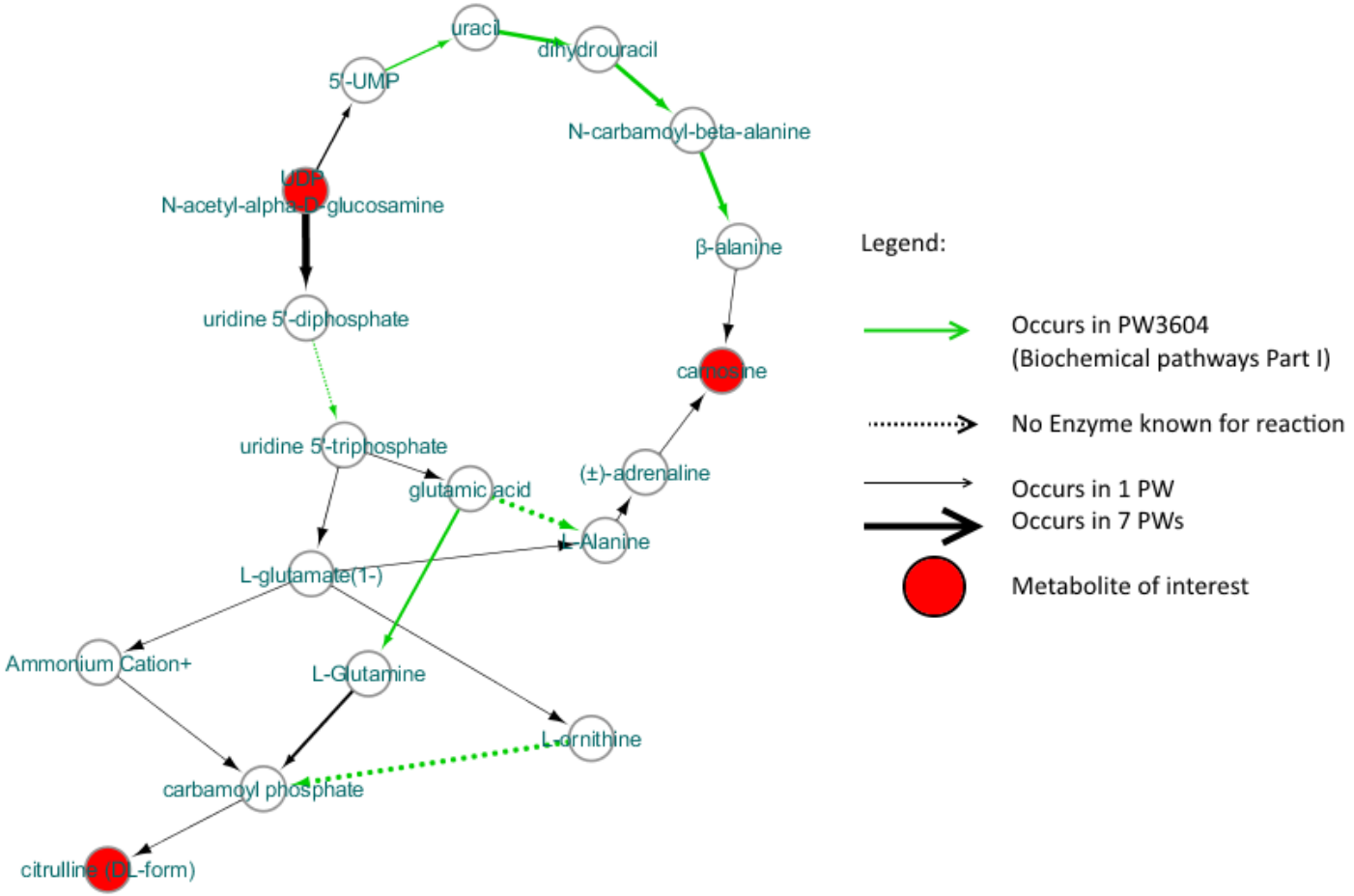
- MetaboLights dataset (MTBLS265) [4]
- Metabolic profiles (LC-MS) in **blood** samples of 15 young (29 ± 4 y of age) and 15 elderly (81 ± 7 y of age) individuals.

[4] **MetaboLights dataset:** http://www.ebi.ac.uk/metabolights/MTBLS265, Chaleckis *et al.* (2016) doi: 10.1073/pnas.1603023113

Dataset 1:


uracil
dihydrouracil
5'-UMP
N-carbamoyl-beta-alanine
UDP
N-acetyl-alpha-D-glucosamine
β-alanine
uridine 5'-diphosphate
carnosine
uridine 5'-triphosphate
(±)-adrenaline
glutamic acid
L-Alanine
L-glutamate(1-)
Ammonium Cation+
L-Glutamine
L-ornithine
carbamoyl phosphate
citrulline (DL-form)

Dataset 1 with additional info:



Maastricht University

[4] **MetaboLights dataset:** http://www.ebi.ac.uk/metabolights/MTBLS265, Chaleckis *et al.* (2016) doi: 10.1073/pnas.1603023113

CONCLUSION

- Calculation of directed subnetwork connecting active metabolites is possible with presented workflow

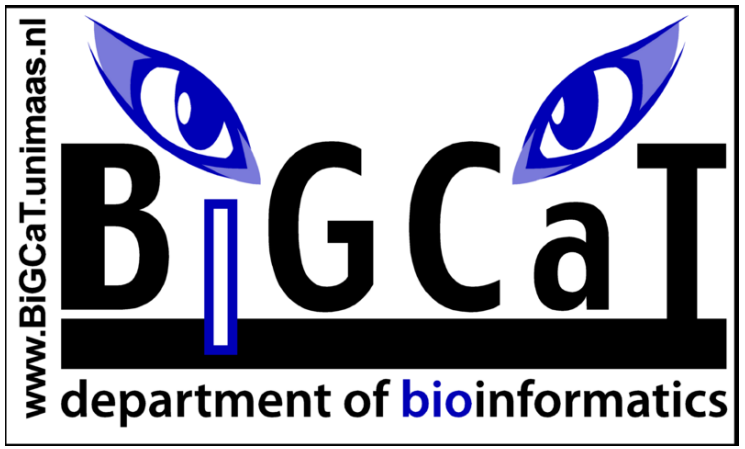
- Neo4j and Cytoscape allow computational calculation for larger networks and advanced visualisation

FUTURE PERSPECTIVE

- Add more pathway knowledge bases (now WikiPathways and Reactome, could add KEGG in the future?)
- Create app for direct visualisation with Cytoscape from Neo4j (first tests have been run)
- Allow for integration with other omics data sources, such as proteomics and transcriptomics

Acknowledgements, questions, discussion

- Martina Kutmon
- Jonathan Melius
- Ryan Miller
- Georg Summer
- Chris T Evelo
- Egon L Willighagen



Maastricht University

Find the original poster @
https://figshare.com/articles/Poster_Visualizing_metabolomics_data_in_directed_biological_networks/5234851