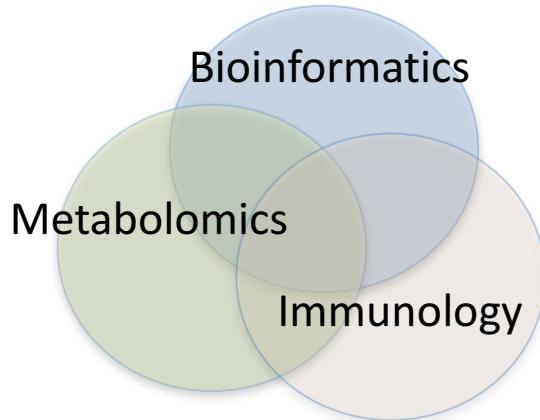
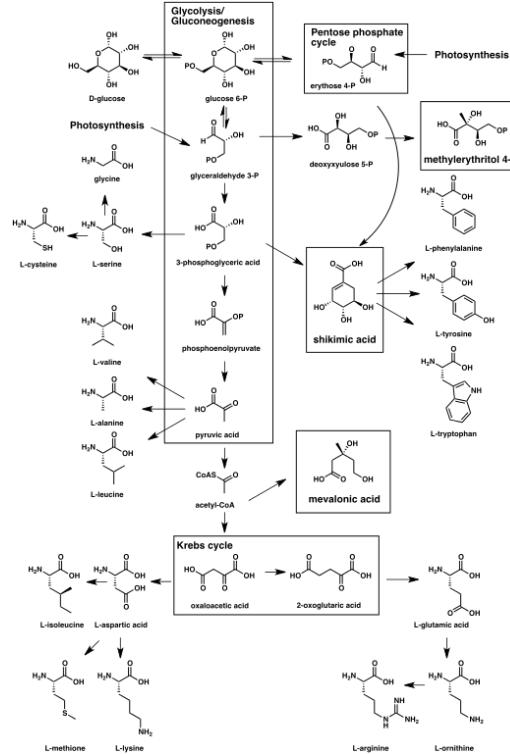


# Mummichog and ongoing work



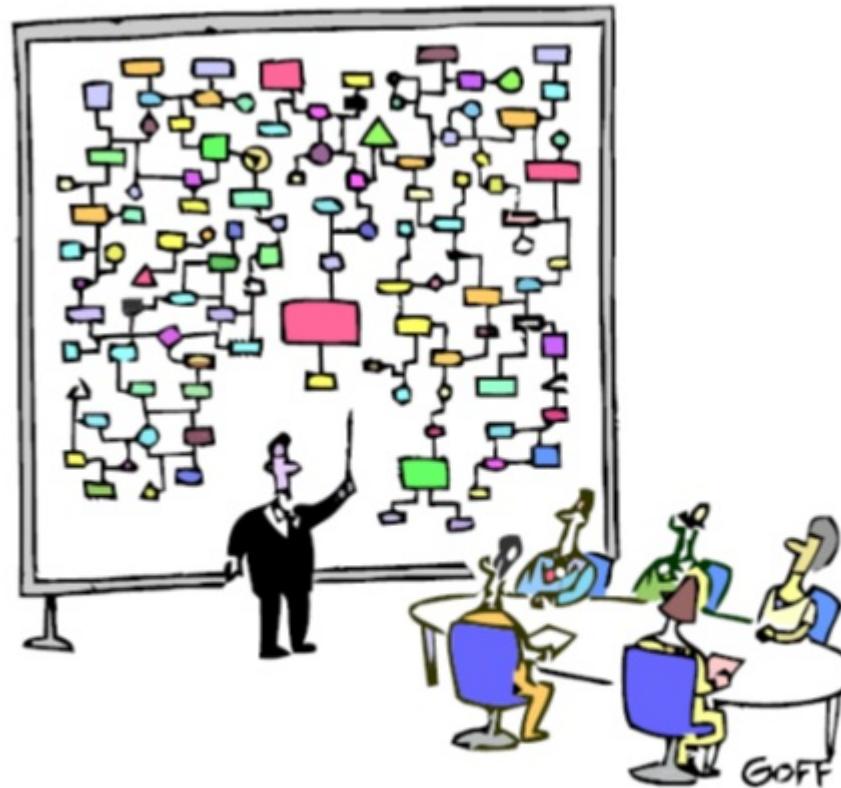
Shuzhao Li, Ph.D  
Assistant Professor  
Department of Medicine  
Emory University  
August 21, 2019

# What's common between *Fish and metabolites?*

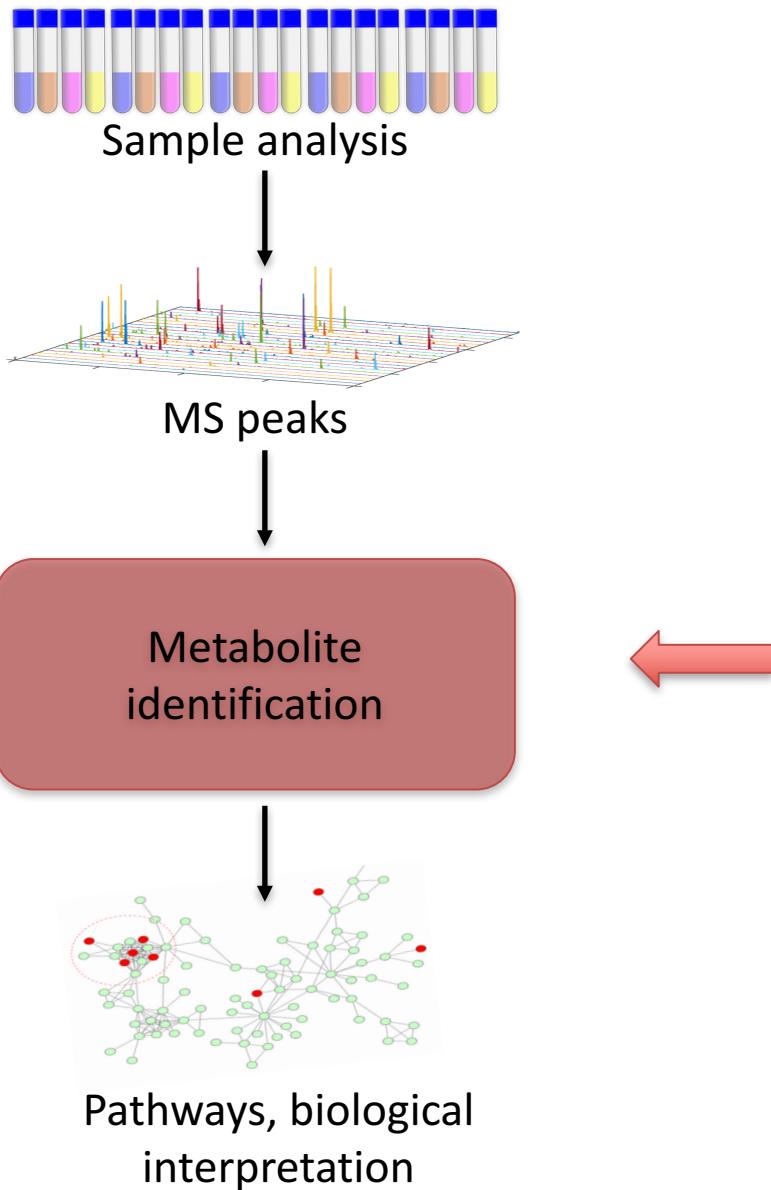


They swim in groups

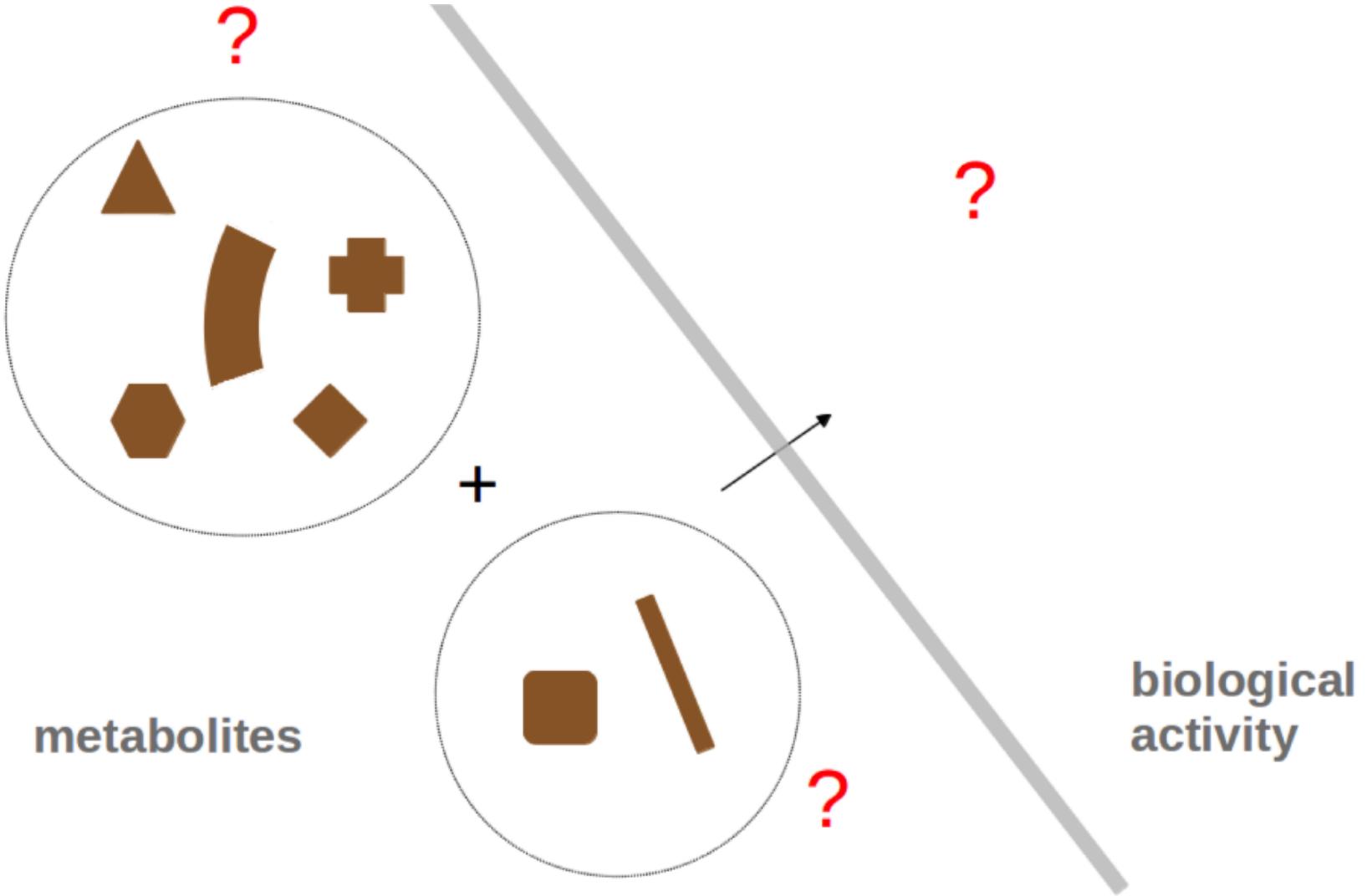
# Lot of pathways are known

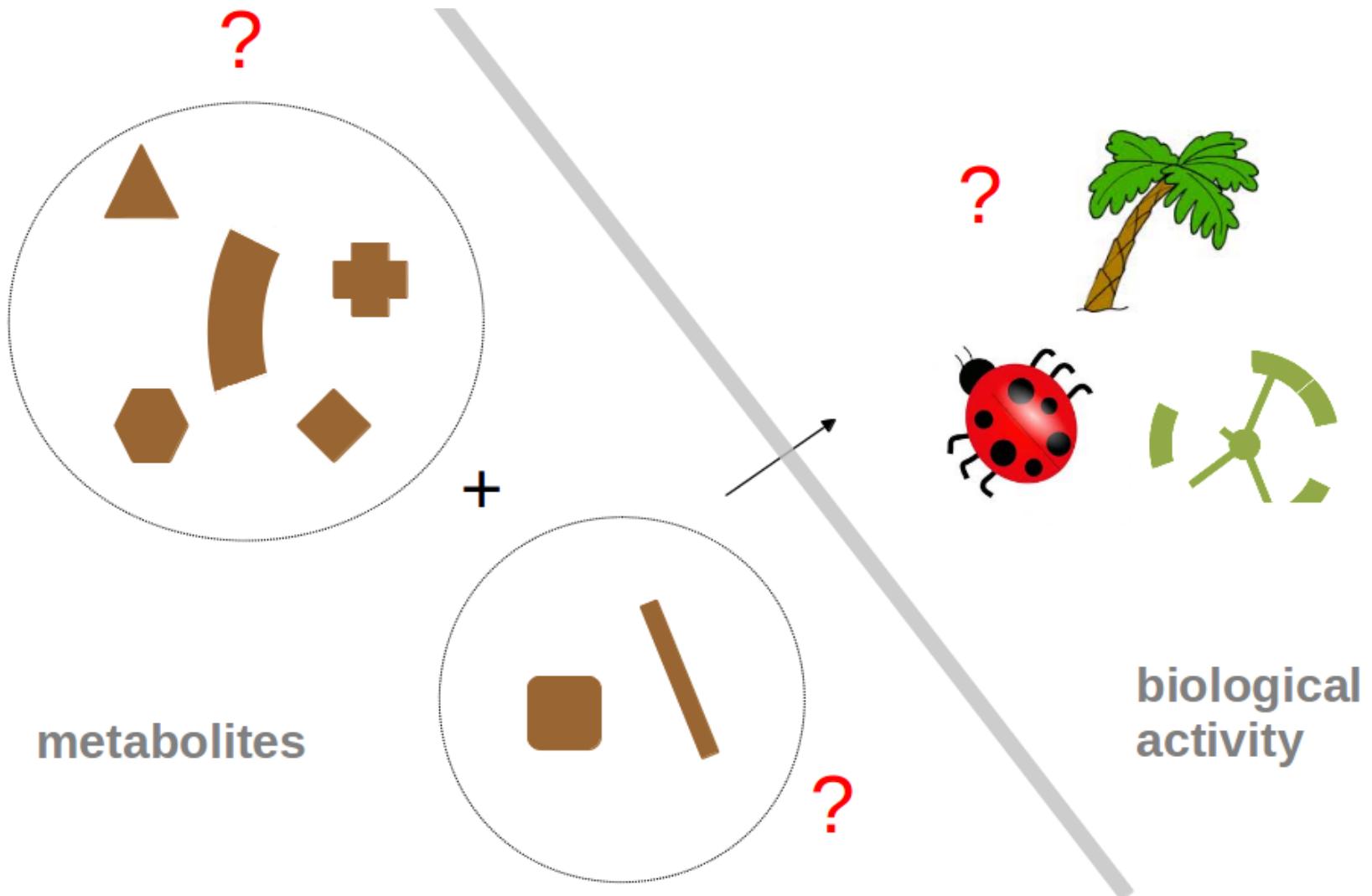


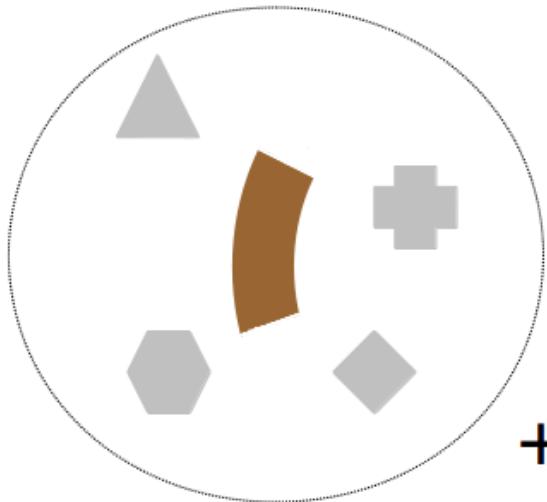
"And that's why we need a computer."



Bottleneck of  
metabolomics



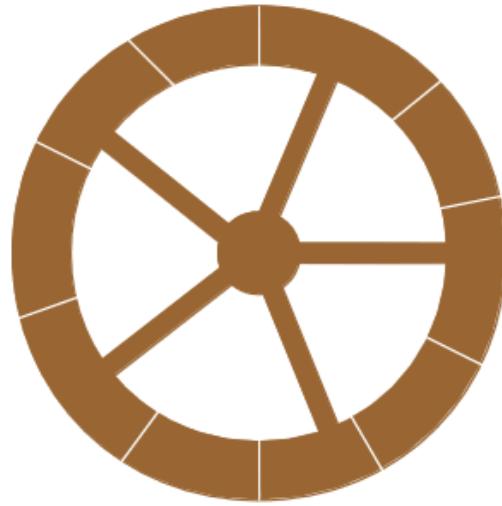




metabolites

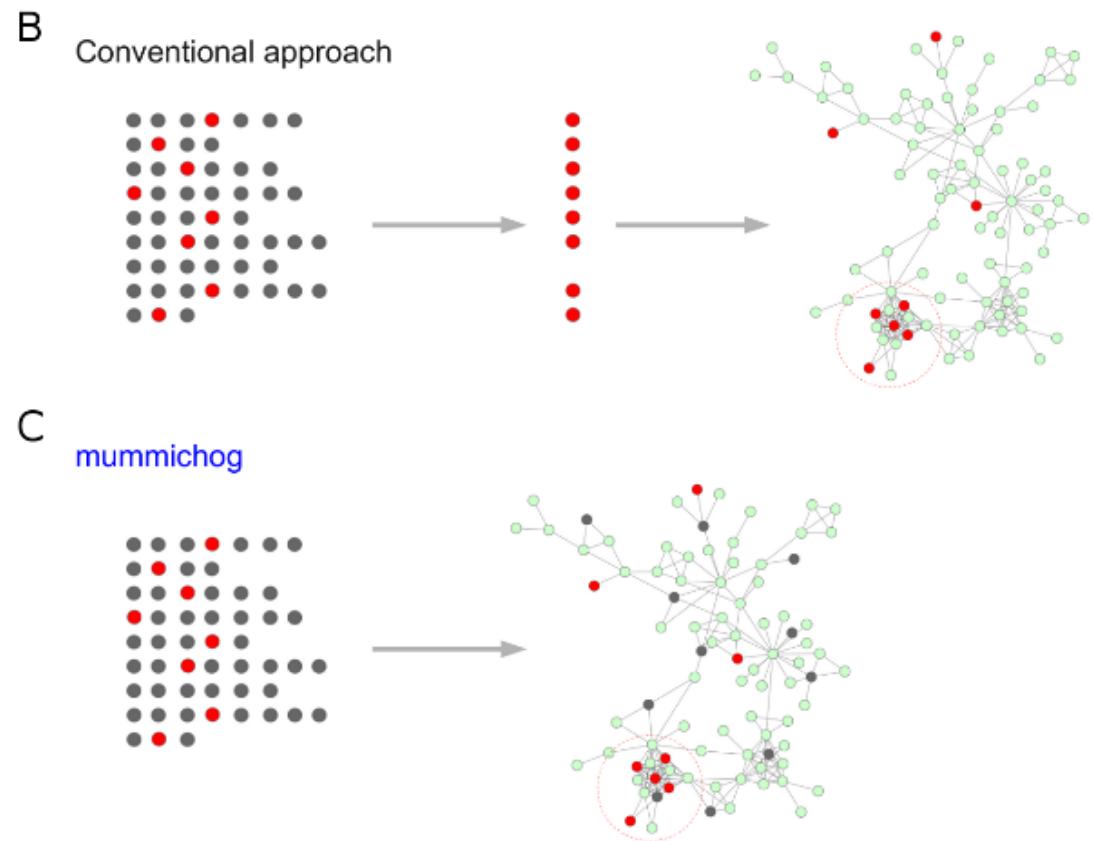
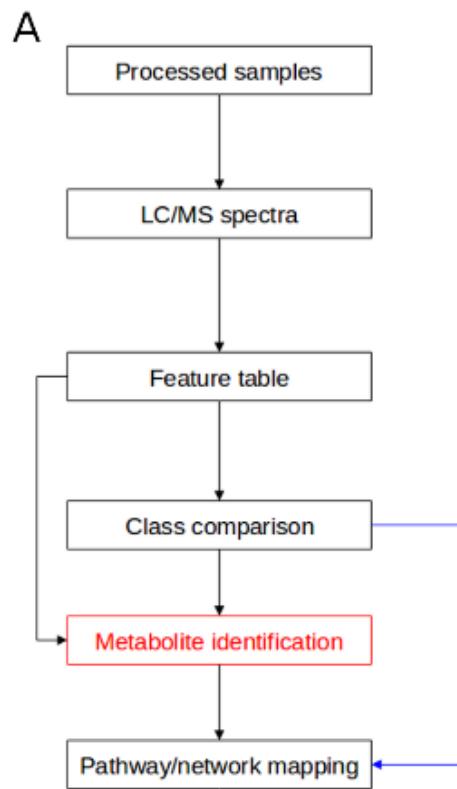


+

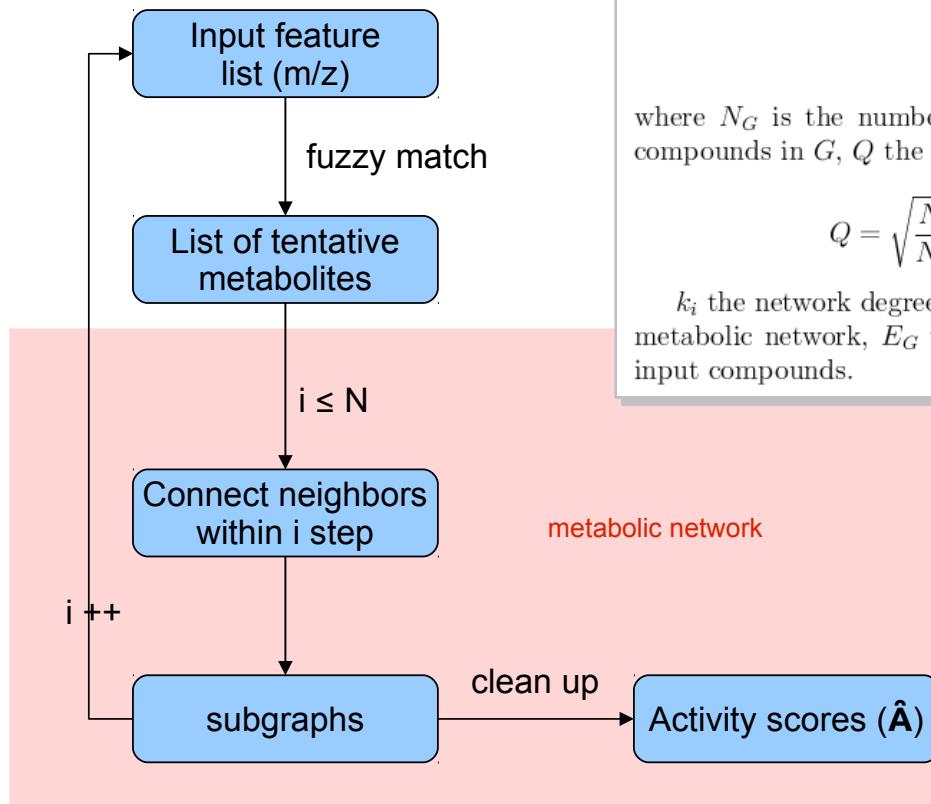


biological  
activity

# *Mummichog* tests metabolite grouping patterns



# Module analysis in *mummichog*



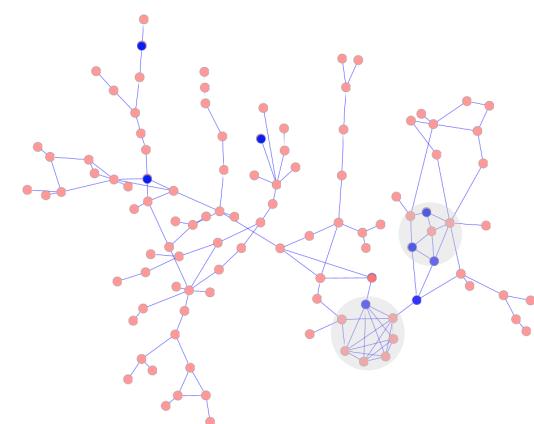
For a subgraph  $G$ , activity score

$$\hat{A} = Q \cdot \frac{N_{I,G}}{N_G}, \quad (1)$$

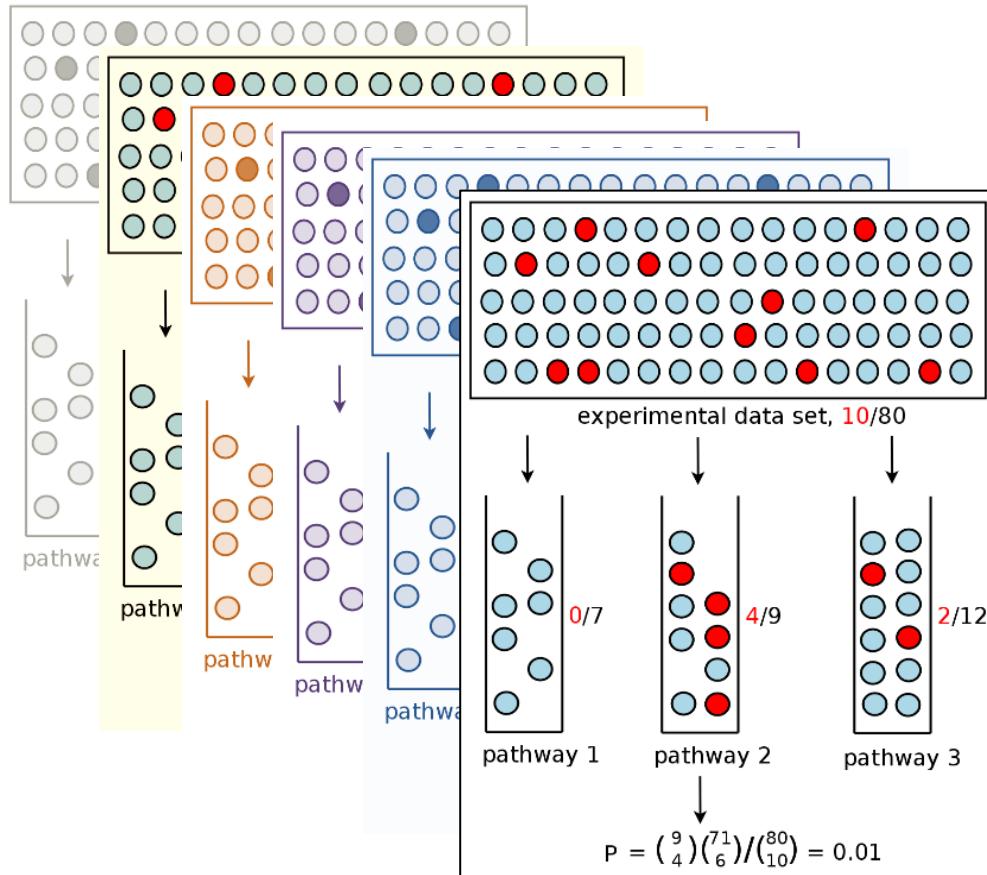
where  $N_G$  is the number of compounds in  $G$ ,  $N_{I,G}$  the number of input compounds in  $G$ ,  $Q$  the adjusted Newman-Girvan modularity:

$$Q = \sqrt{\frac{N_I}{N_G}} \cdot \left( \frac{E_G}{m} - \sum_{i,j} \frac{k_i k_j}{2m} \right) , \quad i, j \in G \quad (2)$$

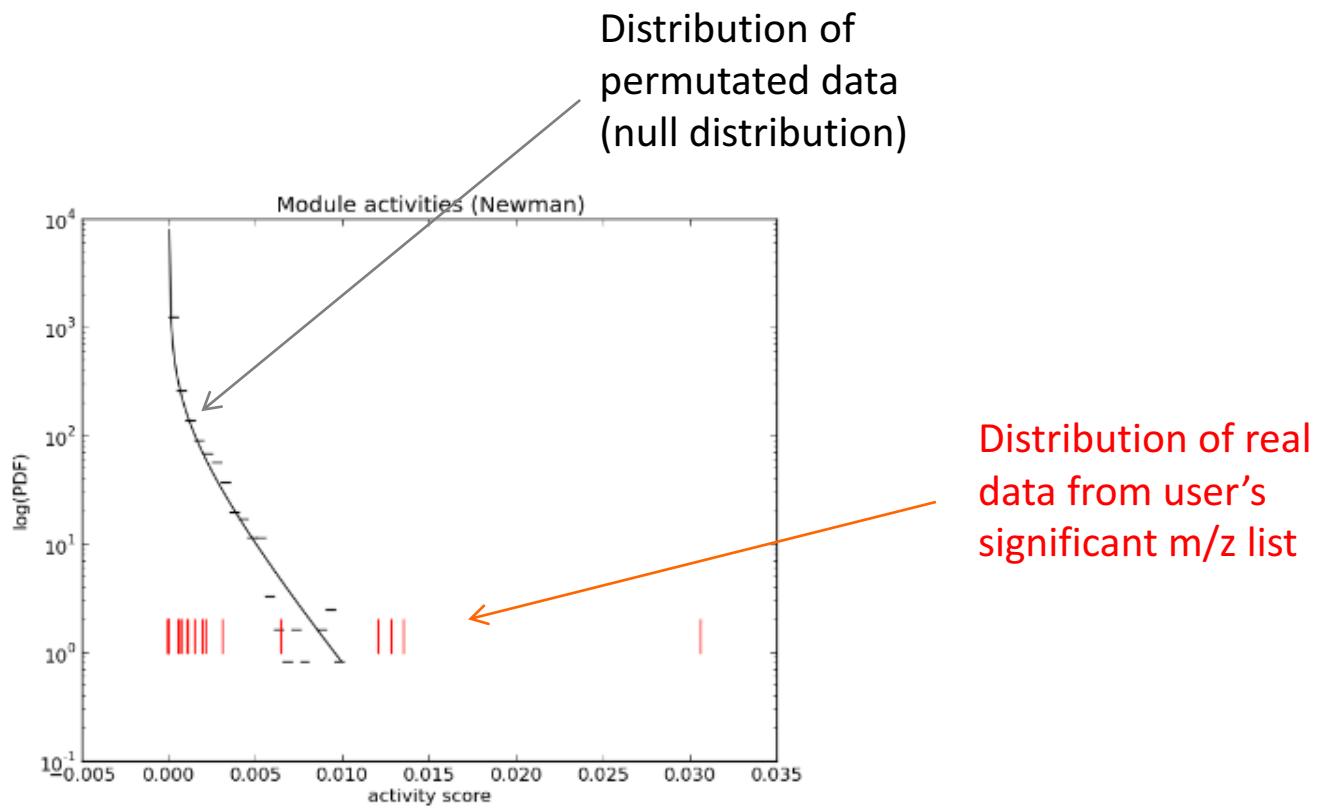
$k_i$  the network degree of compound  $i$ ,  $m$  the total number of edges in the metabolic network,  $E_G$  the total number of edges in  $G$ ,  $N_I$  the number of input compounds.



# Pathway analysis in *mummichog*

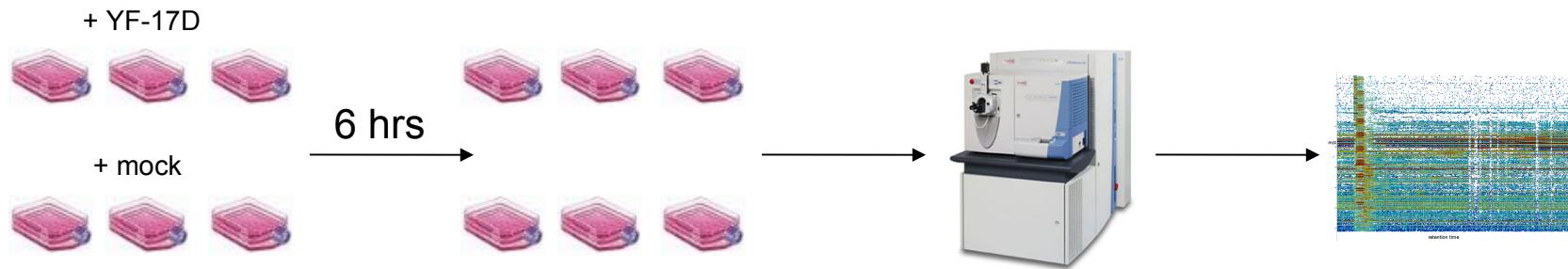


# Testing module/pathway significance in *mummichog*

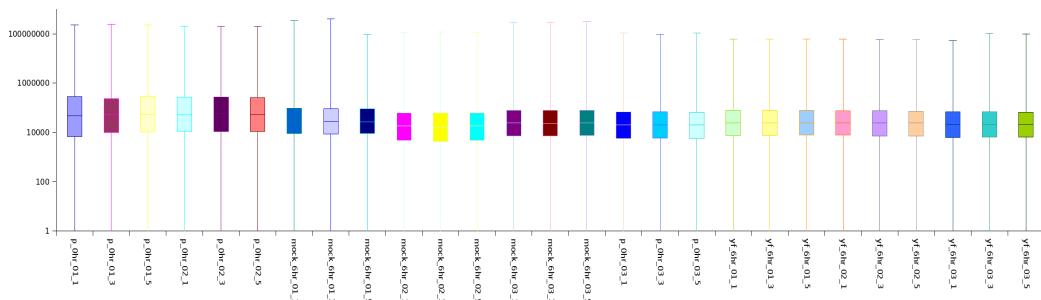


# Case study: viral activation of immune cells

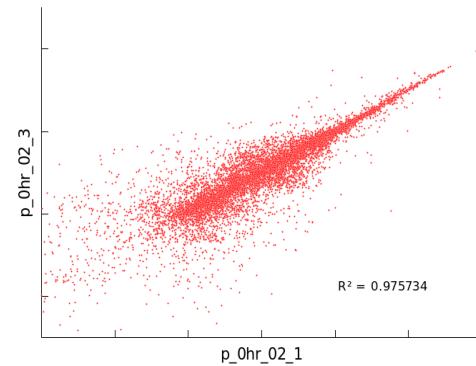
Monocyte derived dendritic cells (moDC)



QA: total ion counts are similar among samples

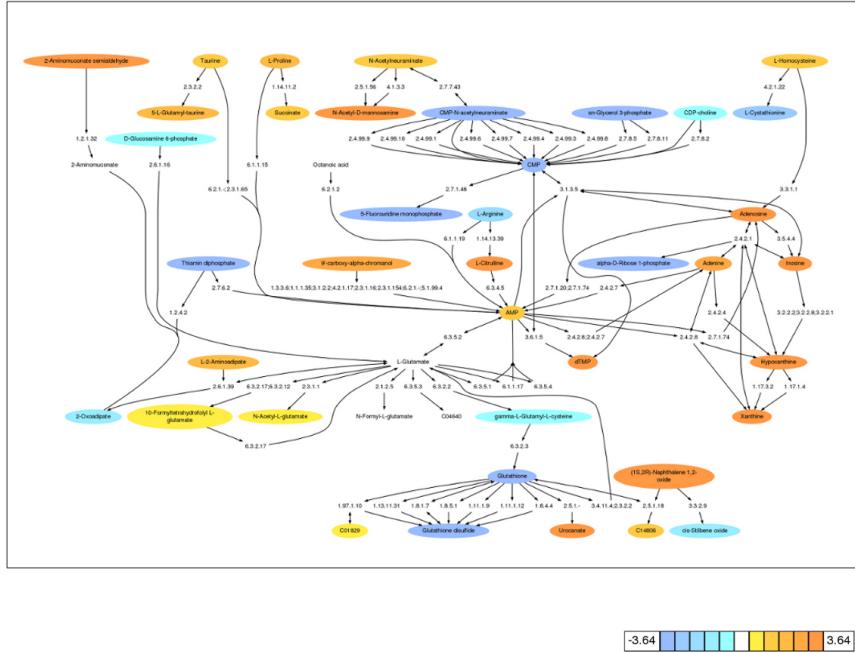


technical replicates, 10,000 features

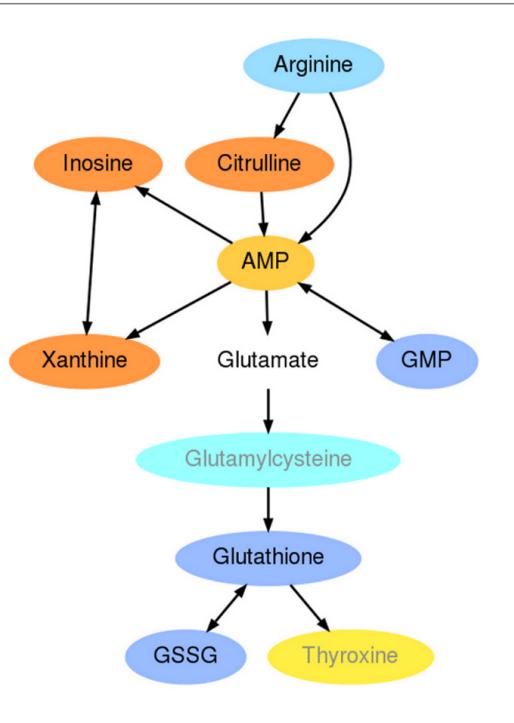


# *Mummichog*: viral activation of immune cells

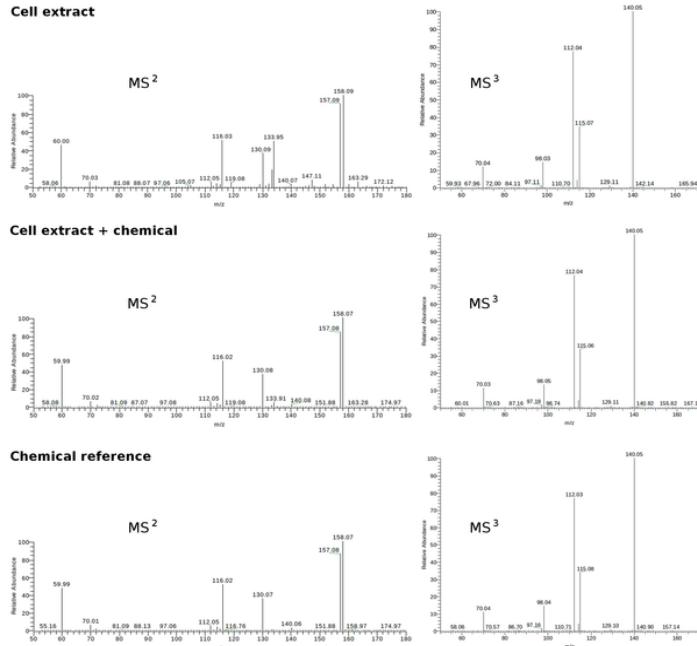
A



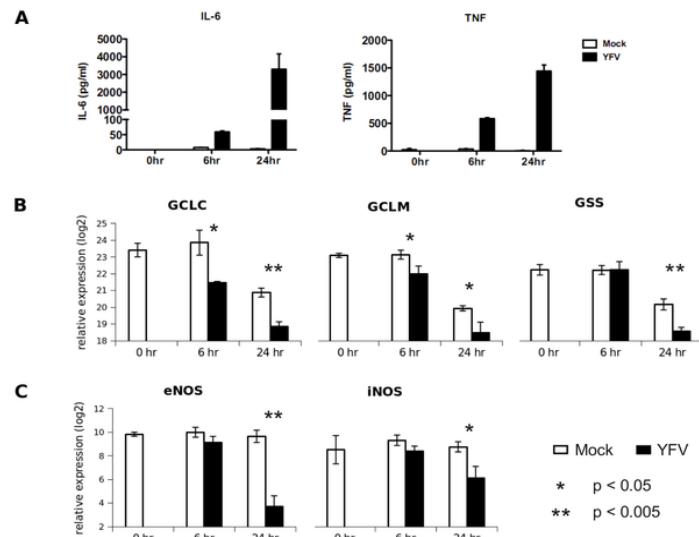
B



# Experimental validation of *mummichog* prediction

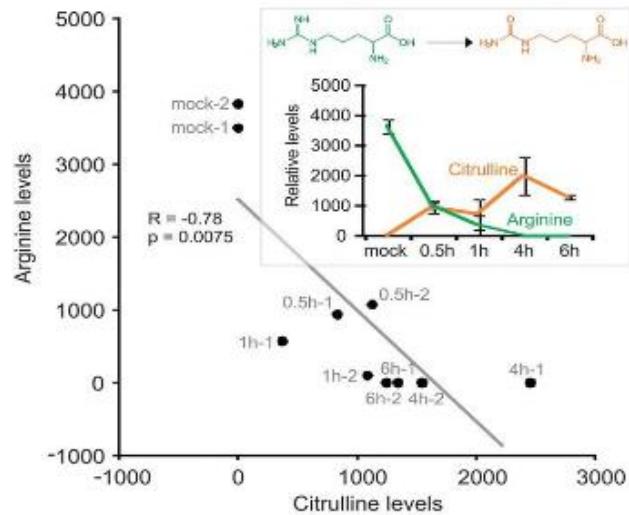


Tandem mass spectrometry confirmed 9/11 metabolites

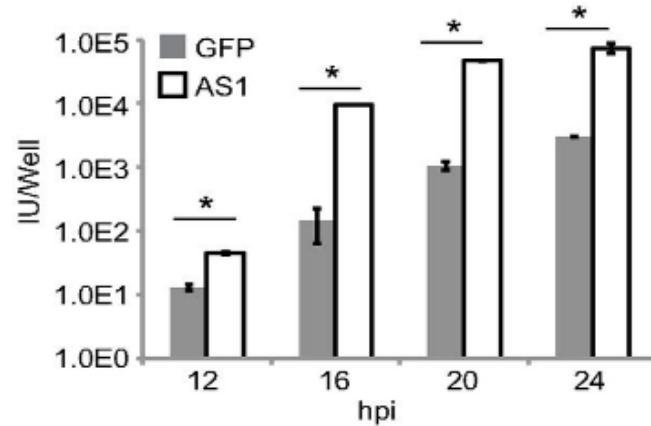


Gene expression supported GSH/GSSG depletion and Arg/Cit conversion

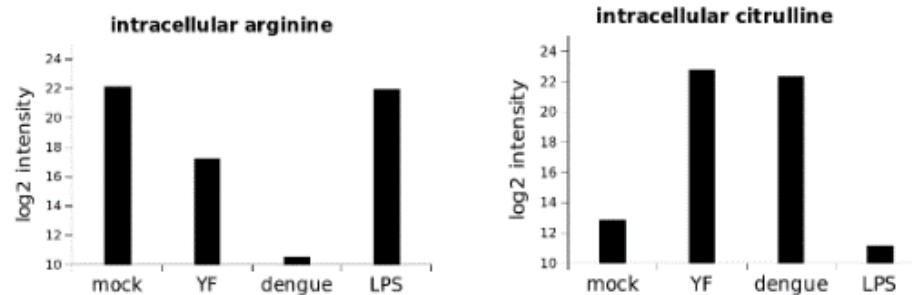
# Arginine as master regulator of viral response



Ravindran et al. 2014. Science 343:313



Argininosuccinate synthetase 1 knockdown led to increased replication of HSV-1.  
Grady, Purdy, Rabinowitz & Shenk. 2013. PNAS 110:E5006.

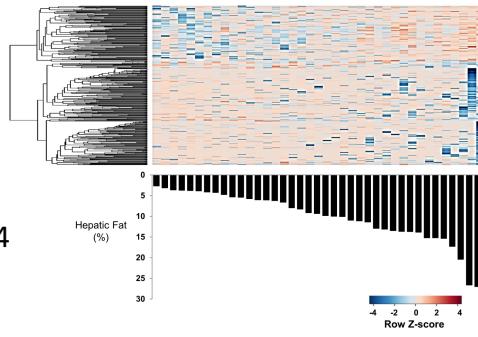


Li et al. 2013. PLoS Computational Biology. 9:e10031323

# Mummichog applications

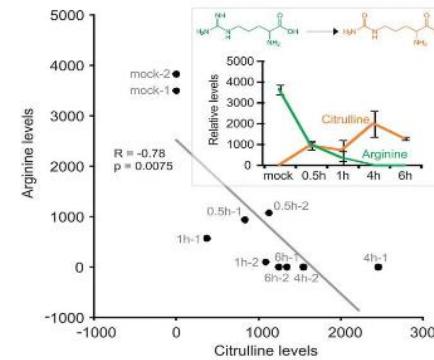
## Epidemiology

Jin et al., 2016.  
*The Journal of pediatrics* 172: 14

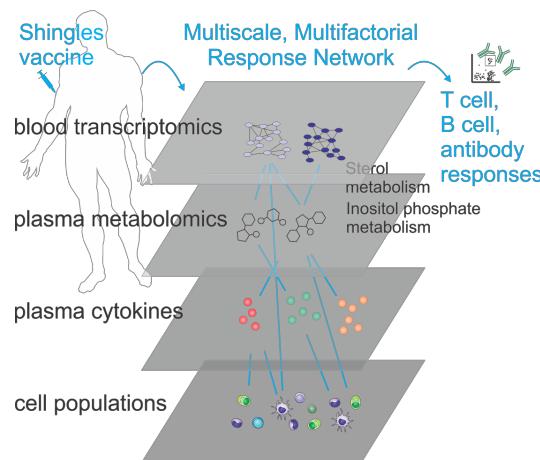


## Molecular mechanisms

Ravindran et al. 2014.  
*Science* 343:313

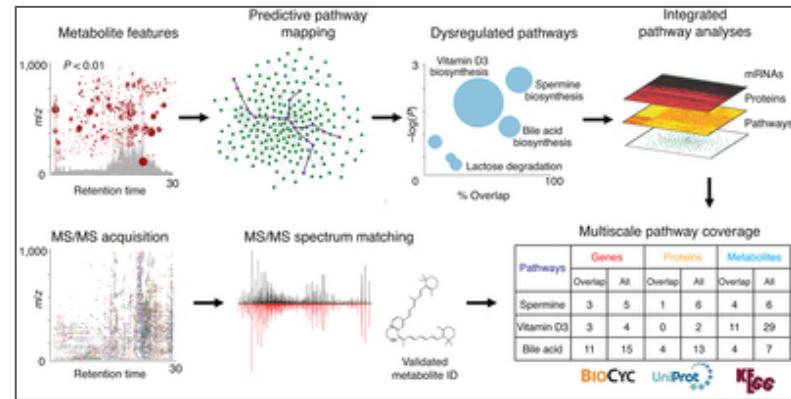


## Multi-omics immune response



Li et al., 2017. *Cell* 169:862

## Bioinformatics platform integration



Huan et al. 2017. *Nature Method* 14:461

## Mummichog pathway and network analysis for metabolomics

Home    Software    Publications    Notebooks    Version 1.0.9    mummichog-server

Mummichog is a free Python program for analyzing data from high throughput, untargeted metabolomics. It leverages the organization of metabolic networks to predict functional activity directly from feature tables, bypassing metabolite identification. Thus, high-quality hypotheses can be quickly generated from a LC-MS data table.

Download and use mummichog. Now via standard Python package index.

OS independent install (version 1):

```
pip install mummichog1
```

Or mummichog 2 (beta test):

```
pip install mummichog
```

Run it in command line:

```
mummichog -f myData --o myResult
```

More to [click "Software"](#).

Example publications that were supported by using mummichog

Li et al. (2017) Metabolic Phenotypes of Response to Vaccination in Humans. *Cell* 169(5): p862-877.

Huan, Tao, et al. "Systems biology guided by XCMS Online metabolomics." *Nature methods* 14.5 (2017): 461.

Xu et al. "Autophagy is essential for effector CD8+ T cell survival and memory formation." *Nature immunology* 15.12 (2014): 1152-1161.

More to [click "Publications"](#).

Jupyter notebooks for data analysis in metabolomics and systems biology

Jupyter notebooks are to data people like lab notebooks to bench scientists. They keep code and result in the same web browser. It's increasingly popular for data analysis and collaboration. We continue posting notebooks as tutorials and for record keeping.

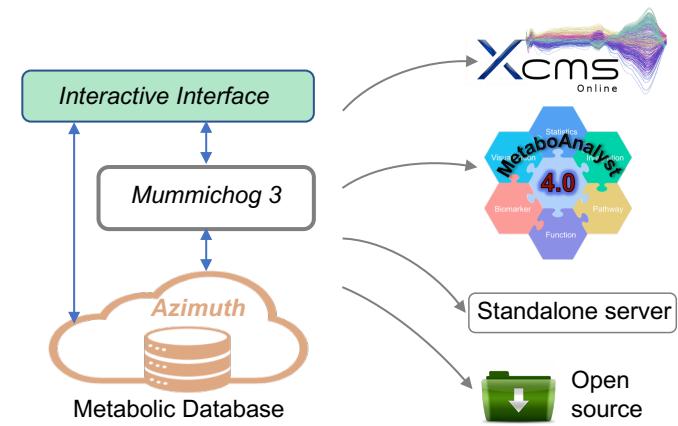
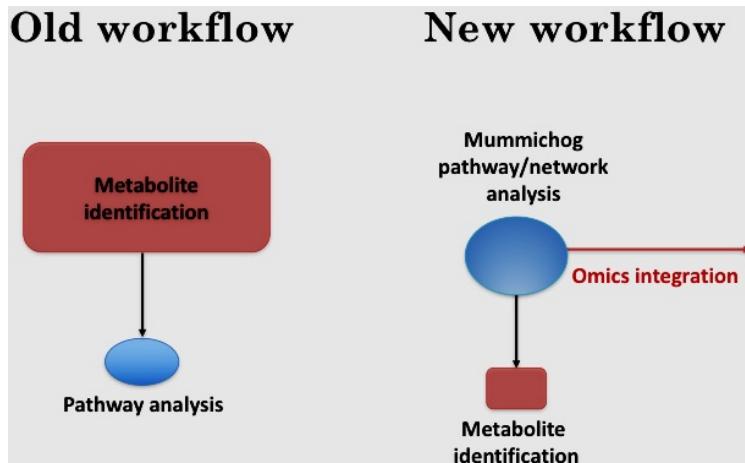
More to [click "Notebooks"](#).

## News

- Web version is now testing at [here](#).
- Mummichog 2 is now on [GitHub](#).
- Mummichog 1 with a web interface is now available on [MetaboAnalyst 4](#).
- A common error, "AttributeError: 'NodeView' object has no attribute 'sort'", is caused by Networkx 2.x, which is not backward compatible. This can be fixed by installing Networkx 1.x via pip in your terminal, "sudo pip install networkx==1.10".
- Mummichog 2 test version is available at [PyPi](#).
- Mummichog version 1.0.10 is available at [PyPi](#).
- Mummichog helped decipher metabolic phenotypes in human vaccination - Li et al. (2017) at [Cell 169\(5\): p862-877](#). Also see commentary "[Orthogonal Data Integration to Define Immunometabolic-Phenotypes](#)" at [Cell Systems](#).
- Emory University Sys/Bio/Info Group runs a monthly meeting on Systems Biology and Bioinformatics. These are casual seminars and discussions, on every first Wednesday of the month, 12 pm, Whitehead Biomedical Research Building, Rm 200. Email Dr. Shuzhao Li to join the mailing list.

# Mummichog & future development

- Active development of version 2 and server
- Separating metabolic models to a new database, updated independently from the software
- Send in your feature requests



- Coupling visual analytics
- Adding compatibility with upstream data processing
- Incorporating research in metabolic network reconstruction, especially using high-resolution mass spectrometry data
- Incorporating network alignment methods for data integration