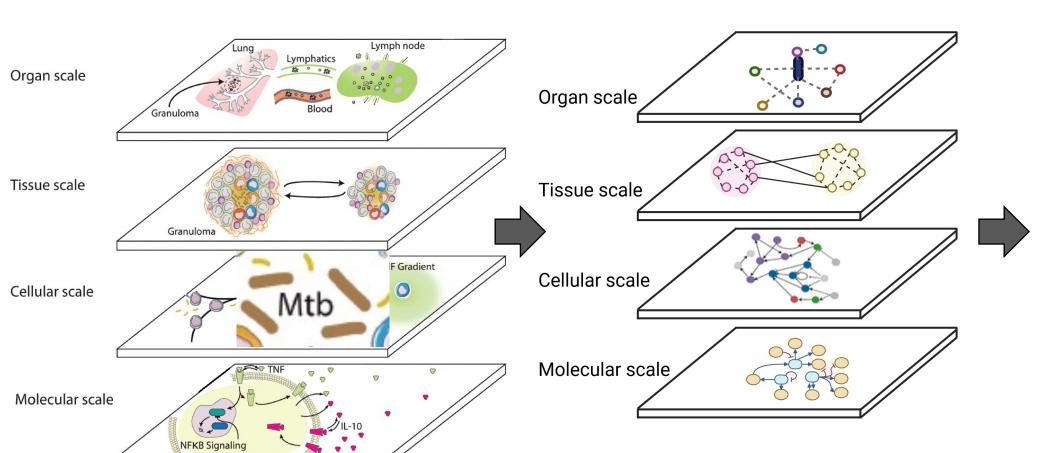


### Goals

- Discuss why networks are useful for analysis
- Discuss annotated vs. data-driven networks
- Method for inferring data-driven network: WGCNA
- Method for mapping genes of interest onto network: GSEA

## Networks can help contextualize biological complexity

**Network Model** 



#### **Mathematical Model**

#### **Organ Rules:**

$$a + b + c = x$$
  
 $a + c - e = x$ 

#### **Tissue Rules:**

$$d+e+f=a$$
  
 $g+h-f=b$ 

#### **Cellular Rules:**

$$j + k + m = g$$
$$j + p - n = f$$
$$n + p - q = d$$

#### **Molecular Rules:**

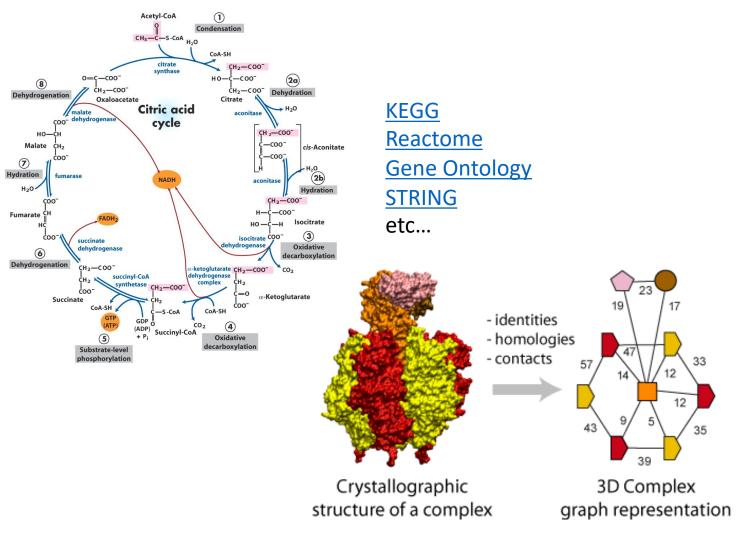
$$r + s + t = m$$
  
 $u + e - v = n$   
 $q + r - f = p$ 

Linderman, et al., 2015, PMID: **25924949** 

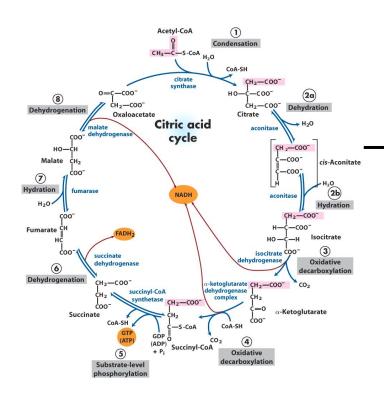
Mast et al., 2014, PMID: 25225336

### Annotated networks

Known interactions from direct characterization



Gene Set Enrichment Analysis (GSEA)



Leading edge subset Gene set S Correlation with Phenotype Random Walk ES(S) Gene List Rank Maximum deviation from zero provides the enrichment score *ES(S)* 

Exper.

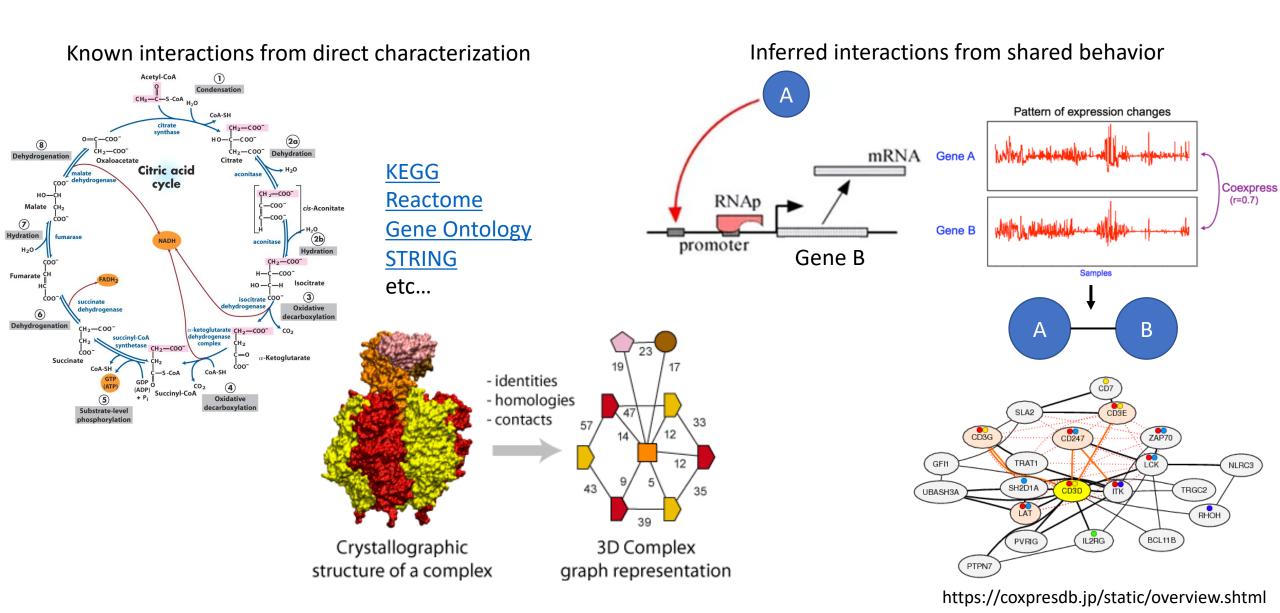
Control

Expression fold-change

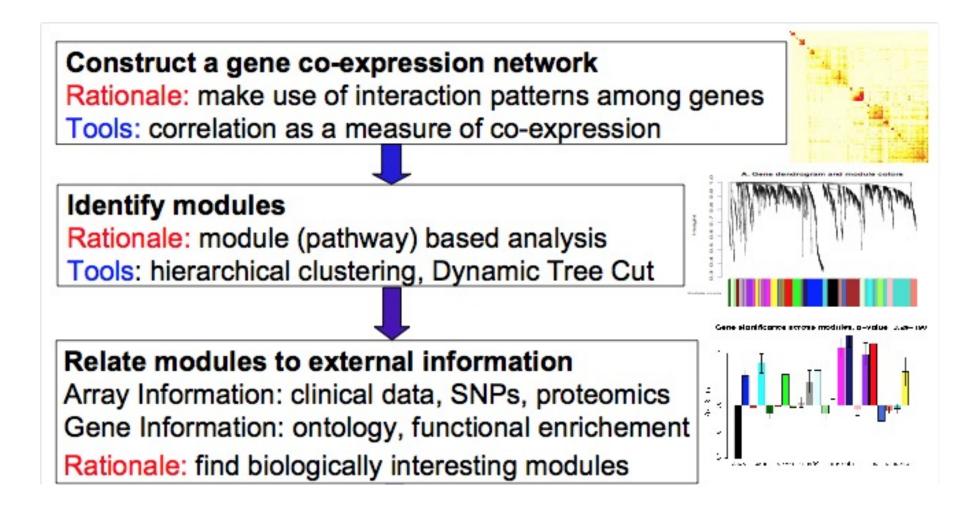
over control

Subramanian, et al., 2005, PMID: **16199517**Sergushichev, 2016, <a href="mailto:doi.org/10.1101/060012">doi.org/10.1101/060012</a>
<a href="https://biostatsquid.com/fgsea-tutorial-gsea/">https://biostatsquid.com/fgsea-tutorial-gsea/</a>

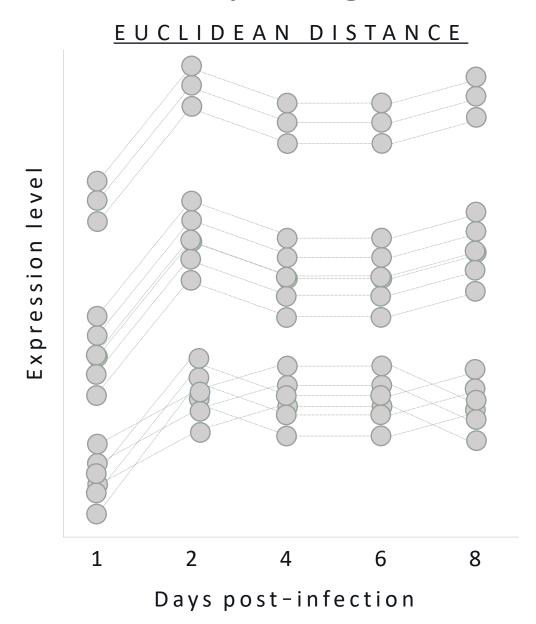
### Annotated networks vs. data-driven networks

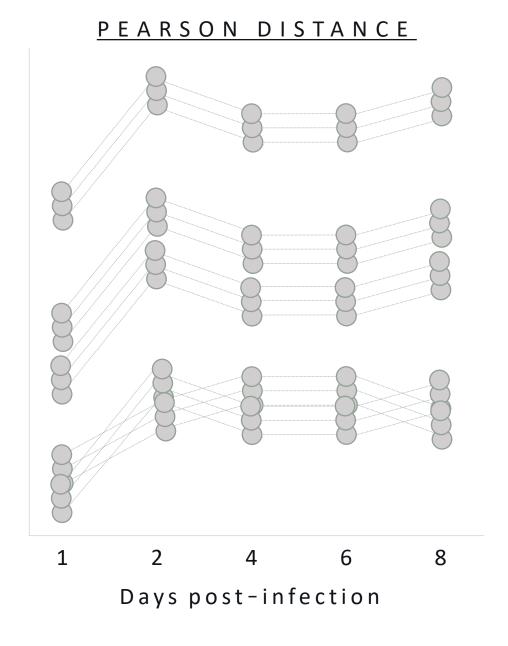


## Weighted Gene Co-expression Network Analysis (WGCNA)

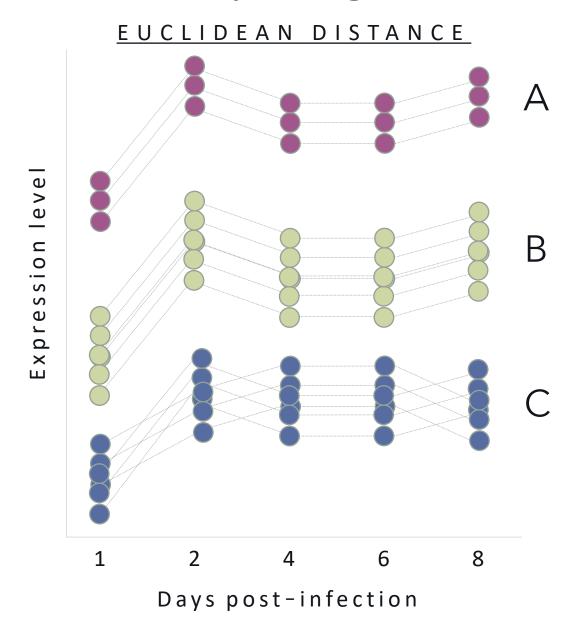


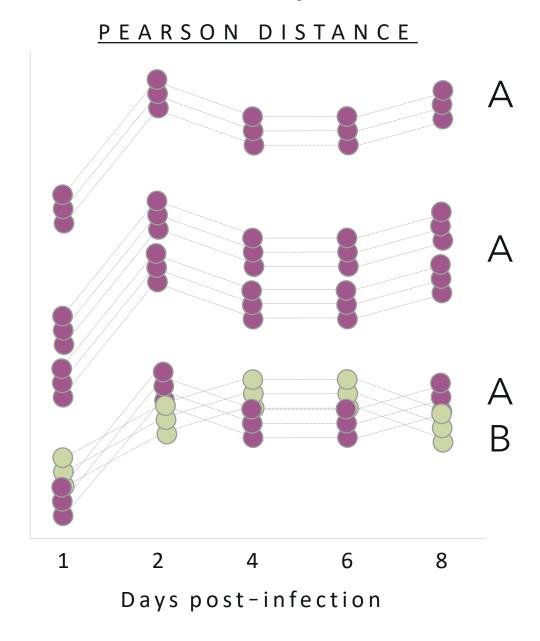
### Comparing Distance Metrics for Co-expression

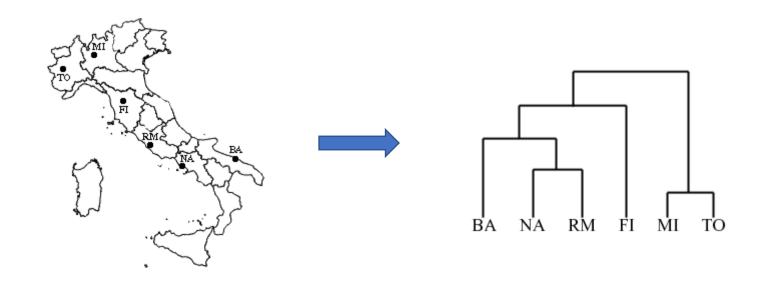




### Comparing Distance Metrics for Co-expression



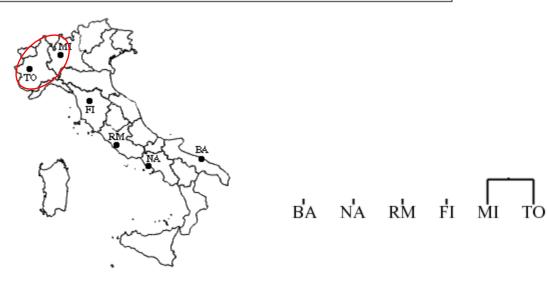




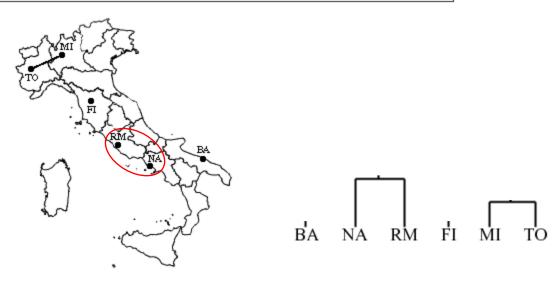
	BA	FI	MI	NA	RM	TO
BA	0	662	877	255	412	996
FI	662	0	295	468	268	400
MI	877	295	0	754	564	138
NA	255	468	754	0	219	869
RM	412	268	564	219	0	669
ТО	996	400	138	869	669	0



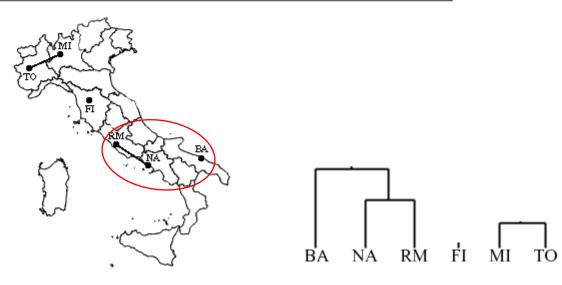
	BA	FI	MI	NA	RM	TO
BA	0	662	877	255	412	996
FI	662	0	295	468	268	400
MI	877	295	0	754	564	138
NA	255	468	754	0	219	869
RM	412	268	564	219	0	669
ТО	996	400	138	869	669	0



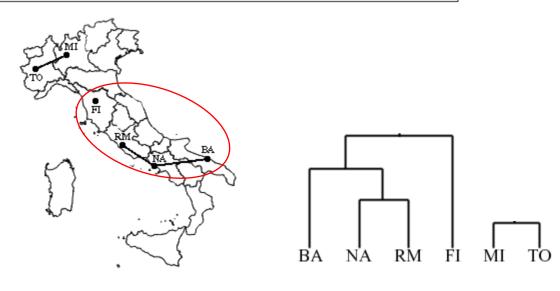
	BA	FI	MI/TO	NA	RM
BA	0	662	877	255	412
FI	662	0	295	468	268
MI/TO	877	295	0	754	564
NA	255	468	754	0	219
RM	412	268	564	219	0



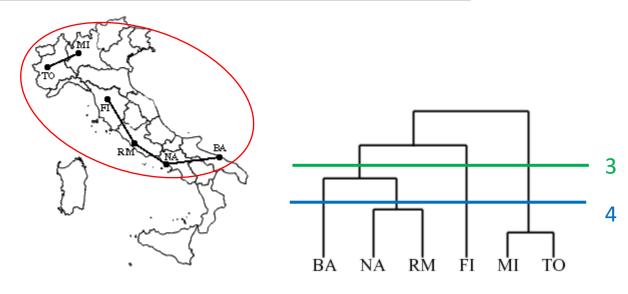
	BA	FI	MI/TO	NA/RM
BA	0	662	877	255
FI	662	0	295	268
MI/TO	877	295	0	564
NA/RM	255	268	564	0



	BA/NA/RM	FI	MI/TO
BA/NA/RM	0	268	564
FI	268	0	295
MI/TO	564	295	0



	BA/FI/NA/RM	MH/TO
BA/FI/NA/RM	0	295
MI/TO	295	0



- \* Height of bar corresponds to how distant samples are from each other
- \*\* Choice of distance cutoff determines number of modules