

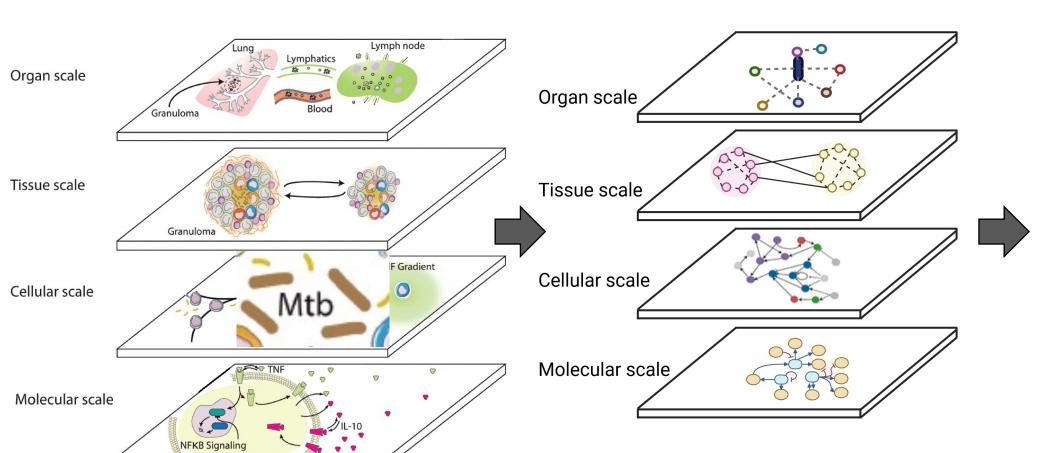
Goals

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

Method for inferring data-driven network: WGCNA

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:

$$r + s + t = m$$

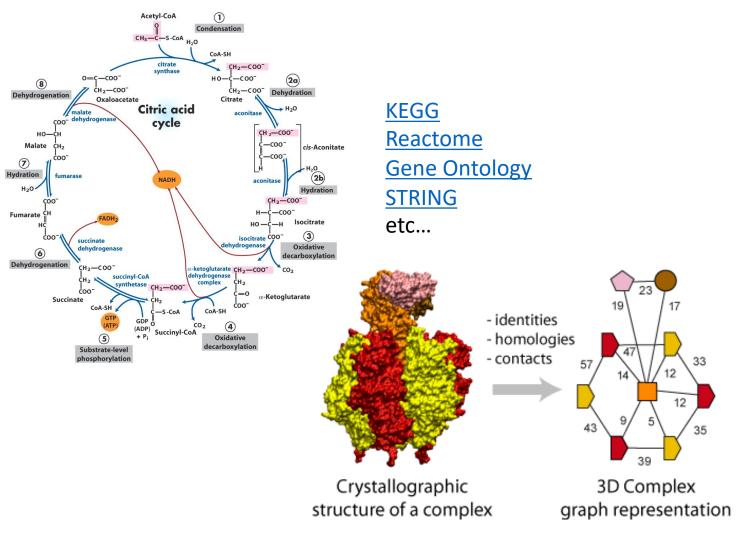
 $u + e - v = n$
 $q + r - f = p$

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

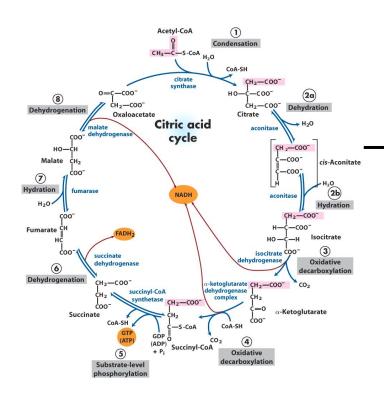
Mast et al., 2014, PMID: 25225336

Annotated networks

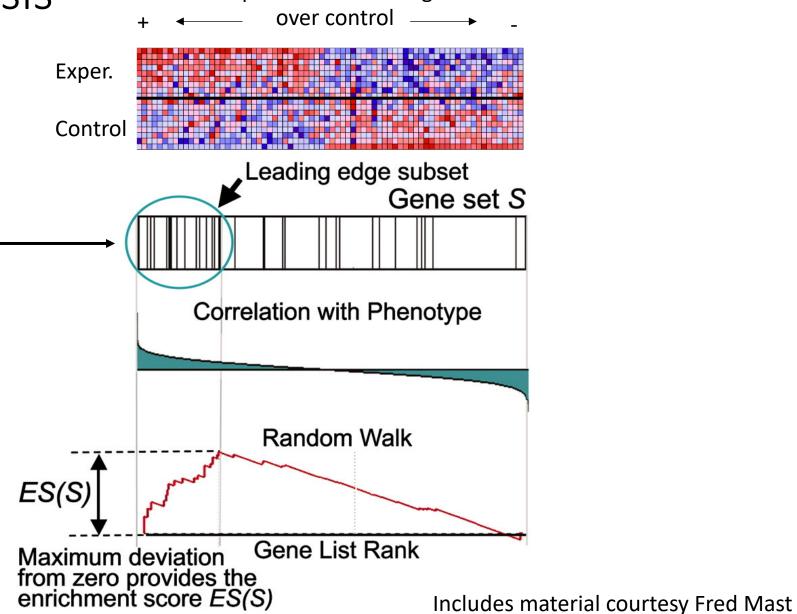
Known interactions from direct characterization



Gene Set Enrichment Analysis (GSEA)

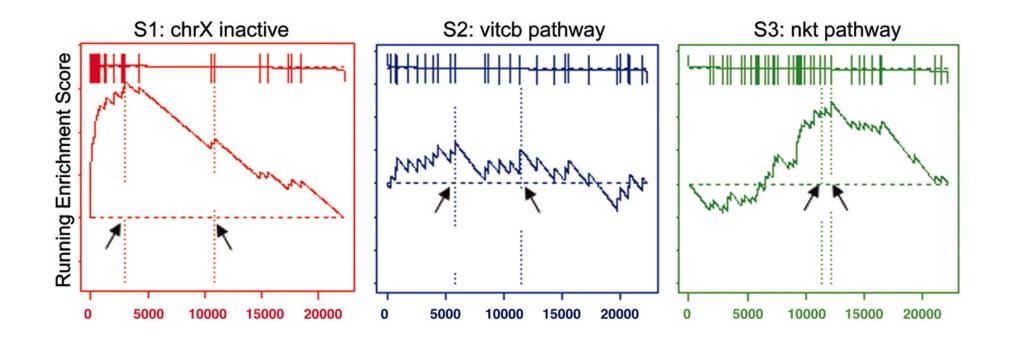


Subramanian, et al., 2005, PMID: **16199517**Sergushichev, 2016, doi.org/10.1101/060012
https://biostatsquid.com/fgsea-tutorial-gsea/

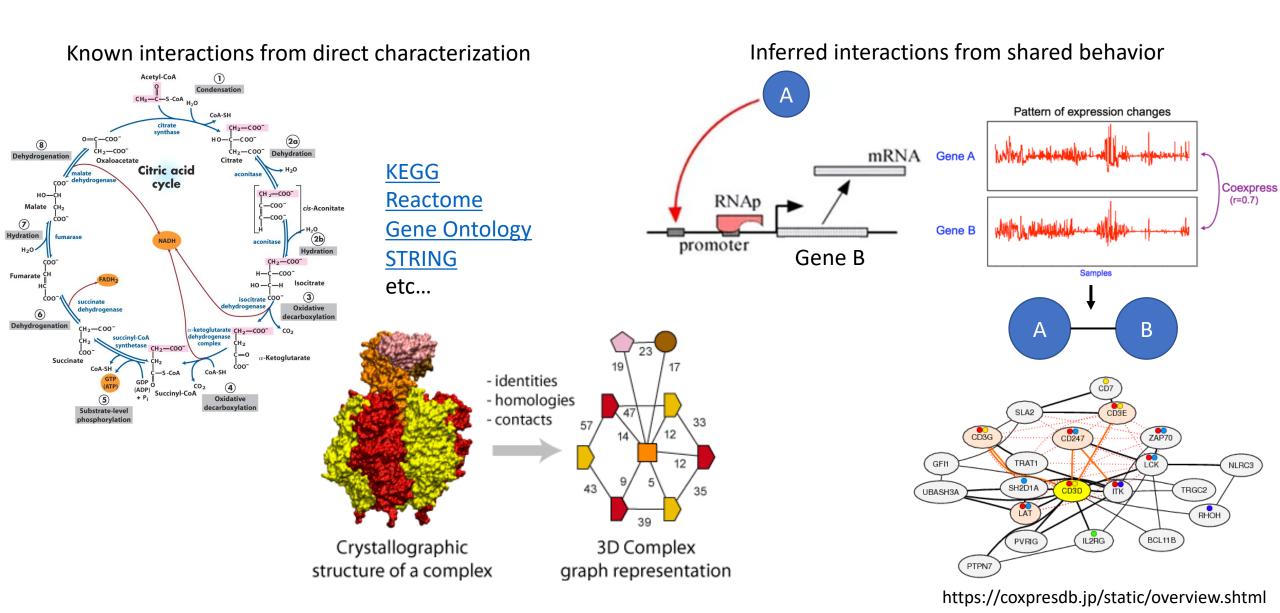


Expression fold-change

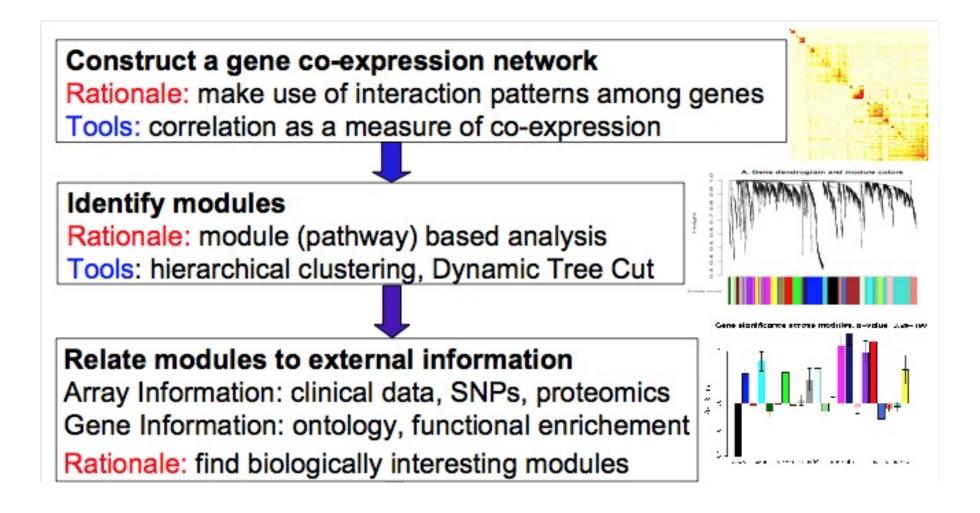
Enrichment scores measure association of gene set with phenotype



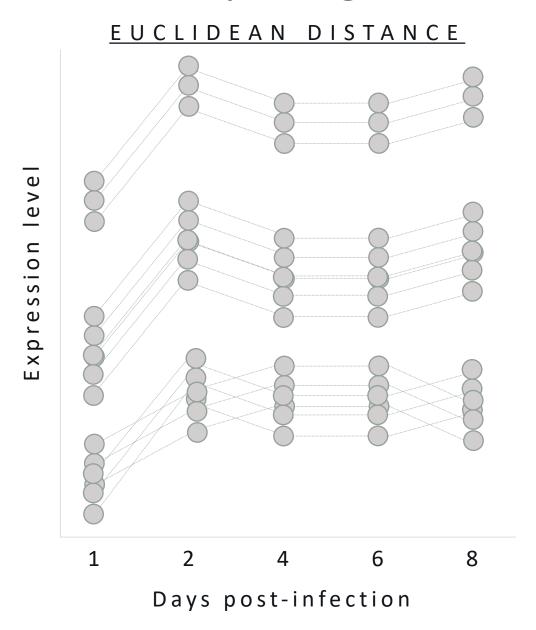
Annotated networks vs. data-driven networks

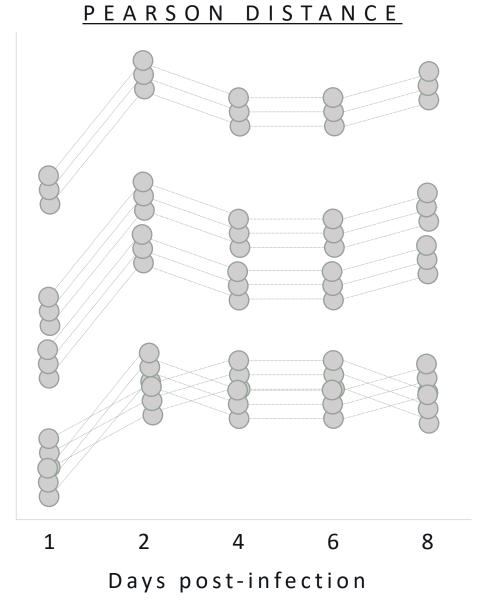


Weighted Gene Co-expression Network Analysis (WGCNA)



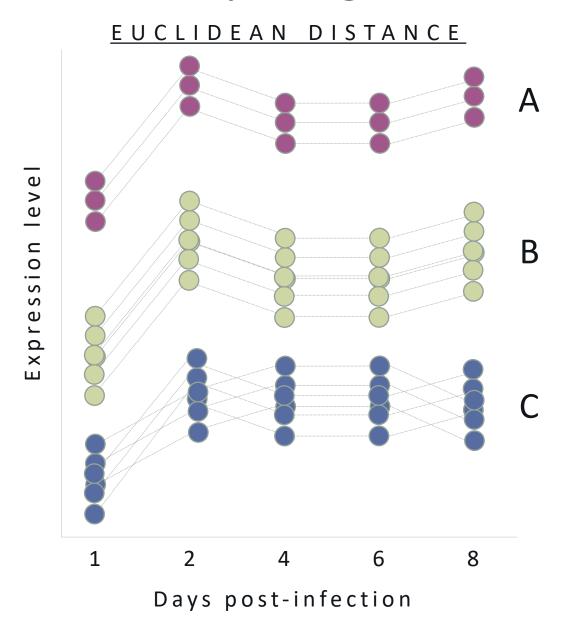
Comparing Distance Metrics for Co-expression

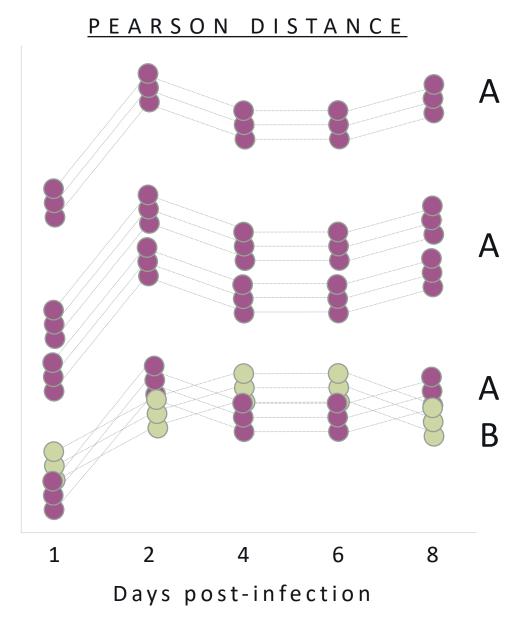




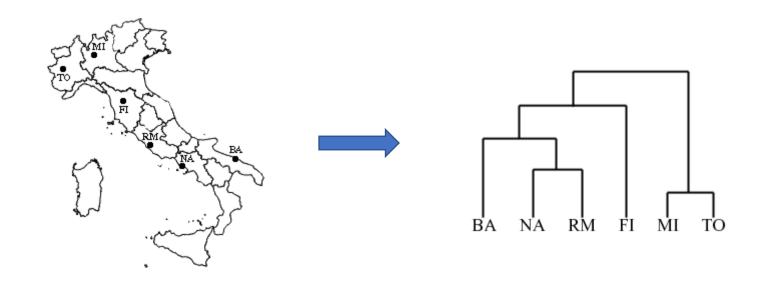
Adapted from slide courtesy Andrew Gustin

Comparing Distance Metrics for Co-expression





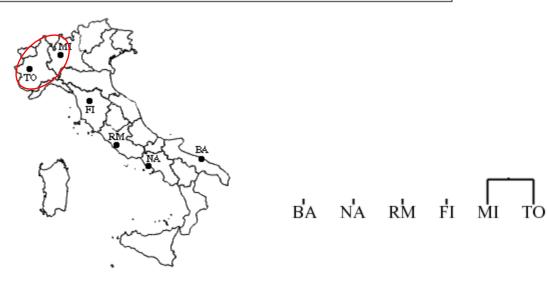
Adapted from slide courtesy Andrew Gustin



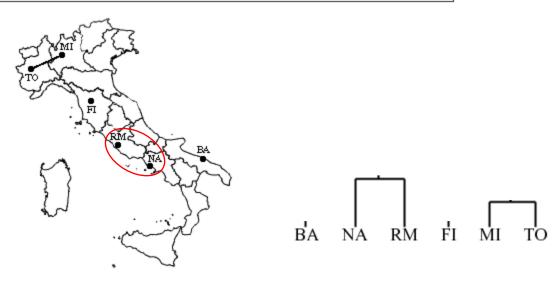
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BA	0	662	877	255	412	996
FI	662	0	295	468	268	400
MI	877	295	0	754	564	138
NA	255	468	754	0	219	869
RM	412	268	564	219	0	669
ТО	996	400	138	869	669	0



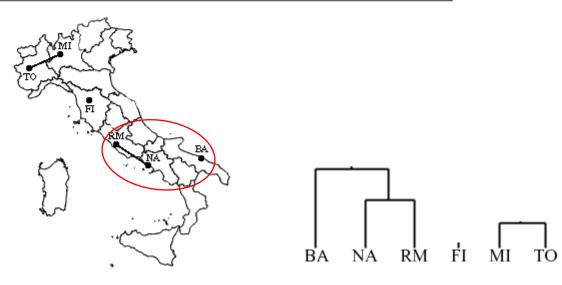
	BA	FI	MI	NA	RM	TO
BA	0	662	877	255	412	996
FI	662	0	295	468	268	400
MI	877	295	0	754	564	138
NA	255	468	754	0	219	869
RM	412	268	564	219	0	669
ТО	996	400	138	869	669	0



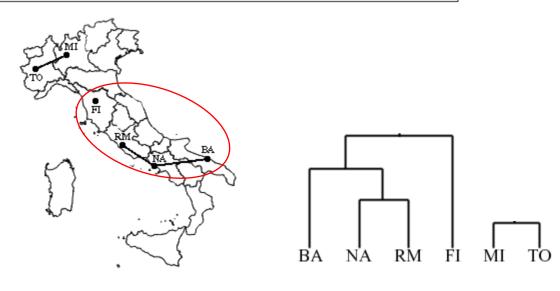
	BA	FI	MI/TO	NA	RM
BA	0	662	877	255	412
FI	662	0	295	468	268
MI/TO	877	295	0	754	564
NA	255	468	754	0	219
RM	412	268	564	219	0



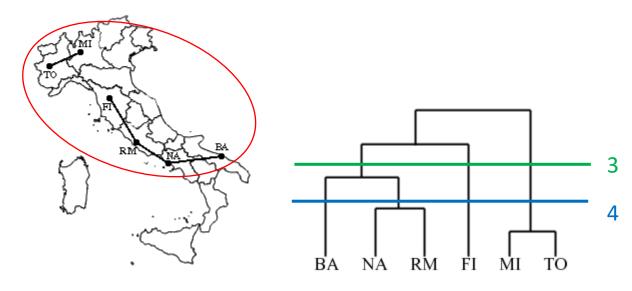
	BA	FI	MI/TO	NA/RM
BA	0	662	877	255
FI	662	0	295	268
MI/TO	877	295	0	564
NA/RM	255	268	564	0



	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	M I/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