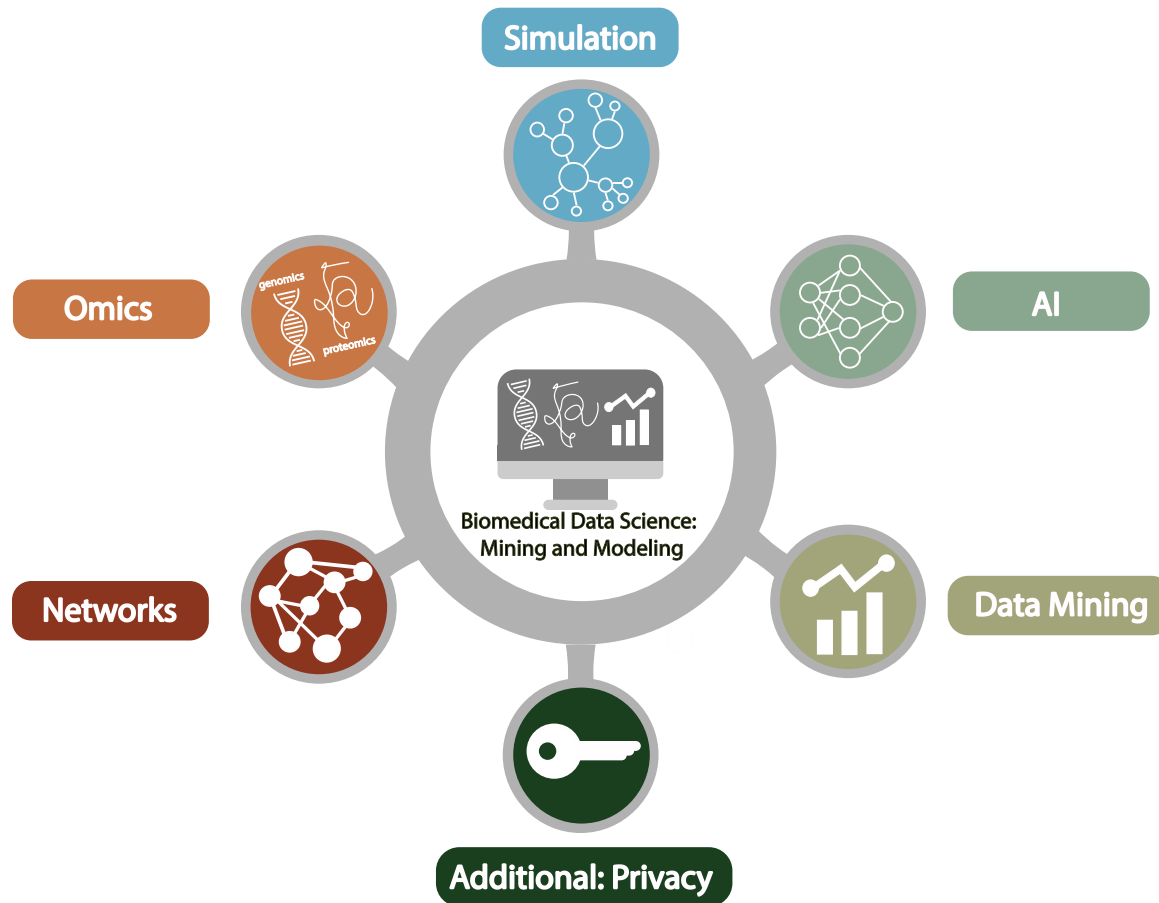


Biomedical Data Science (GersteinLab.org/courses/452)

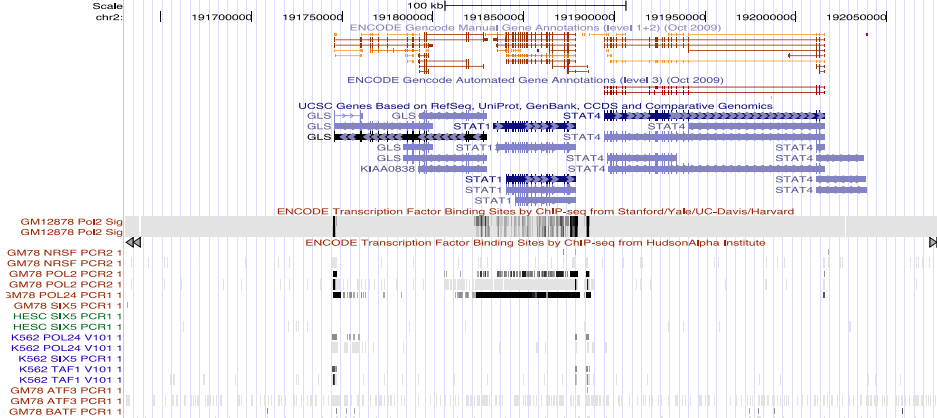
Network Topology -- Intro (25m10a)

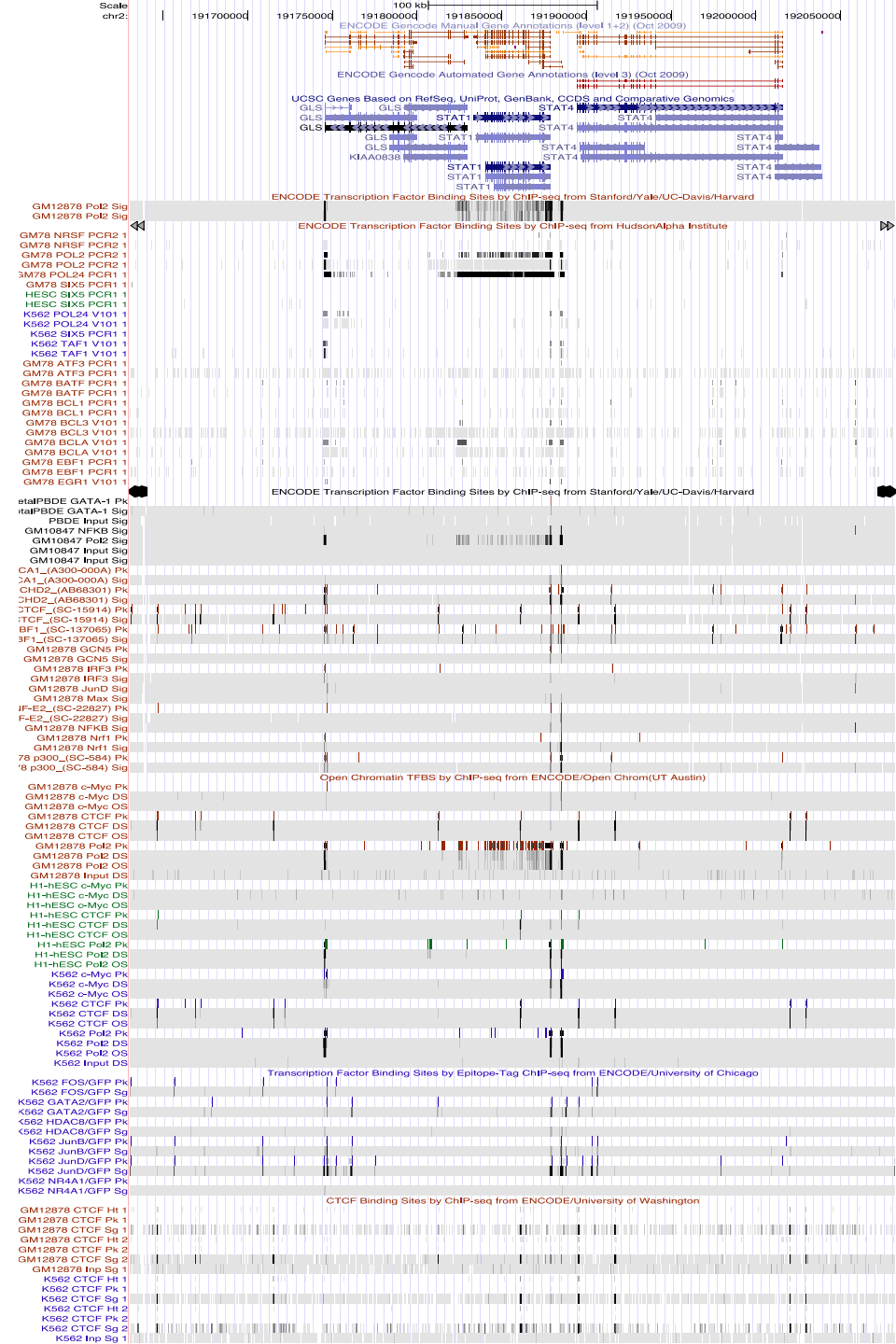


Network Topology

**Reasons for Networks:
Overcome shortcomings
of linear genome annotation**

Current Annotation: 1D Browser Tracks





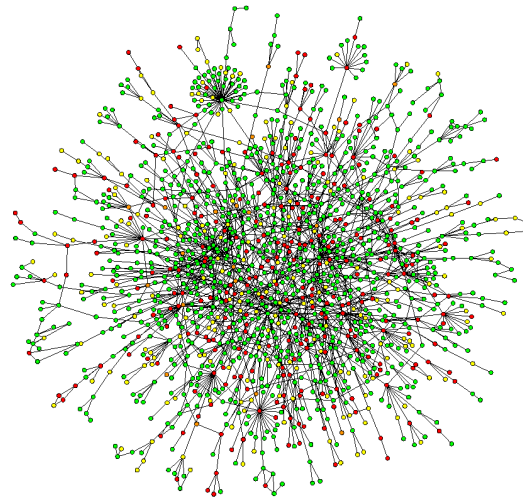
Current Annotation: 1D Browser Tracks

Will this scale to 1000+ tracks? What will next-gen annotation look like?...

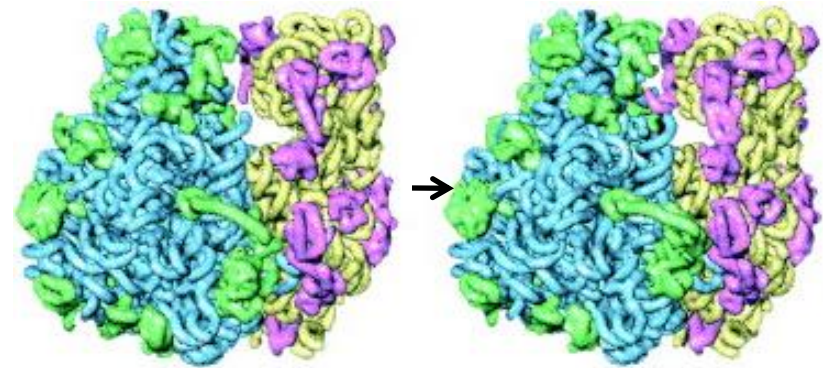
Systems from Parts

GM12878 c-Myc PK
 GM12878 c-Myc OS
 GM12878 CTCF PK
 GM12878 CTCF DS
 GM12878 CTCF OS
 GM12878 Pol2 DS
 GM12878 Pol2 OS
 GM12878 Input DS
 H1-hESC c-Myc PK
 H1-hESC c-Myc OS
 H1-hESC CTCF PK
 H1-hESC CTCF DS
 H1-hESC CTCF OS
 H1-hESC Pol2 PK
 H1-hESC Pol2 DS
 H1-hESC Pol2 OS
 K562 c-Myc PK
 K562 c-Myc DS
 K562 c-Myc OS
 K562 CTCF PK
 K562 CTCF DS
 K562 CTCF OS
 K562 Pol2 PK
 K562 Pol2 DS
 K562 Pol2 OS
 K562 Input DS
 K562 FOS/GFP PK
 K562 FOS/GFP DS
 K562 FOS/GFP OS
 K562 HDAC8/GFP PK
 K562 HDAC8/GFP DS
 K562 HDAC8/GFP OS

Transcription Factor Binding Sites by EpiProteTag ChIP-seq from ENCODE/University of Chicago



~2D: Network Wiring Diagram of a Molecular System



3D & 4D:
Detailed structural
understanding of cellular
machinery
(e.g. ribosome in different
functional states)

1D: Complete Partslist ("Elements" in genomic tracks)

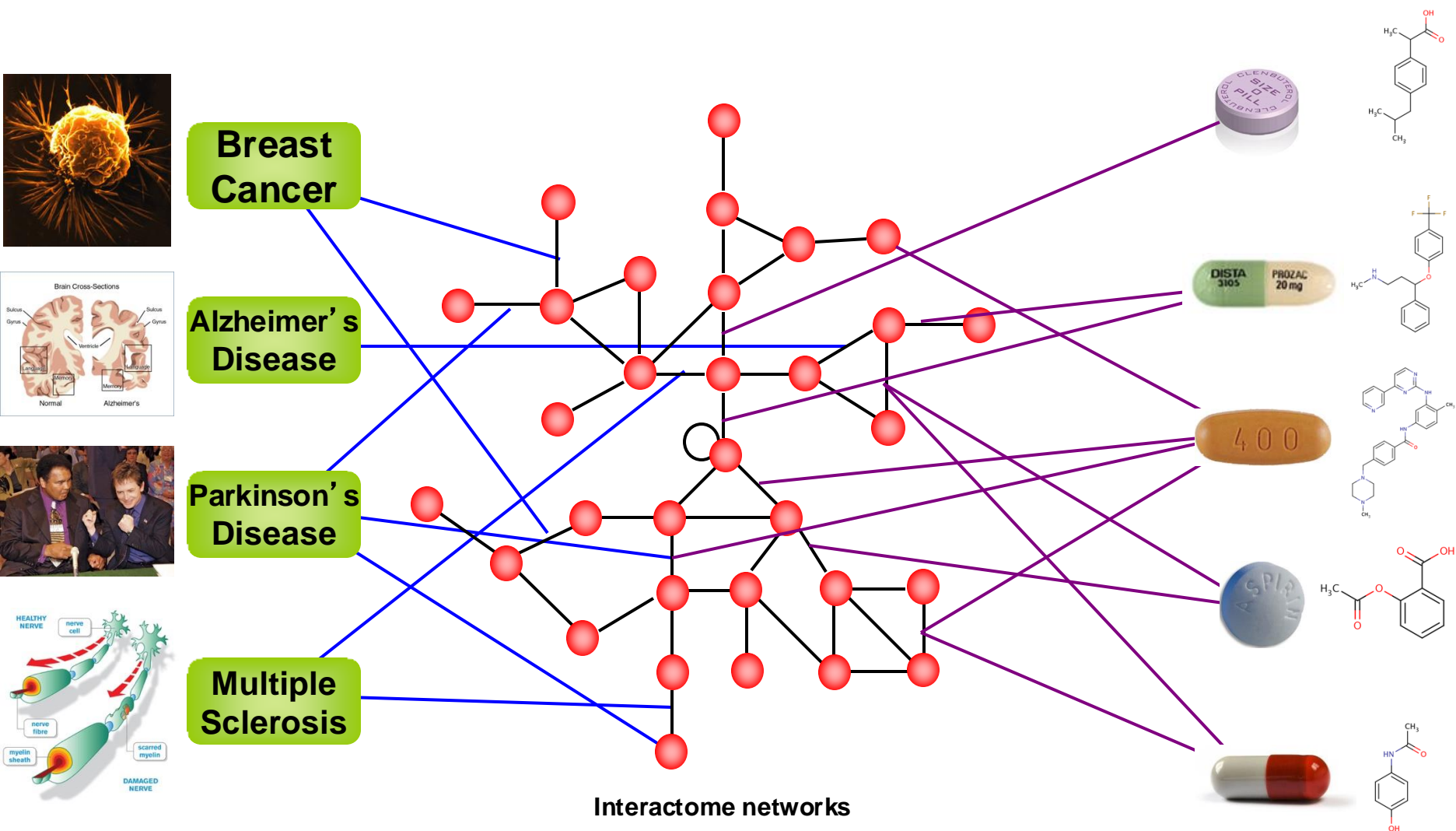
[Jeong et al. Nature, 41:41 1]

[Chiu et al. Trends in Cell Biol, 16:144]

Network Topology

**Reasons for Networks:
Useful way of thinking
about disease**

Network pathology & pharmacology



Interactome Networks and Human Disease

Vol 455 | 23 October 2008 | doi:10.1038/nature07385

nature

ARTICLES

Comprehensive genomic characterization defines human glioblastoma genes and core pathways

The Cancer Genome Atlas Research Network*

Phenotypes

Mendelian disorders

GWAs

Cancer genes

a

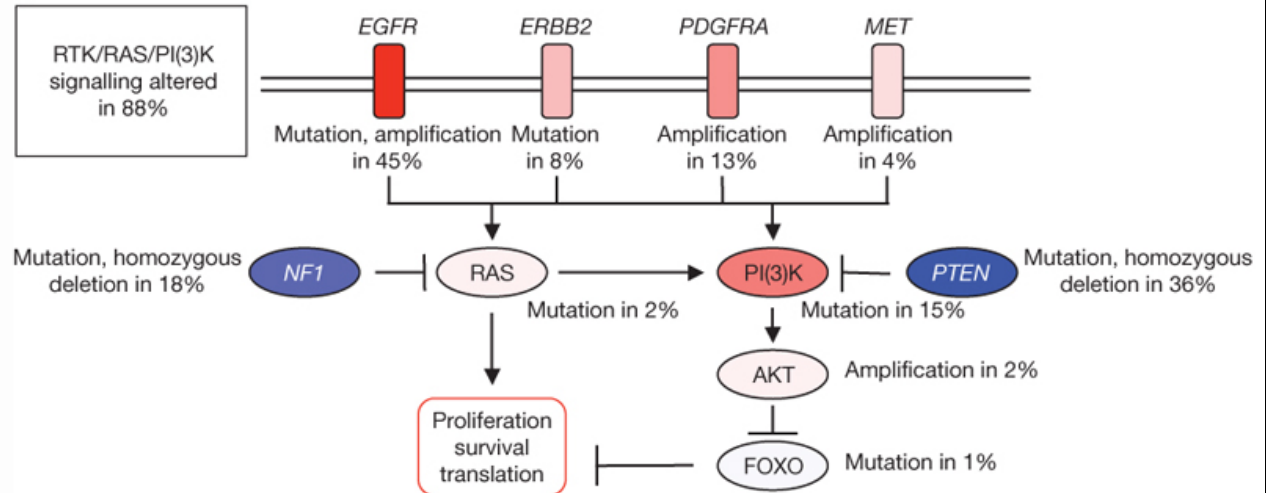
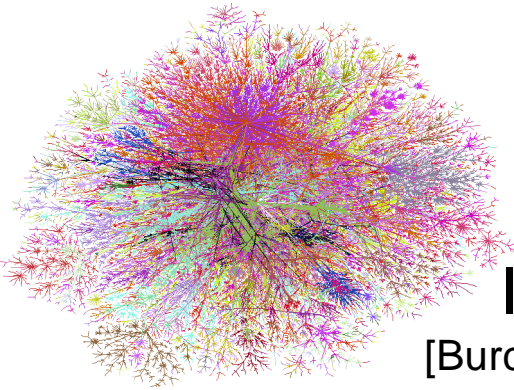


Figure 1. Perturbations in Biological Systems and Cellular Networks May Underlie Genotype-Phenotype Relationships

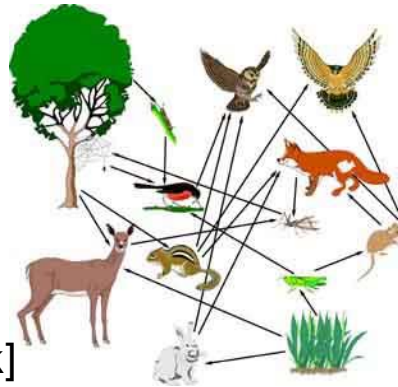
Network Topology

Reasons for Networks: Comprehensive representation, capable of representing many types of biological & non-biological data & bridging between disciplines

Networks as a universal language



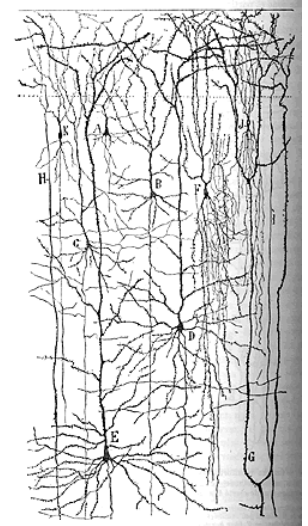
Internet
[Burch & Cheswick]



Food Web



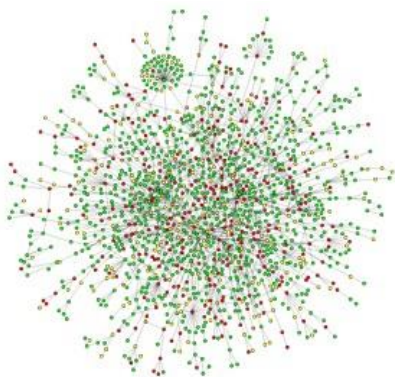
Electronic
Circuit



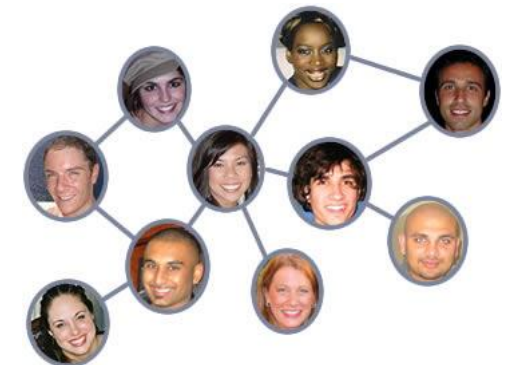
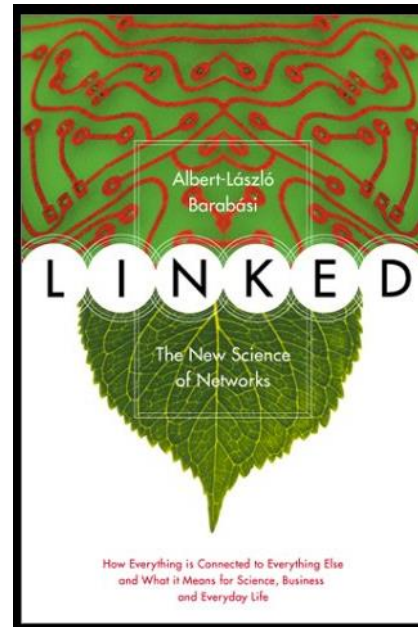
Neural Network
[Cajal]



Disease
Spread
[Krebs]



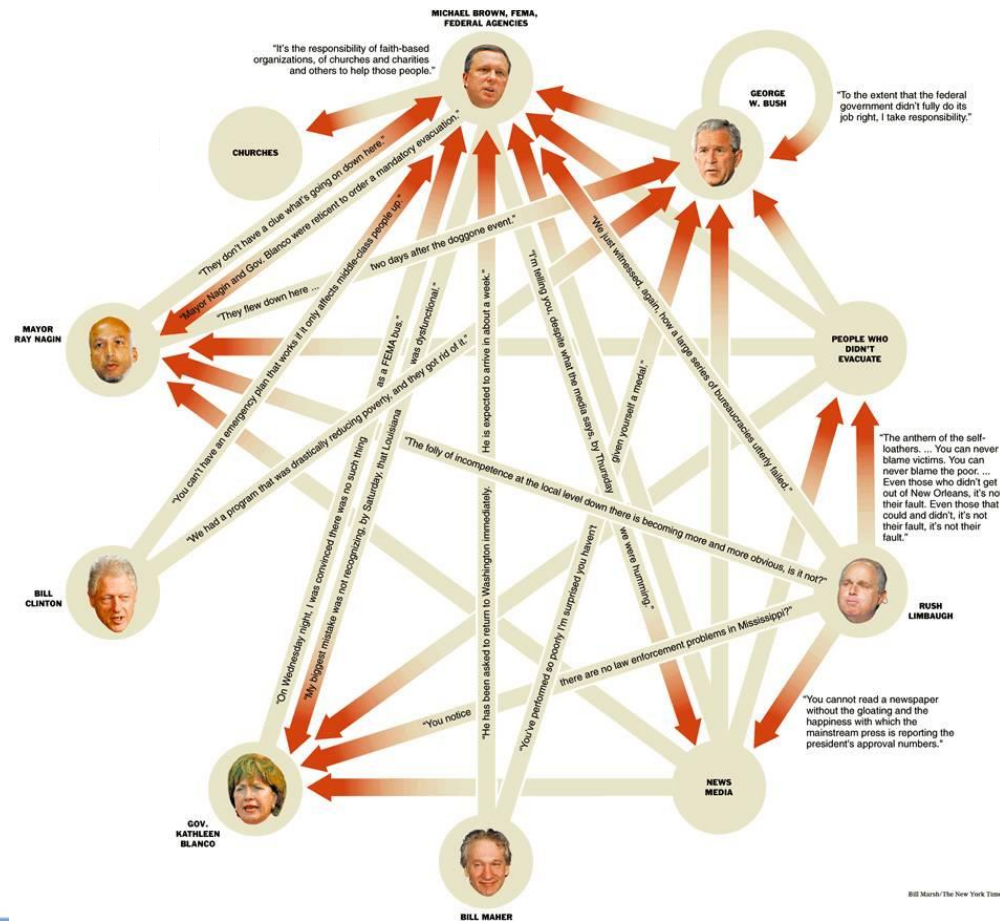
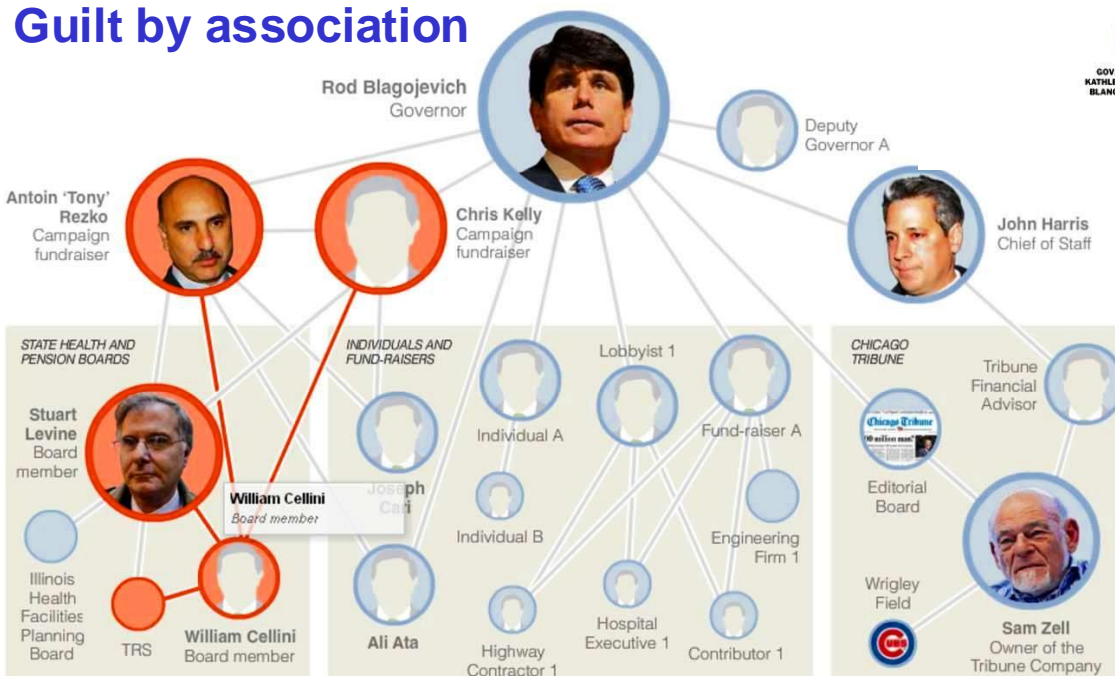
Protein
Interactions
[Barabasi]



Social Network

Using the position in networks to describe function

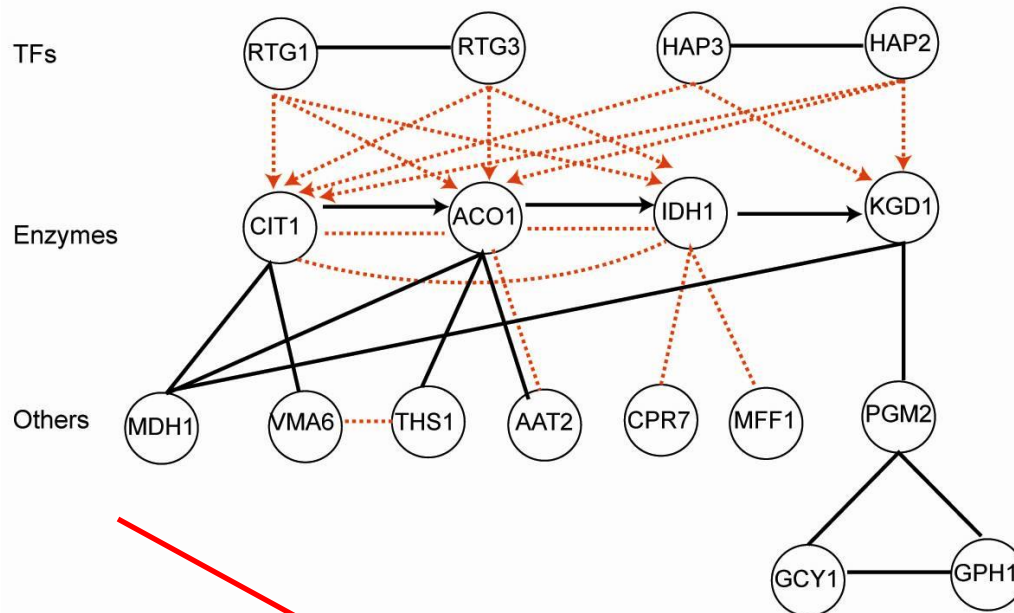
Guilt by association



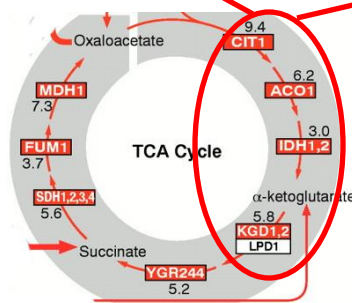
Finding the causal regulator (the "Blame Game")

[NY Times, 2-Oct-05, 9-Dec-08]

Combining networks forms an ideal way of integrating diverse information



- Metabolic pathway
- Transcriptional regulatory network
- Physical protein-protein Interaction
- Co-expression Relationship



Part of the TCA cycle

Genetic interaction
(synthetic lethal)
Signaling pathways

References

- McGillivray, P., Clarke, D., Meyerson, W., Zhang, J., Lee, D., Gu, M., Kumar, S., Zhou, H., & Gerstein, M. (2018). Annual Review of Biomedical Data Science, 1(1), 153–180.

Network analysis as a grand unifier in biomedical data science.

<https://doi.org/10.1146/annurev-biodatasci-080917-013444>

(Section 1.)