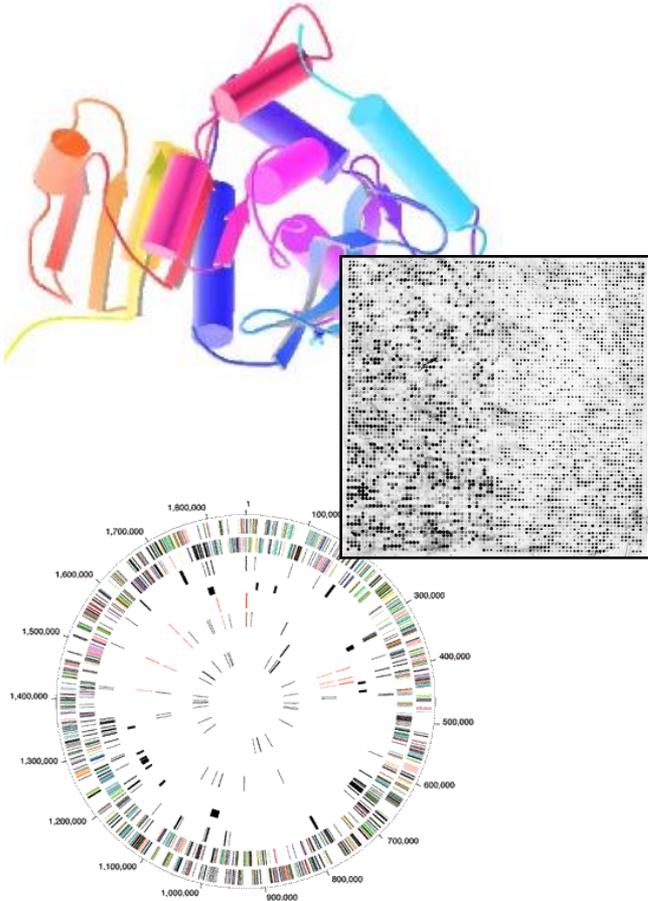


Biomedical Data Science: Analysis of Network Topology -- Intro



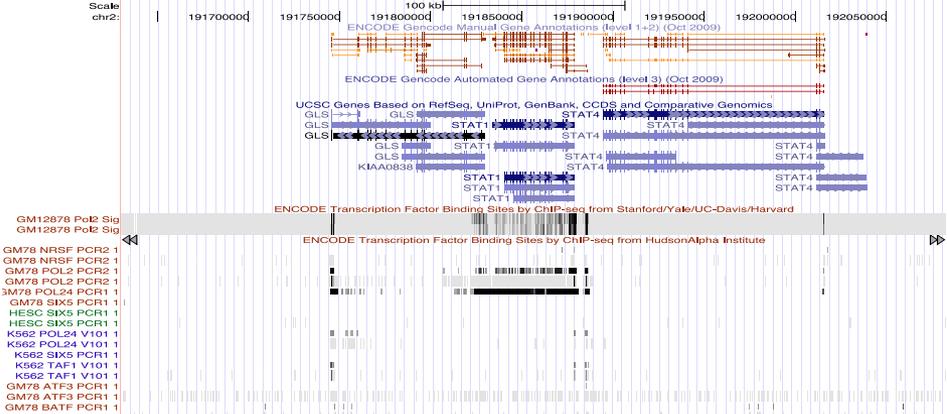
Mark Gerstein, Yale University
gersteinlab.org/courses/452

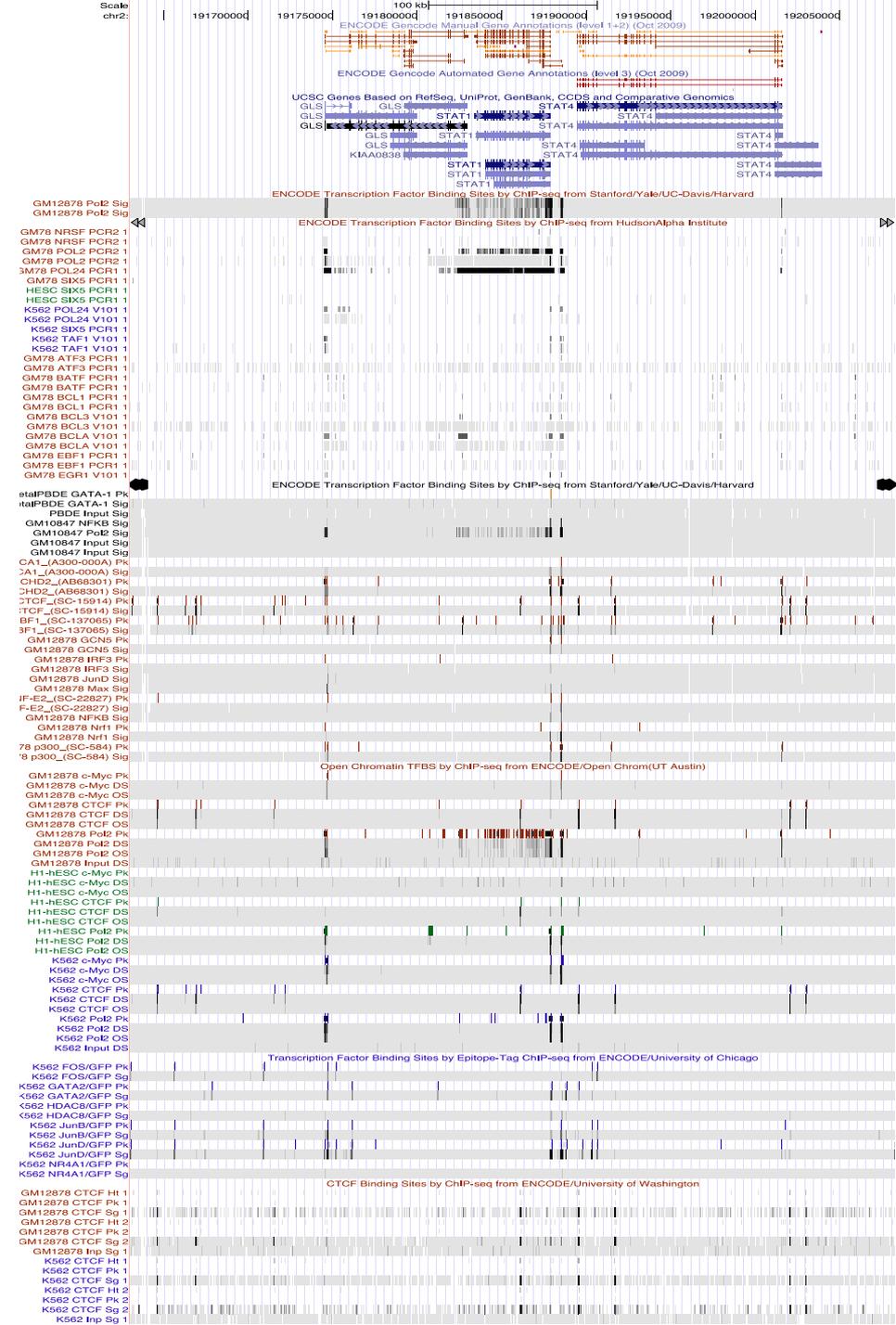
(Last edit in spring '22; pack 22m10a, very similar to M10a from '21.)

Network Topology

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

Current Annotation: 1D Browser Tracks



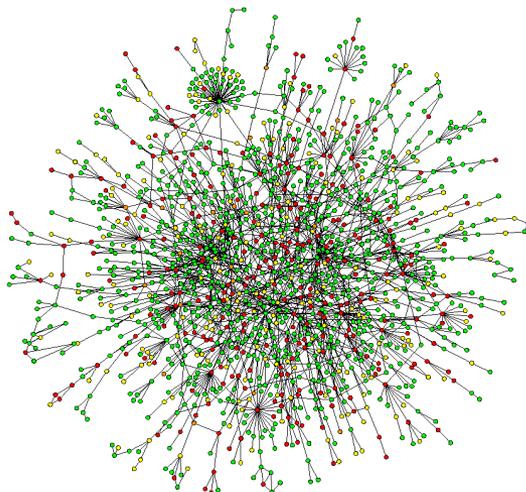
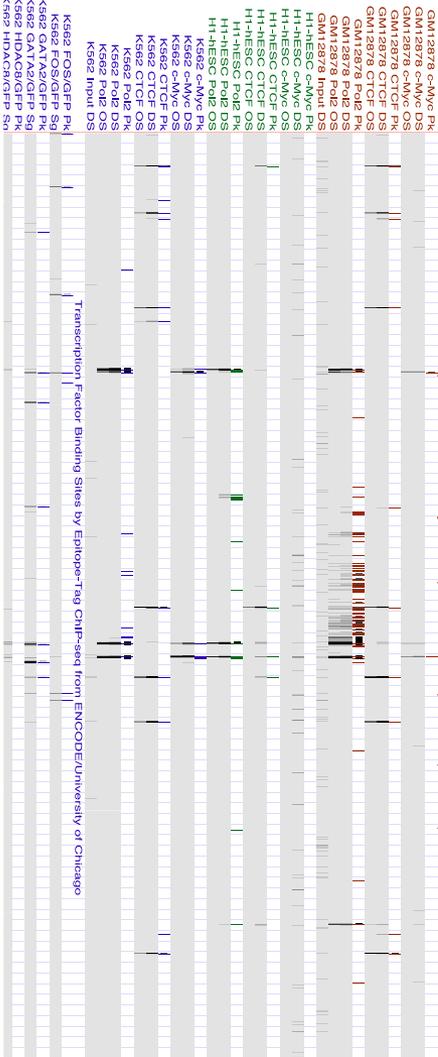


Current Annotation: 1D Browser Tracks

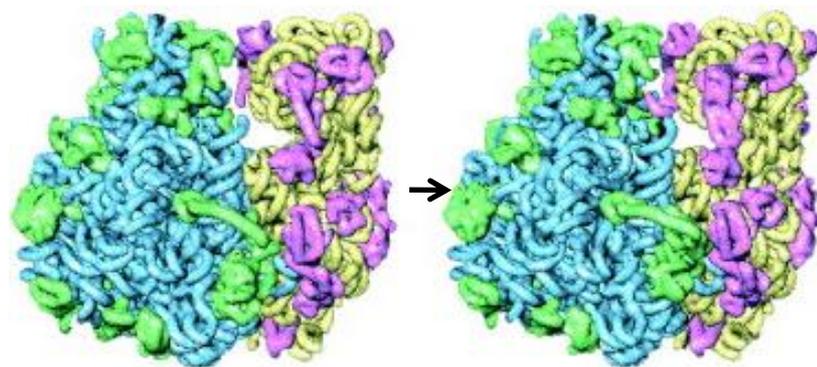
Will this scale to 1000+ tracks? What will next-gen annotation look like?...

Systems from Parts

Networks occupy a midway point in terms of level of understanding



~2D: Network Wiring Diagram of a Molecular System



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

[UCSC genome browser]

[Jeong et al. Nature, 41:411]

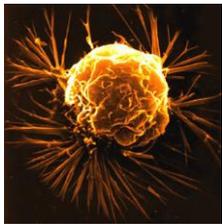
[Chiu et al. Trends in Cell Biol, 16:144]

1D: Complete Partslist (“Elements” in genomic tracks)

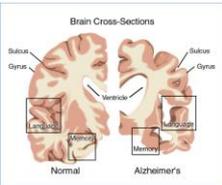
Network Topology

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

Network pathology & pharmacology



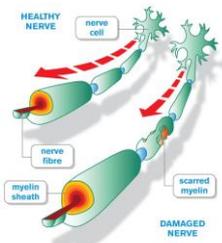
Breast Cancer



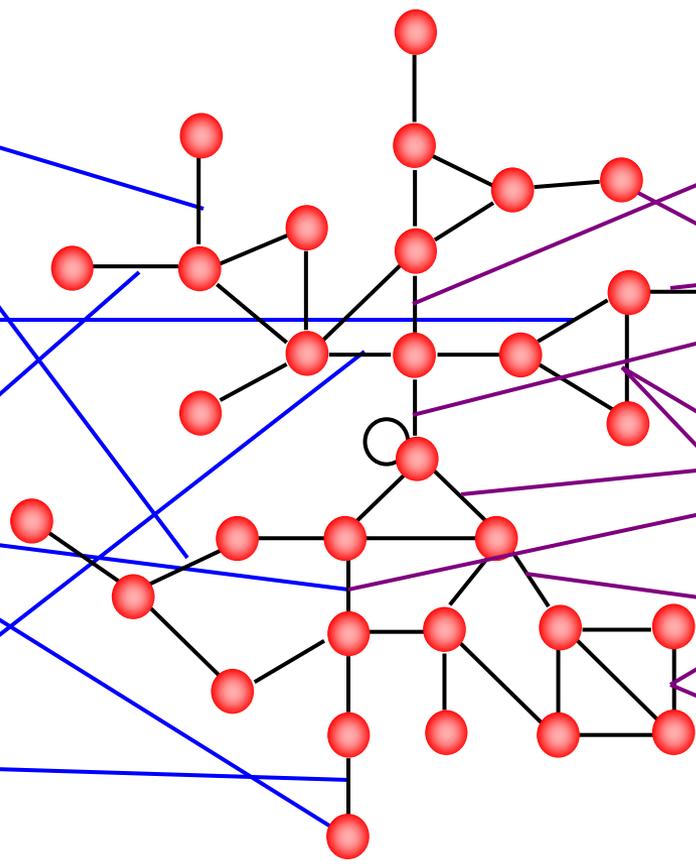
Alzheimer's Disease



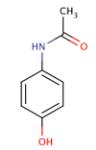
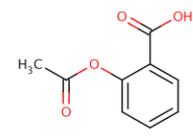
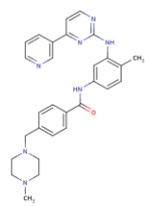
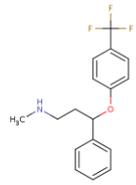
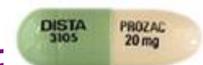
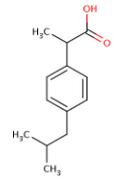
Parkinson's Disease



Multiple Sclerosis



Interactome networks



[Adapted from H Yu]

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*

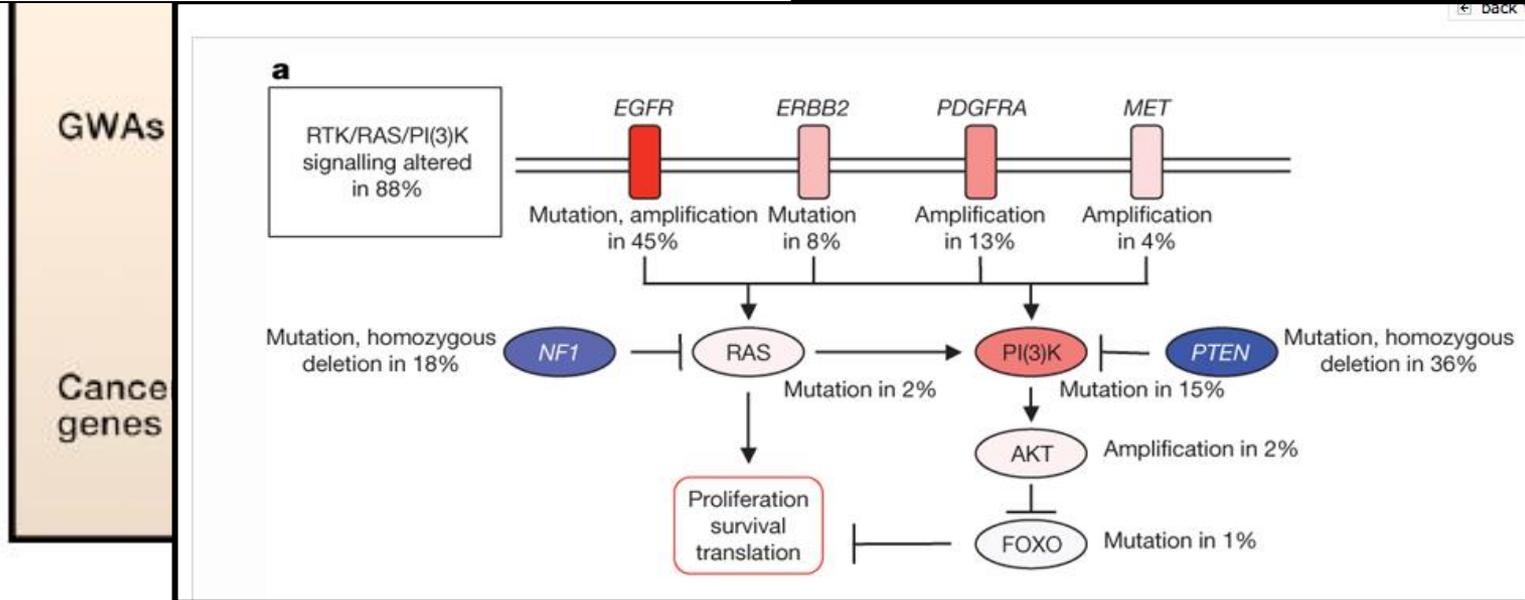
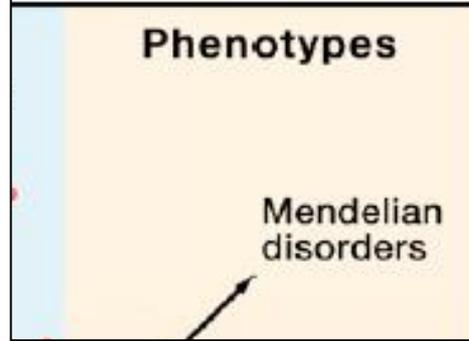
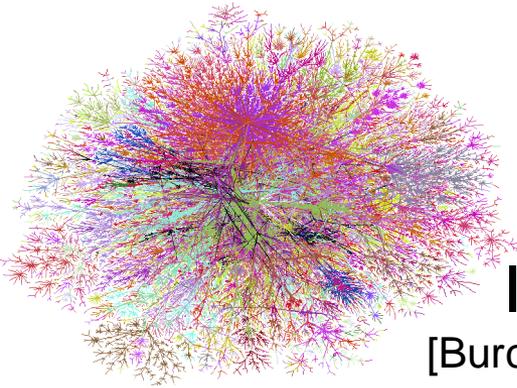


Figure 1. Perturbations in Biological Systems and Cellular Networks May Underlie Genotype-Phenotype Relationships

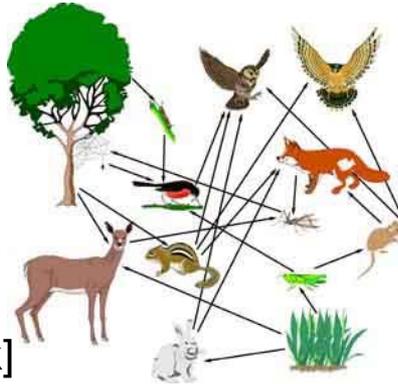
Network Topology

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

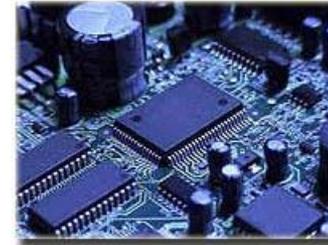
Networks as a universal language



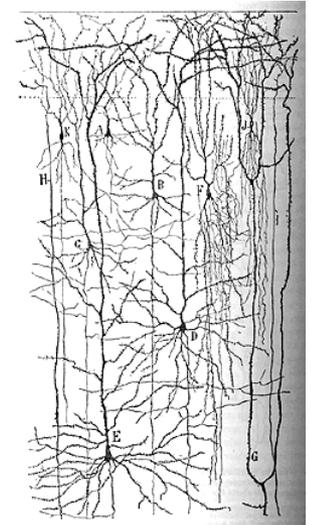
Internet
[Burch & Cheswick]



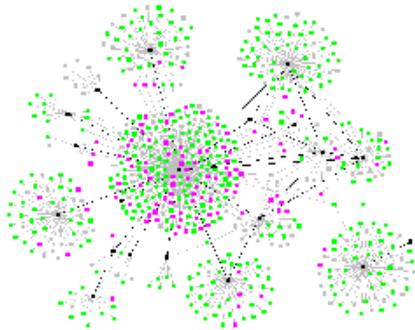
Food Web



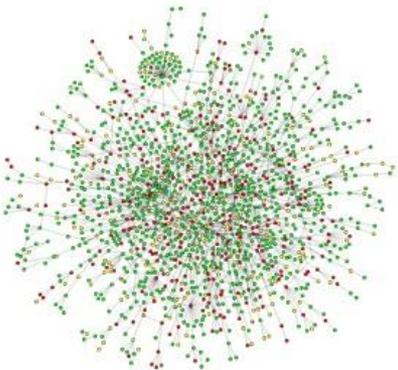
Electronic
Circuit



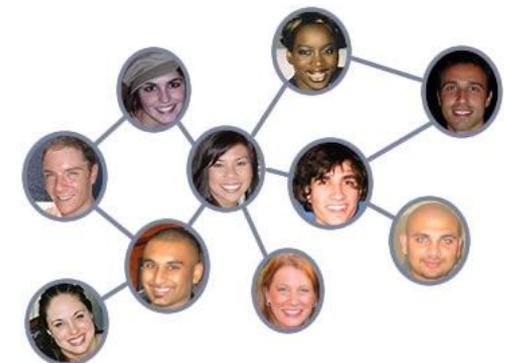
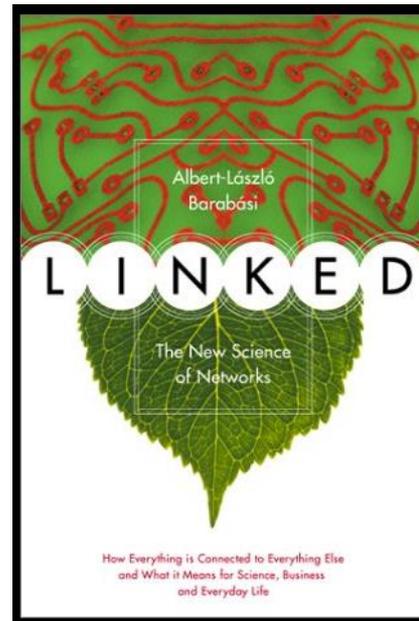
Neural Network
[Cajal]



Disease
Spread
[Krebs]



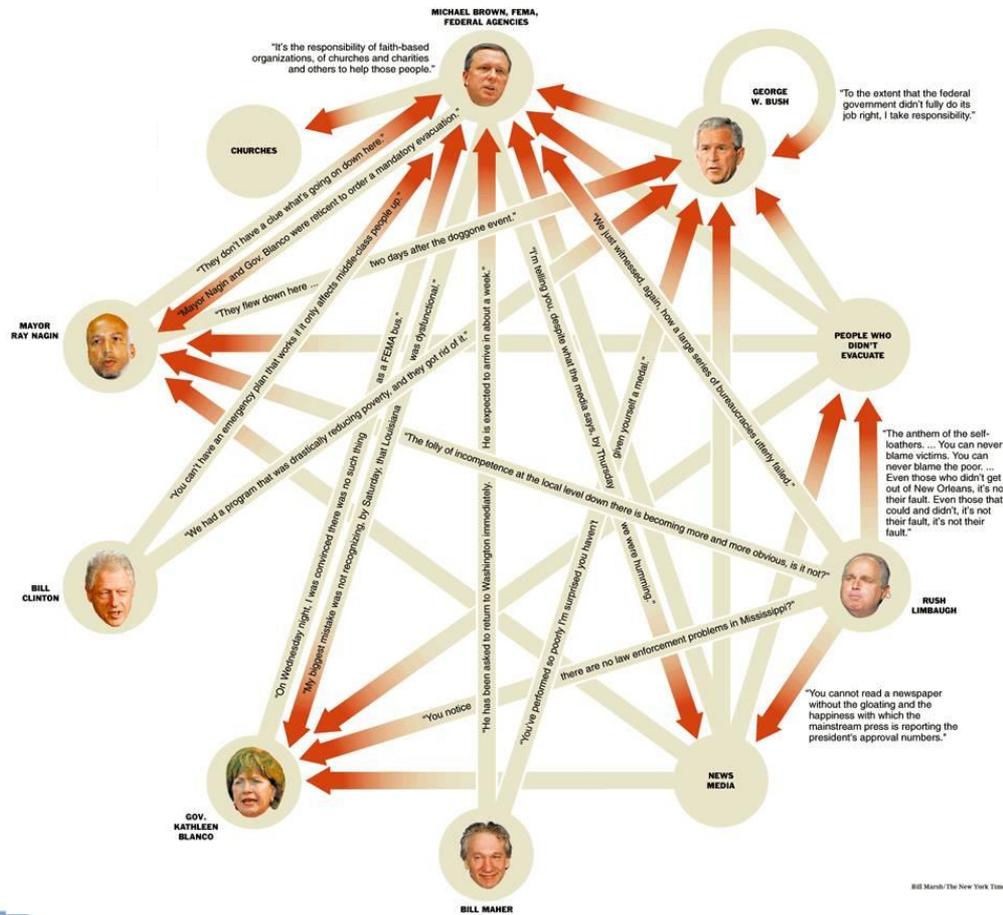
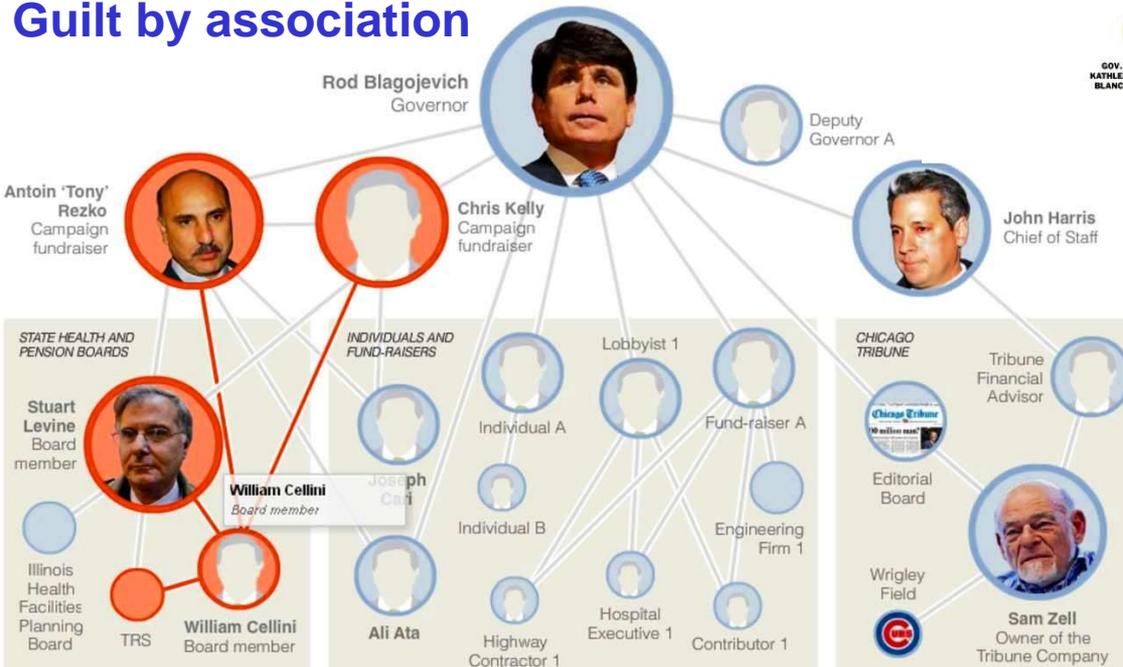
Protein
Interactions
[Barabasi]



Social Network

Using the position in networks to describe function

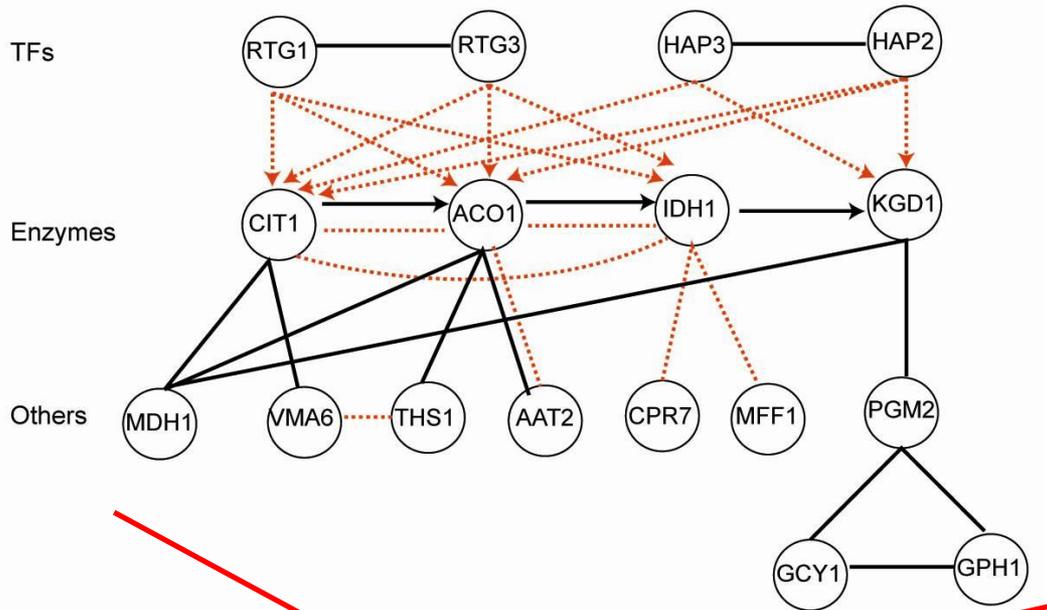
Guilt by association



Finding the causal regulator (the "Blame Game")

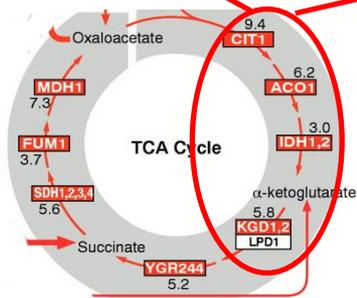
[NY Times, 2-Oct-05, 9-Dec-08]

Combining networks forms an ideal way of integrating diverse information



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

Genetic interaction (synthetic lethal)
Signaling pathways



Part of the TCA cycle