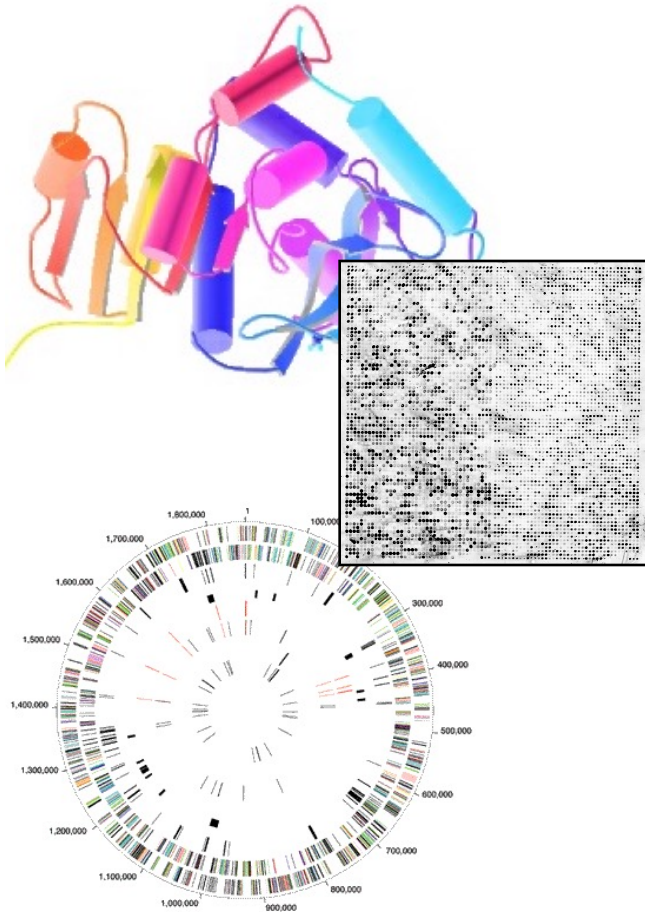


Biomedical Data Science: Analysis of Network Topology A - Intro

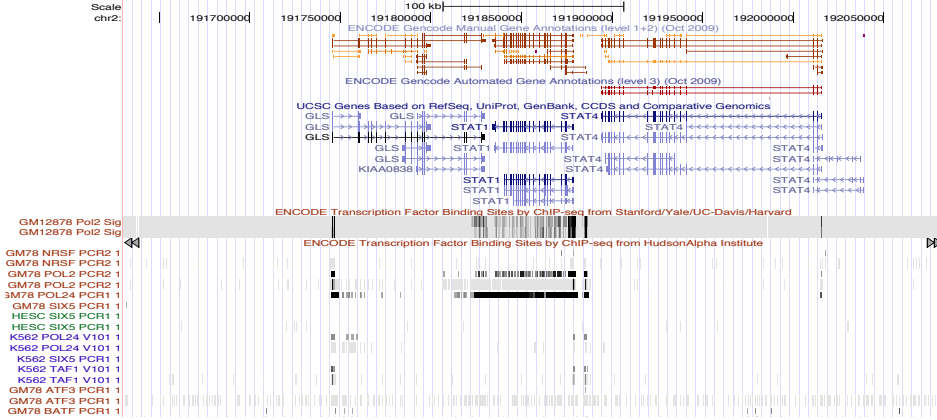


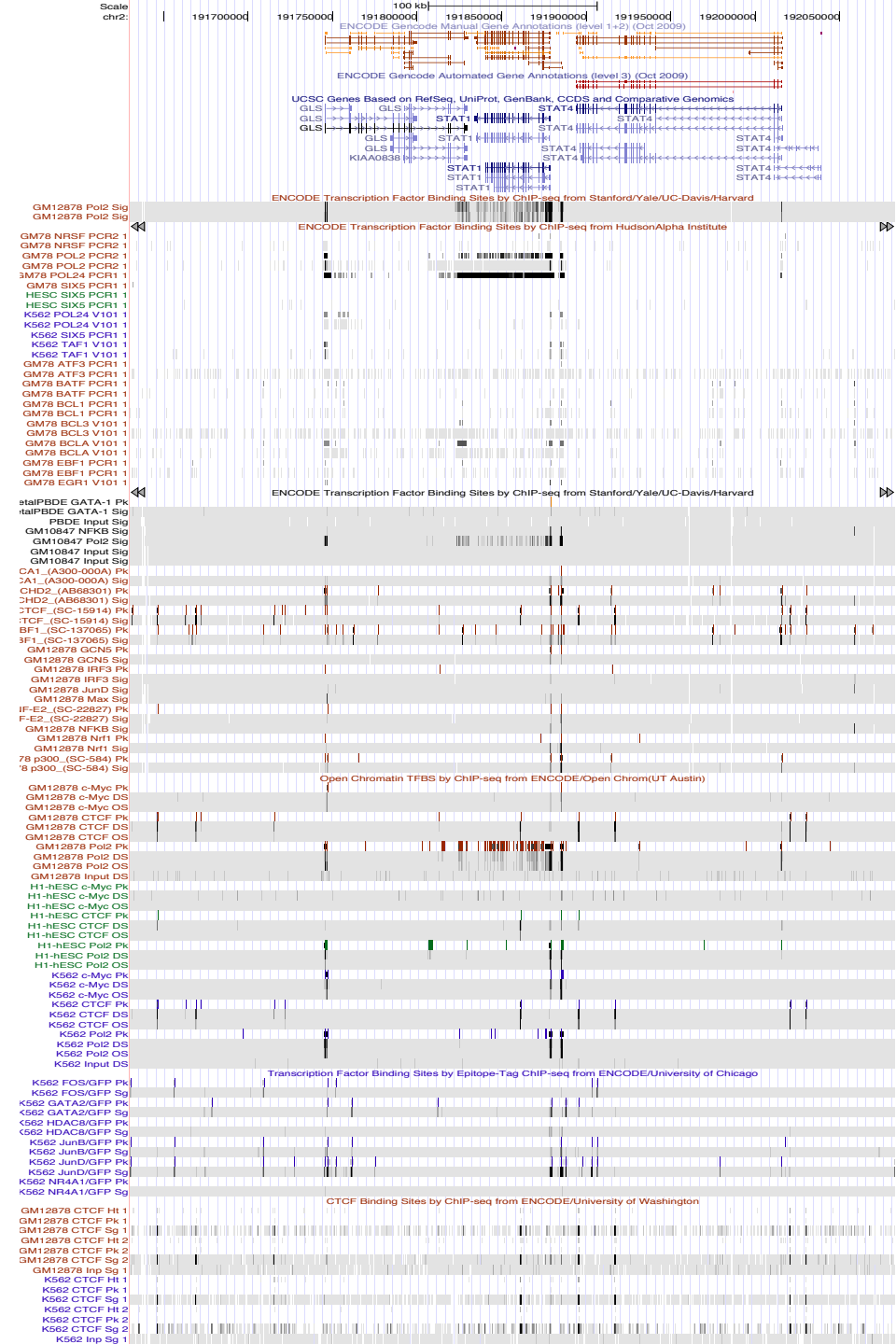
Mark Gerstein, Yale University
gersteinlab.org/courses/452
(last edit in spring '21, final)

Network Topology

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

Current Annotation: 1D Browser Tracks





Current Annotation: 1D Browser Tracks

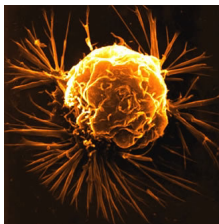
Will this scale to 1000+ tracks? What will next-gen annotation look like?...

Systems from Parts

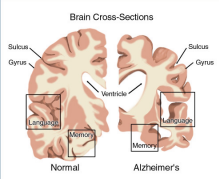
Network Topology

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

Network pathology & pharmacology



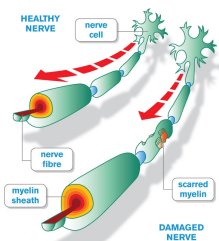
Breast Cancer



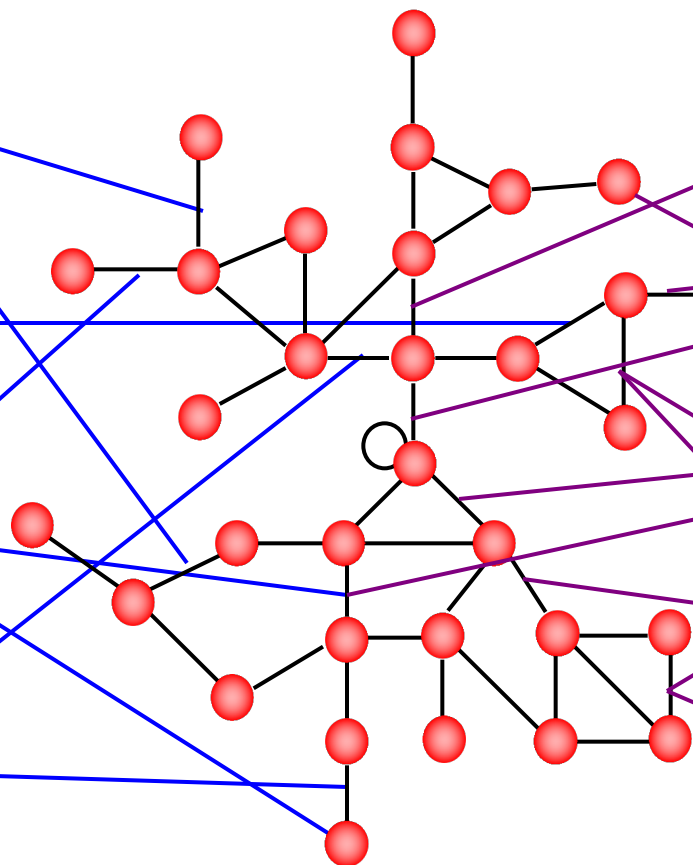
Alzheimer's Disease



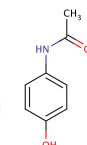
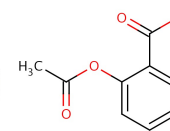
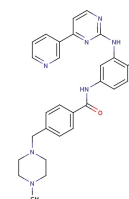
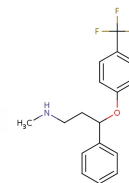
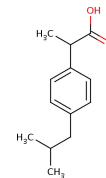
Parkinson's Disease



Multiple Sclerosis



Interactome networks



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

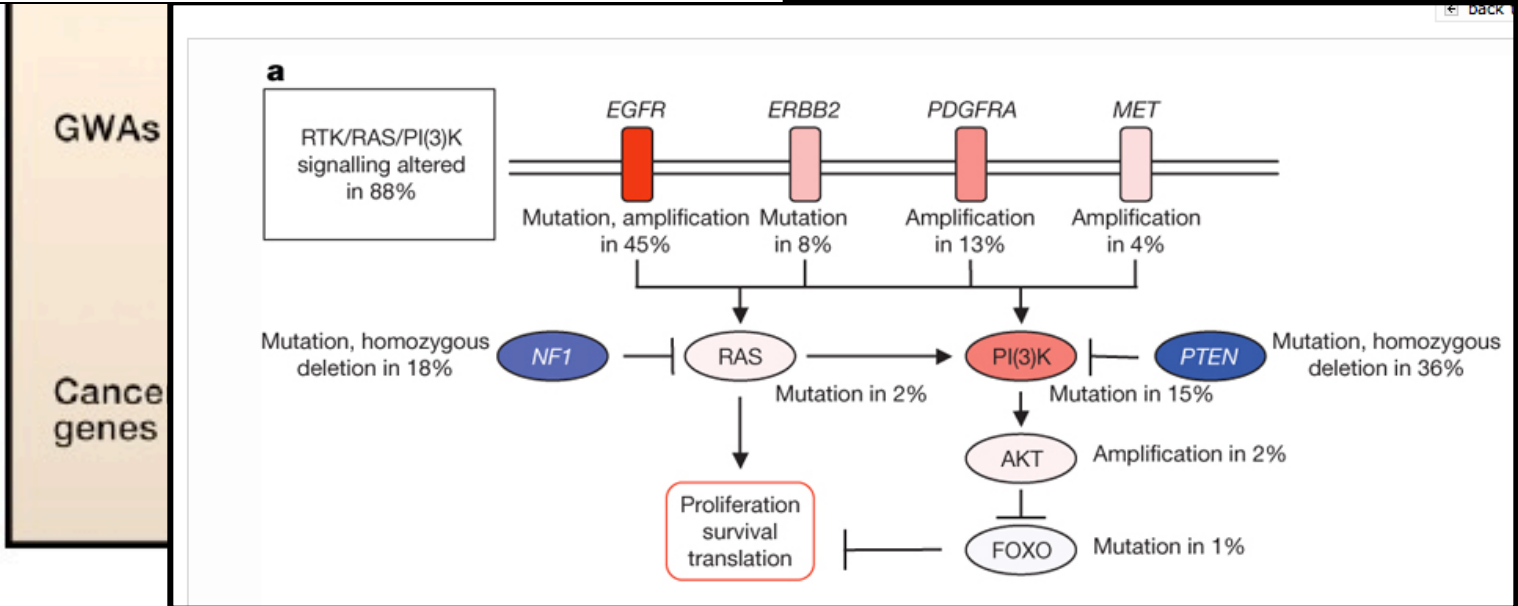
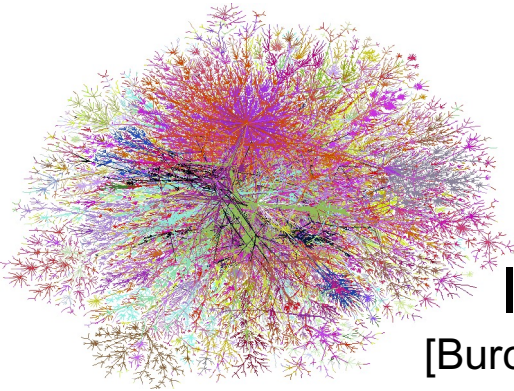


Figure 1. Perturbations in Biological Systems and Cellular Networks May Underlie Genotype-Phenotype Relationships

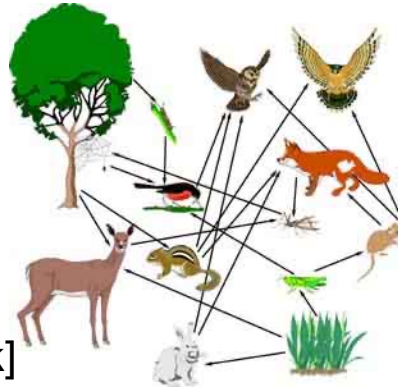
Network Topology

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

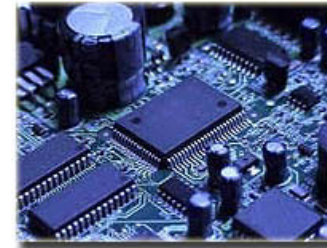
Networks as a universal language



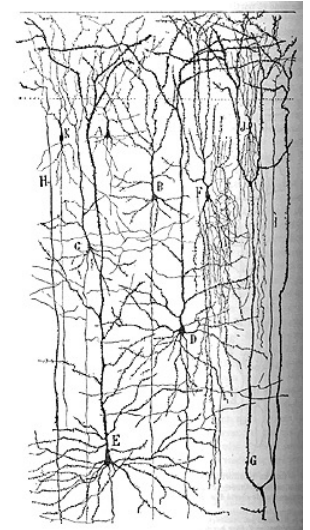
Internet
[Burch & Cheswick]



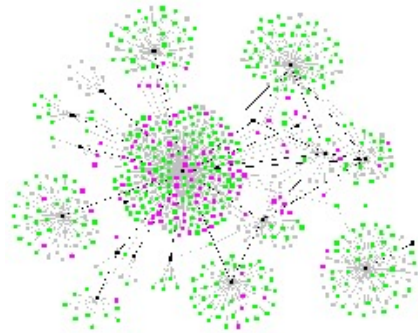
Food Web



Electronic
Circuit



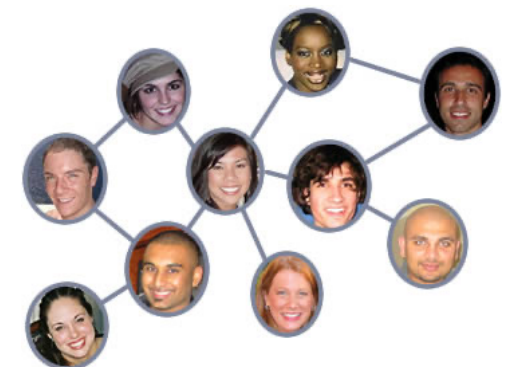
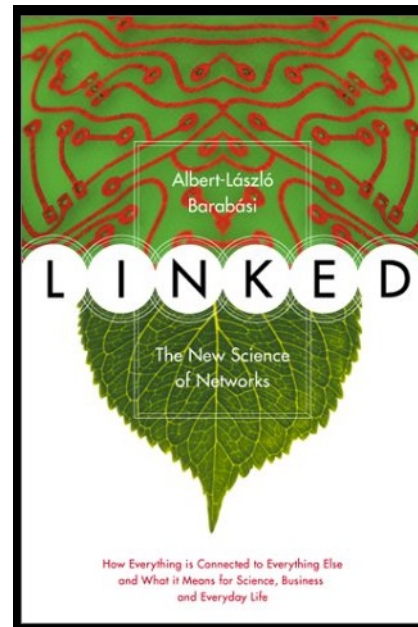
Neural Network
[Cajal]



Disease
Spread
[Krebs]



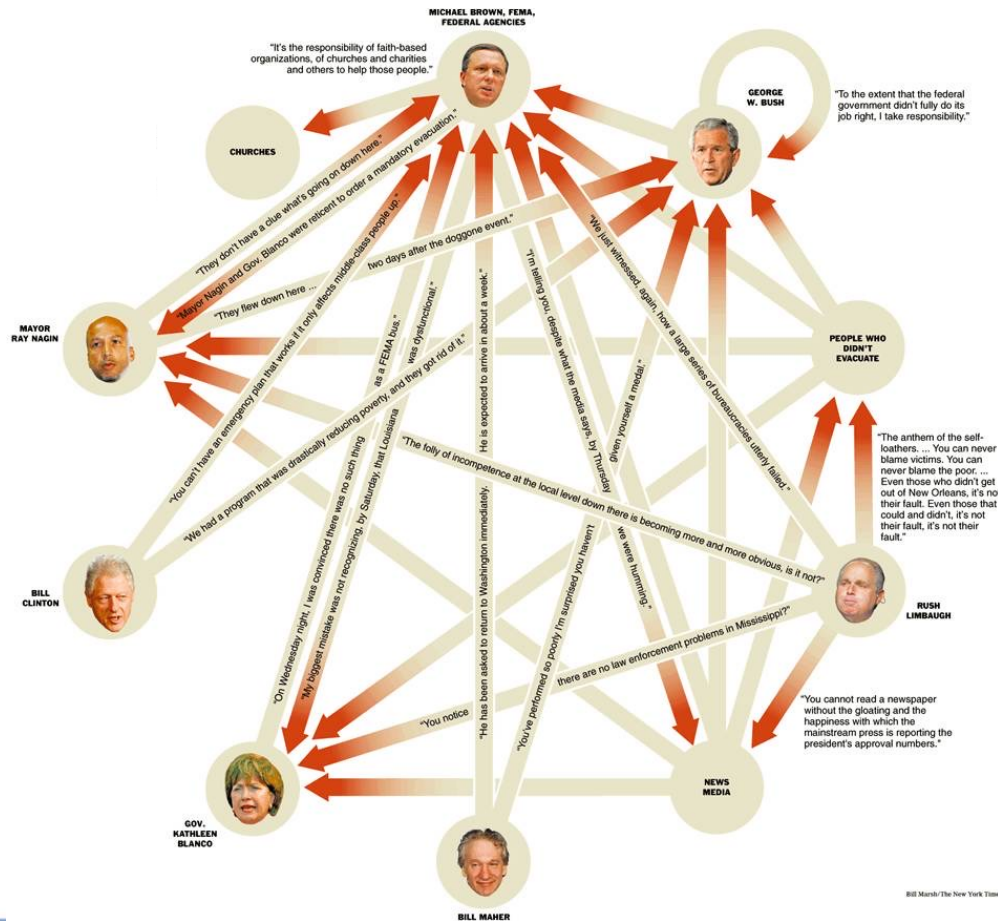
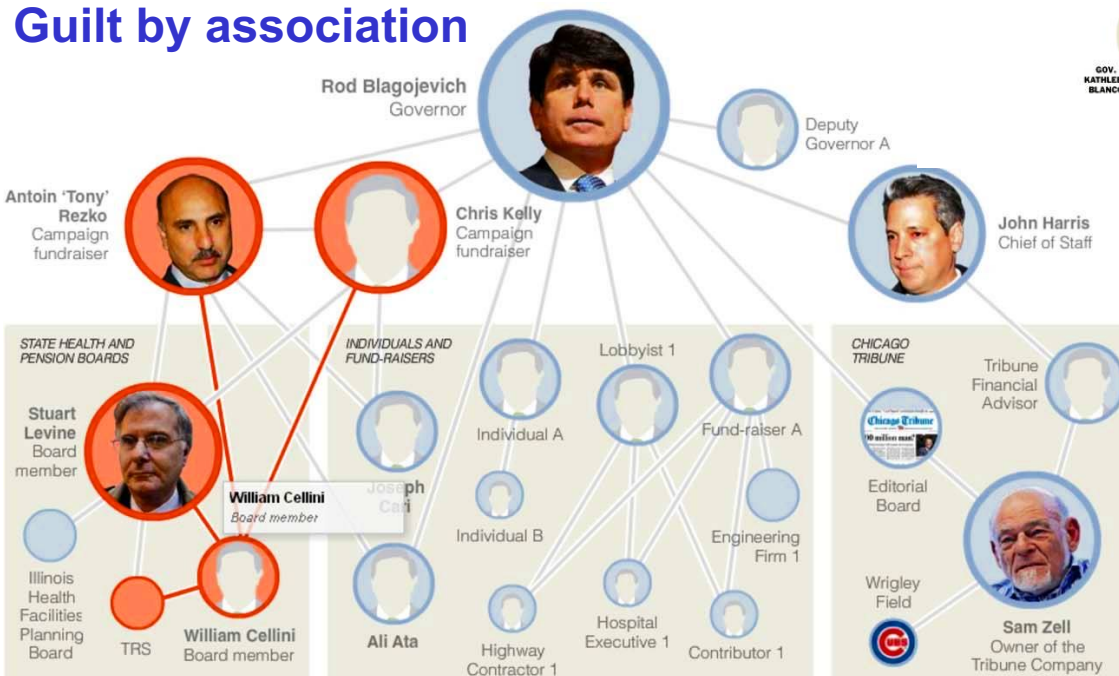
Protein
Interactions
[Barabasi]



Social Network

Using the position in networks to describe function

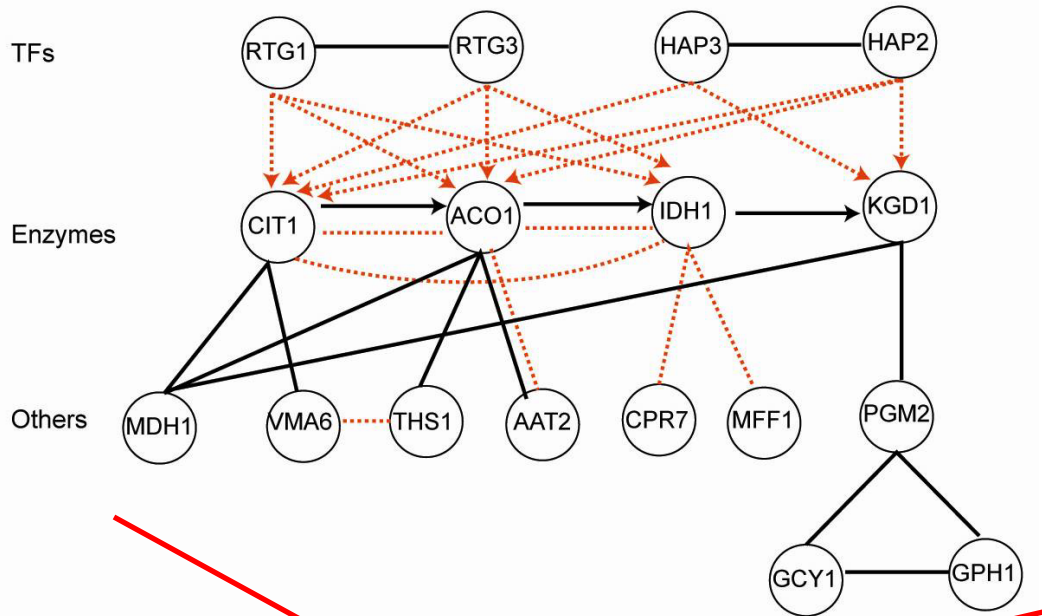
Guilt by association



Finding the causal regulator (the "Blame Game")

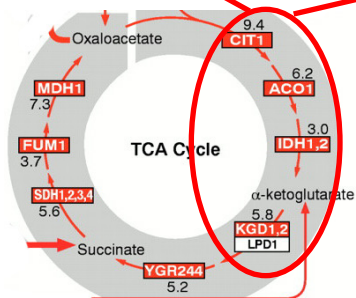
[NY Times, 2-Oct-05, 9-Dec-08]

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

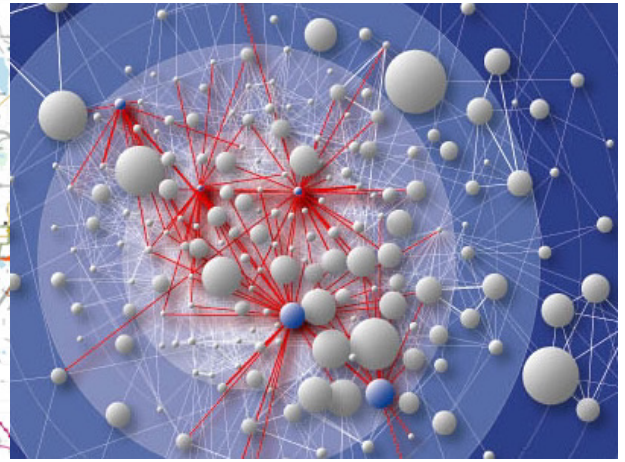
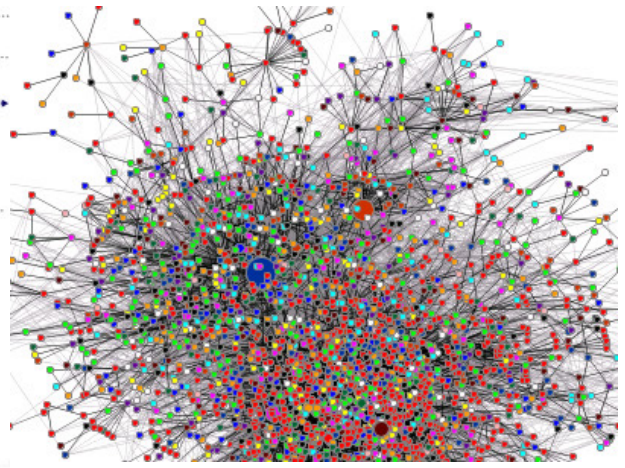
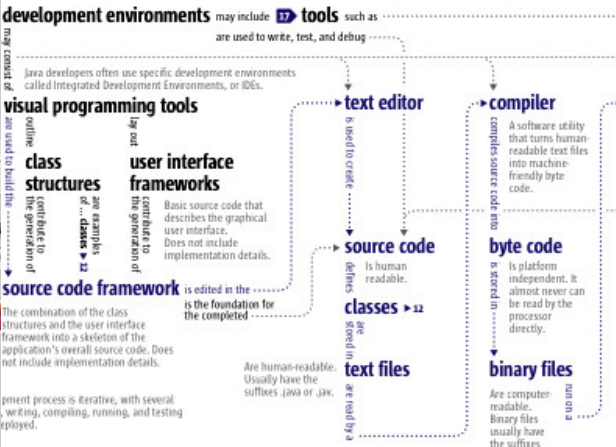


Part of the TCA cycle

Richness of the Visual Representation of Networks

VisualComplexity.com

Some structure (connectivity) but some flexibility (e.g. edge colors and shapes) that can be used to encode additional information



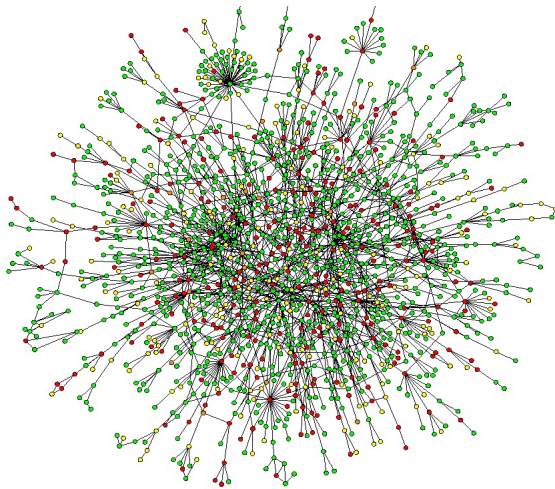
Network Topology

**Building Networks
in Genomics**

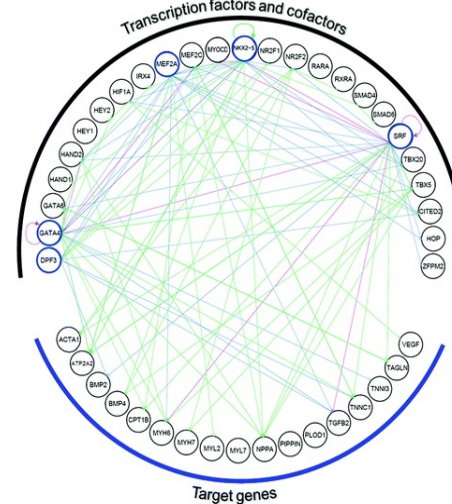
Origin of Networks

- Protein-protein interactions
 - ◇ Phosphorylation networks
- Metabolic Networks
- Regulatory networks
 - ◇ from Chip-Seq (see next slide)
- “Squared” scale
 - ◇ 6K genes in yeast but ~18M potential interactions (6000 chose 2 pairs of interactions)

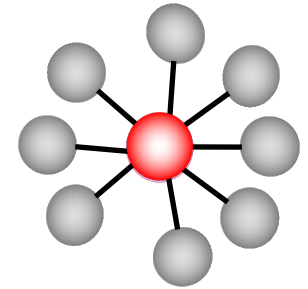
Different Types of Molecular Networks



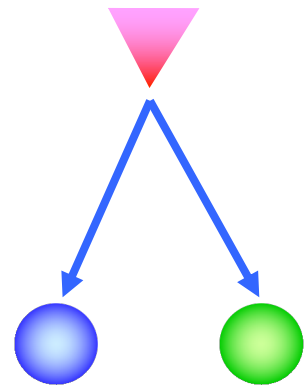
Protein-protein Interaction networks



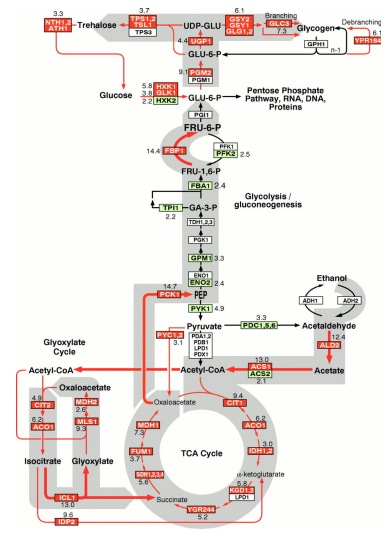
TF-target-gene Regulatory networks



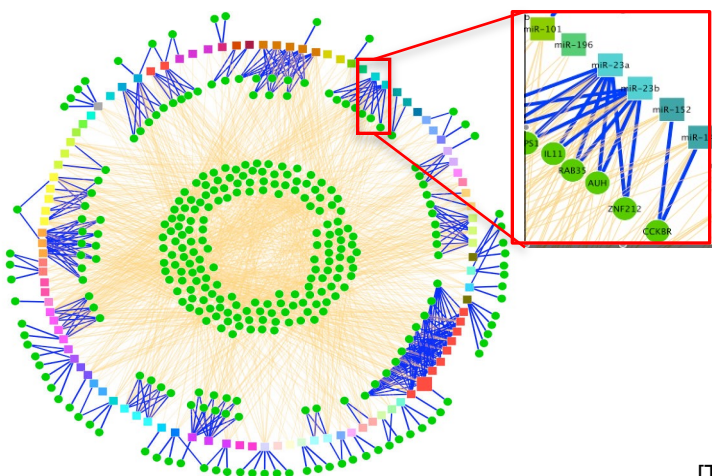
Undirected



Directed



Metabolic pathway networks



miRNA-target networks

[Toenjes, *et al*, *Mol. BioSyst.* (2008); Jeong *et al*, *Nature* (2001); [Horak, *et al*, *Genes & Development*, 16:3017-3033; DeRisi, Iyer, and Brown, *Science*, 278:680-686]