Interactome Networks Discussion

MarK Vidal
MarC Gerstein
Dana Pe’er
Mike Snyder

You
Networks as a universal language

- Internet [Burch & Cheswick]
- Food Web
- Electronic Circuit
- Disease Spread [Krebs]
- Protein Interactions [Barabasi]
- Neural Network [Cajal]
- Social Network

Books:
- Linked: The New Science of Networks
- The New Science of Networks
Genomic analyses of genotype to phenotype relationships

International HapMap Project

1,000 Genomes

Genotype

Phenotype

ENCODE

The Cancer Genome Atlas
Limitations:

**Mendelian traits**
- Incomplete penetrance and variable expressivity
- Pleiotropy or allelic heterogeneity
- Modifier genes

**Complex traits**
- High number of loci
- Small effect per locus
- Challenges from limitations of statistical power
Interactome Networks and Human Disease

Marc Vidal,1,2,* Michael E. Cusick,1,2 and Albert-László Barabási1,3,4,*

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

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
Will this scale to 1000s of tracks? What will the next generation of annotation look like?
Current Encode Annotation: 1D Browser Tracks

Will this scale to 1000s of tracks?

What will the next generation of annotation look like?
ENCODE Networks: wiring diagrams as 2nd Generation Annotation

- Some init. networks generated in mod/ENCODE
- Variety of types (TF=>gene, micro-RNA=>target, 5C, Expr. Corr.)
- Some use interpreting modencode data
More Comprehensive Yeast Networks as a Model of the Future

[Yu et al., PNAS (2006)]
Given this, should we in the future use ENCODE data to systematically generate Reference Networks
Uses of Reference Networks as Scaffolds for Mapping Sequence Variation & Cellular Dynamics

Regulatory Networks Active in Yeast

- Cell cycle
- Sporulation
- Diauxic shift
- DNA damage
- Stress

Mapping the Human ‘Diseasome’
Researchers created a map linking different diseases, represented by circles, to the genes they have in common, represented by squares. Related Article: Redefining Disease, Genes and All

Goh et al PNAS 2007
Networks Discussion

• How can network models help interpreting existing Encode data? Particularly in a disease context?
• How can Encode data address the broader network community?
• How can we systematically define the next phase of encode assays to help define reference networks?
• How can we use these as scaffolds for mapping of other ‘omic information?