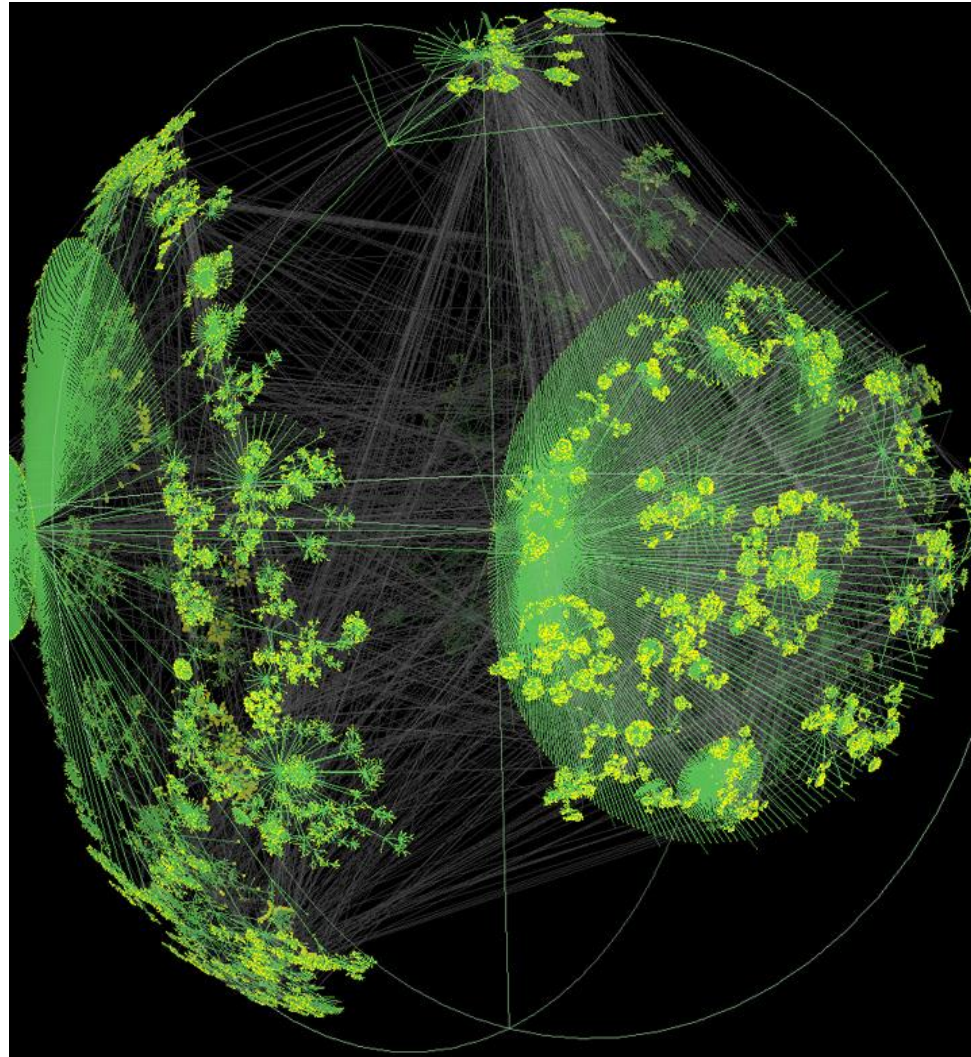# Ch3 Biological Network

Zhuo Wang
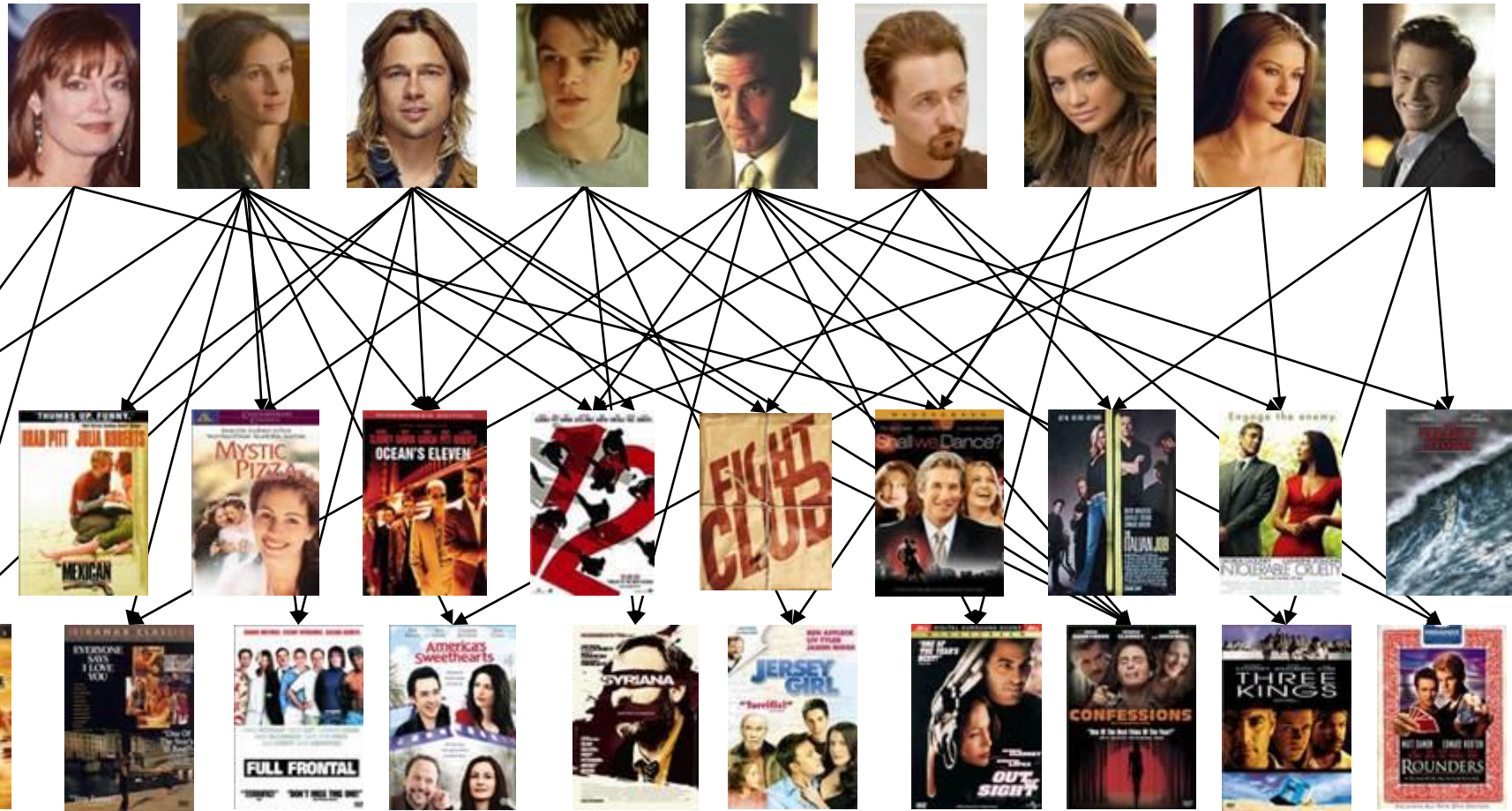*zhuowang@sjtu.edu.cn*

Biological networks

- Introduction
- Biological Networks
  - Protein-Protein Interaction Network
  - Signaling Transduction Network
  - Metabolic Pathway Network
  - Gene Regulatory Network
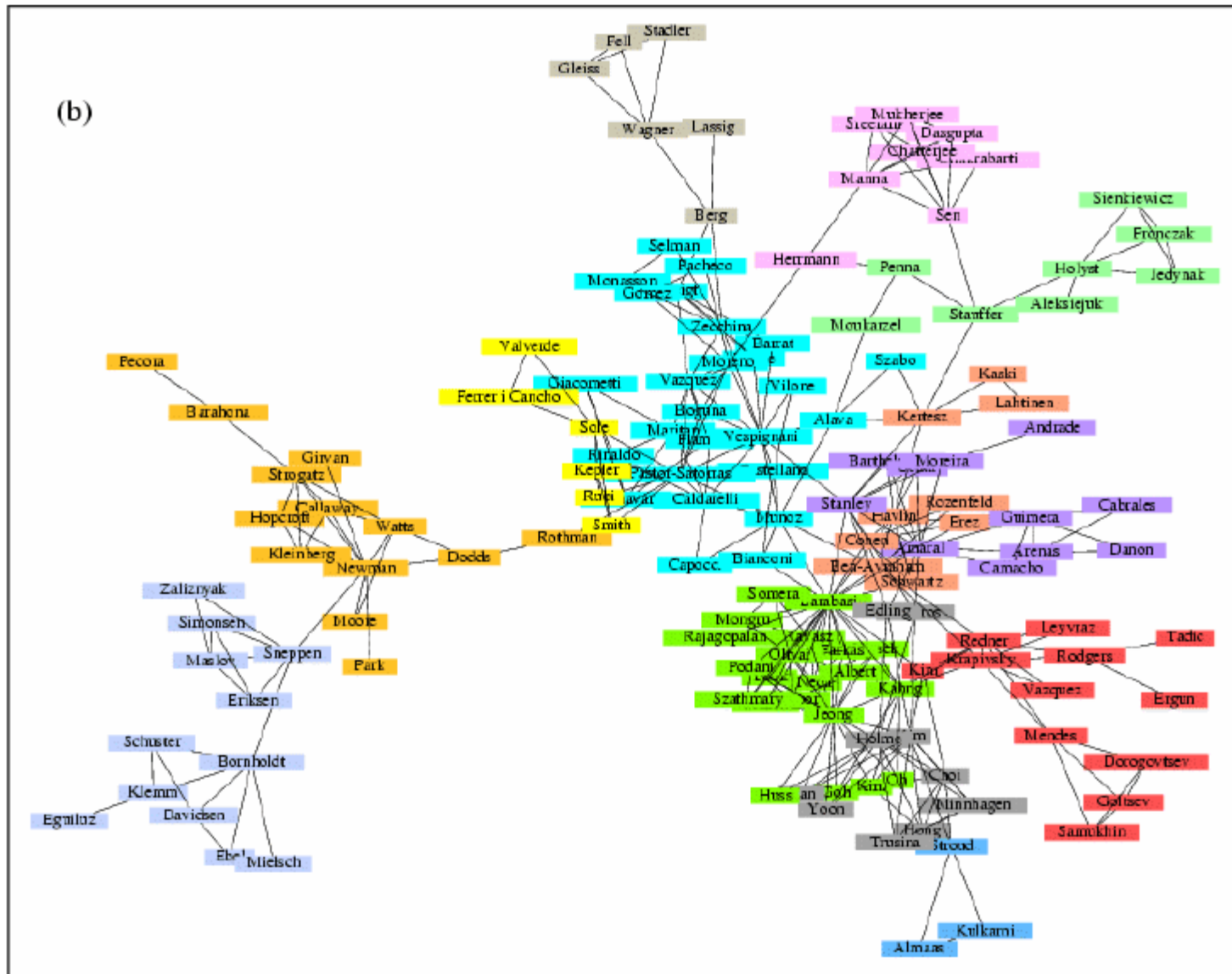 - Expression Network
  - ……
- Discussion

Network Example - The Internet

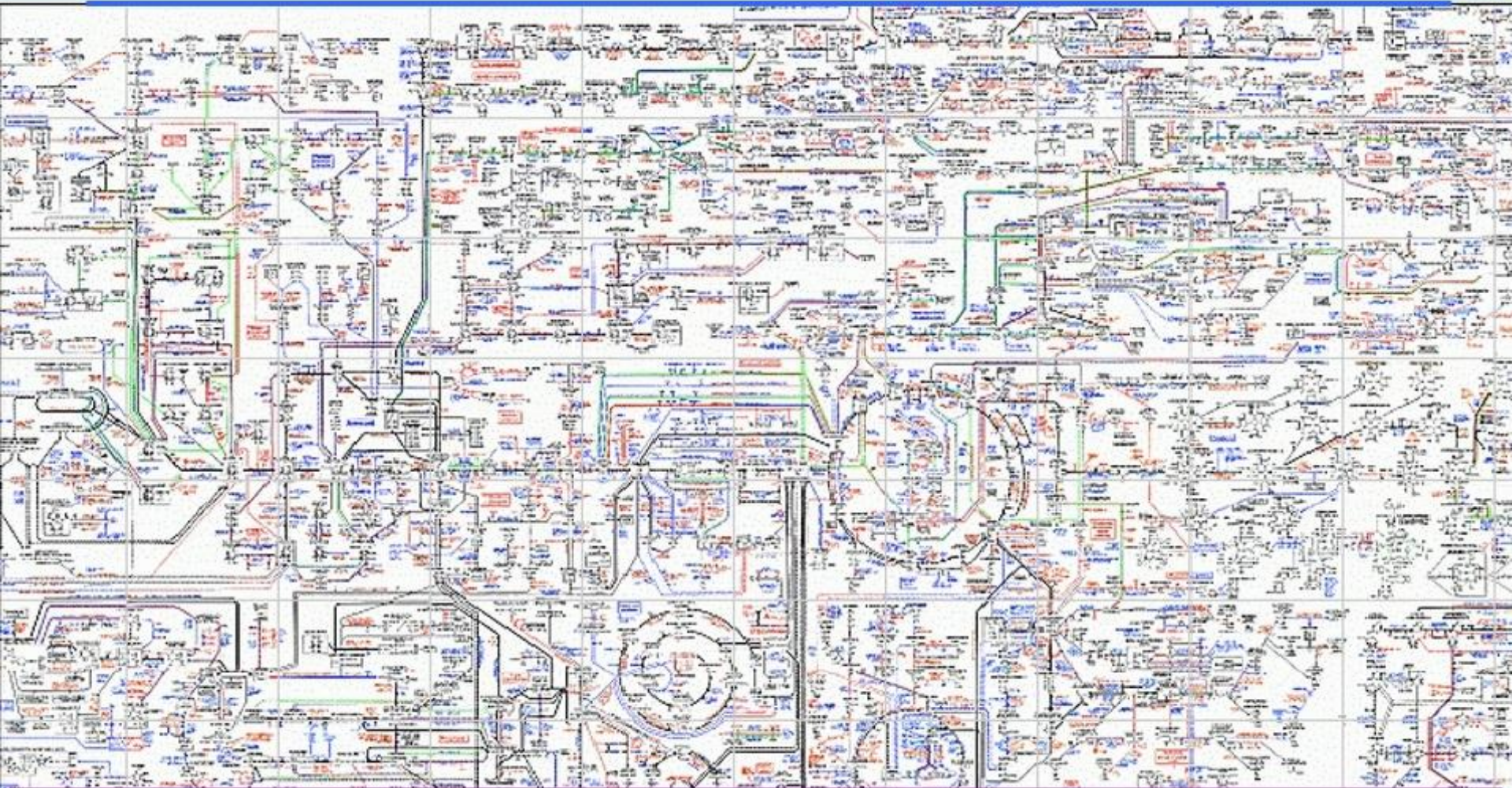# Network of actor co-starring in movies

Networks of scientists' co-authorship of papers
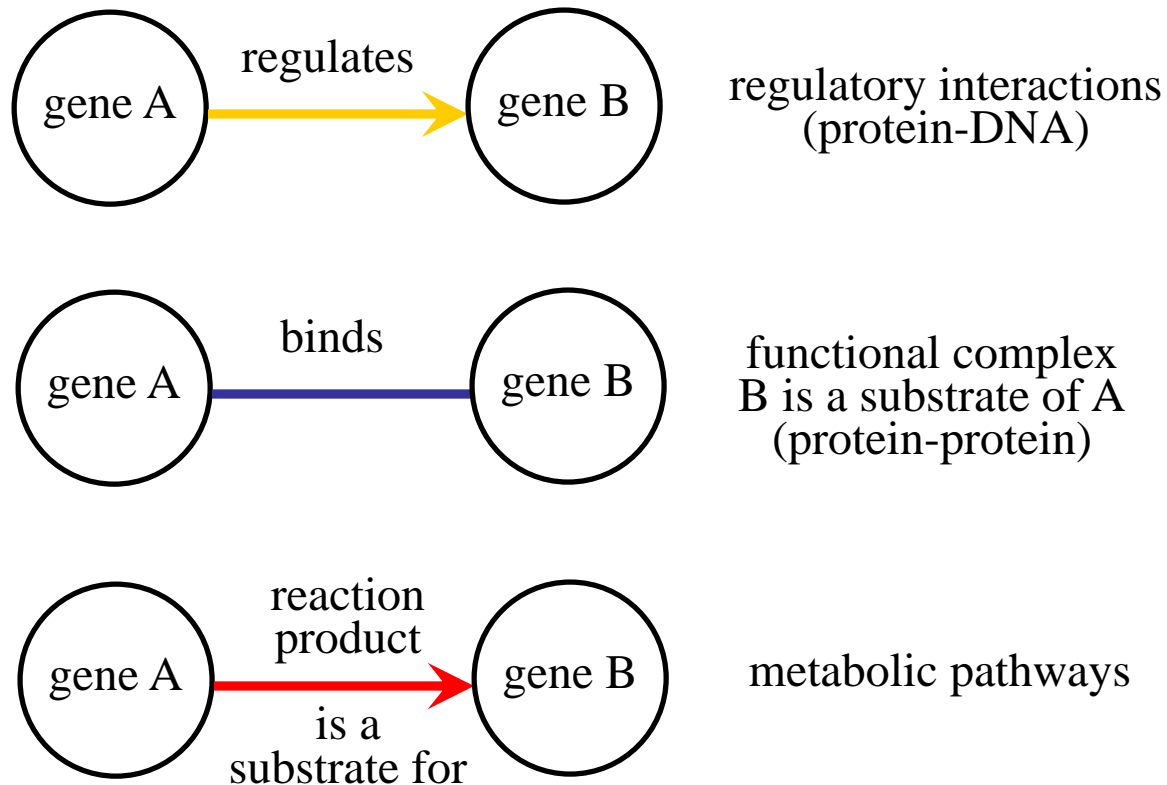
transportation networks: airlines

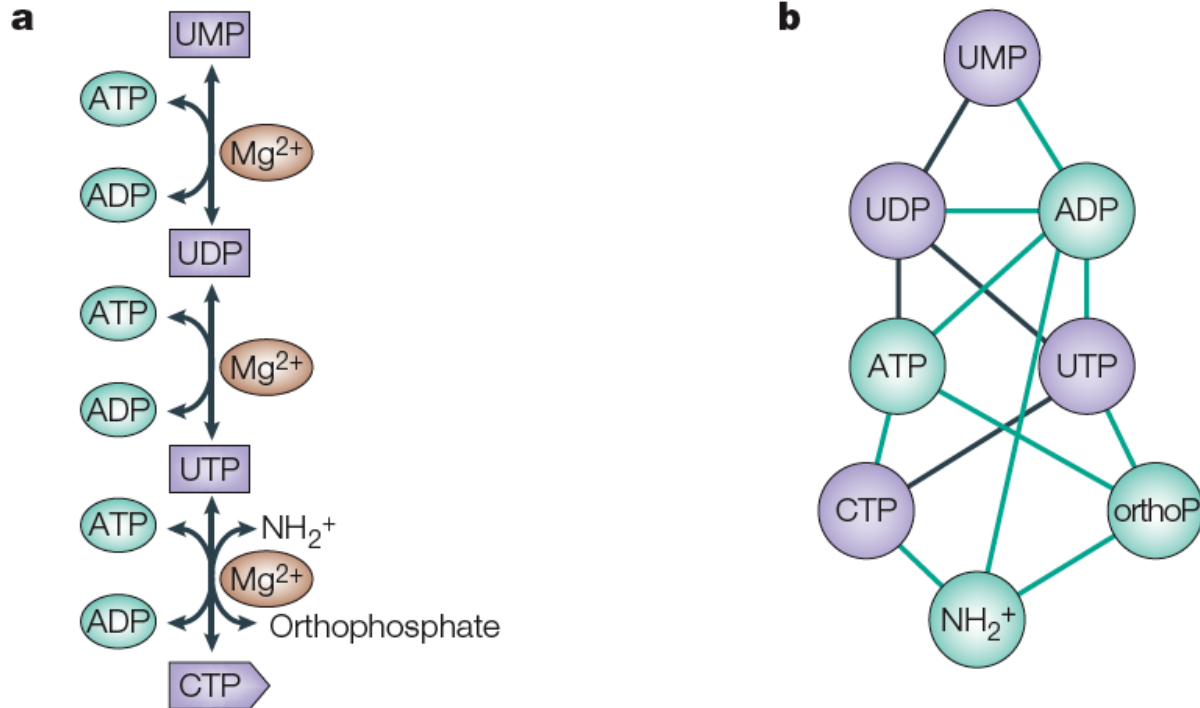# Traits and Phenotypes are Controlled by Molecular Networks

Trying to understand life without knowledge of biochemical network would be like trying to understand Shakespeare without knowledge of English grammar.

Network Representation

Representation of Metabolic Reactions

Networks are found in biological systems of
   varying scales:
   1. Evolutionary tree of life
   2. Ecological networks
   3. Expression networks
   4. Regulatory networks
      - genetic control networks of organisms
   5. The protein interaction network in cells
   6. The metabolic network in cells
   … more biological networks

Why Study Networks?

- It is increasingly recognized that complex systems cannot be described in a reductionist view.

- Understanding the behavior of such systems starts with understanding the topology of the corresponding network.

- Topological information is fundamental in constructing realistic models for the function of the network.
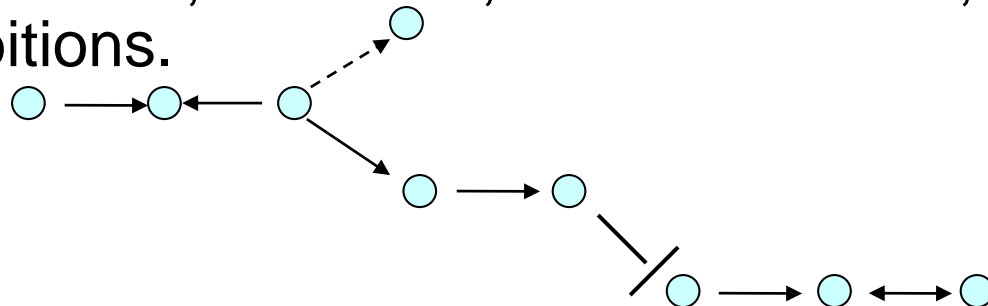
Biological Network Model

- ## Network
  - A linked list of interconnected nodes.

  - Node
    - Protein, peptide, or non-protein biomolecules.

  - ■ Edges
    - ■ Biological relationships, etc., interactions, regulations, reactions, transformations, activation, inhibitions.

Proteins in a cell

- There are thousands of different active proteins in a cell acting as:
  - enzymes, catalysors to chemical reactions of the metabolism
  - components of cellular machinery (e.g. ribosomes)
  - regulators of gene expression
  - Certain proteins play specific roles in special cellular compartments.
  - Others move from one compartment to another as "signals".

Protein Interactions

- Proteins perform a function as a complex rather as a single protein.

- Knowing whether two proteins interact can help us discover unknown proteins' functions:

  - If the function of one protein is known, the function of its binding partners are likely to be related- "guilt by association".

  - Thus, having a good method for detecting interactions can allow us to use a small number of proteins with known function to characterize new proteins.
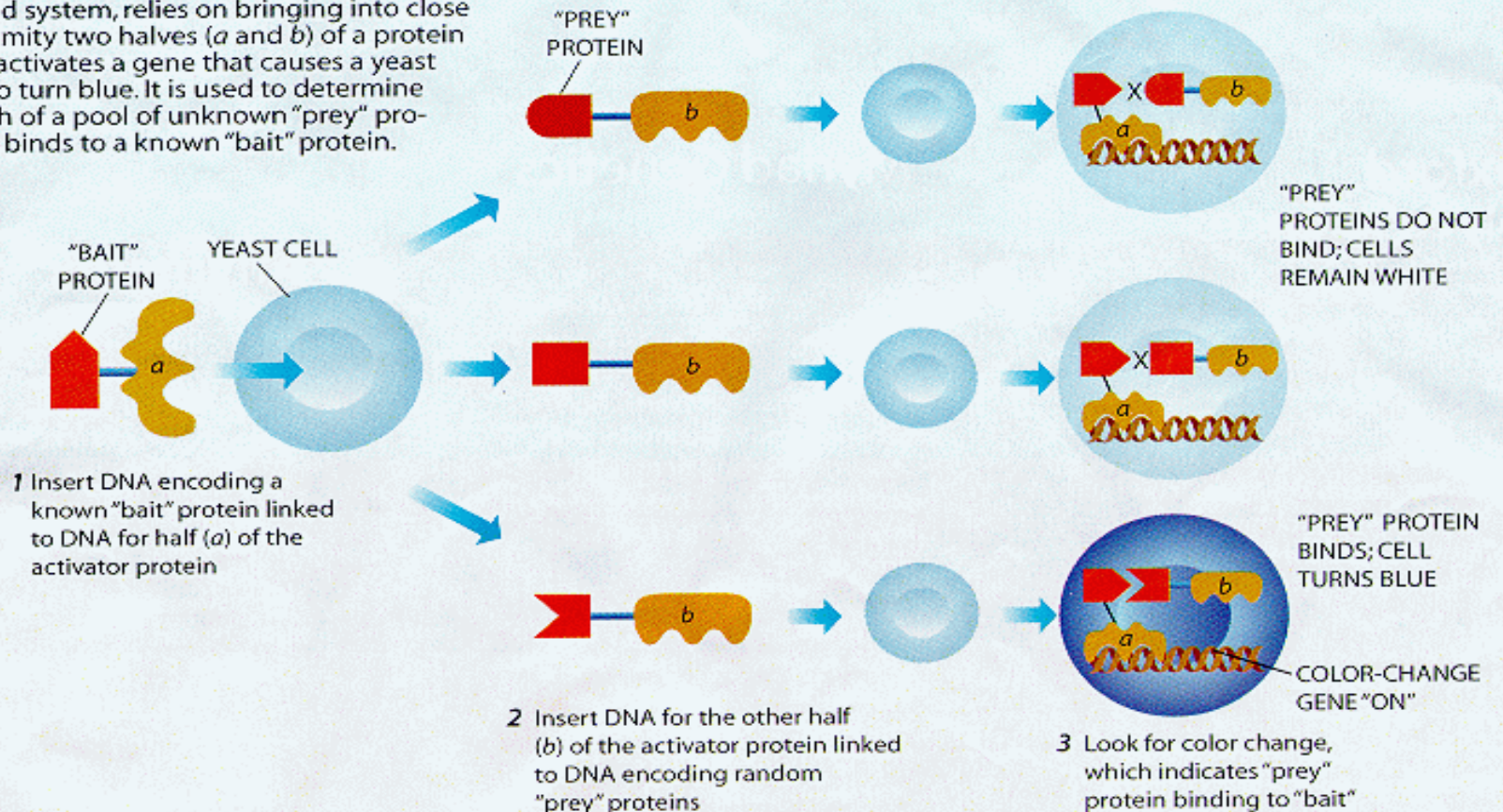
Yeast Two Hybrid

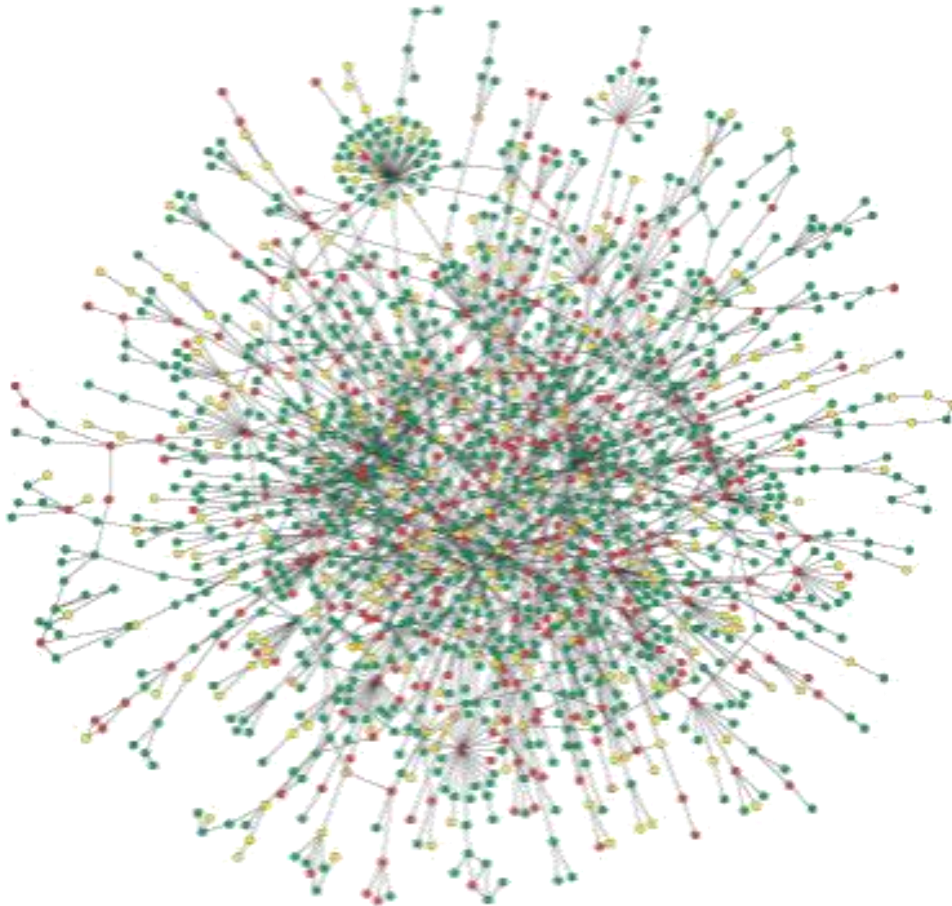P. Uetz, et al. **Nature**, 2000; Ito et al., **PNAS**, 2001; …

Yeast Protein Interaction Network

Nodes: proteins

Links: physical
interactions (binding)

Database for protein interaction

- HPRD
  http://www.hprd.org/

- BioGRID (physic and genetic interaction)
  http://www.thebiogrid.org/

- DIP (experimentally determined)
  http://dip.doe-mbi.ucla.edu/dip/Main.cgi

-- STRING
 https://string-db.org/

HIV病毒蛋白与人体蛋白的互作网络
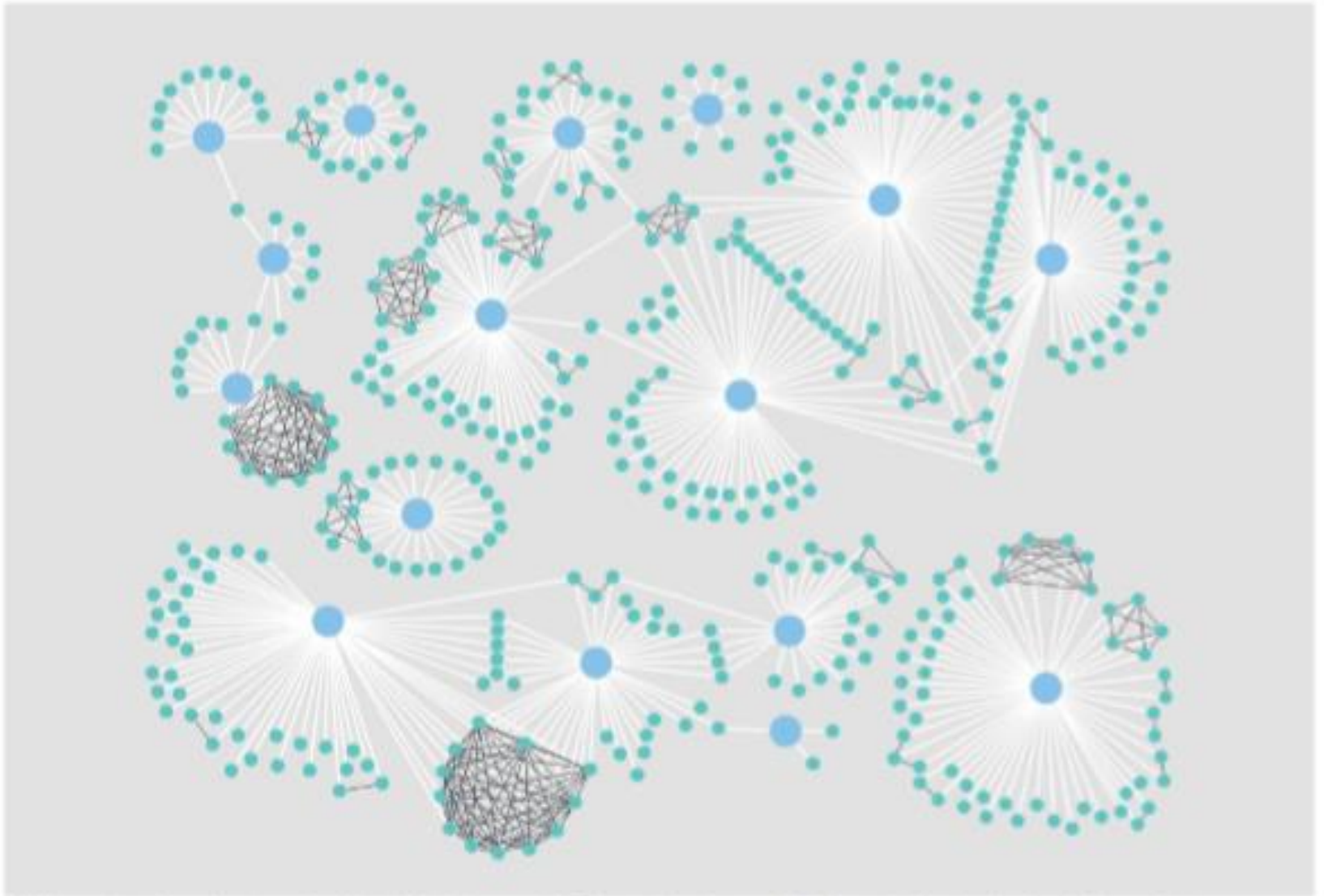
Multiple replicated experiments and sophisticated statistics reveal 497 interactions between 16 HIV proteins (blue) and hundreds of human factors.

Nature (2012), 484: 271.

Signaling Transduction Network

– In biology a **signal** or **biopotential** is an electric quantity (voltage or current or field strength), caused by chemical reactions of charged ions.

– refer to any process by which a cell converts one kind of signal or stimulus into another.

– Another use of the term lies in describing the transfer of information between and within cells, as in signal transduction.

Signaling transduction network
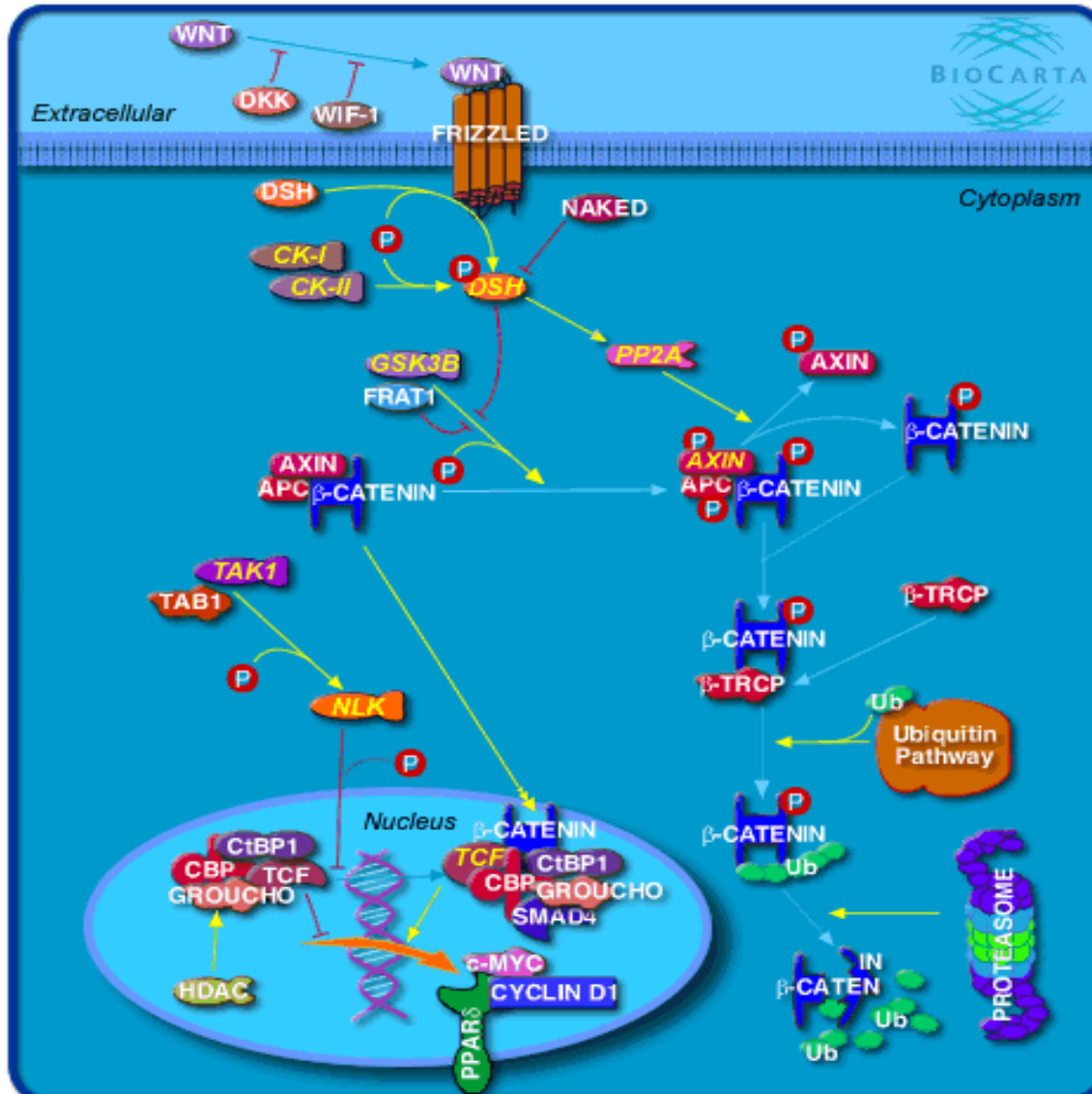
Biocarta

KEGG

STKE

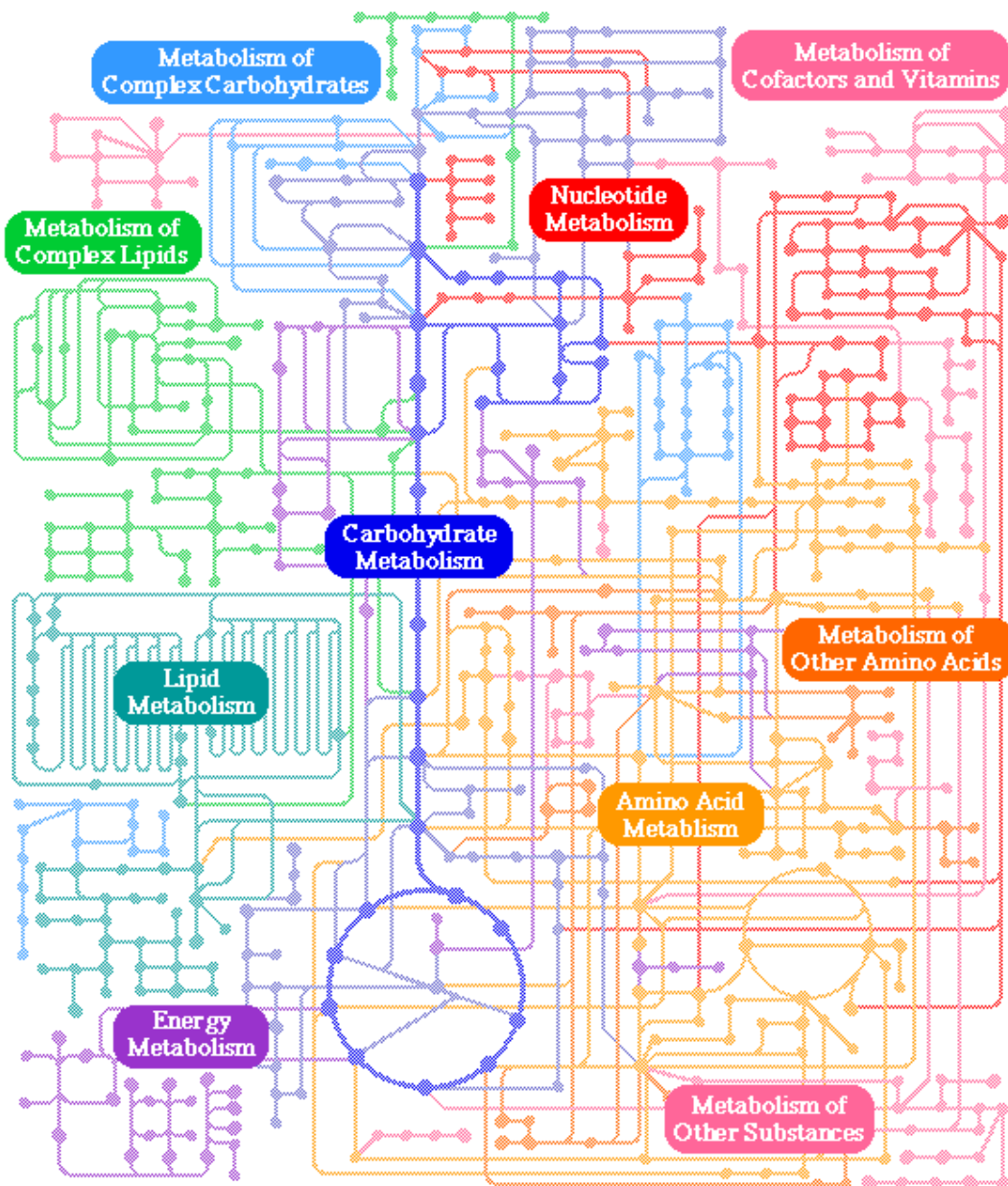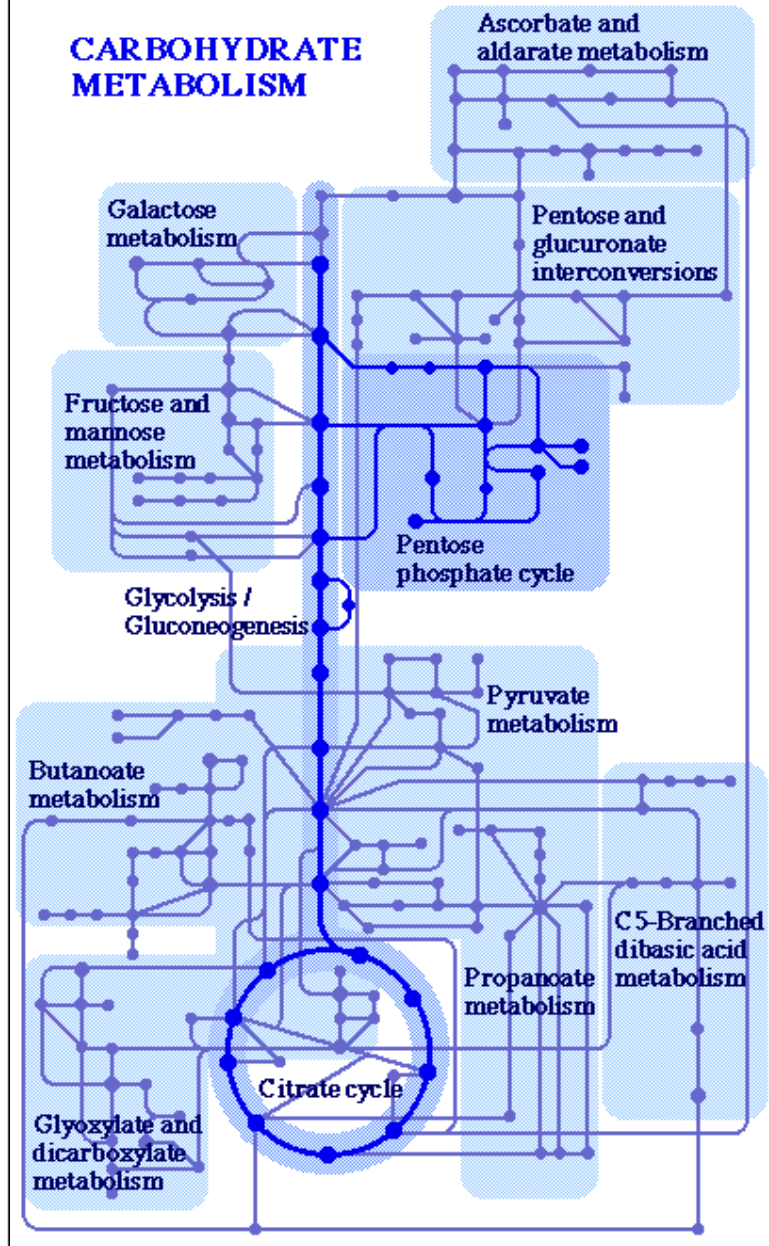# Wnt Signaling pathway in KEGG
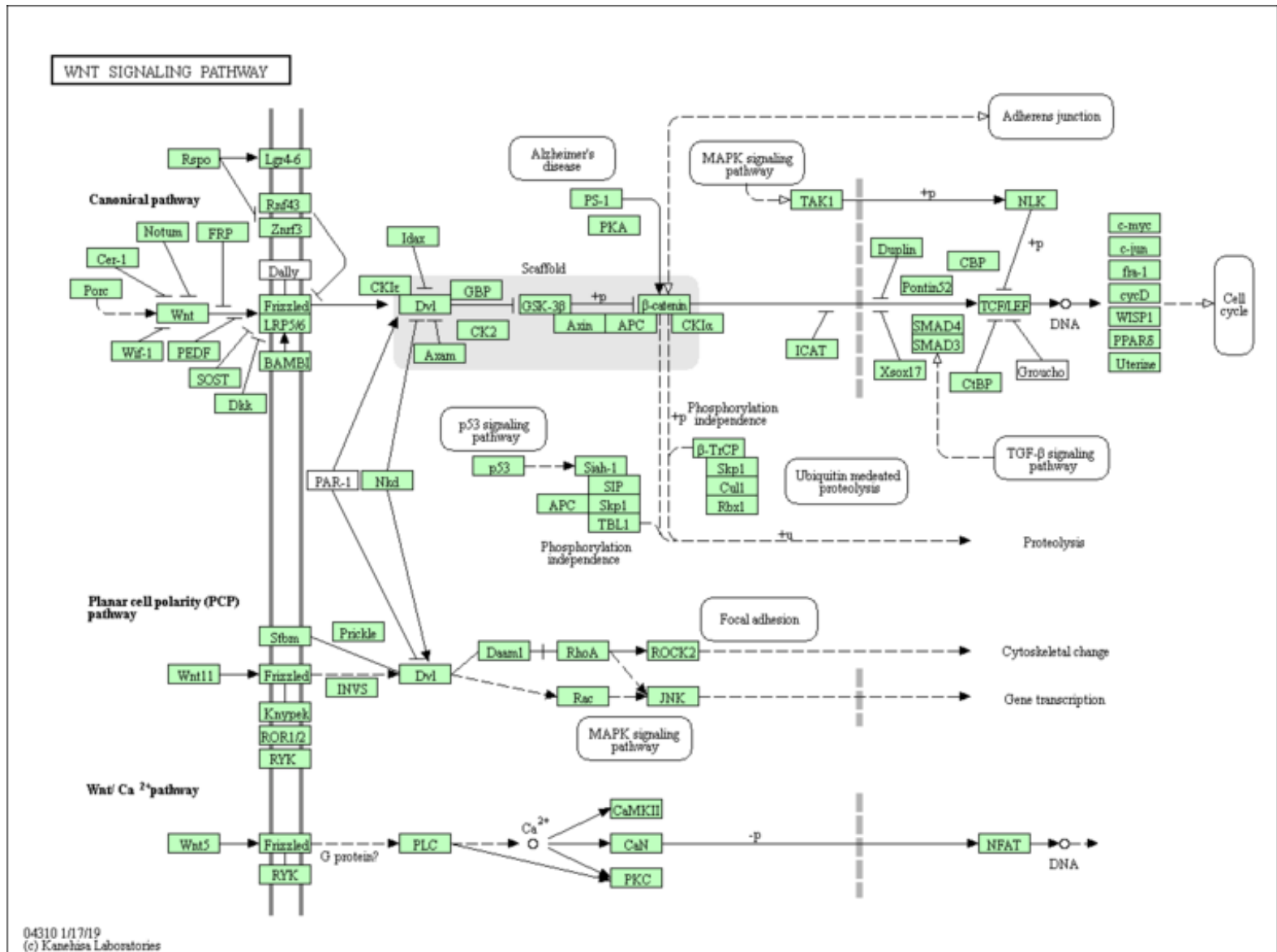
Metabolic Network

– A series of chemical reactions occurring within a cell, catalyzed by enzymes, resulting in either the formation of a metabolic product to be used or stored by the cell, or the initiation of another metabolic pathway
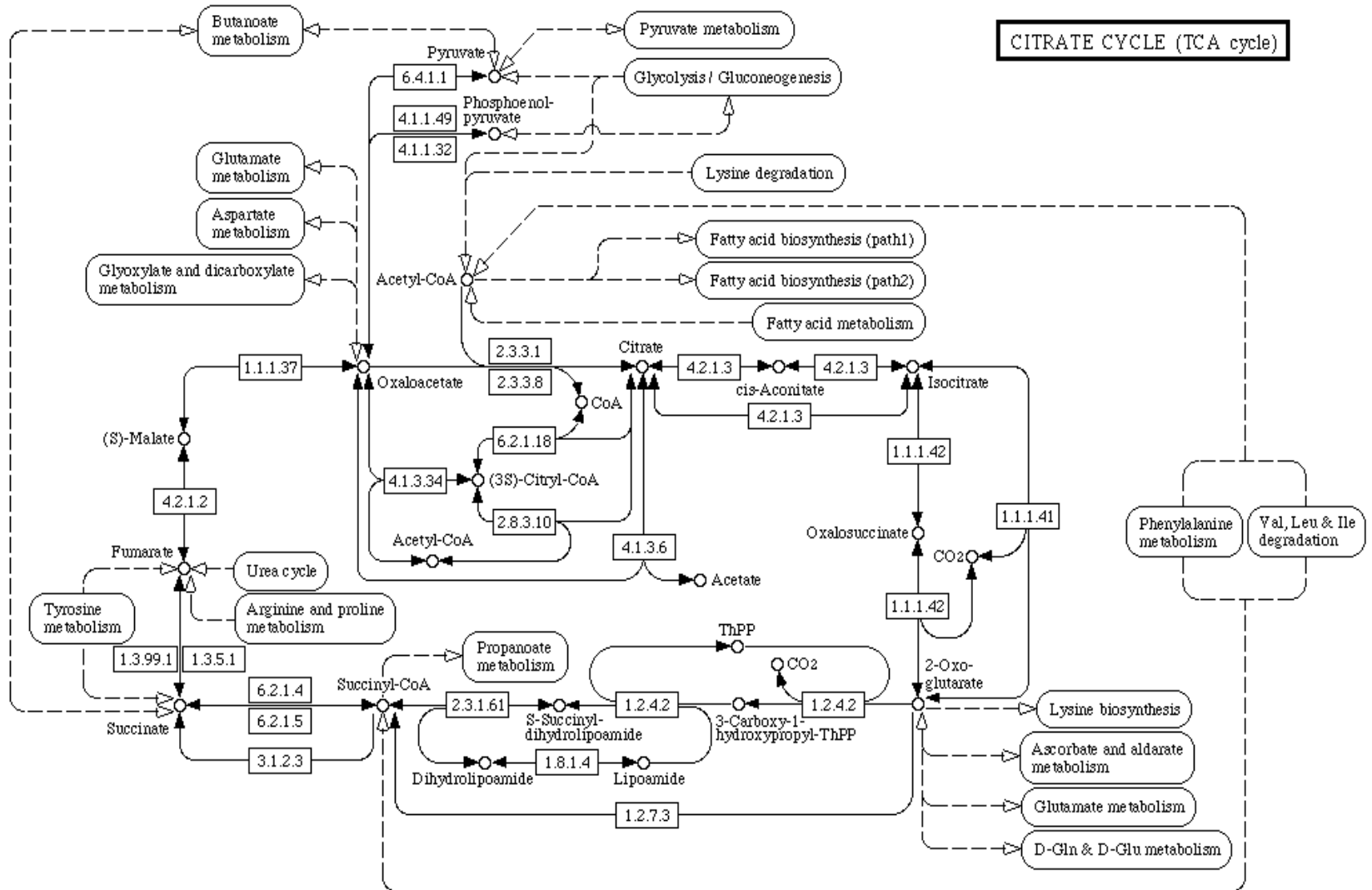
KEGG Metabolic Pathway

METABOLIC PATHWAYS

- Metabolism of Complex Carbohydrates
- Metabolism of Complex Lipids
- Metabolism of Cofactors and Vitamins
- Nucleotide Metabolism
- Carbohydrate Metabolism
- Lipid Metabolism
- Metabolism of Other Amino Acids
- Amino Acid Metablism
- Energy Metabolism
- Metabolism of Other Substances

01100 5/1/00

CARBOHYDRATE METABOLISM

- Ascorbate and aldarate metabolism
- Galactose metabolism
- Pentose and glucuronate interconversions
- Fructose and mannose metabolism
- Pentose phosphate cycle
- Glycolysis / Gluconeogenesis
- Pyruvate metabolism
- Butanoate metabolism
- C 5–Branched dibasic acid metabolism
- Propanoate metabolism
- Citrate cycle
- Glyoxylate and dicarboxylate metabolism

110 10/14/97

Metabolic Pathway Example

CITRATE CYCLE (TCA cycle)

00020 3/19/04

Database for metabolic pathway

KEGG   http://www.genome.jp/kegg/

BioCyc   http://biocyc.org/

PlantCyc http://www.plantcyc.org/

BRENDA http://www.brenda-enzymes.org/

Reactome http://www.reactome.org/

BIGG   http://bigg.ucsd.edu/

Regulatory Network

- A collection of DNA segments (genes) in a cell which interact with each other and with other substances in the cell, thereby governing the rates at which genes in the network are transcribed into mRNA.

Regulatory Network

Regulatory Network Resource

RegulonDB http://regulondb.ccg.unam.mx/

Yeastract   http://www.yeastract.com/

Expression Network

- A network representation of genomic data.
- Inferred from genomic data, i.e. microarray.
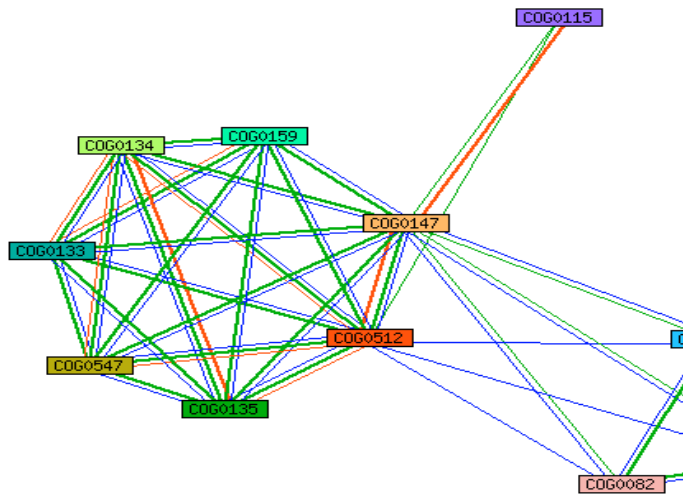
Similarity of gene expression

Your Input:

☐ COG0512 – Anthranilate/para-aminobenzoate synthases component II

Predicted Functional Associations: Score

☐ COG0147 – Anthranilate/para-aminobenzoate synthases component I   0.998
☐ COG0547 – Anthranilate phosphoribosyltransferase   0.958
☐ COG0134 – Indole-3-glycerol phosphate synthase   0.930
☐ COG0135 – Phosphoribosylanthranilate isomerase   0.863
☐ COG0159 – Tryptophan synthase alpha chain   0.843
☐ COG0133 – Tryptophan synthase beta chain   0.791
☐ COG0128 – 5-enolpyruvylshikimate-3-phosphate synthase   0.707
☐ COG0169 – Shikimate 5-dehydrogenase   0.707
☐ COG0115 – Branched-chain amino acid aminotransferase/4-amino-4-deoxychorismate l [...] 0.555
☐ COG0082 – Chorismate synthase   0.454

Discussion

- **Problems**
    - Network Inference
        - Micro Array, Protein Chips, other high throughput assay methods
    - Function prediction
        - The function of 40-50% of the new proteins is unknown
        - Understanding biological function is important for:
            – Study of fundamental biological processes
            – Drug design
            – Genetic engineering
    - Functional module detection
        - Cluster analysis
    - Topological Analysis
        - Descriptive and Structural
        - Locality Analysis
        - Essential Component Analysis
    - Dynamics Analysis
        - Signal Flow Analysis
        - Metabolic Flux Analysis
        - Steady State, Response, Fluctuation Analysis
    - Evolution Analysis

- Biological Networks are very rich networks with very limited, noisy, and incomplete information.
- Discovering underlying principles is very challenging.