Community analysis

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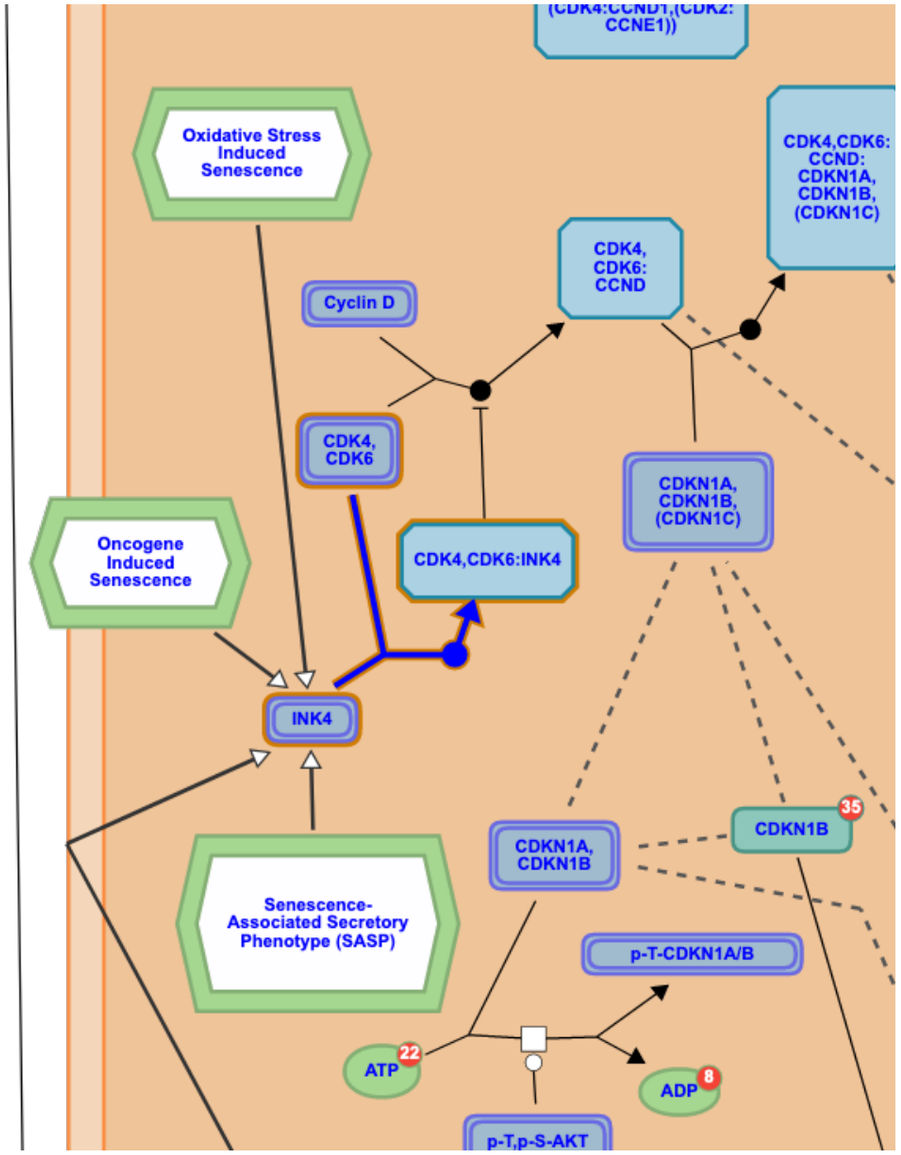
Overview

1. Introduction to network analysis
2. Terminology
3. Network inference
4. Key network properties
5. Community analysis

What are modules?

Modules are physically or functionally associated nodes that work together to achieve a distinct function

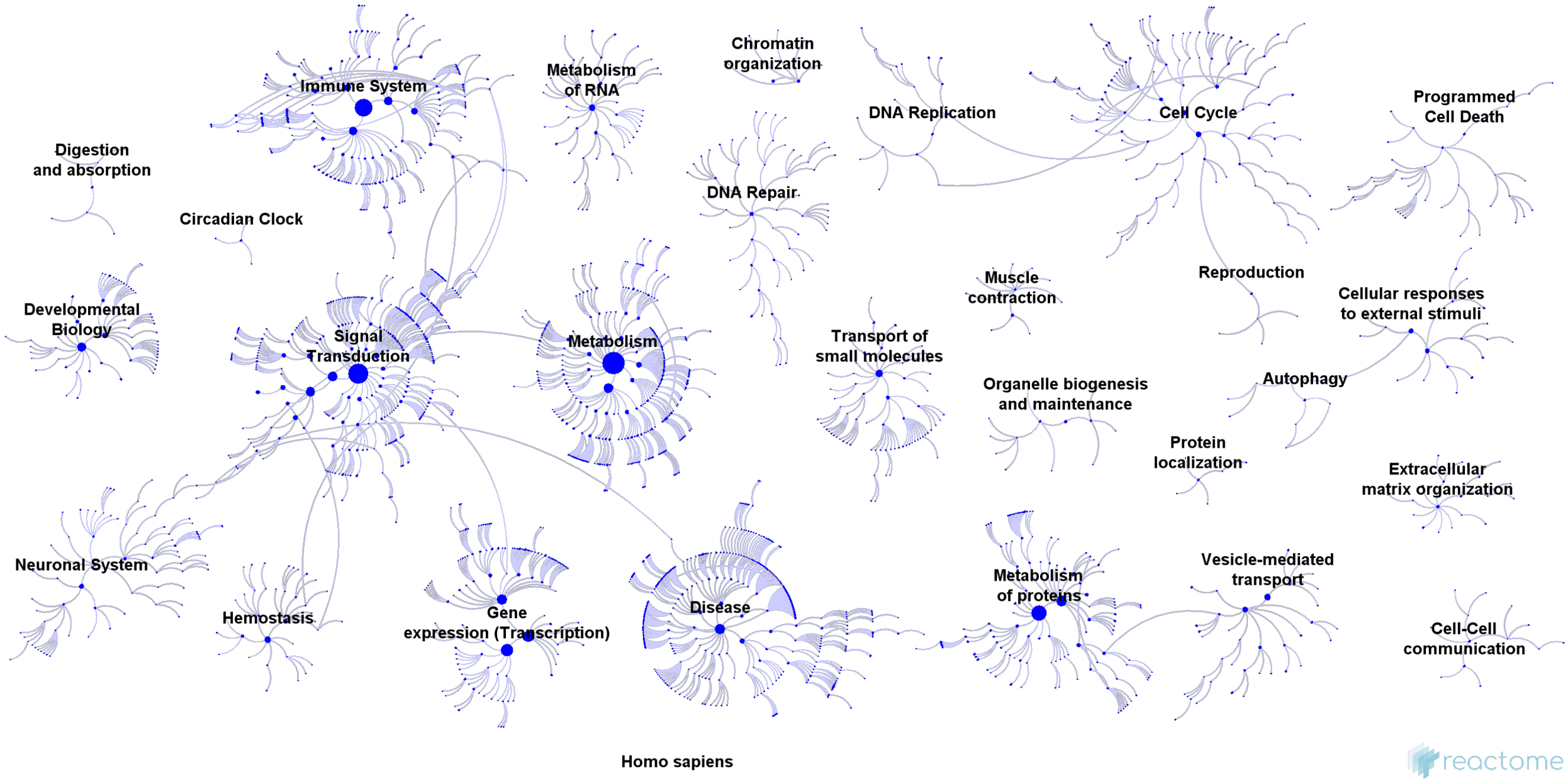
Protein complexes are physical modules



What are modules?

Pathway-associated proteins ***may*** represent functional modules

Gene Ontology



What are modules?

In addition to physical or functional modules, one may identify other types of modules

Topological: derived from their high within-module degree

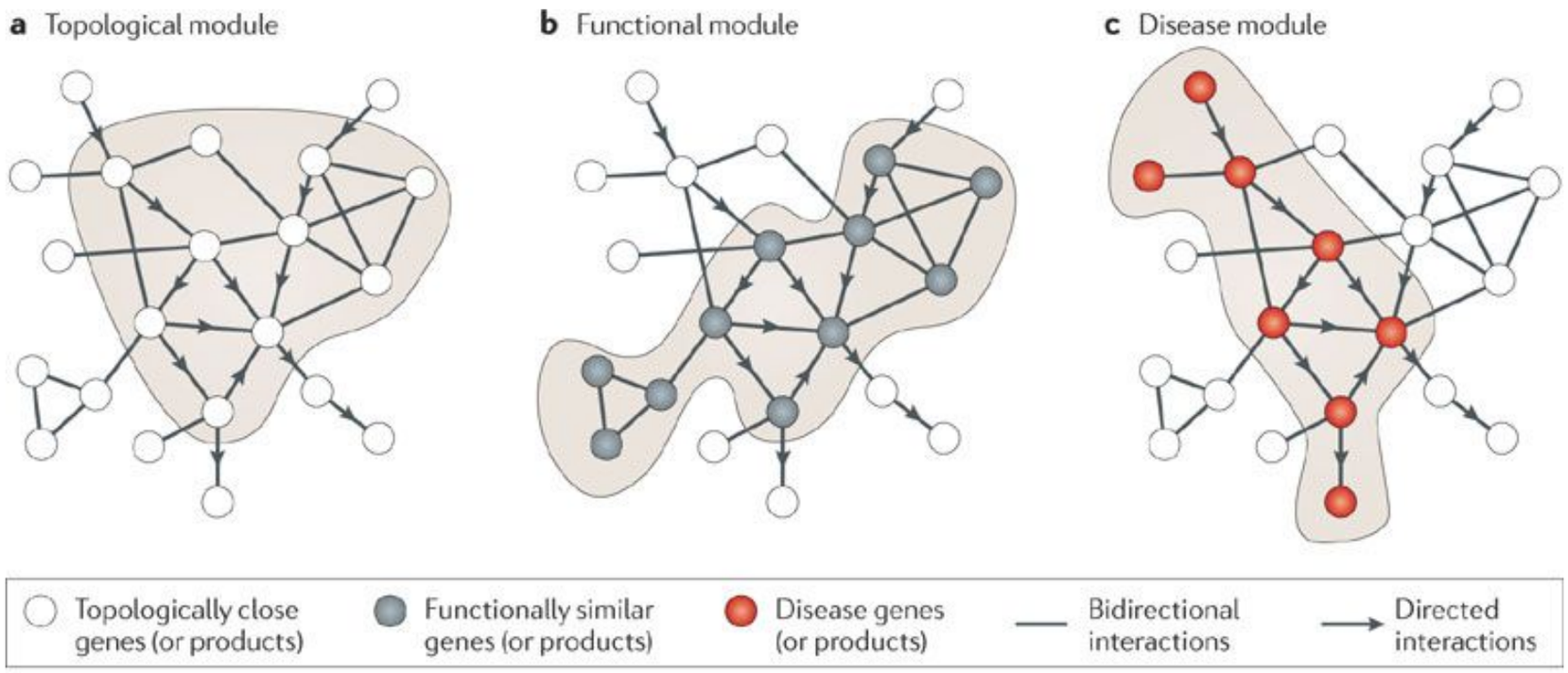
Disease: highly interconnected nodes associated with a disease response

Drug: highly interconnected nodes associated with a drug response

Subgroup: highly interconnected nodes associated with a sample subgroup (e.g. cancer subtype)

Tissue-, cell-type-specific: highly interconnected nodes associated with a specific tissue or cell type

Highly interlinked local regions of a network



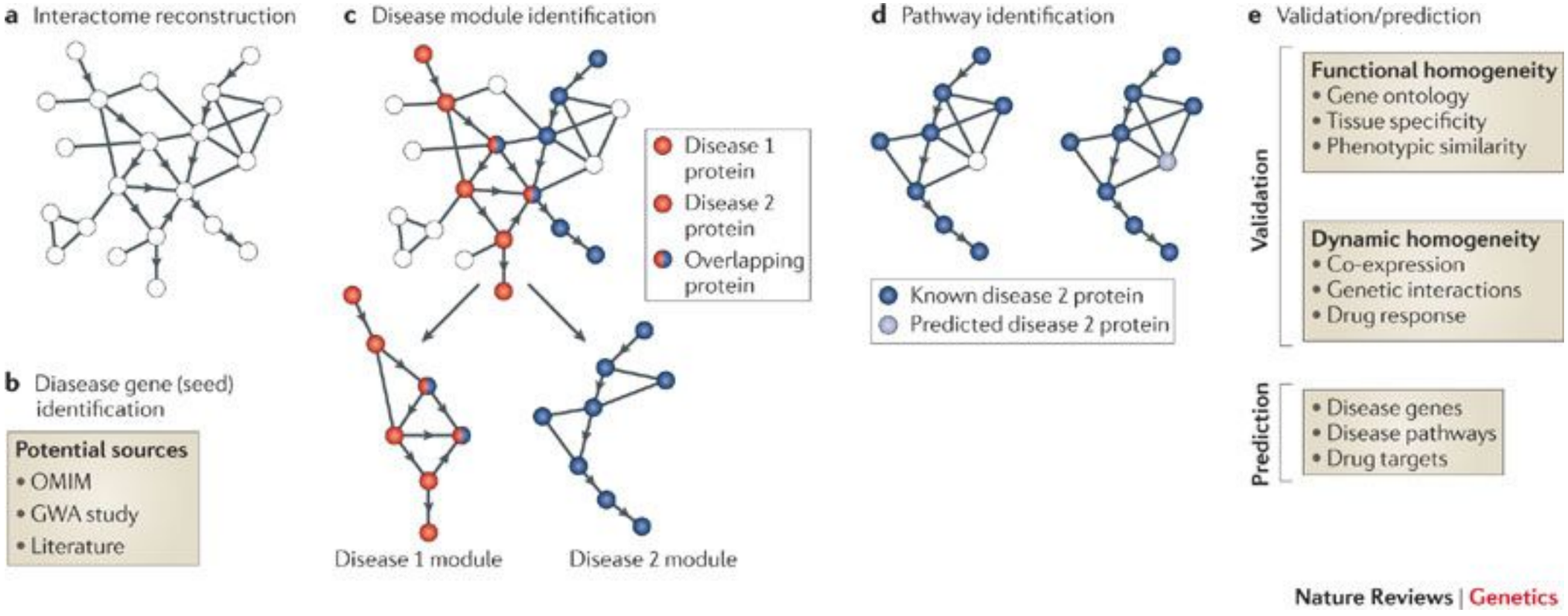
Barabasi 2011

The challenge: identify and characterise modules

Moving from full network to modular characterisation

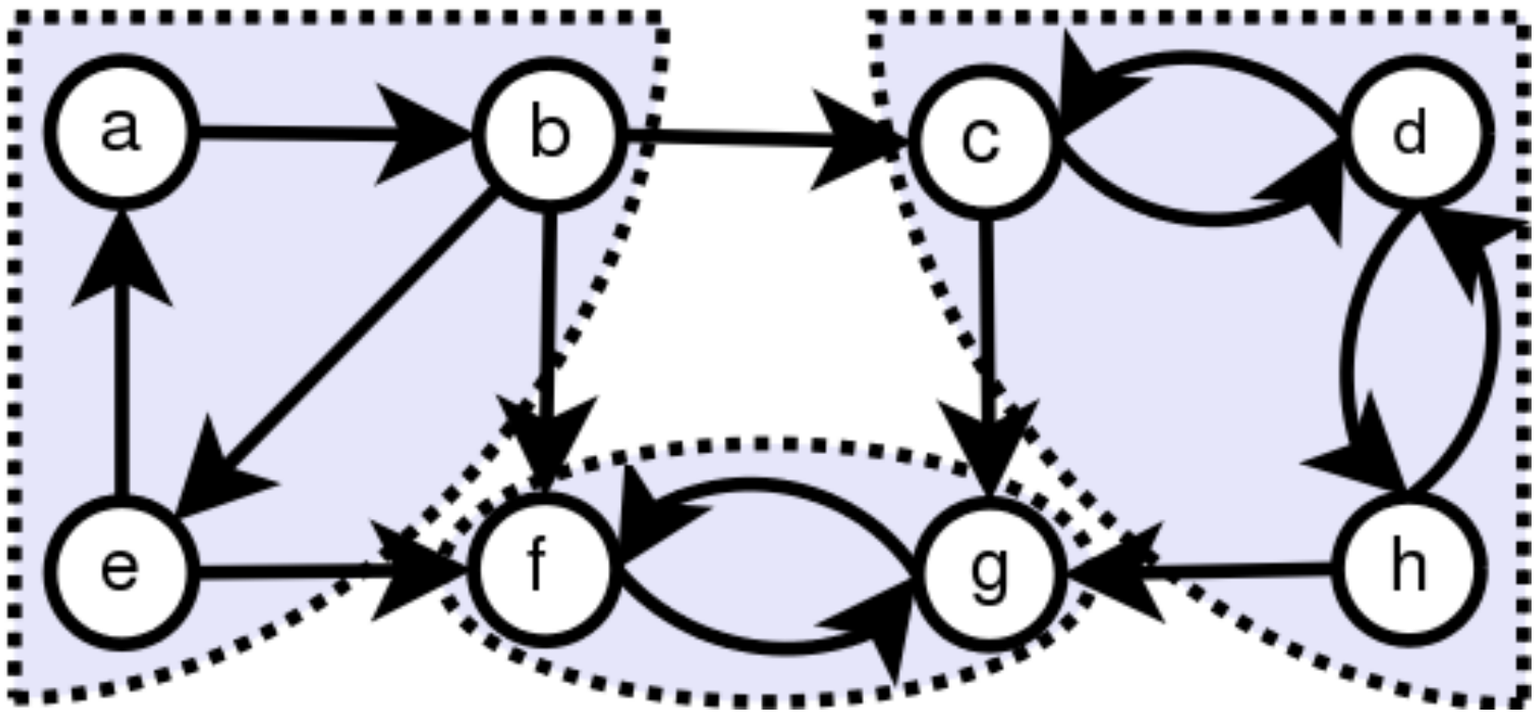
Different features (diseases, biological processes, etc.) may be associated with the same module

Prediction: *in silico*, relies on available knowledge for functional association



Barabasi 2011

Module detection: Connected components



Modularity

Modularity is a property of the network

Modularity (Q) measures the tendency of a graph to be organised into modules

Modules computed by comparing probability that an edge is in a module vs what would be expected in a random network

For a given partitioning of the network into individual groups s, compute

$$Q \propto \sum_{s \in S} [(e_s) - (\text{expected } e_s)]$$

edges in group s

Random network with same number of nodes, edges and degree per node

$-1 < Q < 1$

Q = 1: much higher number of edges than expected by chance

Q = -1: lower number of edges than expected by chance

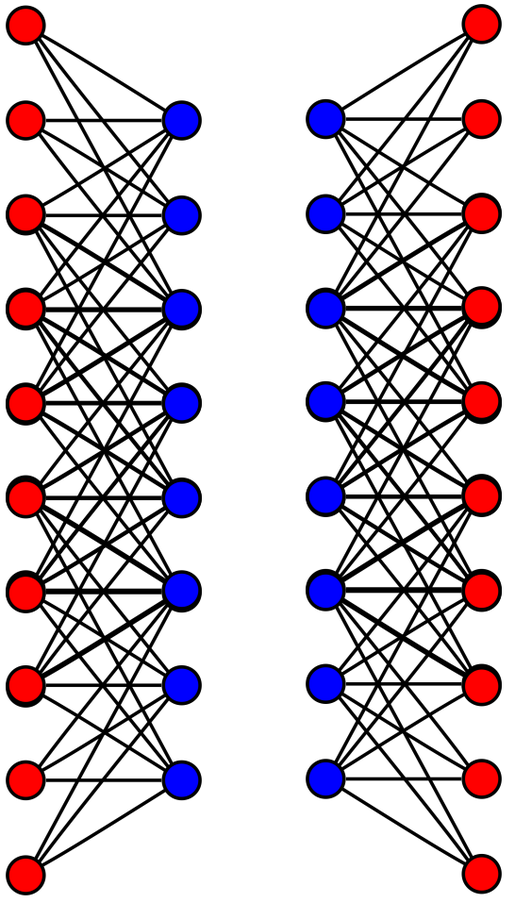
Q > 0.3 - 0.7 means significant community structure

Modularity

Modularity is different than **clustering coefficient**:

Graph composed of two bipartite complete subgraphs:

high Q but low connectivity (C)



Module detection: Louvain algorithm

How to identify modules? Maximise Q

$$Q \propto \sum_{s \in S} [(e_s) - (\text{expected } e_s)]$$

Brute-force approach:

1. Start with 1 node/module
2. Compute distances between nodes
3. Join closest node
4. Re-compute distances between a 2n module and each 1n module
5. Join them if Q increases

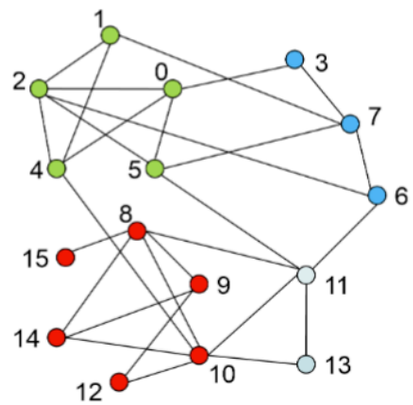
Module detection: Louvain algorithm

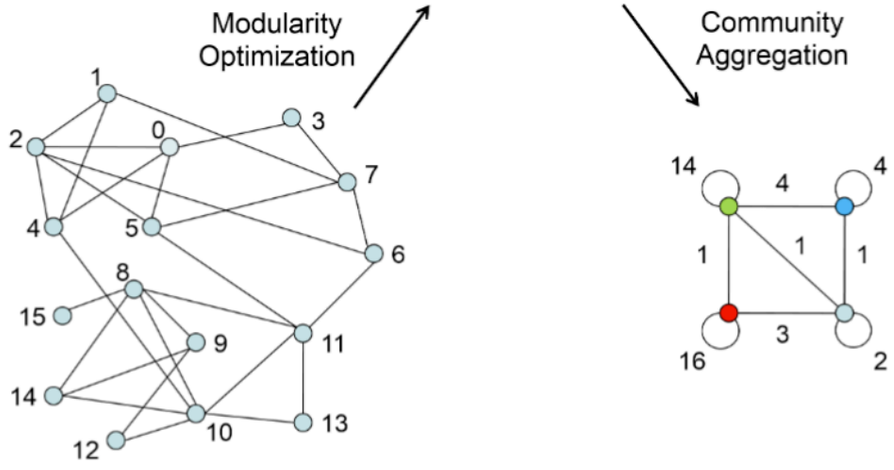
Phase 1: greedy modularity optimisation

1. Start with 1n/community
2. Compute Q by moving *i* to the community of *j*
3. If ΔQ>1, node is placed in community
4. Repeat 1-3 until no improvement is found. Ties solved arbitrarily

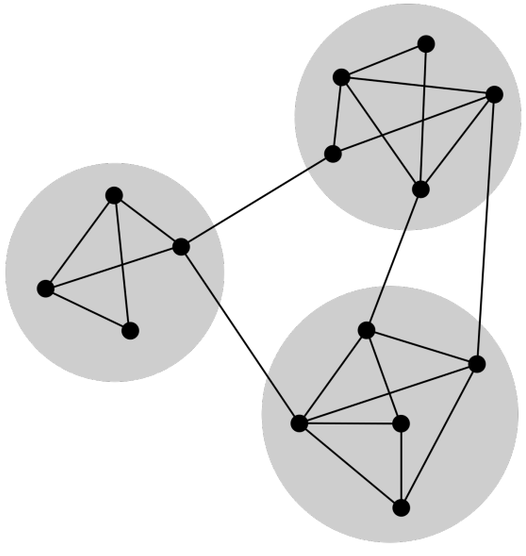
Phase 2: coarse grained community aggregation

5. Link nodes in a community into single node.
6. Self loops show intra-community associations
7. Inter-community weights kept
8. Repeat phase 1 on new network





Other methods:
Walktrap
Label propagation
…
(benchmarking)



Community characterisation

Clustering coefficient and degree distribution

Enrichment analysis

Hypothesis: community-associated features show coordinated changes associated with common biological processes

Can significantly enriched biological processes serve as “validation”?

- Mutual feature associations may reinforce data characterisations not evident by individual features
- …or need of further network curation based on top biological terms

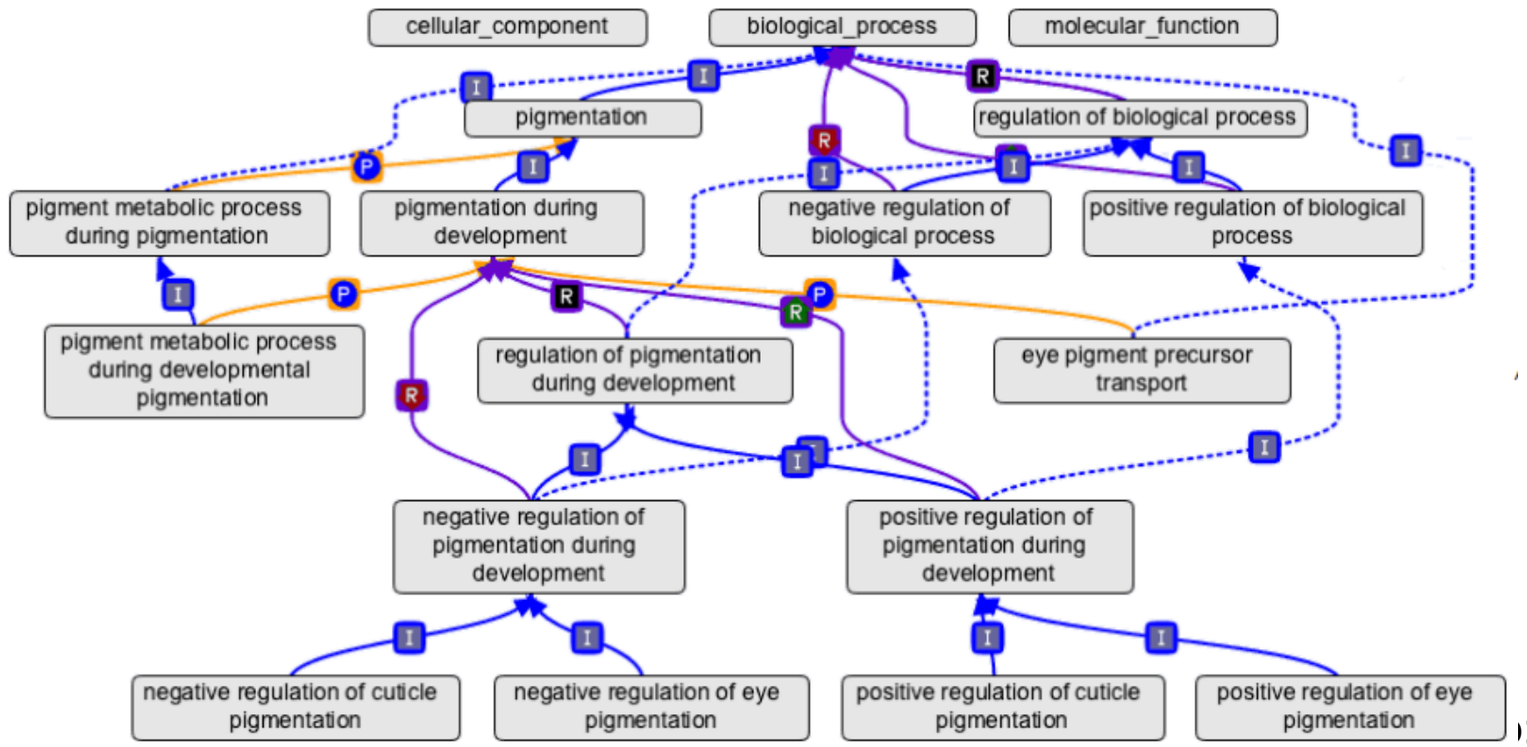
Enrichment analysis

GO-terms, pathways, subcellular location, TF-targets, disease, drugs

Tests for significant overlap between groups

All considerations from standard enrichment analyses apply

Some biological processes may have no biological meaning in your analysis



://geneontology.org/

Enrichment analysis

Important databases with gene-sets:

- MSigDB (gene)
- Enrichr (gene)
- KEGG (metabolite, gene)
- DIANA (miRNA)
- MetaboAnalyst (metabolite)
- DAVID (web)
- Reactome (web)

Creating custom sets and joint sets

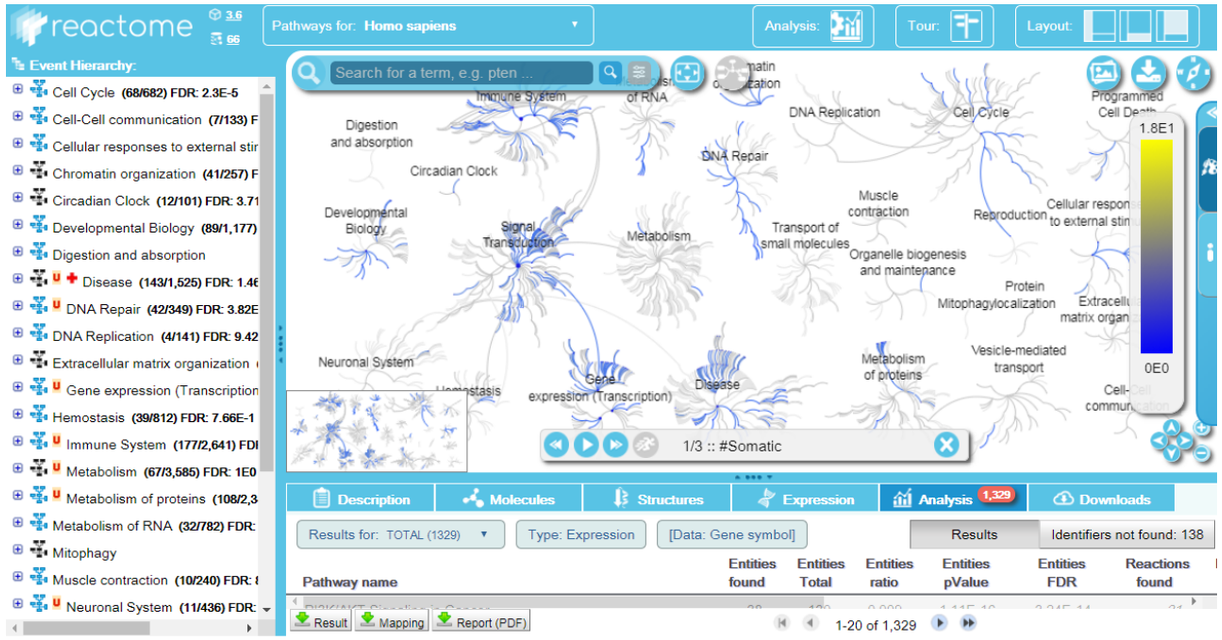
Mapping your data to common IDs

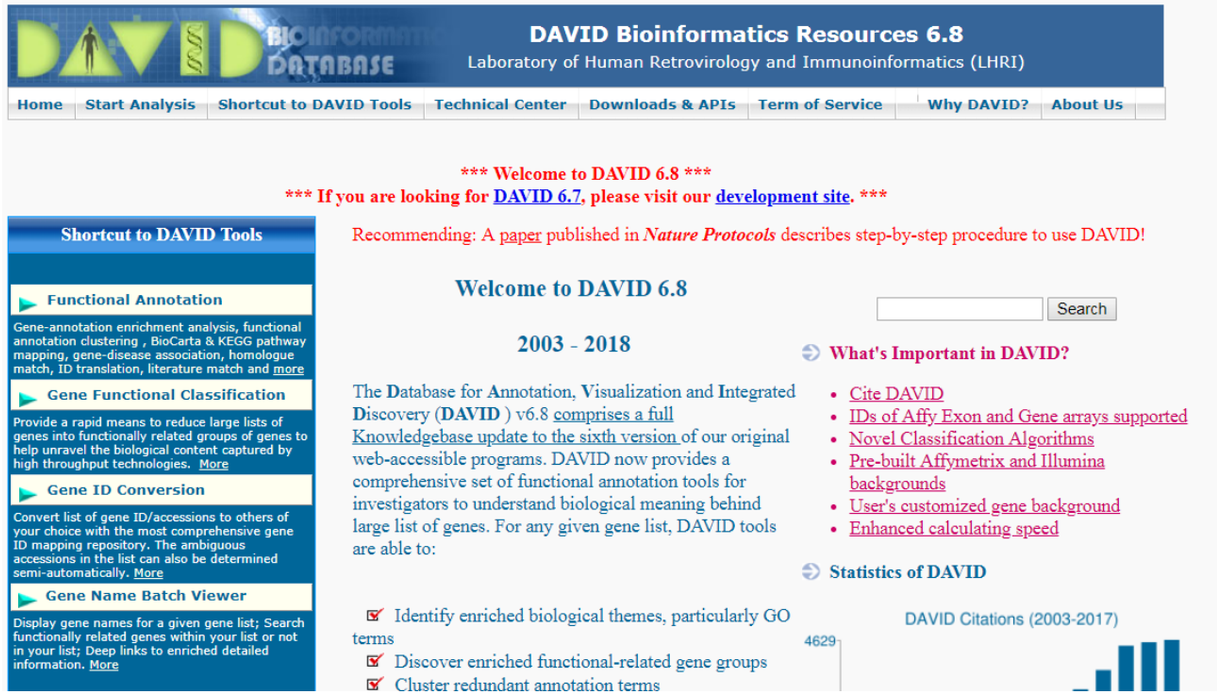
- Easy for genes and proteins: use DAVID, Biomart, or MyGene (in Python or R)
- Hard for other types

Tools for Enrichment analysis

Popular tools for GSEA:

- (most tools above)
- PIANO (highly recommended in R)
- Cytoscape (BINGO plugin)





References as hyperlinks

Additional reading

- Network Science - Textbook on graph theory and network analysis.
- Communication dynamics in complex brain networks - Discussion about whether and how network topology may be applied to study the brain networks.
- A Systematic Evaluation of Methods for Tailoring Genome-Scale Metabolic Models - General review and discussion on methods to use in genome-scale metabolic models.
- Analysis of Biological Networks - General introduction into biological networks, network notation, and analysis, including graph theory.
- Multi-omics approaches to disease - Introduction to how integrative approaches may be applied in disease

Additional references displayed as hyperlinks in each slide.

Additional reading

- Analysis of Biological Networks - General introduction into biological networks, network notation, and analysis, including graph theory.
- Using graph theory to analyze biological networks - overview of the usage of graph theory in biological network analysis
- Survival of the sparsest: robust gene networks are parsimonious - analysis of network complexity and robustness.
- Network biology: understanding the cell's functional organization - Overview of key concepts in biological network structure
- Graph Theory and Networks in Biology - extended perspective on how graph analysis is applied in biology
- Modularity and community structure in networks

Additional references displayed as hyperlinks in each figure.