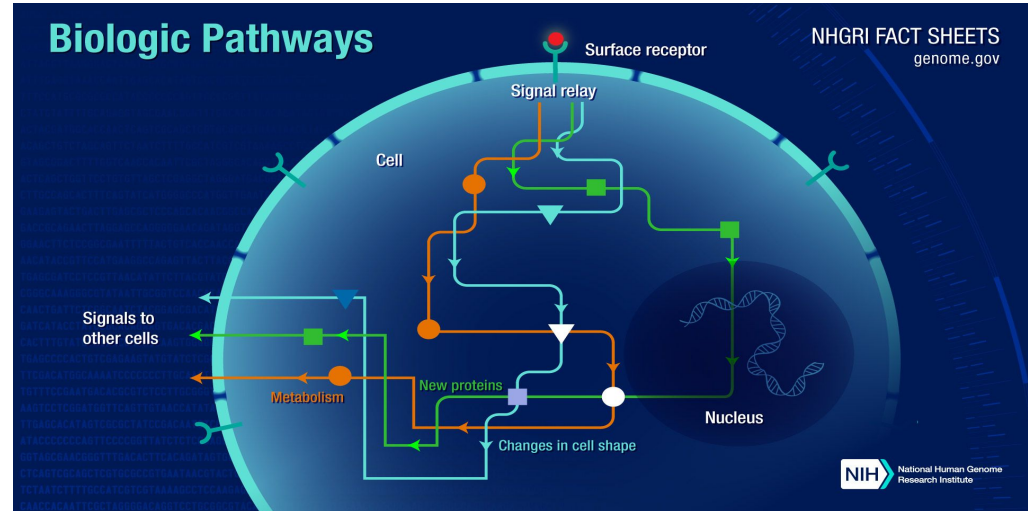


Gene Co-Expression Networks (GCEs): From Clustering to Insights Part 2

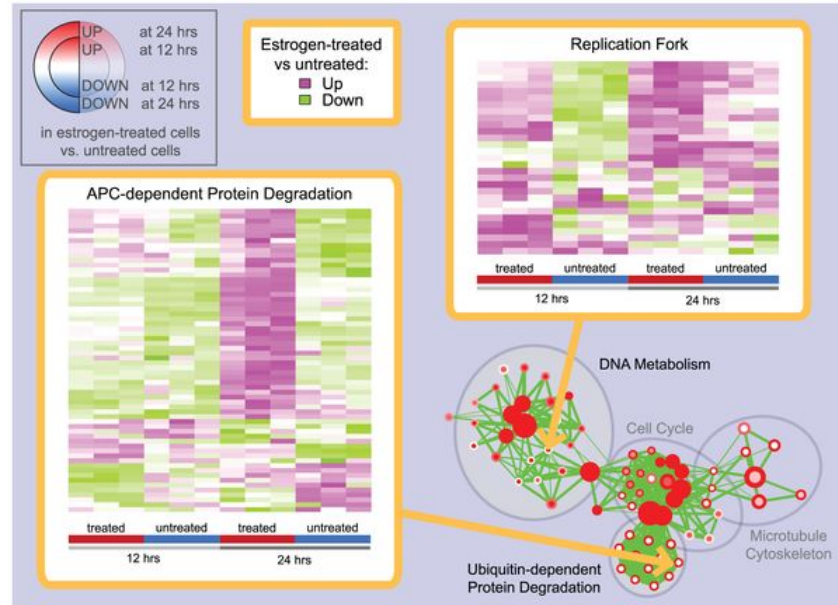
Visualization, Validation &
the Diseasesome

As. univ. Bozdog Alexandru



Validation & Biological Relevance of Modules

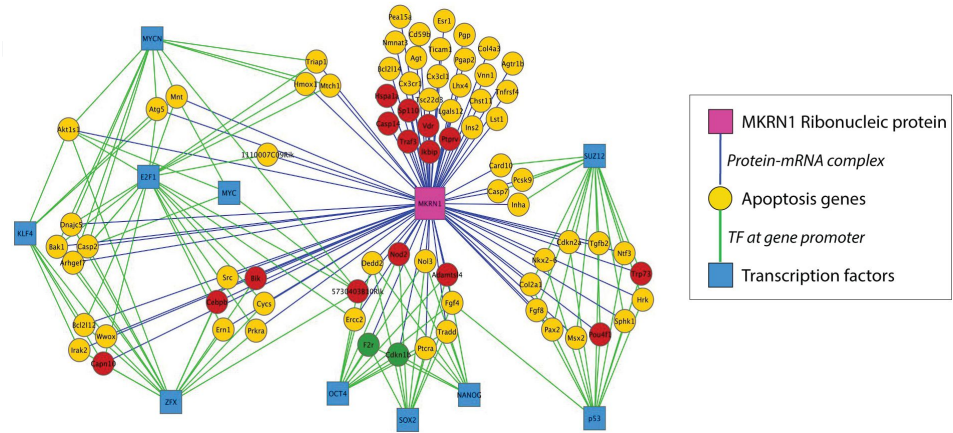
- **Biological validation:** GO/KEGG enrichment analysis.
- **Stability:** bootstrap resampling → do modules persist?
- **Replication:** compare across datasets (e.g. breast vs glioblastoma).
- **Reporting:** correlation metric, threshold/density, community detection algorithm, random seed.



Enrichment map for early-onset colon cancer and overlap with known disease genes. From: Merico, Daniele, et al. "Enrichment map: a network-based method for gene-set enrichment visualization and interpretation." *PLoS one* 5.11 (2010): e13984.

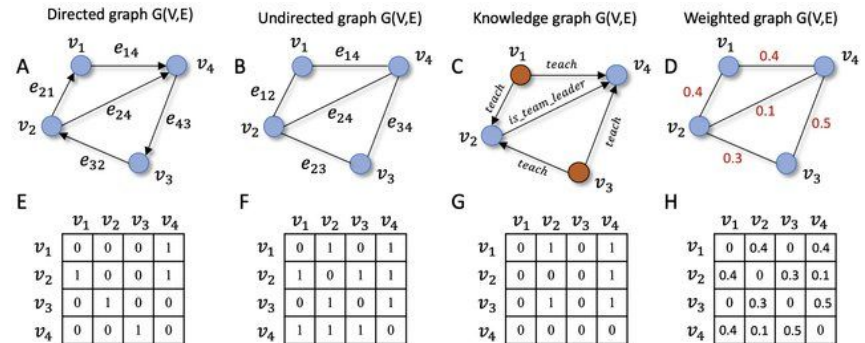
Visualization and Biological Context

- Visualization Tools: Cytoscape, Gephi, NetworkX.
- Identify clusters, hub genes, and patterns.
- Example: Liver tissue—modules enriched for linked to detoxification.



Challenges in GCE Analysis

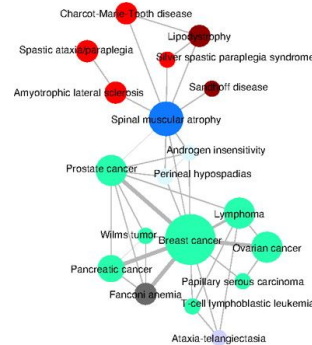
- Noisy data: Requires careful preprocessing and filtering.
- Threshold choice: Balancing noise reduction and meaningful connections.
- Scaling methods:
 - Memory efficiency: Adjacency list vs. matrix.
 - Parallelizing calculations for large datasets.



The DISEASOME: Linking Genes, Modules, and Diseases

- The **DISEASOME** = network of human diseases connected by shared genes, pathways, or molecular mechanisms (Barabási et al., 2007).
- **Co-expression modules** map to **functional gene groups** implicated in specific diseases.
- **Linking modules** → disease phenotypes highlights **comorbidity patterns** and **shared risk factors**.
- Integrates **genomic, transcriptomic, and clinical data** -> systems-level disease map.

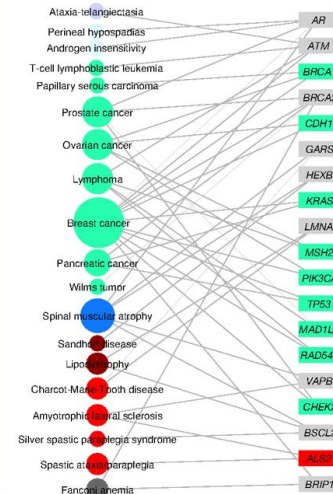
Human Disease Network (HDN)



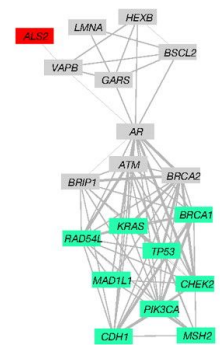
DISEASOME

disease phenotype

disease genome



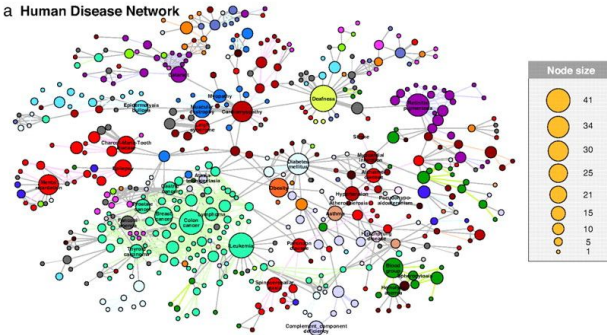
Disease Gene Network (DGN)



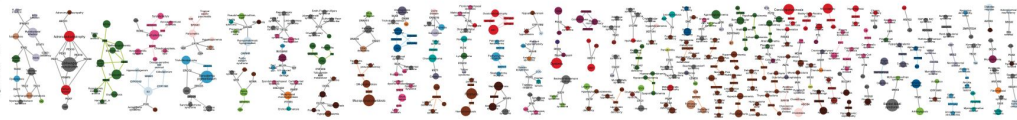
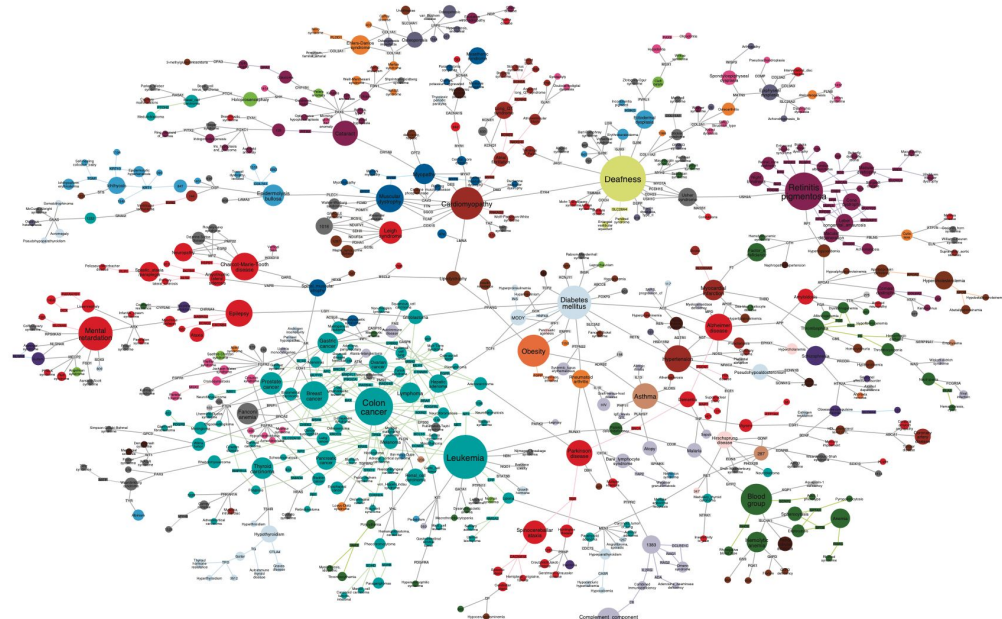
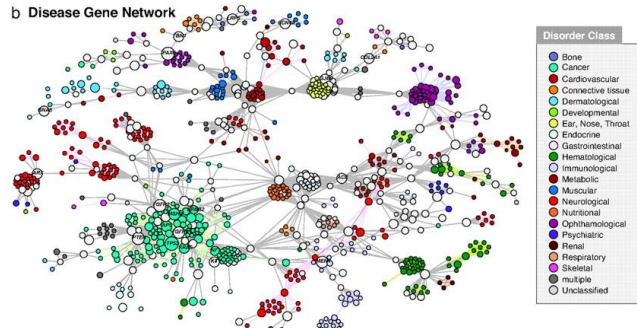
The human diseasome



a Human Disease Network



b Disease Gene Network



Disorder Class

- Bone
- Cancer
- Cardiovascular
- Connective tissue disorder
- Dermatological
- Developmental
- Ear, Nose, Throat
- Endocrine
- Gastrointestinal
- Hematological
- Immunological
- Metabolic
- Muscular
- Neurological
- Nutritional
- Ophthalmological
- Psychiatric
- Renal
- Respiratory
- Skeletal
- multiple
- Unclassified

Disorder Name

1. Alzheimer's disease
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From: <https://barabasi.com/art/work/diseasome>

Key Takeaways and What's Next?

- Gene co-expression networks can be visualized and interpreted using tools like Cytoscape, Gephi, or NetworkX.
- Modules represent groups of genes with correlated expression → often linked to biological functions or pathways.
- Validation is essential: enrichment analysis, stability checks, and replication across datasets.
- The diseasome integrates these modules into a global disease network, connecting genes to phenotypes and comorbidities.
- Applications: cancer research, drug repurposing, systems medicine.
- Next Lab: Applying machine learning for disease classification.

