

SYLLABUS**Network Biology and Biomedicine (BNFO286/MED283)**

TOPIC	LECTURER	TIME /PLACE
1.1 <u>Introduction: why biological networks?</u> Molecular networks bridge genotype to phenotype Networks as next phase of the Genome Project Types of biological networks Network databases and the NDEx cloud Overview of scope and syllabus Course format and expectations	Ideker	Jan 7 LFFB 107
Reading: Newman Ch. 1 p. 1-8, Ch. 5 p. 78-104		
1.2 <u>Network theory and algorithms I</u> Network versus matrix representations Weighted and directed networks Edges based on "co-citation" and correlation Bipartite networks and hypergraphs Degree and cluster coefficient	Ideker	Jan 9 LFFB 107
Reading: Newman Ch. 6.1 - 6.6, p. 109-126; Ch. 6.10 - 6.11, p. 136-141		
Problem Set 1 Assigned		Due Jan 16
2.1 <u>Protein interaction networks I</u> Immunoprecipitation and affinity purification Mass spectrometry analysis	Ideker	Jan 14 LFFB 107
Reading: Huttlin, E. L., Bruckner, R. J., Navarrete-Perea, J., Cannon, J. R., Baltier, K., Gebreab, F., ... & Gygi, S. P. (2021). Dual proteome-scale networks reveal cell-specific remodeling of the human interactome. <i>Cell</i> , 184(11), 3022-3040.		
2.2 <u>Protein interaction networks II</u> Proximity labeling (APEX + BioID) Co-elution (size exclusion chromatography) Residue contact maps (XL-MS)	Ideker	Jan 16
Reading: Kobourov, S. G. (2012). Spring embedders and force directed graph drawing algorithms. arXiv arXiv:1201.3011.		
p Problem Set 2 Assigned. * Part I MUST be completed <u>prior to class 3.1</u> on Jan 21st.		Due Jan 23
3.1 <u>Introduction to network analysis in Cytoscape and Python</u> * Cytoscape and the NDEx infrastructure Cytoscape and NDEx: live hands-on demo Working with Cytoscape and NDEx in Python: live demo	Pillich / Churas	Jan 21 LFFB 107

3.2 Protein interaction networks III Ideker Jan 23
Yeast 2 Hybrid (Y2H) and Proximity Ligation (PLA) LFFB 107
Protein interaction prediction (Naive Bayes, PrePPI)
Protein interaction structural modeling (alphaFold & RoseTTAfold)

Reading: Humphreys, I. R., Pei, J., Baek, M., Krishnakumar, A., Anishchenko, I., Ovchinnikov, S., ... & Baker, D. (2021). Computed structures of core eukaryotic protein complexes. *Science*, 374(6573), eabm4805.

Problem Set 1 Solutions Available

Problem Set 3 Assigned

Due Jan 30

4.1 Genetic interaction networks I Kelly Jan 28
Epistasis versus epistacy; Statistical genetic interactions LFFB 107
Dependency maps and Project Achilles
Mutual exclusivity

Reading: Tsherniak, A. *et al.* Defining a Cancer Dependency Map. *Cell* **170**, 564-576. e16 (2017).

4.2 Genetic interaction networks II Kelly Jan 30
Epistasis and synthetic lethality LFFB 107
Epistatic miniarrays
Combinatorial CRISPR

Reading: Costanzo, M., Hou, J., Messier, V., Nelson, J., Rahman, M., VanderSluis, B., ... & Andrews, B. (2021). Environmental robustness of the global yeast genetic interaction network. *Science*, 372(6542), eabf8424.

Problem Set 2 Solutions Available

Problem Set 4 Assigned

Due Feb 6

5.1 Network organization and modularity I Ideker Feb 4
Degree distributions and the scale-free (power-law) property LFFB 107
Random network models: Erdos-Renyi versus preferential attachment
Pathfinding and shortest paths
Small-world effect and resilience
Components and cliques
Graph partitioning and min-cut

Reading: Newman Ch. 8.1 - 8.6, p. 235-265, Ch. 11.2 - 11.11, p. 354-391

5.2 Network organization and modularity II Ideker Feb 6
Network embedding (node2vec, PINNACLE) LFFB 107
Hierarchical community detection
Network reconstruction of whole-cell structure (i.e. the Gene Ontology)
Hierarchical network visualization tools

Reading: Qin, Y., Huttlin, E. L., Winsnes, C. F., Gosztyla, M. L., Wacheul, L., Kelly, M. R., ... & Ideker, T. (2021). A multi-scale map of cell structure fusing protein images and interactions. *Nature*, 600(7889), 536-542.

Problem Set 3 Solutions Available

Problem Set 5 Assigned

Due Feb 13

6.1 Transcription and chromatin networks I

Ideker

Feb 11

Using gene expression to infer transcriptional interaction

LFFB 107

Approaches from information theory

Approaches using differential equations

Discovery of master regulators

Reading: Replogle J.M., Saunders R.A., Pogson A.N., Hussmann J.A., Lenail A., ... & Weissman J.S. Mapping information-rich genotype-phenotype landscapes with genome-scale Perturb-seq. *Cell*. 2022 Jul 7;185(14): 2559-2575

6.2 Transcriptional and chromatin networks II

Benner

Feb 13

Chromatin immunoprecipitation

LFFB 107

Chromatin capture and HiC methodology

eQTL analysis; integration with genetic perturbations

Reading: Dixon, Jesse R., et al. Topological domains in mammalian genomes identified by analysis of chromatin interactions. *Nature* 485.7398 (2012): 376.

Problem Set 4 Solutions Available

Problem Set: None, prepare for MIDTERM

7.1 **MIDTERM EXAMINATION**

Halmos

Feb 18

LFFB 107

7.2 Network theory and algorithms II

Ideker/Carlin

Feb 20

Closeness and betweenness

LFFB 107

Eigenvector centrality and PageRank

Network propagation and random walks

Application: prediction of gene function

Reading: Newman Ch. 7.1 - 7.4, p. 168-178; Ch. 6.13 - 6.14, p. 152-161

Midterm Solutions Available

8.1 Network-based Genome-Wide Association Studies I

Palmer

Feb 25

Introduction to GWAS

LFFB 107

Association tests and tools – germline variants, common versus rare variants

Fine mapping using transcriptional networks

Reading: Barrio-Hernandez, I., Schwartzenuber, J., Shrivastava, A., Del-Toro, N., Gonzalez, A., Zhang, Q., ... & Beltrao, P. (2023). Network expansion of genetic associations defines a pleiotropy map of human cell biology. *Nature Genetics*, 1-10.

8.2 Network-based Genome-Wide Association Studies II Ideker Feb 27
Network prioritization of germline variants LFFB 107
Identification of mutated subnetworks in cancer (HotNet, NetSig, NBS)
Understanding conserved and shared signals by network co-localization

Reading: Rosenthal, S. B., Wright, S. N., Liu, S., Churas, C., Chilin-Fuentes, D., Chen, C. H., ... & Ideker, T. (2023). Mapping the common gene networks that underlie related diseases. *Nature Protocols*, 1-15.

No new Problem Set assignment, work on team projects

9.1 Using networks for interpretable machine learning Ideker / Pratt March 4
Basic introduction to neural networks (ANNs) LFFB 107
Neural networks coupled to structure (CNNs, LLMs)
Graph neural networks
Coupling ANN architecture to knowledge of biological networks and structures
Application: Translating mutations in genotype to cell growth phenotype
Application: Patient networks

Reading: Elmarakeby, H. A., Hwang, J., Arafeh, R., Crowdis, J., Gang, S., Liu, D., ... & Van Allen, E. M. Biologically informed deep neural network for prostate cancer discovery. *Nature*, 598(7880), 348-352 (2021).

Problem Set 6 Assigned (combined for lectures 7.2 - 9.1) **Due March 13**

9.2 Network comparison and differential analysis Ideker March 6
Cross species studies LFFB 107
Homologs, orthologs and interologs
Algorithms for network alignment
Networks across conditions, Edgetics
Measuring differential genetic interactions
Measuring differential protein interactions
How big is network condition space?

Reading: Sahni, N. *et al.* Widespread Macromolecular Interaction Perturbations in Human Genetic Disorders. *Cell* **161**, 647-660 (2015).1/

Problem Set 5 Solutions Available

No new Problem Set assignment, work on team projects

10 WORK ON TEAM PROJECTS

11 TEAM PROJECT PRESENTATIONS Ideker March 18, 3:00-6:00pm

FINAL PROJECT REPORTS DUE Halmos March 23 Midnight