

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	Apr 4 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	Apr 6 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 Apr 17
2.1 <u>Protein interaction networks I</u> Immunoprecipitation and affinity purification Mass spectrometry analysis	Ideker	Apr 11 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>Genetic interaction networks I</u> Epistasis versus epistacy; Statistical genetic interactions Dependency maps and Project Achilles Mutual exclusivity	Kelly	Apr 13 LFFB 107
Reading: Kobourov, S. G. (2012). Spring embedders and force directed graph drawing algorithms. arXiv arXiv:1201.3011.		
Problem Set 2 Assigned. * Part I MUST be completed <u>prior to class 3.1</u> on April 18.		Due Apr 24
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	Apr 18 LFFB 107
3.2 <u>Genetic interaction networks II</u>	Kelly	Apr 20

Epistasis and synthetic lethality
Epistatic miniarrays
Combinatorial CRISPR

LFFB 107

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 1 Solutions Available
Problem Set 3 Assigned

Due May 1st

4.1 Protein interaction networks II

Ideker

Apr 25

Proximity labeling (APEX + BioID)
Co-elution (size exclusion chromatography)
Residue contact maps (XL-MS)

LFFB 107

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.

4.2 Protein interaction networks III

Ideker

Apr 27

Yeast 2 Hybrid (Y2H) and Proximity Ligation (PLA)
Protein interaction prediction (Naive Bayes, PrePPI)
Protein interaction structural modeling (alphaFold & RoseTTAfold)

LFFB 107

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

Problem Set 2 Solutions Available
Problem Set 4 Assigned

Due May 8

5.1 Network organization and modularity I

Ideker

May 2

Degree distributions and the scale-free (power-law) property
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

LFFB 107

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

May 4

Network embedding (node2vec)
Hierarchical community detection
Network reconstruction of whole-cell structure (i.e. the Gene Ontology)
Hierarchical network visualization tools

LFFB 107

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 May 15

6.1 Transcriptional and chromatin networks I

Benner

May 9

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.

6.2 Transcription and chromatin networks II

Ideker

May 11

Using gene expression to infer transcriptional interaction

LFFB 107

Approaches from information theory

Approaches using differential equations

Discovery of master regulators

Reading: Gardner, T.S., Di Bernardo, D., Lorenz, D. & Collins, J.J. Inferring Genetic Networks and Identifying Compound Mode of Action Via Expression Profiling. *Science* **301**, 102-105 (2003).

Problem Set 4 Solutions Available

Problem Set: None, prepare for MIDTERM

7.1 **MIDTERM EXAMINATION**

Rahman

May 16

LFFB 107

7.2 Network theory and algorithms II

Ideker/Carlin

May 18

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

Problem Set 6 Assigned (combined for lectures 7.2 - 9.1)

Due Jun 1

8.1 Network-based Genome-Wide Association Studies I

Palmer

May 23

Introduction to GWAS

LFFB 107

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

Fine mapping using transcriptional networks

Barrio-Hernandez, I., Schwartzentruber, 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 <u>Network-based Genome-Wide Association Studies II</u>	Ideker	May 25
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 <u>Using networks for interpretable machine learning</u>	Ideker / Pratt	May 30
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).

9.2 <u>Network comparison and differential analysis</u>	Ideker	Jun 1
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).

Problem Set 5 Solutions Available

No new Problem Set assignment, work on team projects

10 WORK ON TEAM PROJECTS

11 <u>TEAM PROJECT PRESENTATIONS</u>	Ideker	Jun 13, 2h block
<u>FINAL PROJECT REPORTS DUE</u>	Rahman	Jun 18 Midnight