BE568: Computational Systems Biology of Human Disease

SPRING 2014

Approved as BME Elective

Course Outline:

Instructors:
Professor Simon Kasif

Time:
MW 6-8pm (subject to change & agreement by all registered students)

LECTURES and Lab Initial Room: LSEB B03 (further notice will follow).

Prerequisites: Junior/Senior or Graduate Student Standing in BME or Bioinformatics. For other disciplines such as medicine, biology, chemistry, physics, engineering or computer science permission of instructor is required.

This course will train students to apply or develop new computational network and machine learning concepts to probe into the systems biology of disease and personalized medicine. The emphasis this semester would be on cancer and diabetes.

The course will cover computational frameworks such as biological networks (including metabolic, regulatory and signal transduction networks), microarray analysis, proteomic analysis, next-generation sequencing, machine learning,
elementary genetics, **pathway modeling and analysis** and other omics technologies to focusing on clinical problems such as cancer, diabetes, inflammation and aging.

The course is aimed at junior/seniors and graduate students in biomedical engineering or bioinformatics. However, students or fellows from other disciplines ranging from medicine and biology to physics or computer science can attend the class with permission of instructor.

There are no exams and grading is based on **bi-weekly homework, reading research papers, class presentations and a team project**. The main aim of this course is to cover general concepts in biological computing that provide the foundation of thinking computationally about anomalous behavior in biological systems relevant to disease mechanisms, **systems biology of disease**, diagnosis, prognosis, **personalized medicine** or **network based drug design**. The course also aims to teach students to work in research teams and develop the skills to plan and coordinate a scientific project.

During the course we will have guest lectures from scientists working in local biotechnology companies or hospitals. For information please contact:

Professor Simon Kasif: kasif@bu.edu

**Goals**

The main aim is to prepare students to apply and develop new concepts in integrative and systems biology of human disease. This involves developing a familiarity with current high-throughput omics technologies, probing the complex systems biology of disease using these biotechnologies: storing, querying and manipulating massive amount of data,
performing analysis of clinically relevant integrative data, producing models of systems across scales, capturing anomalous behavior in biological networks and making and validating predictions made by these network models.

**Tentative Syllabus**

**Tentative Syllabus: Topics Subject to Change**

This course will cover many of the widely used techniques used for network modeling and analysis, systems biology and network modeling of biological systems focusing on detecting dis-regulated networks in disease and identification of novel drug targets and diagnostics.

The class will have a number of invited speakers covering disease biology, rational drug/diagnostic design and network analysis algorithms.

This semester we will focus on cancer but other diseases will be covered including diabetes.

No exams: reading assignments, write-ups of papers and class presentations, lab homework (applying machine learning tools, 2 person groups), final group project (3-4 person project).

There are no programming requirements (we will use widely available tools).

However, different homework (presentation, and write-up) criteria would be applied to graduate students, undergraduate students and students from outside engineering (e.g. biology or chemistry). We will try to form groups from different disciplines for projects.

**Computational Systems Biology of Disease**
**Introductory Cancer Lectures**

Lecture 1: Introduction to Cancer: Lecture by Bob Weinberg Video

Lecture 2: Cancer expanded: One Renegade Cell or a Systemic Process?

Lecture 3a: Biological Networks from E.coli to Human Tissue

Lecture 3b: Broad Introduction to Transcriptional Regulation Networks in Cancer and Signaling Networks in Cancer

Lecture 4: Subtypes of Cancer and Clinically Significant Cancer Phenotypes: Survival Drug Response

Lecture 5: Genomics and Cancer: mutations, copy number variation, epigenomics.

Lecture 6: Epigenomics of Stem Cells and Cancer Stem Cells.

Lecture 7: Diabetes

Lecture 8: Aging and Aging Genes

**Biological Networks**

Lecture 1: Introduction to Networks and Graphs

Lecture 2: Regulatory Networks

Lecture 3: Protein-Protein Interaction Networks (scale free networks)

Lecture 4: Signal Transduction Networks.

Lab Session: Gene Ontology and DAVID Lab Session:
Classification and Network Modeling Methodologies

Machine Learning

Lecture 1: Introduction to Machine Learning

Supervised Learning Methods

Lecture 2: Nearest Neighbor Methods
Lecture 3: Introduction to Decision Trees
Lecture 3: Support Vector Machines
Lab Sessions WEKA1, WEKA2 and Reporting Accuracy (ROC,FDR)

Un-Supervised Learning Methods

Lecture 4. Clustering / Bi-clustering lecture Spectral Graph Clustering Methods, SVD, PCA (principal component analysis)

** advanced topic **: Semi-supervised learning and network learning
Lab Session (Using Gene Pattern)

Lecture 5: Using WEKA, a machine learning environment

Graphical Models

Lecture 1: Probabilistic network (graphical models)
Probabilistic networks (models for gene expression & signaling)

Lecture 2: Network Discovery Algorithms Lab Session:
BN tools, Dynamic Network Simulations

**Personalized Medicine and Network Signatures of Disease**

Introduction to Biomarkers

Lecture 1: Pathways Signatures

Lecture 2: Network Signatures

Lecture 3: Genomic Signatures and Cancer: mutations, copy number variation, epigenomics.

Lecture 4: Cancer Data Analysis Subtypes of Cancer Drug Response Signatures Survival / Metastasis Signatures

Network Signatures for Diabetes and Cancer

Lecture 5: Detailed Cancer Classification with Microarrays Cancer classification with genomic markers

Lecture 6: Introduction to TCGA (Cancer Atlas)

Lab Session: working with Cytoscape and GenePattern

Lab Session: working with Gene Network Enrichment Analysis

**Personalized Medicine and Drugs**

Drug Response Signatures using supervised learning NCI-60 CMAP

**Project Planning and Execution (instead of exam)**

Applying machine learning to develop personalized signatures of drug response

**Optional topics:**
Metabolic Diseases

Metabolic Networks & Insulin Signaling

Diabetes

Lab Session: working with a human metabolic network

Inflammation (immune response)

Innate Immune Response

Adaptive Immune Response

NFKB networks

Lab Session: working with GNEA (detection of inflammation at the molecular network level)

Aging

Conserved Signaling Networks and Longevity

Lab Session: working with Aging Mouse Models

Additional Labs

Probability

Bayes Law, Conditional and Joint Probabilities

Stat. (basic tests, ranked tests)

Gene Pattern: permutations / diagnostic genes and classification

Accuracy/AUC

David Gene Set Enrichment:
GSEA

WEKA 1 WEKA 2

Gene Network Enrichment: GNEA

BN Networks / Graphical Models Network Discovery

Algorithms (THE DREAM COMPETITION)