BME 580.431 Introduction to Computational Medicine I 2016

Part I: 13 class meetings on Computational Physiological Medicine
Raimond Winslow, Sridevi Sarma

Part II: 13 class meetings on Computational Anatomy
Michael Miller, Tilak Ratnanather, Joshua Vogelstein

Lectures: Wednesdays and Fridays, 12:00 – 1:15pm in Hackerman 316
Section: Mondays in Hackerman 316

TA: Kristin Gunnarsdottir
Office Hours: Wednesdays, 11am – 12:00 in Hackerman 111

Personalized Mechanistic Models in the Clinic (Winslow, Project 1):

First reading assignment:
Winslow et al (2012) Computational Medicine: Translating Models to Clinical Care, *Sci. Transl. Med*. 4 158rv11

1) Fri Sept 2 Class:

<u>Overview of Computational Medicine (Lecture)</u>

Two aspects: modeling of disease; personalizing these models and applying them to treat patients

<u>Review the goals of the course:</u>

Hands on experience implementing and fitting models to patient data
Two classes of models: mechanistic; data-driven statistical models

Students will undertake a series of projects. Lecture materials and project assignments will be provided in advance of class meetings. Students are expected to read this material before every class meeting. Class meetings will focus on answering questions about the assigned material, and conducting "hands-on" project work while instructors are available to help.

Students will form project teams of 3-4 students. Each project will require presentation of a (brief) oral summary to the class and/or a written report as specified in the assignment. Class grades in the Comp Physiol portion of the course will be based on our evaluation of both oral and written presentations. Students will be expected to fully document code they develop, document how to run the code on specific data sets, and submit code and data sets to a class GitHub instance. Part of the project grades will be based on: whether or not we can download the codes from Github and easily run them to reproduce test data sets; quality of inline and “Readme” code documentation.

Assigned reading for Winslow:
Saeed et al (2011) Multiparameter Intelligent Monitoring in Intensive Care II: a public-access intensive care unit database. *Crit. Care Med*. 39(5): 952

Sun et al (2009) The cardiac output from blood pressure algorithms trial. *Crit Care Med* 37(1): 72

Sun et al (2005) Estimating cardiac output from arterial blood pressure waveforms: a critical evaluation using the MIMIC II database. *Comp Cardiol.*

Parlikar et al (2007) Model-based estimation of cardiac output and total peripheral resistance. *Computers in Cardiol*. 34: 379

2) Mon Sept 5

LABOR DAY NO SECTION

3) Wed Sept 7 Class:

<u>Model for Estimating CO from arterial BP Measurements (Lecture)</u>

Introduction to GitHub and OneDrive
Project 1 Assignment Distributed

4) Fri September 9 Class: LECTURE Kashif and Marmarelis Applications

<u>Kashif and Marmarelis Applications (Lecture)</u>

Kashif et al (2012). Model-based noninvasive estimation of intracranial pressure from cerebral blood flow velocity and arterial pressure. *Sci. Transl. Med.* 4(129):129ra44

Marmarelis et al (2014) Model-based physiomarkers of cerebral hemodynamics in patients with mild cognitive impairment. *Med. Eng. Phys.* 36(5): 628.

5) Monday Sept 12 Section:

Overview of Project 1 Assignment
Begin in-class work on Project 1

6) Wednesday Sept 14 Class: Work on Project 1

7) Friday Sept 16 Class: Work on Project 1

8) Mon Sept 19 Section: Work on Project 1

Project 1: Coding Progress Assignment submit via GitHub by 12:00 noon

9) Wed Sept 21 Class: Work on Project 1

10) Friday Sept 23 Class:

Project 1 Group Oral Presentations (Slides submitted to GitHub)
Each presentation should be < 15 slides and < 10 minutes.

Assigned Reading for Sarma:
Angus et al (2001). Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care. *Crit. Care Med.* 29: 1303–1310.

Henry et al (2015). A targeted real-time early warning score (TREWScore) for septic shock. *Science Translational Medicine*, Vol 7, Issue 299.

Project 2 Assignment: Students will be given control (non-sepsis) and comparison (sepsis) cohorts in the ~30 MIMIC-II subjects with demographic, clinical, and physiological waveform data; and will construct models of the probability that a given patient has sepsis as a function of their data variables. All data and pseudo code will be provided.

Statistical Models for Clinical State Detection (Sarma, Project 2):

11) Monday Sept 26 Section:

Review the following material:

- Bernoulli random variable
- Data Likelihood function

12) Wed Sept 28 Class:

<u>Sepsis (Lecture):</u> Describe Sepsis and the need for computational approaches to detect adverse clinical states for patients in the ICU.

13) Fri Sept 30 Class:

<u>Lecture:</u>

- Define and discuss Bernoulli random variables

- Define and discuss the Data Likelihood function
- Define and discuss Maximum likelihood estimation (as applied to the Bernoulli random variable): How do we construct a model of a Bernoulli random variable from i.i.d. samples?

14) Monday Oct 3 Section:

Review the following material and data:
- Maximum likelihood estimation
- MATLAB code provided for Project 2

15) Wed Oct 5 Class:

Lecture:
- GLM for the Bernoulli random variable
- Introduction to available PTS data available and MATLAB code

16) Friday Oct 7 Class: Work on Project 2

17) Mon Oct 10 Section: Work on Project 2

18) Wed Oct 12 Class: Work on Project 2

19) Fri Oct 14 Class: Classification Competition

Project 2 group presentations and participate in competition

Structural and Functional Computational Anatomy (Miller, Ratnanather):

20) Mon Oct 17 1st Section (Review of vector optimization: gradients, perturbations)

21) Wed Oct 19 Class

Introduction

- Multiple Modalities: T1,T2, DTI, PET, Spectroscopy
- Neuroinformatics and MRICloud

22) Fri Oct 21 Class (NO CLASS FALL BREAK)

23) Mon Oct 24 Section (Operators and Green's Functions)

24) Wed Oct 26 Class

Matrix Groups and Transformation of Images

- Rotation, Translation, Scale
- Orbit Model of Images

25) Fri Oct 28 class

High Dimensional Vector Fields via Splines and Energy Methods

- Variational Methods and Energy Constraints
- Splines as Green's functions (impulse responses)

26) Mon Oct 31 Section (Functional optimization)

27) Wed Nov 2 Class

Image Analysis, Image Understanding via Templates

- Bijective correspondences and Deformable Templates

28) Fri Nov 4 Class

Small Deformation Spline Models of Vector Fields and Images

- Linear systems model of landmarked images
- Non-linear observer equation for small deformation vector fields

29) Mon Nov 7 section (Jacobians and Inverses)

30) Wed Nov 9 class

High throughput neuroinformatics

- MRICloud and multiple modalities

31) Fri Nov 11 class

Dynamical Systems Models of Images

- Eulerian Flows for Medical Images
- Dynamical Systems Models based on Hamilton's Least Action Principle
- Registering Coordinate Systems via Dense matching

Statistical Connectomics (Vogelstein):

TA Session Contents:

1. Random variables, distributions, statistical models, likelihood
2. Optimization, maximum likelihood
3. Singular value decomposition and Principal Components Analysis
4. K-means and Gaussian Mixture Modeling

32) Mon Nov 14 section

33) Wed Nov 16 class #1

Week 1: Introduction to Brain Graphs

1. What's a graph?
2. What's a connectome/brain-graph and what are they useful for?

Homework:

Read this:
Statistical Analysis of Network Data: Methods and Models, Ch 1 & 2
Clinical applications of the functional connectome
Unraveling the Miswired Connectome: A Developmental Perspective

Write a 1-2 page summary of why understanding connectomics might be important in neurology and/or psychiatry, with >10 citations and 1 figure+caption.

34) Fri Nov 18 class #2

3. How do we estimate connectomes?

Homework:

Read this:
Imaging human connectomes at the macroscale
Mapping brain circuitry with a light microscope
Cellular-resolution connectomics: challenges of dense neural circuit reconstruction

Generate a table listing the pro's and con's of estimating connectomes across the different scales (3 different scales, >5 different desiderata).

35) Mon Nov 21 section (NO CLASS THANKSGIVING)

36) Wed Nov 23 class (NO CLASS THANKSGIVING)

37) Fri Nov 25 class (NO CLASS THANKSGIVING)

38) Mon Nov 28 section

39) Wed Nov 30 class #3

Week 2: Connectomes = Samples from Random Brain Graphs

1. What's a random graph and why do we care?
2. What's an Erdos-Renyi Random Graph?

Homework:

Read this:
[A Survey of Statistical Network Models](), Ch 1, 2, 3

Create Jupyter notebook or Rmarkdown or MATLAB livescript that:

a. Sample several different ER graphs for different values of n & p
b. Plot each as matrices with different sorting of vertices
c. Plot each using with different layouts
d. Write paragraph explaining the pro's and con's for each different plotting style
e. Plot a real connectome in several different ways
f. Write paragraph explaining what you learn about the structure of the connectome from the various visualizations

40) Friday Dec 2 class #4

3. What's a Stochastic Block Model Random Graph?
4. What's an Exponential Family Random Graph?

Homework:

Create Jupyter notebook or Rmarkdown or MATLAB livescript that:

g. Sample several different SBM graphs for different values of n & tau, and B
h. Plot each as matrices with different sorting of vertices
i. Plot each using with different layouts

j. Write paragraph explaining the pro's and con's for each different plotting style
k. Write a paragraph describing whether you think connectomes are approximate samples from SBM, explain why, and also why you might be wrong.

41) Monday Dec 5 section

41) Wed Dec 7 class #5

Week 3: Estimating and Testing in Statistical Connectomics

1. How do I test if my graph has structure?

Homework:

Read this:
A Consistent Adjacency Spectral Embedding for Stochastic Blockmodel Graphs
A semiparametric two-sample hypothesis testing problem for random graphs

Create Jupyter notebook or Rmarkdown or MATLAB livescript that:
l. Estimates the SBM parameters when block identities are known
m. Plots error of parameters vs sample size for several different parameter settings
n. Write paragraph explaining why errors are bigger for some values of the parameters
o. Estimate SBM parameters and block identities
p. Plot errors of parameters & identities vs. sample size for several different parameter settings
q. Write paragraph explaining why errors are bigger in this setting.
r. Estimate the SBM parameters for a connectome
s. Write paragraph describing whether you think the parameters are a good fit, and how the fit might be improved.

42) Fri Dec 9 class #6

2. How do I test if two graphs are different?

Read this:
A semiparametric two-sample hypothesis testing problem for random graphs

Create Jupyter notebook or Rmarkdown or MATLAB livescript that:

t. Sample correlated ER graphs for several different values of n, p, and rho
u. Plot graphs
v. Test if they are correlated
w. Compute the power of the test for a given setting
x. Plot power as a function of sample size
y. Plot 2 different connectomes side-by-side in several different ways
z. Test whether they are different
aa. Write paragraph explaining the results, the degree to which you trust them, why, and how the results could be more believable.

Class ends