**BENG 449 / ENAS 549 - Spring '23** Biomedical Data Analysis

## General Info

- Instructor: Richard Carson
- Office location: Malone 411 and LMP 89A (Med School)
- Student office hours: Malone 214 Tuesday 2:30-3:30pm on weeks when problem sets are due
- Phone: x72814
- email: richard.carson@yale.edu

## About the class: ,

- T, Th 1:00-2:15
- Location: Watson Center A48
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- This course is intended for upper classmen and graduate students who have taken Math 120. It meets the mathematics requirement for BME PhD students
- The course focuses on the analysis of biological and medical data associated with applications of biomedical engineering. It provides relevant background probability and statistics, and analytical approaches for determination of quantitative biological parameters from experimental data. Programming in Matlab to achieve these goals is a major portion of the course.
- The course is divided into *8 units*. Lecture notes are posted online
- Lectures are recorded and available in the Media Library on Canvas
- Course grading: 50% from the problem sets (40% for problem sets 1-7, 10% for final problem set), 20% from the midterm, and 30% from the final.

## Problem sets:

- There will be 7 problem sets, 1 each for the first 7 units.
- Problem sets are due by 11:59 PM one week after the end of each unit.
- There will be a final problem set given during reading period.
- The TF will organize a section on Monday for Matlab programming assistance and review before each problem set assignment is due. The TF will poll the class to choose a good time.
- Problem sets are posted online under Resources/ProblemSets.
- Problem set answers will be posted online under Resources/ProblemSetAnswers.
- "Warm-up" problems with answers are posted under Resources/WarmupProblems
- Problem sets are scored 1 point per problem.
- Late problem set submission policy: For the first and second day after the deadline 10% will be taken off for each late day. After that, no problem sets will be accepted.
- **See additional notes on problem sets** at the end of this document

## Exams:

- There will be a midterm exam in class that covers units 1 – 3.
- There will be a final exam in class that covers units 4-8.

## Matlab

- Matlab is free for students at
    - https://software.yale.edu/software/matlab-student

## Textbooks:

- King and Mody, *Numerical and Statistical Methods for Bioengineering*
  - Link on Resources page
  - http://hdl.handle.net/10079/bibid/9728026
  - On reserve in library
  - Online book: http://site.ebrary.com/lib/yale/docDetail.action?docID=10431397
  - Can download this link from the LinksToTextbooks folder
- Dunn, Constantinides, and Moghe, *Numerical Methods in Biomedical Engineering*
  - Link on Resources page
  - http://hdl.handle.net/10079/bibid/10969392
  - Online book: http://site.ebrary.com/lib/yale/docDetail.action?docID=10167095
  - Can download this link from the LinksToTextbooks folder
- Chapters from:
  - Beck and Arnold, *Parameter Estimation in Engineering and Science*
  - With author's permission
  - In *BackAndArnold* folder on Canvas server

## Class Resources

- All Matlab commands issued in each class are saved in a file under the folder named Matlab Histories
- All lectures will be recorded (MP4 file) and uploaded to the Media Library under Recordings

## Other Resources

- Palm *Introduction to Matlab for Engineers*
- Matlab through Engineering IT (http://www.eng.yale.edu/it/)
  - Including Optimization toolbox and statistics toolbox
  - "Garage" in Dunham
- Cobelli, Foster, and Toffolo *Tracer kinetics in biomedical research from data to model*
  - Online http://site.ebrary.com/lib/yale/Doc?id=10048311
- Jacquez, *Compartmental Analysis in Biology and Medicine*
- Edelstein-Keshet, *Mathematical Models in Biology*
- Murray, *Mathematical Biology I: An Introduction*
- Draper and Smith - *Applied Regression Analysis*
- Cooper, Bloom, and Roth, *The Biochemical Basis of Neuropharmacology*
- Britten, *Essential Mathematical Biology*
- Hoppensteadt and Peskin *Modeling and Simulation in Medicine and the Life Sciences*
- Humphrey and Delange, *An Introduction to Biomechanics*
- PET pharmacokinetic text - *Course web site*
- Carson chapter on PET modeling from Bailey, Townsend, Valk, and Maisey *Positron Emission Tomography: Basic Sciences - Course web site*
- Mendenhall and Scheaffer – *Mathematical Statistics with Applications*
- Boyce and DiPrima *Elementary Differential Equations and Boundary Value Problems*

## Summary

- Introductory Matlab programming: calculations, simulations, and analysis of biomedical data

- Principles of probability/statistics with engineering emphasis: random variables, distributions, expected values, bias, variance, covariance, correlation, propagation of errors
- Modeling and parameter estimation from data: linear and nonlinear least squares estimation (regression models); model fitting to data and model testing/comparison
- Differential equations (ordinary) – simulation and solution with Matlab, Applications of ordinary differential equations including Hodgkin-Huxley

## Schedule:

| Lect. No. | Day | Date | Unit | Topic | Resource | Problem Set Due Date |
|---|---|---|---|---|---|---|
| 1 | Tuesday | 1/17 | 0 | Class intro and Math review | King, Ch. 1 and Appendix A | |
| 2 | Thursday | 1/19 | 1 | Matlab programming | Dunn Ch. 2 and Appendix A | |
| 3 | Tuesday | 1/24 | | Matlab programming and data graphing | | |
| 4 | Thursday | 1/26 | | Mathematical programming examples | | |
| 5 | Tuesday | 1/31 | | Numbers in computers; Debugging Matlab programs | | |
| 6 | Thursday | 2/2 | 2 | Introduction to Probability – random variables – statistical examples | Beck, Ch. 2 | |
| 7 | Tuesday | 2/7 | | Concepts in Probability - expected value and covariance | | PS1 |
| 8 | Thursday | 2/9 | | Discrete and continuous random variables | King, Ch. 3 | |
| 9 | Tuesday | 2/14 | | Simulation and analysis of noisy data in Matlab | | |
| 10 | Thursday | 2/16 | 3 | Linear systems; Maximum likelihood estimation; Cramer-Rao lower bound | King, Ch. 2 | |
| 11 | Tuesday | 2/21 | | Ordinary least squares and residuals | Beck, Ch. 3, 5 | PS2 |
| 12 | Thursday | 2/23 | | Matlab examples of linear fitting and weighted least squares | | |
| 13 | Tuesday | 2/28 | 4 | Linear Algebra, Matrix version of linear regression | Dunn, Appendix C | |
| 14 | Thursday | 3/2 | | Weighted least squares, properties of estimators | Beck, Ch.6 | PS3 |
| 15 | Tuesday | 3/7 | | In-class midterm (units 1-3) | | |
| 16 | Thursday | 3/9 | 5 | Nonlinear equations , root finding, and iterative methods | King, Ch. 5 and 8 | |

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|---|---|---|---|---|---|---|
| 17 | Tuesday | 3/28 | | Parameter estimation - Gauss/Newton and Marquardt/Levenberg | Beck Ch. 7 | PS4 |
| 18 | Thursday | 3/30 | | Matlab examples; Michaelis-Menten and Scatchard analysis | Cooper, Ch. 4, Keshet Ch. 7, Britton Ch. 6 | |
| 19 | Tuesday | 4/4 | 6 | Hypothesis testing and t tests | King, Ch. 4 | |
| 20 | Thursday | 4/6 | | F tests and ANOVA | Dunn, Ch. 9 | PS5 |
| 21 | Tuesday | 4/11 | | Model comparison and selection | Cobelli 8.7 | |
| 22 | Thursday | 4/13 | 7 | Ordinary differential equations (ODEs), Euler, and Runge-Kutta | King, Ch. 6; Dunn, Ch. 7 | |
| 23 | Tuesday | 4/18 | | Runge-Kutta, Hodgkin Huxley, Stability | Dunn 7.7-7.8, Hoppensteadt 3.5, Britton, Ch. 6.5, | PS6 |
| 24 | Thursday | 4/20 | | Compartment Models and Tracer Kinetics | Dunn Ch 7.5;Cobelli, Ch. 4 | |
| 25 | Tuesday | 4/25 | 8 | PET imaging and model fitting | Bailey, Ch. 6, PK Manual | |
| 26 | Thursday | 4/27 | | EM algorithm, image segmentation and reconstruction | Class notes | PS7 |
| | | 4/28-5/4 | | Final PS (Reading period) | | |
| | Sunday | 5/7, 2pm, Watson Center A68 | | “In-class” final (units 4-8) | | |

TF: Nathanial Holderman (nathanial.holderman@yale.edu)
Section times: Monday, 5pm Watson A60

<u>Problem Set Recommendations:</u>

- It is recommended that you **do not wait until the end of the unit to start the problem set**. In general, the material necessary to solve the first few problems is covered in the first lectures of each unit.
- There will be TF session shortly before the problem set sets are due. It is strongly recommended that you **start the problems yourself before the TF session**. In that way, you will be better prepared to ask questions at the TF session, if necessary.

<u>Electronic Problem Set Submission</u>

- It is strongly preferred that you submit your problem sets entirely electronically. For mathematical work, please scan your document and submit electronically.
- Submit your problem sets via Canvas server.
- **Always show your Matlab code**. It is recommended that you copy and paste the Matlab code and graphs into a Word document.
- Please name your problem set files consistently: <last name>_<first name>_PS_problem set number> (e.g., Obama_Barack_PS1.docx). Please be sure the problems are numbered and are in order.
- Problem sets are due by 11:59 PM on the dates listed in the calendar below

<u>Problem Set Guidelines</u>

- Include lots of comments in your code (%..)
- All graphs should be titled – here is the Matlab code to do so:

```
Title('here is your title')
Xlabel('x-axis label, with units')
Ylabel('y-axis label, with units')
Legend('line1 title', 'line2 title', etc)
```

- It helps to keep things organized consistently:
    a. Define all variables (with units) at the start of each problem
    b. Introduce any equations you plan to use
    c. List assumptions
    **d. Show your work**
    e. Box the final answer so that it stands out from other calculations
- If a final answer looks wrong (too large, too small, negative when it should be positive, etc.), discuss why that might be the case. Can you relate the number to anything you know from the real world? Was there some assumption that might have gone awry? Do you have an idea as to where is the bug in your program, but you just can't find it? These types of comments will give you more partial credit if the solution is incorrect.

<u>Problem Set Collaboration Policies:</u>

- For problem sets 1-7, your submissions should be *primarily* your own work. You *may* work together to debug code and solve the problem sets (as well as getting help from the TF). What you submit should represent *your* understanding of the problem and the solution, i.e., you should be able to explain everything in your problem set submissions.
- Do *<u>not</u>* collaborate on the final problem set that is due during reading period. This should be *entirely* your own work.