

# Week 1, Lecture 1 - Introduction, statistics review

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# BIOENGR 188: Machine learning & data-driven modeling in bioengineering

## Lecture:

- ▶ Tuesdays/Thursdays 2:00–3:50pm
- ▶ Boelter Hall 5420

## Lab

- ▶ Fridays, 2:00–3:50pm
- ▶ Bunche Hall 3153

<https://aarmey.github.io/ml-for-bioe/>

# Lecture Slides

- ▶ Lecture slides will be posted on the course website.
- ▶ I'll try to finalize them by the night before, so you can print them out if you want.
- ▶ The slides posted the night before will *not* be everything, but will include space to fill out missing elements during class.

# Textbook / Other Course Materials

- ▶ There is no textbook for this course.
- ▶ I will post related readings prior to each lecture.
- ▶ These will either broaden the scope of material covered in class, or provide critical background.
- ▶ I'll make it clear which is the case.

# Support / Office Hours

## Prof. Meyer

- ▶ Wednesday 11:00-11:50am in Eng V 4129 or by appointment
- ▶ I will usually also stick around after class and am happy to answer questions.

## TAs

- ▶ TBD or by appointment

# Learning Goals:

By the end of the course you will have an increased understanding of:

1. Critical Thinking and Analysis: Understand the process of identifying critical problems, analyzing current solutions, and determining alternative successful solutions.
2. Engineering Design: Apply mathematical and scientific knowledge to identify, formulate, and solve problems in the chosen design area.
3. Computational Modeling: Apply computational tools to solve and optimize engineering problems.
4. Communicate Effectively: Learn how to give an effective presentation. Understand how to communicate progress orally and in written reports.
5. Manage and Work in Teams: Learn to work and communicate effectively with peers to attain a common goal.

# Practical Learning Objectives

By the end of the course you will learn how to:

1. Identify a question that can or cannot be solved by a modeling approach.
2. Determine the prerequisites to applying a modeling method.
3. Implement a number of different modeling methods to answer specific questions.
4. Critically assess modeling results.

# Grade Breakdown

- 30% Final Project
- 20% Homework Assignments
- 30% Midterm
- 20% Class Participation



# Labs

## Where

- ▶ Fridays, 2:00-3:50pm
- ▶ Bunche Hall 3153

## What

- ▶ These are mandatory sessions.
- ▶ You will have an opportunity to get started on each week's implementation and/or work on your project.

# Homework

- ▶ These will be a combination of a computational implementation and other problems.
- ▶ Each will help reinforce the material and provide hands-on experience by implementing what we learn in class.
- ▶ These are meant to challenge you to become comfortable applying the material.
  - ▶ Document your effort
  - ▶ Get started early
  - ▶ Seek answers to your questions in office hours and lab

# Project

- ▶ You will take data from a scientific paper, and implement a machine learning method using best practices.
- ▶ A list of papers with is provided on the website as suggestions.
- ▶ You may also search out options that would be of interest to you.
- ▶ More details to come.
- ▶ First deadline will be to pick a project topic.

# Exams

- ▶ We will have a midterm exam on week 6.
- ▶ You will have a final project in lieu of a final exam.

# Keys to Success

- ▶ Participate in an engaged manner with all in-class and take-home activities.
- ▶ Turn in assignments on time.
- ▶ Work through activities, reading, and problems to ensure your understanding of the material.

If you do these three things, you will do well.

# Introduction

How do we need to learn about the world?

- ▶ What is a measurement?
- ▶ What is a model?

# Three things we need to learn about the world

- ▶ Measurements (data)
- ▶ Models (inference)
- ▶ Algorithms

# Area of Focus

What we will cover spans a range of fields:

- ▶ Engineering (the data)
- ▶ Computational techniques (the algorithms)
- ▶ Statistics (the model)



Why do we need these things to learn about the world?

FILL IN

# Why we need models - Can a biologist fix a radio?



Figure: Lazebnik et al, Cancer Cell, 2002

# Why we need models - Can a biologist fix a radio?

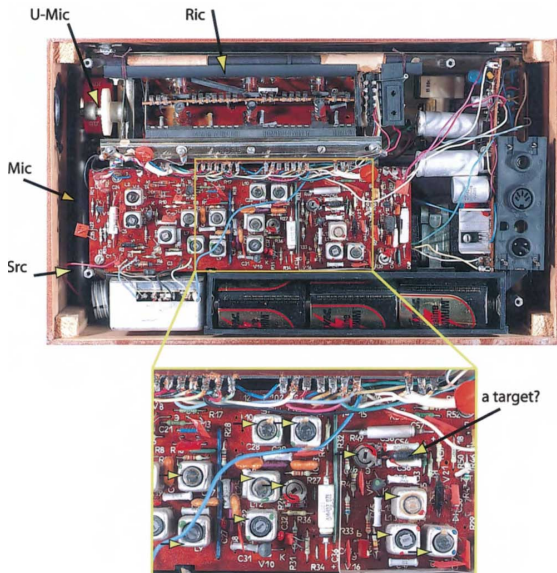


Figure: Lazebnik et al, Cancer Cell, 2002

# Why we need models - Can a biologist fix a radio?

A



B

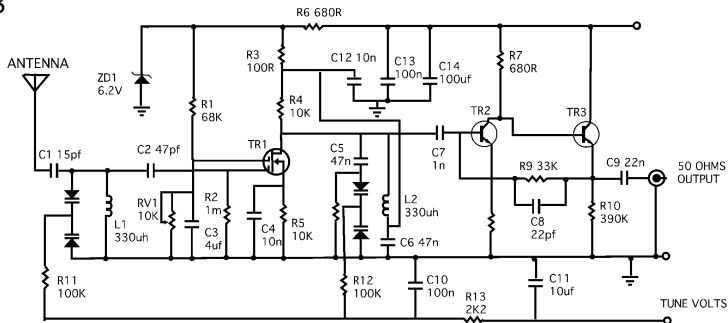


Figure: Lazebnik et al, Cancer Cell, 2002

# Comparisons

- ▶ Multiscale nature
  - ▶ Biology operates on many scales
  - ▶ Same is true for electronics
  - ▶ BUT electronics employ compartmentalization/abstraction to make understandable
- ▶ Component-wise understanding
  - ▶ Only provides basic characterization
  - ▶ Leads to “context-dependent” function

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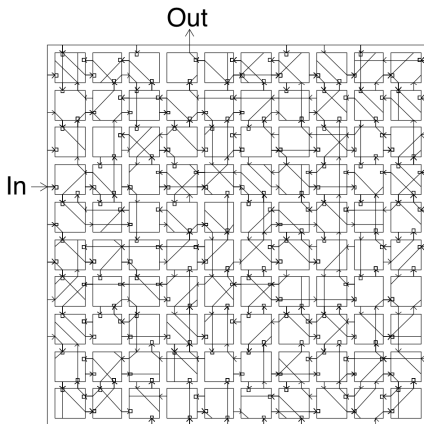


Figure: Thompson et al. Proc. 1st Int. Conf. on Evolvable Systems, 1996

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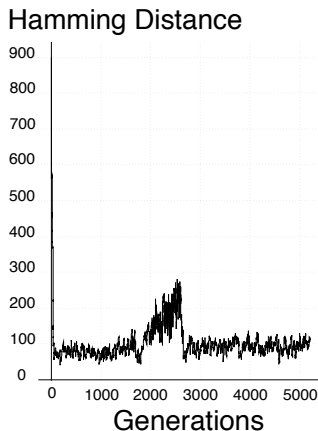


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For many tasks, machine learning can perform better than a human would



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# Data

- ▶ What is a variable?
- ▶ What is an observation?
- ▶ What is N?

# Types of variables

- ▶ Categorical
- ▶ Numerical/continuous
- ▶ Ordinal

# Probability

# Coin toss example

A set of trials: HTHHHTTHHTT

Two possibilities:

- ▶ Fair coin
- ▶ Biased (Heads 60%, Tails 40%)

# Distributions

We've already been talking about these! Distributions describe the range of probabilities that exist for all possible outcomes.

# Other Probabilities

**Conditional probability** The measure of an event given that another event has occurred.

**Marginal distribution** The probability distribution regardless of other observations/factors.

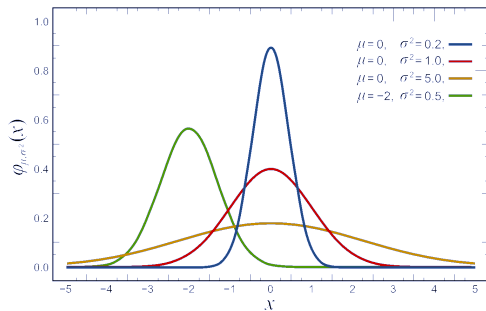
**Joint probability** In a multivariate probability space, the distribution for more than one variable.

**Complementary event** The probability of an event not occurring.

# Normal Distributions

- ▶  $\mu$ : center of the distribution
- ▶  $\sigma$ : standard deviation
- ▶  $\sigma^2$ : variance

$$f(x) = \frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}}$$





# Normal Distributions

For a *standard* normal distribution ( $\mu = 0$ ,  $\sigma = 1$ ):

$$f(x) = \frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}}$$

Area between:

- ▶ One standard deviation: 68%
- ▶ Two stdev: 95%
- ▶ Three stdev: 99.7%

You can normalize any normal distribution to the standard normal.

## Other Distributions

**Normal Distribution** Describes many naturally observed variables and has statistics mean and standard deviation

**Exponential Distribution** Describes the time between events in Poisson Processes

**Poisson** Stochastic process that counts # of events in some  $\Delta T$  time frame

**Rayleigh** Measure of vector magnitude within orthogonal direction is independent

**Gamma** Used in Bayesian statistics, often for modeling waiting times

**Beta** Random variables limited to intervals of finite length (e.g. Allele frequency in population genetics)

**Bernoulli** From binary Bernoulli trial, like a coin flip, describes the probability of observing a single event on next flip

**Binomial** Extension of the Bernoulli trial, describes the # of successes in a sequence of  $n$ -independent binary trials

**Multinomial** Extension of binomial when variable can take on more than two states.

# Distribution moments

The moments of a distribution describe its shape:

$$\mu_n = \int_{-\infty}^{\infty} (x - c)^n f(x) dx$$

First Mean

Second Variance

Third Skewness

Fourth Kurtosis

- ▶ Essential properties to determining how a set of data will behave during analysis
  - ▶ How might your measurements need to change with changes in variance?
  - ▶ What are these values for a normal distribution?

[https://www.che.utah.edu/~tony/course/material/Statistics/12\\_descriptive.php](https://www.che.utah.edu/~tony/course/material/Statistics/12_descriptive.php)

# Sample statistics

If we sampled a number of times ( $n = 3$ , say) many times, we could build a **sampling** distribution of the statistics (e.g. one for the **sample** mean and one for the **sample** standard deviation).

General properties of sampling distributions:

1. The sampling distribution of a statistic often tends to be centered at the value of the population parameter estimated by the statistics
2. The spread of the sampling distributions of many statistics *tends* to grow smaller as sample size  $n$  increases
3. As  $n$  increases, sampling distributions tends towards normality. If a process has mean  $\mu$  and standard deviation  $\sigma$ , then the sample mean  $= \mu$  and the sample standard deviation  $= \sigma/\sqrt{n}$

# Sample statistics

- ▶ This means that as  $n$  increases, the better estimate  $\mu_x$  is of  $\mu$ .
  - ▶ Sample standard deviation is the standard deviation of the mean.
- ▶ When a population distribution is normal, the sampling distribution of the sample statistic is also normal, regardless of  $n$ .
- ▶ And the central limit theorem states that the sampling distribution can be approximated by a normal distribution when the sample size,  $n$ , is sufficiently large.
- ▶ Rule of thumb is that  $n = 30$  is sufficiently large, but there are times when smaller  $n$  will suffice. More  $n$  is required with the higher the skew.

# Hypothesis Testing

In hypothesis testing we state a null hypothesis that we will test and if it's likelihood is less than some value, then we reject it.

For example:

- ▶  $H_0$ : A particular point comes from a normal distribution with mean  $\mu$  (and variance  $\sigma$ ).
- ▶  $H_0$ : Two sets of observations were sampled from distributions with different means.

Relative likelihood of the null hypothesis is the *p-value*.

# T-distribution

When  $n$  is small use the t-distribution with  $n - 1$  degrees of freedom.

- ▶ Ho: Assume  $\mu = \mu_0$  then calculate t.

$$t = \frac{\bar{x} - \mu_0}{s/\sqrt{n}}$$

- ▶ Can think of t designed to be  $z/s$ , where it's sensitive to the magnitude of the difference to the alternate hypothesis and scaled to control for the spread.
- ▶ When comparing the differences between two means: (null hypothesis the means are the same, variances/sizes assumed equal).

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{s_{X_1}^2 + s_{X_2}^2}{n}}}$$

# Effect size

- ▶ The scalar factor scales the t-value
  - ▶ If using a direct gaussian, the estimation of the mean scales with  $1/\sqrt{n}$
  - ▶ Then p-values become significant even though the differences in means is small
- ▶ Exercise caution and report the effect size
  - ▶ For example a 1% difference or a 50% difference in the means

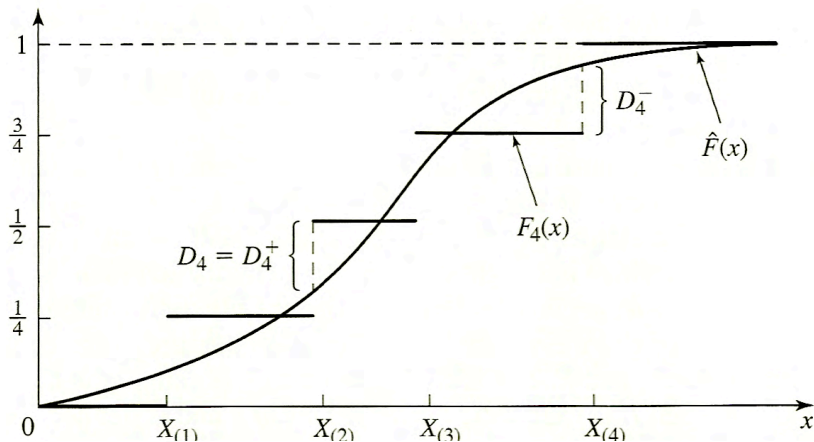


# Kolmogorov-Smirnov Test

- ▶ Comparison of an empirical distribution function with the distribution function of the hypothesized distribution.
- ▶ Does not depend on the grouping of data.
- ▶ Relatively insensitive to outlier points (i.e. distribution tails).

# Kolmogorov-Smirnov Test

- ▶ K-S test is most useful when the sample size is small
- ▶ Geometric meaning of the test statistic:



# Kolmogorov-Smirnov Test

Test statistic:

$$D_n^+ = \max_{1 \leq i \leq n} \left( \frac{i}{n} - \hat{F}(X_{(i)}) \right)$$

$$D_n^- = \max_{1 \leq i \leq n} \left( \hat{F}(X_{(i)}) - \frac{i-1}{n} \right)$$

$$D_n = \max \left( D_n^+, D_n^- \right)$$

Not expressed in one equation with absolute value because distance is assessed from opposite ends for each.

How is this then converted to a p-value?

# Graphical Analysis

- ▶ Plotting a distribution is often more informative than a goodness-of-fit test.
- ▶ Not only assesses deviation, but can explain where it occurs.
- ▶ Many variants:
  - ▶ Q-Q plot
  - ▶ P-P plot
  - ▶ Histogram with fitted distribution

# Testing errors

- ▶ Type I error: error of rejecting  $H_0$  when it is true (false positive)
- ▶ Type II error: not rejecting  $H_0$  when it is false (false negative)
- ▶ Alpha: significance level in the long run  $H_0$  would be rejected this amount of the time falsely. (i.e. We are willing to accept  $\alpha$  in 100 false positives.)

Beware of goodness-of-fit tests because they are unlikely to reject *any* distribution with little data, and are very sensitive to the smallest systematic error with lots of data.

# Multiple hypotheses

We want to test whether the gene expression between two cells differs greater than chance alone. We test the two samples with a p-value cutoff of 0.05:

- ▶ How many false positives would we expect after testing 20 genes?
- ▶ How about 1000 genes?

What about false negatives?

What does this mean when it comes to hypothesis testing?

## Further Reading

- ▶ Computer Age Statistical Inference, Chapters 1 and 2
- ▶ `scipy.stats`