BIOST 546: Machine Learning for Biomedical Big Data

Ali Shojaie

Lecture 1: Introduction
Spring 2017

Course objectives

- An introduction to statistical machine learning methods for analysis of Biomedical Big Data
- Supervised Learning: high dimensional regression and classification, variable selection, support vector machines and random forests
- Unsupervised Learning: clustering and dimension reduction methods
- Pitfalls and challenges of statistical learning methods for analysis of Biomedical Big Data
- We will *not* cover semi-supervised learning, reinforcement learning etc

Course structure

- Homeworks: combination of applied and conceptual questions (30% of total grade)
- You are allowed (and encouraged) to work together on homework problems, but the final solution (codes, implementation, writeup) should be yours
- Project: (40% of total grade)
  - Applications of machine learning methods for analysis of biomedical data, or development of new ideas (more later)
  - Teams of 2, ideally, working on data from your own research
  - Abstract (team members, description of data, project idea etc):
  - Proposal presentation (project description and preliminary results):
  - Final presentation:
- Exam: Last day of class, or exam week, depending on how much we get to cover (30% of total grade)

Resources I

- Instructor: Ali Shojaie, PhD, Department of Biostatistics, UW
  - Office: HSB F642
  - Email: ashojaie@uw.edu
  - Phone: 616-5323
- TA: Asad Haris, Department of Biostatistics, UW
  - Email: aharis@uw.edu
- Office hours:
  - Ali: Tue 12:30-1:30pm, or by appointment.
  - Asad: Wed 10:30am - 11:50am in South Campus Center (SCC) 303, except for the following days:
    - ⋆ on 4/5, 5/3, 5/31 TA OH will be in Foege (Genome Sciences) S060
- Questions are *very* welcome during the class (please interrupt!)
- Class website:

  www.biostat.washington.edu/∼ashojaie/teaching/ML.html

  Handouts, datasets, R code etc will be provided on the website *only*

Resources II

- Recommended reading;
  - Introduction to Statistical Learning: James et al (2013), Springer (free online, includes R labs)
  - Elements of Statistical Learning: Hastie et al (2009) Springer (free online)
  - Machine Learning: Murphy (2012)

Topics

- Linear, and generalized linear regression analysis (logistic regression and survival analysis)
- Resampling methods (bagging, bootstrap)
- Multiple comparison adjustment (family wise error rates, and false discovery rate control)
- Tree-based methods (CART, random forests, and deep learning (time permitting)
- Clustering (hierarchical, k-means, model based, bi-clustering)
- Dimension reduction (principal component analysis, multi-dimensional scaling)

Throughout the course, we will discuss challenges and remedies for biomedical big data

This course

- We will cover the big ideas in statistical machine learning for biomedical big data
  - will not discuss some of the details on theory or formulations
  - will not cover implementation details (i.e. how to solve the optimization problems or code-up the algorithms)
  - will cover practical issues regarding the use of algorithms, particularly related to biomedical big data
- We will focus on using `R`

Why use R?

- Limited point-and-clickability
- Raw output is not what your co-authors (or professors) want to see
- Data manipulation non-trivial
- Formal language, can do almost anything
- Core is written by experts, also contributed packages
- Free! - and available on any sensible platform
- New ML methods implemented as R packages
- Many existing packages for processing and analyzing biomedical data
- You are welcome to use other software/programming languages, but only R is supported in class

Case Studies

- Bring your laptop, with R installed.
- We will try out some of the labs in Introduction to Statistical Learning (ISL) as well as application cases focusing on biomedical data
- To learn more... go through the labs on your own!
  - To make sure you're ready, take a look at Lab 1 (end of Chapter 2) of ISL, and try the commands if needed!!

Prerequisites

- Two main prereqs for the class:
  - Basic statistics and probability: you need to know simple linear regression and hypothesis testing
  - Familiarity with computing: you need to be able to prepare your data for analyses in this class (data wrangling)

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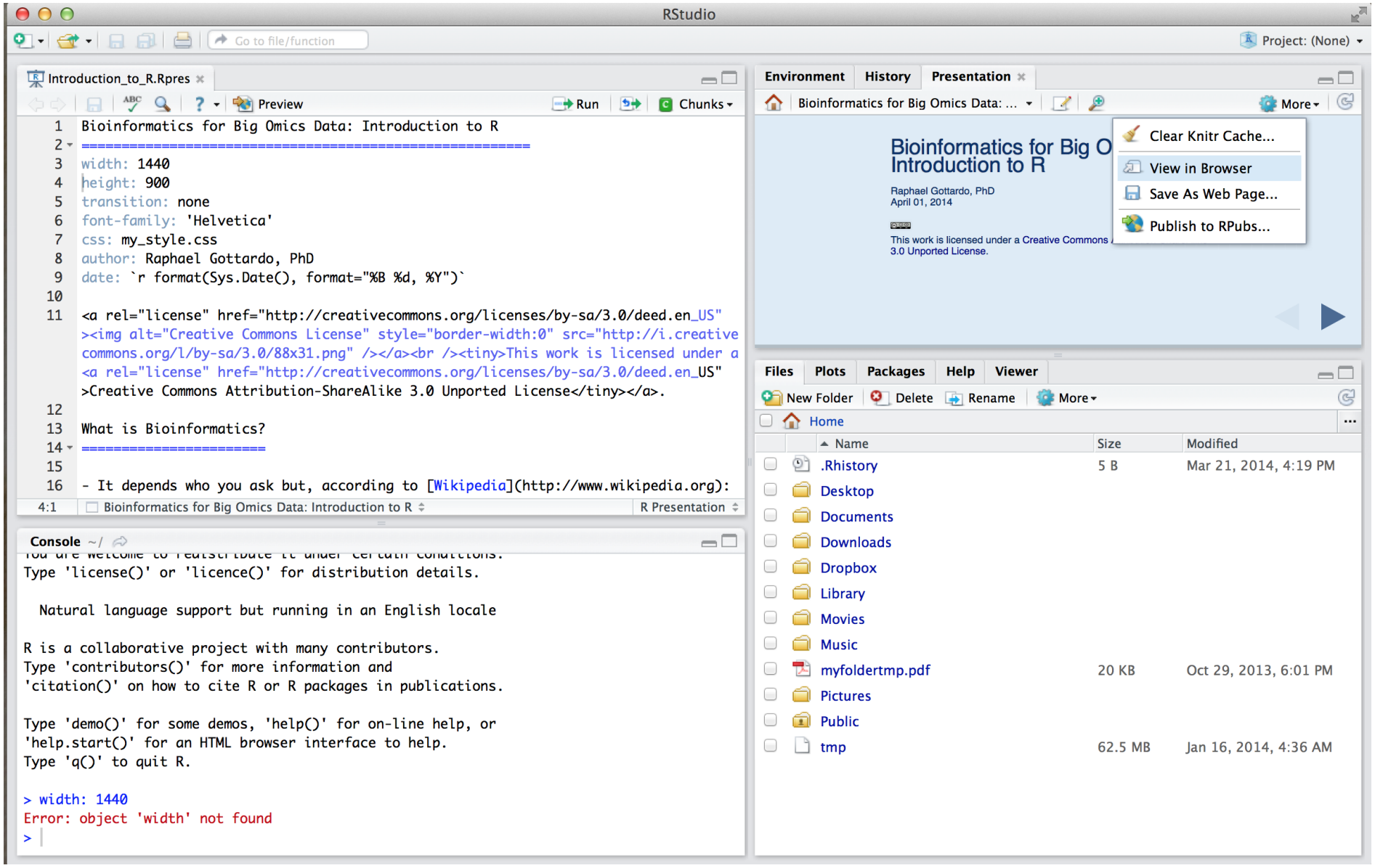
- This course focuses on statistical machine learning methods for analysis of biomedical data, *after the data has been preprocessed*
  - We do not focus on pre-processing of biomedical big data
  - BIOST 544 gives an *Intro to Biomedical Data Science*
  - BIOST 545 focuses on preprocessing of *omics* data. The material (lecture notes, `R` codes, etc) for BIOST 545 are available at `https://github.com/raphg/Biostat-578`
    - ⋆ You need to open the slides in `RStudio`: download the complete folder from the website, and 'open' each of the slides in `RStudio`; you can then choose either *Preview* or choose *Open in Browser* from the *More* menu in the upper right corner.


RStudio
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1 Bioinformatics for Big Omics Data: Introduction to R
2 ==========
3 width: 1440
4 height: 900
5 transition: none
6 font-family: 'Helvetica'
7 css: my_style.css
8 author: Raphael Gottardo, PhD
9 date: `r format(Sys.Date(), format="%B %d, %Y")`
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11
<tiny>This work is licensed under a Creative Commons Attribution-ShareAlike 3.0 Unported License</tiny>.
12
13 What is Bioinformatics?
14 ==========
15
16 - It depends who you ask but, according to [Wikipedia](http://www.wikipedia.org):
4:1
Bioinformatics for Big Omics Data: Introduction to R
R Presentation
Console ~/
Type 'license()' or 'licence()' for distribution details.
Natural language support but running in an English locale
R is a collaborative project with many contributors.
Type 'contributors()' for more information and
'citation()' on how to cite R or R packages in publications.
Type 'demo()' for some demos, 'help()' for on-line help, or
'help.start()' for an HTML browser interface to help.
Type 'q()' to quit R.
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Environment
History
Presentation
Bioinformatics for Big Omics Data: ...
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Introduction to R
Raphael Gottardo, PhD
April 01, 2014
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3.0 Unported License.
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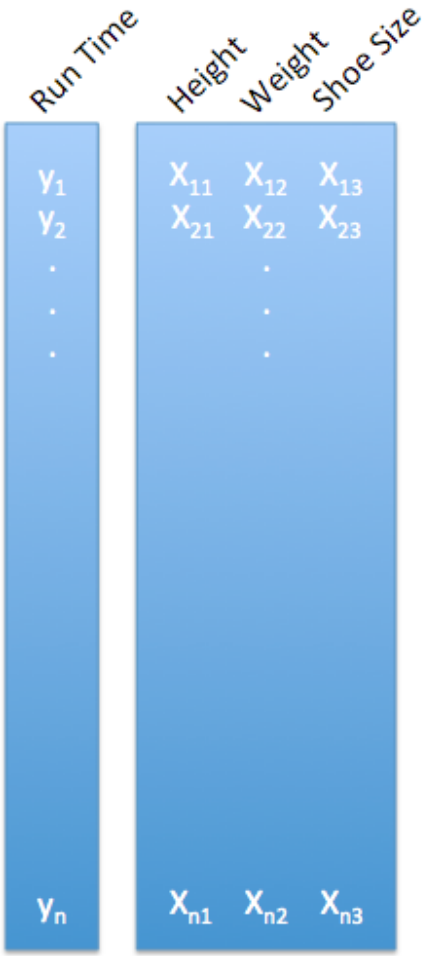
Today's lecture

- What is statistical learning?
- Supervised vs unsupervised learning
- Low-dimensional vs high-dimensional learning

A Simple Example

- Suppose we have $n = 500$ kids for whom we have $p = 3$ measurements: height, weight, and shoe size.
- We wish to predict these kids' 1600-meter run times using these measurements.

A Simple Example



Notation:

- n is the number of observations.
- p the number of variables/features/predictors.
- y is a n-vector containing response/outcome for each of n observations.
- X is a $n \times p$ data matrix.

Linear Regression on a Simple Example

- You can perform linear regression to develop a model to predict run time using height, weight, and shoe size:

$$y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \varepsilon$$

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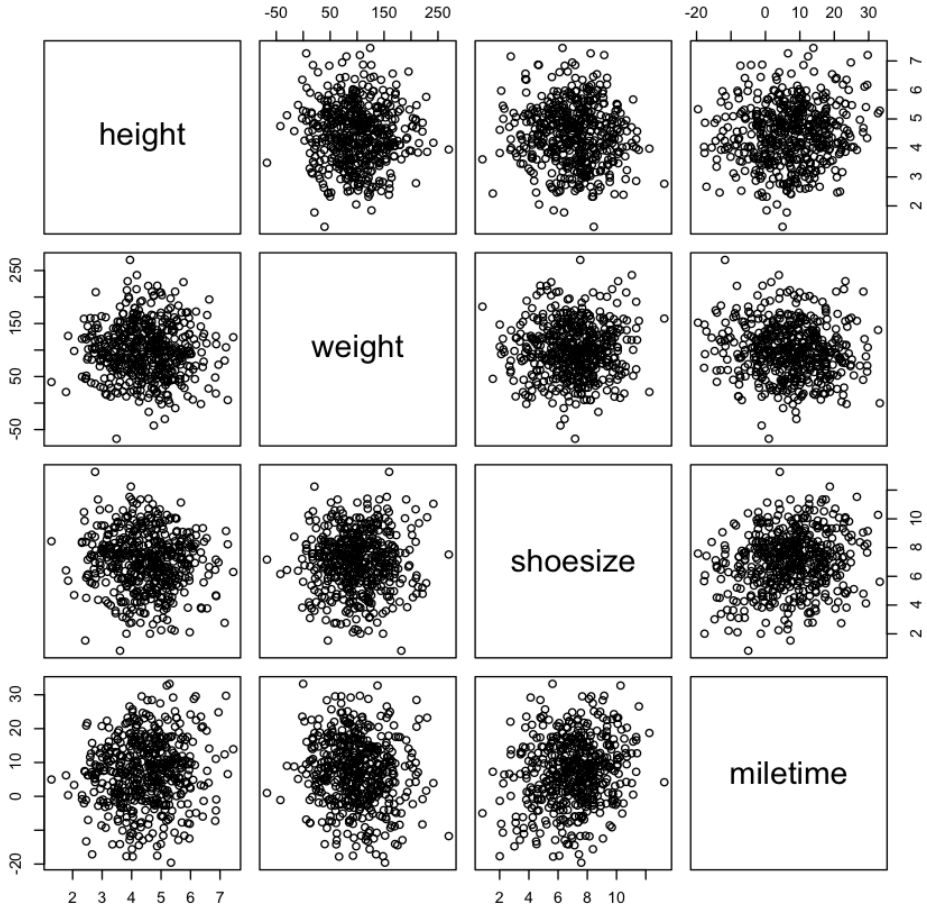
- You can look at the coefficients, p-values, and t-statistics for your linear regression model in order to interpret your results.
- You learned everything (or most of what) you need to analyze this data set in AP Statistics!

A Relationship Between the Variables?



Linear Model Output

	Estimate	Std. Error	T-Stat	P-Value
Intercept	-2.265831	2.644654	-0.857	0.39199
height	1.074814	0.414789	2.591	0.00985 **
weight	-0.021155	0.008482	-2.494	0.01295 *
shoesize	0.955222	0.214449	4.454	1.04e-05 ***

$$\text{RunTime} \approx -2.27 + 1.07 \times \text{Height} - 0.021 \times \text{Weight} + 0.96 \times \text{ShoeSize}.$$

More General Models

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- In both cases, ε is the noise term: we cannot perfectly determine y from $X_1, X_2, \ldots, X_p$, because y *is also a function of* ε, which is not observable
- We are usually not interested in the single data set that we have available: the data set is an *example* of other data sets (e.g. run times of other kids)

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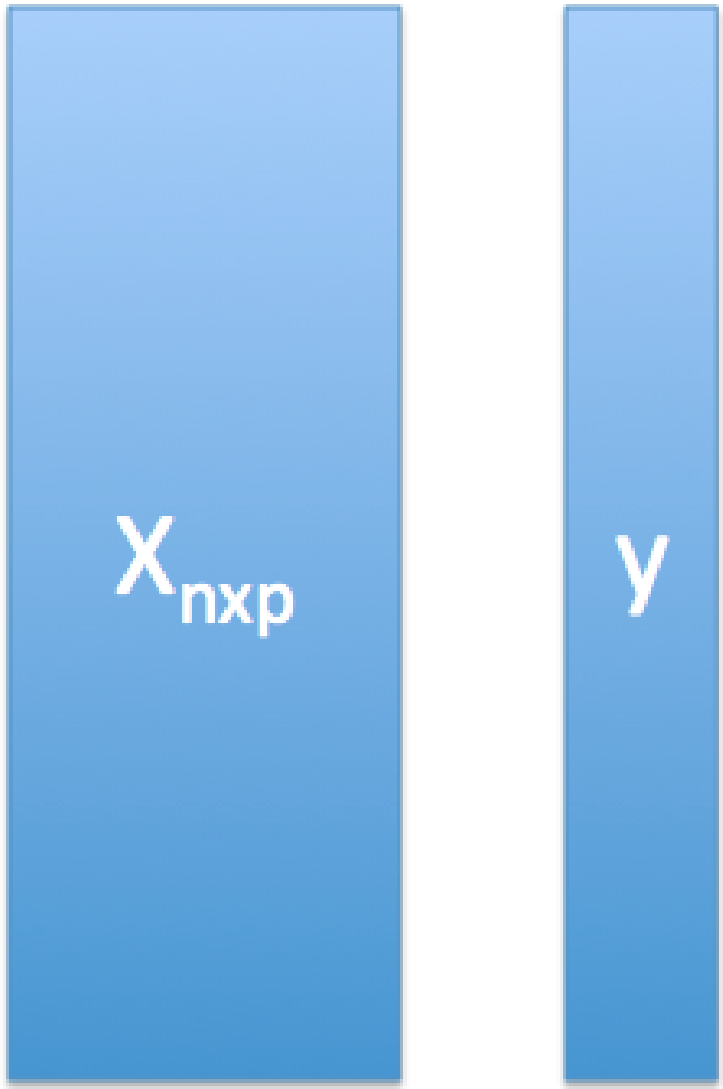
  - $E\left(\hat{f} - f\right)^2$ is called the reducible error
  - $\mathrm{Var}(\varepsilon)$ is called the irreducible error
- These errors are with respect to the 'distribution of data' ...

Low-Dimensional Versus High-Dimensional

- The data set that we just saw is low-dimensional: $n \gg p$.
- Lots of the data sets coming out of modern biological techniques are high-dimensional: $n \approx p$ or $n \ll p$.
- This poses statistical challenges! AP Statistics no longer applies.

Low Dimensional



High Dimensional

What Goes Wrong in High Dimensions?

- Suppose that we include many more predictors in our model, such as
  - 50-yard dash time
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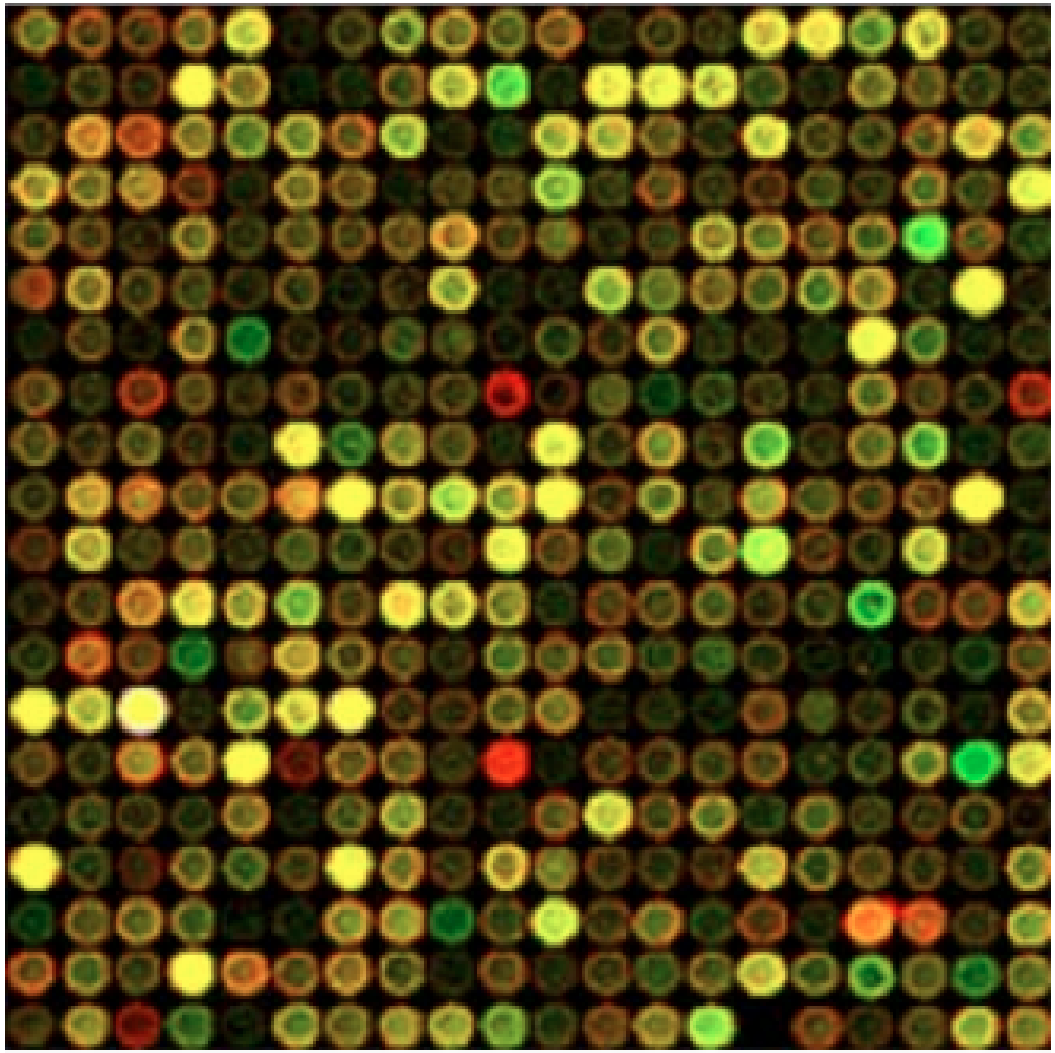
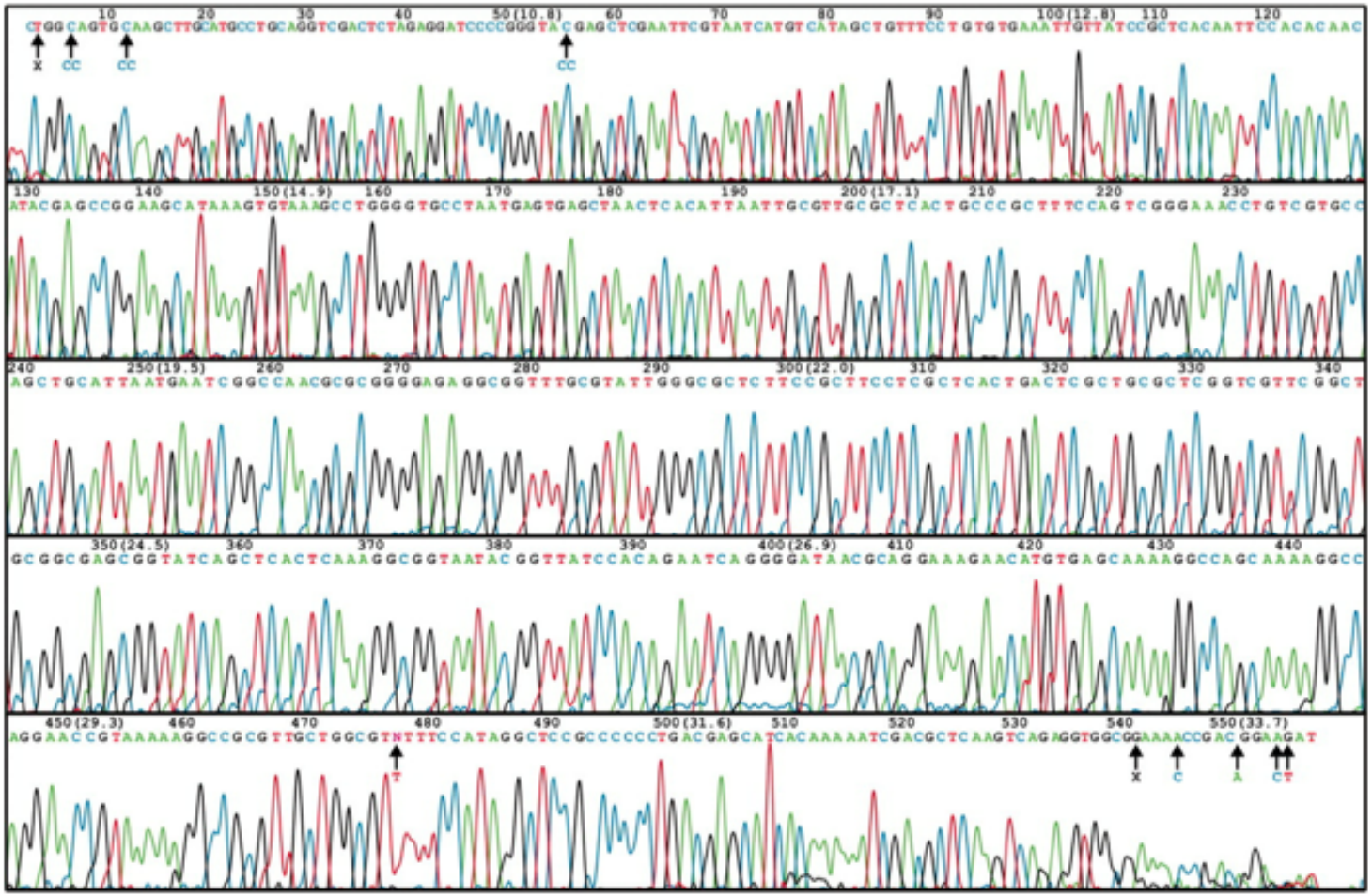
- Overfitting: Model looks great on the data used to develop it, but will perform very poorly on future observations.
- When $p \approx n$ or $p > n$, overfitting is guaranteed unless we are very careful.

Gene Expression Data

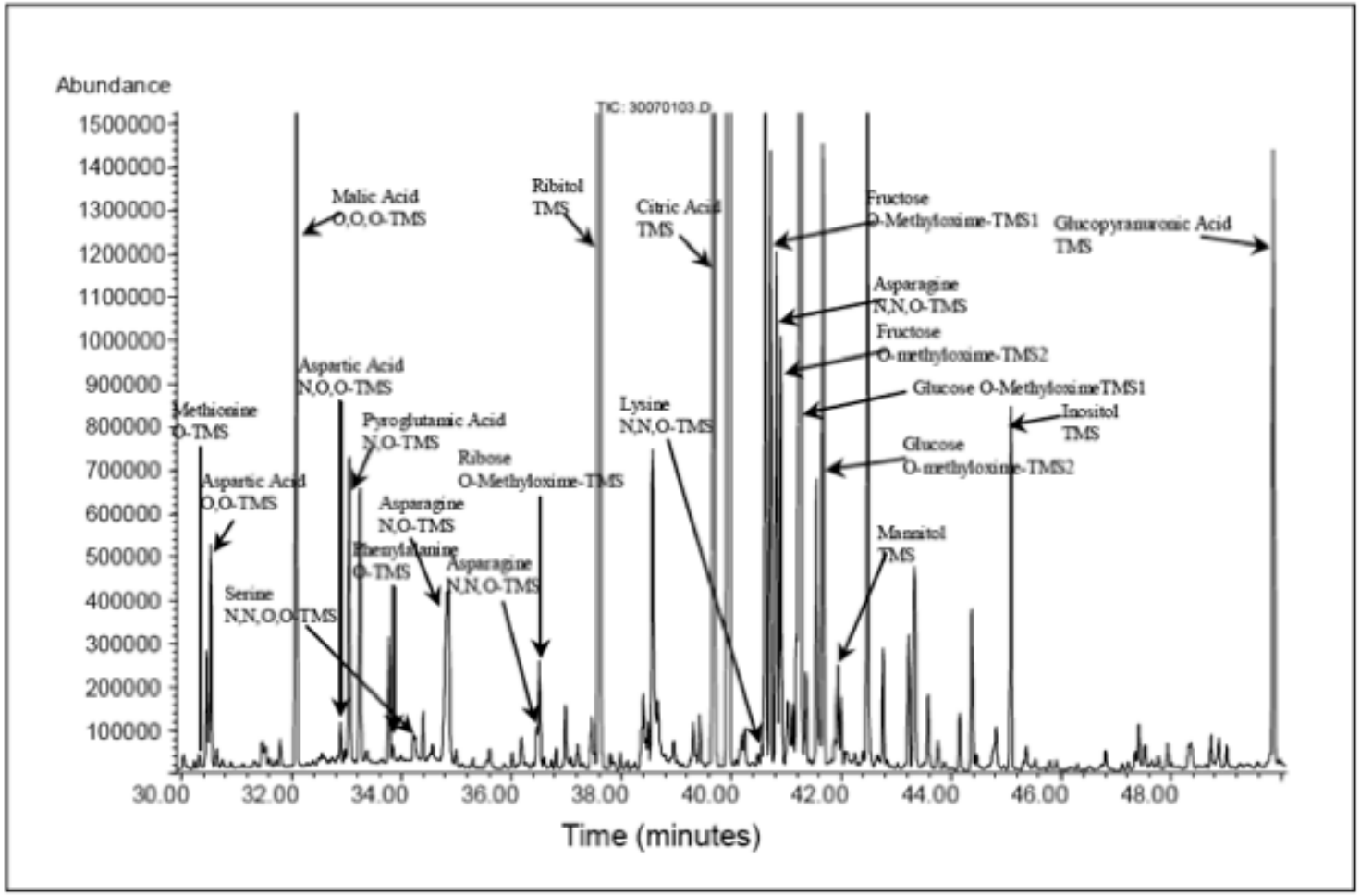


DNA Sequence Data

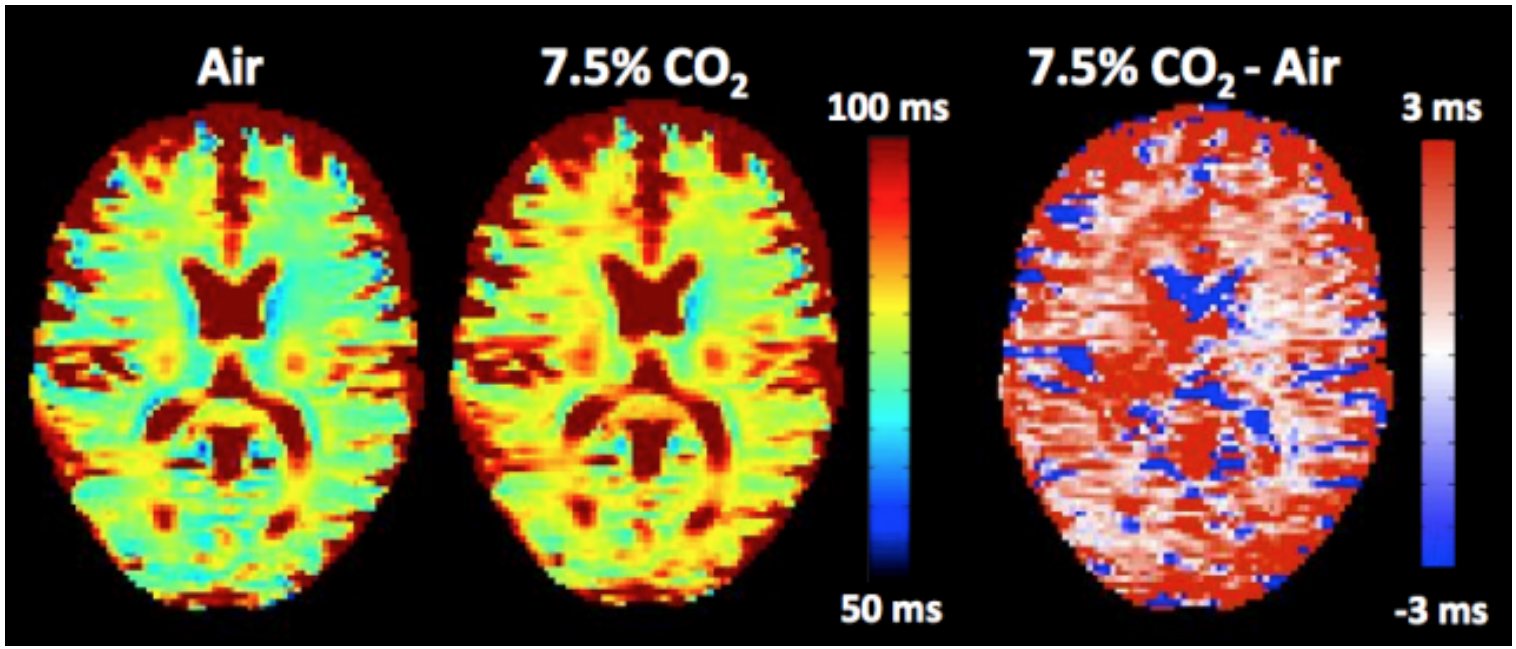


DNAse Hypersensitivity Data

Metabolomic Data



Brain Imaging Data



Electronic Health Records

Biomedical Big Data Analyses

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- Cluster tissue samples on the basis of DNase hypersensitivity... using $n = 200$ cell types and $p = 1,000,000,000$ variables.
- Identify subset of $p = 20,000$ brain regions (variables) whose activities are associated with onset of Alzheimer's disease... using images from $n = 250$ subjects (healthy and diseased).

Why Does Dimensionality Matter?

- Classical statistical techniques, such as linear regression, *cannot* be applied.
- Even very simple tasks, like identifying variables that are associated with a response, must be done with care.
- High risks of overfitting, false positives, and more.

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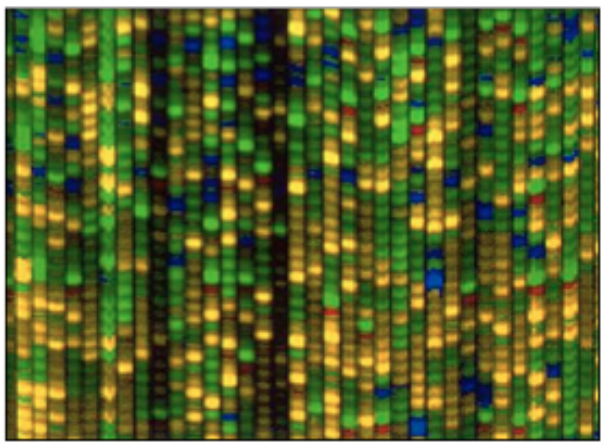
This course: Statistical machine learning tools to obtain generalizable insight from Biomedical Big Data.

Statistical Machine Learning

Google™



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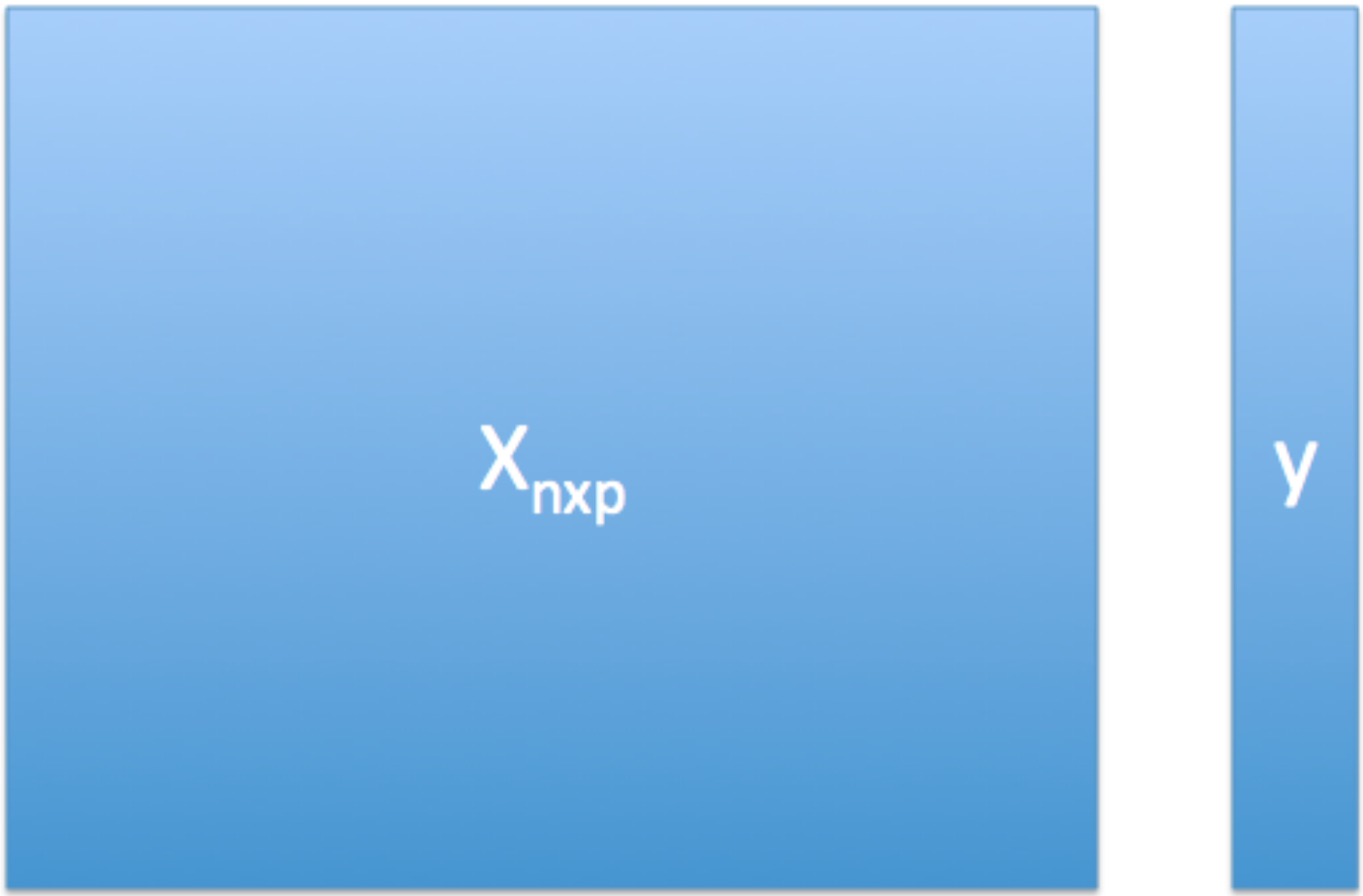
  - Regression
  - Classification
  - Hypothesis Testing
- Unsupervised Learning: Discover the signal/patterns in X, or detect associations within X.
  - Dimension Reduction
  - Clustering

Supervised Learning



Unsupervised Learning

Next Lecture

- A review of regression
- Training and test errors
- Cross validation