Modern Clinical Data Science

Course Notes

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Chapter 1

Overview of Clinical Data Science

The term "data science" has been overused in recent years, and it has become something of a buzzword as a result[1]. However, I think it can best be described as:

> **data science**: Any endeavor in which statistics, machine learning, data analysis, computer science, and information science intersect with domain knowledge.

Data science is about using the machinery of statistics and computer science to solve real-world problems. In the clinical domain, that means incorporating methods from epidemiology, biostatistics, computer science, and machine learning with insights gained from the clinical research literature and the practical experiences of physicians, nurses, hospital administrators, operational teams, and biomedical researchers.

So why is data science considered its own thing, and why am I creating a separate course about it instead of pointing you to Khan Academy, Coursera, etc., all of which have excellent courses on these various technical domains? Because (a) if you tried to learn data science that way, you'd never get anywhere; there are simply too many different subjects you'd have to master, and

[1] See also: "artificial intelligence", "machine learning", "deep learning".

(b) clinical data has issues that are domain-specific, and that rarely come up in general courses on machine learning and related topics. Many times I will think I know what method to use to solve a particular problem, but then when it comes time to gather the data, unusual and unforeseen problems arise. This happens all the time to biomedical and clinical data science researchers, and it is particularly problematic for people who are encountering data analysis and statistical/machine learning methods for the first time. Many assume the problem is them and give up, when in reality they are encountering a genuine difficulty with the data they're working with that the folks doing ad recommendations at Google never have to face.

However, my main reason for doing this is that I believe that in healthcare, clinical and operational teams will increasingly come to rely on data. People who have mastered at least the basic vocabulary of data science will be best positioned to think creatively about how we can improve healthcare using data and analytics, and will be assets to their teams.

1.1 Project Examples

Whenever I teach, I ask students to provide some examples of projects for which they think data and machine learning/statistics could be useful. The following are real examples. There are many and some of them are long, but I encourage you to read through all of them to see the diversity of problems that physicians and folks working in population health, health system operations, etc. come up with.

1. *Unnecessary ER trips.* "Given a number of factors (types of admissions a person has had in the past, number of admissions/re-admissions, social determinants, etc.) can we predict who is going to show up at the emergency room unnecessarily"

2. *Good/poor candidates for program.* "determine if patients are good or poor candidates for one of our specialty care model bundle programs"

3. *Predicting unplanned admissions.* "predicting unplanned inpatient admissions based on many different variables (e.g. chronic conditions,

engagement with primary care, etc.) and how these inputs interact with each other"

4. *Recommending an intervention.* "...stratification/prioritization of care management or other interventions or for clinical decision support...a tool would recommend an appropriate intervention based on the profile of the patient"

5. *Recommending a diagnosis.* "Based on unstructured chat conversations and also structured questions/forms/data...map out possible care pathways. For example, if someone says they have stomach pain, gives their zip code, insurance, pain tolerance and symptoms, and is logged in so we have past history, ask a few more questions and then we could determine they are 45% likely to have ulcer vs. constipation vs. food poisoning vs. appendicitis."

6. *Predicting the amount paid by patients.* "Patient bill estimates - learning from claims data typical amount paid by patients for appointment reasons/types (e.g. estimate of additional services/care administered, and associated cost, based on patient details such as age, gender, etc.)"

7. *Identifying patient subtypes.* "identify cohorts within a population with chronic conditions based on their differences in longitudinal care across the continuum of settings (inpatient, ambulatory, primary care, specialty care, etc.)"

8. *Which conversations are similar?* "using previous chat histories to train (a chatbot) and become more effective/efficient for different, future patient chat experiences"

9. *Predictors of COVID-19 outcomes.* "Get baseline diabetes control marker (HbA1C) and acute glycemic control (inpatient glucose values) and see if either is a stronger predictor of COVID-19 outcomes (ICU, intubation, death)."

10. *Factors influencing mortality in myelofibrosis.* "We see lots of patients who are ineligible for clinical trials based on comorbidities and underlying organ dysfunction. However it is unclear how these factors affect OS. I would like to extract comorbidity data and baseline laboratory factors in patients with myelofibrosis to see how these factors affect mortality,

if controlled for such important factors such as treatment, age, sex, insurance, number of comorbidities, and clinical risk score (DIPSS)."

11. *Non-adherence and difficult-to-treat asthma.* "We want to see whether non-adherence to prescribed inhaled corticosteroids plays a major role in poorly controlled asthma. Difficult-to-treat asthma can be evaluated by the number of ED visits, hospitalizations, prescriptions of prednisone and prescriptions of biological therapies. Using EPIC [we] can obtain medicine reconciliation information, of prescriptions sent, what proportion of those prescriptions were dispensed by Pharmacy. Question is can we find associations between the percentage of prescriptions filled and difficult-to-treat asthma."

12. *Impact of diabetes and hyperglycemia on progression-free survival.* "Aim: Assess the impact of diabetes and hyperglycemia on first-line systemic therapy response (progression-free survival) in patients with advanced non-small cell lung cancer. Diabetes- defined by presence of diagnosis codes coding for diabetes. Hyperglycemia- random glucose >200 ng/dL. Covariates of interest- age, sex, other treatments (RT, surgery), malignancy characteristics (stage, histology), smoking history, ecog (performance status), comorbidities, medications (steroids, anti-hyperglycemics)"

13. *Effect of statin use on MACE.* "Retrospective cohort study in elderly patients with CAD taking statins...exposed group are patients on a high-intensity statin; control group are patients on a moderate- or low-intensity statin. Participants matched based on age, gender, LDL category, and Elixhauser index category...The primary efficacy outcome would be the time-to-first-event of 3-point MACE[2]."

14. *Clustering patients with NAFLD.* "We wanted to understand non-alcoholic fatty liver disease (NAFLD) better, so we developed a cohort of NAFLD patients using EMR-based criteria and then clustered them based on comorbidities, medications, vital signs, and lab values to identify NAFLD subtypes. We then characterized the phenotypes and outcomes of the different subtypes."

[2]MACE stands for "Major Adverse Cardiac Event". The 3-point MACE is a composite of nonfatal stroke, nonfatal myocardial infarction, and cardiovascular death.

1.2 A Taxonomy of Problems

All of these examples describe situations where we want to use data to answer questions of clinical or operational importance. While the details differ in each scenario, the important thing to notice here is that many of the tasks themselves are structurally similar.

For example, all of the items except $7-8$ and 14 describe situations where we want to associate information about a patient with a particular outcome or recommendation. Using information about a patient to estimate the size of a bill (#6) may appear to be a very different problem than uncovering factors influencing myelofibrosis mortality (#10), but the structure of the two problems is similar: the patient features are used as input, and the output is whatever quantity you care about (e.g. the cost to the patient in dollars or the probability of mortality by a certain timepoint).

Learning to see these types of similarities will give you a tremendous amount of power when attacking new problems in clinical data science. It will allow you to confidently deploy methods you used to solve one problem on a wide range of other problems. Each new method you learn then multiplies your capacity to solve problems, rather than adding to it.

Question 1.1

How are items $7-8$ and 14 different from the rest?

Question 1.2

How are items $1-6$ similar to items $9-13$ and how are they different?

Question 1.3

How do items $1-3$ differ from items $4-5$ and how are they similar?

Question 1.4

How do items $1-3$ differ from item 6? How is item 6 different from all of the other items?

Question 1.5

How do items $9-11$ differ from items $12-13$?

1.3 Terms and Contrasts

The basic ways in which clinical data science problems vary can be characterized using a few broad conceptual distinctions. These draw from both traditional clinical disciplines, like epidemiology, as well as machine learning/statistics.

1.3.1 Guidance vs. Understanding

Before beginning any study, it is important to carefully consider the study's goal and how the findings from the study will be used. This will help guide you in choosing appropriate methods. For example, in some studies we care mainly about using data to provide **guidance** that will enable us to perform our jobs better in the future. We may want to predict whether a patient is likely to experience an adverse outcome, or we may want to learn the type of patient who is most likely to benefit from a particular treatment. In these cases, we want the data to guide us in making better choices.

Now, contrast this with a study whose primary goal is scientific **understanding**. In this case, we care more about using data to improve our understanding of a phenomenon than in operationalizing those findings. For example, we may be interested in whether a particular genetic variant affects a phenotype, or we may want to establish a causal link between a particular treatment and an outcome.

The distinction is fuzzy and often imperfect, and the same kinds of methods can often be used in both cases. Depending on the goal, however, one may be willing to make certain compromises. For example, complex, "black box" predictive models (e.g. deep learning models) may be appropriate when the goal is guidance, but offer little in the way of understanding. Conversely, regression models have become the de facto standard for clinical trials and causal inference, but may not lead to optimal predictive ability. In situations

where the primary goal is a rigorous understanding of causal relationships, that may not matter as much.

1.3.2 Observational Study vs. Experiment

In **experimental studies**, the investigator manipulates some aspect of the subjects' experience and studies its effect on the outcome of interest. For example, here is the NIH's definition of a **clinical trial**:

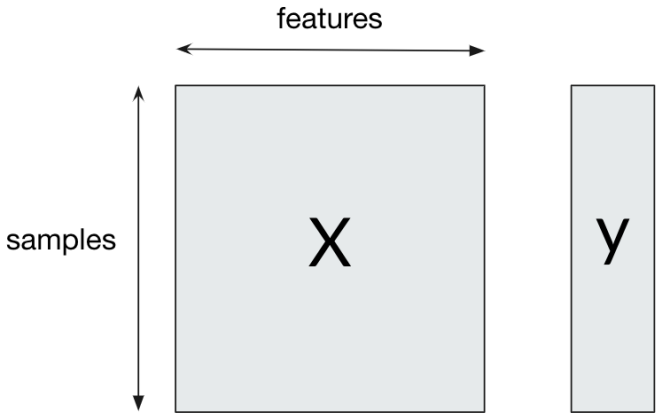
> A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

A clinical trial, therefore, is an experiment, because we control the intervention and monitor the effect of that intervention on one or more outcomes. Usually experimental studies employ some type of **randomization** to ensure that comparisons between different intervention groups are fair.

An **observational study**, in contrast, makes no attempt to interfere with its subjects. Instead, these individuals are simply observed, and inferences are made about the associations between different parameters and the outcome(s). Observational study designs and analytic plans are carefully designed to minimize the effects of different sources of bias that can creep in due to lack of randomization. Although they're not usually referred to using this terminology, virtually all "big data" and machine learning oriented studies in healthcare are observational studies, because they use large datasets that were collected for other purposes.

1.3.3 Types of Machine Learning

This distinction, most often found in discussions of machine learning, refers to the way in which training data is applied to solve a problem. In **supervised learning**, the training data consist of pairs of input features and labels, and the algorithm learns to predict the value of the label from the input features. The general setup for supervised learning looks like this:



In **unsupervised learning**, only the input features are present (i.e. no y) and the algorithm learns to recognize patterns, clusters, or other structure in the inputs. Although they're almost never referred to using this terminology, clinical studies that examine the effect between one or more exposures and an outcome are examples of supervised learning. Studies that attempt to uncover groups, or clusters, of similar patients or samples are examples of unsupervised learning.

There are also two other types of machine learning. In **semi-supervised learning**, a small amount of labeled data is used to create a much larger, weakly-labeled set of training data that is then fed to a supervised learning algorithm. In **reinforcement learning**, an algorithm is trained with a reward system which provides feedback on the quality of the action the system performs in a given situation instead of (as in supervised learning) simply providing the "right answer".

Chapter 2

Classification

Classification is a form of supervised learning in which our goal is to learn a mapping between some features, x, and an output, y. In classification, the output, y, is a category. In **binary classification** (by far the most common), there are only two categories: yes or no, usually represented as "0" (no) or "1" (yes). In **multi-class classification**, there are more than two categories.

To learn an appropriate mapping, we feed **training data** to a **learning algorithm**. Different algorithms learn different types of mappings.

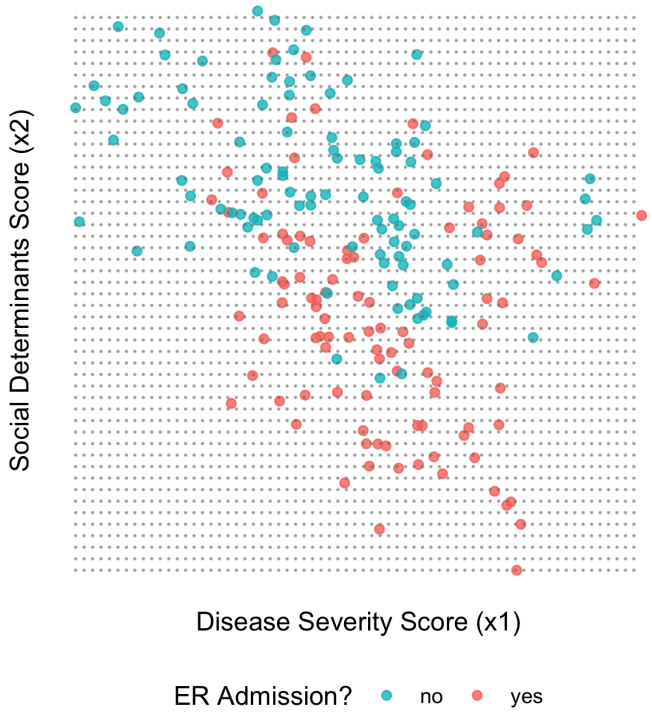
2.1 Definitions

- **Training data:** The data used, along with an appropriate learning algorithm, to create the mapping between input and output. It is composed of **training examples**, a.k.a. **samples**, each consisting of one or more input features and a single output.
- **Test data:** An independent dataset, not used in model training, on which the performance of a trained supervised learning model is evaluated.
- **Feature:** Also known as a **predictor**, or **covariate**, one of the inputs to a supervised learning algorithm.
- **Output:** Also known as the **outcome**, or **label**, the thing you are trying to predict.

- **Feature space:** Envisioning each feature as having its own axis that is orthogonal to all of the other features' axes, the multidimensional space spanned by those axes (or rather: unit vectors in the directions of those axes)
- **Extrapolation:** Making predictions outside the region of the feature space occupied by the training data. This will often lead to errors.

2.2 Visualizing the Classification Problem

Imagine we want to predict whether a patient will be readmitted to the emergency room (ER) within 30 days of hospital discharge. We gather data on two predictors: a disease severity score (x_1), which characterizes the severity of illness, and a social determinants score (x_2), which characterizes the patient's socioeconomic status. We have data on 200 patients.

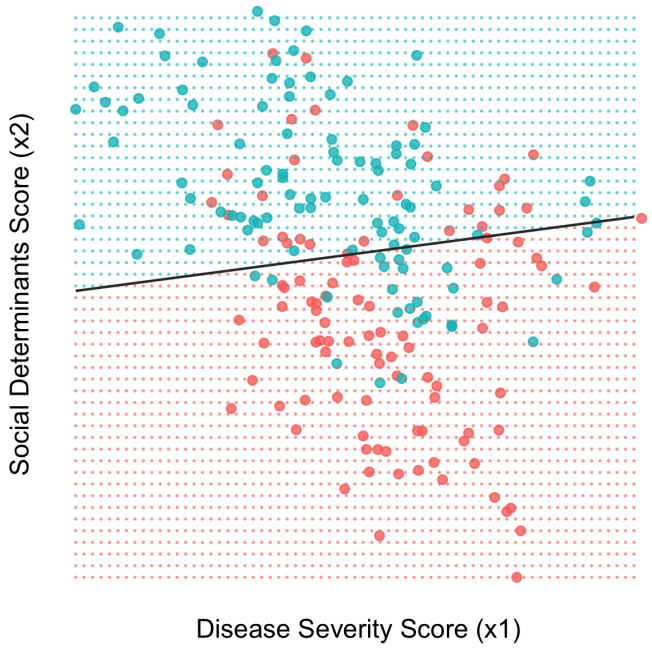


In this figure, the color refers to whether a patient was readmitted (blue = "no", red = "yes"). The location of each point is governed by the patient's disease severity score (x_1, horizontal axis) and social determinants score (x_2, vertical axis). Our goal in classification is to draw a **decision boundary** through this space, on one side of which we will predict that the patient is readmitted, and on the other side not.

2.3 Three Classification Algorithms

2.3.1 Logistic Regression

The simplest decision boundary is, arguably, a line. The logistic regression algorithm simply draws a line[1] through the feature space that divides the positive and negative training examples.

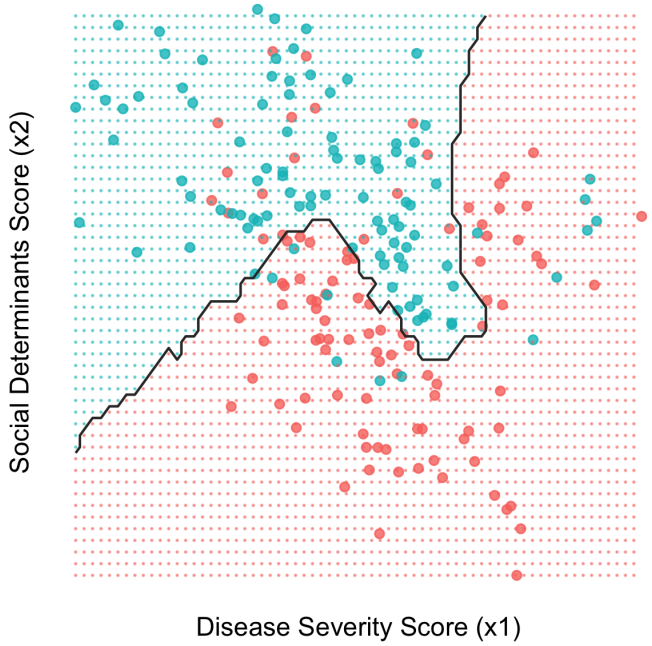


[1] In a higher-dimensional feature space, the decision boundary for logistic regression is a **hyperplane**.

2.3.2 K Nearest Neighbors (KNN)

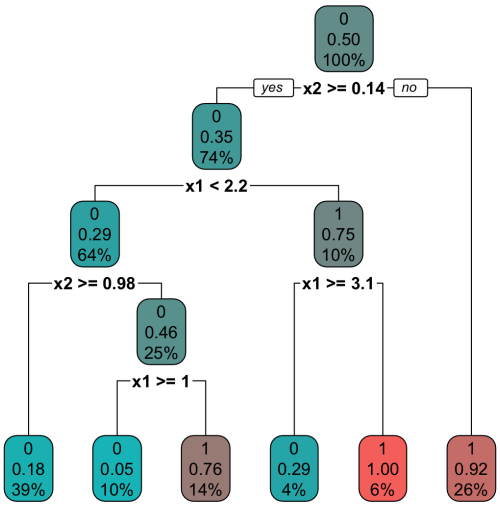
Another approach is to make no assumptions about the shape of the decision boundary. To make a prediction about a new patient, we simply allow the K nearest neighbors to vote. The parameter K must be set independently and is called a **hyperparameter**.

Here is the decision boundary for KNN with $K = 15$:

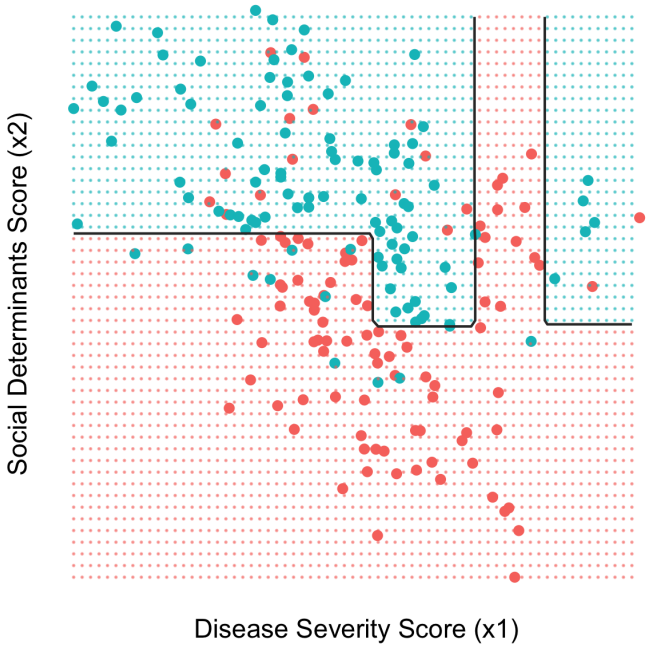


2.3.3 Decision Tree

Finally, we may choose to use our training data to build a decision tree, which will allow us to make predictions on new patients using a series of simple yes/no questions. There are different decision tree learning algorithms, but here is the tree produced by a famous one called CART:



And here is the decision boundary produced by this tree:



Question 2.1

There are six rectangular regions in this picture corresponding to the six leaves of the tree. Identify all six and which leaves they correspond to on the decision tree, above.

Question 2.2

What are the advantages and disadvantages of the decision boundaries produced by:

1. Logistic regression?
2. KNN ($K = 15$)?
3. Decision tree?

Question 2.3

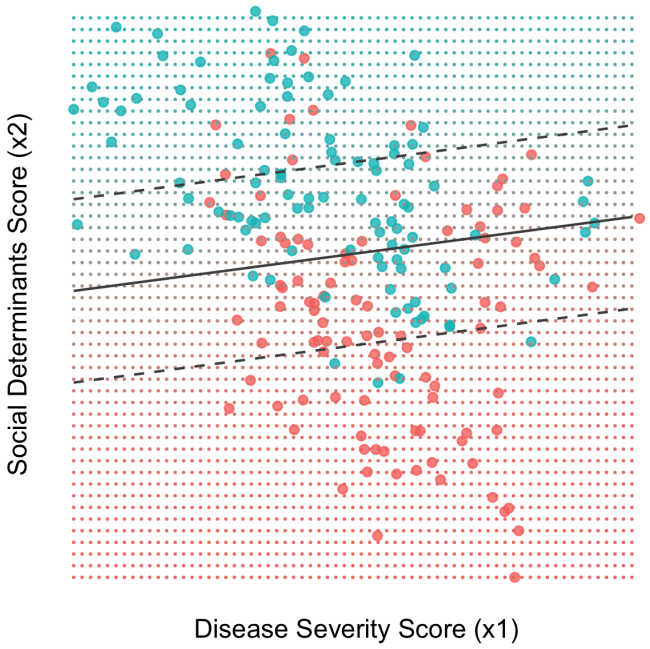
What makes a good classification algorithm? Consider issues of accuracy, generalizability, and speed (both to train the algorithm and to use it to make predictions on new samples).

2.4 Classification with Probabilities

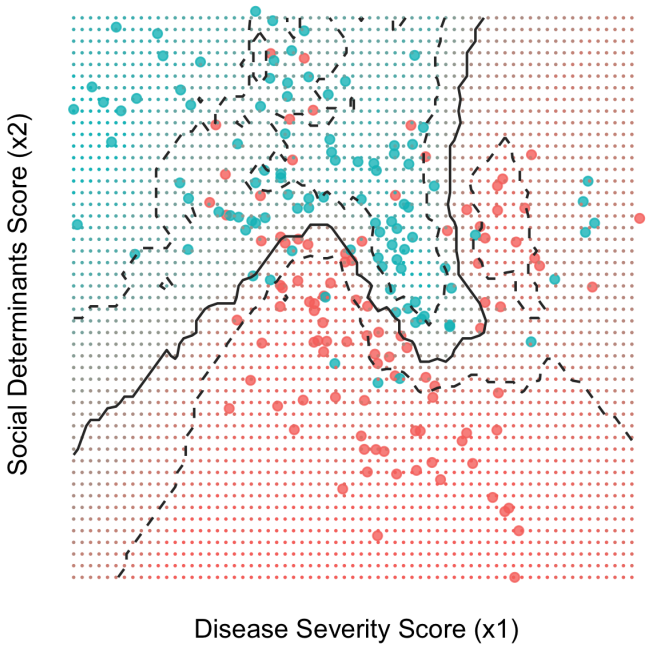
We can think of classification as simply drawing a decision boundary, but underlying each algorithm is a quantitative assessment of each point in the feature space. Each algorithm is, in its own way, able to provide a degree of certainty, or **probability**[2], that a point belongs to the positive outcome class.

For example, here is the feature space of the example we just saw, colored by the probability, according to logistic regression, that a sample at each point should be classified as positive (i.e. the patient will be readmitted to the ER):

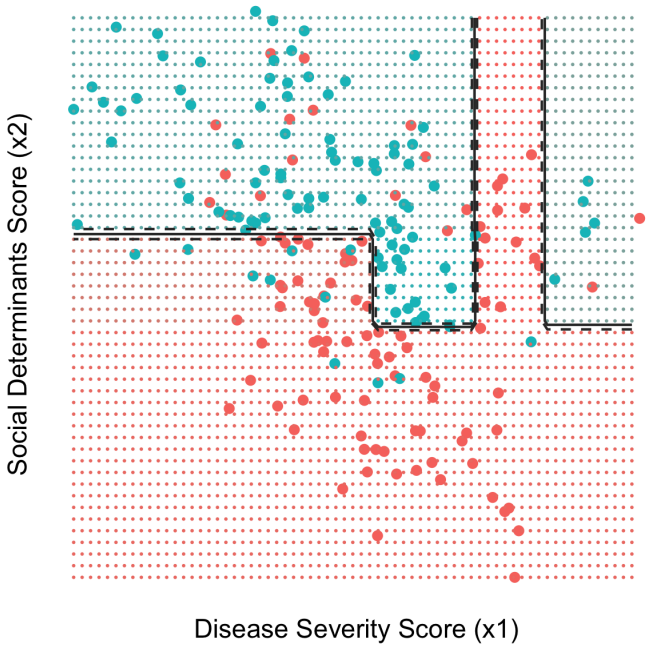
[2]Pedantic footnote: this is a Bayesian definition of probability, as opposed to a frequentist definition. More on that later.



The solid line is the decision boundary, and the dashed lines indicate where the probability of a positive outcome (ER readmission) is 25% (top line) and 75% (bottom line). You can see that the color of the background gets purer red or purer blue the further you get from the decision boundary, but that near the decision boundary, the color is rather murky. That murkiness reflects the algorithm's uncertainty about the outcome. At the decision boundary, it is maximally uncertain. There the probability of a positive outcome is 50%: a coin toss. Here is a similar plot for KNN ($K = 15$):



You can see that the shapes of the 25% and 75% probability lines have much more complex shapes than for logistic regression, but the story is the same: you have regions of pure blue or red, where the algorithm is certain, and you have a murky region near the decision boundary. Now, finally, here is the same plot for the decision tree:



In this case, the color of the background in the different regions is relatively flat. The probability in each rectangular region (corresponding to each leaf of the tree) is constant. It equals the number of red dots in that region divided by the total number of dots. (Convince yourself of this.)

Chapter 3

Regression

Classification is a form of supervised learning in which the outcome is a category. **Regression** is another form of supervised learning in which the outcome is a numeric value. For example, it may be a lab value, physical characteristic (height, weight, etc.), or numeric measurement (e.g. oxygen saturation).

3.1 Visualizing the Regression Problem

Let's consider the same setup from Section 2.2 but this time with a quantitative outcome: a "recurrence biomarker" that indicates the likelihood of recurrence of disease.

Again, we have data on two predictors: a disease severity score (x_1), which characterizes the severity of the illness for which the patient was originally treated, and a social determinants score (x_2), which characterizes a patient's socioeconomic status. We have measurements of x_1 and x_2 on the same 200 patients as in Section 2.2.

This is a plot of the data in a single plane. The color represents the value of the recurrence biomarker – the height of the point above the plane. The goal of regression is to predict the value of the biomarker (y) based on the values of the two predictors, x_1 and x_2.

Question 3.1

Just looking at the two predictors, which one appears to more highly influence the value of the recurrence biomarker? Why?

Question 3.2

Think about the three algorithms we discussed in Chapter 2. Now think about our new task, which is to predict the *numeric value* of the recurrence biomarker as a function of the two predictors, x_1 and x_2.

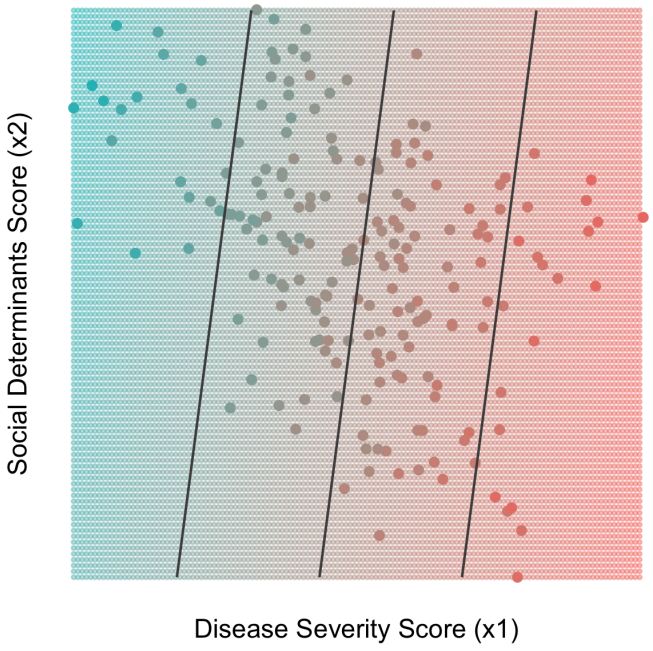
- How might you adapt KNN to deal with this problem?

- How might you adapt a decision tree to deal with this problem?
- How might you adapt logistic regression to deal with this problem? You'll have to "break the algorithm" a bit more this time.

3.2 Three Regression Algorithms

3.2.1 Linear Regression

The regression analogue of logistic regression is **linear regression**[1]. Linear regression creates a hyperplane that slices through the cloud of training datapoints such that it passes as close as possible, on average, to the data. This is, of course, easiest to see when the feature space is two-dimensional, as it is here:

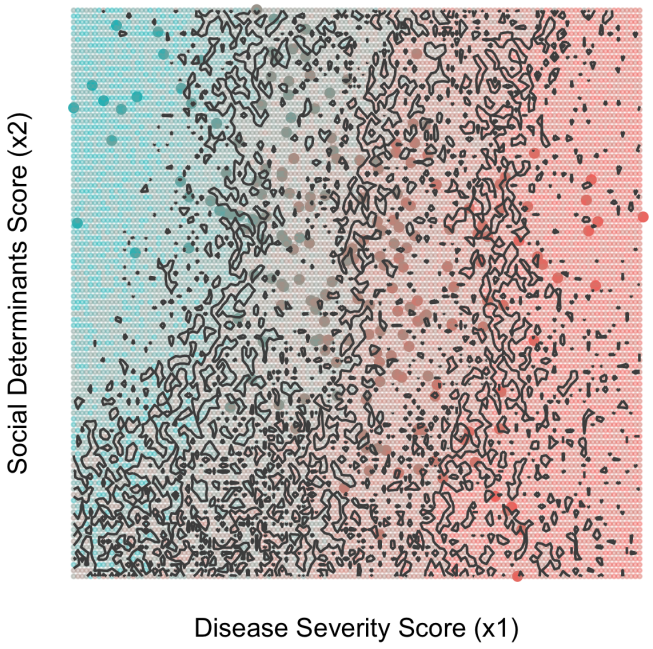


[1]The terminology here is confusing. When we learn about generalized linear models in Chapter 6, you'll see why logistic regression has the word "regression" in its name even though it's a classification algorithm.

The three lines shown here sit on the hyperplane learned by the linear regression model. They are located at heights corresponding to the 25th, 50th, and 75th percentiles of the outcome, y (the biomarker value). The plane tilts downward toward the upper left corner of the $x_1 \times x_2$ grid and upward toward the bottom right corner. It may be helpful to visualize grabbing the $x_1 \times x_2$ plane and rotating/translating it so that it passes through the middle of the training data.

3.2.2 K Nearest Neighbors (KNN)

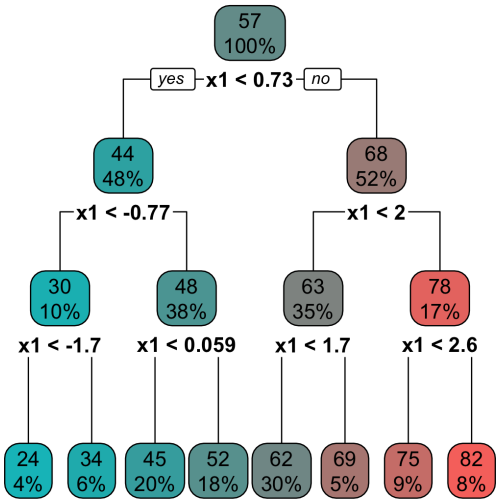
Regression using KNN works very similarly to KNN for classification. In classification, we allow the nearest K points to vote on the label of a new test point. In regression, we **interpolate** between the values of the surrounding points to come up with the value of y for a test point. Typically this is done just by averaging the y values of the nearest K points, but you can also do something more sophisticated, like weight their contributions by distance to the test point. Here is a contour plot of the regression surface produced by KNN ($K = 15$) for our example:



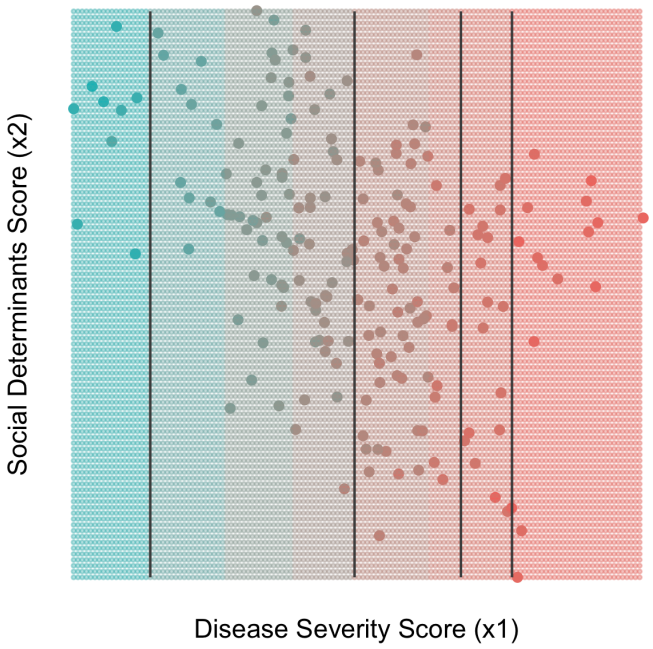
The contours are again drawn at the 25th, 50th, and 75th percentiles of the outcome, y. This looks like a bit of a mess compared to the linear regression plot, but at the same time, the KNN algorithm is able to capture arbitrarily complex relationships between x_1, x_2, and y that can be missed by other regression algorithms.

3.2.3 Decision Tree

Decision tree regression is similar to decision tree classification except that the output at each leaf is not a class label or the probability of membership in the positive training class (both of which are shown on the tree in Section 2.3.3), but a numeric value. That value corresponds to the mean outcome value for the points in that leaf.



The predicted biomarker values for a decision tree trained on this dataset (created using the `rpart` package in R with default parameters) are shown here:



You can see that the decision tree always chooses to split on x_1, the disease severity score, rather than x_2. Revisit Question 3.1 to remind yourself of why this is. The regression surface produced by the decision tree looks like a set of stairs climbing higher and higher as one moves from left to right across the $x_1 \times x_2$ plane. Of course, it would be difficult to climb such stairs, because they are not evenly spaced!

Question 3.3

What are the advantages and disadvantages of each of these three regression algorithms?

Chapter 4

Probability Distributions

Many of the methods we will examine in these workshops depend on basic concepts from probability theory. For example, linear and logistic regression are members of a class of supervised learning algorithms called **generalized linear models** (see Chapter 6) which make assumptions about the type of probability distribution followed by the outcome variable. Decision trees use a concept called **entropy** (see Chapter 9), whose mathematical formulation depends on the probability distribution underlying the outcome. Many **hypothesis tests** (see Chapter 8) likewise rely on probabilistic assumptions about the data. Probability is everywhere.

The following sections review some key probability concepts – in an extremely hand-wavey and non-rigorous way – and the properties of some of the most common probability distributions you will encounter in machine learning and statistics.

4.1 Definitions

A **probability distribution** is just a mathematical function that provides the relative likelihoods of various possible outcomes of an observation. We call the quantity that is being observed a **random variable**. Probability distributions can be discrete or continuous. The random variable involved can be a number, a vector of numbers, a category/class, etc. The **sample space** is the set of all

possible outcomes. The integral (or sum) of the probability distribution over the entire sample space is 1.0. You will often hear probability distributions for continuous random variables referred to as **probability densities**.

Probability distributions are grouped into families that are characterized by their overall shapes. These families contain **parameters** that, when varied, produce different distributions. Specific probability distributions from within a single family can often look quite different.

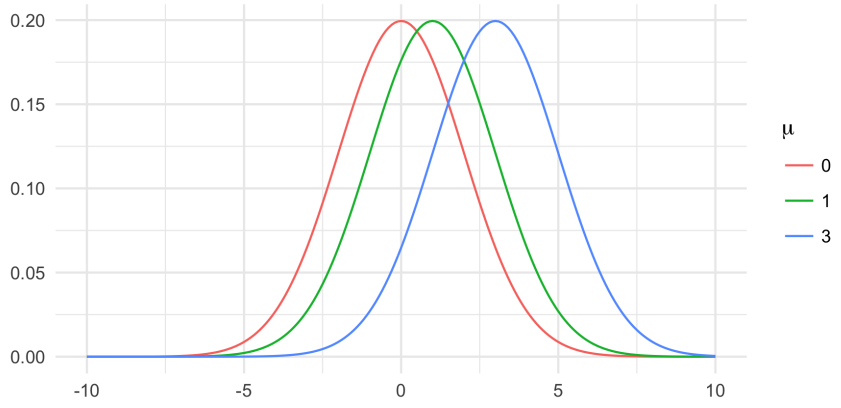
We use the notation $E[x|\theta]$ to refer to the **expected value**, or mean, of a distribution, given its parameter(s), θ. There can be more than one parameter, and it will not always be called θ; this is just an example. We use the notation $\text{var}(x|\theta)$ to refer to the **variance**, or spread, of a distribution around its mean.

4.2 Normal Distribution

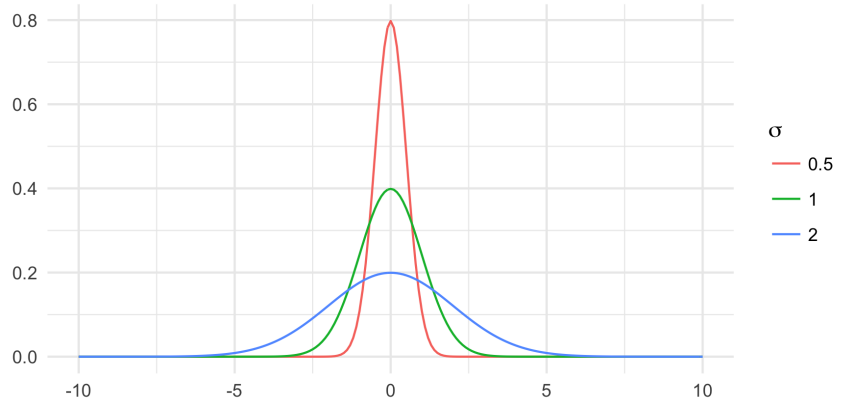
Also called the **Gaussian distribution**, the normal distribution is probably the most well-known continuous probability distribution. It has the following properties:

$$p(x|\mu,\sigma) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}} \qquad E[x|\mu,\sigma] = \mu \qquad \text{var}(x|\mu,\sigma) = \sigma^2$$

where $x \in \mathbb{R}$. We will abbreviate the normal distribution as $\mathcal{N}(\mu,\sigma)$. The value of μ changes the position of the center of the normal distribution.



The value of σ changes the width of the normal distribution.



Question 4.1

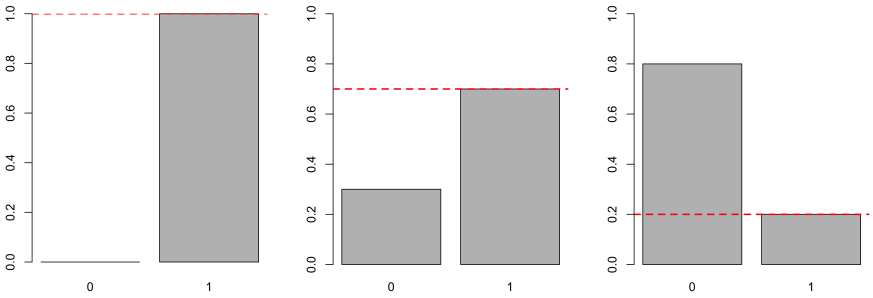
List 5 random variables from medicine or biology that should follow normal distributions.

4.3 Bernoulli Distribution

The **Bernoulli distribution** is a discrete probability distribution with the following properties:

$$p(x|\mu) = \mu^x(1-\mu)^{1-x} \qquad E[x|\mu] = \mu \qquad \text{var}(x|\mu) = \mu(1-\mu)$$

where $x \in \{0, 1\}$. It is used to model events where the outcome is yes/no. Think of it as a weighted coin, with μ the probability that the coin comes up "heads" on a single toss. Here are three Bernoulli distributions with (from left to right) $\mu = 1.0, 0.7, 0.2$. The number along the bottom is x, which can only be 0 or 1.



The **categorical distribution** is a generalization of the Bernoulli distribution to an outcome with more than two levels. The categorical distribution looks like this:

$$p(x|\phi_1, \ldots, \phi_K) = \phi_1^{\mathbb{I}(x=1)} \phi_2^{\mathbb{I}(x=2)} \cdots \phi_K^{\mathbb{I}(x=K)}$$

where $\sum_{k=1}^{K} \phi_k = 1$. The term $\mathbb{I}(x = j)$ is an **indicator**. It equals 1 if $x = j$ and 0 otherwise. For example, $\mathbb{I}(x = 2)$ is 1 if $x = 2$ and 0 otherwise.

Question 4.2

List 5 random variables from medicine or biology that should follow Bernoulli distributions.

4.4 Binomial Distribution

The **binomial distribution** models the number of positive outcomes, x, out of n independent[1] Bernoulli trials, each of which is positive with probability μ. This distribution has the following properties, with $x \in \{0, \ldots, n\}$:

$$p(x|n, \mu) = \binom{n}{x} \mu^x (1-\mu)^{n-x} \qquad E[x|\mu] = n\mu \qquad \text{var}(x|\mu) = n\mu(1-\mu)$$

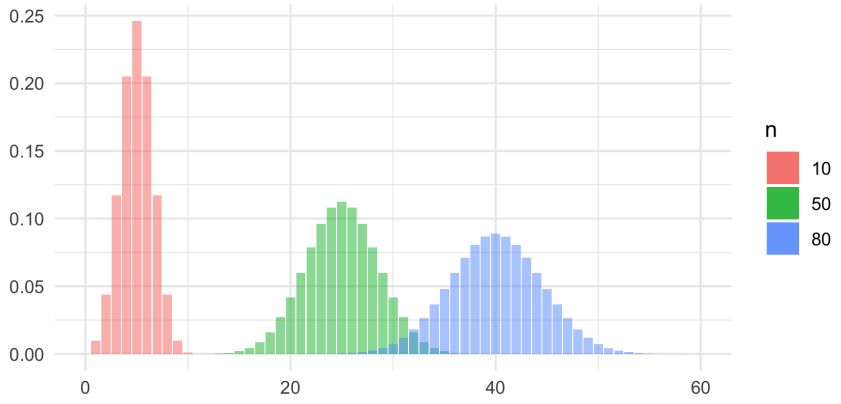
where the notation $\binom{n}{x}$ is defined as:

$$\binom{n}{x} = \frac{n!}{x!(n-x)!}.$$

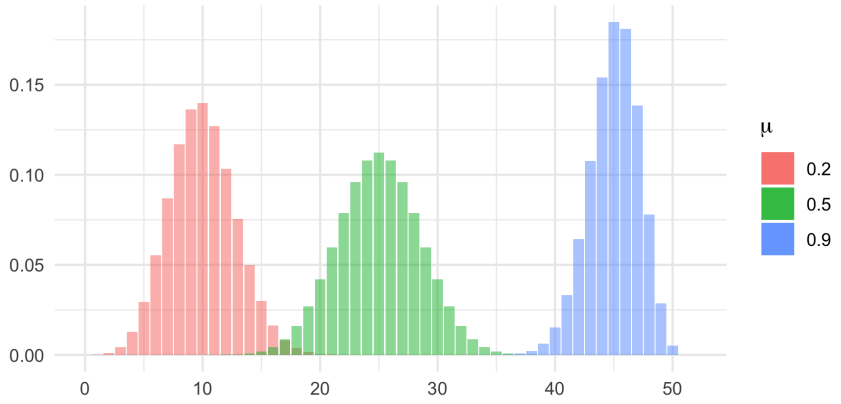
[1]The word **independent** just means that the outcome of one trial does not influence the outcome of any other trial.

This notation denotes the number of ways it is possible to choose x things out of a group of n things, where the ordering doesn't matter. The exclamation point denotes the **factorial function**: $x! = x(x-1)(x-2)\cdots(2)(1)$.

The shape of the binomial distribution is governed by the values of n and μ. Here, we vary n but keep μ constant at 0.5:



And here we vary μ but keep n constant at 50:



Question 4.3

List 5 random variables from medicine or biology that should follow binomial distributions.

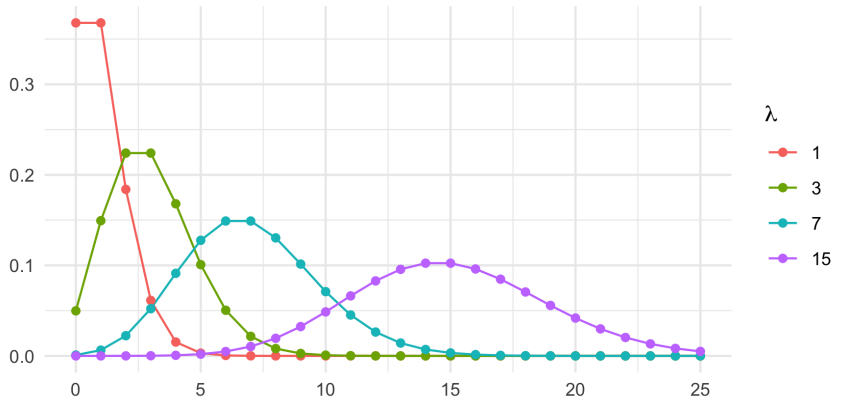
4.5 Poisson Distribution

The **Poisson distribution** is a probability distribution that is often used to model discrete quantitative data, such as counts. It has the following properties:

$$p(x|\lambda) = \frac{e^{-\lambda}\lambda^x}{x!} \qquad E[x|\lambda] = \lambda \qquad \text{var}(x|\lambda) = \lambda$$

where $x \in \{0, 1, 2, \dots\}$. Below are four examples of Poisson distributions. If events of a particular type occur continuously and independently at a constant rate (**Poisson process**), the number of events within a time window of fixed width will be distributed according to the Poisson distribution, with rate parameter λ proportional to the width of the window.

Situations where the population size, n, is large, the probability of an individual event, p, is small, but the expected number of events, np, is moderate (say five or more) can generally be modeled using a Poisson distribution with $\lambda = np$.



Question 4.4

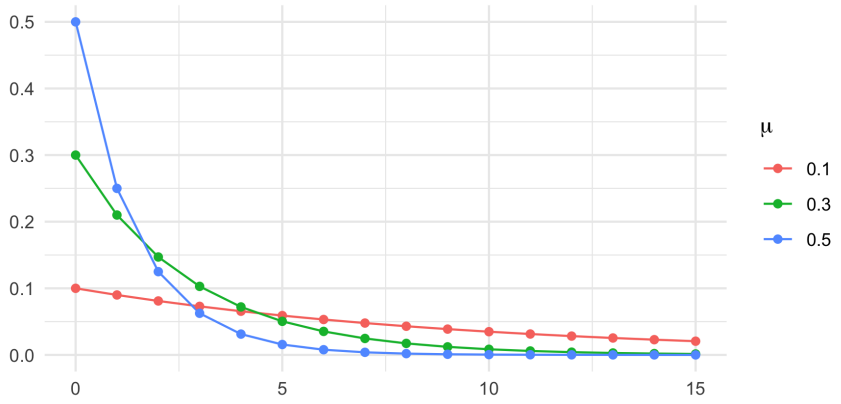
List 5 random variables from medicine or biology that should follow Poisson distributions.

4.6 Geometric

The **geometric distribution** models the number of failures in a sequence of Bernoulli trials before the first success. It has the following properties:

$$p(x|\mu) = (1-\mu)^x \mu \qquad E[x|\mu] = \frac{1-\mu}{\mu} \qquad \text{var}(x|\mu) = \frac{1-\mu}{\mu^2}$$

for $x \in \{0, 1, 2, \dots\}$, where μ refers to the probability (in the Bernoulli trial) that the trial is a success. Some examples of geometric distributions with different μ are shown below:



Question 4.5

List 5 random variables from medicine or biology that should follow Poisson distributions.

4.7 Exponential

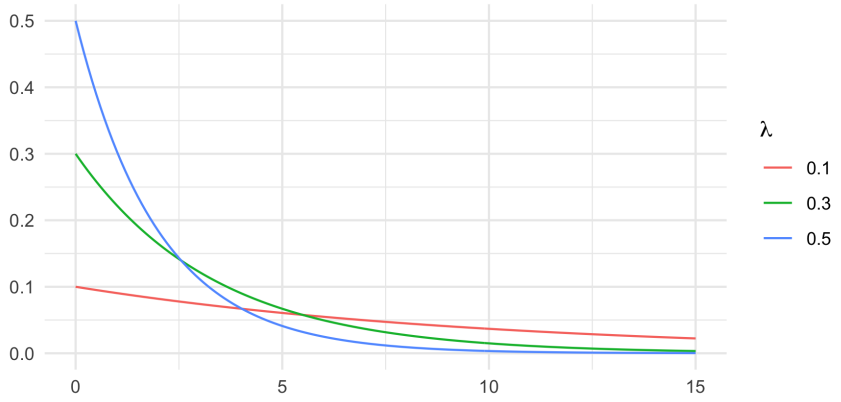
The **exponential distribution** is a continuous probability distribution that models waiting times between events that happen independently and continuously at a constant rate (Poisson process), as well as many other random

variables[2]. It has the following properties:

$$p(x|\lambda) = \lambda e^{-\lambda x} \qquad E[x|\lambda] = \frac{1}{\lambda} \qquad \text{var}(x|\lambda) = \frac{1}{\lambda^2}$$

where $x \in \mathbb{R}^+$ (x is a positive real number, or zero). The exponential distribution is the continuous analogue of the geometric distribution. It is memoryless, which means that the distribution of a waiting time until an event does not depend on how much time has elapsed already.

Here are some different exponential distributions. Compare them to the geometric distribution, above.



Question 4.6

List 5 random variables from medicine or biology that should follow exponential distributions.

4.8 Chi-Squared Distribution

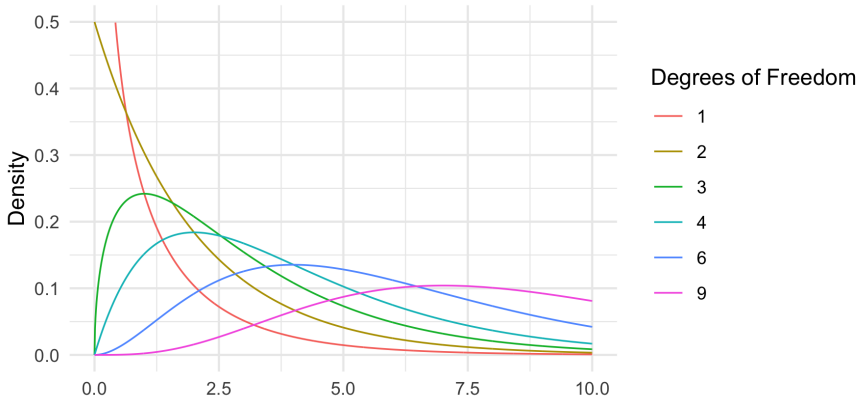
How this distribution arises:

[2]For example, in an epidemiologic model of an infectious process like COVID-19 community spread, exponential waiting times are often used to model transitions between the susceptible, exposed, infectious, and recovered compartments in the model.

1. If $Z \sim \mathcal{N}(0,1)$, the distribution of $U = Z^2$ is called the chi-squared distribution with one degree of freedom.

2. If $U_1, U_2, \ldots, U_k$ are independent χ^2_1 random variables, their sum, $V = \sum_{i=1}^{k} U_i$ follows χ^2_k, a chi-squared distribution with k degrees of freedom.

You'll often see the chi-squared distribution used as the sampling distribution for the sample variance in a variety of statistical hypothesis tests. It looks like this:



The parameter k, the **degrees of freedom**, controls the shape of the chi-squared distribution. The actual formula for the chi-squared distribution looks a bit intimidating, but I'm including it here so you can compare it to the other distributions we've seen:

$$p(x|k) = \frac{1}{2^{k/2}\Gamma(k/2)} x^{k/2-1} e^{-x/2}$$

$$E[x|k] = k \qquad \text{var}(x|k) = 2k$$

The gamma function shown in the denominator of the probability density,

$$\Gamma(z) = \int_0^\infty x^{z-1} e^{-x} dx,$$

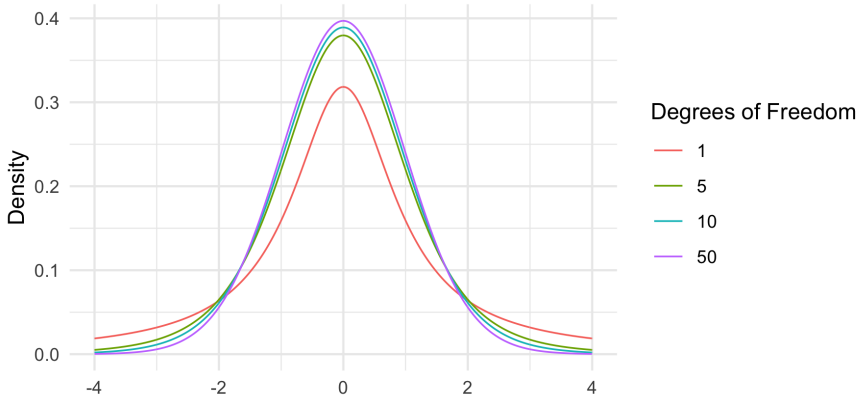
is a generalization of the factorial function to complex numbers. For any positive integer n, $\Gamma(n) = (n-1)!$.

4.9 Student's T Distribution

If $Z \sim \mathcal{N}(0,1)$ and $U \sim \chi^2_k$ and Z and U are independent,

$$T = \frac{Z}{\sqrt{U/k}} \sim t_k$$

or in words, the statistic T follows a t-distribution with k degrees of freedom. The T distribution plays an important role in a family of statistical hypothesis tests called T-tests.



Again, the functional form of the T distribution is a bit intimidating, but I'm including it for completeness:

$$p(x|k) = \frac{\Gamma\left(\frac{k+1}{2}\right)}{\sqrt{k\pi}\,\Gamma\left(\frac{k}{2}\right)}\left(1+\frac{x^2}{k}\right)^{-\frac{k+1}{2}}$$

$$E[x|k] = 0 \quad \text{for } k > 1\text{; otherwise undefined}$$

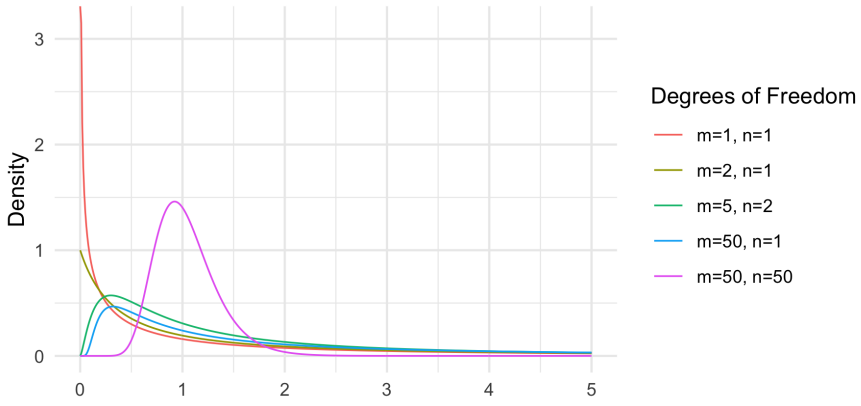
$$\text{var}(x|k) = \begin{cases} \frac{k}{k-2} & k > 2 \\ \infty & 1 < k \leq 2 \\ \text{undefined} & \text{otherwise} \end{cases}$$

4.10 F Distribution

If U and V are independent χ^2 random variables with m and n degrees of freedom,

$$W = \frac{U/m}{V/n} \sim F_{m,n}$$

or in words, the statistic W follows an F distribution with m and n degrees of freedom. I'm not writing out the functional form of the F distribution here because it's too awful-looking, but graphically it looks like this:



Note that if $T \sim t_k$, then $T^2 \sim F_{1,k}$. The F-distribution plays an important role in a class of statistical analysis techniques called **ANalysis Of VAriance**, or **ANOVA**.

Question 4.7

For each of the following experimental conditions, which distribution (from those listed above) provides the best model for how the data $x^{(1)}, \ldots, x^{(n)}$ are generated?

(a) You are observing several patients' skin in a clinical study to see how long it takes them to develop a rash. You take a picture each day. Let $x^{(i)}$ be the number of days of *no rash* before the rash occurs.

Patient ID (i)	$x^{(i)}$
1	4
2	1
3	0
4	2
5	2
6	4
7	3
8	1
9	0
10	1

(b) Same situation as above except that instead of taking a picture each day, the patient texts you at the moment he/she observes a rash. The data look like this, where $x^{(i)}$ is the time (in days) at which patient i develops a rash:

Patient ID (i)	$x^{(i)}$
1	2.25
2	3.43
3	0.68
4	0.04
5	3.78
6	5.65
7	2.88
8	3.88
9	2.83
10	1.87

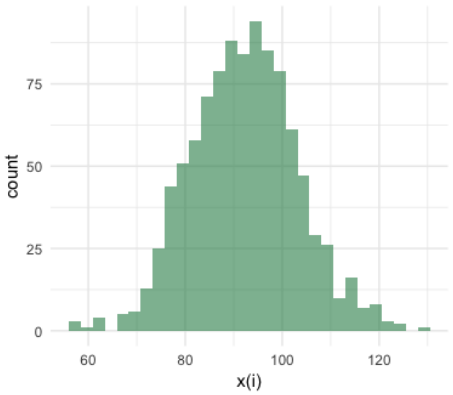
(c) Imagine you are Ladislaus Bortkiewicz, and you are modeling the number of persons killed by mule or horse kicks in the Prussian army per year. You have data from the late 1800s over the course of 20 years. Let $x^{(i)}$ be the number of people killed in year i.

Year (i)	$x^{(i)}$	Year (i)	$x^{(i)}$
1	8	11	9
2	10	12	7
3	5	13	10
4	3	14	12
5	10	15	8
6	8	16	7
7	7	17	8
8	2	18	8
9	6	19	10
10	11	20	7

(d) Every year, 10 scientists go to the same geographic area (same Lyme prevalence) and they each collect 40 ticks. They test each tick for Lyme disease and record the number of ticks that have Lyme. Let $x^{(i)}$ be the number of ticks with Lyme in the ith scientist's bunch.

Scientist ID (i)	$x^{(i)}$
1	8
2	9
3	14
4	15
5	12
6	7
7	6
8	8
9	8
10	14

(e) You have waist circumference data on 1045 men aged 70 and above (see Dey's 2002 paper in the Journal of the American Geriatric Society). It looks like this:


75
50
25
0
count
60
80
100
120
x(i)

Chapter 5

Maximum Likelihood Estimation*

Beneath our discussions of classification, regression, and probability distributions in Chapters 2, 3, and 4 lies the tricky problem of **model fitting**. We've seen what classification and regression models look like, but we still haven't addressed how to fit these models using training data.

Linear and logistic regression models are fit using a technique called **maximum likelihood (ML) estimation**, in which the model parameters are adjusted to maximize the joint probability of the observed data, or likelihood, given the model.

For example, consider the five different datasets from Question 4.7. In each case, you have some data and an assumption about which probability distribution the data are drawn from. The job of maximum likelihood estimation is to use the data to identify the correct distributional parameters, such as μ and σ (in the case of the normal distribution) or λ (in the case of the Poisson distribution). This process is a type of **statistical inference**.

5.1 The Likelihood and Log-Likelihood

Let $p(x|\theta)$ be the probability distribution that governs our data. Here, θ stands in for all of the parameters we want to fit.

If we draw independent[1] samples from $p(x|\theta)$, the **joint probability density function** for all n observations is:

$$p(x^{(1)}, x^{(2)}, \ldots, x^{(n)}|\theta) = \prod_{i=1}^{n} p(x^{(i)}|\theta).$$

Since the data are known but the parameter(s) θ are unknown, we will view this quantity as a function of θ. This is just a change in notation:

$$\mathcal{L}(\theta) = \prod_{i=1}^{n} p(x^{(i)}|\theta).$$

The higher the joint probability of the data (the more "likely" the data are) given θ, the higher the value of this function. We call $\mathcal{L}(\theta)$ the **likelihood**[2]. Frequently we will want to work with the logarithm of the likelihood, which we call the **log-likelihood**, because it has some nice properties, including allowing us to manipulate sums instead of products[3]:

$$\log \mathcal{L}(\theta) = \sum_{i=1}^{n} \log p(x^{(i)}|\theta).$$

In maximum likelihood estimation, we seek to find the θ for which the likelihood (or log-likelihood) is maximized. We do this by taking derivatives

[1] Independent sampling just means that the values of different samples do not depend on each other. When the samples are drawn independently from the same distribution, their joint probability density is just the product of the individual probability densities (which are all the same).

[2] The distributions we have discussed so far are from a broad family of probability distributions called the **exponential family**. One of the properties of this family is that the log-likelihood is concave. Practically speaking, this means that if we maximize the log-likelihood by setting derivatives equal to zero, we are guaranteed to (a) get only one solution, and (b) find a maximum (not a minimum or an inflection point).

[3] Note that if the function $f(z)$ has a maximum at z', the function $\log f(z)$ will also have a maximum at z', because the logarithmic function is monotonically increasing. So we will get the same parameter estimate(s) either way.

of the log-likelihood with respect to the various parameters and setting them equal to zero. The best-fit parameter estimates obtained in this way are called the **maximum likelihood estimates (MLEs)**.

In some simple cases, the MLEs can be calculated analytically. We will now go through a bunch of examples of how to find the MLEs of the probability distributions we saw in Chapter 4.

5.2 Bernoulli MLE

The Bernoulli distribution is described in Section 4.3. Our goal is to find the parameter, μ, of this distribution, given some observed data, $x^{(1)}, \ldots, x^{(n)}$. The data will consist of a list of 1s and 0s, since Bernoulli random variables can only take the values 0 or 1.

To find $\hat{\mu}$, our MLE for μ, we first write down the log-likelihood:

$$\begin{aligned}
\log \mathcal{L}(\mu) &= \sum_{i=1}^{n} \log p(x^{(i)}|\mu) \\
&= \sum_{i=1}^{n} \log \left(\mu^{x^{(i)}} (1-\mu)^{1-x^{(i)}} \right) \\
&= \sum_{i=1}^{n} \left[x^{(i)} \log(\mu) + (1-x^{(i)}) \log(1-\mu) \right]
\end{aligned}$$

Then we take the derivative of the log-likelihood with respect to μ:

$$\frac{d}{d\mu} \log \mathcal{L}(\mu) = \sum_{i=1}^{n} \left[\frac{x^{(i)}}{\mu} - \frac{1-x^{(i)}}{1-\mu} \right]$$

The MLE of μ will occur when the likelihood is maximized, which happens when the first derivative equals zero. So to solve for $\hat{\mu}$, we set the derivative

equal to zero and rearrange:

$$\sum_{i=1}^{n}\left[\frac{x^{(i)}}{\hat{\mu}}-\frac{1-x^{(i)}}{1-\hat{\mu}}\right]=0 \implies (1-\hat{\mu})\sum_{i=1}^{n}x^{(i)}=\hat{\mu}\sum_{i=1}^{n}(1-x^{(i)})$$
$$\implies \boxed{\hat{\mu}=\frac{1}{n}\sum_{i=1}^{n}x^{(i)}}$$

We see that the MLE, $\hat{\mu}$, is simply the sum of our data – i.e. the number of data points where the outcome is 1 – divided by the total number of observations.

This makes sense: if you want to know the probability that a coin will come up heads, a good way to estimate it is to flip the coin a bunch of times and calculate the fraction of observations in which the coin comes up heads.

5.3 Binomial MLE

The binomial distribution is described in Section 4.4. We will make one notational change from that section, which is to call the number of Bernoulli trials m instead of n, since we are using n to refer to the number of data samples. To keep things simple, we will assume that m is a known quantity. As before, we first write down the log-likelihood:

$$\begin{aligned}\log\mathcal{L}(\mu) &= \sum_{i=1}^{n}\log p(x^{(i)}|m,\mu)\\ &= \sum_{i=1}^{n}\log\left[\binom{m}{x}\mu^{x}(1-\mu)^{m-x}\right]\\ &= \sum_{i=1}^{n}\left[\log(m!)-\log(x!)-\log((m-x)!)+x^{(i)}\log(\mu)+(m-x^{(i)})\log(1-\mu)\right]\end{aligned}$$

Then we take the derivative of the log-likelihood with respect to μ:

$$\frac{d}{d\mu}\log\mathcal{L}(\mu)=\sum_{i=1}^{n}\left[\frac{x^{(i)}}{\mu}-\frac{m-x^{(i)}}{1-\mu}\right]$$

We set this equal to zero and solve for $\hat{\mu}$ (the maximum likelihood estimate of μ):

$$\sum_{i=1}^{n}\left[\frac{x^{(i)}}{\hat{\mu}}-\frac{m-x^{(i)}}{1-\hat{\mu}}\right]=0 \implies (1-\hat{\mu})\sum_{i=1}^{n}x^{(i)}=\hat{\mu}\sum_{i=1}^{n}(m-x^{(i)})$$
$$\implies \boxed{\hat{\mu}=\frac{1}{nm}\sum_{i=1}^{n}x^{(i)}}$$

Question 5.1

Interpret this finding. Does the MLE for μ make intuitive sense to you? Think through a few of your examples from Question 4.3.

5.4 Normal MLE

The normal distribution is described in Section 4.2. We will follow the same procedure as in the previous two sections, except that now we have two parameters to solve for, μ and σ, instead of one. First, we write down the log-likelihood:

$$\begin{aligned}\log\mathcal{L}(\mu,\sigma)&=\sum_{i=1}^{n}\log p(x^{(i)}|\mu,\sigma)\\&=\sum_{i=1}^{n}\log\left(\frac{1}{\sqrt{2\pi\sigma^2}}e^{-\frac{(x^{(i)}-\mu)^2}{2\sigma^2}}\right)\\&=-\frac{n}{2}\log(2\pi)-\frac{n}{2}\log\sigma^2-\frac{1}{2\sigma^2}\sum_{i=1}^{n}\left(x^{(i)}-\mu\right)^2\end{aligned}$$

To find the MLE for μ, we take the derivative of the log-likelihood with respect to μ:

$$\frac{\partial}{\partial\mu}\log\mathcal{L}(\mu,\sigma)=\frac{1}{\sigma^2}\sum_{i=1}^{n}\left(x^{(i)}-\mu\right)$$

We set this equal to zero and solve for $\hat{\mu}$ (the maximum likelihood estimate of μ):

$$\frac{1}{\sigma^2}\sum_{i=1}^{n}\left(x^{(i)}-\mu\right)=0 \implies \boxed{\hat{\mu}=\frac{1}{n}\sum_{i=1}^{n}x^{(i)}}$$

To find the MLE for σ, we then take the derivative of the log-likelihood with respect to σ:

$$\frac{\partial}{\partial\sigma}\log\mathcal{L}(\mu,\sigma)=-\frac{n}{\sigma}+\frac{1}{\sigma^3}\sum_{i=1}^{n}\left(x^{(i)}-\mu\right)^2$$

We set this equal to zero and solve for $\hat{\sigma}$ (the maximum likelihood estimate of σ)[4]. Note that the answer depends on our previously calculated MLE for μ:

$$-\frac{n}{\hat{\sigma}}+\frac{1}{\hat{\sigma}^3}\sum_{i=1}^{n}\left(x^{(i)}-\mu\right)^2=0 \implies \boxed{\hat{\sigma}=\sqrt{\frac{1}{n}\sum_{i=1}^{n}\left(x^{(i)}-\hat{\mu}\right)^2}}$$

Question 5.2

Interpret these findings. Do the MLEs for μ and σ make intuitive sense to you? Think through a few of your examples from Question 4.1.

[4]One detail: it turns out this estimate is biased because it depends on the MLE for μ. An unbiased version has $n-1$ in the denominator instead of n. The effect of this is minimal unless n is small.

5.5 Poisson MLE

The Poisson distribution is described in Section 4.5. To find the MLE for λ, its mean, we first (as usual) write down the log-likelihood:

$$\begin{aligned}
\log \mathcal{L}(\lambda) &= \sum_{i=1}^{n} \log p(x^{(i)}|\lambda) \\
&= \sum_{i=1}^{n} \log \left(\frac{e^{-\lambda} \lambda^{x^{(i)}}}{x^{(i)}!} \right) \\
&= \sum_{i=1}^{n} \left[-\lambda + x^{(i)} \log(\lambda) - \log(x^{(i)}!) \right]
\end{aligned}$$

Now we take the derivative of the log-likelihood with respect to λ:

$$\frac{d}{d\lambda} \log \mathcal{L}(\lambda) = \sum_{i=1}^{n} \left[-1 + \frac{x^{(i)}}{\lambda} \right]$$

We set this equal to zero and solve for $\hat{\lambda}$ (the maximum likelihood estimate of λ):

$$\sum_{i=1}^{n} \left[-1 + \frac{x^{(i)}}{\hat{\lambda}} \right] = 0 \implies \boxed{\hat{\lambda} = \frac{1}{n} \sum_{i=1}^{n} x^{(i)}}$$

Question 5.3

Interpret this finding. Does the MLE for λ make intuitive sense to you? Think through a few of your examples from Question 4.4.

5.6 Geometric MLE

The geometric distribution is described in Section 4.6. To find the MLE for μ, we first write down the log-likelihood:

$$\begin{aligned}\log \mathcal{L}(\mu) &= \sum_{i=1}^{n} \log p(x^{(i)}|\mu) \\ &= \sum_{i=1}^{n} \log \left((1-\mu)^{x^{(i)}} \mu \right) \\ &= \sum_{i=1}^{n} \left[x^{(i)} \log(1-\mu) + \log(\mu) \right]\end{aligned}$$

Now we take the derivative of the log-likelihood with respect to μ:

$$\frac{d}{d\mu} \log \mathcal{L}(\mu) = \sum_{i=1}^{n} \left[-\frac{x^{(i)}}{1-\mu} + \frac{1}{\mu} \right]$$

We set this equal to zero and solve for $\hat{\mu}$ (the maximum likelihood estimate of μ):

$$\begin{aligned}\sum_{i=1}^{n} \left[-\frac{x^{(i)}}{1-\hat{\mu}} + \frac{1}{\hat{\mu}} \right] = 0 \implies \frac{n}{\hat{\mu}} &= \frac{1}{1-\hat{\mu}} \sum_{i=1}^{n} x^{(i)} \\ \implies \boxed{\hat{\mu} = \frac{n}{\sum_{i=1}^{n} (x^{(i)} + 1)}}\end{aligned}$$

Question 5.4

Interpret this finding. Does the MLE for μ make intuitive sense to you? Think through a few of your examples from Question 4.5.

5.7 Exponential MLE

The exponential distribution is described in Section 4.7. To find the MLE for λ, we first write down the log-likelihood:

$$\begin{aligned}\log \mathcal{L}(\lambda) &= \sum_{i=1}^{n} \log p(x^{(i)}|\lambda) \\ &= \sum_{i=1}^{n} \log \left(\lambda e^{-\lambda x^{(i)}}\right) \\ &= \sum_{i=1}^{n} \left[\log(\lambda) - \lambda x^{(i)}\right]\end{aligned}$$

Now we take the derivative of the log-likelihood with respect to λ:

$$\frac{d}{d\lambda} \log \mathcal{L}(\lambda) = \sum_{i=1}^{n} \left[\frac{1}{\lambda} - x^{(i)}\right]$$

We set this equal to zero and solve for $\hat{\lambda}$ (the maximum likelihood estimate of λ):

$$\sum_{i=1}^{n} \left[\frac{1}{\hat{\lambda}} - x^{(i)}\right] = 0 \implies \boxed{\hat{\lambda} = \frac{n}{\sum_{i=1}^{n} x^{(i)}}}$$

Question 5.5

Interpret this finding. Does the MLE for λ make intuitive sense to you? Think through a few of your examples from Question 4.6.

5.8 Summary

The table below contains a summary of the MLEs of various parameters from some common probability distributions.

Distribution	Parameter	ML Estimate	Domain of $x^{(i)}$
Univariate Normal	μ	$\frac{1}{n}\sum_{i=1}^{n} x^{(i)}$	$\mathbb{R}$
	σ	$\frac{1}{n}\sum_{i=1}^{n}\left(x^{(i)}-\hat{\mu}\right)^2$	$\mathbb{R}$
Multivariate Normal	μ	$\frac{1}{n}\sum_{i=1}^{n} x^{(i)}$	$\mathbb{R}^m$
	$\mathbf{\Sigma}$	$\frac{1}{n}\sum_{i=1}^{n}(x^{(i)}-\hat{\mu})(x^{(i)}-\hat{\mu})^T$	$\mathbb{R}^m$
Bernoulli	μ	$\frac{1}{n}\sum_{i=1}^{n} x^{(i)}$	$\{0,1\}$
Binomial (fixed m)	μ	$\frac{1}{nm}\sum_{i=1}^{n} x^{(i)}$	$\{0,1,\ldots,m\}$
Poisson	λ	$\frac{1}{n}\sum_{i=1}^{n} x^{(i)}$	$\{0,1,\ldots\}$
Geometric	μ	$\frac{n}{\sum_{i=1}^{n}(x^{(i)}+1)}$	$\{0,1,\ldots\}$
Exponential	λ	$\frac{n}{\sum_{i=1}^{n} x^{(i)}}$	$\mathbb{R}^+$

Question 5.6

In Question 4.7, we examined several examples of experimental conditions and datasets and discussed which probability distribution best modeled each one. Using the formulas above and the actual datasets from Question 4.7, calculate the MLEs for the parameter(s) of your chosen probability distributions.

Chapter 6

Generalized Linear Models*

Generalized linear models (GLMs) are a class of supervised learning models that form a convenient bridge between machine learning and traditional statistics. The basic idea behind a GLM is that your outcome variable (a.k.a. response variable, see Chapter 2), y, follows a probability distribution. The expected value, or mean, of that distribution is related to the values of the predictors (a.k.a. covariates; see Chapters 2 and 3), $x_1, \ldots, x_p$ in a model-specific way.

We will focus on three classes of GLM: **linear regression**, which models data where the outcome, y, is numeric ($y \in \mathbb{R}$); **logistic regression**, in which the outcome is binary ($y \in \{0, 1\}$), and **loglinear (Poisson) regression**, in which the outcome is a positive integer, or count ($y \in \{0, 1, 2, \ldots\}$). We have seen linear regression already in Chapter 3 and logistic regression in Chapter 2. There are many more GLMs corresponding to outcomes that follow other types of probability distributions.

6.1 Model Assumptions

In GLMs, the predictors can be anything – interval, ordinal, or nominal – regardless of the specific model one chooses. However, there are several other assumptions that are important to consider before fitting one of these models:

- We assume that the outcome follows a certain type of distribution (e.g. Bernoulli distribution for a logistic regression model, normal for linear, etc.) conditional on the predictors. This assumption is baked into the model structure. It is, therefore, important to consider whether the outcome distribution you chose actually makes sense for your particular problem. It is generally not advisable to use a linear regression model, for example, when your outcome is a count.
- We assume that the predictors are fixed and known, and thus have no error associated with their measurements[1].
- We assume that the predictors enter the model as a linear combination. This is why GLMs are referred to as "linear models".
- We assume that the n samples in our dataset are collected independently, so that the errors of the n sample outcomes are uncorrelated[2].

6.2 Modeling the Predictors

All of the GLMs we will see today incorporate a **linear combination** of predictors. A linear combination is an expression constructed from a set of terms by multiplying each term by a constant and adding the results. We denote the number of predictors in the model by p and the vector of predictors by x, where

$$x = \begin{bmatrix} 1 \\ x_1 \\ x_2 \\ \vdots \\ x_p \end{bmatrix}$$

and we have included a "1" as the first element to allow for an **intercept**. We write $x^{(i)}$ to denote the vector of predictors associated with the ith training example. The coefficients of the linear combination (i.e. the model parameters

[1] Bayesian versions of these models relax this assumption, but we will not encounter these until much later

[2] Think back to our formulation of the likelihood in Chapter 5 and how it depended on the samples' being independent and identically distributed, or iid.

we are hoping to learn) are denoted by:

$$\beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \\ \vdots \\ \beta_p \end{bmatrix}$$

and we often express the linear combination as an inner product, written as

$$\beta^T x = \beta_0 + \sum_{j=1}^{p} \beta_j x_j.$$

Generalized linear models model the **expected value** of the outcome, $E[y]$, as a function of this linear combination of predictors. The function that relates the two is called the **link function**. Different types of GLM use different link functions.

6.3 Linear Regression

The linear regression model has a long history of development before the advent of GLMs, so it's typically taught in its own course with all of the associated model diagnostics, goodness of fit tests, etc. long before a student ever sees other GLMs. I think a comparative approach is more effective, which is why we're doing it this way[3].

6.3.1 Modeling the Outcome

In linear regression, we assume that the outcome, y, follows a normal distribution (see Section 4.2), conditional on the values of the predictors. Recall that the normal distribution is a continuous probability distribution with the

[3]The other thing about linear regression models is that they are usually fit using least squares methods instead of maximum likelihood. The parameter estimates are the same in both cases, as we will see much later.

following properties:

$$p(y|\mu,\sigma) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(y-\mu)^2}{2\sigma^2}} \qquad E[y|\mu,\sigma] = \mu \qquad \text{var}(y|\mu,\sigma) = \sigma^2$$

where $y \in \mathbb{R}$.

6.3.2 Linking the Predictors to the Outcome

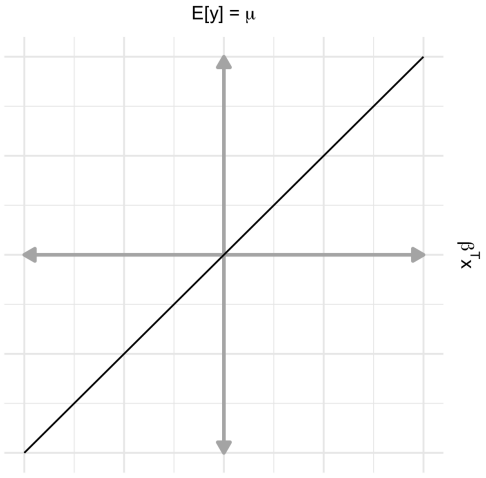
In linear regression, the mean of the outcome distribution, which is normal, can be any real number. We therefore use the **identity link**, setting $E[y]$ directly equal to the linear combination of predictors. Since the outcome is normal, we know that $E[y] = \mu$, the mean of the normal distribution. We therefore write:

$$E[y] = \mu = \beta^T x \tag{6.1}$$

which is usually rearranged and rewritten as:

$$y = \beta^T x + \varepsilon$$

where $\varepsilon \sim N(0, \sigma^2)$. The relationship between $E[y]$ and $\beta^T x$ is shown below.



6.4 Logistic Regression

Logistic regression models data where the outcome is binary; i.e. where y is "yes" or "no". Variants of logistic regression, called **multinomial logistic regression** and the **proportional odds model**, can also be used to model data where the outcome contains multiple categories that either have an ordering (ordinal) or do not (nominal). We will see how this works in a second.

6.4.1 Modeling the Outcome

In logistic regression the outcome, y, is either 0 or 1. We model it using the Bernoulli distribution (see Section 4.3), which is a discrete probability distribution with the following properties:

$$p(y|\mu) = \mu^y(1-\mu)^{1-y} \qquad E[y|\mu] = \mu \qquad \text{var}(y|\mu) = \mu(1-\mu)$$

where $y \in \{0, 1\}$.

6.4.2 Linking the Predictors to the Outcome

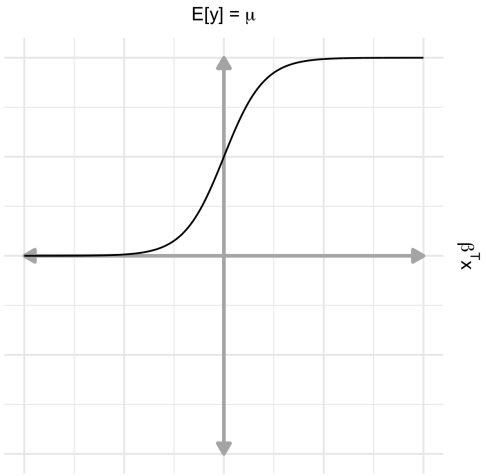
In logistic regression, the mean of the outcome distribution, which is Bernoulli, is a probability. It must therefore be a real number between 0 and 1. No matter how large or small $\beta^T x$ gets, the value of $E[y] = \mu$ cannot be outside this range. We therefore apply the **logistic function**, $f(x) = 1/(1+\exp(-x))$, which has the range $(0, 1)$, to $\beta^T x$ to squash it:

$$E[y] = \mu = \frac{1}{1+\exp\left(-\beta^T x\right)} \tag{6.2}$$

The relationship between $E[y]$ and $\beta^T x$ is shown below. We typically invert the model to write

$$\log \frac{\mu}{1-\mu} = \beta^T x$$

which is the standard form of the logistic regression model. The function $\log\left(\mu/(1-\mu)\right)$ is called the logit, and in logistic regression we say we use the **logit link**.



6.5 Poisson Regression

In Poisson regression, the outcome is a count. This type of regression is less common than linear and logistic regression, but we include it here mainly so you can see how the ideas from GLM extend to many different classes of outcome distributions within the exponential family.

6.5.1 Modeling the Outcome

In Poisson regression, we model the outcome using the Poisson distribution, which is a discrete probability distribution with the following properties:

$$p(y|\lambda) = \frac{e^{-\lambda}\lambda^y}{y!} \qquad E[y|\lambda] = \lambda \qquad \text{var}(y|\lambda) = \lambda$$

where $y \in 0, 1, 2, \ldots$.

6.5.2 Linking the Predictors to the Outcome

In Poisson regression, the mean of the outcome distribution, which is Poisson, is the expected value of a count. It must therefore be a real number greater

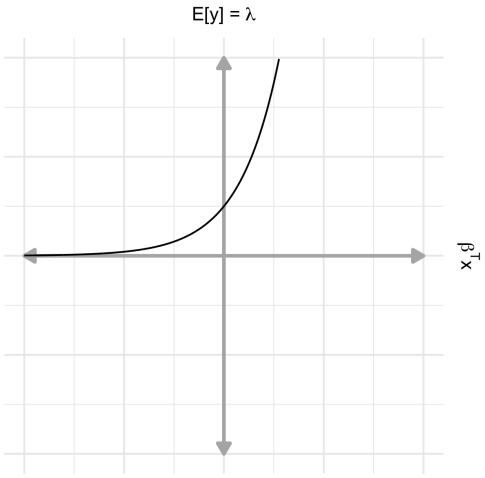
than or equal to zero. In particular, no matter how small $\beta^T x$ gets, the value of $E[y] = \lambda$ cannot be negative. We therefore exponentiate $\beta^T x$ to ensure that the result is greater than zero:

$$E[y] = \lambda = \exp(\beta^T x) \tag{6.3}$$

The relationship between $E[y]$ and $\beta^T x$ is shown below. We typically invert the model to write

$$\log(\lambda) = \beta^T x$$

which is the standard form of the Poisson regression model. We say we use the **log link**.



6.6 Maximum Likelihood for GLMs

GLMs are typically fit using maximum likelihood estimation (see Chapter 5). A full treatment of MLE for GLMs is outside the scope of these notes, but I've put the start of the calculations for each type of model below.

6.6.1 Linear Regression

The likelihood for the linear regression model is:

$$\mathcal{L}(\mu^{(1)}, \ldots, \mu^{(n)}, \sigma) = \prod_{i=1}^{n} \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left[-\frac{(y^{(i)} - \mu^{(i)})^2}{2\sigma^2}\right]$$

where we use $\mu^{(i)}$ to represent the model's estimate of the mean of the outcome at the position of training example i. We can use Equation 6.1 to rewrite this as a function of the predictors:

$$\mathcal{L}(\beta, \sigma) = \prod_{i=1}^{n} \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left[-\frac{(y^{(i)} - \beta^T x^{(i)})^2}{2\sigma^2}\right]$$

Taking the log, we obtain the log-likelihood:

$$\log \mathcal{L}(\beta, \sigma) = -\frac{n}{2}\log(2\pi) - \frac{n}{2}\log(\sigma^2) - \frac{1}{2\sigma^2}\sum_{i=1}^{n}\left(y^{(i)} - \beta^T x^{(i)}\right)^2$$

Taking derivatives of the log-likelihood with respect to the βs, we find that we can maximize the likelihood by minimizing the sum-squares: $\sum_{i=1}^{n}\left(y^{(i)} - \beta^T x^{(i)}\right)^2$.

6.6.2 Logistic Regression

The likelihood for the logistic regression model is:

$$\mathcal{L}(\mu^{(1)}, \ldots, \mu^{(n)}) = \prod_{i=1}^{n} {\mu^{(i)}}^{y^{(i)}} (1 - \mu^{(i)})^{1-y^{(i)}}$$

Rewriting this as a function of the predictors, we get:

$$\mathcal{L}(\beta) = \prod_{i=1}^{n} \left(\frac{1}{1 + \exp(-\beta^T x^{(i)})}\right)^{y^{(i)}} \left(\frac{\exp(-\beta^T x^{(i)})}{1 + \exp(-\beta^T x^{(i)})}\right)^{1-y^{(i)}}$$

Taking the log, we obtain the log-likelihood:

$$\log \mathcal{L}(\beta) = \sum_{i=1}^{n} \left[-y^{(i)} \log \left[1 + \exp(-\beta^T x^{(i)}) \right] + (1 - y^{(i)}) \log \left[1 + \exp(-\beta^T x^{(i)}) \right] \right]$$

Again, we will take derivatives of the log-likelihood with respect to the βs to maximize it. However, we cannot solve for the optimal βs analytically; numerical optimization methods are used to perform the optimization.

6.6.3 Loglinear (Poisson) Regression

The likelihood for the Poisson regression model is:

$$\mathcal{L}(\lambda^{(1)}, \ldots, \lambda^{(n)}) = \prod_{i=1}^{n} \frac{{\lambda^{(i)}}^{y^{(i)}} e^{-\lambda^{(i)}}}{y^{(i)}!}$$

Rewriting this as a function of the predictors, we get:

$$\mathcal{L}(\beta) = \prod_{i=1}^{n} \frac{\exp\left(y^{(i)} \beta^T x^{(i)}\right) e^{-\exp\left(\beta^T x^{(i)}\right)}}{y^{(i)}!}$$

Taking the log, we obtain the log-likelihood:

$$\log \mathcal{L}(\beta) = \sum_{i=1}^{n} \left[y^{(i)} \beta^T x^{(i)} - \exp(\beta^T x^{(i)}) - \log(y^{(i)}!) \right]$$

As with logistic regression, we cannot solve for the optimal βs analytically; numerical optimization methods are used.

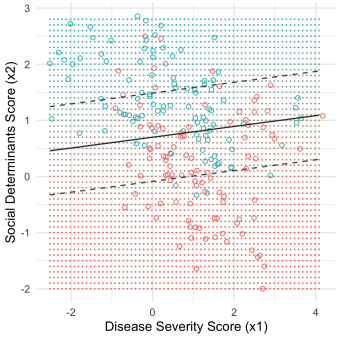
Chapter 7

Fitting and Interpreting GLMs

Generalized linear models (Chapter 6) are just one way to approach supervised learning. However, they are by far the most common approach in the clinical research literature. Linear and logistic regression are established, standard methods for clinical data analysis in contexts where you want to relate the effects of one or more predictors to an outcome that is a number or a class (e.g. yes/no). Because of this, it is important to know how to interpret these models – e.g., what the coefficients, standard errors, and model diagnostics mean – and how to fit them using software.

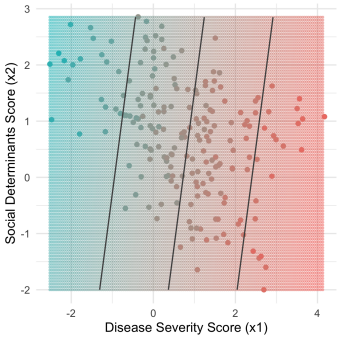
7.1 Examples from Chapters 2 and 3

In Chapter 2, we saw an example where information about two predictors – a disease severity score (x_1) and a social determinants score (x_2) – was used to predict a binary outcome: whether a patient would be readmitted to the ER within 30 days of discharge. In Chapter 3, we used the same two predictors to predict the numeric level of a disease recurrence biomarker. Here are pictures of the logistic regression model from Chapter 2 and the linear regression model from Chapter 3 with their fitted model summary output. Note: These pictures include axis labels, whereas those from Chapters 2 and 3 did not.




```r
m3 <- glm(y ~ x1 + x2, data = df, family = "binomial")
summary(m3)
```

```
Call:
glm(formula = y ~ x1 + x2, family = "binomial", data = df)

Deviance Residuals:
     Min        1Q    Median        3Q       Max
-1.88232  -0.90614  -0.05965   0.86579   2.28489

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)   0.9780     0.2945   3.321 0.000897 ***
x1            0.1344     0.1372   0.980 0.327272
x2           -1.3981     0.2316  -6.035 1.59e-09 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 277.26  on 199  degrees of freedom
Residual deviance: 209.54  on 197  degrees of freedom
AIC: 215.54

Number of Fisher Scoring iterations: 4
```




```r
m2 <- glm(y ~ x1 + x2, data = df, family = "gaussian")
summary(m2)
```

```
Call:
glm(formula = y ~ x1 + x2, family = "gaussian", data = df)

Deviance Residuals:
     Min        1Q    Median        3Q       Max
-11.9218   -3.1032    0.2891    2.8316   12.5813

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  49.8600     0.5370  92.844  < 2e-16 ***
x1           10.4372     0.2855  36.555  < 2e-16 ***
x2           -1.8824     0.3609  -5.215 4.63e-07 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for gaussian family taken to be 22.74456)

    Null deviance: 45983.6  on 199  degrees of freedom
Residual deviance:  4480.7  on 197  degrees of freedom
AIC: 1197.4

Number of Fisher Scoring iterations: 2
```

Question 7.1

Interpret the meaning of the coefficients of x_1 and x_2 in the linear regression model.

Question 7.2

Interpret the meaning of the intercept in the linear regression model.

Question 7.3

Interpret the meaning of the coefficients of x_1 and x_2 in the logistic regression model.

Question 7.4

Interpret the meaning of the intercept in the logistic regression model.

7.2 Standard Errors and Hypothesis Tests

The magnitudes of the coefficients in these models matter only in relation to:

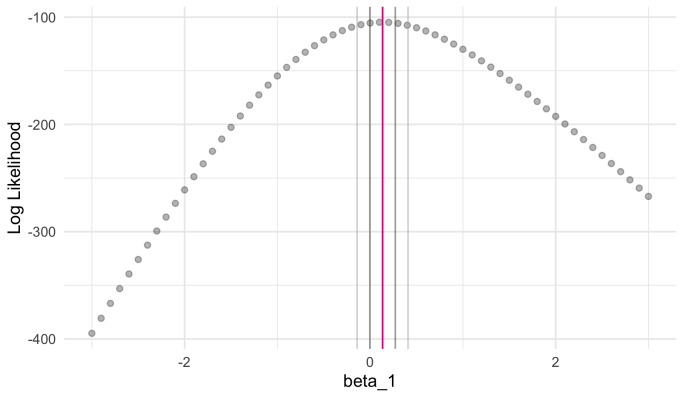
1. The scale on which the predictors are measured.
2. The amount of uncertainty the model has about their values.

For example, if a predictor varies only across a tiny range of values, its model coefficient may be large, since it quantifies the change in the link-function-transformed outcome when the predictor changes by 1.0. However, that doesn't mean that the predictor itself is important to the outcome[1].

Similarly, the model may be highly uncertain about a coefficient's value, owing to factors like a small dataset (small n) or collinearity among the

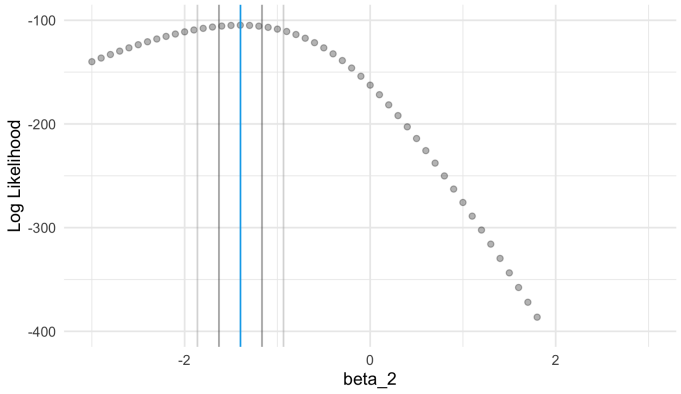
[1]This is one reason many advocate **scaling** and **centering** predictors before fitting a model. Centering means subtracting the mean value of a predictor from all of its individual measurements so that the mean of each centered predictor is zero. Scaling means dividing the values of each predictor by their standard deviation, so that the standard deviation of each predictor is 1.0. This enables the relative magnitudes of the model coefficients to be compared directly.

predictors. Mathematically, high uncertainty means that the value of the likelihood doesn't change very rapidly as you move away from the maximum likelihood estimate of a coefficient. For example, here is how the log-likelihood for the logistic regression example above changes when we vary β_1 (the coefficient of x_1), keeping β_0 (the intercept) and β_2 (the coefficient of x_2) fixed at their MLEs:



The gray vertical lines are related to the **standard error** of the model coefficient, which is in turn related to the "flatness" of the likelihood surface around the MLE. The gray lines are situated at 1 and 2 standard errors away from the MLE in either direction. You can see that in the case of β_1, the gray lines overlap zero. The value zero (no effect) is a plausible estimate of the impact of x_1 on the outcome.

Contrast this with how the log-likelihood varies around the MLE for β_2:



Here the standard error is larger, but the magnitude of the coefficient is also larger, so the range of the gray lines does not overlap zero. These findings are reflected in the relative values of the **Z-statistic** (`z value`) and **P-value** (`Pr(>z|)`) in the model output for the two coefficients. Whether a coefficient's value is likely to be nonzero is typically evaluated using a formalism called a **hypothesis test**. We will discuss hypothesis tests in much greater detail in Chapter 8.

7.3 Case Study: Linear Regression

The following data come from an early study that examined the possible link between air pollution and mortality. The authors examined 60 cities throughout the United States and recorded the following data:

MORT	Total age-adjusted mortality from all causes, in deaths per 100,000 population
PRECIP	Mean annual precipitation (in inches)
EDUC	Median number of school years completed for persons of age 25 years or older
NONWHITE	Percentage of the 1960 population that is nonwhite
NOX	Relative pollution potential of oxides of nitrogen
SO2	Relative pollution potential of sulfur dioxide

Note: "Relative pollution potential" refers to the product of the tons emitted per day per square kilometer and a factor correcting the SMSA dimensions and exposure.

We want to predict the value of `MORT` (y) using the predictors `PRECIP`, `EDUC`, `NONWHITE`, `NOX`, and `SO2` (x_1, x_2, x_3, x_4 and x_5). Here is the GLM output for this model in R:

```
Call:
glm(formula = MORT ~ PRECIP + EDUC + NONWHITE + NOX + SO2,
    family = "gaussian", data = d)

Deviance Residuals:
   Min      1Q  Median      3Q     Max
```

```
-91.38  -18.97   -3.56   16.00   91.83

Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept) 995.63646   91.64099  10.865 3.35e-15 ***
PRECIP        1.40734    0.68914   2.042 0.046032 *
EDUC        -14.80139    7.02747  -2.106 0.039849 *
NONWHITE      3.19909    0.62231   5.141 3.89e-06 ***
NOX          -0.10797    0.13502  -0.800 0.427426
SO2           0.35518    0.09096   3.905 0.000264 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for gaussian family taken to be 1375.723)

    Null deviance: 228275  on 59  degrees of freedom
Residual deviance:  74289  on 54  degrees of freedom
AIC: 611.56

Number of Fisher Scoring iterations: 2
```

Side note: Most models can be fit multiple ways. Linear regression models are normally fit using **ordinary least squares** and the `lm` package, as opposed to maximum likelihood and the `glm` package. The coefficients and most of the output are exactly the same:

```
Call:
lm(formula = MORT ~ PRECIP + EDUC + NONWHITE + NOX + SO2,
   data = d)

Residuals:
   Min     1Q Median     3Q    Max
-91.38 -18.97  -3.56  16.00  91.83

Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept) 995.63646   91.64099  10.865 3.35e-15 ***
PRECIP        1.40734    0.68914   2.042 0.046032 *
EDUC        -14.80139    7.02747  -2.106 0.039849 *
NONWHITE      3.19909    0.62231   5.141 3.89e-06 ***
NOX          -0.10797    0.13502  -0.800 0.427426
```

```
SO2           0.35518    0.09096   3.905 0.000264 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 37.09 on 54 degrees of freedom
Multiple R-squared:  0.6746,  Adjusted R-squared:  0.6444
F-statistic: 22.39 on 5 and 54 DF,  p-value: 4.407e-12
```

Question 7.5

Interpret the values of each of these coefficients. Based on the coefficient values and their standard errors, which predictor(s) do you think have the greatest impact on mortality?

Question 7.6

In this model, is the effect of one predictor (say, `PRECIP`) impacted by the value(s) of any of the other predictor(s)? How does this differ from the other regression algorithms we've seen (KNN and decision trees)? What are the advantages and disadvantages of this choice?

7.4 Case Study: Logistic Regression

The goal of this study was to identify risk factors associated with giving birth to a low birth weight baby (a baby weighing less than 2500 grams). Infant mortality rates and birth defect rates are very high for low birth weight babies. A woman's behavior during pregnancy (including diet, smoking habits, and receiving prenatal care) can greatly alter the chances of carrying the baby to term and, consequently, of delivering a baby of normal birth weight.

Data were collected on 189 women, 59 of which had low birth weight babies and 130 of which had normal birth weight babies.

LOW	Low birth weight (0 = birth weight $\geq$ 2500 g; 1 = birth weight $<$ 2500 g)
AGE	Age of mother in years
LWT	Mother's weight in pounds at last menstrual period
RACE	Race (1 = white, 2 = black, 3 = other)
SMOKE	Smoking status during pregnancy (1 = yes, 0 = no)
PTL	History of premature labor (0 = none, 1 = one, etc.)
HT	History of hypertension (0 = no, 1 = yes)
UI	Presence of uterine irritability (0 = no, 1 = yes)
FTV	Number of physician visits during the first trimester
BWT	Birth weight in grams

SOURCE: Hosmer and Lemeshow (2000) *Applied Logistic Regression: Second Edition*. Data were collected at Baystate Medical Center, Springfield, Massachusetts during 1986.

We would like to predict LOW based on all of the other covariates except BWT. (Why not use BWT?) The GLM output of this model is:

```
Call:
glm(formula = LOW ~ AGE + LWT + RACE + SMOKE + PTL + HT + UI +
    FTV, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.8946  -0.8212  -0.5316   0.9818   2.2125

Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  0.480623   1.196888   0.402  0.68801
AGE         -0.029549   0.037031  -0.798  0.42489
LWT         -0.015424   0.006919  -2.229  0.02580 *
RACE2        1.272260   0.527357   2.413  0.01584 *
RACE3        0.880496   0.440778   1.998  0.04576 *
SMOKE        0.938846   0.402147   2.335  0.01957 *
PTL          0.543337   0.345403   1.573  0.11571
HT           1.863303   0.697533   2.671  0.00756 **
UI           0.767648   0.459318   1.671  0.09467 .
FTV          0.065302   0.172394   0.379  0.70484
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 234.67  on 188  degrees of freedom
Residual deviance: 201.28  on 179  degrees of freedom
AIC: 221.28

Number of Fisher Scoring iterations: 4
```

Question 7.7

In this model, is the effect of one predictor (say, `AGE`) impacted by the value(s) of any of the other predictor(s)? How does this differ from the other classification algorithms we've seen (KNN and decision trees)? What are the advantages and disadvantages of this choice?

Question 7.8

Comment on how the variable `RACE` enters into the model here. Does this make sense in light of what that variable means and how it potentially interacts with the other study variables?

Question 7.9

Interpret the values of each of these coefficients. Based on the coefficient values and their standard errors, which predictor(s) do you think have the greatest impact on whether or not a woman has a low birthweight baby?

7.5 Case Study: Poisson Regression

These data come from a study of nesting horseshoe crabs. Each of the 173 observed female horseshoe crabs had a male crab resident in her nest. The study investigated factors affecting whether the female crab had any other males, called *satellites*, residing nearby. (Source: Agresti, *Categorical Data Analysis*, Table 4.3. Data courtesy of Jane Brockmann, Zoology Department, University of Florida; study described in *Ethology* **102**: 1-21, 1996.)

SATELL	Number of satellites
COLOR	Color of the female crab (1 = light medium, 2 = medium, 3 = dark medium, 4 = dark)
SPINE	Spine condition (1 = both good, 2 = one work or broken, 3 = both worn or broken)
WIDTH	Carapace width of the female crab (cm)
WEIGHT	Weight of the female crab (g)

The GLM output of this model is:

```
Call:
glm(formula = satell ~ color + spine + width + weight, family = "poisson",
    data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-3.0126  -1.8846  -0.5406   0.9448   4.9602

Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept) -0.3435447  0.9684204  -0.355  0.72278
color       -0.1849325  0.0665236  -2.780  0.00544 **
spine        0.0399764  0.0568062   0.704  0.48160
width        0.0275251  0.0479425   0.574  0.56588
weight       0.0004725  0.0001649   2.865  0.00417 **
---
Signif. codes:  0 ’***’ 0.001 ’**’ 0.01 ’*’ 0.05 ’.’ 0.1 ’ ’ 1

(Dispersion parameter for poisson family taken to be 1)

    Null deviance: 632.79  on 172  degrees of freedom
Residual deviance: 551.85  on 168  degrees of freedom
AIC: 917.15

Number of Fisher Scoring iterations: 6
```

Question 7.10

Comment on how the variables `color` and `spine` are coded here. Does this make sense in light of what those variables mean?

Question 7.11

Interpret the values of each of these coefficients. Based on the coefficient values and their standard errors, which predictor(s) do you think have the greatest impact on the number of male satellites around a nesting female horseshoe crab?

Chapter 8

Hypothesis Testing DRAFT

Hypothesis testing is the central idea underpinning most of the analysis you'll find in the clinical and biomedical research literature[1]. There are multiple types of hypothesis testing, but the most common type is **null hypothesis testing**, most of the theory of which originated from the statistician R.A. Fisher. In null hypothesis testing, you create a model of how your data should look under default conditions, and then you look to see whether your data deviate appreciably from the model. You quantify your data's deviation from the model by calculating a **test statistic**. One can view this type of hypothesis testing as a form of **anomaly detection**.

The statisticians Jerzy Neyman and Karl Pearson instead favored the use of hypothesis testing as a **model comparison** tool. In their view, you would set up multiple different models and then quantify each model's fit to your data to choose the best one. Fisher hated this approach because it meant accepting one or more models as truth, when in reality it's impossible to account for all potential scenarios.

Most of the hypothesis tests we use today (T-tests, chi-squared tests, etc.) follow Fisher's approach. Likelihood ratio tests and Bayesian methods adhere more to the Neyman-Pearson philosophy.

[1] I should state that there is still a lot of controversy around the whole idea of hypothesis testing and whether p-values should be used at all, etc.

8.1 Basic Steps of a Hypothesis Test

1. *Create an initial **research hypothesis**.* A hypothesis is an assertion that is capable of being proved false, such as, "If the subject has this genetic mutation, his risk of developing cancer will increase."

2. *State the **null hypothesis**.* The null hypothesis corresponds to the default, or baseline, position; for our example, the null hypothesis might be, "The events 'has mutation' and 'has cancer' are statistically independent." For some techniques, you also need to state an **alternative hypothesis**, which is the hypothesis that is contrary to the null[2].

3. *List statistical assumptions.* E.g. in **parametric** hypothesis testing methods, we assume the data follow some particular probability distribution under the null. **Nonparametric** methods do not make this assumption.

4. *Decide on an appropriate test and test statistic.* The **test statistic** quantifies the degree of deviation of your observed data from what you would expect under the null hypothesis[3].

5. *Derive the distribution of the test statistic under the null.* This is called the **null distribution**.

6. *Select a significance level under which you'll reject the null.* The **significance level**, usually written as α, is the probability of a type I error, which is when you reject the null even if it is true (false positive result).

7. *Compute the observed value of the test statistic from the data.*

8. *Decide whether or not to reject the null hypothesis.*

[2]The alternative hypothesis is the hypothesis that is contrary to the null hypothesis. It is usually taken to be that the observations are the result of a real effect (with some amount of chance variation superposed). As mentioned above, there was a huge controversy between R.A. Fisher and Jerzy Neyman/Karl Pearson over the use of alternative hypotheses. Fisher said you shouldn't use them because rejecting the null doesn't mean accepting that there's a true effect. Neyman and Pearson thought you should use them because it gave statistical tests more power. Most of hypothesis testing ended up following Fisher's approach.

[3]Some definitions: A **statistic** is just some quantity that summarizes a set of data, or gives some information about the value of a parameter. A **sufficient statistic** is a statistic that gives the maximum amount of information about a parameter that can possibly be obtained from the sample data.

8.2 Definitions

- **Type I Error:** When a hypothesis test rejects the null even though the null is true (also called a **false positive**). The type I error rate is usually denoted by α.
- **Type II Error:** When a hypothesis test fails to reject the null even though it is false (also called a **false negative**). The type II error rate is usually denoted by β.
- **P-value:** The probability of obtaining a test statistic at least as extreme as the one that was actually obtained, assuming the null is true. A p-value can be **one-sided** or **two-sided**. The difference lies in the definition of "extreme". In a one-sided test, we find the probability that the test statistic is at least as extreme *in the same direction* as the one we observed. In a two-sided test, we find the probability that the test statistic is at least as extreme *in either direction* (positive or negative deviation). In most cases, this has the practical effect of doubling the p-value.
- **Power:** The probability that a hypothesis test will reject the null when the null is false (that the test will detect a true effect if the effect is there). Usually denoted $1 - \beta$.

8.3 The Z-Test

8.4 Student's T-tests

The T-test (actually a family of tests) deals with situations where you have data that are assumed to be normally distributed, and you want to draw a conclusion about the mean of that distribution.

8.4.1 One Sample T-test

Assume you have a dataset $x^{(1)}, \ldots, x^{(n)}$, of real numbers that you can plausibly assume are normally distributed. You want to test whether the mean of

your data is equal to a fixed value, μ_0. You can do this using a test statistic

$$T = \frac{\overline{x} - \mu_0}{s/\sqrt{n}}$$

which follows a T-distribution with $n-1$ degrees of freedom under the null hypothesis that the means are the same. Here $\overline{x}$ refers to the sample mean, and s refers to the sample standard deviation, which is the square root of the sample variance, s^2:

$$s = \sqrt{\frac{1}{n-1}\sum_{i=1}^{n}(x^{(i)} - \overline{x})^2}$$

8.4.2 One-Sample T-test vs. Z-test

A one-sample T-test looks a lot like a Z-test (example from slides). Here is the difference:

- A Z-test assumes that the population standard deviation, σ, is fixed and known with 100% certainty so that the test statistic follows a normal distribution.
- The T-test estimates the population standard deviation from the data. The sample variance follows a chi-squared distribution with $n-1$ degrees of freedom, where n is the sample size. In this case, the test statistic follows a Student's T-distribution with $n-1$ degrees of freedom.

If you have enough samples, the sample standard deviation approaches the population standard deviation and the T-test becomes a Z-test. But when n is small, the T-test is quite a bit more conservative.

8.4.3 Two Independent Samples, Equal Variance

Assume you have a dataset $x^{(1)}, \ldots, x^{(n)}$ and another dataset $y^{(1)}, \ldots, y^{(m)}$. You assume that both are drawn from normal distributions with equal variance but potentially different means. You want to test whether the means are equal.

The test statistic

$$T = \frac{\overline{x} - \overline{y}}{s_p \sqrt{\frac{1}{n} + \frac{1}{m}}}$$

where

$$s_p^2 = \frac{(n-1)s_x^2 + (m-1)s_y^2}{m+n-2}$$
$$s_x^2 = \frac{1}{n-1}\sum_{i=1}^{n}(x^{(i)} - \overline{x})^2$$
$$s_y^2 = \frac{1}{m-1}\sum_{i=1}^{m}(y^{(i)} - \overline{y})^2$$

follows a t-distribution with $m + n - 2$ degrees of freedom.

8.4.4 Two Independent Samples, Unequal Variance

Sometimes you have two independent samples but cannot assume the variances are equal. In this case, you can use **Welch's T-test**, which uses the test statistic

$$T = \frac{\overline{x} - \overline{y}}{s_{xy}}$$

where

$$s_{xy} = \sqrt{\frac{s_x^2}{n} + \frac{s_y^2}{m}}.$$

This test statistic approximately follows a t-distribution with degrees of freedom given by the Welch-Sattherwaite Equation

$$\text{d.f.} = \frac{\left(\frac{s_x^2}{n} + \frac{s_y^2}{m}\right)^2}{\frac{(s_x^2/n)^2}{n-1} + \frac{(s_y^2/m)^2}{m-1}}$$

8.4.5 Matched Pairs

Assume you have a data set of matched pairs. This could be a set of measurements of the same individuals taken at two different points in time, for example. You want to test whether the second set of values have changed relative to the first set of values.

Question 8.1

Why does the output for the linear regression model in Section 7.1 use a T-test to test the hypotheses for the regression coefficients while the logistic regression model uses a Z-test?

8.5 Mann-Whitney Test

All of these variants of the T-test make assumptions about the normality of the data. Sometimes you want to compare the means of two groups but you aren't sure whether the normal assumption holds. In this case, you might want to try a **nonparametric** alternative to the two-sample T-test called the **Mann-Whitney Test**, or Wilcoxon Rank Sum Test.

Some interesting points about nonparametric tests:

- There are no distributional assumptions.
- Most nonparametric methods replace data by their ranks, which are invariant to any monotonic transformation of the data.
- Compare this to the T-test: If you use the log-transform of the data instead of the original values and do a T-test on them, the p-value can change. But with ranks that doesn't happen.
- Replacing the data by ranks also makes the test less sensitive to outliers.
- But remember, there is no free lunch: You will always lose power relative to a parametric test if you use the nonparametric alternative in a case where the distributional assumptions of the parametric test are true.

8.6 Pearson's Chi-Squared Test

Imagine you have data on two discrete covariates for a number of different subjects. You want to test whether the value of one covariate depends on the value of the other. **Pearson's chi-squared test** is used to assess the independence of row and column values in contingency tables, provided the cell counts are high enough.

We make some assumptions:

- The data are sampled randomly from a fixed population where each member of the population has an equal probability of selection.
- Expected counts for each cell must be sufficiently high. A common rule is 5 or more in all cells of a 2×2 table, and 5 or more in 80% of cells in larger tables, but no cells with zero counts.
- The observations are independent of each other. One observation should not be influenced in any way by the other observations taken before or after it.

The chi-squared test works by calculating expected counts in all $r \times c$ cells of the table (r = number of rows, c = number of columns) and then measuring the data's deviation from those expected counts. The **chi-squared test statistic** has the form

$$X^2 = \sum_{i=1}^{r} \sum_{j=1}^{c} \frac{(O_{ij} - E_{ij})^2}{E_{ij}}$$

where O refers to "observed count" and E to "expected count". This test statistic follows a chi-squared distribution with $(r-1)(c-1)$ degrees of freedom.

8.7 Fisher's Exact Test

For small sample sizes, the assumptions underlying Pearson's chi-squared test are no longer true. In these cases, it is common to replace the chi-squared test

with something called **Fisher's Exact Test**, which calculates an exact p-value directly by considering every possible outcome.

8.8 Tests of Normality

Chapter 9

Decision Trees DRAFT

Decision trees were developed as an alternative to neural networks in the 1970s. They can be used either for classification or regression. There are several algorithms for fitting decision trees, all of which are heuristic, because the general problem of learning an optimal decision tree for a dataset is NP-complete. All algorithms for tree learning are **greedy** and are not guaranteed to give the optimal solution.

9.1 Tree Learning Algorithms

9.2 Regression Trees

9.2.1 Entropy and Information Gain

Today we will discuss the ID3 algorithm for building decision trees, which relies on the concepts of entropy and information gain. **Entropy**, usually abbreviated H, is a measure of the uncertainty in the value of a random variable. It is the number of bits (on average) required to describe the outcome of the random variable. Here is the formula for the entropy of the discrete probability distribution governing the outcome of a random variable, X:

$$H(X) = -\sum_x P(X = x) \log_2 \left(P(X = x)\right)$$

For a Bernoulli random variable, there are only two possible outcomes: 0 and 1. The entropy of this random variable is given by:

$$H_{\text{Bernoulli}} = -\mu \log_2(\mu) - (1 - \mu) \log_2(1 - \mu)$$

where μ, as usual, is the probability the outcome is 1.

Let Y be the outcome variable of a training set. Let X be some other random variable defined over the training set. It could be one of the original predictors or some arbitrary combination of them. **Information gain** is defined as:

$$\begin{aligned} \text{Gain}(Y, X) &= H(Y) - \sum_x P(X = x)\ H(Y|X = x) \\ &= H(Y) - H(Y|X) \end{aligned}$$

It is a measure of how much our uncertainty in the value of Y is reduced by knowing X.

9.2.2 The ID3 Algorithm

Here is the algorithm:

1. Start with a single node representing the entire dataset.
2. At each current leaf node in the tree:
   (a) Compute the information gain for each feature in turn.
   (b) Split on the one with the highest information gain.
3. Return to Step 2. Stop the recursion when either the class distributions at the leaf nodes are entirely pure (all data points at a leaf have the same outcome class), or there are no more variables left to split on.

9.2.3 Decision Tree Regression

So far we've assumed that our outcome is discrete. But what happens if it's numeric? (That is, what if we want to perform regression instead of classification?)

In that case, we use **standard deviation reduction** instead of information gain to decide which variables to split on. The sample standard deviation of an outcome, y, is defined as:

$$S(Y) = \sqrt{\frac{\sum_i (y^{(i)} - \overline{y})}{n-1}}$$

The procedure is identical to the ID3 algorithm except you use conditional standard deviation instead of information gain to decide on features. We define

$$S(Y, X) = \sum_x P(X = x)\ S(Y(X = x))$$

and at each current leaf node, we split on the variable where the reduction in standard deviation, $S(Y) - S(Y, X)$, is the highest.

9.2.4 Numeric Predictors

So far we've also assumed that our predictors are discrete. But decision trees can handle numeric predictors as well. There are many different strategies for deciding on an optimal split for a predictor. Two simple ones:

- Split at the median or mean of the predictor.
- Order the datapoints on the value of the predictor and consider each possible split, looking for the one that gives the greatest information gain/standard deviation reduction. So for example, if you have a predictor called "age" and its values are $10, 11, 16, 18, 20$, and 35, consider all $N - 1 = 5$ possible split points. (This is the approach used by C4.5, a successor to ID3.)

If you have a large dataset, the second option is probably not practical, but you can downsample your dataset first and then look for the optimal cut point(s).

What if the outcome is numeric? In that case, we can use **standard deviation reduction** instead of information gain to decide which variables to split on. The sample standard deviation of an outcome, y, is defined as:

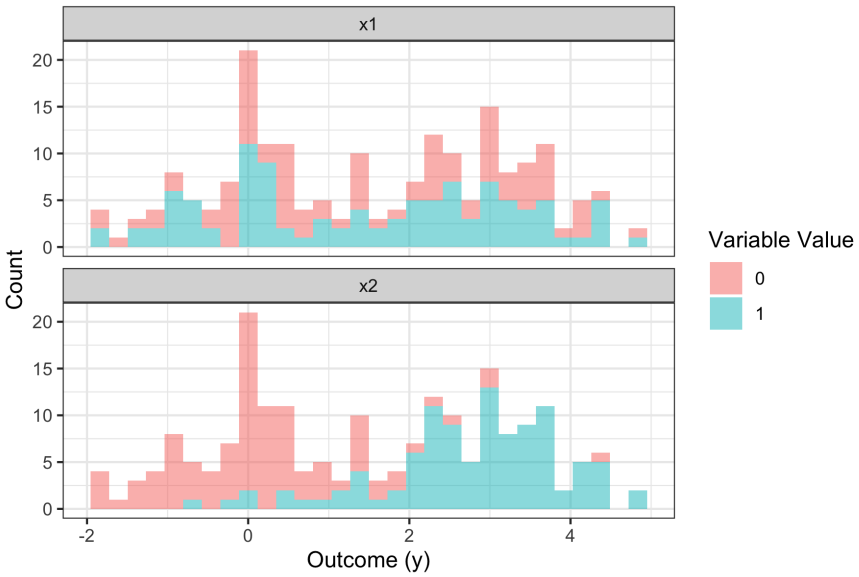
$$S(Y) = \sqrt{\frac{\sum_i (y^{(i)} - \overline{y})^2}{n-1}}$$

where $\overline{y}$ is the overall mean of the outcome. The procedure is identical to the ID3 algorithm (see Chapter 9) except you use conditional standard deviation instead of information gain to decide on features. We define

$$S(Y, X) = \sum_{x \in \text{Values(X)}} \frac{|Y(X = x)|}{|Y|} S(Y(X = x))$$

and at each current leaf node, we split on the variable where the reduction in standard deviation, $S(Y) - S(Y, X)$, is the highest.

For example, imagine you had a dataset similar in structure to our example, but instead of two real-valued predictors, you have two binary predictors, x_1 and x_2. The decision tree algorithm could choose either one of them to split on first. Here are the distributions of outcome values associated with x_1 and x_2.



Question 9.1

Which of these two variables, x_1 or x_2, would make the most sense for a decision tree to split on? What would such a split look like and what would the output value of the tree (the predicted value of y) be for each side of the split?

Chapter 10

The Bias-Variance Tradeoff
DRAFT

In classification, **model complexity** (i.e. the effective number of parameters the model must fit) is typically related to the intricacy and complexity of the decision boundary; the more parameters in the model, the more complex the boundary.

10.1 Goodness of Fit vs. Generalizability

Training vs. test error

10.2 Bias vs. Variance

This figure shows the training and test error for KNN as a function of K for a classification example similar to the one discussed in Chapter 2, as well as the training and test error for a linear model (which doesn't vary with K). You can see that the curves have characteristic shapes that vary with K. It turns out these shapes reflect a general principle for all supervised learning called the **bias-variance tradeoff**.

The bias-variance tradeoff: KNN example. The Bayes error rate, or **ir-**

reducible error, is the probability an instance is misclassified by a classifier that knows the true class probabilities given the predictors. From *Elements of Statistical Learning*, Figure 2.4.

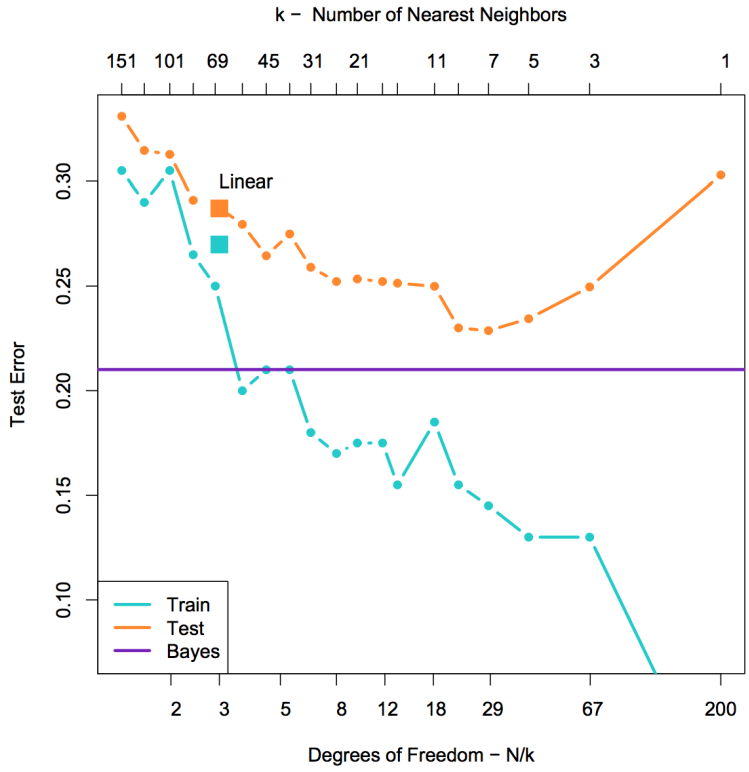
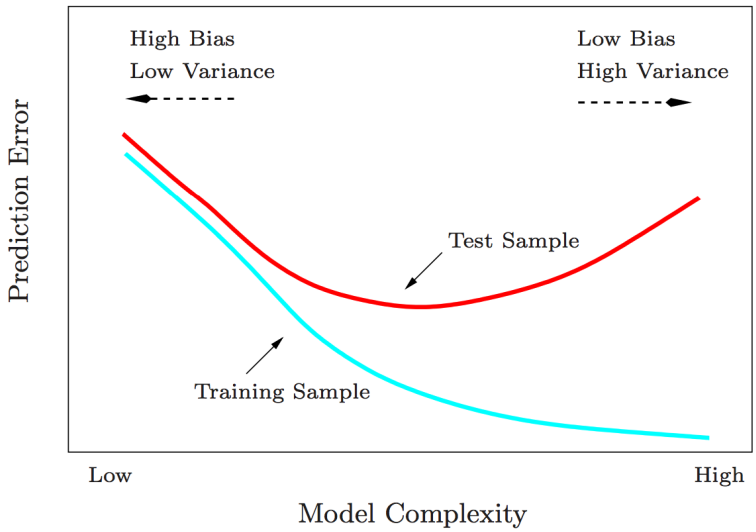
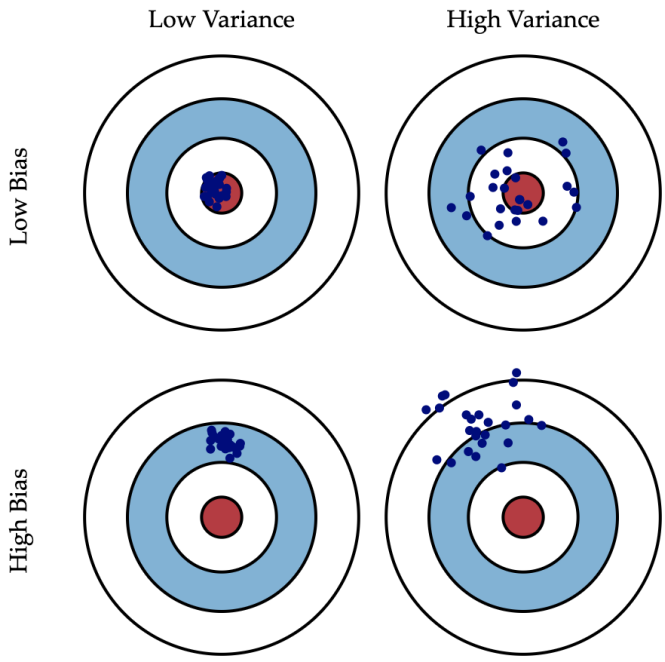


Illustration of training vs. test error as a function of model complexity, as well as the bias-variance tradeoff. From *Elements of Statistical Learning*, Figure 2.11.



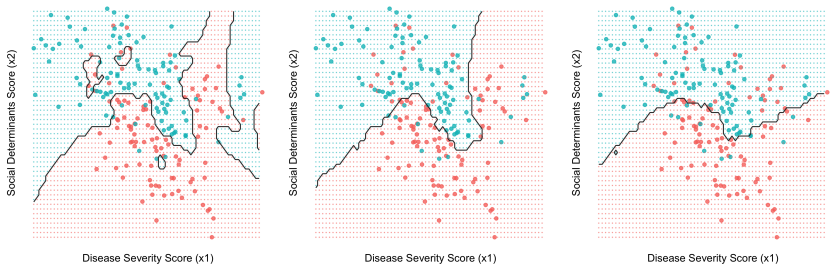
A graphical illustration of the difference between bias and variance. Think of each dot as representing a single test example evaluated under the same model trained on slightly different datasets. The center of the target is the prediction the model should make for that test example. In the case of high bias and low variance, all of the models are off, but they are "wrong in the same way". If you average their predictions, the answer is still way off the mark. In the case of high variance, the models all make very different predictions on the same training example. However, their predictions are off in random directions from the center, so if you average their outputs, you'll get closer to the right answer.



10.3 Overfitting vs. Underfitting

Question 10.1

What are the advantages and disadvantages of KNN with low K (e.g. $K = 3$) vs. high K (e.g. $K = 50$)? The decision boundaries for the previous example with (left to right) $K = 3, 15$, and 50 are shown below.



Question 10.2

We have discussed bias and variance in the context of classification (a yes/no outcome). How would training and test error, overfitting vs. underfitting, etc. be quantified if the outcome was a number, as in a regression problem (Chapter 3)?

Chapter 11

Feature Engineering and Feature Selection

The methods we've studied in Chapters 2 and 3, as well as all other supervised (and unsupervised) machine learning algorithms, all depend on the concept of a **feature**. A feature is some aspect of each training example that the model designer believes will influence its relationship to the outcome, or that captures some aspect of the data in a way that is relevant to the problem he/she is trying to solve.

Before any algorithm can be applied, therefore, it is necessary to decide how to represent the data: which features to include and how to extract them from the raw data. This task is called **feature engineering**. In most cases, the model designer will also want to incorporate some form of **feature selection**: a process that automatically or semi-automatically decides which features are most relevant to the model and discards the others.

Question 11.1

Choose 2-3 examples from the list of problems in Section 1.1. Describe the setup of each problem and what types of features one would need to collect to build an accurate/useful model.

11.1 Sample Dataset

The so-called "Pima Indians diabetes dataset" was collected in the 1980s. It includes information on 768 women from the Pima people, who live near Phoenix, Arizona. The Pima were, as of the late 1980s, under continuous study by the National Institute of Diabetes and Digestive and Kidney Diseases because of their high incidence of diabetes[1]. There are eight predictors in the dataset and one outcome. The predictors are:

Predictor	Description
Pregnancies	Number of times pregnant
Glucose	Plasma glucose concentration in a two-hour oral glucose tolerance test
BloodPressure	Diastolic blood pressure (mm Hg)
SkinThickness	Triceps skin fold thickness (mm)
Insulin	Two-hour serum insulin (μU/mL)
BMI	Body mass index (weight in kg/(height in m)^2)
DiabetesPedigreeFunction	Diabetes pedigree function (developed by research team; described in paper)
Age	Age in years

The outcome is whether or not the woman went on to develop type II diabetes within 5 years from the time of the survey.

Question 11.2

Why is coding this outcome as 0/1, or yes/no, potentially problematic?

[1]The causative factors behind this high diabetes rate are not clear. Some scholars believe that it was driven by a sudden shift in diet during the last century from traditional agricultural crops to processed foods, together with a decline in physical activity L. O. Schulz, P. H. Bennett, E. Ravussin, J. R. Kidd, K. K. Kidd, J. Esparza, and M. E. Valencia. "Effects of traditional and western environments on prevalence of type 2 diabetes in Pima Indians in Mexico and the US". in: *Diabetes Care* 29.8 (2006), pp. 1866–1871.

Question 11.3

What type of problem is this? What methods should we consider when solving this problem? Name at least three learning algorithms that might be appropriate.

11.2 Feature Engineering

Feature engineering mostly depends on domain expertise. There are three major analytical considerations when performing feature engineering: how the raw data is represented/summarized into features, how those features enter the model (e.g., do they need to be transformed or combined), and how different features are related to each other.

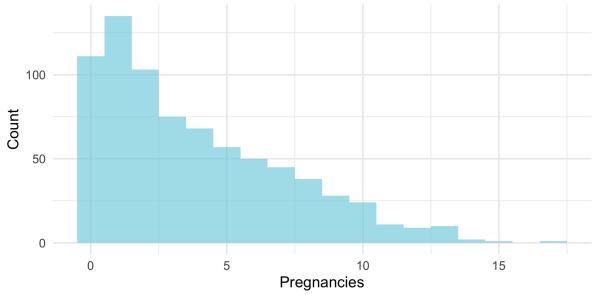
11.2.1 Representation

Rarely will raw data, especially observational data, feed directly into a model. More often, one must decide how to design features that capture aspects of the data that are likely to be important to the model.

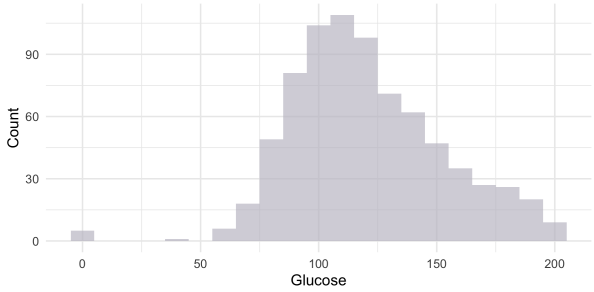
Question 11.4

These histograms show the distributions of the individual predictors in the Pima dataset. In each case, what is one alternative way that the same information could be represented as a feature? For predictors 2–6, what do you think the zero values mean and how should they be dealt with?

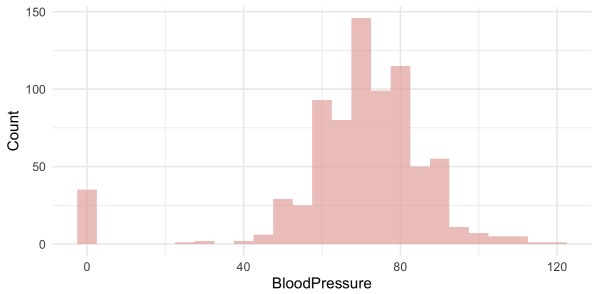
1. Pregnancies



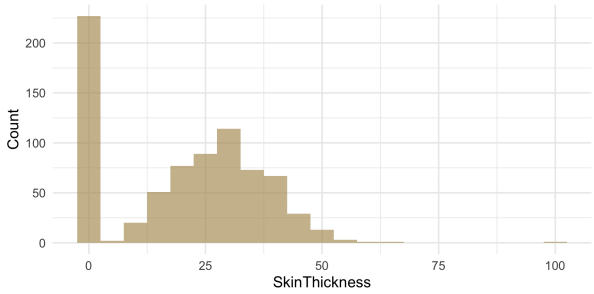
2. Glucose



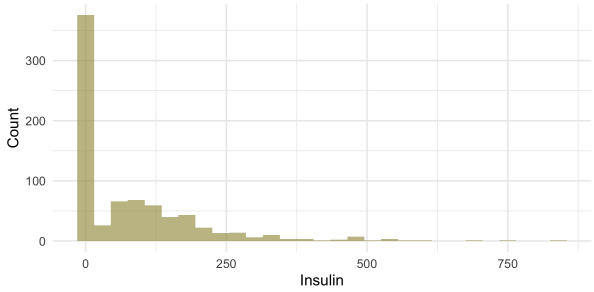
3. BloodPressure



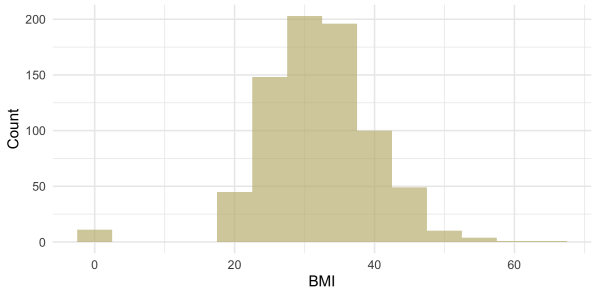
4. SkinThickness



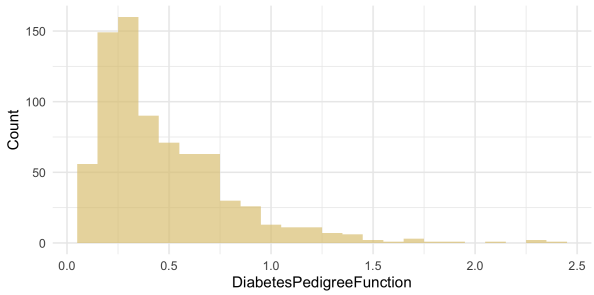
5. Insulin



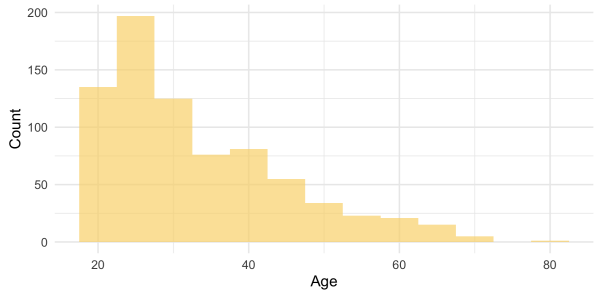
6. BMI



7. DiabetesPedigreeFunction



8. Age



Question 11.5

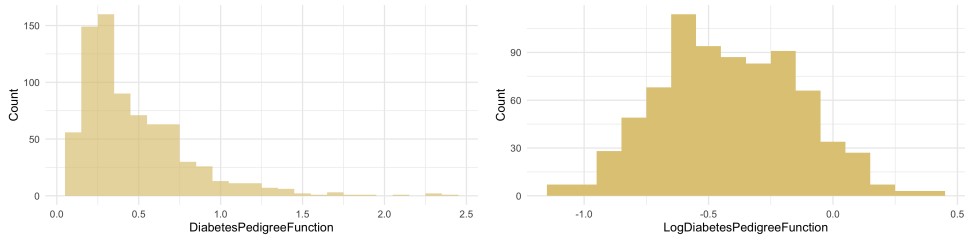
The type of study design here is called a **prospective cohort study**. How would you collect information on these eight predictors if this were a **retrospective cohort study** (e.g., if you collected information about these women and their subsequent development of diabetes from the EHR)? How might this change affect how you extract and code the predictors?

11.2.2 Transformations

Depending on the learning algorithm you're using and the goal of your project, you may or may not decide to employ transformations. A **transformation** is simply the application of a deterministic mathematical function to your data. In a supervised learning problem, you can transform one or more of the predictors and/or the outcome. Transformations are used to improve the interpretability of the model and/or to ensure that the model fulfills the assumptions of the statistical inference method(s) being used (e.g., a hypothesis test).

For example, here is what happens to the "diabetes pedigree function" predictor in the Pima dataset when we employ a common transformation called a **log transformation**[2]:

[2]Here we are using log base 10, but you could also perform a similar transformation with the natural log, $\log_2$, etc.



Question 11.6

In the log transformation shown here, we simply replace each value, x, by $\log_{10}(x)$. Every unit increase on a $\log_{10}$ scale corresponds to a 10-fold multiplication on the usual scale of the predictor. If you put the log-transformed predictor into a regression model in place of the original (linear is the easiest to understand, but you could also consider logistic, Poisson, etc.), how would that change your interpretation of the model?

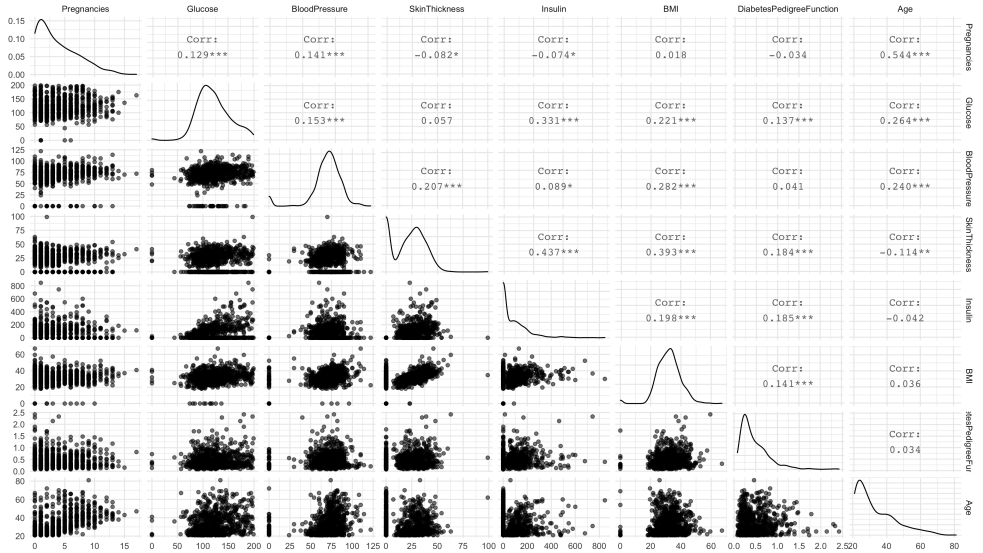
Political science, economics, sociology, and related disciplines, which are heavily dependent on the use of linear regression models and hypothesis tests, rely extensively on transformations. In my experience, machine learning folks spend almost no time on them because their primary concern is predictive accuracy, not model interpretation. Machine learning practitioners, however, very frequently **scale and center** their predictors (see footnote in Section 7.2), which is another type of transformation. We will get into more detail on transformations as we continue to learn about regression models.

11.2.3 Correlations and Redundancy

Including dozens or hundreds of predictors in a model does not guarantee that each contributes independent information. A good rule of thumb for any model is that it should be **parsimonious**: it should accomplish its goal with as little complexity and as few parameters as possible.

Finding a parsimonious model often means identifying sources of redundancy in a dataset. Often, two or more variables will be **correlated**, meaning that the value of one provides at least some information about the value of the other(s). A good way to alert yourself to the presence of highly correlated predictors is to create some sort of **correlogram**, or scatterplot matrix, which

looks at associations between all pairs of variables. A correlogram for the Pima dataset is below.



Question 11.7

This correlogram quantifies correlation using a metric called the **Pearson correlation coefficient**. Which pairs of predictors are the most tightly correlated? Are they positively or negatively correlated? How might you modify your dataset to eliminate redundancies in the information contributed by the different predictors?

Including correlated predictors is not always a bad thing, especially if your goal is prediction rather than model interpretation (see I. Guyon and A. Elisseeff. "An introduction to variable and feature selection". In: *Journal of Machine Learning Research* 3.Mar (2003), pp. 1157–1182, Figures 1, 2, and 3). The presence of correlations will also affect different types of models in different ways, and some suffer more than others.

For example, here are eight univariate logistic regression models that capture the effect of each predictor in the Pima dataset on the outcome of diabetes vs. no diabetes:

```
Call:
glm(formula = Outcome ~ Pregnancies, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.4433  -0.8741  -0.7782   1.2707   1.7003

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) -1.17675    0.12312  -9.558  < 2e-16 ***
Pregnancies  0.13716    0.02291   5.986 2.15e-09 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 956.21  on 766  degrees of freedom
AIC: 960.21

Number of Fisher Scoring iterations: 4
```

```
Call:
glm(formula = Outcome ~ BloodPressure, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.0797  -0.9389  -0.9000   1.4097   1.6838

Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept)   -1.140092   0.299822  -3.803 0.000143 ***
BloodPressure  0.007425   0.004141   1.793 0.072994 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 990.13  on 766  degrees of freedom
AIC: 994.13

Number of Fisher Scoring iterations: 4
```

```
Call:
glm(formula = Outcome ~ Insulin, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.5736  -0.9129  -0.8563   1.3761   1.5370

Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept) -0.8145101  0.0943584  -8.632  < 2e-16 ***
Insulin      0.0022988  0.0006535   3.518 0.000435 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 980.81  on 766  degrees of freedom
AIC: 984.81

Number of Fisher Scoring iterations: 4
```

```
Call:
glm(formula = Outcome ~ DiabetesPedigreeFunction, family = "binomial",
    data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.7889  -0.9032  -0.8213   1.3510   1.6441

Coefficients:
                         Estimate Std. Error z value Pr(>|z|)
(Intercept)               -1.1473     0.1379  -8.319  < 2e-16 ***
DiabetesPedigreeFunction   1.0828     0.2340   4.627  3.7e-06 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 970.86  on 766  degrees of freedom
AIC: 974.86

Number of Fisher Scoring iterations: 4
```

```
Call:
glm(formula = Outcome ~ Glucose, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-2.1096  -0.7837  -0.5365   0.8566   3.2726

Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept) -5.350080   0.420827  -12.71   <2e-16 ***
Glucose      0.037873   0.003252   11.65   <2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 808.72  on 766  degrees of freedom
AIC: 812.72

Number of Fisher Scoring iterations: 4
```

```
Call:
glm(formula = Outcome ~ SkinThickness, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.0781  -0.9455  -0.8508   1.3900   1.5439

Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept)   -0.829853   0.126816  -6.544    6e-11 ***
SkinThickness  0.009862   0.004773   2.066   0.0388 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 989.19  on 766  degrees of freedom
AIC: 993.19

Number of Fisher Scoring iterations: 4
```

```
Call:
glm(formula = Outcome ~ BMI, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.9209  -0.9178  -0.6838   1.2351   2.7244

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) -3.68641    0.40896  -9.014  < 2e-16 ***
BMI          0.09353    0.01205   7.761 8.45e-15 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 920.71  on 766  degrees of freedom
AIC: 924.71

Number of Fisher Scoring iterations: 4
```

```
Call:
glm(formula = Outcome ~ Age, family = "binomial", data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-1.7809  -0.8512  -0.7505   1.2811   1.6950

Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept) -2.047511   0.238847  -8.572  < 2e-16 ***
Age          0.042026   0.006587   6.380 1.77e-10 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 950.72  on 766  degrees of freedom
AIC: 954.72

Number of Fisher Scoring iterations: 4
```

The coefficients on each predictor here are called the **unadjusted coefficients**, and the p-values on the predictor-specific hypothesis tests are called **unadjusted p-values**. If you exponentiate a coefficient in a univariate logistic regression model, you get an **unadjusted odds ratio**[3]. Here is a summary table:

Predictor	Unadjusted Coefficient	Unadjusted Odds Ratio	Unadjusted P-value
Pregnancies	0.137	1.147	<0.001
Glucose	0.038	1.039	<0.001
BloodPressure	0.007	1.007	0.073
SkinThickness	0.010	1.010	0.039
Insulin	0.002	1.002	<0.001
BMI	0.094	1.100	<0.001
DiabetesPedigreeFunction	1.083	2.953	<0.001
Age	0.042	1.043	<0.001

Now let's create one big logistic regression model that includes all eight predictors. This is called a **multivariate** model. The coefficients, exponentiated coefficients, and p-values are often called **adjusted** in this case, or one might say that the odds ratio measures the effect of one predictor, **controlling for** the effects of the other predictors. Here are the adjusted estimates:

Predictor	Adjusted Coefficient	Adjusted Odds Ratio	Adjusted P-value
Pregnancies	0.123	1.131	<0.001
Glucose	0.035	1.036	<0.001
BloodPressure	-0.013	0.987	0.011
SkinThickness	0.001	1.001	0.929
Insulin	-0.001	0.999	0.186
BMI	0.090	1.094	<0.001
DiabetesPedigreeFunction	0.945	2.573	0.002
Age	0.015	1.015	0.111

[3]See Chapter 6 if you don't understand why you're exponentiating or where the term "odds ratio" comes from. The odds ratio compares the odds of having a positive outcome among two groups separated by a one unit difference of the predictor in question, all else being the same.

Question 11.8

How can the odds ratio for Insulin be so close to 1.0 yet its p-value so low? (Hint: See Section 7.2.)

Question 11.9

Why might the coefficient and p-value for SkinThickness change so much in the shift from unadjusted to adjusted?

11.3 Feature Selection

The process of feature selection is largely about eliminating redundancies and useless predictors in an effort to come up with the most parsimonious model possible. In many cases, it is also about increasing the accuracy of model interpretation. There are three basic approaches to feature selection: filters, wrappers, and embedded methods.

11.3.1 Filters

Filter methods select subsets of variables as a preprocessing step, *independently of the chosen model*. These methods use **proxy measures** to rank variables; the proxy measure is often chosen to be computationally fast so that large numbers of features can be sifted through quickly.

A predetermined threshold of the proxy measure is usually used to determine which features pass to the multivariate modeling stage. Alternatively, the modeler may decide on a fixed number of features to include. Some examples of filter methods include:

- Any kind of univariate model (e.g. univariate logistic or linear regression)
- Any kind of hypothesis test (e.g. t-test, chi-squared test; see Chapter 8)
- Any kind of correlation coefficient (e.g. Pearson, Spearman)

- Mutual information[4]

$$MI(X_i, Y) = \sum_x \sum_y P(X_i = x, Y = y) \log \frac{P(X_i = x, Y = y)}{P(X_i = x)P(Y = y)}$$

- Variance thresholding (simply remove features with low variance)

Question 11.10

If you wanted to use the univariate logistic regression models above in Section 11.2.3 as a filter for a downstream model (potentially not even multivariate logistic regression - it could be a decision tree, etc.), how would you rank them and how would you decide on an appropriate cutoff?

Question 11.11

How would you apply a filter-based selection method in a case where you had dozens of different predictors of different types (e.g. some categorical, some binary, some numeric)?

Question 11.12

How might you choose the appropriate threshold for a filter-based method in a data-driven way?

Question 11.13

What is problematic about testing each potential feature, one at a time?

11.3.2 Wrappers

Wrapper methods use a search algorithm to traverse the space of possible features, evaluating each subset by running the chosen model using that subset. They are generally computationally intensive (e.g., imagine trying to

[4]The mutual information, in another format, is the most common splitting criterion used for decision trees; see Chapter 9. In the case of continuous variables, the sums are replaced by integrals.

find the optimal subset of 10,000 features, or even 50) so **heuristics** generally have to be used to pare down the search space. Some examples of wrapper methods include:

- **Exhaustive search.** Try all possible subsets of features. If there are m features, this means trying 2^m possible subsets.
- **Forward selection.** Start with a baseline (e.g., intercept only) model. Add in each of m possible predictors individually and take the best one based on some performance criterion. Repeat, adding one predictor at each step, until the performance criterion stops getting better or you run out of predictors.
- **Backward elimination.** Start with a complete model (all predictors included). Try removing each predictor and take the one whose removal causes the performance criterion to increase the most. Repeat, removing one predictor at each step, until the performance criterion stops getting better or you are left with no predictors (null model).
- **Forward-backward selection.** A combination of forward selection and backward elimination.
- **Simulated annealing.** Add or remove predictors with some probability depending on how well the model is doing. At each stage, if the new model is better, accept it; it becomes the new baseline. If the new model is worse, accept it with some probability, p, that decreases over time according to a "cooling schedule". This helps prevent the variable selection process from getting stuck in local optima.

Question 11.14

Why is exhaustive search problematic for almost any reasonably sized m?

Question 11.15

Here is the output of forward selection for the Pima example, using R's *MASS* package and the **Akaike Information Criterion (AIC)** as the model performance metric.

```
Start:  AIC=995.48
```

```
Outcome ~ 1
                          Df Deviance    AIC
+ Glucose                  1   808.72 812.72
+ BMI                      1   920.71 924.71
+ Age                      1   950.72 954.72
+ Pregnancies              1   956.21 960.21
+ DiabetesPedigreeFunction 1   970.86 974.86
+ Insulin                  1   980.81 984.81
+ SkinThickness            1   989.19 993.19
+ BloodPressure            1   990.13 994.13
<none>                         993.48 995.48

Step:  AIC=812.72
Outcome ~ Glucose

                          Df Deviance    AIC
+ BMI                      1   771.40 777.40
+ Pregnancies              1   784.95 790.95
+ DiabetesPedigreeFunction 1   796.99 802.99
+ Age                      1   797.36 803.36
<none>                         808.72 812.72
+ SkinThickness            1   807.07 813.07
+ Insulin                  1   807.77 813.77
+ BloodPressure            1   808.59 814.59

Step:  AIC=777.4
Outcome ~ Glucose + BMI

                          Df Deviance    AIC
+ Pregnancies              1   744.12 752.12
+ Age                      1   755.68 763.68
+ DiabetesPedigreeFunction 1   762.87 770.87
+ Insulin                  1   767.79 775.79
+ BloodPressure            1   769.07 777.07
<none>                         771.40 777.40
+ SkinThickness            1   770.20 778.20

Step:  AIC=752.12
Outcome ~ Glucose + BMI + Pregnancies

                          Df Deviance    AIC
+ DiabetesPedigreeFunction 1   734.31 744.31
+ BloodPressure            1   738.43 748.43
+ Age                      1   742.10 752.10
```

```
<none>                          744.12 752.12
+ Insulin                  1    742.43 752.43
+ SkinThickness            1    743.60 753.60

Step:  AIC=744.31
Outcome ~ Glucose + BMI + Pregnancies +
          DiabetesPedigreeFunction

               Df Deviance    AIC
+ BloodPressure  1   728.56 740.56
+ Insulin        1   731.51 743.51
<none>               734.31 744.31
+ Age            1   732.51 744.51
+ SkinThickness  1   733.06 745.06

Step:  AIC=740.56
Outcome ~ Glucose + BMI + Pregnancies +
          DiabetesPedigreeFunction +
          BloodPressure

               Df Deviance    AIC
+ Age            1   725.46 739.46
+ Insulin        1   725.97 739.97
<none>               728.56 740.56
+ SkinThickness  1   728.00 742.00

Step:  AIC=739.46
Outcome ~ Glucose + BMI + Pregnancies +
          DiabetesPedigreeFunction +
          BloodPressure + Age

               Df Deviance    AIC
+ Insulin        1   723.45 739.45
<none>               725.46 739.46
+ SkinThickness  1   725.19 741.19

Step:  AIC=739.45
Outcome ~ Glucose + BMI + Pregnancies +
          DiabetesPedigreeFunction +
          BloodPressure + Age + Insulin

               Df Deviance    AIC
<none>               723.45 739.45
+ SkinThickness  1   723.45 741.45
```

What does the final model look like? Which predictor is missing from the final model? Note: AIC is an estimate of out-of-sample prediction error and depends on the likelihood; thus it does not work for models that do not calculate some form of likelihood.

Question 11.16

Here is the output of backward selection for the Pima example, again using R's *MASS* package and AIC as the model performance metric.

```
Start:  AIC=741.45
Outcome ~ Pregnancies + Glucose + BloodPressure + SkinThickness +
    Insulin + BMI + DiabetesPedigreeFunction + Age

                          Df Deviance    AIC
- SkinThickness            1   723.45 739.45
- Insulin                  1   725.19 741.19
<none>                         723.45 741.45
- Age                      1   725.97 741.97
- BloodPressure            1   729.99 745.99
- DiabetesPedigreeFunction 1   733.78 749.78
- Pregnancies              1   738.68 754.68
- BMI                      1   764.22 780.22
- Glucose                  1   838.37 854.37

Step:  AIC=739.45
Outcome ~ Pregnancies + Glucose + BloodPressure + Insulin + BMI +
    DiabetesPedigreeFunction + Age

                          Df Deviance    AIC
<none>                         723.45 739.45
- Insulin                  1   725.46 739.46
- Age                      1   725.97 739.97
- BloodPressure            1   730.13 744.13
- DiabetesPedigreeFunction 1   733.92 747.92
- Pregnancies              1   738.69 752.69
- BMI                      1   768.77 782.77
- Glucose                  1   840.87 854.87
```

What does the final model look like? How does it compare to the model obtained through forward selection?

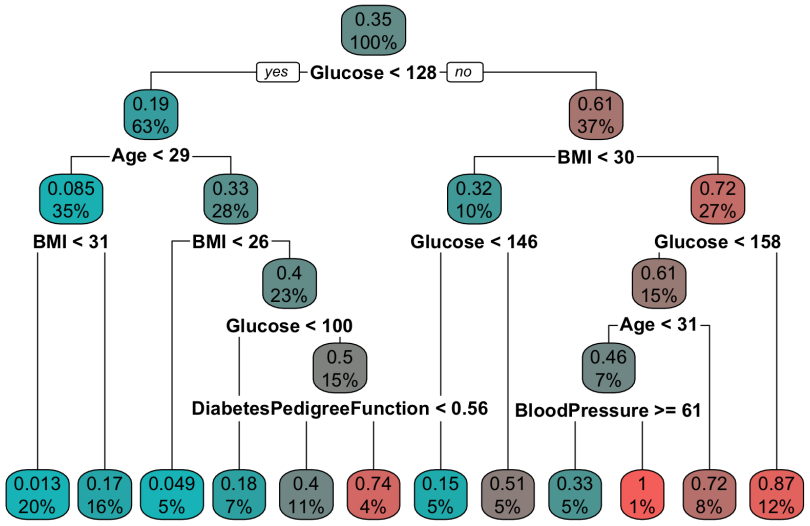
11.3.3 Embedded Methods

Embedded methods perform feature selection during the process of model training. They are usually specific to a particular type of model.

One example of an embedded method is a decision tree (see Chapter 9), which implicitly performs feature selection by placing the most informative predictors at the top of the tree and ignoring those that are unassociated with the outcome.

Question 11.17

Here is the decision tree produced by CART, using information gain/mutual information as the splitting criterion as usual:



Which features were selected for this tree and which were ignored? How were the features transformed from their original forms in the dataset?

Another example of an embedded method is **regularization**. The easiest way to understand regularization is through our discussion of maximum likelihood estimation for GLMs in Chapter 6. The goal of maximum likelihood

estimation is to find the set of model coefficients, βs, that maximize the joint probability (likelihood) of our observed data given the model. The trouble with this is that more complex models, with more parameters, will generally fit the data better: i.e. produce a higher likelihood.

Regularization addresses this by introducing a penalty term on the likelihood that is proportional to the size of the parameters. In L_1 regularization, a.k.a. **Lasso**, the penalty term is proportional to the absolute values of the coefficients. It looks like this:

$$\lambda \sum_{j=1}^{p} |\beta_j|$$

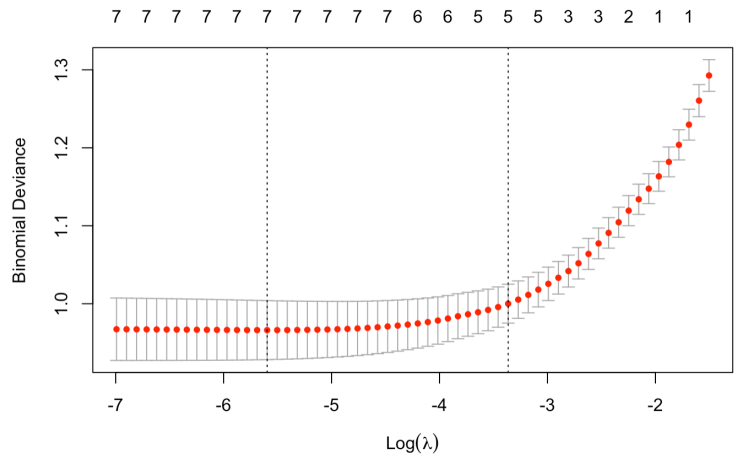
where p is the number of predictors. This creates a tradeoff in the model between the likelihood and the number of parameters. During optimization, the model will set the coefficients on predictors to zero if including those predictors does not sufficiently improve the likelihood. The relative importance of the penalty term and likelihood is adjusted using the parameter λ. We will see regularized regression methods in much greater detail in Chapter 12.

Question 11.18

Here is the raw model output from the multivariate logistic regression model that includes all eight predictors:

```
Call:
glm(formula = Outcome ~ . - LogDiabetesPedigreeFunction, family = "binomial",
    data = d)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-2.5566  -0.7274  -0.4159   0.7267   2.9297

Coefficients:
                           Estimate Std. Error z value Pr(>|z|)
(Intercept)              -8.4046964  0.7166359 -11.728  < 2e-16 ***
Pregnancies               0.1231823  0.0320776   3.840 0.000123 ***
Glucose                   0.0351637  0.0037087   9.481  < 2e-16 ***
BloodPressure            -0.0132955  0.0052336  -2.540 0.011072 *
SkinThickness             0.0006190  0.0068994   0.090 0.928515
Insulin                  -0.0011917  0.0009012  -1.322 0.186065
BMI                       0.0897010  0.0150876   5.945 2.76e-09 ***
DiabetesPedigreeFunction  0.9451797  0.2991475   3.160 0.001580 **
Age                       0.0148690  0.0093348   1.593 0.111192
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 993.48  on 767  degrees of freedom
Residual deviance: 723.45  on 759  degrees of freedom
AIC: 741.45

Number of Fisher Scoring iterations: 5
```

Now let's consider what happens when we use a L_1 regularized logistic regression model, produced using the R package *glmnet*. Here is what happens to the model's error (assessed using 10-fold cross validation; measured using a metric called **binomial deviance**) when we vary λ:




```
Measure: Binomial Deviance

      Lambda Measure      SE Nonzero
min 0.004468  0.9686 0.02647       7
1se 0.028723  0.9922 0.02118       5
```

We choose λ to be equal to the value that produces the minimum deviance. Here are the coefficients of the final model:

```
9 x 1 sparse Matrix of class "dgCMatrix"
                                      1
(Intercept)               -8.048785391
Pregnancies                0.115632123
Glucose                    0.033559189
BloodPressure             -0.010901115
SkinThickness              .
Insulin                   -0.000837989
BMI                        0.083305233
DiabetesPedigreeFunction   0.847558021
Age                        0.013503422
```

Compare this output to the results of models obtained through forward and backward selection methods, as well as to the full (unregularized) logistic regression model. What are the advantages and disadvantages of the regularization approach vs. wrappers and filters?

Chapter 12

Lasso, Ridge, and Elastic Net
DRAFT

Sometimes when building regression models, you run into issues like the following:

- You have more predictors, p, than you have samples, n.
- Your predictors are highly correlated.

Both of these conditions can lead to models that are highly unstable. Maybe they fit your training data well, but if you change your training set even a tiny bit, the coefficients shift wildly. It becomes very hard to trust the coefficient values under these circumstances. One way to combat this is to introduce a **penalty** on the values of the coefficients. There are different types of penalty (see slides) that do different things. Relevant terms include: **ridge regression**, **Lasso**, and **elastic net**.

Chapter 13

Random Forests DRAFT

A random forest is just a collection (or **ensemble**) of decision trees whose "votes" are uncorrelated. The trees vote to produce a final prediction.

Two details are important to the construction of random forests:

1. Each tree is built using a subset of training examples sampled with replacement from the original training set. This is called **bagging** (bootstrap aggregating). Typically around 2/3 of training examples are used per tree. Note that bagging is a general-purpose procedure that can be used for other models besides random forests.

2. For each split, the tree considers not all m predictor variables, but only a randomly-chosen subset, usually of size approximately $\sqrt{m}$ (for classification problems) or $m/3$ (for regression problems). This keeps you from building the same tree over and over again and ensures that the votes from different trees are uncorrelated.

Here are two bagged samples of size 6 from the dataset in Table **??**.

ID	friends (X_1)	money (X_2)	free time (X_3)	happy (Y)
5	1	0	0	0
4	0	0	0	0
2	1	1	1	0
10	1	0	0	1
8	1	0	1	1
10	1	0	0	1

ID	friends (X_1)	money (X_2)	free time (X_3)	happy (Y)
5	1	0	0	0
6	0	0	0	0
2	1	1	1	0
5	1	0	0	0
9	0	0	1	1
7	1	2	1	1

Question 3.11: Use a random forest to fit the data from the low birth-weight example used in the logistic regression model, above. Use the following commands exactly as shown to ensure it all runs smoothly and you can view the output:

```
library(randomForest)
d <- read.delim("../data/logistic-lowbwt-data.tsv")
d$RACE <- as.factor(d$RACE)   # <- ensure RACE coded as factor
d$LOW <- as.factor(d$LOW)     # <- ensure LOW coded as factor
r <- randomForest(LOW ~ AGE + LWT + RACE + SMOKE + PTL + HT + UI + FTV, data = d, ntree = 100, do.trace = TRUE)
plot(r)
```

The random forest will report a number called the **out-of-bag (OOB)** error as it runs. To calculate OOB error, the trees are allowed to vote on the points that were *not* used in their construction. This provides an ongoing estimate of the generalization error of the algorithm, so you can see if adding more trees is likely to help.

What is the (approximate) overall OOB error? What is it for the positive outcome class only? The negative outcome class only?

Chapter 14

Boosting DRAFT

Each decision tree within a random forest provides a full model of some subset of the training data. The trees are fully grown and have low bias - most of their generalization error comes from their high variance (they overfit to details of their individual training sets). Averaging the votes from the different trees reduces this variance and increases accuracy.

There is also a different approach, called **boosting**, that uses an ensemble of *biased* learners. As more learners are added, the importance of datapoints that have been previously misclassified is upweighted so that subsequent learners will "focus on" those points. Averaging the votes from the different classifiers reduces the overall bias and increases accuracy in a way distinct from bagging/random forests.

14.0.1 AdaBoost

The first boosting algorithm was called **AdaBoost**, which is what we will look at today. Assume we have a training set

$$\{(x^{(1)}, y^{(1)}), \ldots, (x^{(n)}, y^{(n)})\}.$$

We will start by assuming a binary outcome, $Y \in \{1, -1\}$. The $x^{(i)}$ are feature vectors of length p. Assume we have p total classifiers (for example, one classifier based on each feature in your training data).

1. Initialize the observation weights to $w_i = \frac{1}{N}$ for $i = 1, \ldots, N$.
2. For $m = 1, \ldots, M$:
   (a) Calculate the weighted errors of the available classifiers using the current training weights, w_i. Select the classifier $G_m(x)$ that minimizes the weighted training error.
   (b) Compute
   $$\text{err}_m = \frac{\sum_{i=1}^{N} w_i \cdot \mathcal{I}(y^{(i)} \neq G_m(x^{(i)}))}{\sum_{i=1}^{N} w_i}$$
   (c) Compute voting weight for classifier m:
   $$\alpha_m = \log\left(\frac{1 - \text{err}_m}{\text{err}_m}\right)$$
   (d) Set
   $$w_i := w_i \cdot \exp\left[\alpha_m \cdot \mathcal{I}(y^{(i)} \neq G_m(x^{(i)}))\right]$$
   for $i = 1, \ldots, N$.
3. Output
   $$G(x) = \text{sign}\left[\sum_{m=1}^{M} \alpha_m G_m(x)\right]$$
   .

We will now apply AdaBoost to the "happiness" example.

14.0.2 Gradient Boosting

Jerome Friedman and Leo Breiman generalized AdaBoost into a general framework called **gradient boosting**. In this framework, of which AdaBoost is a subset, there are three components:

1. A loss function to be optimized.
2. Weak learners to make predictions.
3. An additive model that adds the contributions of different weak learners to minimize the loss function.

We don't have time to get into the details of the gradient boosting framework today, but its basic advantage is that it formulates the boosting process in such a way that any differentiable loss function can be used. In addition, although classification trees or regression trees are usually the weak learners (and technically, Friedman defined "gradient boosting" as a model that uses trees as learners) the framework is general enough to encompass other types of weak learners.

Chapter 15

Missing Data DRAFT

Chapter 16

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