BIOST 546: Machine Learning for Biomedical Big Data

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Lecture 2: Linear Regression for Big Data
Spring 2017

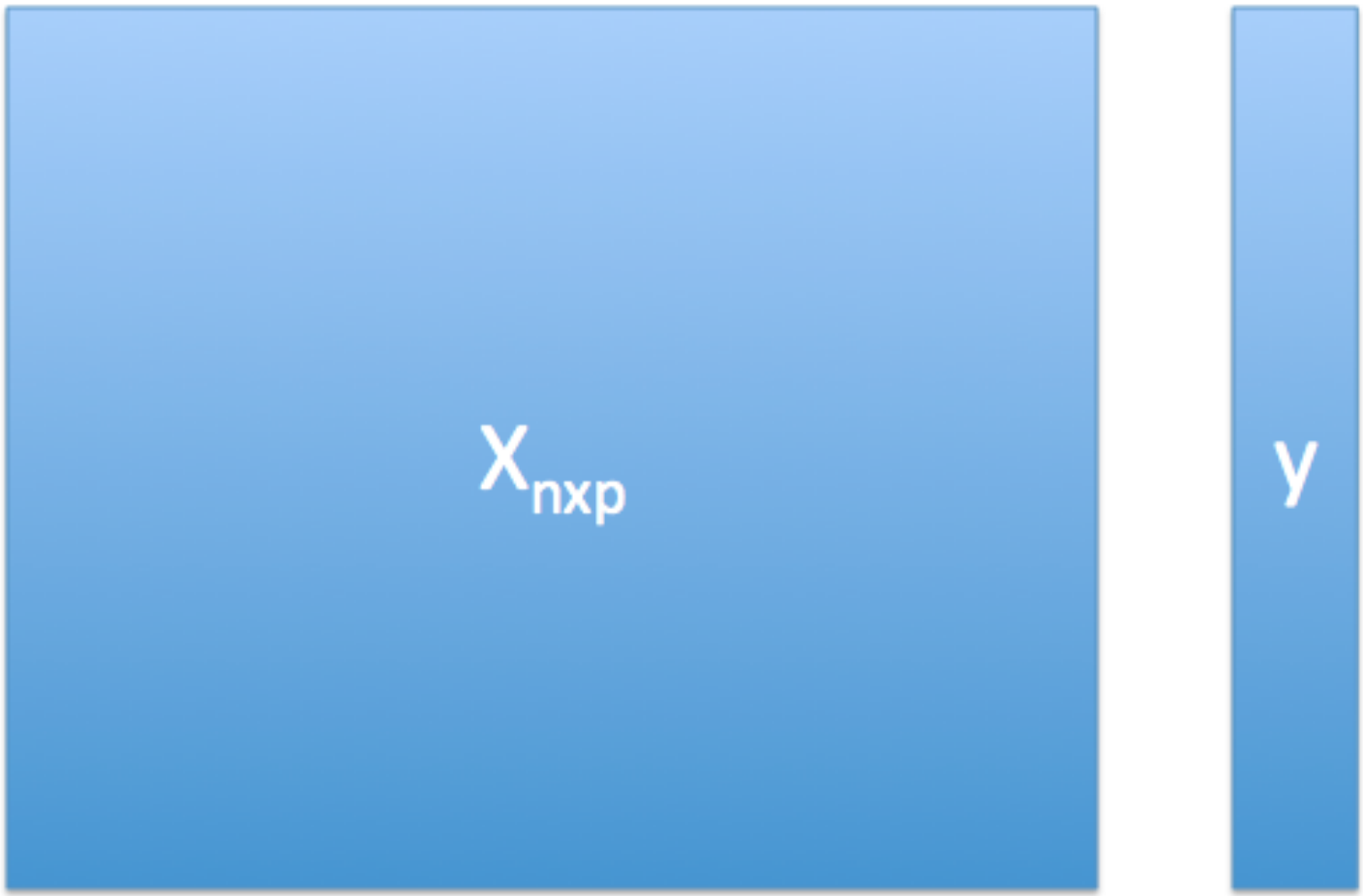
Recap

- Overview of statistical learning
- Supervised vs Unsupervised learning
- Challenges of Biomedical Big Data (briefly)

Today

- Overview of linear regression
- Overfitting
- Training and test errors
- Cross validation

Supervised Learning



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  - subtype of glioblastoma
- This lecture: Regression.

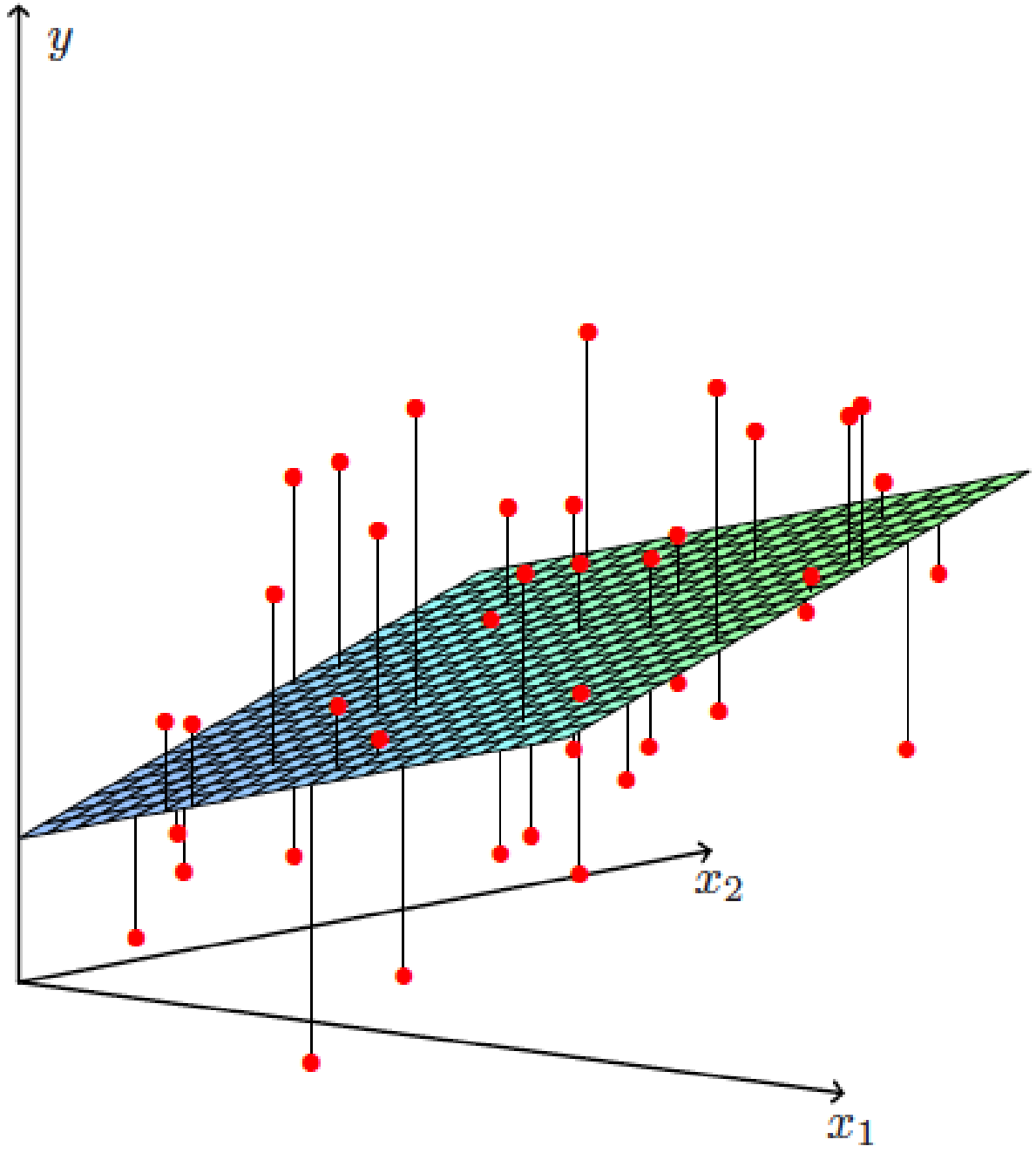
Linear Models

- We have n observations, for each of which we have p predictor measurements and a response measurement.
- Want to develop a model of the form

$$y_i = \beta_0 + \beta_1 X_{i1} + \ldots + \beta_p X_{ip} + \varepsilon_i.$$

- Here ε_i is a noise term associated with the ith observation.
- Must estimate $\beta_0, \beta_1, \ldots, \beta_p$ – i.e. we must fit the model.

Linear Model With $p = 2$ Predictors



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- This is not a linear model:

$$y_i = \beta_1^{X_{i1}} + \sin(\beta_2 X_{i2}) + \varepsilon_i.$$

Linear Models in Matrix Form

- For simplicity, ignore the intercept β_0.
  - Assume $\sum_{i=1}^{n} y_i = \sum_{i=1}^{n} X_{ij} = 0$; in this case, $\beta_0 = 0$.
  - Alternatively, let the first column of $\mathbf{X}$ be a column of 1's.
- In matrix form, we can write the linear model as

$$\mathbf{y} = \mathbf{X}\beta + \varepsilon,$$

i.e.

$$\begin{pmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{pmatrix} = \begin{pmatrix} X_{11} & X_{12} & \dots & X_{1p} \\ X_{21} & X_{22} & \dots & X_{2p} \\ \vdots & \vdots & \ddots & \vdots \\ X_{n1} & X_{n2} & \dots & X_{np} \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_2 \\ \vdots \\ \beta_p \end{pmatrix} + \begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{pmatrix}.$$

Least Squares Regression I

- There are a lot of ways we could fit the model

$$\mathbf{y} = \mathbf{X}\beta + \varepsilon.$$

- Most common approach in classical statistics is least squares:

$$\underset{\beta}{\text{minimize}} \left\{ \|\mathbf{y} - \mathbf{X}\beta\|^2 \right\}.$$

  Here $\|\mathbf{a}\|^2 \equiv \sum_{i=1}^{n} a_i^2$.

- We are looking for $\beta_1, \ldots, \beta_p$ such that

$$\sum_{i=1}^{n} (y_i - (\beta_1 X_{i1} + \ldots + \beta_p X_{ip}))^2$$

  is as small as possible.

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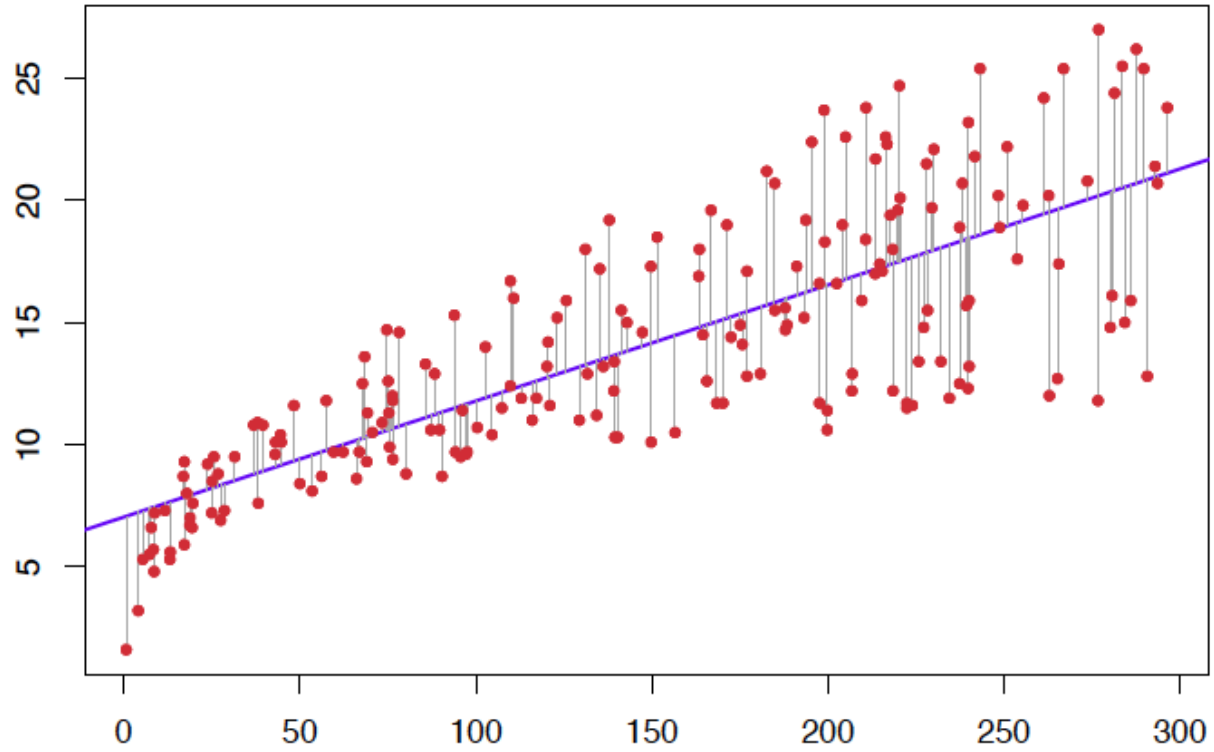
- In the last lecture we also mentioned that we want to find $\hat{f}$ such that the reducible error is minimized...
- In linear regression, we "assume" that f is linear, and so the problem reduces to finding the best combination of $\beta_1, \ldots, \beta_p$

Least Squares



- Horizontal axis: predictor
- Vertical axis: response
- Red dots: observations
- Blue line: least squares line

Blue line is positioned to minimize the sum of squared lengths of the gray lines.

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$$MSE = \frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{y}_i)^2 = \frac{1}{n}\sum_{i=1}^{n}(y_i - (\hat{\beta}_1 X_{i1} + \ldots + \hat{\beta}_p X_{ip}))^2.$$

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- Big $R^2 \Leftrightarrow$ Small Training Error.

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- When using linear regression, we assume that $f(X_1, \ldots, X_p) = X_1\beta_1 + \ldots + X_p\beta_p$
- If this assumption is true, then the least squares estimate is *unbiased*. However, even if not, then it is still useful...

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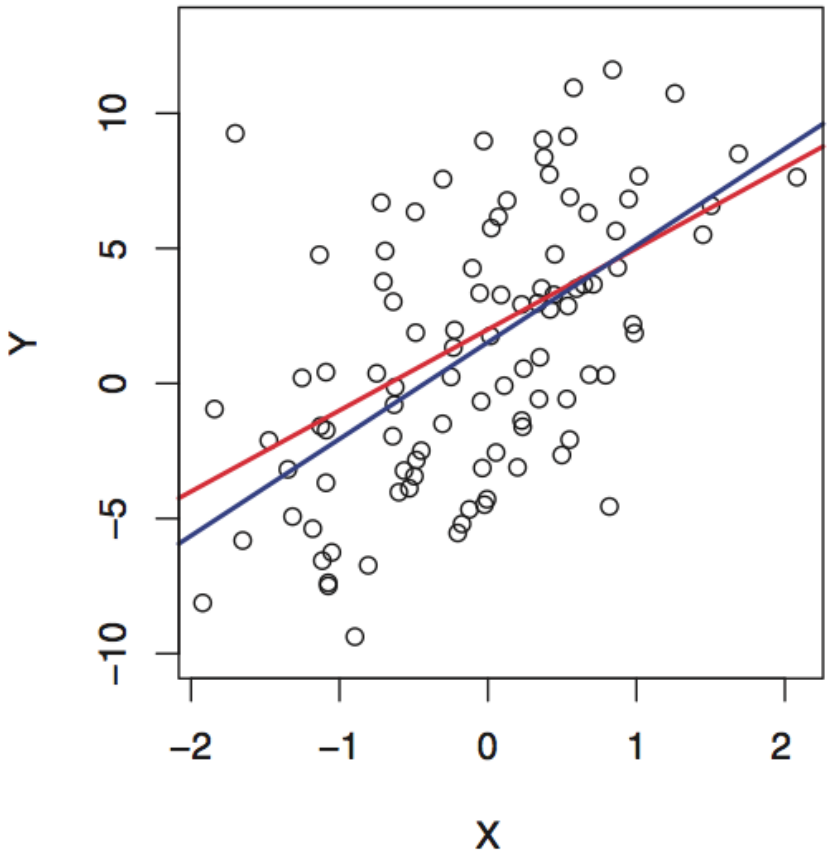

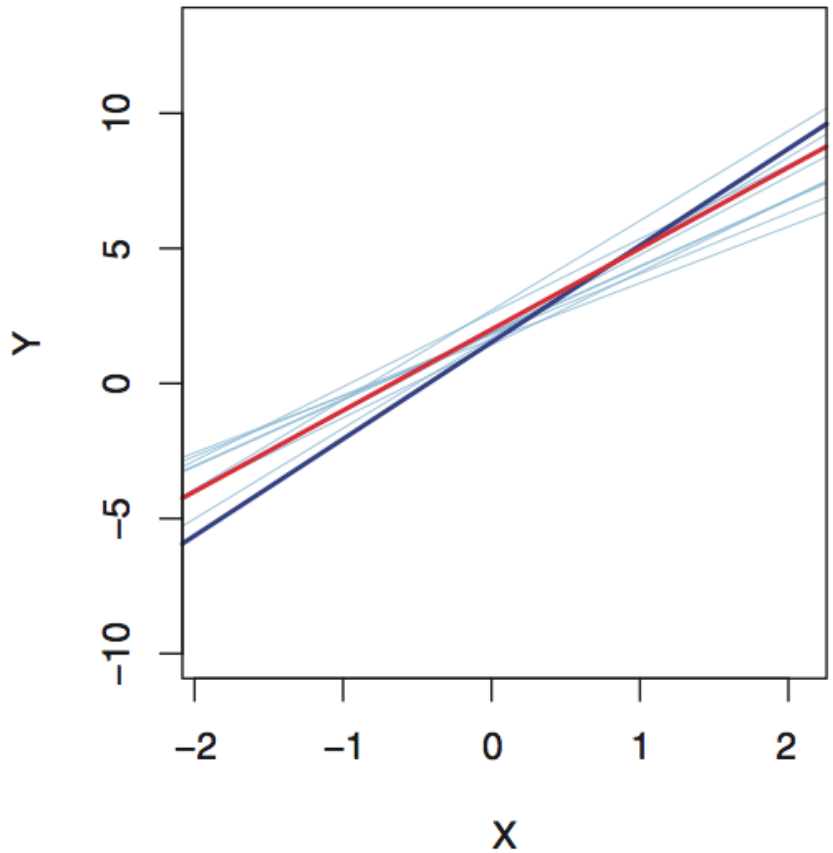

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Least Squares as More Variables are Included

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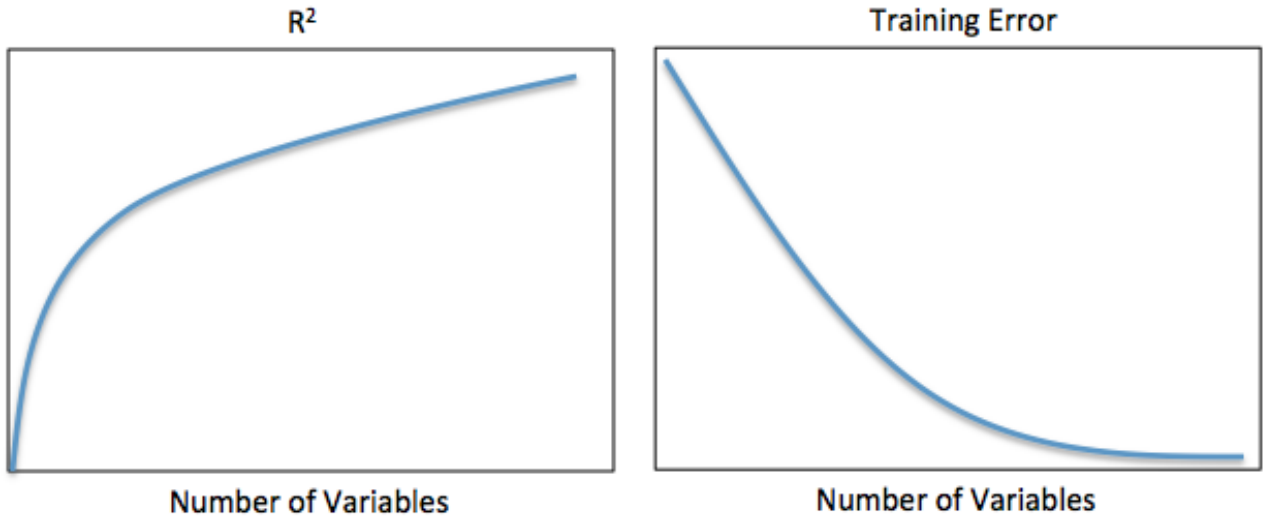
- We really care about the model's performance on test observations – observations not used to fit the model.

The Problem

As we add more variables into the model...



... the training error decreases and the R^2 increases!

Why is this a Problem?

- We really care about the model's performance on observations not used to fit the model!
  - We want a model that will predict the survival time of a new patient who walks into the clinic!
  - We want a model that can be used to diagnose cancer for a patient not used in model training!
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  - We want to predict risk of diabetes for a patient who wasn't used to fit the model!
- What we really care about:

$$(y_{test} - \hat{y}_{test})^2,$$

where

$$\hat{y}_{test} = \hat{\beta}_1 X_{test,1} + \ldots + \hat{\beta}_p X_{test,p},$$

and (X_{test}, y_{test}) was not used to train the model.

- The test error is the average of $(y_{test} - \hat{y}_{test})^2$ over a bunch of test observations.

Training Error versus Test Error

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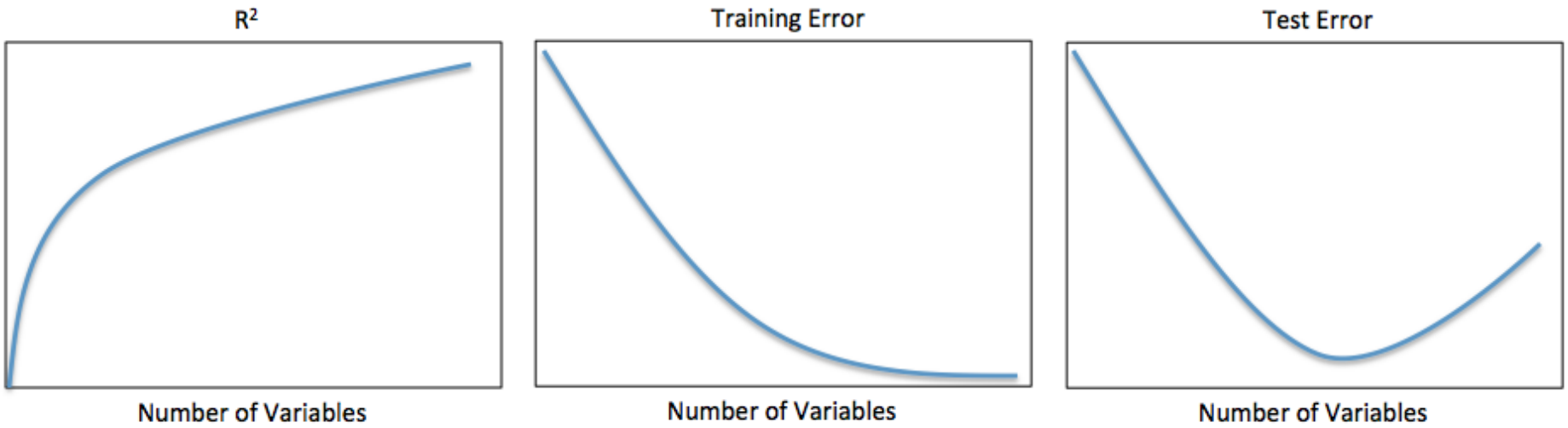

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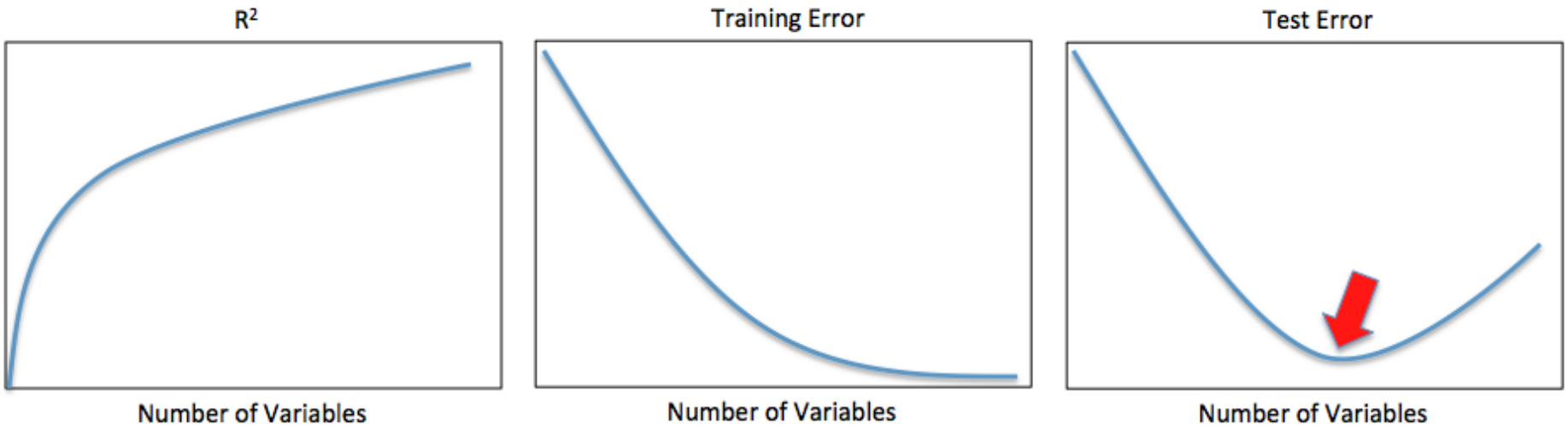

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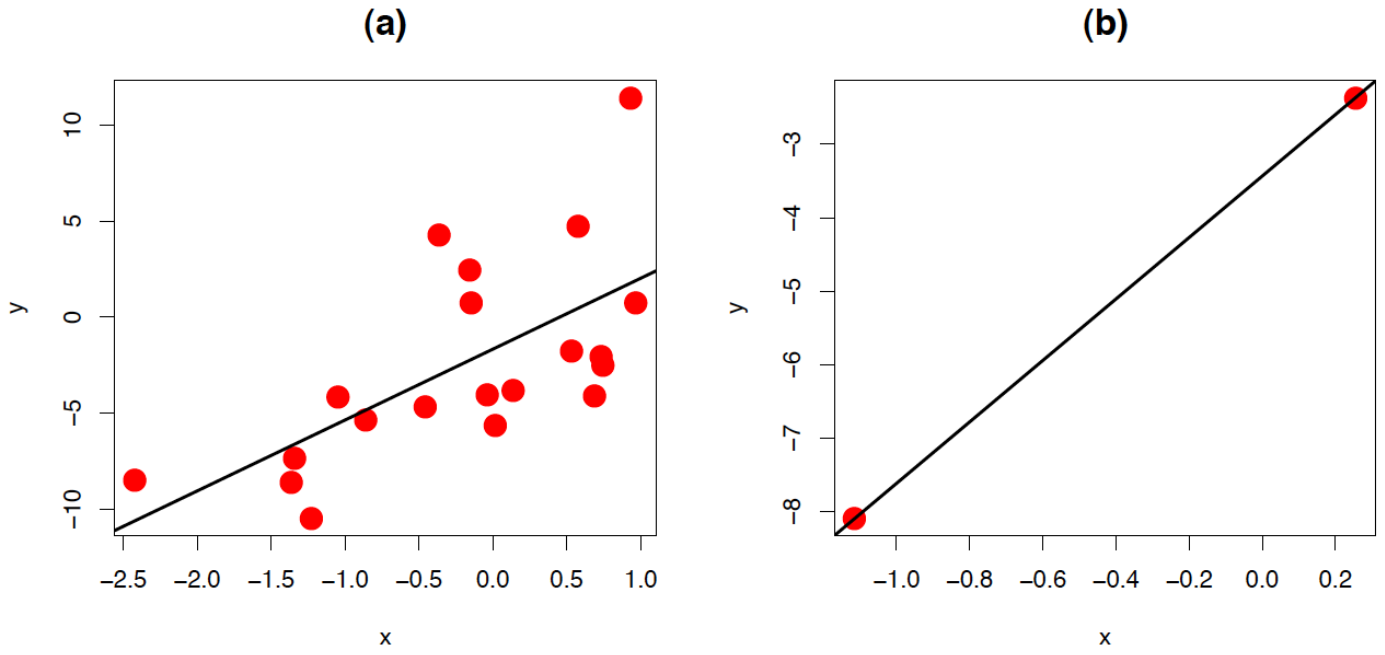
Why the Number of Variables Matters

- Linear regression will have a very low training error if p is large relative to n.
- A simple example:



- When $n \leq p$, you can always get a perfect model fit to the training data!
- But the test error will be awful.

Model Complexity, Training Error, and Test Error

- In this course, we will consider various types of models.
- We will be very concerned with model complexity: e.g. the number of variables used to fit a model.
- As we fit more complex models – e.g. models with more variables – the training error will always decrease.
- But the test error might not.
- As we will see, the number of variables in the model is not the only – or even the best – way to quantify model complexity.

An Example In R

```
xtr <- matrix(rnorm(100*100),ncol=100)
xte <- matrix(rnorm(100000*100),ncol=100)
beta <- c(rep(1,10),rep(0,90))
ytr <- xtr%*%beta + rnorm(100)
yte <- xte%*%beta + rnorm(100000)
rsq <- trainerr <- testerr <-  NULL
for(i in 2:100){
mod <- lm(ytr~xtr[,1:i])
rsq <- c(rsq,summary(mod)$r.squared)
beta <- mod$coef[-1]
intercept <- mod$coef[1]
trainerr <- c(trainerr, mean((xtr[,1:i]%*%beta+intercept - ytr)^2))
testerr <- c(testerr, mean((xte[,1:i]%*%beta+intercept - yte)^2))
}
par(mfrow=c(1,3))
plot(2:100,rsq,xlab='No of Variables',ylab="R Squared",log="y")
abline(v=10,col="red")
plot(2:100,trainerr,xlab='No of Variables',ylab="Training Error",log="y")
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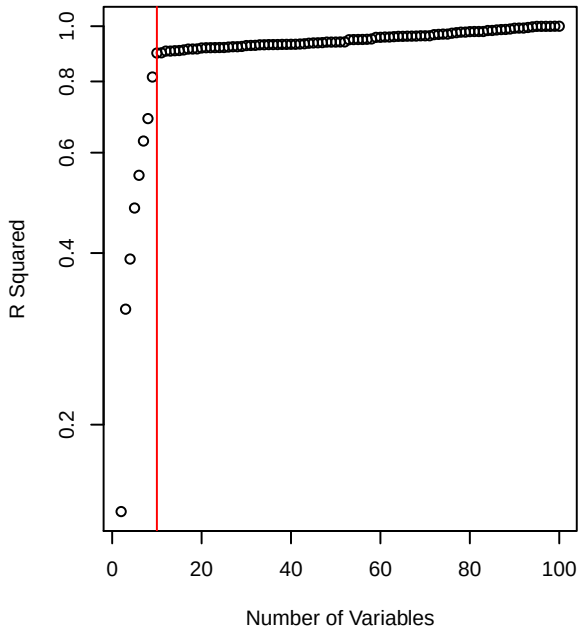
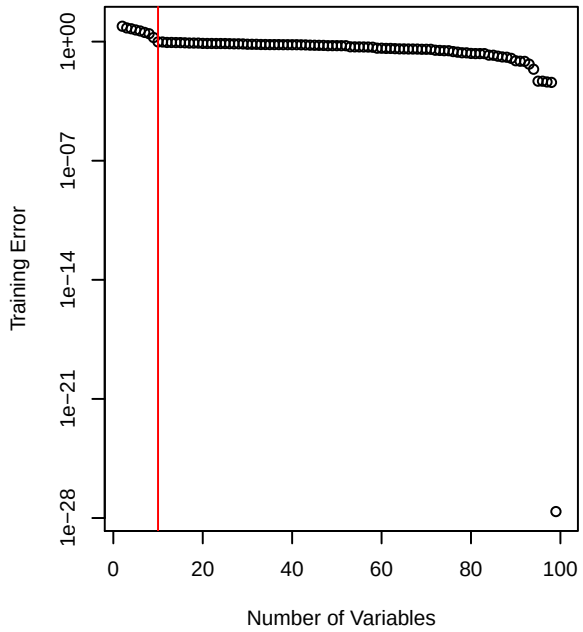
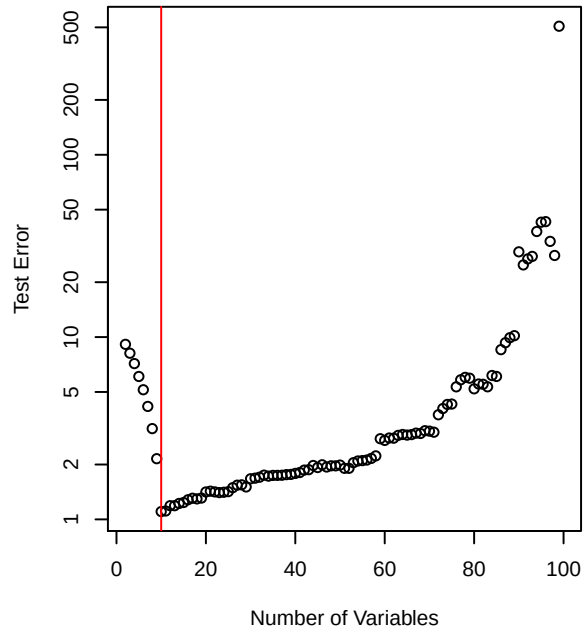
Output of R Code







- 1st 10 variables are related to response; remaining 90 are not.
- R^2 increases and training error decreases as more variables are added to the model.
- Test error is lowest when only signal variables in model.

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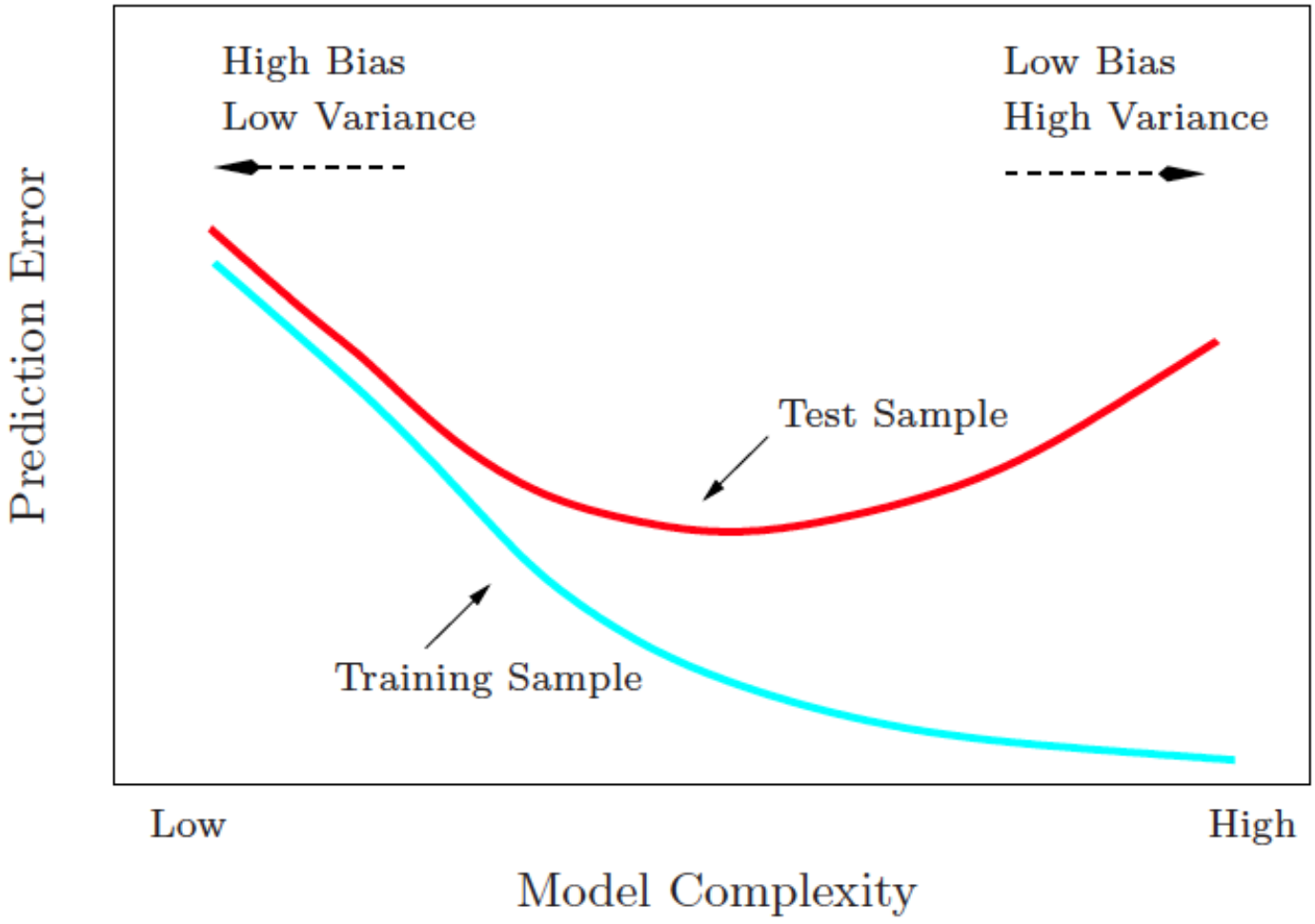
- There is a bias-variance trade-off. We want a model that is sufficiently complex as to have not too much bias, but not so complex that it has too much variance.

A Really Fundamental Picture



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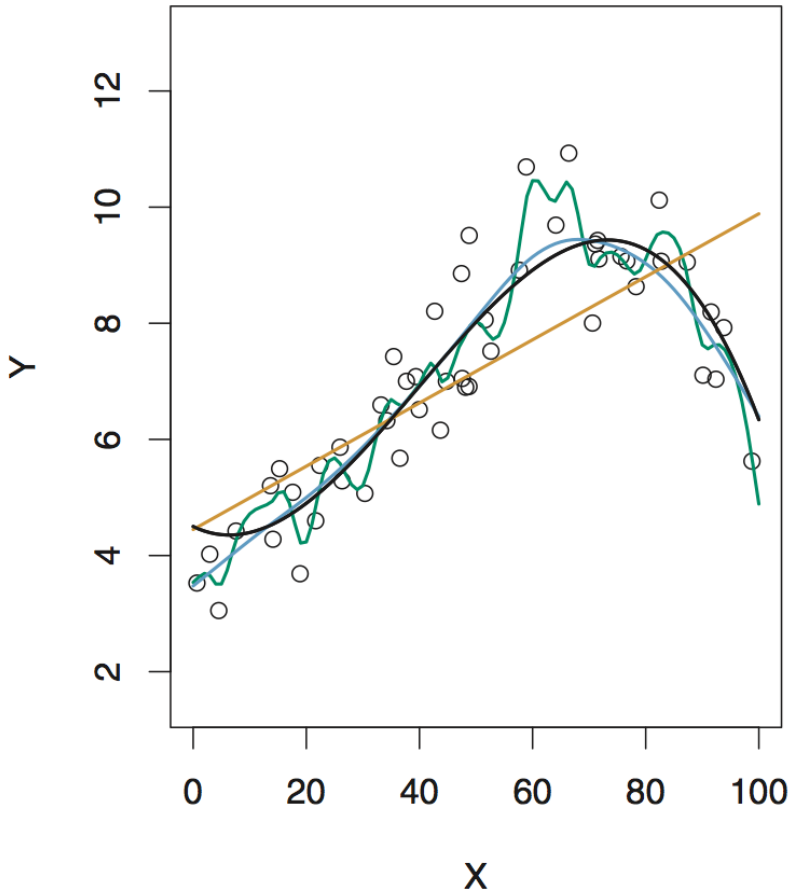

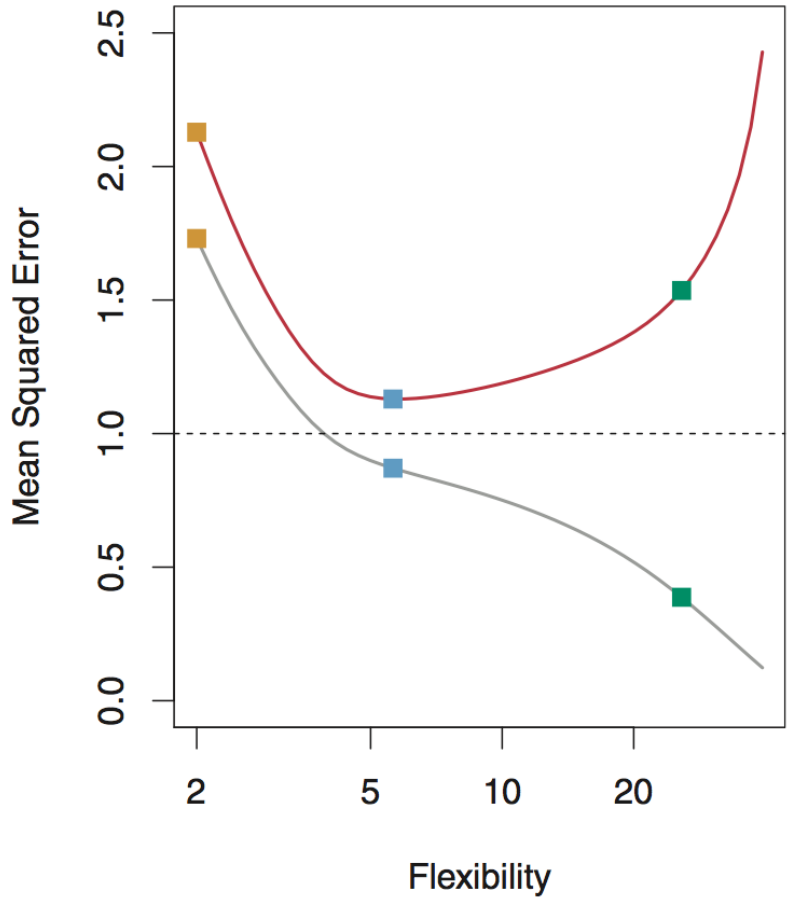

Bias-Variance Tradeoff

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- For general (non-linear) models we can define the MSE in a similar way

$$MSE = \frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{y}_i)^2 = \frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{f}(X_{i1}, \ldots, X_{ip}))^2$$

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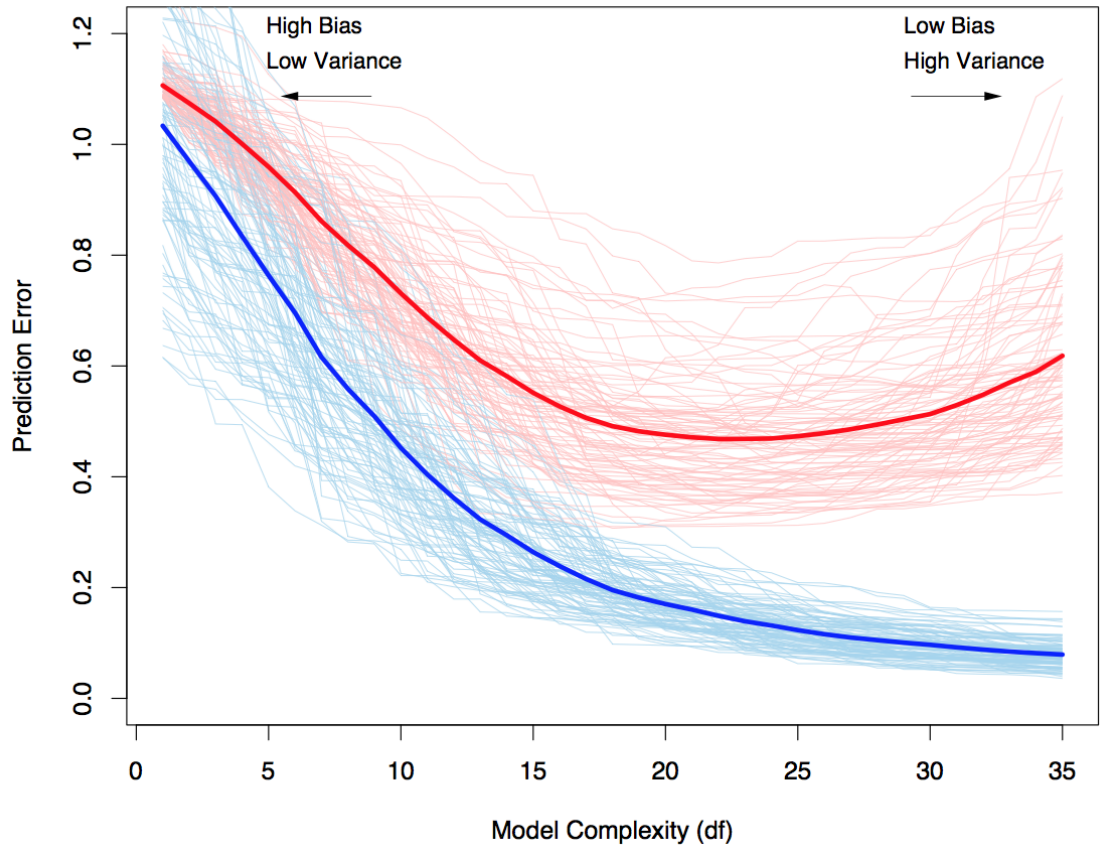

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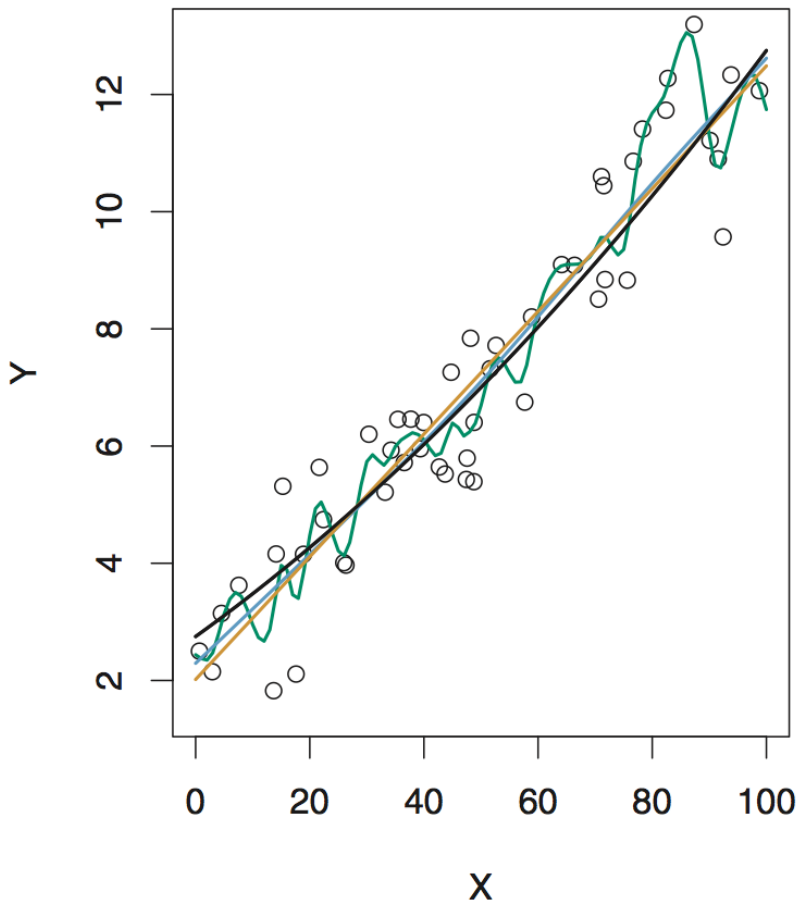

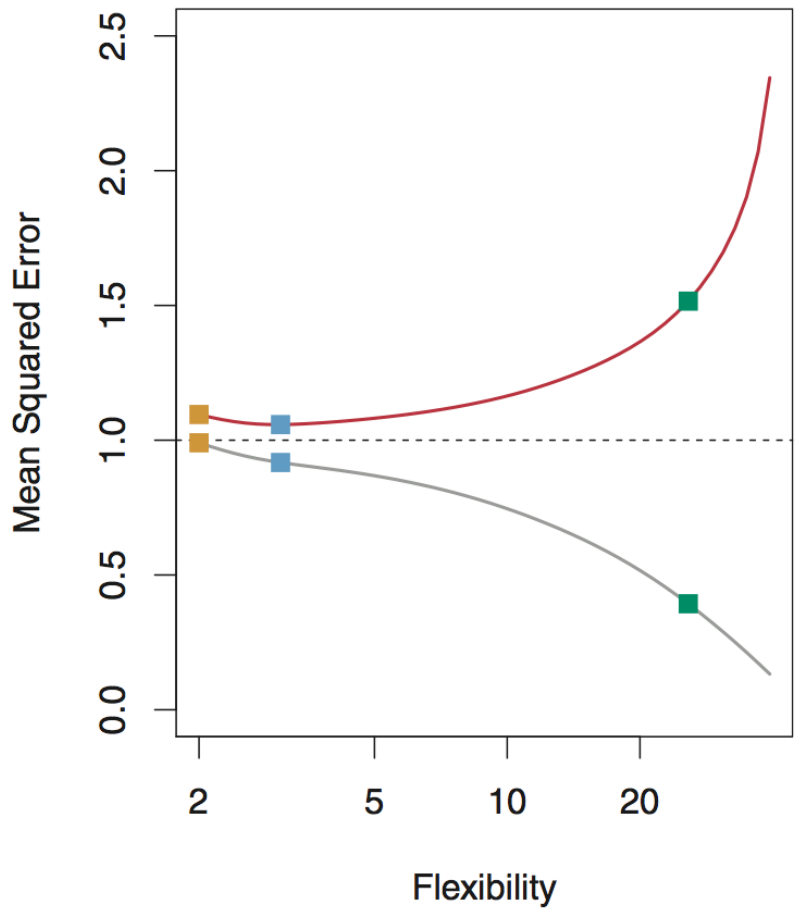

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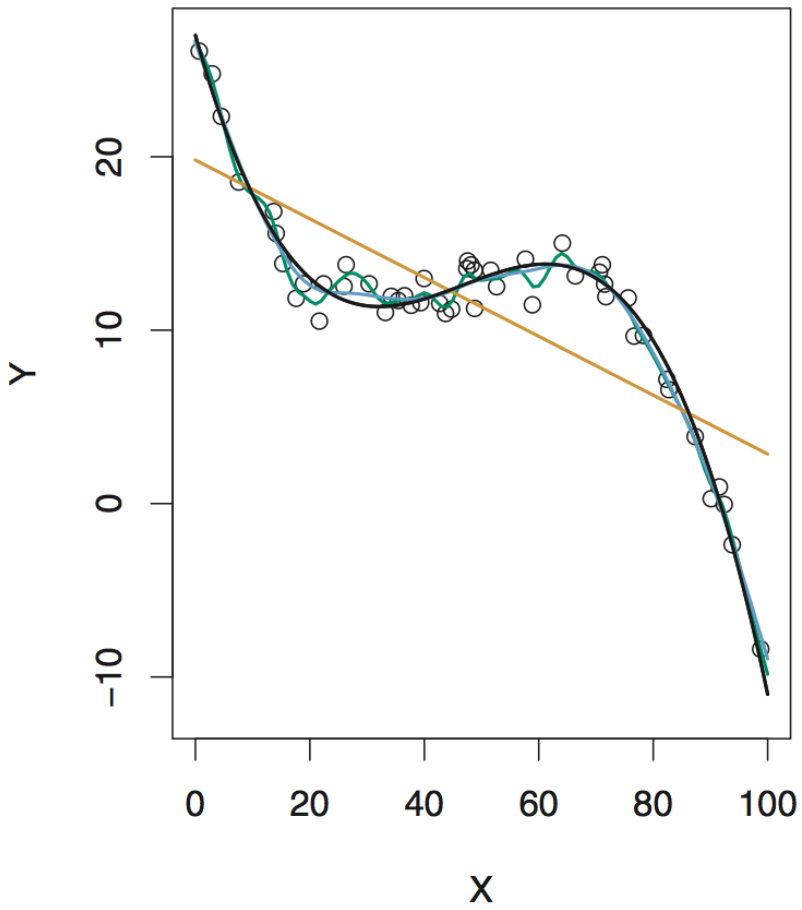

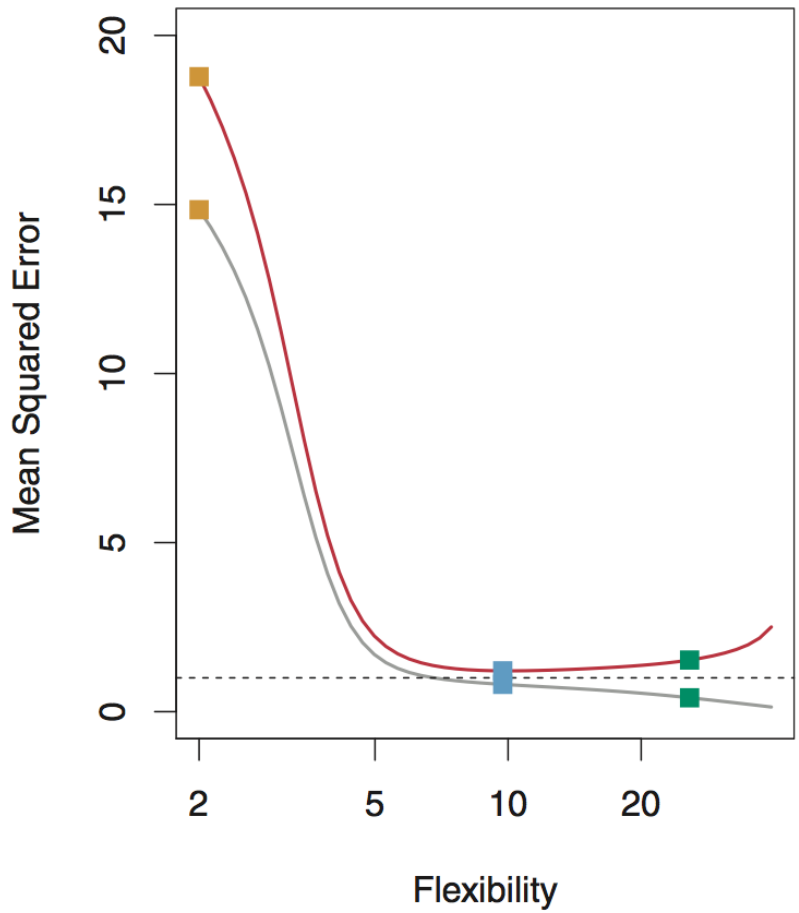

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- How can we estimate the test error?

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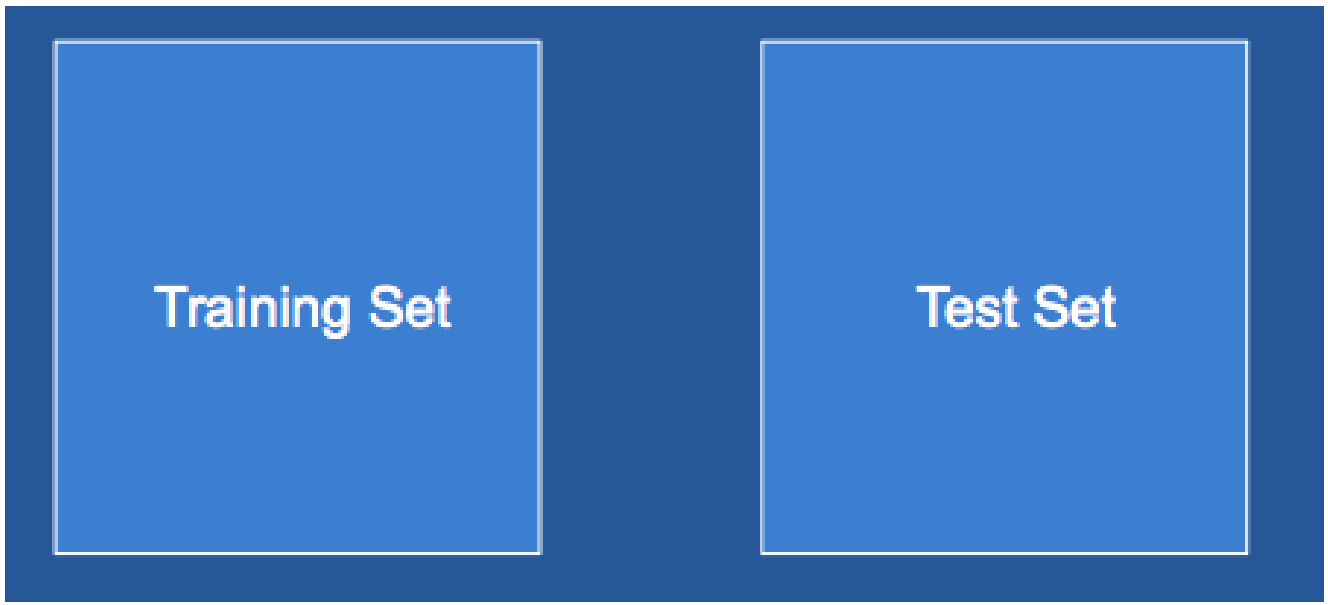

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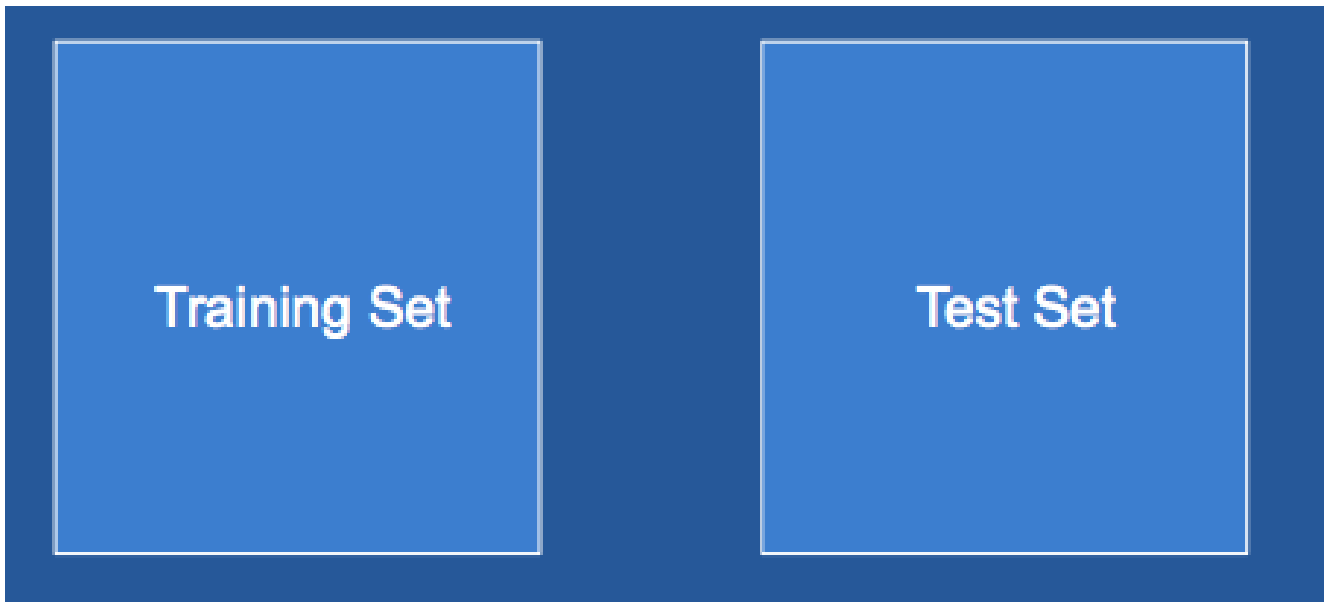

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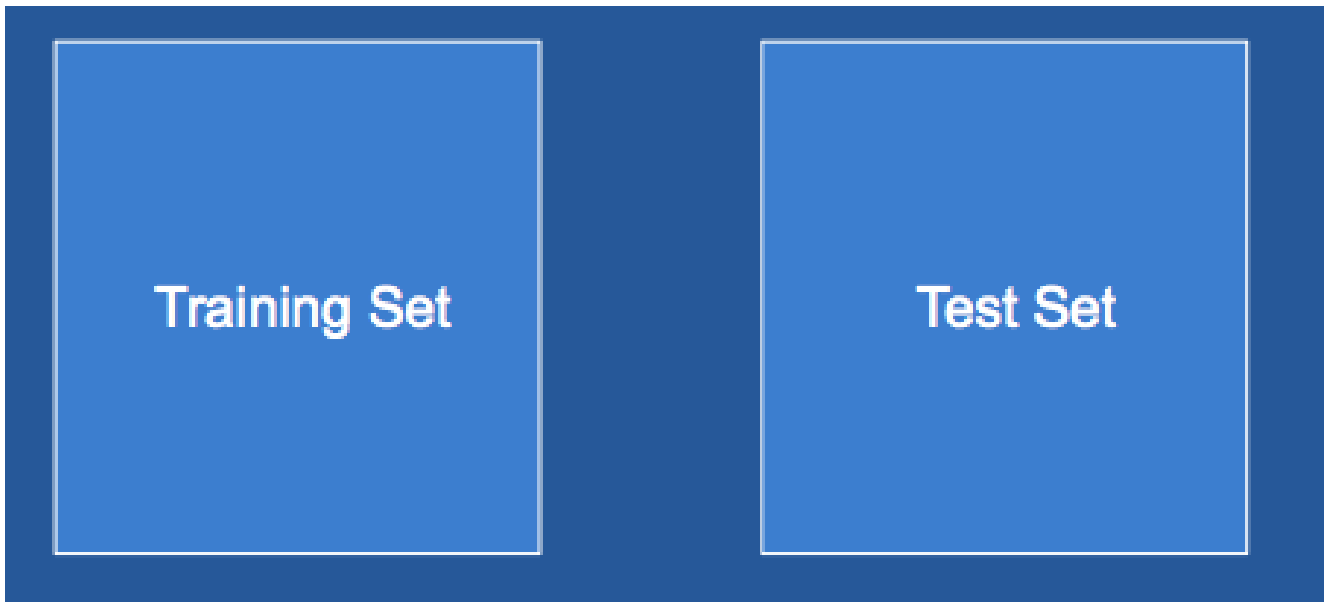

Q: Can there ever, under any circumstance, be sample overlap between the training and test sets?
A: Absolutely Not!

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You can't peek at the test set until you are completely done all aspects of model-fitting on the training set!

How to Estimate the Test Error?

To get an estimate of the test error of a particular model on a future observation:

1. Split the samples into a training set and a test set.
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But remember: no peeking!

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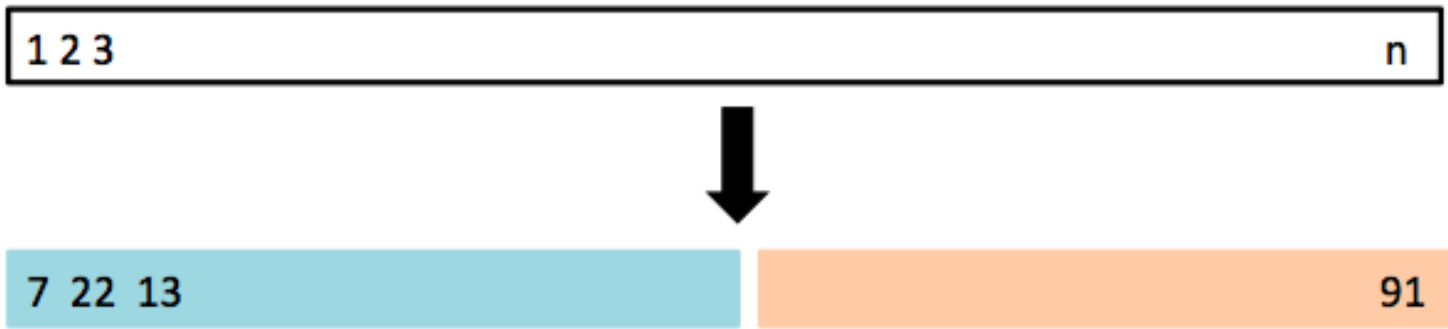
  3. K-fold cross-validation.
- In what follows, assume that we have split the data into a training set and a test set, and the training set contains n observations.

Validation Set Approach

Split the n observations into two sets of approximately equal size. Train on one set, and evaluate performance on the other.



Validation Set Approach

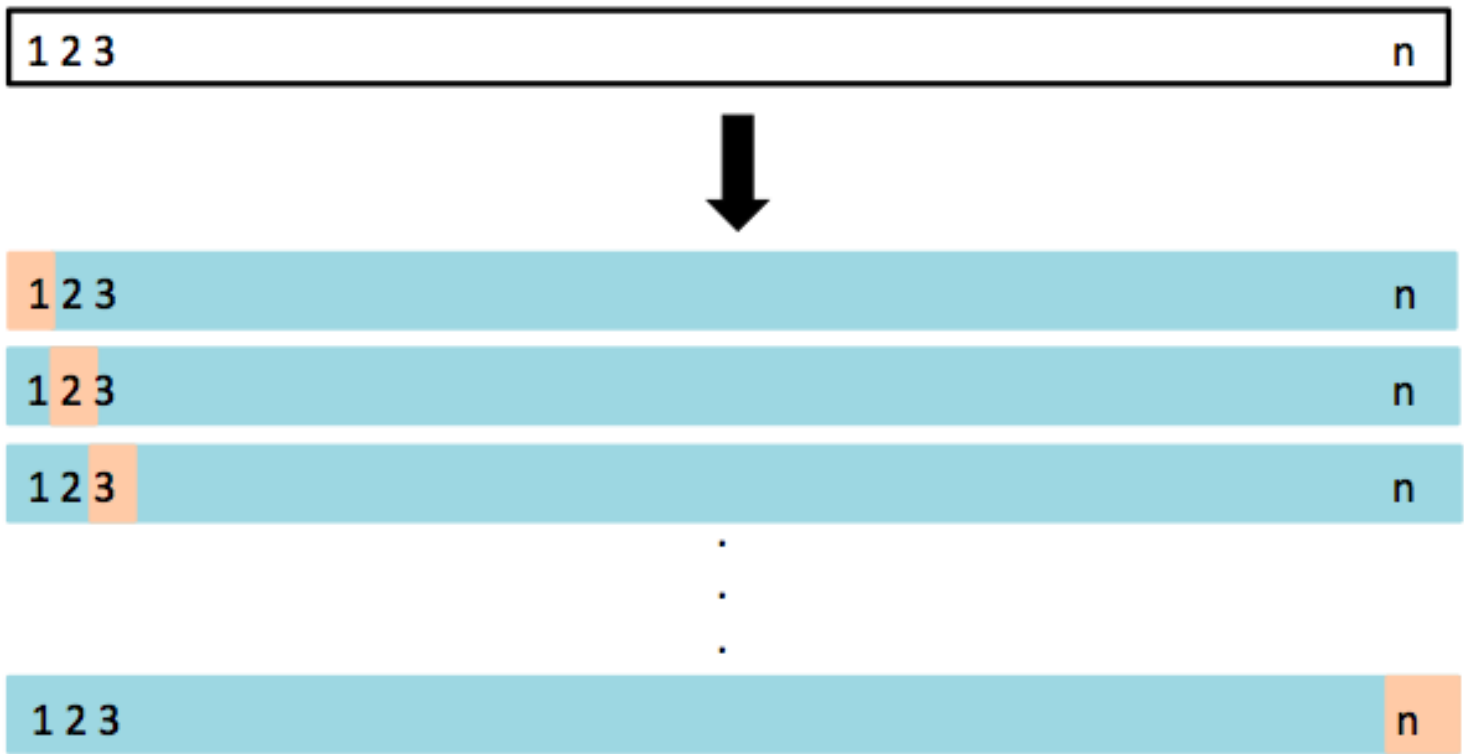
For a given model, we perform the following procedure:

1. Split the observations into two sets of approximately equal size, a training set and a validation set.
   a. Fit the model using the training observations. Let $\hat{\beta}_{(train)}$ denote the regression coefficient estimates.
   b. For each observation in the validation set, compute the error, $e_i = (y_i - \mathbf{x}_i^T \hat{\beta}_{(train)})^2$.
2. Calculate the total validation set error by summing the e_i's over all of the validation set observations.

Out of a set of candidate models, the "best" one is the one for which the total error is smallest.

Leave-One-Out Cross-Validation

Fit n models, each on $n-1$ of the observations. Evaluate each model on the left-out observation.



Leave-One-Out Cross-Validation

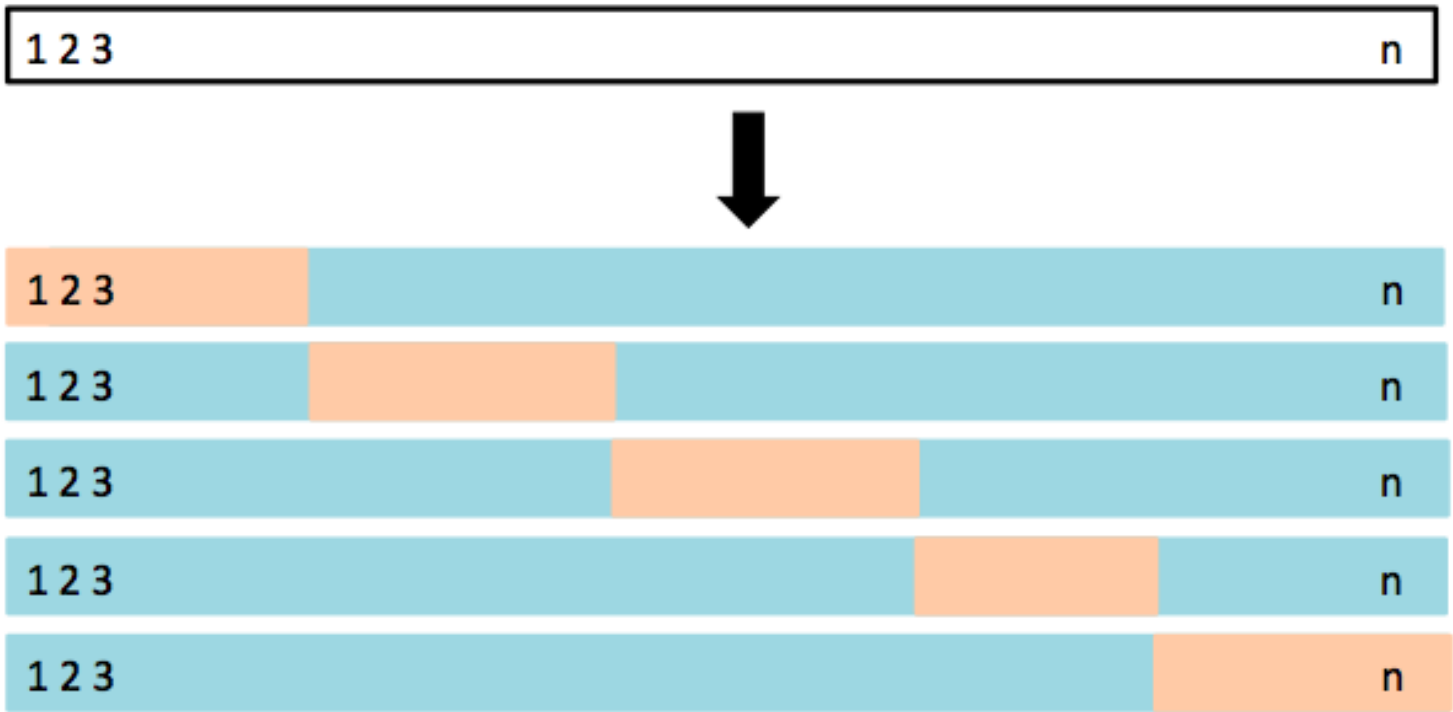
For a given model, we perform the following procedure:

1. For $i = 1, \ldots, n$:
   a. Fit the model using observations $1, \ldots, i-1, i+1, \ldots, n$. Let $\hat{\beta}_{(i)}$ denote the regression coefficient estimates.
   b. Compute the test error, $e_i = (y_i - \mathbf{x}_i^T \hat{\beta}_{(i)})^2$.
2. Calculate $\sum_{i=1}^{n} e_i$, the total CV error.

Out of a set of candidate models, the "best" one is the one for which the total error is smallest.

5-Fold Cross-Validation

Split the observations into 5 sets. Repeatedly train the model on 4 sets and evaluate its performance on the 5th.



K-fold cross-validation

A generalization of leave-one-out cross-validation. For a given model, we perform the following procedure:

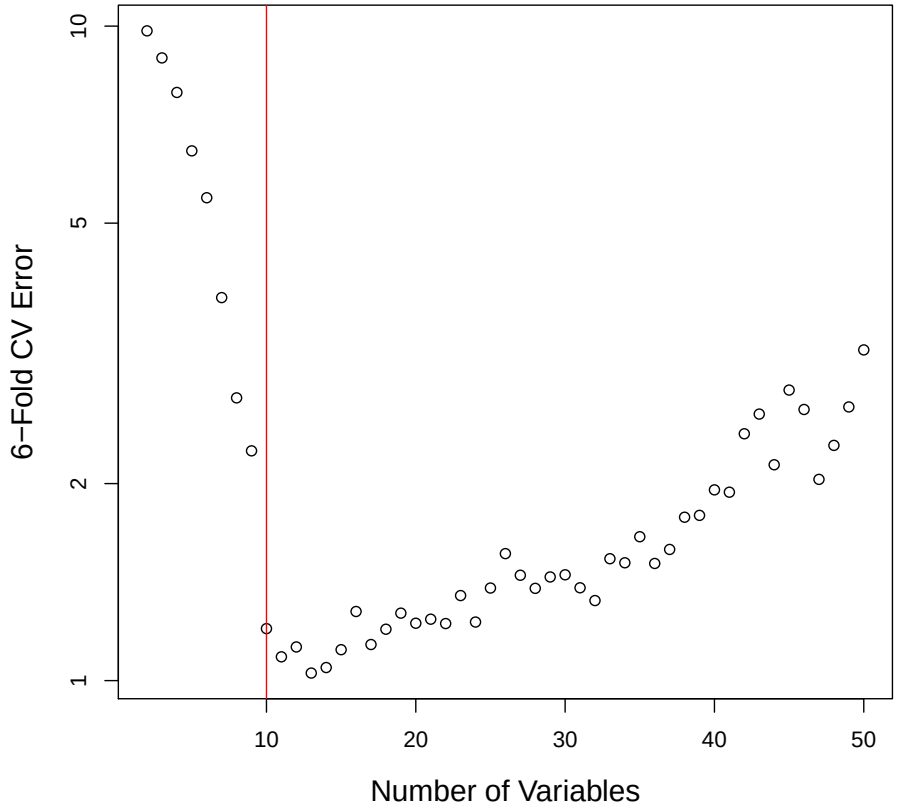
1. Split the n observations into K equally-sized folds.
2. For $k = 1, \ldots, K$:
   a. Fit the model using the observations not in the kth fold.
   b. Let e_k denote the test error for the observations in the kth fold.
3. Calculate $\sum_{k=1}^{K} e_k$, the total CV error.

Out of a set of candidate models, the "best" one is the one for which the total error is smallest.

An Example In R

```
xtr <- matrix(rnorm(100*100),ncol=100)
beta <- c(rep(1,10),rep(0,90))
ytr <- xtr%*%beta + rnorm(100)
cv.err <- NULL
for(i in 2:50){
dat <- data.frame(x=xtr[,1:i],y=ytr)
mod <- glm(y~.,data=dat)
cv.err <- c(cv.err, cv.glm(dat,mod,K=6)$delta[1])
}
plot(2:50, cv.err, xlab="Number of Variables",
ylab="6-Fold CV Error", log="y")
abline(v=10, col="red")
```

Output of R Code



- Six-fold CV identifies the model with just over ten predictors.
- First ten predictors contain signal, and the rest are noise.

After Estimating the Test Error on the Training Set...

After we estimate the test error using the training set, we refit the “best" model on all of the available training observations. We then evaluate this model on the test set.

Big Picture

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Summary: Four-Step Procedure

1. Split observations into training set and test set.
2. Fit a bunch of models on training set, and estimate the test error, using cross-validation or validation set approach.
3. Refit the best model on the full training set.
4. Evaluate the model's performance on the test set.

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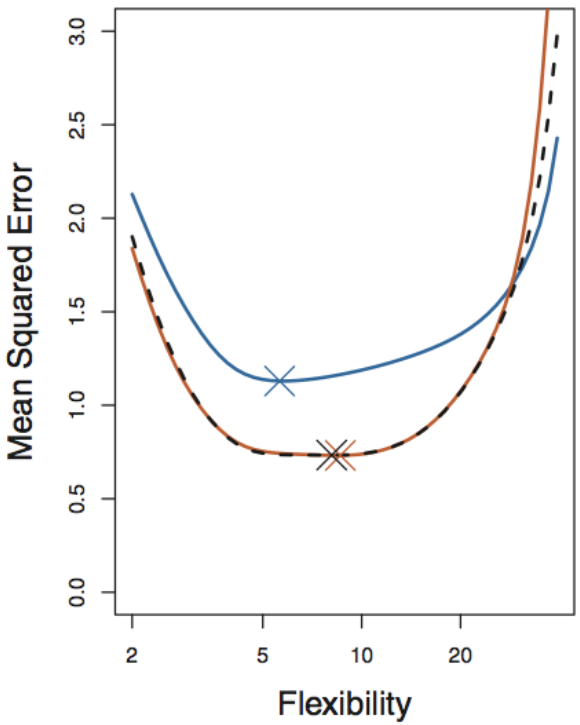
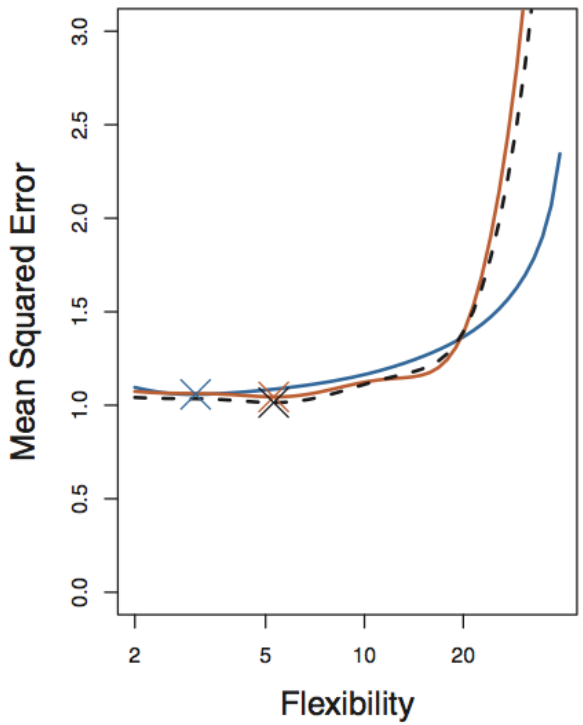
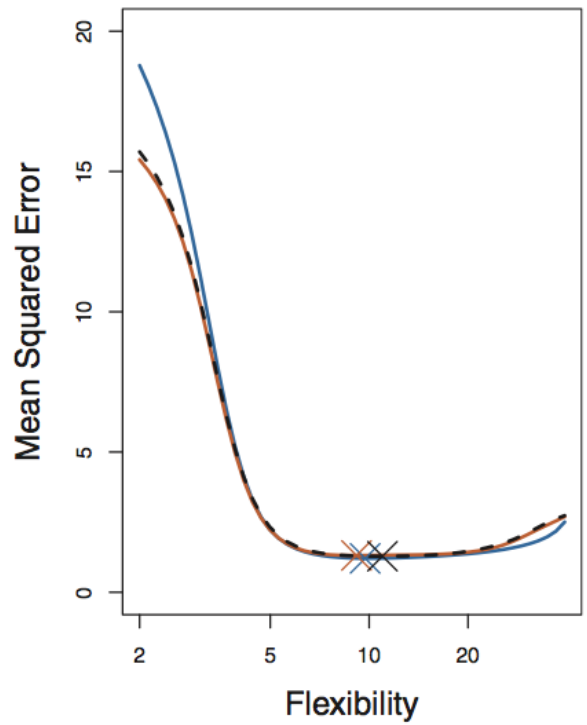
  - decide which model is best among a set of candidate models: in this case, the actual estimate of MSE is not very important, as long as the location of the minimum MSE value is correct

Cross Validation in Practice







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- In practice k-fold CV with k between 5 to 10 often gives good results

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A: In general, we are choosing between a whole bunch of models, and we will use the cross-validation or validation set approach to pick between these models. If we use the resulting estimate as a final estimate of test error, then this could be an extreme underestimate, because one model might give a lower estimated test error than others by chance. To avoid having an extreme underestimate of test error, we need to evaluate the "best" model obtained on an independent test set. *This is particularly important in high dimensions!!*

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- These are alternatives to fitting a linear model using least squares.
- Each of these approaches will allow us to choose the level of complexity – e.g. the number of variables in the model.

The Fundamental Truth About High-Dimensional Data

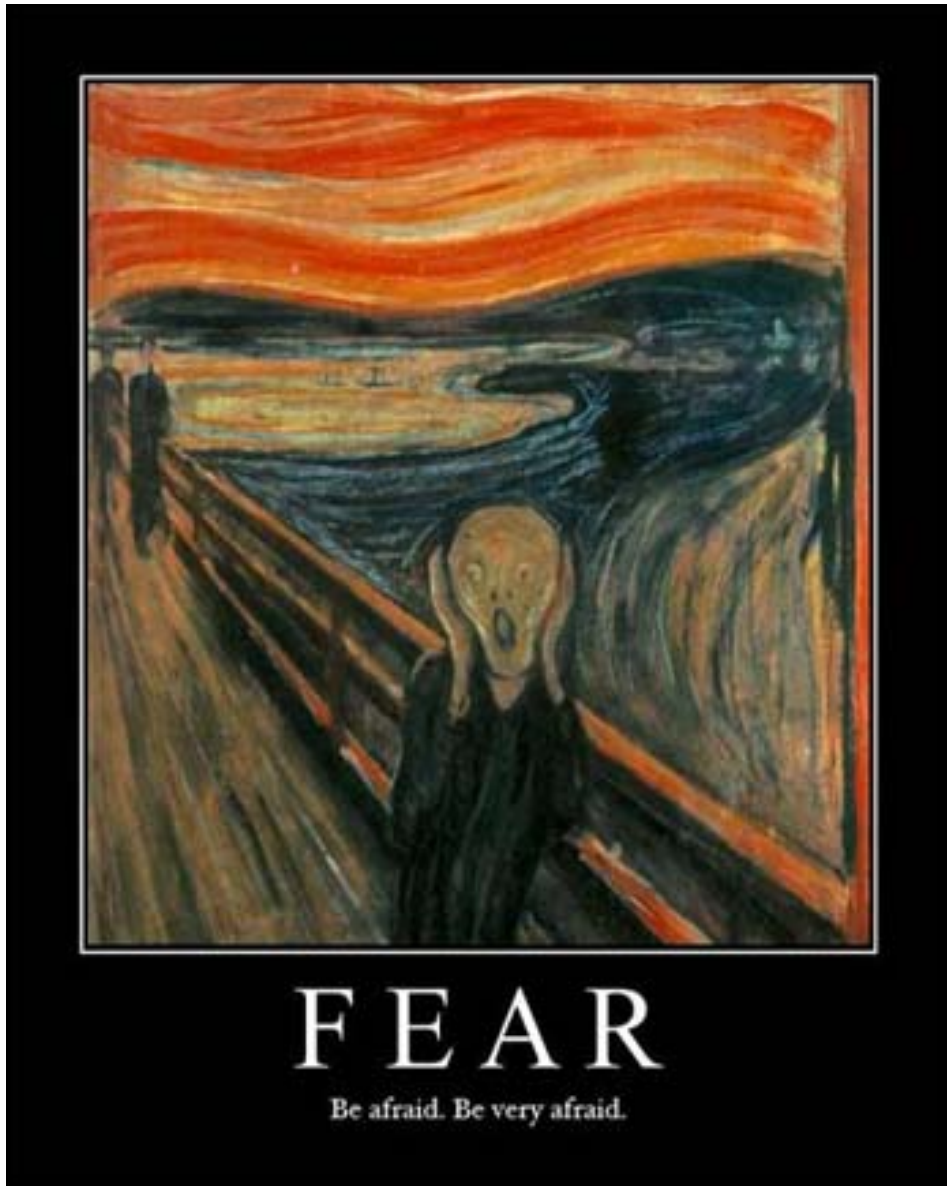
If you

- fit your model carelessly;
- do not properly estimate the test error;
- or select a model based on training set rather than test set performance;

then you will woefully overfit your training data, leading to a model that looks good on training data but will perform atrociously on future observations.

Our intuition breaks down in high dimensions, and so rigorous model-fitting is crucial.

The Curse of Dimensionality



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Q: A data set with more variables is better than a data set with fewer variables, right?

A: Not necessarily!

Noise variables – such as genes whose expression levels are not truly associated with the response being studied – will simply increase the risk of overfitting, and the difficulty of developing an effective model that will perform well on future observations.

On the other hand, more signal variables – variables that are truly associated with the response being studied – are always useful!

Every Biostatisticians' Favorite Anecdote

A biostatistician walks into a collaborator's office with a list of genes found to be predictive of survival time in a condition of interest....

Wise Words

In high-dimensional data analysis, common mistakes are simple, and simple mistakes are common.

– Keith Baggerly

Before You're Done with Your Analysis

- Estimate the test error.
- Do a "sanity check" whenever possible.
  - "Spot-check" the variables that have the largest coefficients in the model.
  - Rewrite your code from scratch. Do you get the same answer again?

Fitting models in high-dimensions: one mistake away from disaster!