Supervised Learning: Regression, Part II

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Linear Models in High Dimensions

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- When p is large, least squares regression will lead to very low training error but terrible test error.
- We will now see some approaches for fitting linear models in high dimensions, $p \gg n$.
- These approaches also work well when $p \approx n$ or $n > p$.

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- For instance, these biomarkers could be:
  - the expression levels of genes measured using a microarray.
  - protein levels.
  - mutations in genes potentially implicated in breast cancer.
- How can we develop a model with low test error in this setting?

Remember

- We have n training observations.
- Our goal is to get a model that will perform well on future test observations.
- We'll incur some bias in order to reduce variance.

Variable Pre-Selection

The simplest approach for fitting a model in high dimensions:

1. Choose a small set of variables, say the q variables that are most correlated with the response, where $q < n$ and $q < p$.
2. Use least squares to fit a model predicting y using only these q variables.

This approach is simple and straightforward.

Variable Pre-Selection in R

```
xtr <- matrix(rnorm(100*100),ncol=100)
beta <- c(rep(1,10),rep(0,90))
ytr <- xtr%*%beta + rnorm(100)
cors <- cor(xtr,ytr)
whichers <- which(abs(cors)>.2)
mod <- lm(ytr~xtr[,whichers])
print(summary(mod))
```

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- For a range of values of q, we can perform the validation set approach, leave-one-out cross-validation, or K-fold cross-validation in order to estimate the test error.
- Then choose the value of q for which the estimated test error is smallest.

Estimating the Test Error For a Given q

This is the right way to estimate the test error using the validation set approach:

1. Split the observations into a training set and a validation set.
2. Using the training set only:
    a. Identify the q variables most associated with the response.
    b. Use least squares to fit a model predicting y using those q variables.
    c. Let $\hat{\beta}_1, \ldots, \hat{\beta}_q$ denote the resulting coefficient estimates.
3. Use $\hat{\beta}_1, \ldots, \hat{\beta}_q$ obtained on training set to predict response on validation set, and compute the validation set MSE.

Estimating the Test Error For a Given q

This is the wrong way to estimate the test error using the validation set approach:

1. Identify the q variables most associated with the response on the full data set.
2. Split the observations into a training set and a validation set.
3. Using the training set only:
   a. Use least squares to fit a model predicting y using those q variables.
   b. Let $\hat{\beta}_1, \ldots, \hat{\beta}_q$ denote the resulting coefficient estimates.
4. Use $\hat{\beta}_1, \ldots, \hat{\beta}_q$ obtained on training set to predict response on validation set, and compute the validation set MSE.

Frequently Asked Questions

- **Q:** Does it really matter how you estimate the test error?
  A: Yes.

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- **Q:** Does it really matter how you estimate the test error?
  A: Yes.
- **Q:** Would anyone make such a silly mistake?
  A: Yes.

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- The variable pre-selection approach is simple and easy to implement — all you need is a way to calculate correlations, and software to fit a linear model using least squares.

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- But it might not work well: just because a bunch of variables are correlated with the response doesn't mean that when used together in a linear model, they will predict the response well.
- What we really want to do: pick the q variables that best predict the response.
- Many methods have been developed to achieve this over the past 10-20 years! We cover few of them in this module.

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  - When $p = 3$, $2^p = 8$.
  - When $p = 6$, $2^p = 64$.
  - When $p = 250$, there are $2^{250} \approx 10^{80}$ possible models. According to www.universetoday.com, this is around the number of atoms in the known universe.
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- Ridge regression and the lasso instead control model complexity by using an alternative to least squares, by shrinking the regression coefficients.
- This is known as regularization or penalization.

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- Why does correlation matter?
  - Suppose that X_1 and X_2 are highly correlated with each other... assume $X_1 = X_2$ for the sake of argument.
  - And suppose that the least squares model is

$$\hat{y} = X_1 - 2X_2 + 3X_3.$$

  - Then this is also a least squares model:

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- Bottom Line: When there are too many variables, the least squares coefficients can get crazy!
- This craziness is directly responsible for poor test error.
- It amounts to too much model complexity.

A Solution: Don't Let the Coefficients Get Too Crazy

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- Equivalently, find $\boldsymbol{\beta}$ that minimizes
$$\|\mathbf{y} - \mathbf{X}\boldsymbol{\beta}\|^2$$
subject to the constraint that
$$\sum_{j=1}^{p} \beta_j^2 \leq s.$$

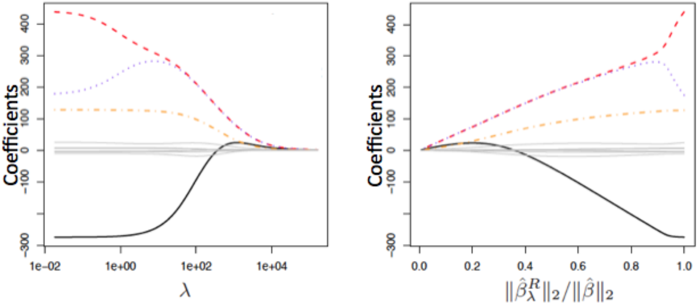
Ridge Regression

- Ridge regression coefficient estimates minimize

$$\|\mathbf{y} - \mathbf{X}\boldsymbol{\beta}\|^2 + \lambda \sum_j \beta_j^2.$$

- Here λ is a nonnegative tuning parameter that shrinks the coefficient estimates.
- When $\lambda = 0$, then ridge regression is just the same as least squares.
- As λ increases, then $\sum_{j=1}^{p} (\hat{\beta}_{\lambda,j}^R)^2$ decreases — i.e. coefficients become shrunken towards zero.
- When $\lambda = \infty$, $\hat{\boldsymbol{\beta}}_{\lambda}^{R} = 0$.

Ridge Regression As λ Varies



Ridge Regression In Practice

- Perform ridge regression for a very fine grid of λ values.
- Use cross-validation or the validation set approach to select the optimal value of λ — that is, the best level of model complexity.
- Perform ridge on the full data set, using that value of λ.

Example in R

```
xtr <- matrix(rnorm(100*100),ncol=100)
beta <- c(rep(1,10),rep(0,90))
ytr <- xtr%*%beta + rnorm(100)
library(glmnet)
cv.out <- cv.glmnet(xtr,ytr,alpha=0,nfolds=5)
print(cv.out$cvm)
plot(cv.out)
cat("CV Errors", cv.out$cvm,fill=TRUE)
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cat("Coefficients", as.numeric(coef(cv.out)),fill=TRUE)
cat("Number of Zero Coefficients",
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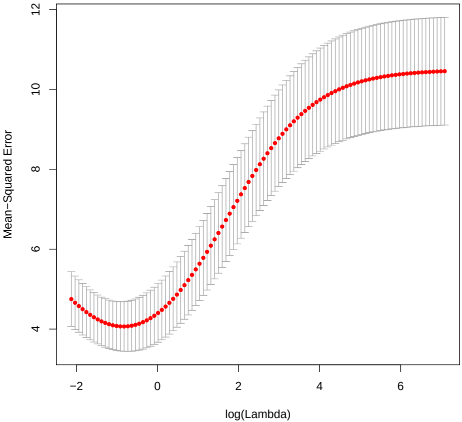
R Output



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- The lasso involves performing a little tweak to ridge regression so that the resulting model contains mostly zeros.
- In other words, the resulting model is sparse. We say that the lasso performs feature selection.
- The lasso is a very active area of research interest in the statistical community!

The Lasso

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- So lasso is just like ridge, except that β_j^2 has been replaced with $|\beta_j|$.

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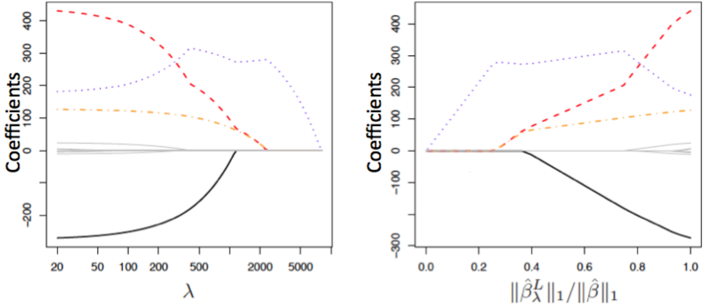
  - When $\lambda = 0$, we get least squares.
  - When λ is very large, we get $\hat{\beta}_\lambda^L = 0$.
- But unlike ridge, lasso will give some coefficients exactly equal to zero for intermediate values of λ!

Lasso As λ Varies



Lasso In Practice

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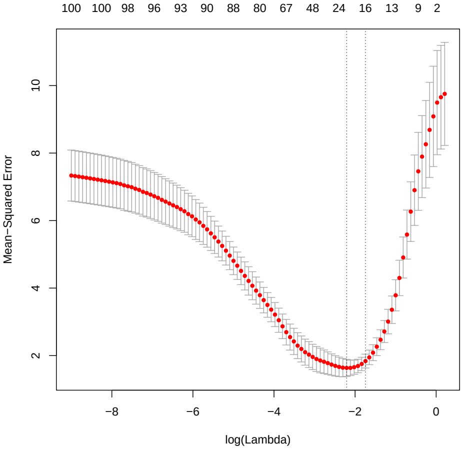
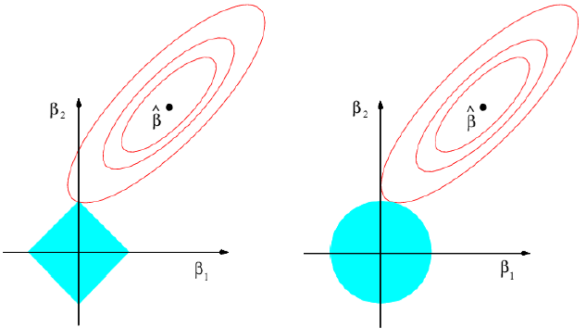

100 100 98 96 93 90 88 80 67 48 24 16 13 9 2
Mean−Squared Error
2
4
6
8
10
−8
−6
−4
−2
0
log(Lambda)

Ridge and Lasso: A Geometric Interpretation



Let's Try It Out in R!

Chapter 6 R Lab, Part 2
www.statlearning.com

Pros/Cons of Each Approach

Approach	Simplicity?*	Sparsity?**	Predictions?***
Pre-Selection	Good	Yes	So-So
Ridge	Medium	No	Great
Lasso	Bad	Yes	Great

* How simple is this model-fitting procedure? If you were stranded on a desert island with pretty limited statistical software, could you fit this model?
** Does this approach perform feature selection, i.e. is the resulting model sparse?
*** How good are the predictions resulting from this model?

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- Some approaches will work better than others. For instance:
  - Lasso will work well if it's really true that just a few features are associated with the response.
  - Ridge will do better if all of the features are associated with the response.
- If somebody tells you that one approach is "best"... then they are mistaken. Politely contradict them.
- While no approach is "best", some approaches are wrong (e.g.: there is a wrong way to do cross-validation)!

Predicting Age Using DNA Methylation Data

- Comparison on 6 data sets
- SPC: A method based on dimension reduction (not discussed here).
- Elastic Net: A hybrid between ridge and lasso.
- SVM: We'll see it next lecture in the classification context.
- Citation: Zhuang et al., BMC Bioinformatics, 2012

Didn't I Tell You? No Best Method!

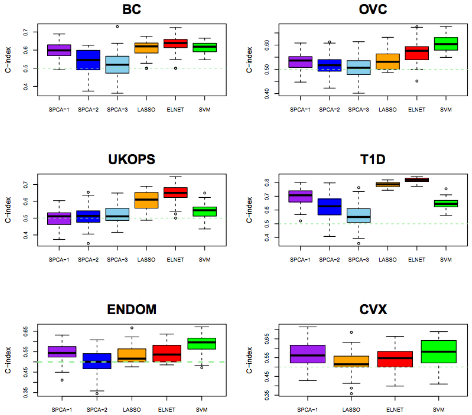

Figure 6 Classification method comparison of SPCA1, SPCA2, SPCA3, LASSO, ELNET and SVM, using age as the phenotype of interest, for each of the 6 DNAm studies with available age information. A total of 50 training-test set partitions were used, so each boxplot contains 50 data points. C-index (y-axis) measures the concordance index between the DNAm age predictor score and age itself. Dashed green line denotes the null hypothesis of no association.

High C-index indicates a low test error.

Bottom Line

Much more important than what model you fit is how you fit it.

- Was cross-validation performed properly?
- Did you select a model (or level of model complexity) based on an estimate of test error?

Discussion Questions

A collaborator comes to you and says:

I really don't like this LASSO thing; I tried it on my data and it the resulting model only explained 15% of the variability in my data... Then I tried variable pre-selection, and I was able to get it to explain 95%! Why would anyone ever use the LASSO???

What do you think is happening?

Discussion Questions

What if instead they said:

I really don't like this variable pre-selection thing; I tried it on my data and it the resulting model only explained 15% of the variability in my data... Then I tried the LASSO, and I was able to get it to explain 95%! Why would anyone ever use variable pre-selection???

Discussion Questions

Finally, what if they said:

I really love the LASSO. I was originally just using standard linear regression and the resulting model only explained 15% *of the variability in my data... Then I tried the LASSO, and I was able to get it to explain* 95%*!*

What do you think is happening here?

Discussion Questions

A collaborator came to me and said:

"I am reviewing a paper where the authors claim to be able to predict the flu, by looking at serum gene expression values 3 weeks before symptom onset. This seems impossible, but I can't find an obvious error in the paper"

Discussion Questions

Looking at the paper, the authors had used the following pipeline:

- Took banked blood from 100 patients (50 subsequently diagnosed with flu, 50 were not).
- They separately looked at the correlation of expression of each gene with flu-status, and selected the 70 top genes
- They split into a training and test set.
- On the training set they ran 5-fold cross validation to come up with an optimal aggregation of kernel-SVM, logistic regression, and boosted classification trees
- They evaluated this on the test set, and found almost perfect classification.

Discussion Questions

What is going on???

Did they go on to create an enormously successful biotech company?