

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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- ▶ We want q that minimizes the test error.
- ▶ 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 $\hat{\beta}_1, \dots, \hat{\beta}_q$ denote the resulting coefficient estimates.
3. Use $\hat{\beta}_1, \dots, \hat{\beta}_q$ 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 $\hat{\beta}_1, \dots, \hat{\beta}_q$ denote the resulting coefficient estimates.
4. Use $\hat{\beta}_1, \dots, \hat{\beta}_q$ 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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- ▶ 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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- ▶ Unfortunately, this is computationally intractable:
 - ▶ 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

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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.

Crazy Coefficients

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- ▶ When $p > n$, some of the variables are **highly correlated**.
- ▶ 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:

$$\hat{y} = 100000001X_1 - 100000002X_2 + 3X_3.$$

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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**.

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subject to the constraint that

$$\sum_{j=1}^p \beta_j^2 \leq s.$$

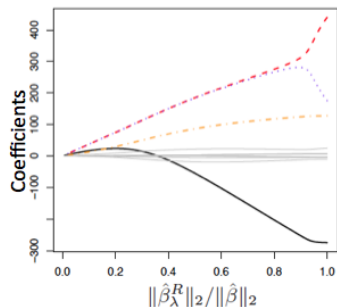
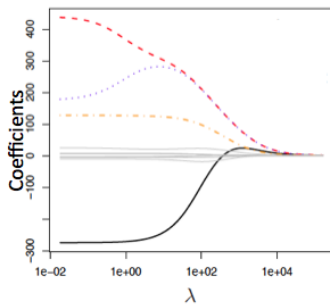
Ridge Regression

- ▶ Ridge regression coefficient estimates minimize

$$\|y - X\beta\|^2 + \lambda \sum_j \beta_j^2.$$

- ▶ 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 $\lambda = \infty$, $\hat{\beta}_{\lambda}^R = 0$.

Ridge Regression As λ Varies



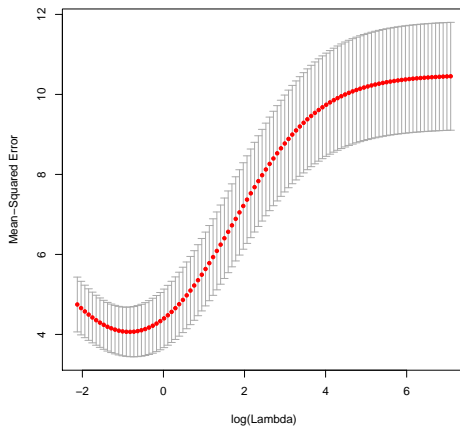
Ridge Regression In Practice

- ▶ 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)
cat("Lambda with smallest CV Error",
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cat("Coefficients", as.numeric(coef(cv.out)),fill=TRUE)
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R Output



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- ▶ The lasso is a very active area of research interest in the statistical community!

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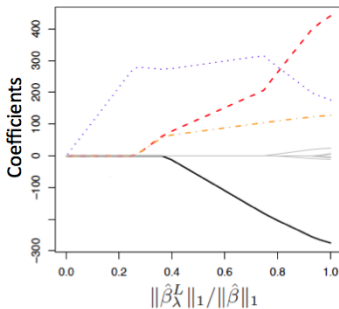
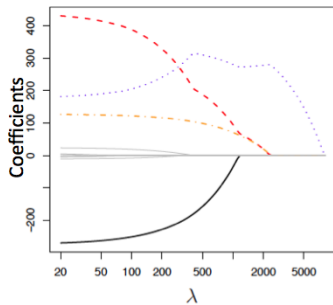
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 - ▶ When $\lambda = 0$, we get least squares.
 - ▶ When λ is very large, we get $\hat{\beta}_{\lambda}^L = 0$.
- ▶ But unlike ridge, **lasso will give some coefficients exactly equal to zero for intermediate values of λ !**

Lasso As λ Varies



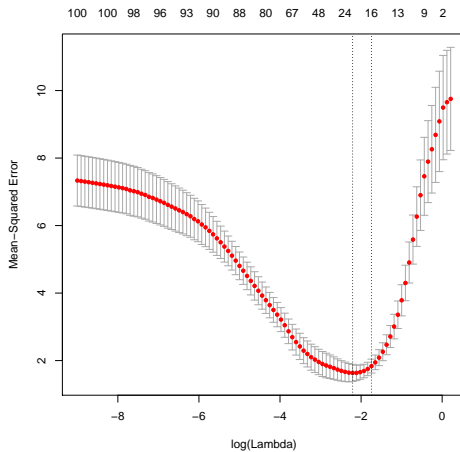
Lasso In Practice

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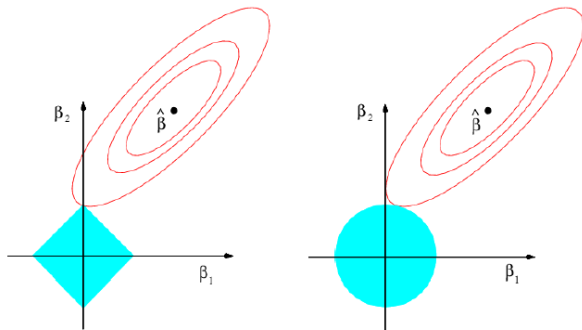
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R Output



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?

No “Best” Approach

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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!

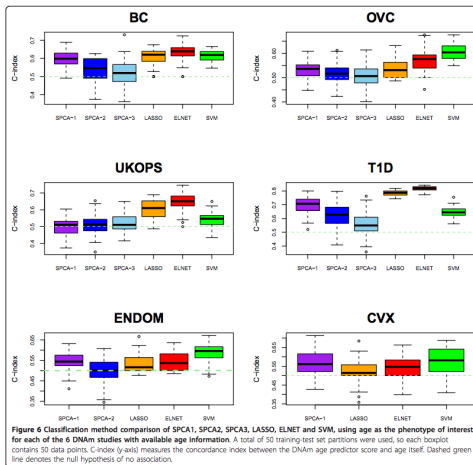


Figure 6 Classification method comparison of SPCA1, SPCA2, SPCA3, LASSO, ELNET and SVM, using age as the phenotype of interest, for each of the 6 DNAm studies with available age information. A total of 50 training-test set partitions were used, so each boxplot contains 50 data points. C-index (y-axis) 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 forward stepwise regression???

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?