Supervised Learning:
Regression, Part II

Noah Simon & Ali Shojaie

July 15-17, 2020
Summer Institute in Statistics for Big Data
University of Washington

Linear Models in High Dimensions

- When p is large, least squares regression will lead to very low training error but terrible test error.

Linear Models in High Dimensions

- 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 $n > p$.

Motivating example

- We would like to build a model to predict survival time for breast cancer patients using a number of clinical measurements (tumor stage, tumor grade, tumor size, patient age, etc.) as well as some biomarkers.

Motivating example

- We would like to build a model to predict survival time for breast cancer patients using a number of clinical measurements (tumor stage, tumor grade, tumor size, patient age, etc.) as well as some biomarkers.
- For instance, these biomarkers could be:

Motivating example

- We would like to build a model to predict survival time for breast cancer patients using a number of clinical measurements (tumor stage, tumor grade, tumor size, patient age, etc.) as well as some biomarkers.
- For instance, these biomarkers could be:
  - the expression levels of genes measured using a microarray.

Motivating example

- We would like to build a model to predict survival time for breast cancer patients using a number of clinical measurements (tumor stage, tumor grade, tumor size, patient age, etc.) as well as some biomarkers.
- For instance, these biomarkers could be:
  - the expression levels of genes measured using a microarray.
  - protein levels.

Motivating example

- We would like to build a model to predict survival time for breast cancer patients using a number of clinical measurements (tumor stage, tumor grade, tumor size, patient age, etc.) as well as some biomarkers.
- 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.

Motivating example

- We would like to build a model to predict survival time for breast cancer patients using a number of clinical measurements (tumor stage, tumor grade, tumor size, patient age, etc.) as well as some biomarkers.
- 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))
```

How Many Variable to Use?

- We need a way to choose q, the number of variables used in the regression model.

How Many Variable to Use?

- We need a way to choose q, the number of variables used in the regression model.
- We want q that minimizes the test error.

How Many Variable to Use?

- We need a way to choose q, the number of variables used in the regression model.
- 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.

How Many Variable to Use?

- We need a way to choose q, the number of variables used in the regression model.
- 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 $\hat{\beta}_1, \ldots, \hat{\beta}_q$ 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.

Frequently Asked Questions

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

A Better Approach

- 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.

A Better Approach

- 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.
- 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.

A Better Approach

- 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.
- 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.

A Better Approach

- 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.
- 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.

Best Subset Selection

- Ideally, we would like to consider all possible models using a subset of the p predictors.

Best Subset Selection

- Ideally, we would like to consider all possible models using a subset of the p predictors.
- In other words, we'd like to consider all 2^p possible models.

Best Subset Selection

- Ideally, we would like to consider all possible models using a subset of the p predictors.
- In other words, we'd like to consider all 2^p possible models.
- This is called best subset selection.

Best Subset Selection

- Ideally, we would like to consider all possible models using a subset of the p predictors.
- In other words, we'd like to consider all 2^p possible models.
- This is called best subset selection.
- 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.
  - Not feasible to consider so many models!

Best Subset Selection

- Ideally, we would like to consider all possible models using a subset of the p predictors.
- In other words, we'd like to consider all 2^p possible models.
- This is called best subset selection.
- 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.
    - Not feasible to consider so many models!

Ridge Regression and the Lasso

- Best subset selection does a discrete search through model space, considering subsets of the predictors, and fitting each of the resulting models using least squares. Model complexity is controlled by using subsets of the predictors.

Ridge Regression and the Lasso

- Best subset selection does a discrete search through model space, considering subsets of the predictors, and fitting each of the resulting models using least squares. Model complexity is controlled by using subsets of the predictors.
- Ridge regression and the lasso instead control model complexity by using an alternative to least squares, by shrinking the regression coefficients.

Ridge Regression and the Lasso

- Best subset selection does a discrete search through model space, considering subsets of the predictors, and fitting each of the resulting models using least squares. Model complexity is controlled by using subsets of the predictors.
- 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

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

Crazy Coefficients

- 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:

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

Crazy Coefficients

- 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:

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

- 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

- Recall that least squares involves finding $\boldsymbol{\beta}$ that minimizes

$$\|\mathsf{y} - \mathsf{X}\boldsymbol{\beta}\|^2.$$

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

- Recall that least squares involves finding $\boldsymbol{\beta}$ that minimizes

$$\|\mathsf{y} - \mathsf{X}\boldsymbol{\beta}\|^2.$$

- Ridge regression involves finding $\boldsymbol{\beta}$ that minimizes

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

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

- Recall that least squares involves finding $\boldsymbol{\beta}$ that minimizes

$$\|\mathsf{y} - \mathsf{X}\boldsymbol{\beta}\|^2.$$

- Ridge regression involves finding $\boldsymbol{\beta}$ that minimizes

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

- Equivalently, find $\boldsymbol{\beta}$ that minimizes

$$\|\mathsf{y} - \mathsf{X}\boldsymbol{\beta}\|^2$$

  subject to the constraint that

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

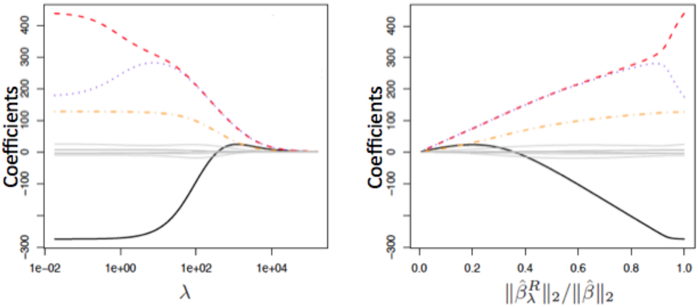
Ridge Regression

- Ridge regression coefficient estimates minimize

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

- 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



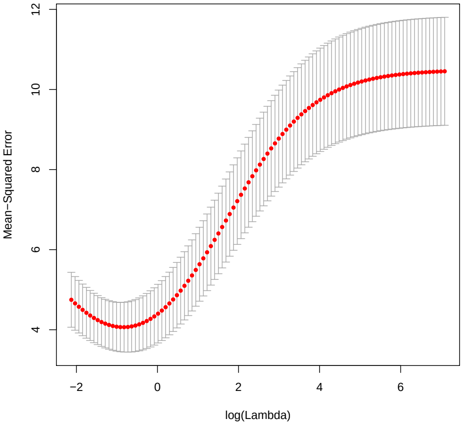
Ridge Regression In Practice

- 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)
cat("Lambda with smallest CV Error",
cv.out$lambda[which.min(cv.out$cvm)],fill=TRUE)
cat("Coefficients", as.numeric(coef(cv.out)),fill=TRUE)
cat("Number of Zero Coefficients",
sum(abs(coef(cv.out))<1e-8),fill=TRUE)
```

R Output



Drawbacks of Ridge

- Ridge regression is a simple idea and has a number of attractive properties: for instance, you can continuously control model complexity through the tuning parameter λ.

Drawbacks of Ridge

- Ridge regression is a simple idea and has a number of attractive properties: for instance, you can continuously control model complexity through the tuning parameter λ.
- But it suffers in terms of model interpretability, since the final model contains all p variables, no matter what.

Drawbacks of Ridge

- Ridge regression is a simple idea and has a number of attractive properties: for instance, you can continuously control model complexity through the tuning parameter λ.
- But it suffers in terms of model interpretability, since the final model contains all p variables, no matter what.
- Often want a simpler model involving a subset of the features.

Drawbacks of Ridge

- Ridge regression is a simple idea and has a number of attractive properties: for instance, you can continuously control model complexity through the tuning parameter λ.
- But it suffers in terms of model interpretability, since the final model contains all *p* variables, no matter what.
- Often want a simpler model involving a subset of the features.
- The lasso involves performing a little tweak to ridge regression so that the resulting model contains mostly zeros.

Drawbacks of Ridge

- Ridge regression is a simple idea and has a number of attractive properties: for instance, you can continuously control model complexity through the tuning parameter λ.
- But it suffers in terms of model interpretability, since the final model contains all p variables, no matter what.
- Often want a simpler model involving a subset of the features.
- 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.

Drawbacks of Ridge

- Ridge regression is a simple idea and has a number of attractive properties: for instance, you can continuously control model complexity through the tuning parameter λ.
- But it suffers in terms of model interpretability, since the final model contains all p variables, no matter what.
- Often want a simpler model involving a subset of the features.
- 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

- The lasso involves finding $\boldsymbol{\beta}$ that minimizes

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

The Lasso

- The lasso involves finding $\boldsymbol{\beta}$ that minimizes

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

- Equivalently, find $\boldsymbol{\beta}$ that minimizes

$$\|\mathsf{y} - \mathsf{X}\boldsymbol{\beta}\|^2$$

subject to the constraint that

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

The Lasso

- The lasso involves finding $\boldsymbol{\beta}$ that minimizes

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

- Equivalently, find $\boldsymbol{\beta}$ that minimizes

$$\|\mathsf{y} - \mathsf{X}\boldsymbol{\beta}\|^2$$

  subject to the constraint that

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

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

The Lasso

- Lasso is a lot like ridge:

The Lasso

- Lasso is a lot like ridge:
  - λ is a nonnegative tuning parameter that controls model complexity.

The Lasso

- Lasso is a lot like ridge:
  - λ is a nonnegative tuning parameter that controls model complexity.
  - When $\lambda = 0$, we get least squares.

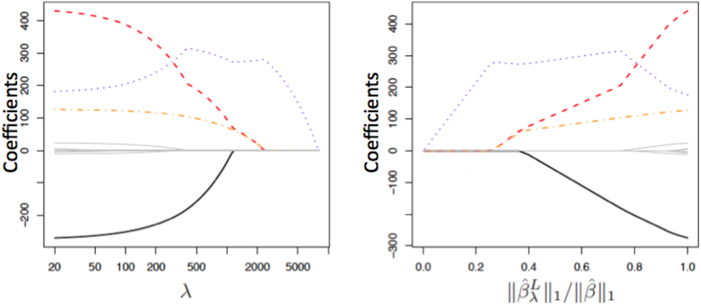
The Lasso

- Lasso is a lot like ridge:
  - λ is a nonnegative tuning parameter that controls model complexity.
  - When $\lambda = 0$, we get least squares.
  - When λ is very large, we get $\hat{\beta}^L_\lambda = 0$.

The Lasso

- Lasso is a lot like ridge:
  - λ is a nonnegative tuning parameter that controls model complexity.
  - When $\lambda = 0$, we get least squares.
  - When λ is very large, we get $\hat{\beta}^L_\lambda = 0$.
- But unlike ridge, lasso will give some coefficients exactly equal to zero for intermediate values of λ!

Lasso As λ Varies



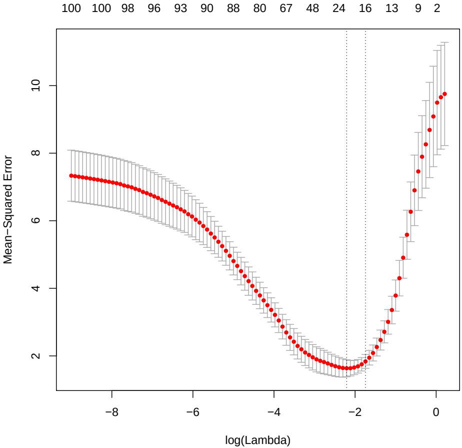
Lasso In Practice

- Perform lasso 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 the lasso on the full data set, using that value of λ.

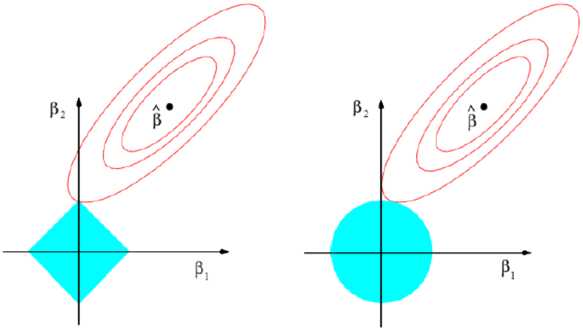
Example in R

```
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=1,nfolds=5)
print(cv.out$cvm)
plot(cv.out)
cat("CV Errors", cv.out$cvm,fill=TRUE)
cat("Lambda with smallest CV Error",
cv.out$lambda[which.min(cv.out$cvm)],fill=TRUE)
cat("Coefficients", as.numeric(coef(cv.out)),fill=TRUE)
cat("Number of Zero Coefficients",sum(abs(coef(cv.out))<1e-8),
fill=TRUE)
```

R Output


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?

No “Best” Approach

- There is no “best” approach to regression in high dimensions.

No “Best” Approach

- There is no “best” approach to regression in high dimensions.
- 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.

No “Best” Approach

- There is no “best” approach to regression in high dimensions.
- 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!

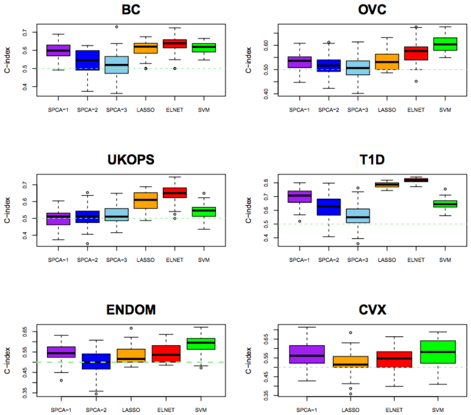


Figure 6 Classification method comparison of SPCA1, SPCA2, SPCA3, LASSO, ELNET and SVM, using age as the phenotype of interest, for each of the 6 DNAm studies with available age information. A total of 50 training-test set partitions were used, so each boxplot contains 50 data points. C-index (y-axis)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