Sparse Linear Regression: the LASSO

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High Dimensional Linear Regression

Setting: Common in genomics, biomedicine, climatology

- Data $(x_1, y_1) \ldots, (x_n, y_n) \in \mathbb{R}^{p+1} \times \mathbb{R}$ with $p >> n$
- Interested in fitting linear model $y = X\,\beta + \varepsilon$

Sparsity: Assumption (sometimes a goal) of regression analysis

- Only a small number s of the available features are related to the response; other features unimportant
- True coefficient vector β has only s non-zero components

Sparse Linear Regression

Common goals

- Prediction: Find sparse $\hat{\beta}$ so that $x^t\hat{\beta}$ close to y for new (x, y)
- Feature selection: Identify the “true” features, i.e., $\{j : \beta_j = 0\}$

Issue: For OLS and Ridge all estimated coefficients are non-zero

LASSO: Least absolute shrinkage and selection operator

- Replace ridge penalty $\sum_{j=0}^{p} \beta_j^2$ by ℓ_1-penalty $\sum_{j=0}^{p} |\beta_j|$
- The ℓ_1 penalty enforces sparsity but preserves convexity

LASSO Regression

Task: Given design matrix X, response vector y, and parameter $\lambda \geq 0$, find coefficients $\hat{\beta}_\lambda^{\text{LASSO}}$ minimizing

$$\tilde{R}_{n,\lambda}(\beta) \;=\; \frac{1}{2}||y - X\beta||^2 \,+\, \lambda\,||\beta||_1$$

- $||y - X\beta||^2$ measures fit of linear model
- $||\beta||_1 = \sum_{j=0}^{p} |\beta_j|$ measures magnitude of coefficient vector
- Parameter λ controls tradeoff between fit and magnitude

Key fact: The ℓ_1-penalty forces some coefficients $\hat{\beta}^{\text{LASSO}}$ to be *exactly* zero

- Increasing λ tends to increase number of zero coefficients in $\hat{\beta}^{\text{LASSO}}$

LASSO Estimation as a Convex Program

Fact: For every $\lambda \geq 0$ objective $\tilde{R}_{n,\lambda}(\beta)$ is a convex function of β

Fact: Minimizing $R_\lambda(\beta)$ is Lagrangian form of the mathematical program

$$\min f(\beta) = ||y - X\beta||^2 \text{ subject to } ||\beta||_1 \leq t$$

where t depends on λ. Objective function and constraint set are convex.

Upshot: Zero-ing property follows from *geometry* of the ℓ_1-penalty

Estimating the Penalty Parameter λ

Good prediction: Find λ such that $R(\hat{\beta}_\lambda^{\text{LASSO}})$ is small

- Independent test set
- Cross-validation

Theory: If $y = X\,\beta + \varepsilon$ with $\varepsilon \sim \mathcal{N}_n(0, \sigma^2 I)$ theory suggests

1. Find good estimate $\hat{\sigma}^2$ of the noise variance σ^2
2. Choose parameter

$$\lambda \;=\; \sqrt{\frac{2\hat{\sigma}^2 \log p}{n}}$$

Estimating the Penalty Parameter, cont

Idea: If response y is independent of X then β should be 0

Procedure: For $k = 1, \ldots, 20$ do the following

1. Randomly permute components of y to get dummy response y_π
2. Apply LASSO to (y_π, X) with different values of λ
3. Let $\lambda_k =$ smallest λ such that $\hat{\beta}^{\text{LASSO}} = 0$

Estimated penalty parameter is $\hat{\lambda} =$ median$(\lambda_1, \ldots, \lambda_k)$

Example: B-cell gene expression data

Background: Data from Basso et al. 2005, Affymetrix microarrays

1. Samples: Samples of $n = 211$ normal and tumor tissue
2. Feature vector: Expression measurements of $p = 6,248$ genes
3. Response: Expression of single ADA gene

Question: How does the expression of `ADA` depend on the expression of the 6248 other genes?

OLS Solution

```
R > summary(my_model)

Call:
lm(formula = ADA ~ ., data = gene_expressions)

Residuals:
ALL 211 residuals are 0: no residual degrees of freedom!

Coefficients: (6038 not defined because of singularities)
                Estimate Std. Error t value Pr(>|t|)
(Intercept)   -412.40983         NA      NA       NA
CDH2            -1.86356         NA      NA       NA
MED6             7.10850         NA      NA       NA
NR2E3           -1.40334         NA      NA       NA
ACOT8            3.48331         NA      NA       NA
ABI1            -5.88529         NA      NA       NA
GNPDA1           0.28055         NA      NA       NA
TANK            -6.02434         NA      NA       NA
HGC6.3          -0.79016         NA      NA       NA
C1orf68         -1.21752         NA      NA       NA
LOC100129361     0.20853         NA      NA       NA
OLFM1                 NA         NA      NA       NA
TIMM17A               NA         NA      NA       NA
N4BP2L2               NA         NA      NA       NA
MCRS1                 NA         NA      NA       NA
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Residual standard error: NaN on 0 degrees of freedom
Multiple R-squared:      1, Adjusted R-squared:    NaN
F-statistic:   NaN on 210 and 0 DF, p-value: NA
```

Ridge Solution

- R function selects penalty parameter λ based on the variance explained by the first 8 PCs. [1]
- Note: coefficient estimates for every feature are non-zero

```
R > ridge.fit = linearRidge(ADA~., data = gene_expressions)
R > ridge.fit$coef[,"nPCs8"]
          CDH2           MED6          NR2E3          ACOT8
  1.390812e-02  -3.920405e-02   2.380735e-02  -1.577109e-02

  ABI1          GNPDA1           TANK          HGC6.3
  1.902280e-04  -5.952662e-03   1.141530e-02   5.133231e-02

       C1orf68   LOC100129361           CD24          HDAC5
 -5.509269e-02  -3.030931e-02  -4.909134e-02  -5.526016e-03

PDCD6          BCL2L11          SH2B3           GNE
1.990365e-02   2.167638e-02  -3.561387e-02  -1.047401e-01
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 R > length(which(coef(ridge.fit) == 0))
[1] 0
```
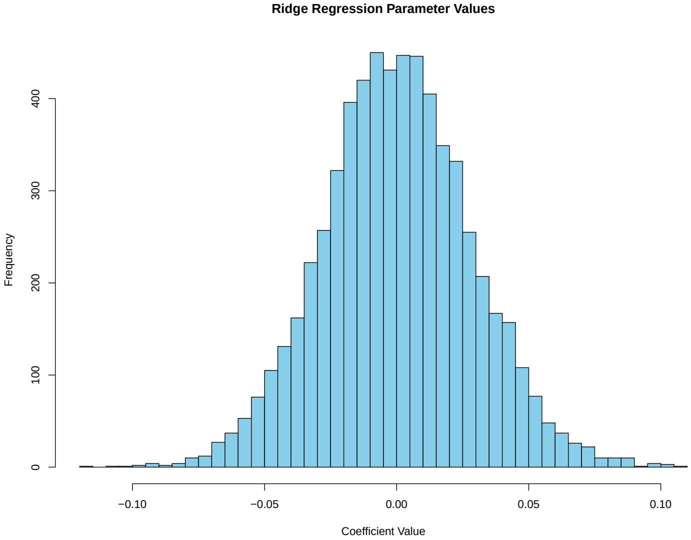

[1] From Cule & De Iorio (2012). A semi-automatic method to guide the choice of ridge parameter in ridge regression

Histogram of Ridge Coefficients



LASSO Solution

- R function selects penalty parameter λ using 10-fold CV

```
R > lasso.fit = Lasso(as.matrix(gene_expressions)[,-1], as.matrix(gene_expressions)[,1], fix.lambda = FALSE)
R > lasso.fit
$beta0
[1] 11.85041
$beta
    [1]  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000
         0.000000000  0.000000000  0.000000000  0.000000000
   [10]  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000
        0.000000000 -0.143888739  0.000000000  0.000000000
   [19]  0.113587487  0.000000000  0.000000000  0.000000000  0.000000000
        0.000000000  0.000000000  0.000000000  0.000000000
   [28]  0.000000000  0.000000000  0.000000000  0.000000000  0.000000000
        0.000000000  0.000000000  0.000000000  0.000000000
   [ reached getOption("max.print") -- omitted 6212 entries ]
$lambda
[1] 0.09383066
```

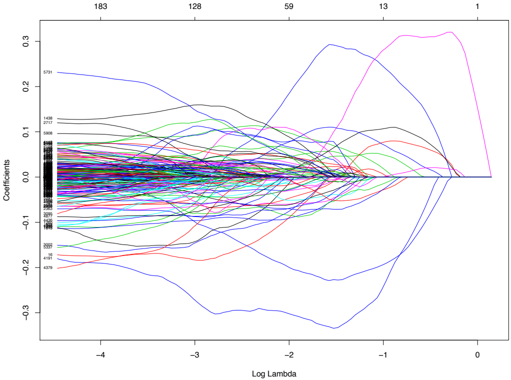
LASSO Solution Cont.

- LASSO sets most coefficients to zero. Only 84 are non-zero.

```
R > length(which(lasso.fit$beta != 0))
[1] 84
R > colnames(gene_expressions)[which(lasso.fit$beta != 0)]
  [1] "SH2B3"     "PIGK"      "ACTR2"     "MBNL2"     "POP7"      "RRAGB"
         "RBM14"     "FBLN5"     "RAD51AP1"  "RALBP1"
 [11] "GLMN"      "FILIP1L"   "AP2S1"     "CLCN4"     "ZNF384"    "DLG1"
         "AGXT"      "EPHA7"     "F12"       "FABP4"
 [21] "FCN1"      "ABCF1"     "TMCC1"     "PDS5B"     "ZHX3"      "SEPT6"
        "RRS1"      "SCFD1"     "MCF2L"     "KHNYN"
 [31] "COG4"      "ODZ4"      "GCG"       "PELP1"     "AHDC1"     "RNF115"
        "GNAT2"     "ANGPT2"    "GUCA2A"    "GZMB"
 [41] "HBD"       "HLA.DPA1"  "HSD17B1"   "IDH3B"     "ACADS"     "AQP1"
         "ITGA1"     "L1CAM"     "ST20"      "MSMB"
 [51] "MYO6"      "NFATC1"    "KRT76"     "FAM8A1"    "PIK3C2B"   "SSH1"
         "ZNF821"    "PSG11"     "PTHLH"     "GATAD1"
 [61] "RAD52"     "RGS16"     "BCL9"      "RPS4X"     "RPS27"     "CCL5"
         "SLC4A3"    "SNAPC1"    "BTG1"      "UBE2E1"
 [71] "VRK1"      "ZNF23"     "ZNF76"     "DDX39B"    "ACTL6A"    "VNN2"
         "WASF1"     "CD1D"      "MS4A3"     "NRXN1"
 [81] "TMPRSS11D" "POLR1C"    "MDC1"      "TMED10"
```

LASSO Solution Cont.

```
R > model  <- cv.glmnet(as.matrix(gene_expressions)[,-1], as.matrix(gene_expressions)[,1],  standardize=TRUE)
R > plot(model$glmnet.fit ,  ”lambda”,  label=TRUE)
```


Coefficients
Log Lambda