Supervised Learning: Penalized Regression for Other Data Types

Jean Feng & Ali Shojaie

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Data of Different Types

- ► Simple continuous response
- ► Binary response
- ► Count data
- ► Survival outcome

Different Data Need Different Models

- ► Simple continuous response: squared error
- ► Binary response: logistic loss (0-1/hinge loss for other methods)
- ► Count data: Poisson loss
- ► Survival outcome: Cox loss

Data generating mechanisms \rightarrow (log)likelihood \rightarrow Loss function

Our usual Gaussian model

$$y_i = \beta_0 + x_i^{\top} \beta + \epsilon_i$$

with ϵ_i iid $N(0, \sigma^2)$

The likelihood:

$$\mathcal{L}(\beta \mid x, y) = (2\pi\sigma^2)^{n/2} \exp{-\frac{1}{2\sigma^2} \sum_{i=1}^{n} (y_i - x_i^\top \beta)^2}$$

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our usual least squares criterion!

Logistic model

$$\log\left(\frac{p_i}{1-p_i}\right) = \beta_0 + x_i^{\top} \beta$$

with
$$p_i = P(Y_i = 1 \mid x_i)$$

The likelihood:

$$\begin{split} \mathcal{L}(\beta \mid x, y) &= &\prod_{i} \rho_{i}^{y_{i}} (1 - \rho_{i})^{(1 - y_{i})} \\ &= &\prod_{i} \mathsf{expit}(\beta_{0} + x_{i}^{\top} \beta)^{y_{i}} \Big(1 - \mathsf{expit}(\beta_{0} + x_{i}^{\top} \beta) \Big)^{(1 - y_{i})} \end{split}$$

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which is solved in logistic regression.

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► Poisson Model:

$$\log (E[y_i \mid x_i]) = \beta_0 + \beta^\top x_i$$

is used to model rare events

- ► deaths from TB each year in the US
- counts from sequencing data for gene expression
- ▶ limit of Binomial likelihood for a large number of trials with a really biased coin (e.g. $\pi = 3/1000$)

give rise to Poisson regression

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► For Poisson regression: glmnet(x,y,family = "Poisson")

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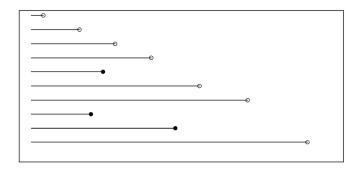
- ► Cox Model (nested multinomials):
 - \triangleright x_i : features
 - \triangleright y_i : time on study
 - \triangleright z_i : indicator of fail/censoring

Consider likelihood conditional on failure times:

$$P(\text{person } j \text{ fails at time } t \mid \text{a failure at time } t) = \frac{e^{x_j^\top \beta}}{\sum_{k \text{ at risk at } t} e^{x_k^\top \beta}}$$

We're interested in **length** of survival time...

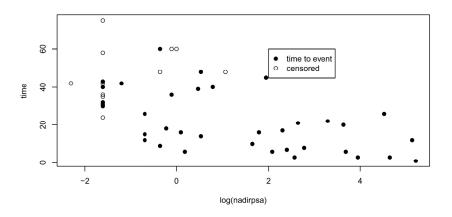
We're interested in **length** of survival time... but not everyone dies;



Survival time (all start at zero)

At random, we see survival time T or just know that T > C

Results are somewhat intuitive...



What do you think the effect of nadirpsa is?

Surv objects

The 'outcome' in survival analysis involves both an observed time and a censoring status. These are packaged in a Surv object.

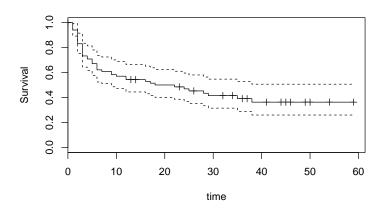
- library(survival) has many features for low-dim. data
- Surv(time, event) is the simplest form (for simple right-censoring data)
- ightharpoonup event tells R whether we saw T or just T > C
- ► Full *T*, *C* terminology a bit cumbersome, censoring is instead shown with a +

```
> library(survival)
Loading required package: splines
> tumor.surv <- with(tumor, Surv(time, event) )
> tumor.surv[1:10]
[1] 0+ 1+ 4+ 7+ 10+ 6 14+ 18+ 5 12
```

Always check this! Is your censoring setup correctly?

Survival Curves

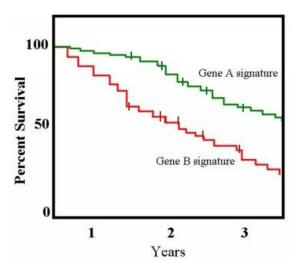
The most common, 'intuitive' summary, also known as Kaplan-Meier curves



plot(survfit(tumor.surv ~ 1))

Survival Curves

Can e.g. compare different groups



Gene B signature < Gene A signature

- ► Generally want a classification of high vs low risk:
- ► Given a Cox-model
 - ▶ with *p* genomic features
 - ightharpoonup and coefficient vector β

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How do we choose c? cross-validation! (CV survival curves)

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Can use regularization:

$$\min \ell(\beta) + \lambda \|\beta\|_1$$

Example: Gene Expression Example

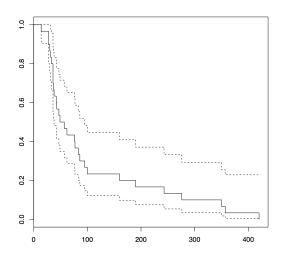
Building a prognostic classifier for patients with advanced bladder cancer receiving chemotherapy:

- ► GEO-GSE5287
- ▶ 30 patients
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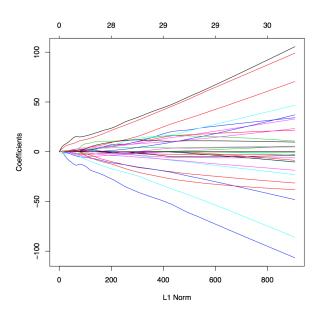
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Very easy to run lasso:

```
fit <- glmnet(X, Surv(time, status), family = "cox")
plot(fit)</pre>
```



Cross validation for KM in HD

This is a bit more tricky, as we may need to cross validate for each pair of candidate c and λ :

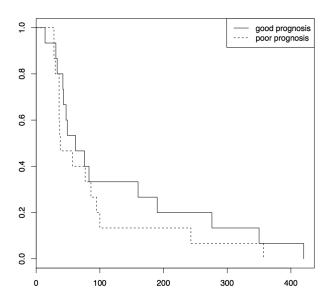
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- 1. Break data into folds
- 2. For each fold k
 - 2.1. Train on all data except kth fold to find $\hat{\beta}$
 - 2.2. Calculate score $\eta_i = x_i^{\top} \hat{\beta}$ for all i in the left-out fold
- 3. Split the data into *i* with $\eta_i \leq c$ and $\eta_i > c$
- 4. Plot KM curves!

Choose the best KM plot!

```
> unord <- match(1:30,obs.ord)
> test.pred <- matrix(0,ncol = 100, nrow = 30)
> for(fold in 1:3){
+ ind.train <- obs.ord[((fold-1)*10 + 1):(fold*10)]
+ fit.train <- glmnet(X[ind.train,], Surv(time[ind.train],status[ind.train]), family="cox")
+ test.pred[-ind.train,] <- predict(fit.train, X[-ind.train,])
+}
> k <- 80
> plot(survfit(Surv(time,status)~(test.pred[,k] > median(test.pred[,k]))),
+ lty = c(1,2))
> legend("topright", c("good prognosis","poor prognosis"), lty = c(1,2))
```



Not so great!

Log-Likelihood Recap

- ► Losses are often based on generative model or error structure
- ► Minimize Negative Log Likelihood
- ► Can add sparsity/ridge/other penalties

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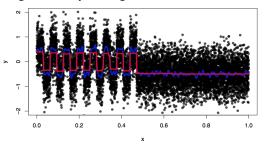
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$$\min \ell(\beta) + \lambda \sum_{k} \|\beta^{(k)}\|_2$$

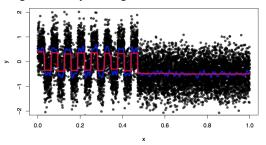
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$$\min \ell(\beta) + \lambda \sum_{j} |\beta_j - \beta_{j-1}|$$

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- ► This is a very active area of research!!