

Supervised Learning: Penalized Regression for Other Data Types

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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**

Log-Likelihood Loss

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

Log-Likelihood Loss

Our usual Gaussian model

$$y_i = \beta_0 + \mathbf{x}_i^\top \boldsymbol{\beta} + \epsilon_i$$

with ϵ_i iid $N(0, \sigma^2)$

The likelihood:

$$\mathcal{L}(\boldsymbol{\beta} \mid \mathbf{x}, \mathbf{y}) = (2\pi\sigma^2)^{n/2} \exp - \frac{1}{2\sigma^2} \sum (y_i - \mathbf{x}_i^\top \boldsymbol{\beta})^2$$

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our usual **least squares** criterion!

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Logistic model

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

with $p_i = P(Y_i = 1 \mid \mathbf{x}_i)$

The likelihood:

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which is solved in **logistic regression**.

Log-Likelihood Loss

Other examples:

Log-Likelihood Loss

Other examples:

- ▶ **Poisson Model:**

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

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")`

Log-Likelihood Loss

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Other examples:

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

Consider likelihood conditional on failure times:

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

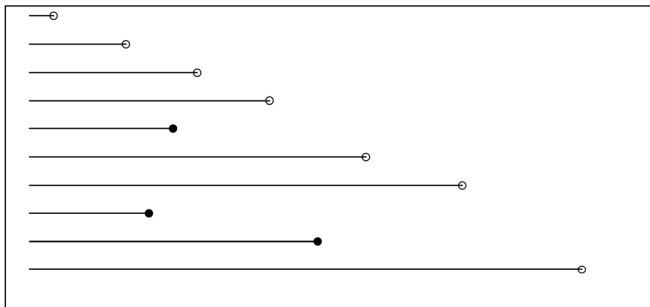
Survival Outcome

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

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

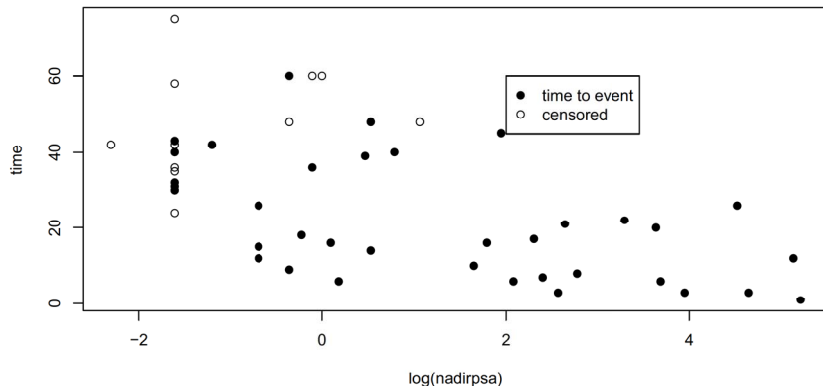


Survival time (all start at zero)

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

Survival Outcome

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.

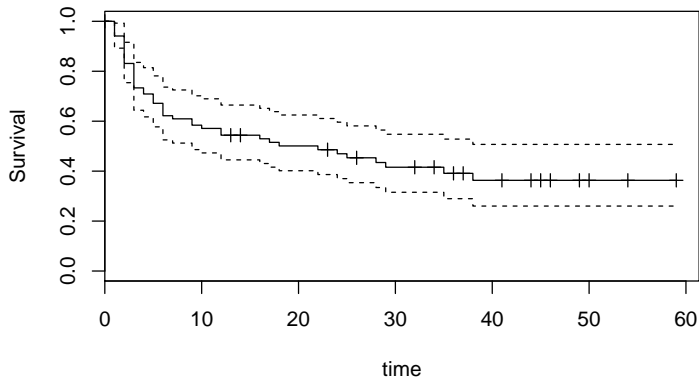
- ▶ `library(survival)` has many features for low-dim. data
- ▶ `Surv(time,event)` is the simplest form (for simple right-censoring data)
- ▶ `event` tells R whether we saw T or just $T > C$
- ▶ Full T , C terminology a bit cumbersome, censoring is instead shown with a $+$

```
> 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

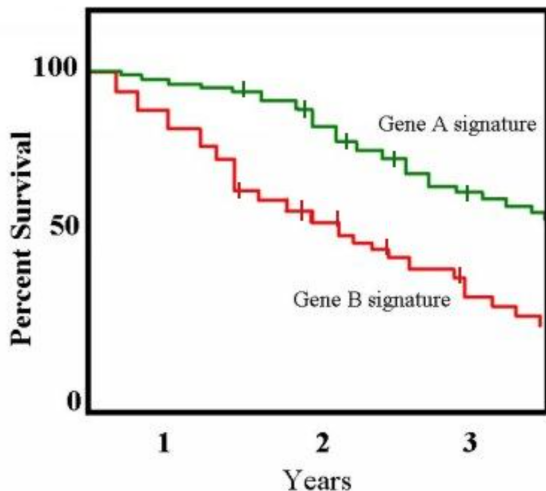
The most common, 'intuitive' summary, also known as **Kaplan-Meier** curves



```
plot(survfit(tumor.surv ~ 1))
```


Survival Curves

Can e.g. compare different groups



Gene B signature < Gene A signature

Building prognostic survival classifiers

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

We know observations with larger $x_i^\top \beta$ are higher risk!

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How do we choose c ?

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

Cox Regression in HD

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Can use regularization:

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

Example: Gene Expression Example

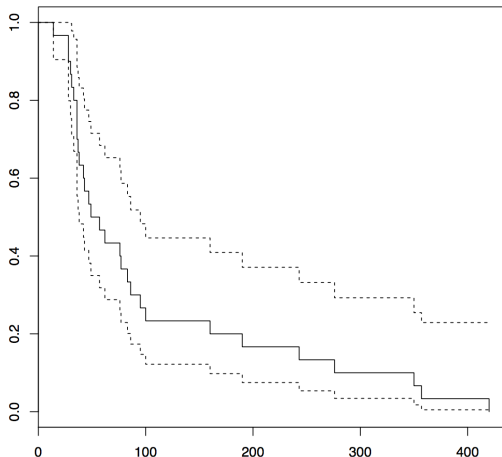
Building a prognostic classifier for patients with advanced bladder cancer receiving chemotherapy:

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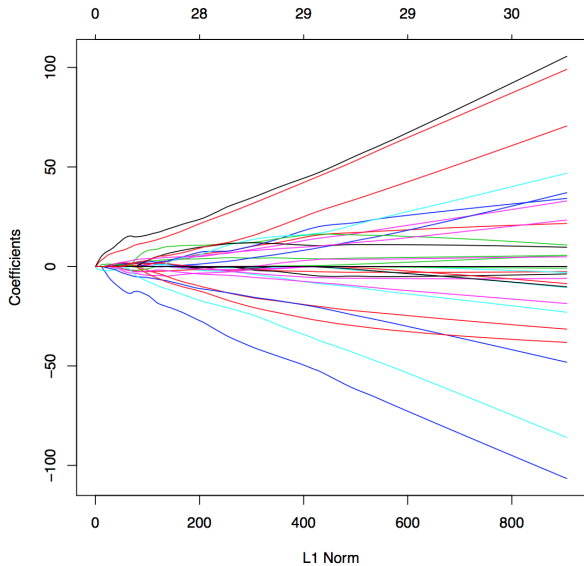


Cox Regression in HD

Very easy to run lasso:

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

Cox Regression in HD



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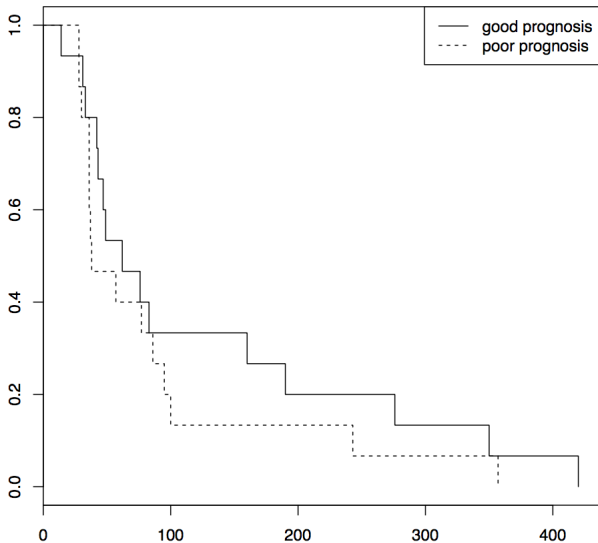
1. Break data into folds
2. For each fold k
 - 2.1. Train on all data except k th fold to find $\hat{\beta}$
 - 2.2. Calculate **score** $\eta_i = x_i^\top \hat{\beta}$ for all i in the left-out fold
3. Split the data into i with $\eta_i \leq c$ and $\eta_i > c$
4. Plot KM curves!

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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 - ▶ Genes in the same pathway
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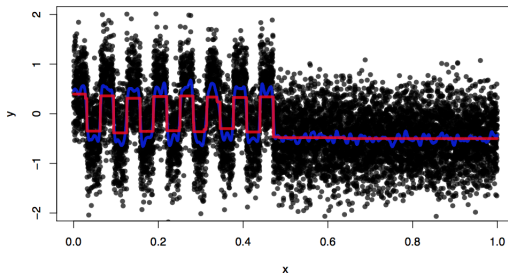
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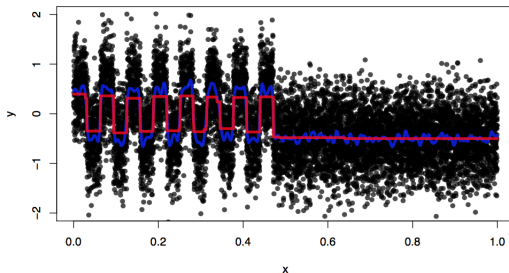
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- ▶ **Fused sparsity:**
 - ▶ To encourage similarity among consecutive covariates



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

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 - ▶ Hierarchical sparsity
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- ▶ There are various other types of penalties
 - ▶ Hierarchical sparsity
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 - ▶ ...
- ▶ This is a very active area of research!!