

# Exercises and Solutions - Analysis of High-Dimensional Data

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## 1 Diabetes data and linear regression

The data that we consider consist of 442 diabetes patients, with the response of interest being a quantitative measure of disease progression one year after baseline. There are ten baseline variables — age, sex, body-mass index, average blood pressure, and six blood serum measurements — plus quadratic terms, giving a total of  $p = 64$  features.

1. Read the diabetes data set and make a histogram for the response variable  $y$ . Describe the distribution of the variable.
2. Create a scatterplot matrix for the 5 first variables in the data set. Use `pairs` or `ggpairs`.
3. Randomly assign patients to training and test data (use `sample`).
4. Run a univariate regression model with `bmi` as covariate. Study the `summary` output.
  - How do you interpret the regression coefficients for `bmi`?
  - What is the meaning of the *multiple R-squared*?
  - What is the *residual standard error*?

- Generate a scatter plot of `y` against `bmi` and add the regression line with confidence band (use `geom_smooth, method="lm"`).
  - Draw the Tukey Anscombe plot and the QQ plot (check `?plot.lm`). What are these two plots telling us?
5. Run a multiple regression model using all covariates. Study the `summary` output.
    - What does change in the interpretation of the coefficient for `bmi`?
    - What do you conclude from the *multiple R-squared*?
    - Create a Tukey Anscombe plot and a QQ plot.
  6. Calculate the RSS for both models. Write down your observation.
  7. Compare the two models using the `anova` function. What do you conclude?

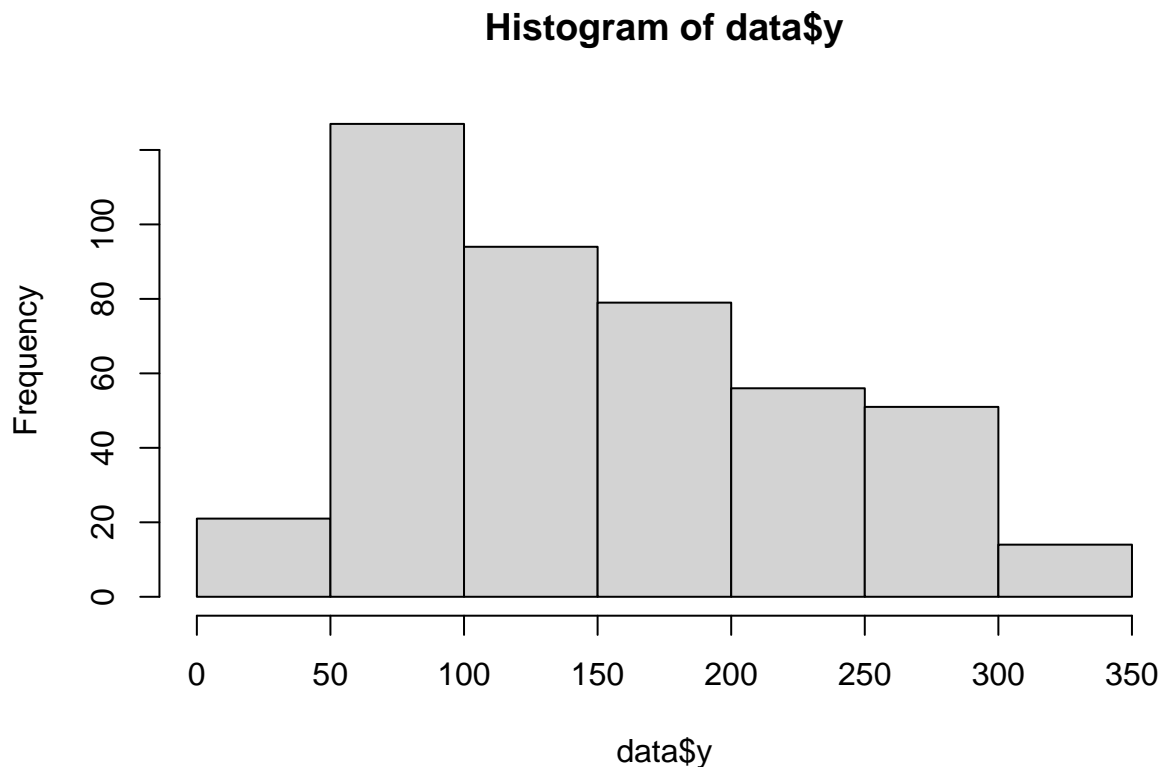
Solution to the exercise.

Read the data set.

```
diabetes <- readRDS(file="data/diabetes.rds")
data <- as.data.frame(cbind(y=diabetes$y,diabetes$x2))
colnames(data) <- gsub(":", ".", colnames(data))
```

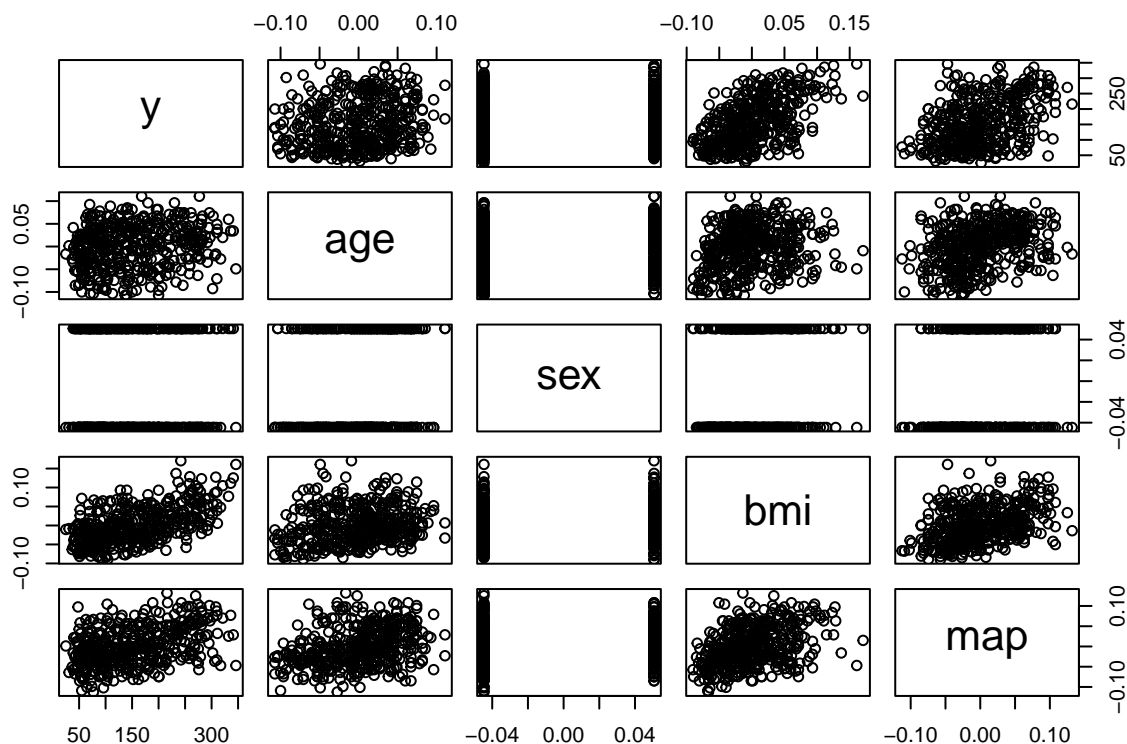
Generate a histogram of `y`.

```
hist(data$y)
```



The distribution is right-skewed. Scatterplot matrix of the diabetes data.

```
pairs(data[,1:5])
```



Create training and test data.

```
train_ind <- sample(seq(nrow(data)),size=nrow(data)/2)
data_train <- data[train_ind,]
xtrain <- as.matrix(data_train[,-1])
ytrain <- data_train[,1]
data_test <- data[-train_ind,]
xtest <- as.matrix(data_test[,-1])
ytest <- data_test[,1]
```

Fit a univariate regression model.

```
fit1 <- lm(y~bmi,data=data_train)
summary(fit1)
```

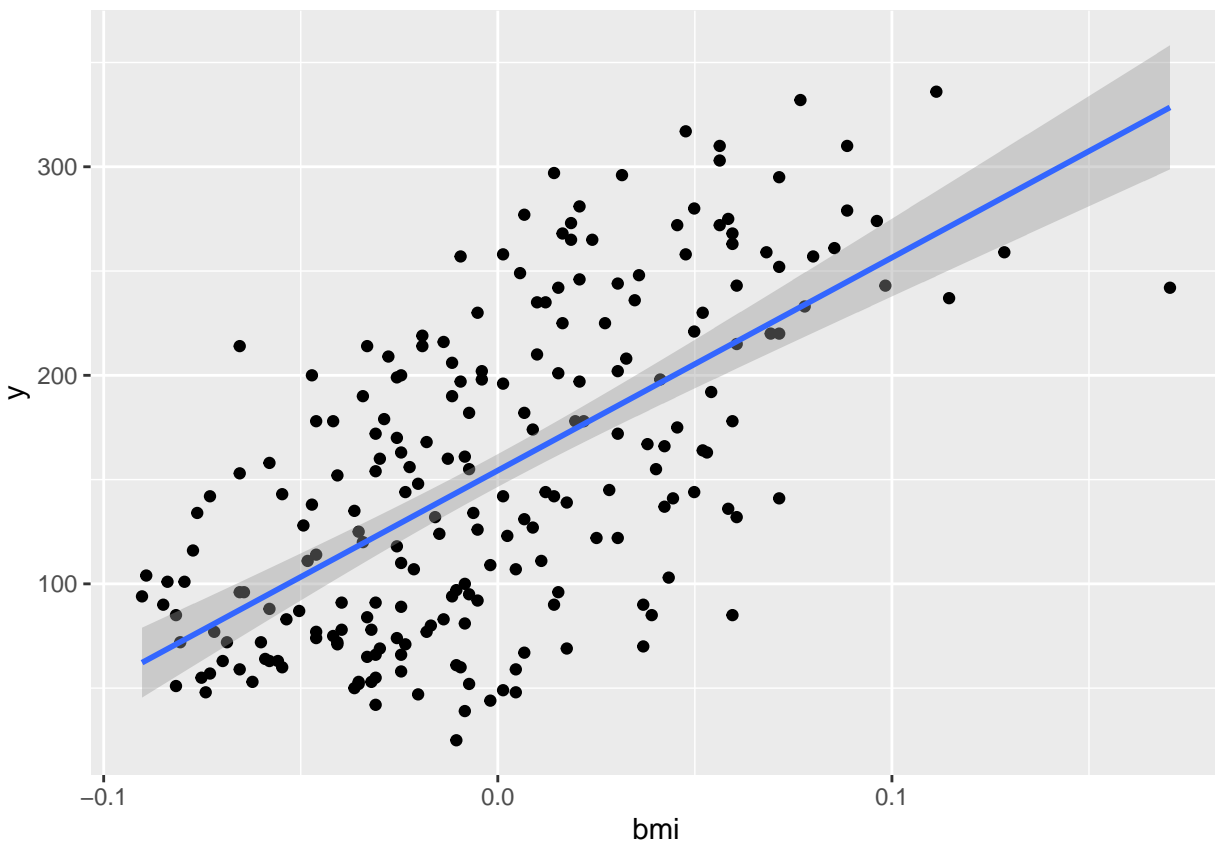
```
##
## Call:
## lm(formula = y ~ bmi, data = data_train)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -130.142  -43.428   -1.243   47.474  128.068
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   154.362     3.987   38.71  <2e-16 ***
## bmi          1020.821    84.546   12.07  <2e-16 ***
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 59.25 on 219 degrees of freedom
## Multiple R-squared:  0.3996, Adjusted R-squared:  0.3969
## F-statistic: 145.8 on 1 and 219 DF,  p-value: < 2.2e-16
```

Scatter plot with regression line.

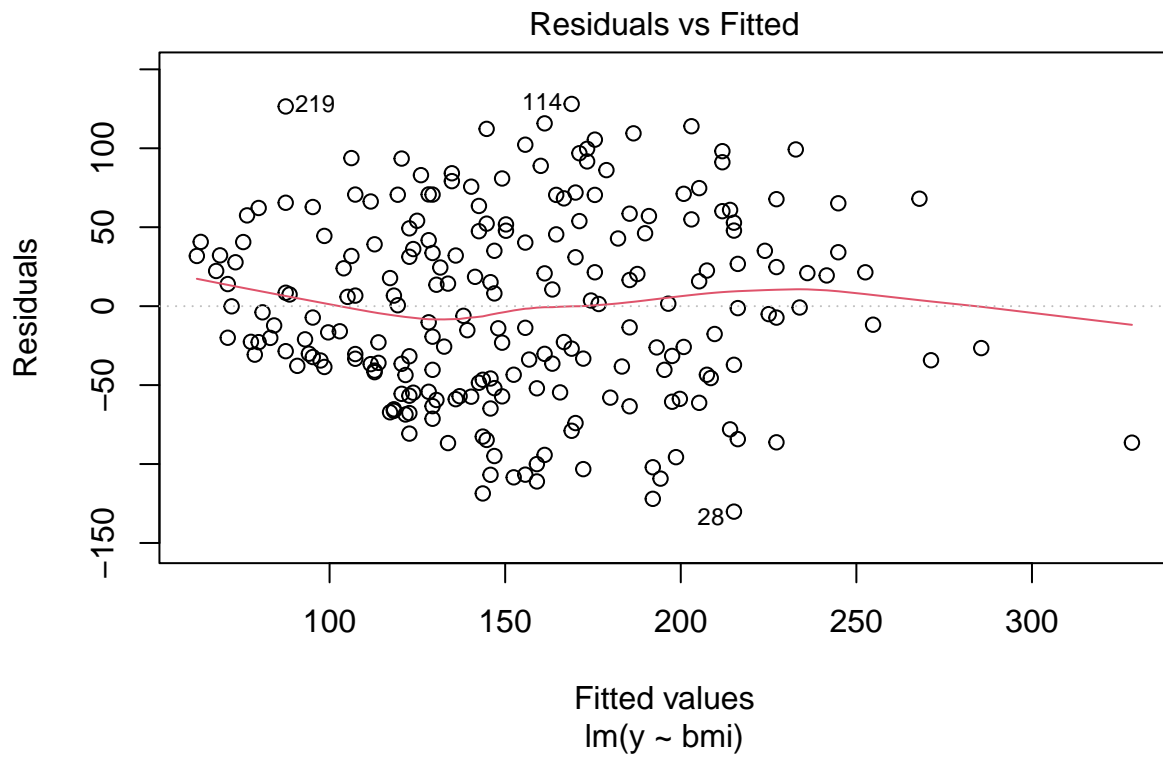
```
data_train%>%
  ggplot(data=.,aes(x=bmi,y=y))+
  geom_point()+
  geom_smooth(method="lm")
```

```
## `geom_smooth()` using formula 'y ~ x'
```



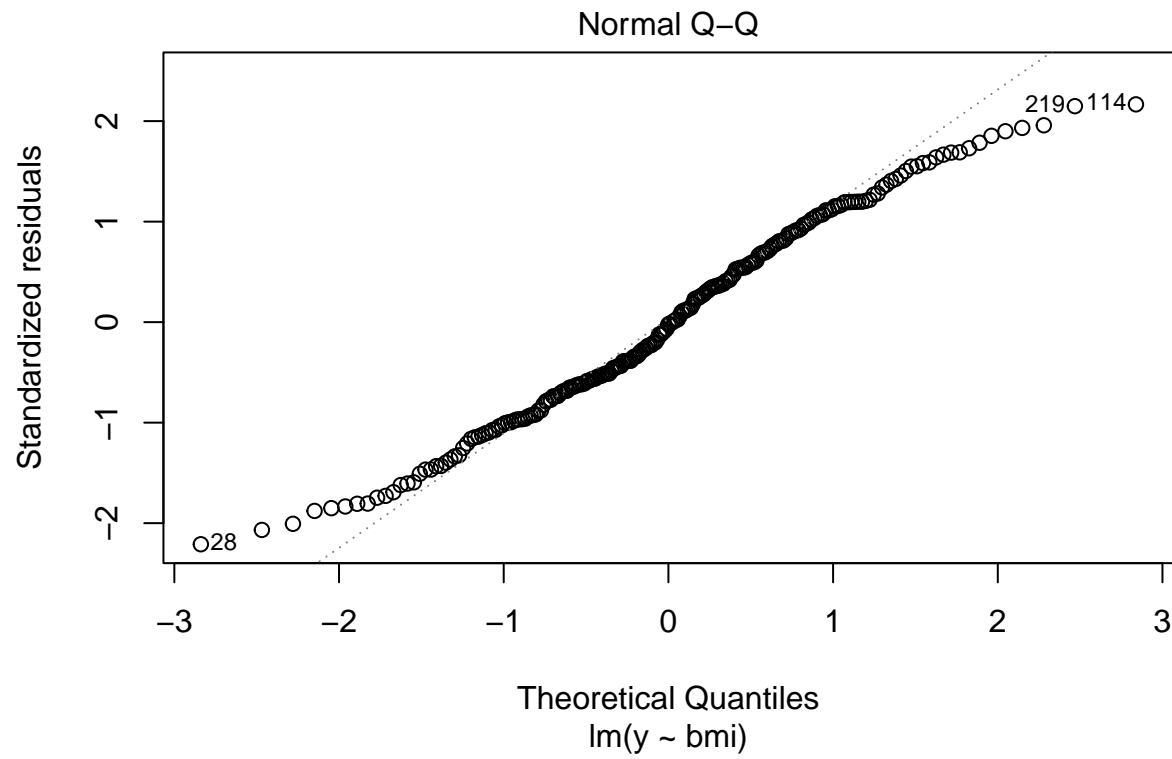
The Tukey Anscombe plot. The residuals scatter around the 0 line and do not show any systematic pattern. This indicates that the residuals are independent and have mean 0.

```
plot(fit1,which=1) # Tukey Anscombe plot
```

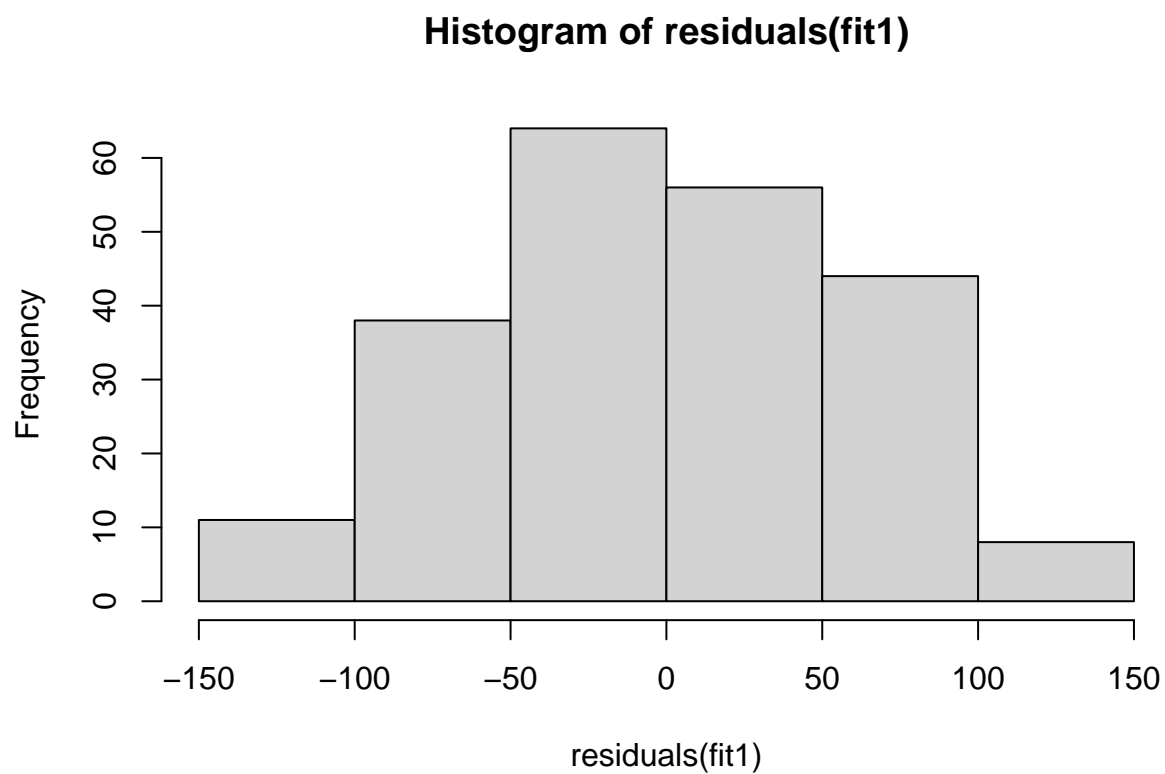


The QQ plot. This plot is used to check the normality assumption of the residuals. The residuals show slight tendency to be right-skewed (see also the histogram).

```
plot(fit1,which=2) # Tukey Anscombe plot
```

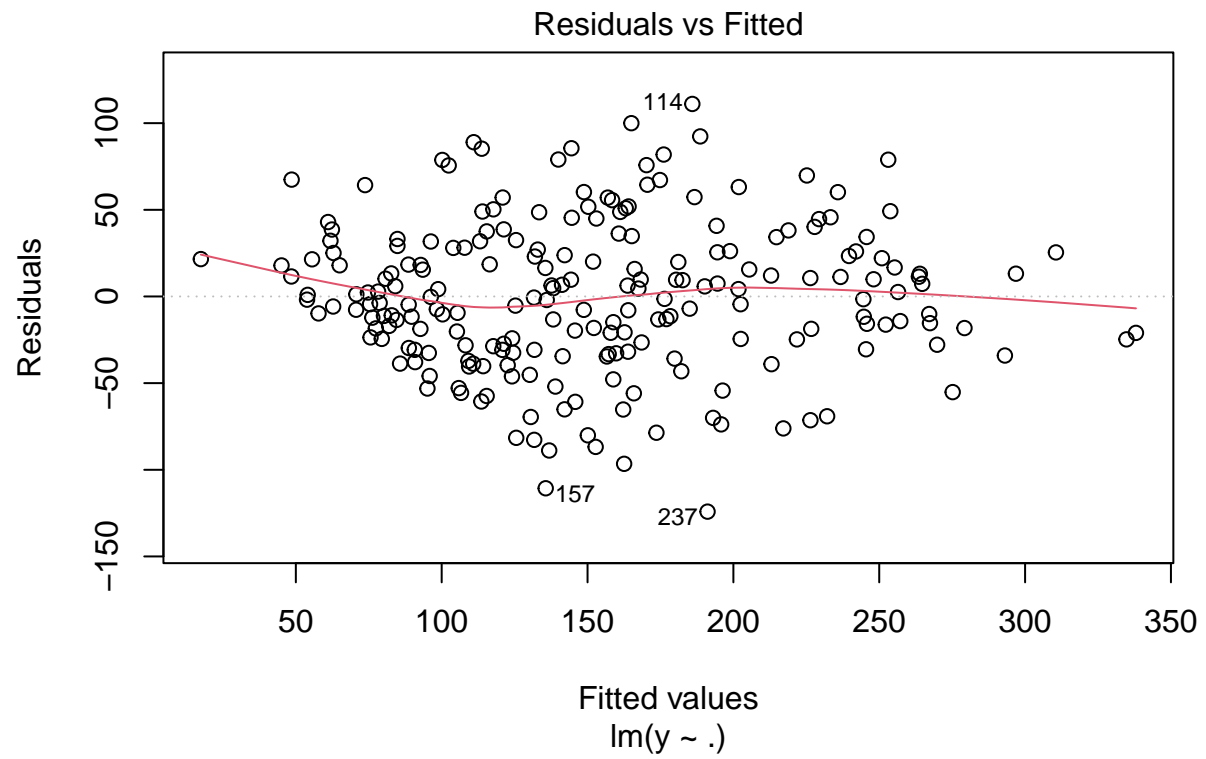


```
hist(residuals(fit1))
```



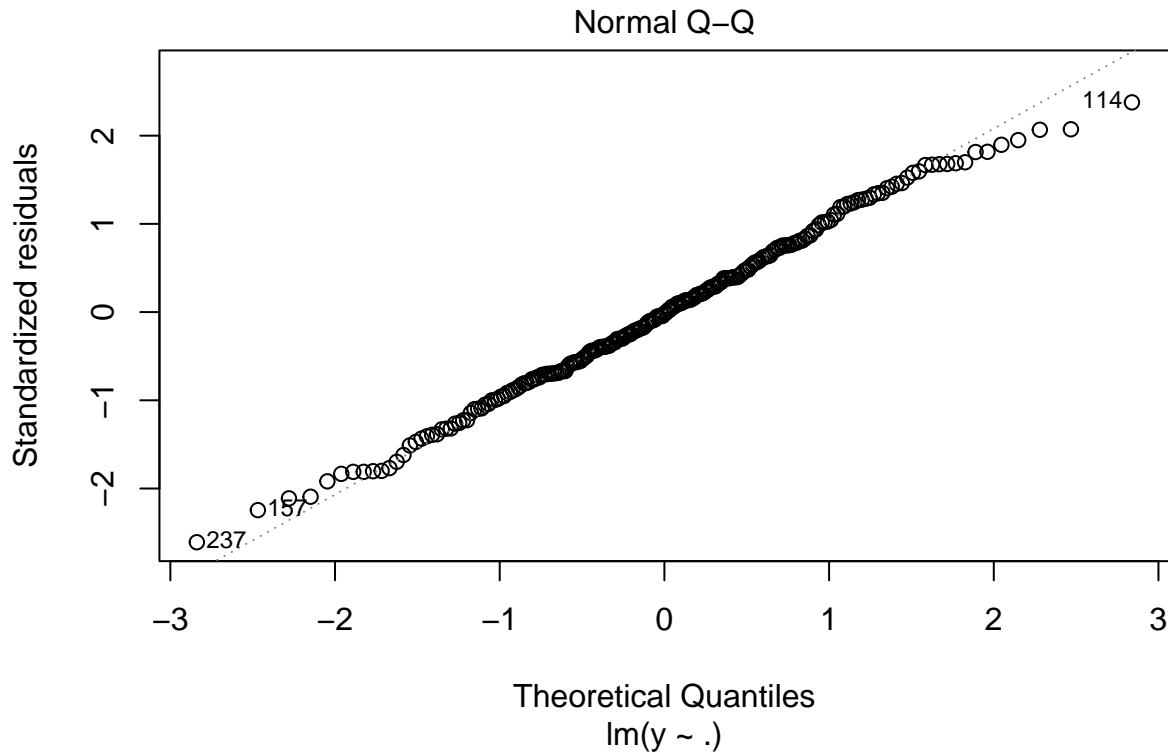
We run the multiple regression model with all covariates. We print the `summary` and create TA and QQ plots.

```
fit2 <- lm(y~.,data=data_train)
#summary(fit2)
plot(fit2,which=1)
```



```
plot(fit2, which=2)
```





Calculate the RSS.

```
sum(residuals(fit1)^2)
```

```
## [1] 768871.6
```

```
sum(residuals(fit2)^2)
```

```
## [1] 402679.3
```

Compare the 2 models using the `anova` function.

```
anova(fit1,fit2)
```

```
## Analysis of Variance Table
```

```
##
```

```
## Model 1: y ~ bmi
```

```
## Model 2: y ~ age + sex + bmi + map + tc + ldl + hdl + tch + ltg + glu +
```

```
##   `age^2` + `bmi^2` + `map^2` + `tc^2` + `ldl^2` + `hdl^2` +
```

```
##   `tch^2` + `ltg^2` + `glu^2` + age.sex + age.bmi + age.map +
```

```
##   age.tc + age.ldl + age.hdl + age.tch + age.ltg + age.glu +
```

```
##   sex.bmi + sex.map + sex.tc + sex.ldl + sex.hdl + sex.tch +
```

```
##   sex.ltg + sex.glu + bmi.map + bmi.tc + bmi.ldl + bmi.hdl +
```

```
##   bmi.tch + bmi.ltg + bmi.glu + map.tc + map.ldl + map.hdl +
```

```
##   map.tch + map.ltg + map.glu + tc.ldl + tc.hdl + tc.tch +
```

```
##   tc.ltg + tc.glu + ldl.hdl + ldl.tch + ldl.ltg + ldl.glu +
```

```
##   hdl.tch + hdl.ltg + hdl.glu + tch.ltg + tch.glu + ltg.glu
```

```
##   Res.Df    RSS Df Sum of Sq    F    Pr(>F)
```

```
## 1      219 768872
```

```
## 2      156 402679 63      366192 2.2518 2.595e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

## 2 Diabetes data and model validation

In the previous section we developed 2 models to predict  $y$ . In this section we explore the generalizability of these models.

1. Calculate the RMSEs on the training data. Which model will perform best on future data?
2. Use the test data and make scatter plots of the observed against predicted outcomes. Use `ggplot` to create one plot per model and add the regression line (`geom_smooth`) and the “ $y=x$ ” (`geom_abline`) line to the graph. This plot is also called “calibration plot”. The model is “well” calibrated if the regression line agrees with the “ $y=x$ ” line.
3. Generate boxplots of `predicted - observed` for the 2 models. What do you conclude?
4. Calculate the generalization error, i.e., the RMSE on the test data.

Solution to the exercise.

We calculate the RMSEs on the training data. RMSE on training data tells you how good the model “fits” the data. We cannot make any conclusion about the generalizability of the models based on RMSEs on training data.

```
RMSE(data_train$y,predict(fit1,newdata=data_train))
```

```
## [1] 58.98353
```

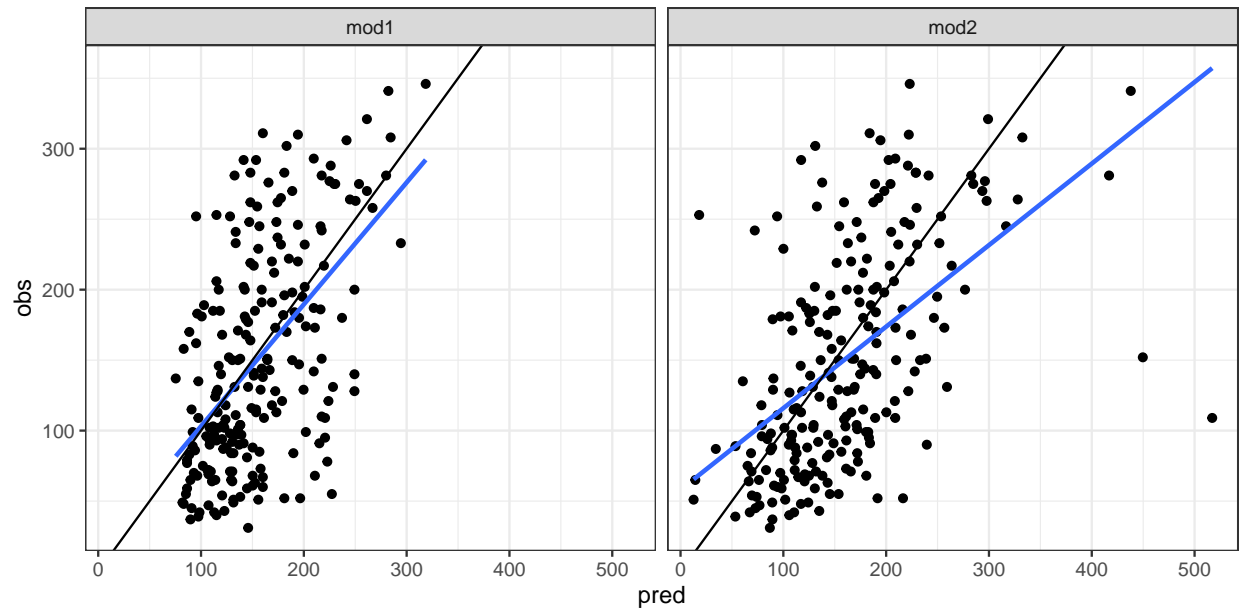
```
RMSE(data_train$y,predict(fit2,newdata=data_train))
```

```
## [1] 42.68581
```

We draw calibration plots for the 2 models. Model 1 calibrates slightly better.

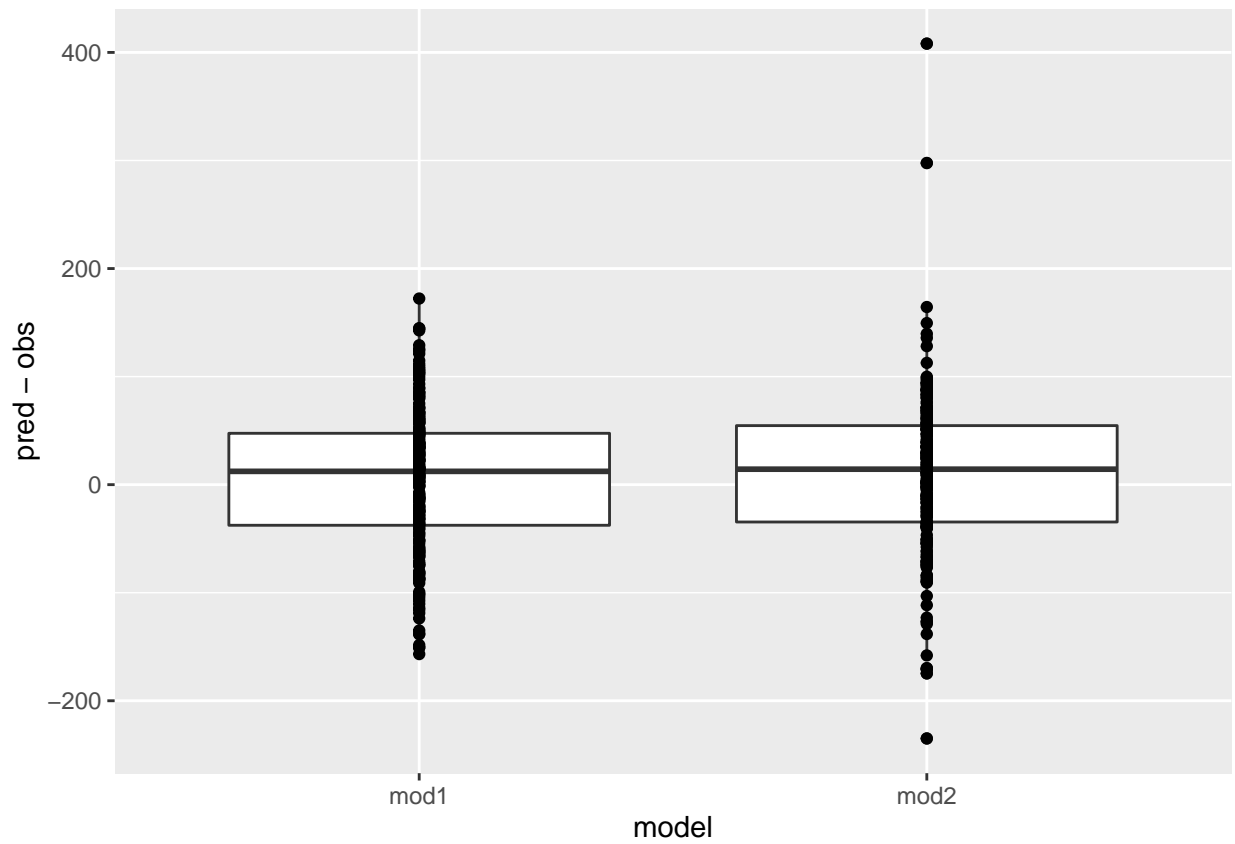
```
dd <- data.frame(pred=c(predict(fit1,newdata=data_test),
                             predict(fit2,newdata=data_test)),
                  obs = rep(data_test$y,times=2),
                  model=rep(c("mod1","mod2"),each=nrow(data_test))
)
dd%>%
  ggplot(.,aes(x=pred,y=obs))+
  geom_point()+
  geom_smooth(se=FALSE,method="lm")+
  geom_abline(slope=1,intercept=0)+
  theme_bw()+
  facet_wrap(~model)
```

```
## `geom_smooth()` using formula 'y ~ x'
```



Boxplots of predicted minus observed.

```
dd%>%
  ggplot(.,aes(x=model,y=pred-obs))+
  geom_boxplot()+
  geom_point()
```



Calculate RMSEs on test data.

```
RMSE(data_test$y, predict(fit1, newdata=data_test))
```

```
## [1] 65.83956
```

```
RMSE(data_test$y, predict(fit2, newdata=data_test))
```

```
## [1] 73.09069
```

### 3 Calculus, optimization and OLS

1. Consider the function  $f(x) = 2x^2 + x - 5$ . Draw a plot of the function.
2. Use `optimize` to find the minimum of  $f(x)$ .
3. Obtain the minimum of  $f(x)$  by taking the derivative and setting equal to zero.
4. Show that  $\|a\|_2^2 = a^T a$ .
5. Use the result in 4. and show that  $\mathbf{RSS}(\beta) = \mathbf{y}^T \mathbf{y} - 2\mathbf{y}^T \mathbf{X}\beta + \beta^T \mathbf{X}^T \mathbf{X}\beta$ .
6. Invoke the result obtained in 4. and show that

$$\frac{\partial}{\partial \beta} \mathbf{RSS}(\beta) = -2\mathbf{X}^T \mathbf{y} + 2\mathbf{X}^T \mathbf{X}\beta.$$

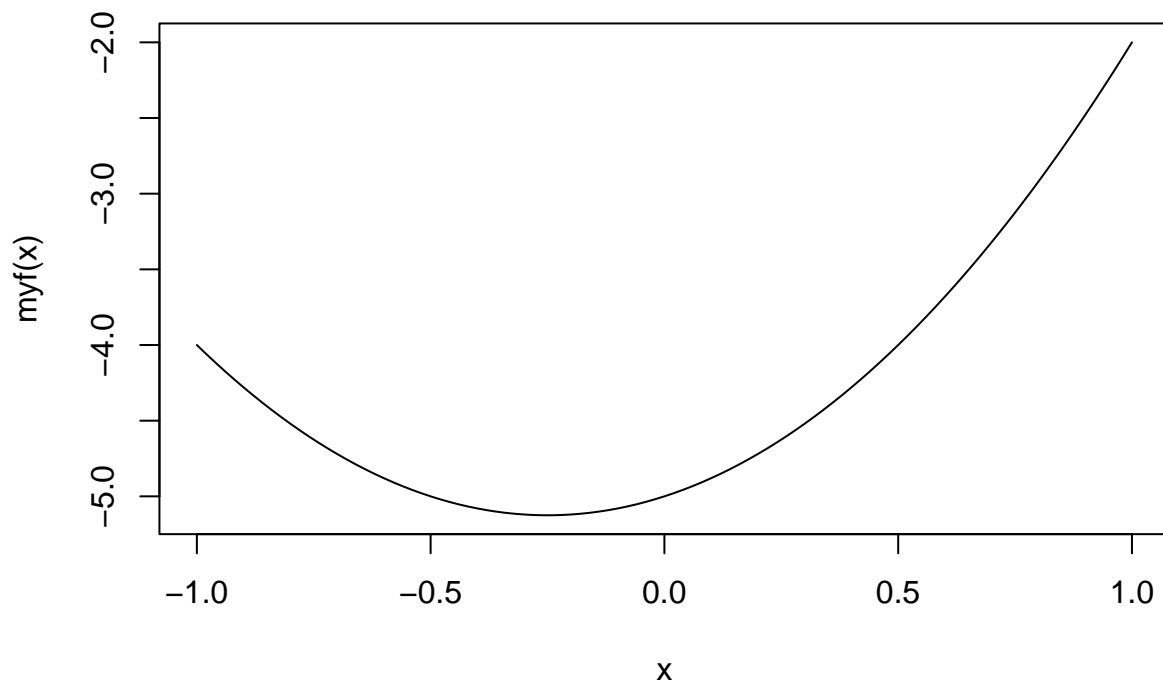
Hint: review the “Identities” section of Wikipedia.

7. Do you understand the derivation of the least squares estimator?

Solution to the exercise.

Plot of the function.

```
myf <- function(x){  
  2*x^2 + x -5  
}  
curve(myf, from=-1, to=1)
```



```
optimize(myf,interval=c(-5,5))
```

```
## $minimum
## [1] -0.25
##
## $objective
## [1] -5.125
```

## 4 Diabetes data and regularization

The task is to use the diabetes data to construct a model that predicts the response  $y$  (disease progression) based on covariates. The two hopes are, that the model would produce accurate baseline predictions of response for future patients, and also that the form of the model would suggest which covariates were important factors in disease progression.

1. Read the prostate cancer data set.
2. Run forward stepwise regression. Which is the first variable included in the selection process? Print the coefficients of the AIC-optimal model as a table.
3. Fit Ridge regression. Show the trace plot and the cross-validation plot.
4. Run the Lasso approach and show the trace and the cross-validation plots.
5. Calculate the root-mean-square errors (RMSE) for all 3 models on the test data and compare with the performance of the full model. Which model generalizes best?
6. Plot the regression coefficients for all 3 models.

The solution to this exercise.

Read the data set and create training and test data.

```

diabetes <- readRDS(file="data/diabetes.rds")
data <- as.data.frame(cbind(y=diabetes$y,diabetes$x2))
colnames(data) <- gsub(":", ".", colnames(data))
train_ind <- sample(seq(nrow(data)),size=nrow(data)/2)
data_train <- data[train_ind,]
xtrain <- as.matrix(data_train[,-1])
ytrain <- data_train[,1]
data_test <- data[-train_ind,]
xtest <- as.matrix(data_test[,-1])
ytest <- data_test[,1]

```

We perform forward stepwise regression.

```

# Forward regression
fit0 <- lm(y~1,data=data_train)
up.model <- paste("~",
  paste(
    colnames(data_train[,-1]),collapse=" + "
  )
)
fit.fw <- stepAIC(fit0,direction="forward",
  scope=list(lower=fit0,
    upper=up.model
  ),
  trace = FALSE
)
#summary(fit.fw)

```

The selection process is depicted in the following table.

```

kable(as.data.frame(fit.fw$anova),digits=2,
  booktabs=TRUE)

```

Step	Df	Deviance	Resid. Df	Resid. Dev	AIC
	NA	NA	220	1224479.0	1906.99
+ bmi	1	432530.48	219	791948.5	1812.68
+ ltg	1	147003.16	218	644945.4	1769.31
+ age.sex	1	35078.91	217	609866.4	1758.95
+ bmi.map	1	25028.66	216	584837.8	1751.68
+ tch.glu	1	19656.88	215	565180.9	1746.13
+ map	1	12391.56	214	552789.3	1743.23
+ sex	1	8803.80	213	543985.6	1741.68
+ tch	1	15827.49	212	528158.1	1737.16
+ age.hdl	1	6044.29	211	522113.8	1736.61
+ map.glu	1	4928.04	210	517185.7	1736.52
+ sex.bmi	1	4853.26	209	512332.5	1736.43
+ sex.ldl	1	5863.58	208	506468.9	1735.89
+ ldl.tch	1	4589.59	207	501879.3	1735.88
+ hdl	1	4721.73	206	497157.6	1735.79

The regression coefficients and the corresponding statistics of the AIC-optimal model are shown next.

```

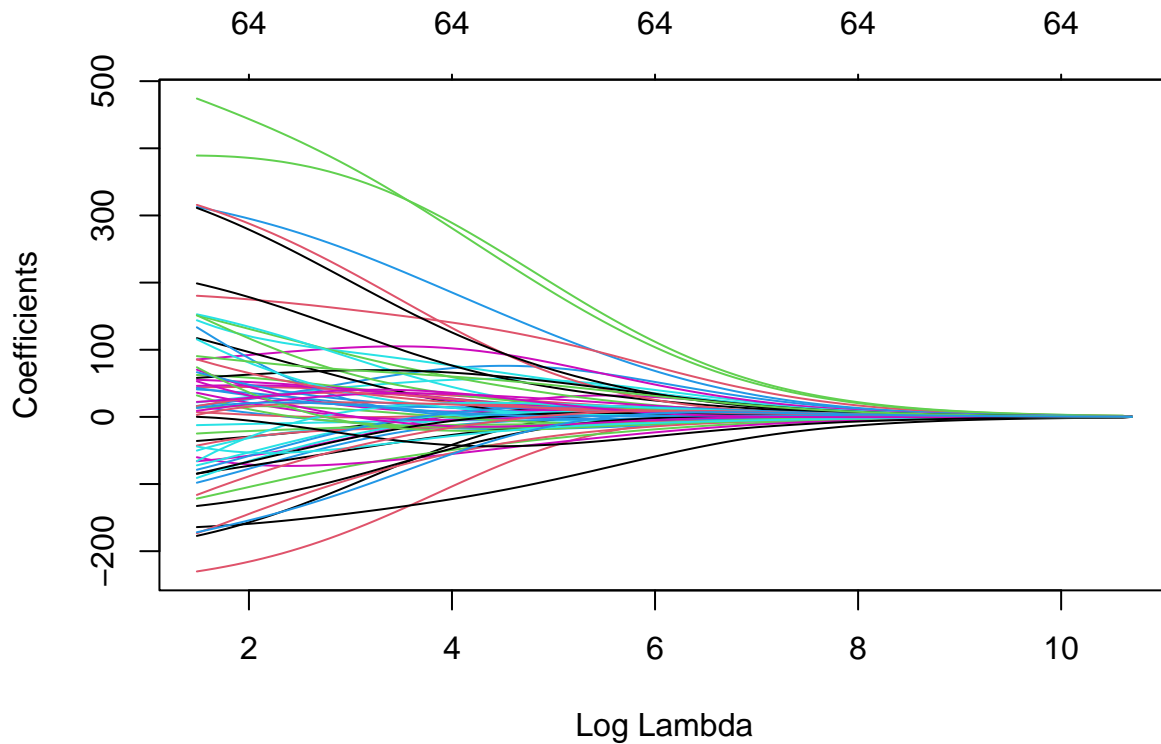
kable(broom::tidy(fit.fw),digits=2,
  booktabs=TRUE)

```

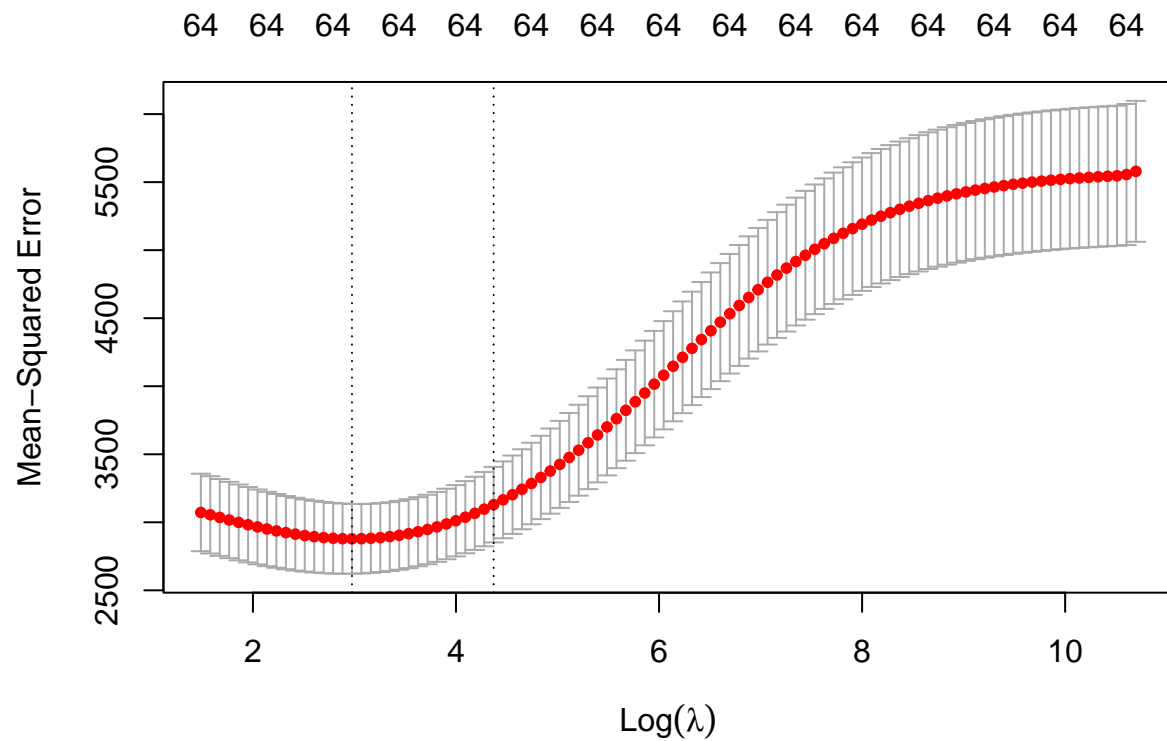
term	estimate	std.error	statistic	p.value
(Intercept)	149.48	3.36	44.46	0.00
bmi	498.45	90.20	5.53	0.00
ltg	508.36	97.22	5.23	0.00
age.sex	325.74	78.25	4.16	0.00
bmi.map	273.15	81.50	3.35	0.00
tch.glu	172.41	82.21	2.10	0.04
map	284.36	81.90	3.47	0.00
sex	-228.89	82.47	-2.78	0.01
tch	124.08	137.12	0.90	0.37
age.hdl	127.70	75.31	1.70	0.09
map.glu	-148.64	84.25	-1.76	0.08
sex.bmi	148.88	79.45	1.87	0.06
sex.ldr	-175.30	86.71	-2.02	0.04
ldr.tch	165.13	114.47	1.44	0.15
hdl	-151.10	108.02	-1.40	0.16

We continue by fitting Ridge regression. We show the trace plot and the cross-validation plot.

```
# Ridge
set.seed(1515)
fit.ridge <- glmnet(xtrain,ytrain,alpha=0)
fit.ridge.cv <- cv.glmnet(xtrain,ytrain,alpha=0)
plot(fit.ridge,xvar="lambda")
```



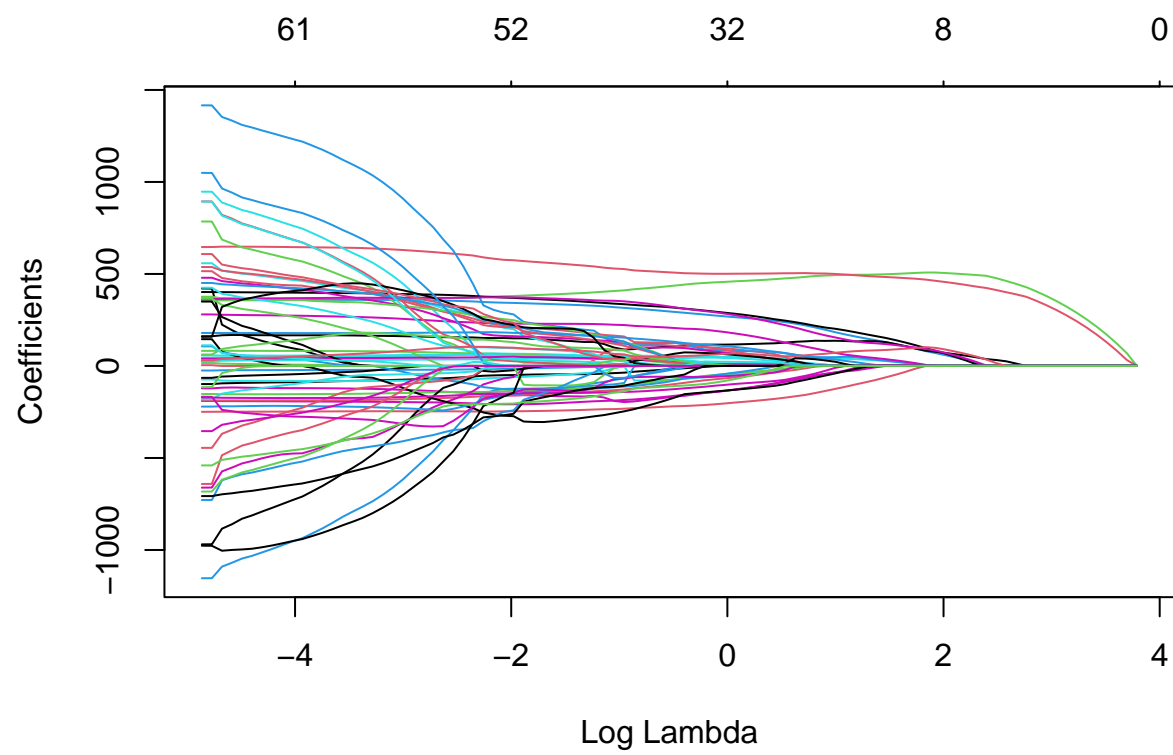
```
plot(fit.ridge.cv)
```



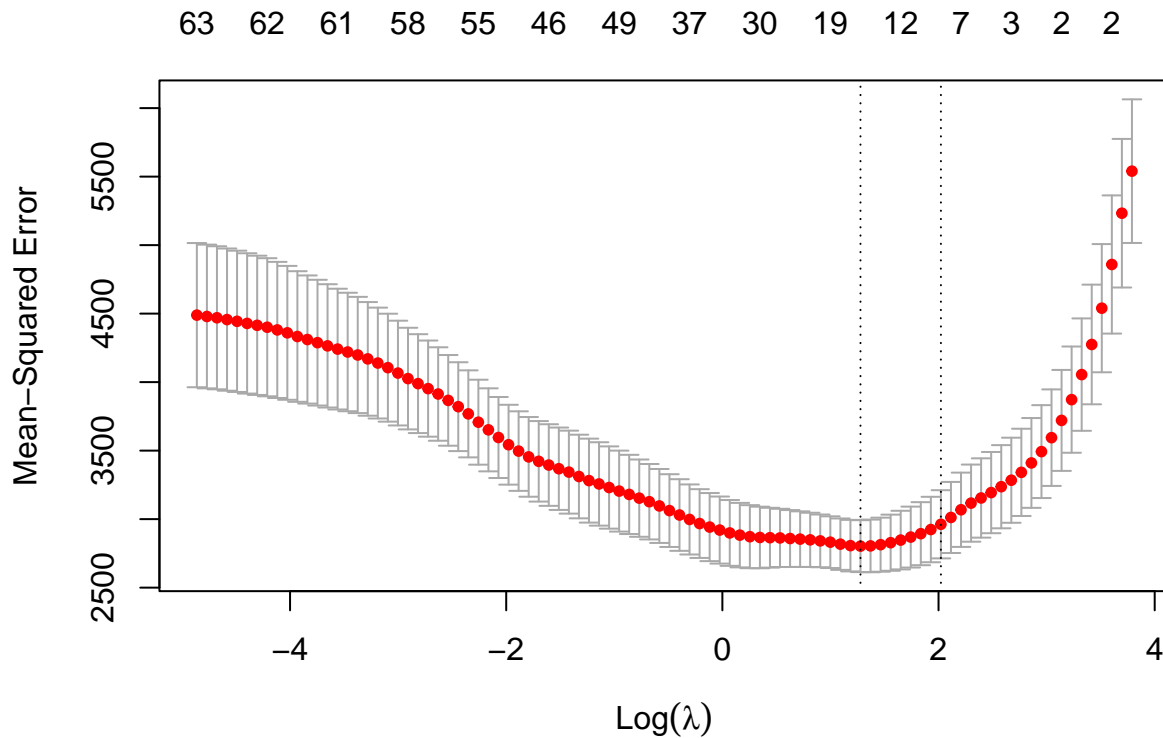
Finally, we run the Lasso approach and show the trace and the cross-validation plots.

```
# Lasso
set.seed(1515)
fit.lasso <- glmnet(xtrain,ytrain,alpha=1)
fit.lasso.cv <- cv.glmnet(xtrain,ytrain,alpha=1)
plot(fit.lasso,xvar="lambda")
```





```
plot(fit.lasso.cv)#fit.lasso.cv$lambda.1se
```

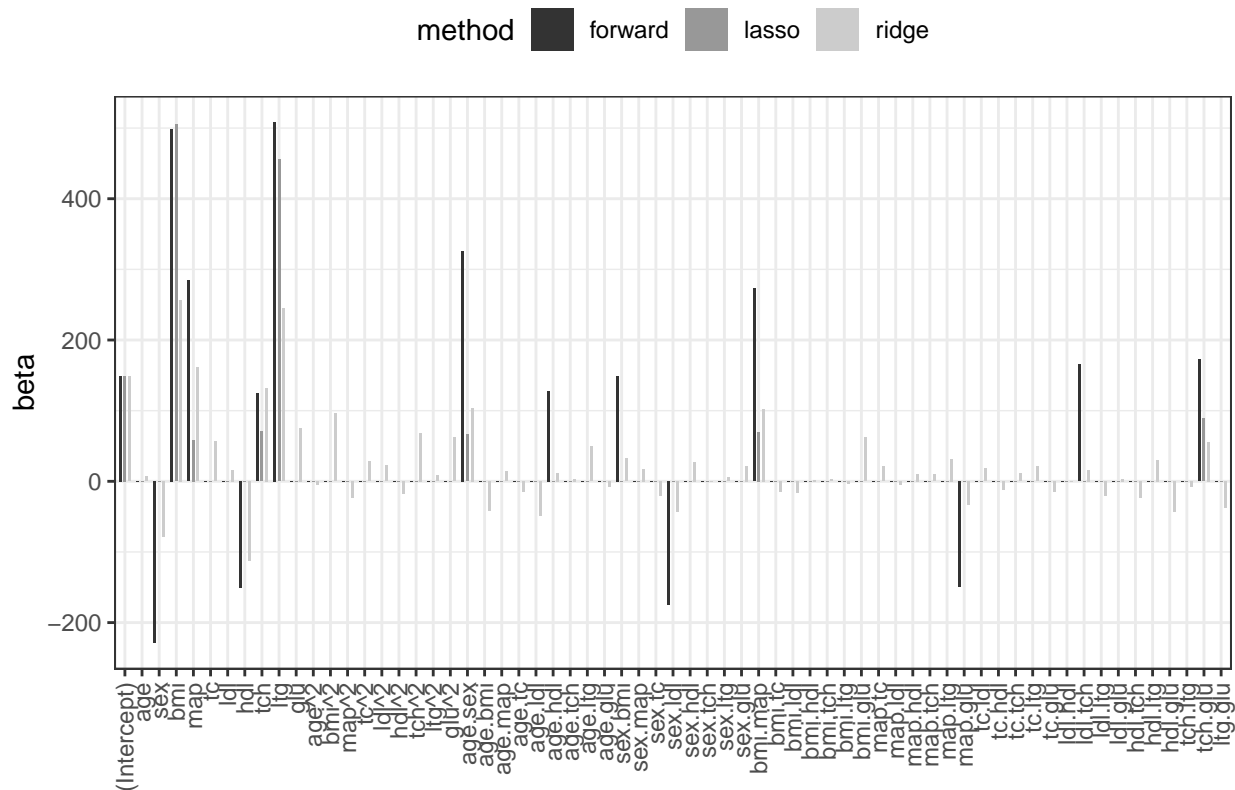


We calculate the root-mean-square errors (RMSE) on the test data and compare with the full model.

```
# Full model
fit.full <- lm(y~.,data=data_train)
# RMSE
pred.full <- predict(fit.full,newdata=data_test)
pred.fw <- predict(fit.fw,newdata=data_test)
pred.ridge <- as.vector(predict(fit.ridge,newx=xtest,s=fit.ridge.cv$lambda.1se))
pred.lasso <- as.vector(predict(fit.lasso,newx=xtest,s=fit.lasso.cv$lambda.1se))
res.rmse <- data.frame(
  method=c("full","forward","ridge","lasso"),
  rmse=c(RMSE(pred.full,ytest),RMSE(pred.fw,ytest),RMSE(pred.ridge,ytest),RMSE(pred.lasso,ytest)))
kable(res.rmse,digits = 2,
      booktabs=TRUE)
```

method	rmse
full	77.72
forward	60.54
ridge	61.96
lasso	59.43

The Lasso has the lowest generalization error (RMSE). We plot the regression coefficients for all 3 methods.



## 5 Closed form solution for Ridge regression

1. Show that the Ridge optimization problem has the closed form solution

$$\hat{\beta}_{\lambda}^{\text{Ridge}} = (\mathbf{X}^T \mathbf{X} + \lambda \mathbf{I})^{-1} \mathbf{X}^T \mathbf{y}.$$

Hint: calculate the gradient of the loss function  $\ell_{\text{Ridge}}(\beta|\mathbf{y}, \mathbf{X}) = \text{RSS}(\beta) + \lambda \|\beta\|_2^2$ , set equal to zero and solve for  $\beta$ .

2. Use the code below to generate simulated data. Use the formula from the script to calculate the Ridge coefficients for  $\lambda = 35$ . Compare the coefficients with those obtained using `glmnet`. Hint: Read the following blog on how to scale the  $\lambda$ .

```
set.seed(1)

# simulate data
n <- 20
p <- 15
x <- matrix(rnorm(n * p), n, p)
y <- x[,1:4] %*% c(2, -2, 2, -2) + rnorm(n)
```

Solution to the exercise.

## Closed form solution for Ridge regression

$$\hat{\beta}_c^{\text{ridge}} = \underset{\|\beta\|_2^2 \leq c}{\operatorname{argmin}} \quad \|y - X\beta\|_2^2$$

Lagrange multiplier

$$\Leftrightarrow \quad \underset{\text{minimize}}{\quad} \underbrace{\|y - X\beta\|_2^2 + \lambda \|\beta\|_2^2}_{\equiv \mathcal{L}(\beta)}$$

$$\Leftrightarrow \quad \frac{\partial \mathcal{L}(\beta)}{\partial \beta} \stackrel{!}{=} 0$$

$$\|y - X\beta\|_2^2 = (y - X\beta)^T (y - X\beta) = \cancel{y^T y} - \cancel{y^T X \beta} - \cancel{\beta^T X^T y} + \beta^T \cancel{X^T X \beta}$$

$\downarrow \frac{\partial}{\partial \beta} \quad \downarrow \frac{\partial}{\partial \beta} \quad \downarrow \frac{\partial}{\partial \beta}$   
 $0 \quad X^T y \quad X^T y \quad 2X^T X \beta$

$$\Rightarrow \frac{\partial}{\partial \beta} \|y - X\beta\|_2^2 = -2X^T y + 2X^T X \beta$$

$$\|\beta\|_2^2 = \sum_{j=1}^p \beta_j^2 \quad \Rightarrow \quad \frac{\partial}{\partial \beta} \|\beta\|_2^2 = 2\beta$$

$$\Rightarrow \quad \frac{\partial \mathcal{L}(\beta)}{\partial \beta} = -2X^T y + 2X^T X \beta + \lambda 2\beta \stackrel{!}{=} 0$$

$$\Leftrightarrow \quad X^T X \beta + \lambda \beta \stackrel{!}{=} X^T y$$

$$\Leftrightarrow \quad (X^T X + \lambda I) \beta \stackrel{!}{=} X^T y$$

$$\Leftrightarrow \quad \hat{\beta} = (X^T X + \lambda I)^{-1} X^T y$$

□

We obtain the Ridge coefficients using `glmnet`.

```
my.lambda <- 35
fit.ridge <- glmnet(x,y,alpha=0,lambda=my.lambda,
                    intercept=FALSE,standardize = FALSE,thresh = 1e-20,exact=TRUE)
coef.ridge <- as.vector(coef(fit.ridge))[-1]
head(coef.ridge)
```

```
## [1] 0.27330465 -0.24799766 0.19686435 -0.21942808 0.05302251 -0.02458886
```

Next we calculate the coefficients based on the formula from the script. Note that we need to re-scale the lambda.

```
sd_y <- sqrt(var(y)*(n-1)/n)[1,1]
my.lambda2 <- n*my.lambda/sd_y
coef.ridge2 <- solve(t(x)%*%x+my.lambda2*diag(nrow=ncol(x)))%*%t(x)%*%y
head(coef.ridge2)[,1]
```

```
## [1] 0.27031012 -0.24528806 0.19469189 -0.21696366 0.05244081 -0.02429057
```

## 6 Bayesian interpretation of Ridge regression (difficult)

1. Write down the log-likelihood of the linear regression model. Note:  $Y_i = X_i^T \beta + \epsilon_i$ , where  $\epsilon_1, \dots, \epsilon_n$  iid  $N(0, \sigma^2)$  and  $\mathbf{X}$  is a fixed  $n \times p$  design matrix.
2. Find the expression for the maximum likelihood estimator.
3. Assuming a prior distribution  $\beta_1, \dots, \beta_p$  iid  $\sim N(0, \tau^2)$ , derive the posterior distribution of  $\beta$  and show that the maximum a posteriori estimator (MAP) coincides with the Ridge estimator.

The solution to this exercise.

## Likelihood of linear regression

$$p(y_i | x_i, \beta, \sigma^2) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{(y_i - x_i^T \beta)^2}{2\sigma^2}\right)$$

$$\log p(y_i | x_i, \beta, \sigma^2) \propto -\log \sigma - \frac{(y_i - x_i^T \beta)^2}{2\sigma^2}$$

$$\log p(y | X, \beta, \sigma^2) = \sum_{i=1}^n \log p(y_i | x_i, \beta, \sigma^2) \propto -n \log \sigma - \frac{1}{2\sigma^2} \|Y - X\beta\|_2^2$$

## Maximum Likelihood for linear regression

$$A) \max_{\beta} \log p(y | X, \beta, \sigma^2) \Leftrightarrow \min_{\beta} \|Y - X\beta\|_2^2 \Leftrightarrow \hat{\beta}^{OLS}$$

$$B) \max_{\sigma} \log p(y | X, \beta, \sigma^2) \Leftrightarrow \frac{\partial}{\partial \sigma} \log p(y | X, \beta, \sigma^2) \stackrel{!}{=} 0$$

$$\frac{\partial}{\partial \sigma} \log p(y | X, \hat{\beta}^{OLS}, \sigma^2) = \frac{-n}{\sigma} + \frac{1}{2\sigma^3} \|Y - X\hat{\beta}^{OLS}\|_2^2 \stackrel{!}{=} 0$$

$$\hat{\sigma}^2 = \frac{\|Y - X\hat{\beta}^{OLS}\|_2^2}{n}$$

## Posteriori distribution

$$p(\beta | y, X) = \frac{p(y | X, \beta) p(\beta)}{p(y | X)} \propto -p \log \tau - \frac{1}{2\tau^2} \|\beta\|_2^2$$

$$\log p(\beta | y, X) \propto \log p(y | X, \beta) + \log p(\beta) \\ \propto -n \log \sigma - \frac{1}{2\sigma^2} \|Y - X\beta\|_2^2 - p \log \tau - \frac{1}{2\tau^2} \|\beta\|_2^2$$

$$\Rightarrow \max_{\beta} \log p(\beta | y, X) \Leftrightarrow \min_{\beta} \|Y - X\beta\|_2^2 + \left(\frac{\sigma^2}{\tau^2}\right) \|\beta\|_2^2$$

## 7 Elastic net mixing parameter and cross-validation

1. Load the `hdi` package and read the riboflavin data set (`?riboflavin`).
2. Run the Lasso and generate the trace plot.
3. Run the Elastic net with mixing parameters  $\alpha = 0.25, 0.5, 0.75$  and 1 and compare the cross-validation curves. Hint: use the `foldid` argument in `glmnet`.
4. Show the selected genes for the best performing model.

The solution to this exercise.

We first load the data and check the data structure.

```
library(hdi)
```

```
## Loading required package: scalreg
```

```
library(glmnet)
```

```
riboflavin <- readRDS(file="data/riboflavin.rds")
```

```
str(riboflavin)
```

```
## 'data.frame': 71 obs. of 2 variables:
```

```
## $ y: num -6.64 -6.95 -7.93 -8.29 -7.31 ...
```

```
## $ x: 'AsIs' num [1:71, 1:4088] 8.49 7.64 8.09 7.89 6.81 ...
```

```
## ..- attr(*, "dimnames")=List of 2
```

```
## .. ..$ : chr [1:71] "b_Fbat107PT24.CEL" "b_Fbat107PT30.CEL" "b_Fbat107PT48.CEL" "b_Fbat107PT52.CEL"
```

```
## .. ..$ : chr [1:4088] "AADK_at" "AAPA_at" "ABFA_at" "ABH_at" ...
```

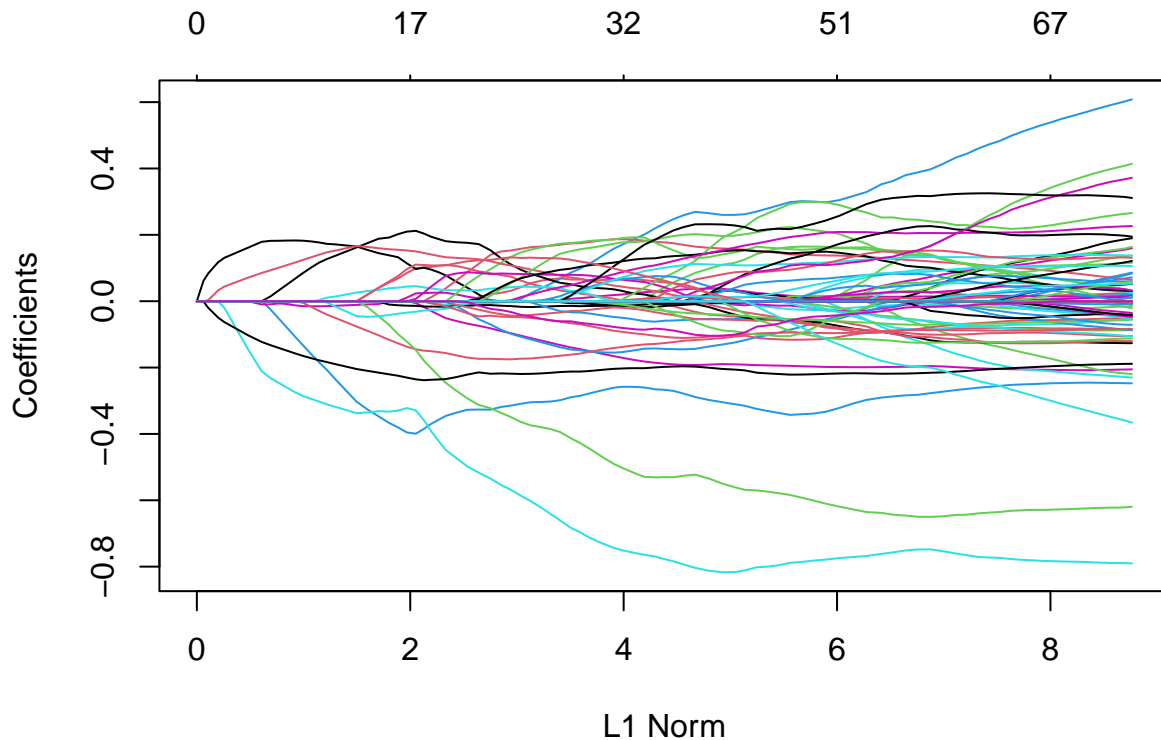
Next we setup the design matrix and the response variable and we run the Lasso.

```
x <- riboflavin[,-1]
```

```
y <- riboflavin[,1]
```

```
fit <- glmnet(x = x, y = y)
```

```
plot(fit)
```



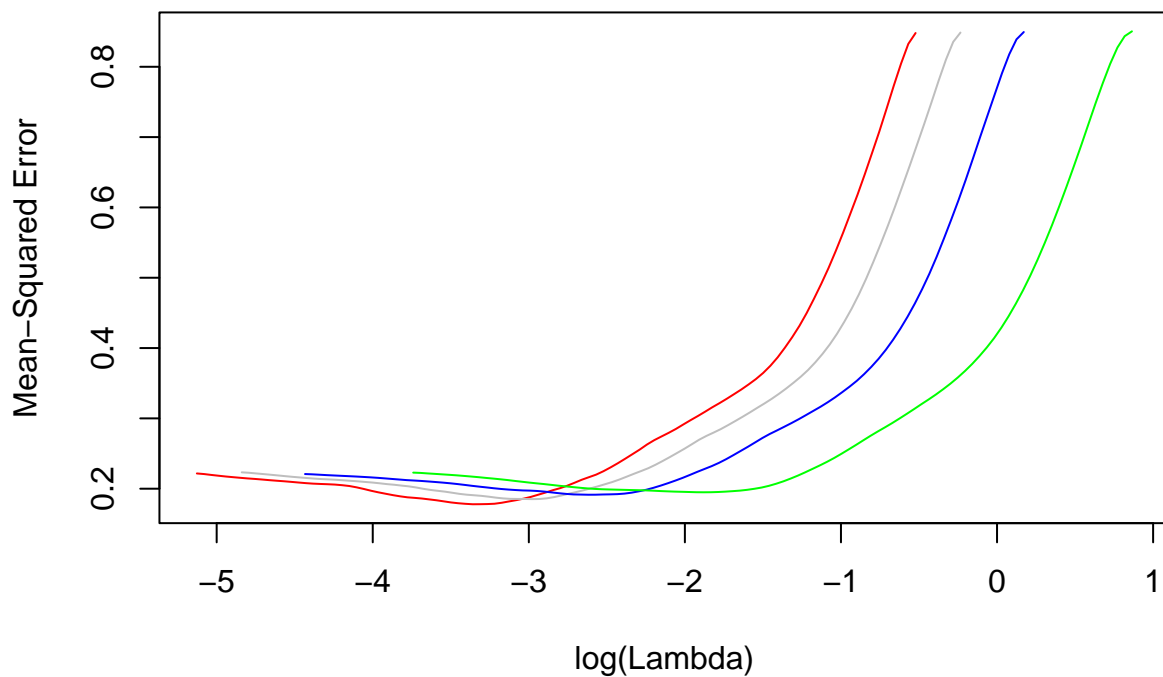
We run 10-fold cross-validation for the different mixing parameters and plot the error curves.

```
set.seed(1)
n.fold <- 10
foldid <- sample(1:n.fold, size = length(y), replace = TRUE)
cv1 <- cv.glmnet(x, y, foldid = foldid, alpha = 1)
cv2 <- cv.glmnet(x, y, foldid = foldid, alpha = 0.75)
cv3 <- cv.glmnet(x, y, foldid = foldid, alpha = 0.5)
cv4 <- cv.glmnet(x, y, foldid = foldid, alpha = 0.25)

t.lambdarange <- range(log(c(cv1$lambda,
                           cv2$lambda,
                           cv3$lambda,
                           cv4$lambda)))

t.crange <- range(c(cv1$cvm, cv2$cvm, cv3$cvm, cv4$cvm))
plot(log(cv1$lambda), cv1$cvm,
     pch = 19, col = "red",
     xlab = "log(Lambda)",
     ylab = cv1$name,
     type = "l",
     xlim = t.lambdarange,
     ylim = t.crange)
lines(log(cv2$lambda), cv2$cvm, pch = 19, col = "grey")
lines(log(cv3$lambda), cv3$cvm, pch = 19, col = "blue")
lines(log(cv4$lambda), cv4$cvm, pch = 19, col = "green")
```





Finally, we print the gene names of the non-zero coefficients.

```
## Get selected genes
b <- as.matrix(coef(cv1))
rownames(b)[b!=0]
```

```
## [1] "(Intercept)" "ARGF_at"      "DNAJ_at"      "GAPB_at"      "LYSC_at"      "PKSA_at"      "SPOIISA_at"
## [10] "XKDS_at"      "XTRA_at"      "YBFI_at"      "YCDH_at"      "YCGO_at"      "YCKE_at"      "YCLB_at"
## [19] "YDDK_at"      "YEBC_at"      "YEZB_at"      "YFHE_r_at"    "YFIR_at"      "YHDS_r_at"    "YKBA_at"
## [28] "YRVJ_at"      "YTGB_at"      "YURQ_at"      "YXLD_at"      "YXLE_at"      "YYDA_at"
```

```
## By default, the selected variables are based on the largest value of
## lambda such that the cv-error is within 1 standard error of the minimum
```

## 8 Ridge and Lasso for the orthonormal design (difficult)

1. Calculate the Ridge and the Lasso solution for the special case of an orthonormal design matrix.

The solution to this exercise.

## Ridge and Lasso for orthonormal design

orthonormal design  $\Rightarrow \boxed{X^T X = I}$

$$\hat{\beta}^{OLS} = (X^T X)^{-1} X^T y = X^T y$$

Note:  $\hat{\beta}^{OLS T} \hat{\beta}^{OLS} = y^T X X^T y$

$$\begin{aligned} \|y - X\beta\|_2^2 &= (y - X\beta)^T (y - X\beta) \because \\ &= y^T y - y^T X\beta - \beta^T X^T y + \beta^T X^T X \beta \\ &= y^T y - 2 \beta^T \underbrace{X^T y}_{\hat{\beta}^{OLS}} + \beta^T \beta \\ &\propto -2 \beta^T \hat{\beta}^{OLS} + \beta^T \beta \end{aligned}$$

$$\begin{aligned} \text{Ridge: } \frac{\partial}{\partial \beta} (-2 \beta_j \hat{\beta}_j^{OLS} + \beta_j^2 + \lambda \beta_j^2) &\stackrel{!}{=} 0 \\ -2 \hat{\beta}_j^{OLS} + 2 \beta_j + 2 \lambda \beta_j &\stackrel{!}{=} 0 \\ \Rightarrow (1 + \lambda) \beta_j &\stackrel{!}{=} \hat{\beta}_j^{OLS} \\ \Rightarrow \hat{\beta}_j^{ridge} &\stackrel{!}{=} \frac{1}{1 + \lambda} \hat{\beta}_j^{OLS} \end{aligned}$$

$$\text{Lasso: } \frac{\partial}{\partial \beta} (-2 \beta_j \hat{\beta}_j^{OLS} + \beta_j^2 + \lambda |\beta_j|) \stackrel{!}{=} 0$$

$$\text{If } \beta_j \neq 0 \quad -\hat{\beta}_j^{OLS} + \beta_j + \frac{\lambda}{2} \text{sgn}(\beta_j) \stackrel{!}{=} 0$$

$$\Rightarrow \hat{\beta}_j^{ridge} = \text{sgn}(\hat{\beta}_j^{OLS}) \left( |\hat{\beta}_j^{OLS}| - 0.5 \lambda \right)_+$$

## 9 Logistic regression and splines

We explore logistic regression based on the South African heart disease data. Proceed as follows:

1. Fit a univariate logistic regression model with **age** as the covariate. Calculate the odds-ratio and elaborate on the interpretation.
2. Predict the probability of heart disease at age 65.
3. Fit a logistic regression model including all covariates. Run stepwise backward selection. Which variables are excluded? What is the AIC value of the final model?
4. Fit a logistic regression model using four natural cubic spline bases for each term in the model. Run backward selection and summarise the final model. Plot the natural cubic spline functions for the age term (use **termplot**). What does the plot tell you?

The solution to this exercise.

We load the data and fit a logistic regression with age as the covariate.

```
sahd <- readRDS(file="data/sahd.rds")
fit <- glm(chd~age, data=sahd, family=binomial )
summary(fit)

##
## Call:
## glm(formula = chd ~ age, family = binomial, data = sahd)
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.4321  -0.9215  -0.5392   1.0952   2.2433
##
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept) -3.521710    0.416031  -8.465  < 2e-16 ***
## age          0.064108    0.008532   7.513 5.76e-14 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 596.11  on 461  degrees of freedom
## Residual deviance: 525.56  on 460  degrees of freedom
## AIC: 529.56
##
## Number of Fisher Scoring iterations: 4
```

The odds ratio for age is given next.

```
exp(coef(fit)[2])
```

```
##      age
## 1.066208
```

This means that an increase of 1 year in age leads to a 6.6% increase in the odds of having a heart disease.

The estimated probability of having a heart disease at age 65 can be calculated using the **predict** function.

```
predict(fit,newdata=data.frame(age=65),type="response")
```

```
##      1
```

```
## 0.6559532
```

Alternatively, we can use the inverse logit formula.

```
lp <- coef(fit)[1]+coef(fit)[2]*65  
exp(lp)/(exp(lp)+1)
```

```
## (Intercept)  
## 0.6559532
```

We fit a logistic regression model including all covariates. Then we perform stepwise backward selection using stepAIC.

```
fit.full <- glm(chd~sbp+tobacco+ldl+famhist+obesity+alcohol+age,  
               data=sahd,  
               family="binomial")  
fit.bw <- stepAIC(fit.full,direction = "backward",trace=FALSE)
```

The terms removed in each step are provided in the next table.

```
kable(as.data.frame(fit.bw$anova),digits=3,booktabs=TRUE)
```

Step	Df	Deviance	Resid. Df	Resid. Dev	AIC
	NA	NA	454	483.174	499.174
- alcohol	1	0.019	455	483.193	497.193
- sbp	1	1.104	456	484.297	496.297
- obesity	1	1.147	457	485.444	495.444

The variables alcohol, sbp and obesity are excluded from the model. The AIC values are provided in the table above. We can also re-calculate the AIC for the final model.

```
AIC(fit.bw)
```

```
## [1] 495.4439
```

We fit a logistic regression model using natural splines.

```
# Computes the logistic regression model using natural splines (note famhist is included as a factor):  
form <- "chd ~ ns(sbp,df=4) + ns(tobacco,df=4) + ns(ldl,df=4) + famhist + ns(obesity,df=4)+ ns(alcohol  
form <- formula(form)  
fit <- glm( form, data=sahd, family=binomial )  
  
# stepwise backward selection  
fit.bw <- stepAIC(fit,direction="backward",trace = 0)  
kable(as.data.frame(fit.bw$anova),digits=3,booktabs=TRUE)
```

Step	Df	Deviance	Resid. Df	Resid. Dev	AIC
	NA	NA	436	457.632	509.632
- ns(alcohol, df = 4)	4	0.456	440	458.088	502.088

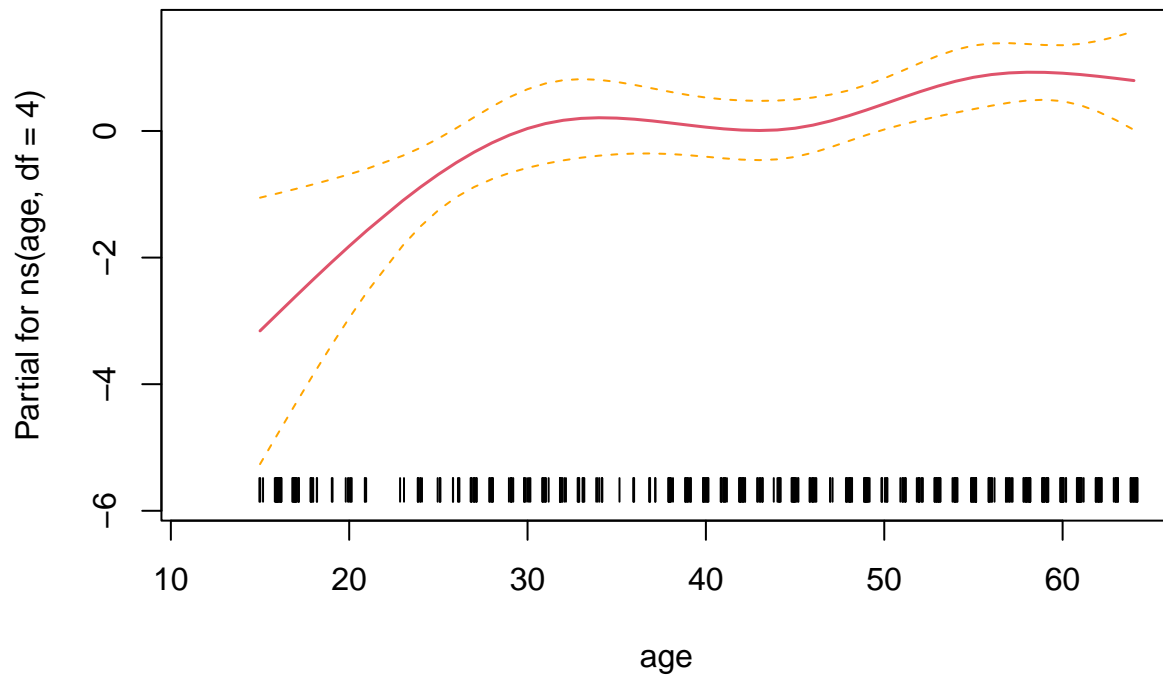
The summary of the final model is provided next.

```
kable(as.data.frame(drop1(fit.bw, test="Chisq" )),digits=2,booktabs=TRUE)
```

	Df	Deviance	AIC	LRT	Pr(>Chi)
	NA	458.09	502.09	NA	NA
ns(sbp, df = 4)	4	467.16	503.16	9.08	0.06
ns(tobacco, df = 4)	4	470.48	506.48	12.39	0.01
ns(ldl, df = 4)	4	472.39	508.39	14.31	0.01
famhist	1	479.44	521.44	21.36	0.00
ns(obesity, df = 4)	4	466.24	502.24	8.15	0.09
ns(age, df = 4)	4	481.86	517.86	23.77	0.00

We can plot the natural spline function for the first term as follows.

```
termplot(fit.bw, se=TRUE, rug=TRUE, term=6)
```



The plot shows how the log-odds change with age (keeping the other variables fixed). We observe a slight deviation from linearity, i.e. the log-odds increase more strongly for age <35 than for age >35.

## 10 Decision trees, Random Forest and AdaBoost

In this exercise we explore decision trees based on the South African heart disease data.

1. Load the South African heart disease data and grow a decision tree using `rpart`. Visualize the tree using `rpart.plot`. How many leaf nodes has the tree?
2. Re-grow the tree but now relax the “default” control parameters (choose `rpart.control(cp=0, minsplit=50)`). How many leaves has the tree now?
3. Plot the cross-validation error against the complexity parameter  $\alpha$ . What is the tree size of the optimal model?

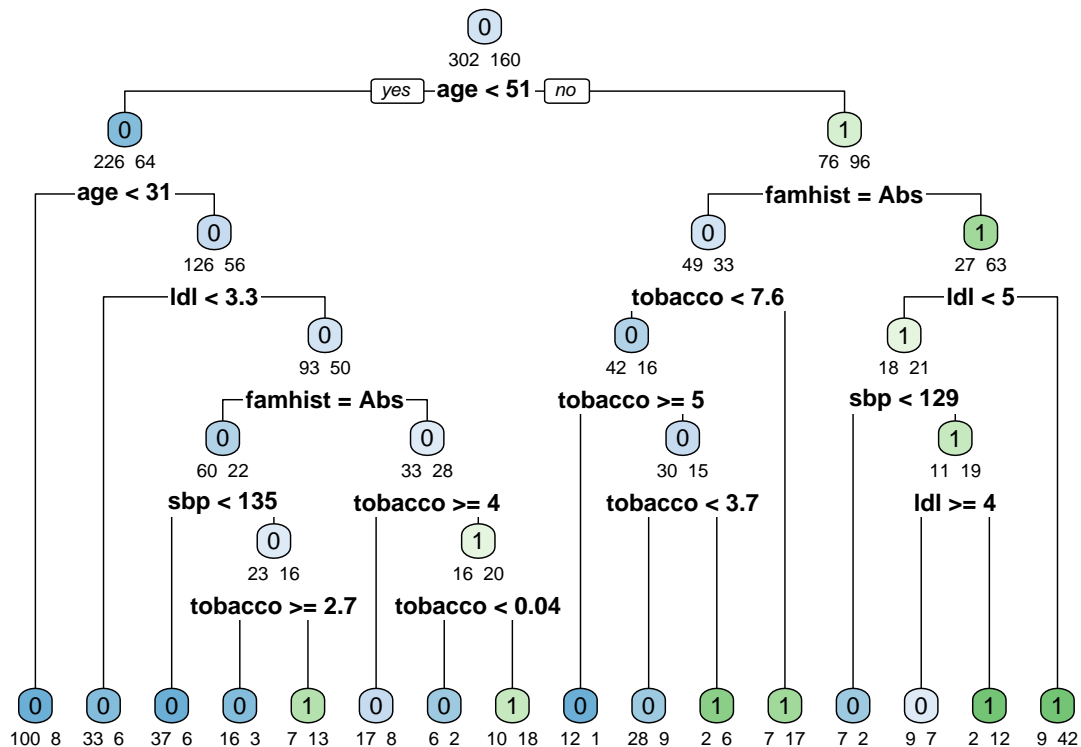
4. Prune the tree using `prune` and by choosing `cp` ( $=\alpha$ ) to achieve minimal cross-validation error.
5. Calculate the confusion matrix and the misclassification error.
6. Generate a bootstrap sample. Grow a tree and calculate the out-of-bag error.
7. Fit a random forest using `randomForest`. Plot the fitted object. What is this plot telling us? Calculate the variable importance. Which are the most important variables?
8. Run AdaBoost using `gbm`. What is the prediction for a patient with covariates `sbp=100`, `tobacco=0`, `ldl=5`, `famhist="Present"`, `obesity=25`, `alcohol=10` and `age=50`. Compute the variable importance.

The solution to this exercise.

First we read the data and grow the tree.

```
# load packages
library(rpart)
library(rpart.plot)

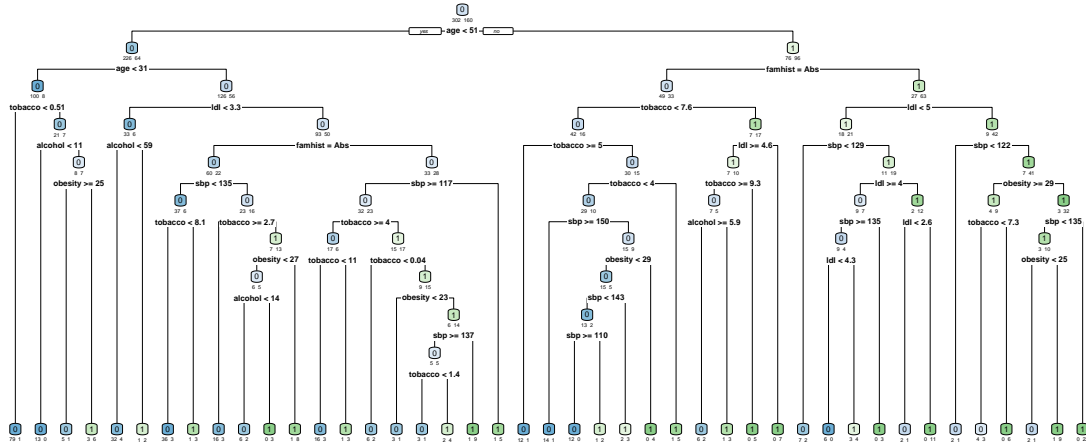
# grow a classification tree
fit.tree <- rpart(chd~.,data=sahd,method="class")
rpart.plot(fit.tree,extra=1,under=TRUE,tweak = 1.2,faclen=3)
```



We re-grow the tree using different control parameters.

```
# controlling the growth of the tree with rpart.control
# cp: improvement in each split needs to be > cp
# minsplit: minimal number of samples in a node inorder to do a split
fit.tree2 <- rpart(chd~.,data=sahd,method="class",
  control = rpart.control(cp = 0,minsplit=10)
)
```

```
rpart.plot(fit.tree2,extra=1,under=TRUE,tweak = 1.2,faclen=3)
```



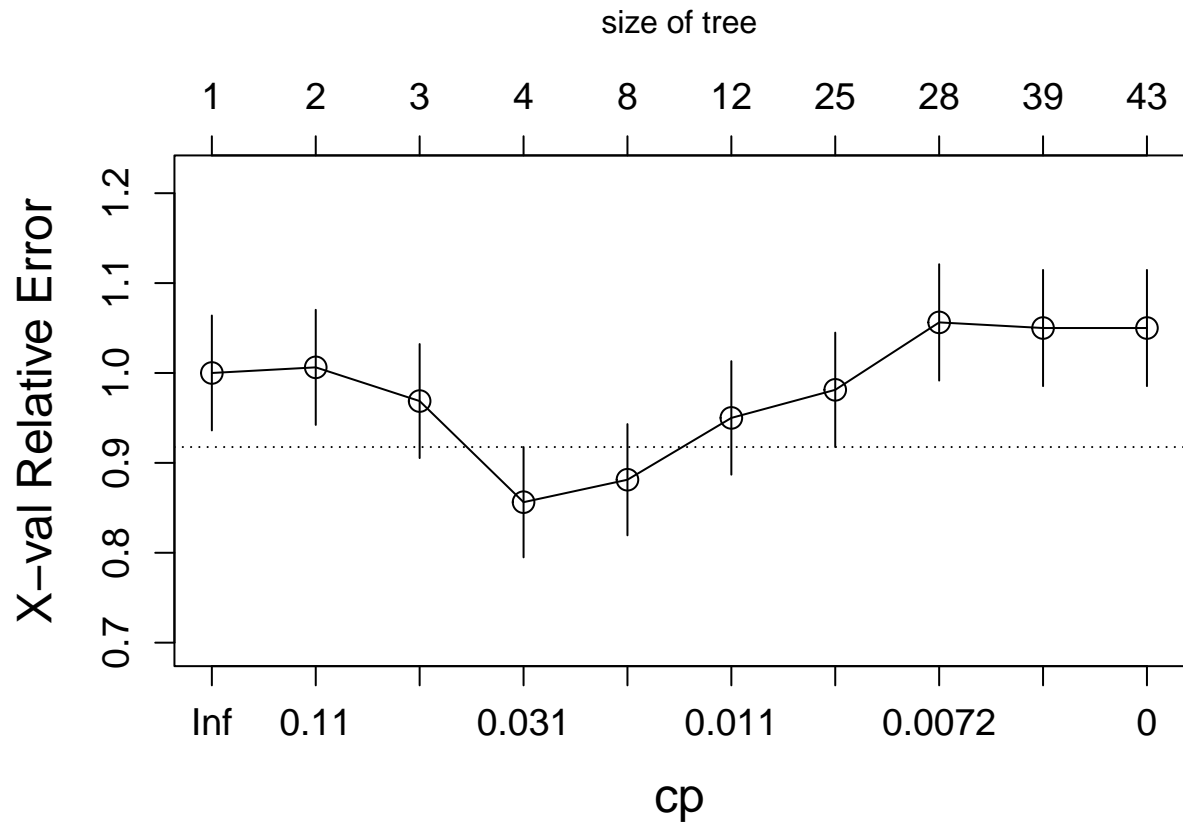
We can get the tree size from the cptable (tree size=number of leaves=number splits+1).

```
fit.tree2$cptable[fit.tree2$cptable[, "CP"] == 0, "nsplit"] + 1 # number of leaves
```

```
## [1] 43
```

Next, we plot the cross-validation error against the complexity parameter  $\alpha$ .

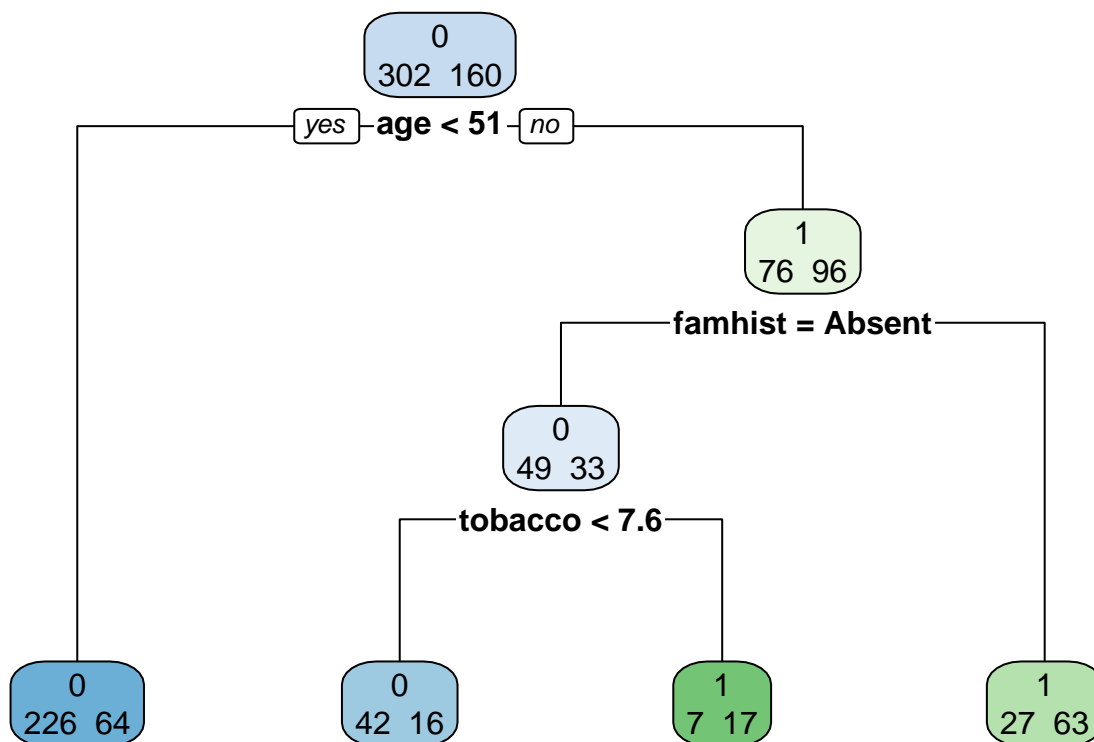
```
plotcp(fit.tree2, cex.lab=1.5, cex.axis=1.2, cex=1.5)
```



We prune the tree and visualize the result.

```
# prune the tree
fit.prune<- prune(fit.tree2,
                  cp=fit.tree2$cptable[which.min(fit.tree2$cptable[, "xerror"]), "CP"])
rpart.plot(fit.prune, extra=1)
```





Finally, we compute the confusion matrix and the misclassification error.

```
# confusion matrix of actual and fitted class labels
table(Actual=sahd$chd,Fitted=predict(fit.prune,type="class"))
```

```
##      Fitted
## Actual  0   1
##      0 268  34
##      1  80  80
```

```
# missclassification error
mean(sahd$chd!=predict(fit.prune,type="class"))
```

```
## [1] 0.2467532
```

We sample with replacement (bootstrap sample).

```
set.seed(1)
inthebag <- sample(1:nrow(sahd),size=nrow(sahd),replace=TRUE)
outofbag <- setdiff(1:nrow(sahd),inthebag)
```

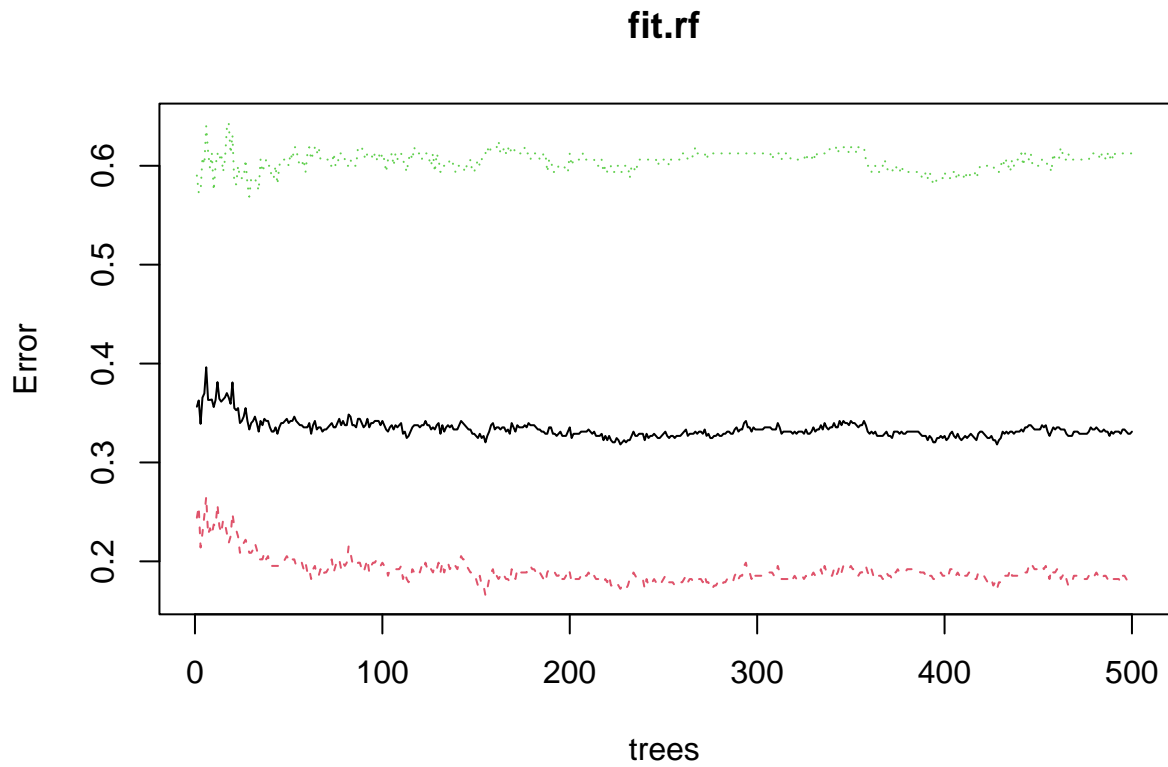
We fit a tree on the in-the-bag samples and calculate the misclassification error on the out-of-bag samples.

```
fit.in <- rpart(chd~.,data=sahd[inthebag,],method="class")
pred.oob <- predict(fit.in,newdata=sahd[outofbag,],type="class")
mean(sahd$chd[outofbag]!=pred.oob)
```

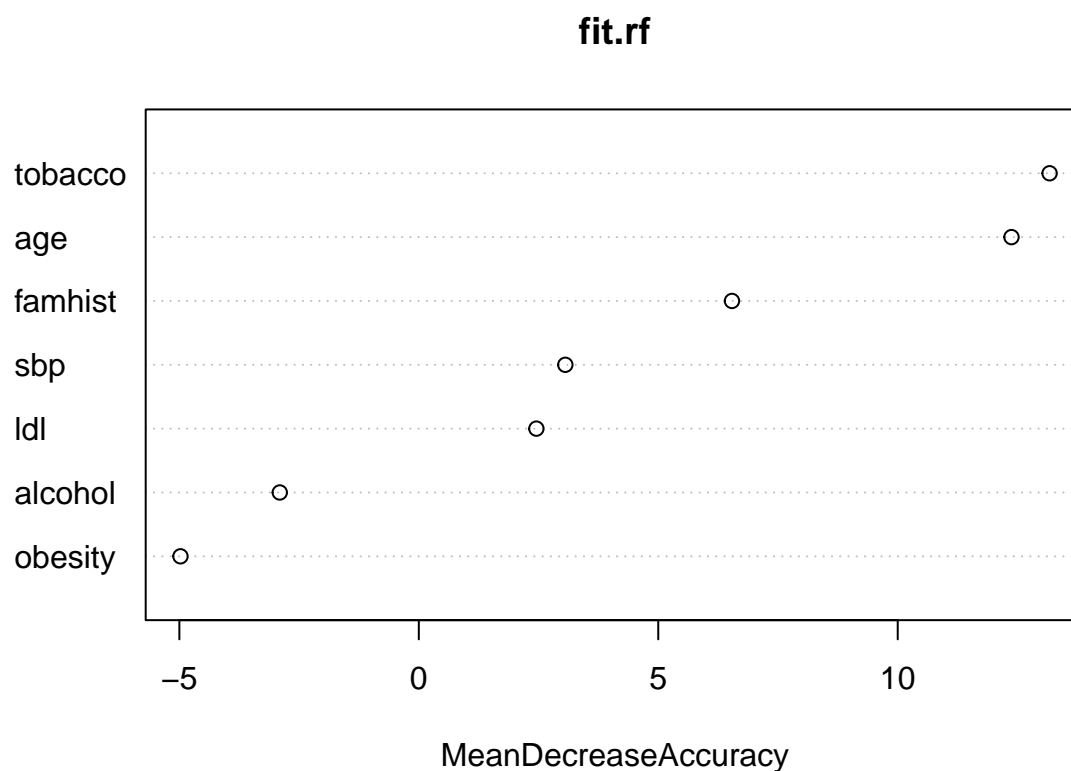
```
## [1] 0.3559322
```

We fit the random forest, plot the error as a function of the number of trees and plot the variable importance.

```
library(randomForest)
sahd$chd <- factor(sahd$chd)
fit.rf <- randomForest(chd~.,data=sahd,importance=TRUE)
plot(fit.rf)
```

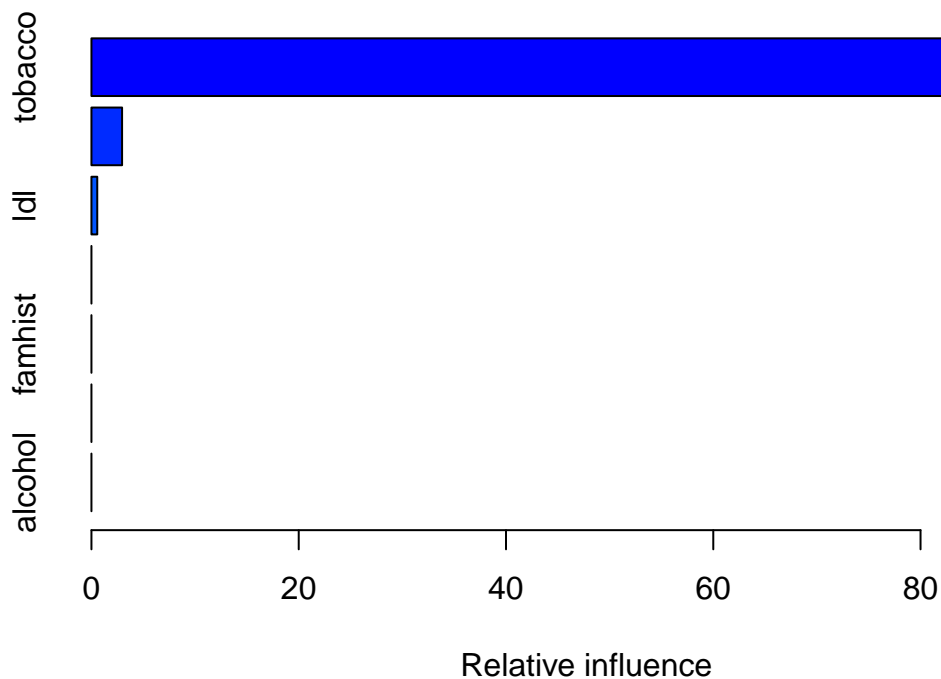


```
varImpPlot(fit.rf,type=1)
```



We run AdaBoost using `gbm` and by specifying `distribution = "adaboost"`. The `summary` provides a measure of variable importance. Prediction can be made using `predict`.

```
fit.boost <-gbm(chd~.,data=sahd,distribution = "adaboost") # note: for adaboost the outcome must be num  
summary(fit.boost)
```



```
##           var      rel.inf
## tobacco tobacco 96.4821033
## age         age  2.9567803
## ldl         ldl  0.5611164
## sbp         sbp  0.0000000
## famhist famhist 0.0000000
## obesity obesity 0.0000000
## alcohol alcohol 0.0000000

newd <- data.frame(sbp=100,tobacco=0,ldl=5,famhist=factor("Present"),obesity=25,alcohol=10,age=50)
predict(fit.boost,
        newdata=newd,
        type="response" )

## Using 100 trees...
## [1] 1
```

## 11 Phoneme recognition

In this exercise we investigate prediction of phonemes based on digitized speech data.

1. Read the data set, subset the phonemes “aa” and “ao” and create training and test data.

```
dat <- readRDS(file="data/phoneme.rds")
dat2 <- dat[dat$g%in%c("aa","ao"),]

dtrain <- dat2[grepl("^train",dat2$speaker),-c(1,259)]
```

```

xtrain <- as.matrix(dtrain[,-257])
ytrain <- ifelse(dtrain$g=="ao",1,0)
dtest <- dat2[grepl("^test",dat2$speaker),-c(1,259)]
xtest <- as.matrix(dtest[,-257])
ytest <- ifelse(dtest$g=="ao",1,0)

dtrain$y <- ytrain
dtest$y <- ytest
dtrain <- dtrain[,-257]
dtest <- dtest[,-257]

```

2. Plot the log-periodogram as a function of frequency for 5 examples each of the phonemes “aa” and “ao”.
3. Fit a logistic regression model and evaluate the training and test misclassification errors.
4. Run Lasso regression and evaluate the training and test misclassification errors.
5. In the previous approaches we assumed logit-link

$$\text{logit}(x; \beta) = \sum_{j=1}^{256} X_j \beta_j.$$

Next we assume that the coefficients are a smooth function of the frequency  $\beta(f)$ , i.e.

$$\beta(f) = \sum_{m=1}^{\nu} h_m(f) \theta_m,$$

where  $h_m$  are B-spline basis functions for a natural cubic spline with  $\nu = 12$  degrees of freedom (defined on the set of frequencies). Consider filtered inputs  $x^* = \mathbf{H}^T x$  and fit  $\theta$  by logistic regression on the  $x^*$ . Evaluate the training and test misclassification errors.

6. Plot the coefficients of the different models.

The solution to this exercise.

We prepare the data set.

```

library(splines)
dat <- readRDS(file="data/phoneme.rds")
dat2 <- dat[dat$g%in%c("aa","ao"),]

dtrain <- dat2[grepl("^train",dat2$speaker),-c(1,259)]
xtrain <- as.matrix(dtrain[,-257])
ytrain <- ifelse(dtrain$g=="ao",1,0)
dtest <- dat2[grepl("^test",dat2$speaker),-c(1,259)]
xtest <- as.matrix(dtest[,-257])
ytest <- ifelse(dtest$g=="ao",1,0)

dtrain$y <- ytrain
dtest$y <- ytest
dtrain <- dtrain[,-257]
dtest <- dtest[,-257]

```

We plot the log-periodograms.

```

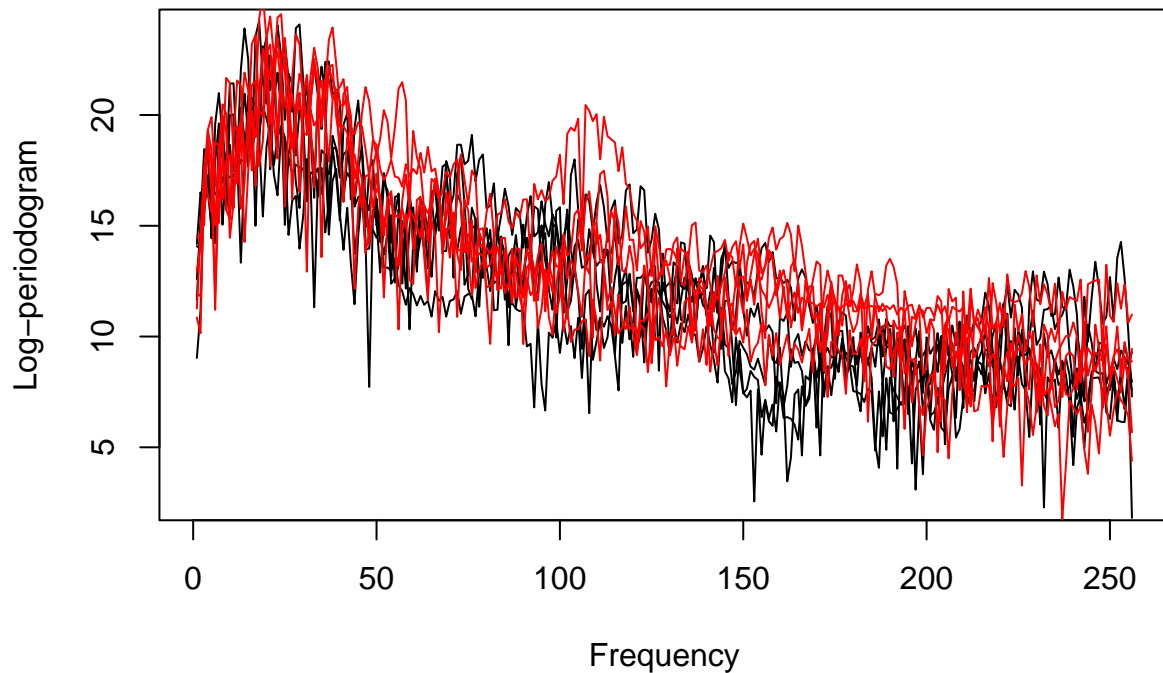
id.ao <- sample(which(ytrain==1),5)
id.aa <- sample(which(ytrain==0),5)
plot(xtrain[id.ao[1],,type="l",

```

```

      xlab="Frequency",ylab="Log-periodogram")
for(i in 2:5){
  lines(xtrain[id.ao[i],])
}
for(i in 1:5){
  lines(xtrain[id.aa[i],],col="red")
}

```



We run logistic regression and calculate the train and test errors.

```

# logistic regression
fit <- glm(y~.,data=dtrain,family=binomial)
coef.glm <- coefficients(fit)
pred_train <- as.numeric((predict(fit,type="response")>0.5))
pred_test <- as.numeric((predict(fit,type="response",newdata=dtest)>0.5))
mean(pred_train!=ytrain)

```

```
## [1] 0.09311424
```

```
mean(pred_test!=ytest)
```

```
## [1] 0.2437358
```

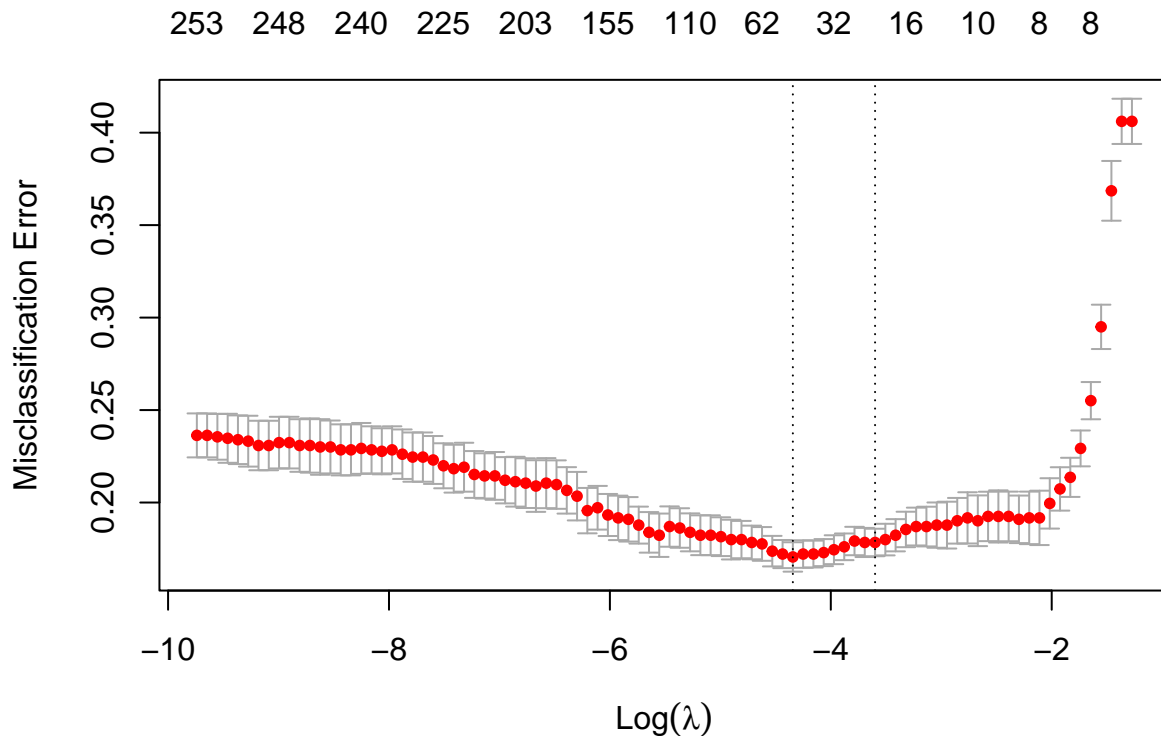
We run Lasso regression and calculate the train and test errors.

```

# lasso regression
fit.glmnet <-glmnet(xtrain,ytrain,family = "binomial",alpha=1)
cv.glmnet <- cv.glmnet(xtrain,ytrain,family = "binomial",type.measure = "class",
                      alpha = 1,nfolds = 10)

```

```
coef.lasso <- as.numeric(coefficients(fit.glmnet,s = cv.glmnet$lambda.1se))[-1]
plot(cv.glmnet)
```



```
pred_train <- c(predict(fit.glmnet,xtrain,s = cv.glmnet$lambda.1se,type = "class"))
pred_test <- c(predict(fit.glmnet,xtest,s = cv.glmnet$lambda.1se,type = "class"))
mean(pred_train!=ytrain)
```

```
## [1] 0.170579
```

```
mean(pred_test!=ytest)
```

```
## [1] 0.2072893
```

We use the natural cubic spline basis with  $\nu = 12$  to express the coefficients as a smooth function of the frequencies. We calculate the train and test errors.

```
# coefficient smoothing
hmat <- ns(x=1:256,df=12)
xstar <- xtrain%*%hmat
fit.smooth <- glm(dtrain$y~.,data=data.frame(xstar),family="binomial")
coef.smooth <- as.numeric(hmat%*%coef(fit.smooth)[-1])
pred_train <- as.numeric((predict(fit.smooth,type="response")>0.5))
pred_test <- as.numeric((predict(fit.smooth,type="response",newdata=data.frame(xtest%*%hmat))>0.5))

mean(pred_train!=ytrain)
```

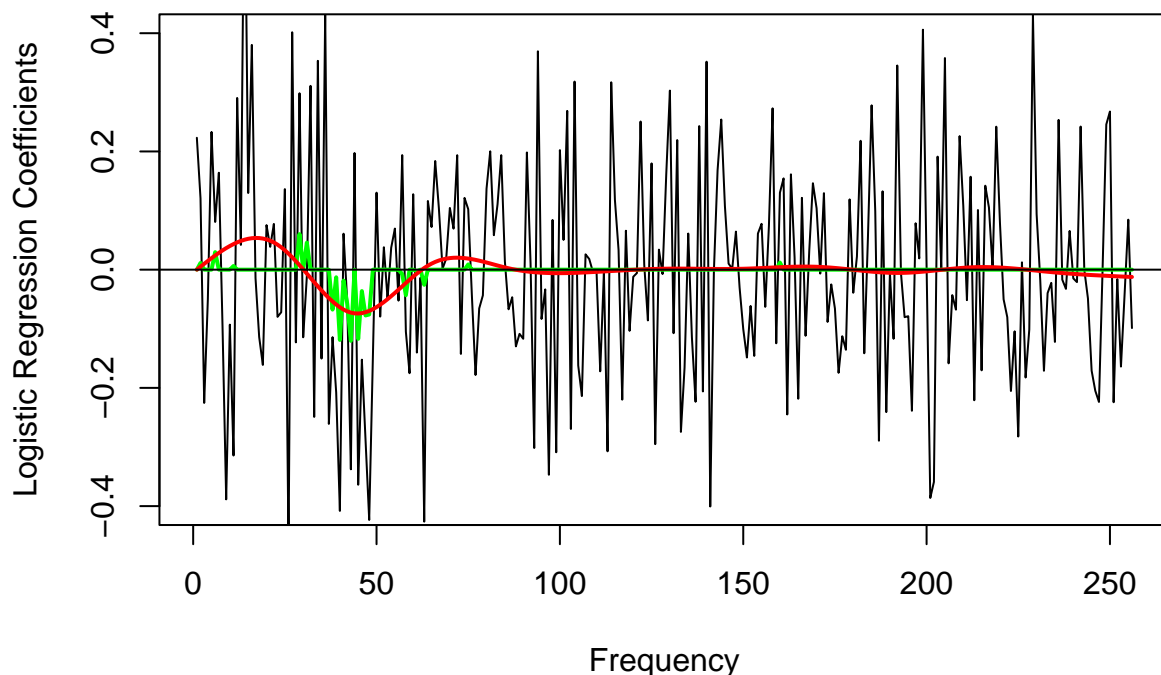
```
## [1] 0.1690141
```

```
mean(pred_test!=ytest)
```

```
## [1] 0.1867882
```

We plot the regression coefficients.

```
plot( coef.glm[-1],  
      ylim=c(-0.4,+0.4),  
      type="l",  
      xlab="Frequency",  
      ylab="Logistic Regression Coefficients" )  
lines(coef.lasso,col="green",lwd=2)  
lines(coef.smooth,col="red",lwd=2)  
abline(h=0)
```



## 12 Survival analysis and the Lymphoma data

In this exercise we explore the Lymphoma data set to predict survival based on gene expression data.

1. Load the Lymphoma data and make a histogram of the survival times.
2. Plot the estimated survival curve using `survfit` (Kaplan-Meier method).
3. Fit a Cox regression model with the first three genes as predictors. Use the function `coxph`.
4. Build a predictive model using `glmnet` (data pre-processing: use the top 100 genes and scale the resulting predictor matrix). Which genes are selected? What is the C-index for the optimal tuning parameter?



5. Use the predictive model and classify patients into “good” and “poor” prognostic groups by thresholding the linear predictor at zero. Calculate the Kaplan-Meier curves for the two groups. What is your conclusion? Do you have any concerns?
6. The linear predictor scores computed in 5. are biased as they are evaluated on the same data for which they were computed. We now use a variant of cross-validation, known as *pre-validation*, in order to obtain a fair evaluation of the model. Calculate a pre-validated data set using the code below and calculate the Kaplan-Meier curves for patients with good and poor prognosis.

```
# split data into K=5 folds
n.fold <- 5
foldid <- sample(1:n.fold, size = nrow(x), replace = TRUE)

# pre-validation
dat.preval <- data.frame(y)
dat.preval$lp <- NA

for (i in 1:n.fold){

  # train model on samples not in the kth fold
  omitk <- which(foldid==i)
  fitk <- cv.glmnet(x[-omitk,], y.surv[-omitk,],
                   family="cox",
                   type.measure="C",
                   nfolds = 5,
                   alpha=1)

  # calculated linear predictor on samples in the kth fold
  lp <- predict(fitk,
               newx=x[omitk,],
               s=cv.coxnet$lambda.min,
               type="link")
  dat.preval$lp[omitk] <- lp
}
```

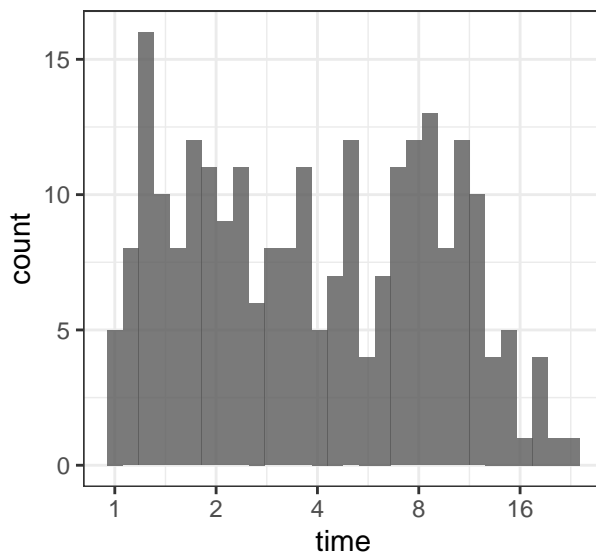
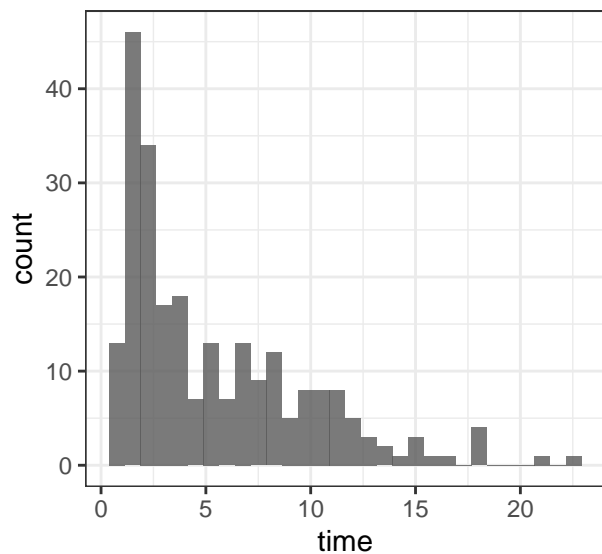
Solution to the exercise.

We load the data set.

```
# read gene expression matrix
x <- read.table("data/lymphx.txt")%>%
  as.matrix

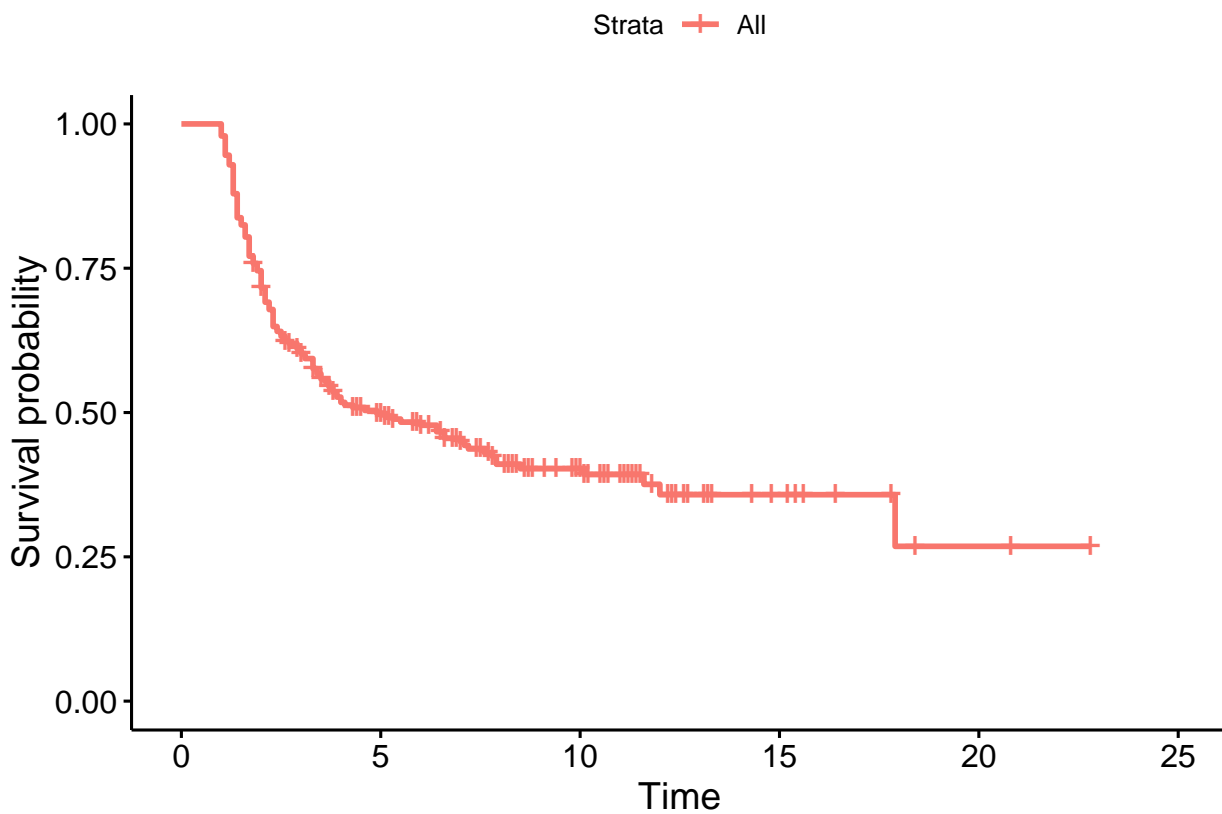
# read survival data
y <- read.table("data/lymphtime.txt", header = TRUE)%>%
  as.matrix
```

Plot the distribution of the survival times.



Plot of the Kaplan-Meier estimates.

```
dat <- data.frame(y)
fit.surv <- survfit(Surv(time, status) ~ 1,
                    data = dat)
ggsurvplot(fit.surv, conf.int=FALSE)
```



Fit a Cox regression model.

```

dat <- data.frame(cbind(y,x[,1:3]))
fit <- coxph(Surv(time,status)~.,data=dat)
summary(fit)

```

```

## Call:
## coxph(formula = Surv(time, status) ~ ., data = dat)
##
##      n= 240, number of events= 138
##
##           coef exp(coef) se(coef)      z Pr(>|z|)
## V1  0.6382     1.8931   0.4504  1.417   0.156
## V2 -0.5778     0.5611   0.4023 -1.436   0.151
## V3 -0.1508     0.8600   0.3785 -0.398   0.690
##
##      exp(coef) exp(-coef) lower .95 upper .95
## V1    1.8931     0.5282   0.7831   4.577
## V2    0.5611     1.7822   0.2551   1.234
## V3    0.8600     1.1627   0.4095   1.806
##
## Concordance= 0.559  (se = 0.028 )
## Likelihood ratio test= 4.46  on 3 df,   p=0.2
## Wald test               = 4.66  on 3 df,   p=0.2
## Score (logrank) test = 4.66  on 3 df,   p=0.2

```

Build a predictive model using glmnet. Data pre-processing.

```

# filter for top genes (highest variance) and scale the input matrix
topvar.genes <- order(apply(x,2,var),decreasing=TRUE)[1:100]
x <- scale(x[,topvar.genes])

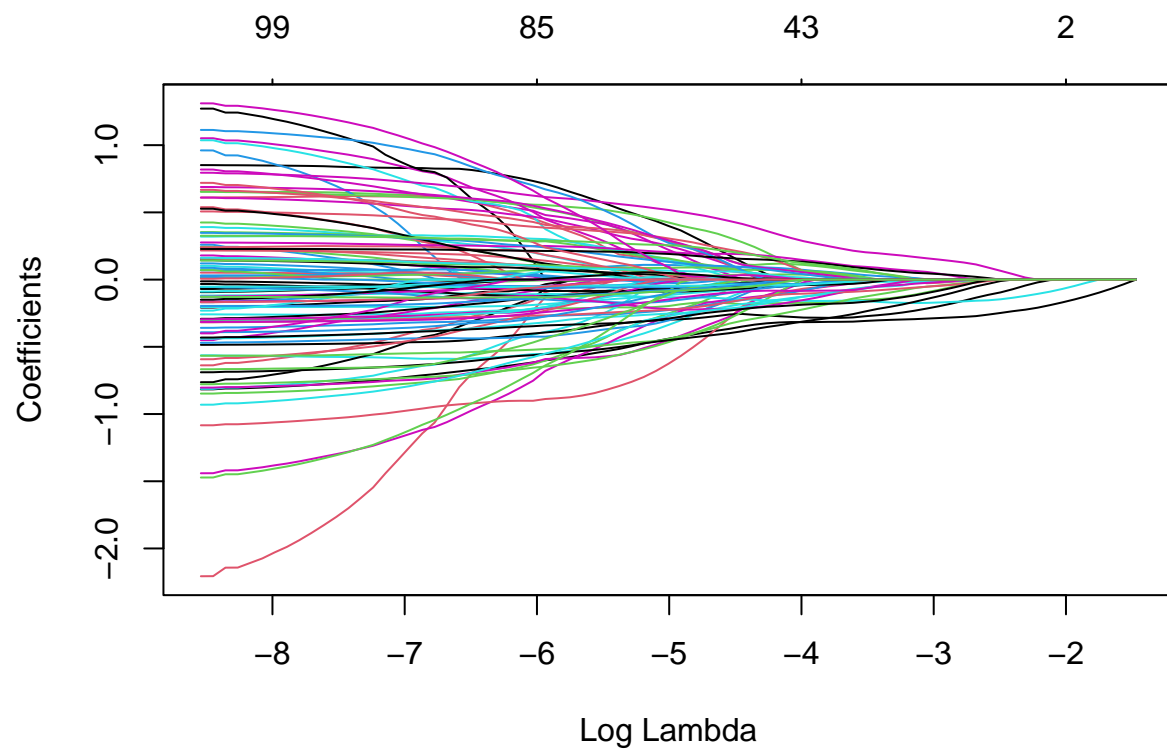
```

Run glmnet using family="cox".

```

set.seed(1)
y.surv <- Surv(y[, "time"], y[, "status"])
fit.coxnet <- glmnet(x, y.surv, family = "cox")
plot(fit.coxnet, xvar="lambda")

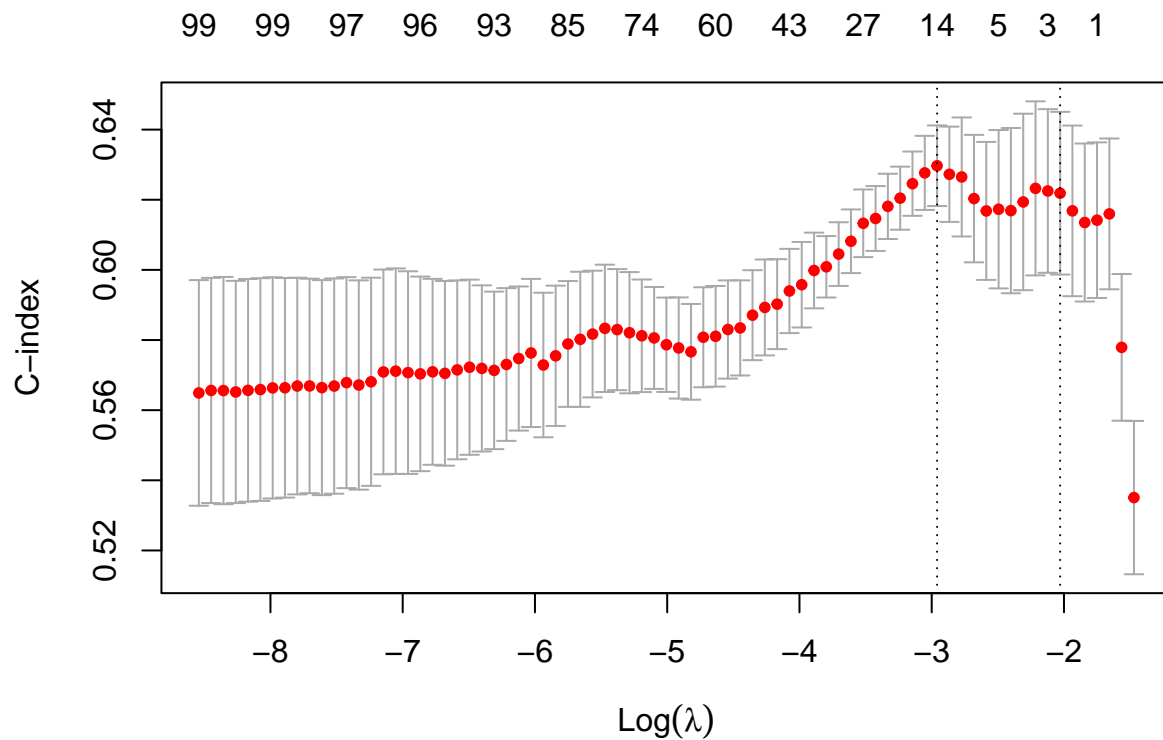
```



Calculate the cross-validated C-index.

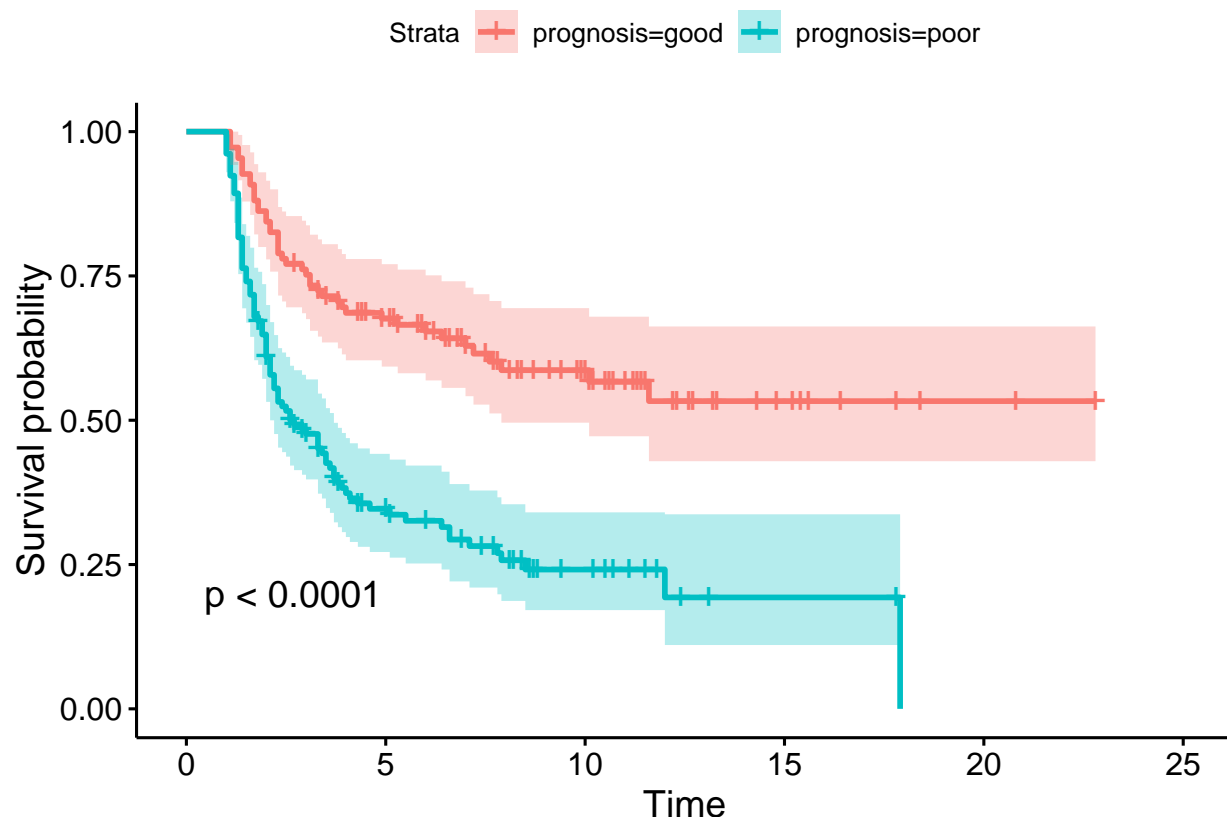
```
cv.coxnet <- cv.glmnet(x,y.surv,
                      family="cox",
                      type.measure="C",
                      nfolds = 5)

plot(cv.coxnet)
```



Classify patients into groups with good and poor prognosis (based on thresholding the linear predictor at zero).

```
# linear predictor
lp <- predict(fit.coxnet,
              newx=x,
              s=cv.coxnet$lambda.1se,
              type="link")
dat <- data.frame(y)
dat$prognosis <- ifelse(lp>0,"poor","good")
fit.surv <- survfit(Surv(time, status) ~ prognosis,
                  data = dat)
ggsurvplot(fit.surv, conf.int = TRUE, pval=TRUE)
```



The curves are very well separated. However, these linear predictor scores are biased: we are evaluating their performance on the same data for which they were computed.

In order to obtain a fair evaluation of the model we calculate a pre-validated data set.

```
set.seed(150381)

# split data into K=5 folds
n.fold <- 5
foldid <- sample(1:n.fold, size = nrow(x), replace = TRUE)

# pre-validation
dat.preval <- data.frame(y)
dat.preval$lp <- NA

for (i in 1:n.fold){

  # train model on samples not in the kth fold
  omitk <- which(foldid==i)
  fitk <- cv.glmnet(x[-omitk,], y.surv[-omitk,],
                    family="cox",
                    type.measure="C",
                    nfolds = 5,
                    alpha=1)

  # calculated linear predictor on samples in the kth fold
  lp <- predict(fitk,
```

```

newx=x[omitk,],
s=cv.coxnet$lambda.min,
type="link")
dat.preval$lp[omitk] <- lp
}

```

Plot the Kaplan-Meier curves for the good and poor prognostic groups based on the pre-validated data.

```

dat.preval$prognosis <- ifelse(dat.preval$lp>0,"poor","good")
fit.surv <- survfit(Surv(time, status) ~ prognosis,
                    data = dat.preval)
ggsurvplot(fit.surv,conf.int = TRUE,pval=TRUE)

```

