Solution to Final module

Problem 1. (10 points) MLE and bootstrap for Poisson data.

A random sample from the Poisson distribution $poisson(\lambda = e^{\theta})$ is provided in the file "DataPois.txt".

(a) What is the sample size n? What is the sample mean $\bar{Y}$?

(b) Find the value of MLE $\hat{\theta}$ on this data set *using numerical method*. NO credit is given if you used an analytic formula to find MLE.

(c) Test the null hypothesis that $\theta = 1$ at level 0.05, using a bootstrap confidence interval. Do NOT use analytic formula for MLE in your calculation. Use numerical optimization as in part (b). What is your conclusion? Can you find the p-value?

Solutions:1a)

```
> str(y)
 num [1:120] 3 5 3 1 2 1 2 1 0 2 ...
> #MEan of the sample
> print("mean of th esample is:")
[1] "mean of th esample is:"
> mean(y)
[1] 1.816667
```

Sample size : 120

Mean of the sample is 1.816667

1b)

```
> llh <- function(x) - sum(log(dpois(y, lambda=exp(x))))
> print("the vaue of theta is:")
[1] "the vaue of theta is:"
> optim(0, llh)$par
[1] 0.5970703
```

The value of θ is 0.5970703

1c)

```
> quantile(boot.xbar,c(0.025,0.975))
     2.5%     97.5%
0.4435547 0.7378906
```

We can thus conclude that the theta value lies between (0.4435547, 0.7378906)

Thus we reject the NULL HYPOTHESIS

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Problem 2. (20 points) ANOVA

We analyze the data set NCI60 data from the ISLR library. (This data set was used in Homework 11).

(a) Delete the cancer types with only one or two cases ("K562A-repro", etc.). Keep only the cancer types with more than 3 cases.

(b) Analyze the expression values of the first gene in the data (first column). Does the first gene express differently in different types of cancers? If so, in which pairs of cancer types does the first gene express differently? (Use FDR adjustment.)

(c) Check the model assumptions for analysis in part (b). Is ANOVA analysis appropriate here?

(d) Apply ANOVA analysis to each of the 6830 genes. At FDR level of 0.05, how many genes express differently among different types of cancer patients?

Solutions:

2a)

```
library(ISLR)
> nci.data<- NCI60$data
> nci.labs<- NCI60$labs
> data <- NULL
> z=1
> for (i in 1:64){
+   if (sum(nci.labs==(nci.labs[i])) <= 3){
+     data[z] <- i
+     z=z+1
+   }
+ }
> new.data <- nci.data[-data,]
> new.labs <- nci.labs[-data]
```

2b)

```
> anova(lm(gene ~ new.labs))
Analysis of Variance Table

Response: gene
          Df Sum Sq Mean Sq F value  Pr(>F)
new.labs   7 2.8931 0.41331  2.3272 0.03928 *
Residuals 49 8.7021 0.17759
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The p value obtained is 0.03928 which is less than 0.05, we can say that thre is no evidence that the gene is expressed differently, thus we reject the NULL hypothesis

Solution to Final module

```
> pairwise.t.test(gene, new.labs, p.adjust.method = 'fdr')

        Pairwise comparisons using t tests with pooled SD

data:  gene and new.labs

          BREAST CNS  COLON LEUKEMIA MELANOMA NSCLC OVARIAN
CNS       0.34   -    -     -        -        -     -
COLON     0.35   0.10 -     -        -        -     -
LEUKEMIA  0.42   0.11 0.93  -        -        -     -
MELANOMA  0.93   0.34 0.34  0.34     -        -     -
NSCLC     0.34   0.93 0.10  0.10     0.34     -     -
OVARIAN   0.34   0.93 0.10  0.12     0.37     0.99  -
RENAL     0.93   0.34 0.34  0.35     0.93     0.34  0.34

P value adjustment method: fdr
```

As all the p-value are >0.05 its difficult to distinguish between the types of cancers.

2c)

```
> shapiro.test(residuals(lm(gene ~ new.labs)))

        Shapiro-Wilk normality test

data:  residuals(lm(gene ~ new.labs))
W = 0.9795, p-value = 0.4414
```

We fail to reject NULL hypothesis as the p-value is 0.4414 which is less than 0.05.

```
> bptest(lm(gene ~ new.labs), studentize = FALSE)

        Breusch-Pagan test

data:  lm(gene ~ new.labs)
BP = 8.8392, df = 7, p-value = 0.2644
```

We cant reject the NULL hypothesis as p-value is 0.2644 which is less than 0.05.

2d)

```
> anova <- apply(new.data, 2, function(x) anova(lm(x ~ new.labs))$Pr[1])
> p.fdr <- p.adjust(p=anova, method="fdr")
> sum(p.fdr<0.05)
[1] 2808
```

2808 genes were expressed differently

Solution to Final module

Problem 3. (10 points) Regression

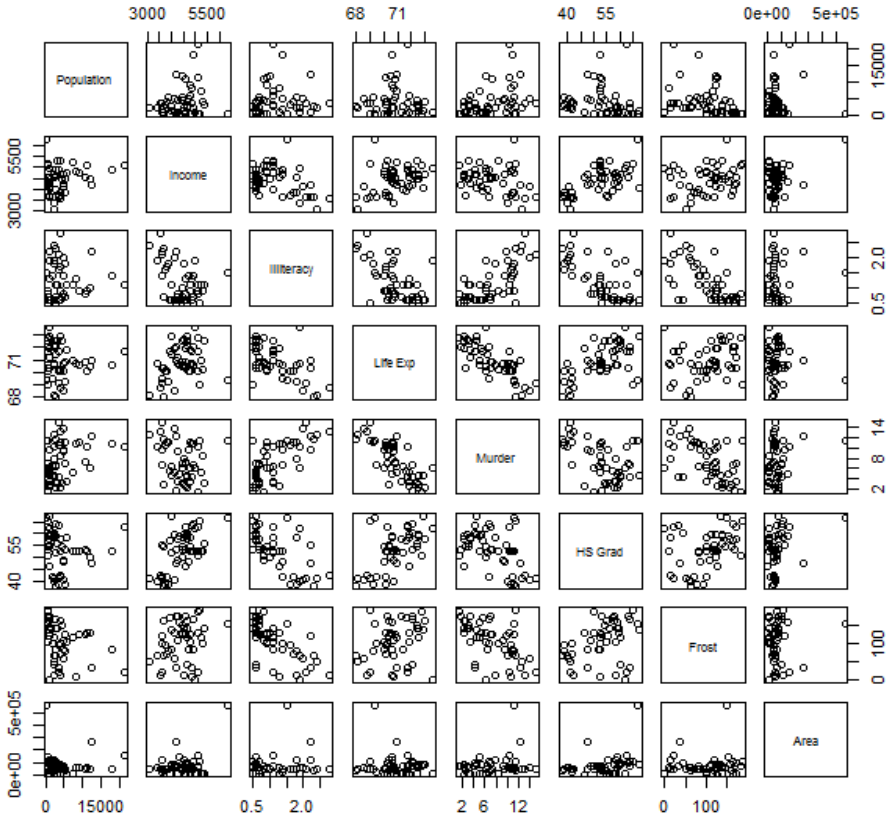
We consider the regression analysis on the state.x77 data set. In the module 9, we regressed the life expectancy on three variables: the murder rates, percentage of high-school graduates and mean number of frost days.

(a) Make pairwise scatterplots for all variables in the data set. Which variables appears to be linearly correlated with the life expectancy based on the scatterplots?

(b) Conduct a regression analysis different from the example analysis in module 9. We regress the life expectancy on three variables: the per capita income (Income), the illiteracy rate (Illiteracy) and mean number of frost days (Frost). What is your regression equation? In this regression analysis, which of the three variables affect the life expectancy significantly?

(c) Find delete-one-cross-validated mean square errors $\frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{y}_{(-i)})^2$ for this regression model. Here y_i is the i-th response (life expectancy), $\hat{y}_{(-i)}$ is the prediction of the i-th response from the regression fit without using that observation.

Solutions: 3a)



Solution to Final module

Murder, HS Grad, Frost and illiteracy appear to be correlated with life expectancy

3b)

The equation for regression analysis is

Life.Exp = 72.5+ 0.0002income – 1.56 illiteracy – 0.006 frost

As per this equation illiteracy plays a more significant role in life expectancy.

3c)

```
> error <- mean(error)
> print(error)
[1] 1.345143
```

The delete one cross validated error is 1.345143

Solution to Final module

Problem 4. (60 points) Predicting B-cell differentiation with gene expression.
We analyze data for the B-cell patients in the ALL data set in the textbook.
(a) Select gene expression data for only the B-cell patients. The analysis in following parts will only use these gene expression data on the B-cell patients.
(b) Select only those genes whose coefficient of variance (i.e., standard deviation divided by the mean) is greater than 0.2. How many genes are selected?
(c) We wish to conduct clustering analysis to study natural groupings of the patients predicted by the gene expression profiles. For this analysis, we first need to reduce the number of genes studied. The filter in (b) is one such choice. Please comment on what filtering methods you would use to choose genes, other than the filter in (b). What would you consider as the best gene filter in this case.

(d) Conduct a hierarchical clustering analysis with filtered genes in (b). (For uniformity in grading, we ask everyone to use the filter in (b). It may not be your best filter in (c).) How do the clusters compare to the B-stages? How does do the clusters compare to the molecule biology types (in variable ALL$mol.biol)? Provide the confusion matrices of the comparisons, with 4 clusters.

(e) Draw two heatmaps for the expression data in (d), one for each comparison. Using colorbars to show the comparison types (B-stages or molecule biology types). The clusters reflect which types better: B-stages or molecule biology types?

(f) We focus on predicting the B-cell differentiation in the following analysis. We merge the last two categories "B3" and "B4", so that we are studying 3 classes: "B1", "B2" and "B34". (Ignore the unknown type "B" in the analysis.) Use linear model (limma library) to select genes that expresses differently among these three classes at FDR of 0.05. How many genes are selected?

(g) Fit SVM and the classification tree on these selected genes in part (f), evaluate their performance with delete-one-cross-validated misclassification rate.

(h) We select the genes passing both filters in (b) and (f). How many genes are selected? Redo part (g) on these genes passing both filters.

(i) Which classifier you will consider best among the classifiers studied in part (g)

Solutions: 4a)

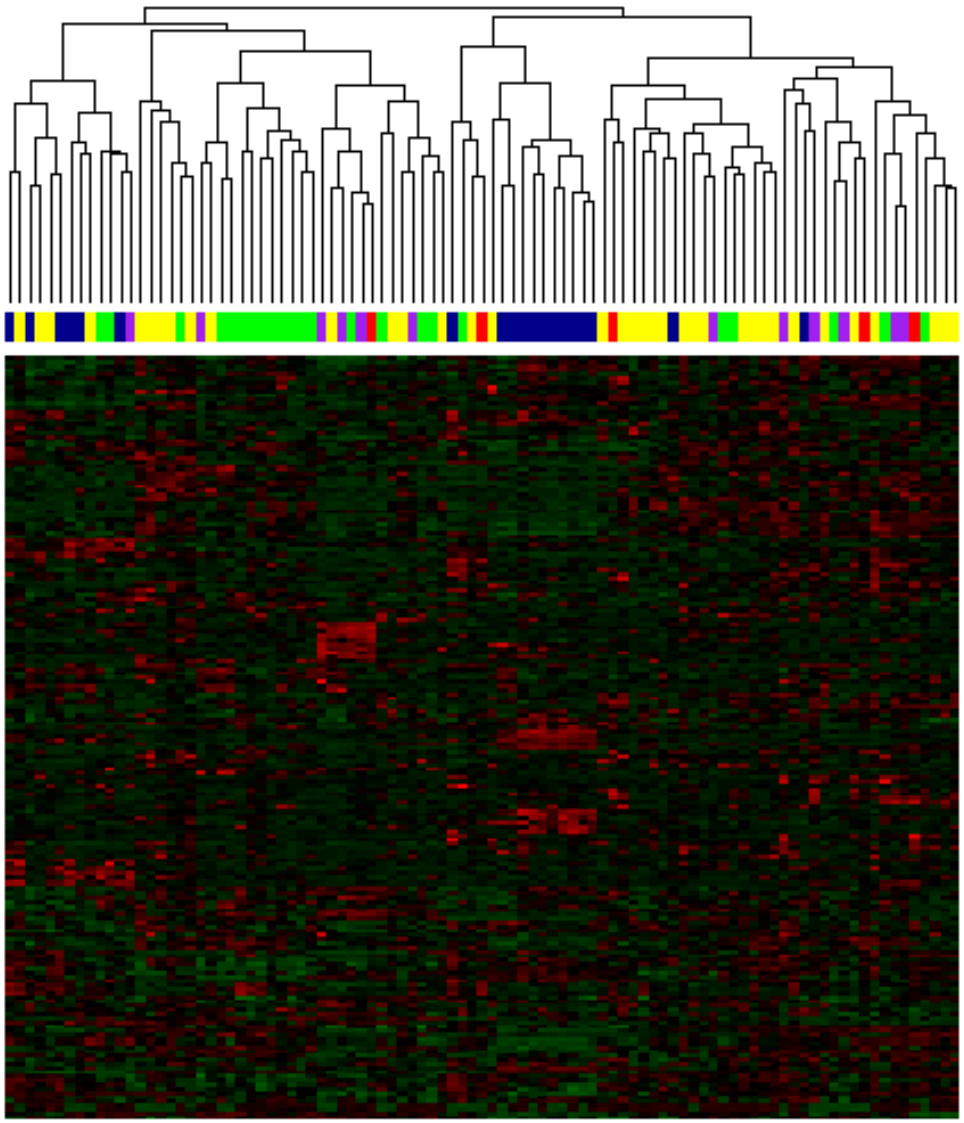
```
 > ALL.B <- ALL[,which(ALL$BT %in% c("B","B1","B2","B3","B4"))]
> B.data <- exprs(ALL.B)
> str(B.data)
 num [1:12625, 1:95] 7.6 5.05 3.9 5.9 5.93 ...
 - attr(*, "dimnames")=List of 2
  ..$ : chr [1:12625] "1000_at" "1001_at" "1002_f_at" "1003_s_at" ...
  ..$ : chr [1:95] "01005" "01010" "03002" "04006" ...
```

Solution to Final module

4b)

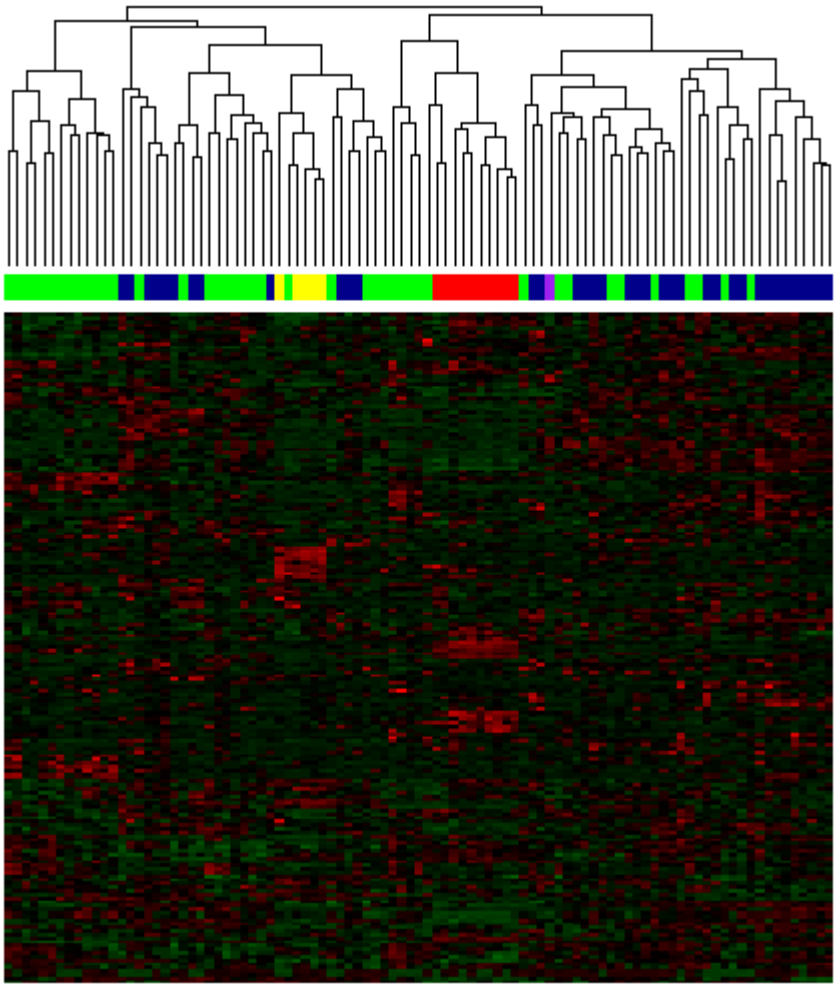
Selecting the genes whose coefficience of variance is greater than 0.2 , we get 184 genes

4e)



Most of the B1 is in the first cluster. Most of the B2 (yellow) is in the second cluster. Most of the B3 (green) is in the first cluster.

Solution to Final module



Most of the green(NEG) is in the first cluster. Entire yellow(E2A/PBXI) is in the first cluster. Entire red(ALL/AF4) and (p15/p16) are in the second cluster. I think the clusters reflect molecular biology types better.

4c) Shapiro–Wilks test has the power to detect even small deviations from normality and score them as significant. Thus we use Shapiro-Wilks test.

Solution to Final module

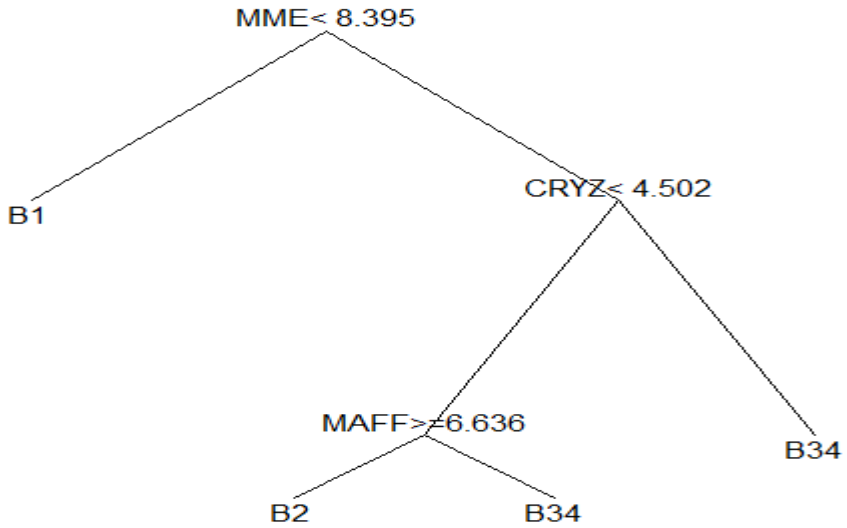
4d)

```
> table(ALL$BT[1:95,drop=T],cluster)
    cluster
      1  2  3  4
  B   3  1  1  0
  B1  2  0 11  6
  B2 20 10  2  4
  B3  5 15  1  2
  B4  6  5  0  1
> table(ALL$mol.bio[1:95],cluster)
           cluster
             1  2  3  4
  ALL1/AF4   0  0 10  0
  BCR/ABL   25 12  0  0
  E2A/PBX1   0  5  0  0
  NEG       10 14  5 13
  NUP-98     0  0  0  0
  p15/p16    1  0  0  0
```

4f)

Using linear model I could select 1169 genes.

4g)



Solution to Final module

For SVM

Delete one cross validated misclassification rate is 0.3

```
> mcr.cv<-mean(mcr.raw)
> mcr.cv
[1] 0.3
```

For classification tree Delete one cross validated misclassification rate is 0.102

```
> tree.cv <- mean(tree.raw)
> tree.cv
[1] 0.102
```

4h)

Passing both the filters in (b) and (f) we can get 55 genes.

4i)

I think the genes in (h) is better as we are filtering down using more rigorous filtering methods

Problem 5

5a) Code in r script