Solutions to Midterm Module

Problem 1 (10 points)

X follows a distribution with pdf $f_X(x) = 2.469862(xe^{-x^2}), x = 1,2,3$; while Y follows a distribution with pdf $f_Y(y) = 2ye^{-y^2}, y > 0$.

a) Find E(X), E(Y), sd(X) and sd(Y).

b) If X and Y are independent, find E(2X-3Y) and sd(2X-3Y).

Solutions:

a) Find E(X), E(Y), sd(X) and sd(Y).

```
> # Finding E(X)

> X.Range<- c(1,2,3)
> f.x<- function(x) 2.469862*(x*exp(-x^2))
> f_x<- function(x) f.x(x)*(x %in% X.Range)
> E.X<- sum(X.Range*f_x(X.Range))
> print("The E(X) is ")
[1] "The E(X) is "
> print(E.X)
[1] 1.092303
```

⇨ The value of E(X) is 1.092303

```
> # Finding E(Y)

> f.Y<- function(y) 2*(y*exp(-y^2))*(0<=y & y<=Inf)
> E.Y<- integrate(function(y) y*f.Y(y), lower=0, upper=Inf)$value
> print("The E(Y) is")
[1] "The E(Y) is"
> print(E.Y)
[1] 0.8862269
```

⇨ The value of E(Y) is 0.8862269

```
> # Finding sd(X)

> X.Range<-c(1,2,3)
> f.x<- function(x) 2.469862*(x*exp(-x^2))
> f_x<- function(x) f.x(x)*(x %in% X.Range)
> E.X<- sum(X.Range*f_x(X.Range))
> # findind variance
> Var.X<- sum((X.Range-E.X)^2 * f_x(X.Range))
> # finding standard deviatioin
> sd.X<- sqrt(Var.X)
> print("the sd(x) is")
[1] "the sd(x) is"
> print (sd.X)
[1] 0.2925953
```

⇨ The value of sd(x) is 0.2925953

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```
> # Finding sd(Y)

> f.Y<- function(y) 2*(y*exp(-y^2))*(0<=y & y<=Inf)
> E.Y<- integrate(function(y) y*f.Y(y), lower=0, upper=Inf)$value
> Var.Y<-integrate(function(y) (y-E.Y)^2*f.Y(y), lower=0, upper=Inf)$value
> sd.Y<- sqrt(Var.Y)
> print("The sd(Y) is")
[1] "The sd(Y) is"
> print(sd.Y)
[1] 0.4632514
```

⇨ The value of sd(Y) is 0.4632514

b) If X and Y are independent, find E(2X-3Y) and sd(2X-3Y).

```
> # Finding E(2X-3Y)

> (2*(E.X) - 3*(E.Y))
[1] -0.4740746
```

⇨ The value of E(2X-3Y) is -0.4740746

```
> # Finding sd(2X-3Y)

> Var<- (4*Var.X)+(9*Var.Y)
> sd<- sqrt(Var)
> print("The sd(2X-3Y) is")
[1] "The sd(2X-3Y) is"
> print(sd)
[1] 1.507934
```

⇨ The value of sd(2X-3Y) is 1.507934

Solutions to Midterm Module

Problem 2 (10 points)
X follows a standard normal distribution N(mean=0, sd=1), and Y follows a Chi-square distribution with degrees of freedom df=4. Assume that X and Y are independent. Please estimate $E(\frac{X^2}{X^2+Y})$ accurate to two decimal places.

Solution:

```
> # X follows standard normal distribution

> X<- rnorm(10000, mean=0, sd=1)
> # Y follows chi-square distribution
> Y<- rchisq(10000, df=4)
> # solving the equation
> eqn <- (X^2)/(X^2+Y)
> E.eqn<-mean(eqn)
> print(E.eqn)
[1] 0.1985588
```

⇨ The estimate of E(X^2 / (X^2+Y)) is 0.1985588

Problem 3 (10 points)
Suppose we decide to use the Monte Carlo method to check coverage of a 95% confidence interval (CI) formula. We generated nsim=1000 data sets from the known distribution, calculate the 95% confidence interval on each data set and check the empirical coverage (that is, the proportion of those 1000 confidence intervals that contains the true parameter). Suppose that the CI formula is wrong, and the true coverage is only 92%. What is the probability that our empirical coverage is greater than 94%?

Solution:

```
> 1-pbinom(940,1000,0.92)
[1] 0.006617437
```

⇨ The probability that the empirical coverage is greater than 94% is 0.006617437

Solutions to Midterm Module

Problem 4 (10 points)

A random sample from the normal distribution $N(mean = \theta, sd = \theta)$ is provided in the file "normalData.txt". Find the value of MLE $\hat{\theta}$ on this data set.

Instructions on inputting the data set:

You should download the file, put it in the working directory of your R session.

Then load it using command

y<-as.numeric(t(read.table(file = "normalData.txt", header=T)))

Solutions:

```
> # download the file, put it in the working directory of your R session.
> getwd()
[1] "C:/Users/Neha/Documents"
> # load it using command
> y<-as.numeric(t(read.table(file = "normalData.txt", header=T)))
>
> c(sqrt(sum((y-mean(y))^2)/length(y)))
[1] 2.599879
```

⇨ The Value of MLE $\hat{\theta}$ for this set is 2.599879

Problem 5 (10 points)

On the Golub et al. (1999) data set, complete the following:

a) Use the t-test to test how many genes have mean expression values greater than 0.6. Use a FDR of 10%.

b) Find the gene names of the top five genes with mean expression values greater than 0.6.

Solution:

a) Use the t-test to test how many genes have mean expression values greater than 0.6. Use a FDR of 10%.

```
 > # finding the genes with mean expression greater than 0.6
> mean <- p.values<0.05
> print(" The genes with mean expression greater than 0.6")
[1] " The genes with mean expression greater than 0.6"
> sum(p.values<0.05)
[1] 526
> # using FDR of 10%
> p.fdr<-p.adjust(p = p.values, method="fdr")
> print("the no of genes have mean expression values greater than 0.6 after 1
0% FDR are")
```

Solutions to Midterm Module

```
[1] "the no of genes have mean expression values greater than 0.6 after 10% F
DR are"
> sum(p.fdr<0.10)
[1] 502
```

- ⇨ The genes with mean expression greater than 0.6 = 526
- ⇨ After using FDR = 502

b) Find the gene names of the top five genes with mean expression values greater than 0.6.

```
> genes <- order(p.fdr, decreasing = FALSE)[1:5]
> print("gene names of the top five genes with mean expression values greater
than 0.6.")
[1] "gene names of the top five genes with mean expression values greater tha
n 0.6."
> golub.gnames[genes, 2]
[1] "HnRNP-E2 mRNA"
[2] "Ornithine decarboxylase antizyme, ORF 1 and ORF 2"
[3] "GB DEF = Polyadenylate binding protein II"
[4] "RPS14 gene (ribosomal protein S14) extracted from Human ribosomal protei
n S14 gene"
[5] "GAPD Glyceraldehyde-3-phosphate dehydrogenase"
```

Solutions to Midterm Module

Problem 6 (35 points)
On the Golub et al. (1999) data set, compare the "GRO3 GRO3 oncogene" (at row 2715) with the "MYC V-myc avian myelocytomatosis viral oncogene homolog" (at row 2302). I will refer to those two genes as GRO3 gene and MYC gene for short in the following:

a) Draw a histogram of the GRO3 gene expression values.

b) Draw a scatterplot of the GRO3 gene expression values versus MYC gene expression values, labeled with different colors for ALL and AML patients.

c) Use a parametric t-test to check (the alternative hypothesis) if the mean expression value of GRO3 gene is less than the mean expression value of MYC gene.

d) Use a formal diagnostic test to check the parametric assumptions of the t-test. Is the usage of the t-test appropriate here?

e) Use a nonparametric test to check (the alternative hypothesis) if the *median* difference between the expression values of GRO3 gene and the expression values of MYC gene is less than zero.

f) Calculate a nonparametric 95% one-sided upper confidence interval for the *median* difference between the expression values of GRO3 gene and of MYC gene.

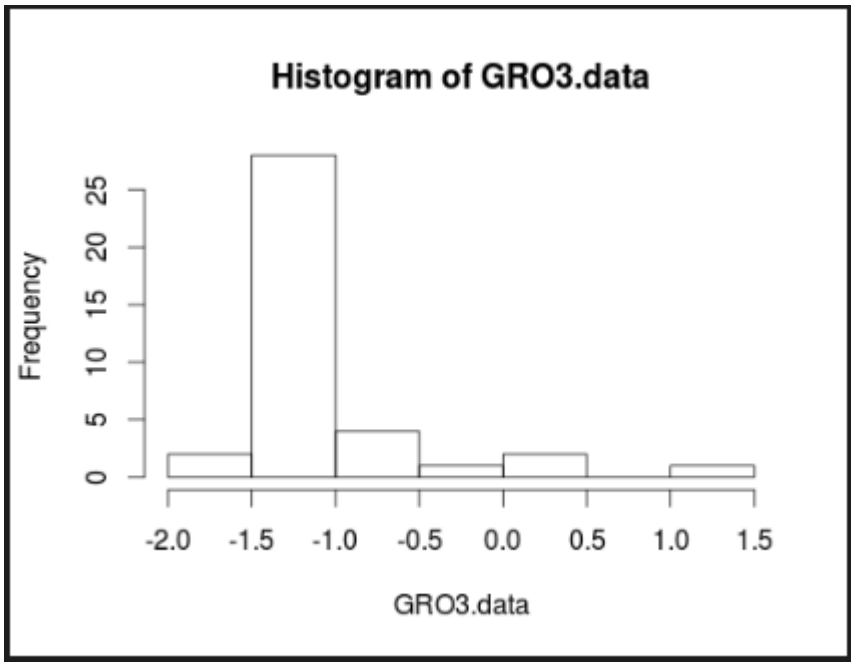
g) Calculate a nonparametric bootstrap 95% one-sided upper confidence interval for the *mean* difference between the expression values of GRO3 gene and of MYC gene.

Solution:

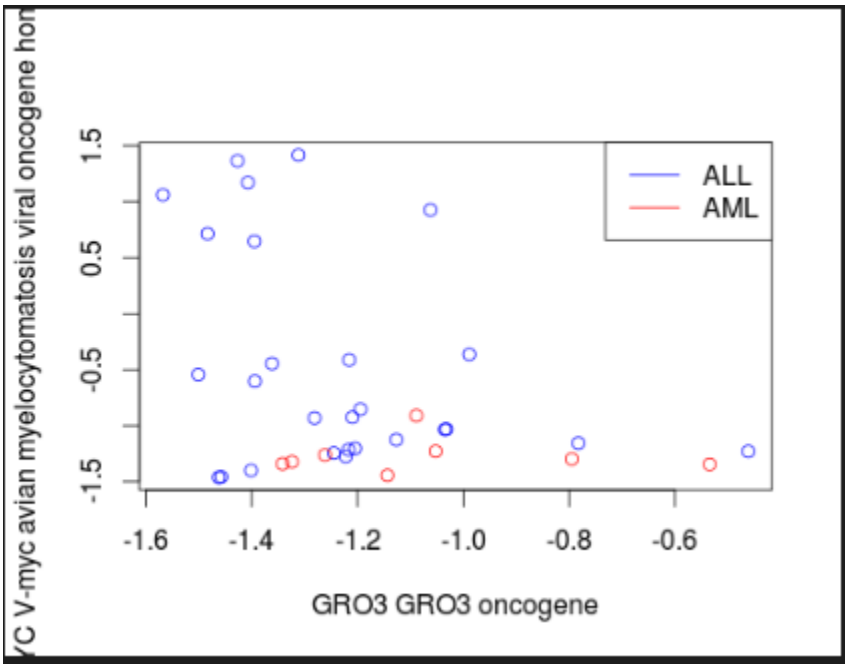
6a) Draw a histogram of the GRO3 gene expression values.

```
> data(golub, package = "multtest")
> gol.fac <- factor(golub.cl,levels=0:1, labels= c("ALL","AML"))
> # a) Draw a histogram of the GRO3 gene expression values.
> # row index of GRO3 gene is 2715. getting the data for GRO3
> GRO3.data = golub[2715,]
> # to draw a histogram
> hist(GRO3.data)
```

Solutions to Midterm Module



6b) b) Draw a scatterplot of the GRO3 gene expression values versus MYC gene expression values, labeled with different colors for ALL and AML patients



Solutions to Midterm Module

```
> data(golub, package = "multtest")
> gol.fac <- factor(golub.cl,levels=0:1, labels= c("ALL","AML"))
> # a) Draw a histogram of the GRO3 gene expression values.
> # row index of GRO3 gene is 2715. getting the data for GRO3
> GRO3.data = golub[2715,]
> # to draw a histogram
> hist(GRO3.data)
> MYC.data = golub[2302,]
> # row index of GRO3 gene is 2715. getting the data for GRO3
> GRO3.data<- golub[2715,]
> ALL.x<- golub[2715, gol.fac=="ALL"]
> AML.x<- golub[2715, gol.fac=="AML"]
> ALL.y<- golub[2302, gol.fac=="ALL"]
> AML.y<- golub[2302, gol.fac=="AML"]
> # to draw a scatterplot
> plot(ALL.x,ALL.y,xlab=golub.gnames[2715,2],ylab=golub.gnames[2302,2], col="
blue")
> points(AML.x,AML.y, col="red")
> legend("topright",c("ALL","AML"),col=c("blue","red"),lty=c(1,1))
```

6c) Use a parametric t-test to check (the alternative hypothesis) if the mean expression value of GRO3 gene is less than the mean expression value of MYC gene.

H_0 : Mean(GRO3)- Mean(MYC) > 0

- ⇨ H_0 : mean(GRO3) > Mean(MYC)

H_A : Mean(GRO3) < Mean (MYC)

The p value is 0.03718

- ⇨ As p-value is small, we can reject The NULL HYPOTHESIS and accept the mean expression of GRO3 is less than mean expression of MYC

```
> # applying t-test
> t.test(GRO3.data, MYC.data, paired=T, alternative = "less" )

        Paired t-test

data:  GRO3.data and MYC.data
t = -1.8363, df = 37, p-value = 0.03718
alternative hypothesis: true difference in means is less than 0
95 percent confidence interval:
        -Inf -0.02909346
sample estimates:
mean of the differences
             -0.3580716
```

Solutions to Midterm Module

6 **d)** Use a formal diagnostic test to check the parametric assumptions of the t-test. Is the usage of the t-test appropriate here?

```
> shapiro.test(golub[2715,])

        Shapiro-Wilk normality test

data:  golub[2715, ]
W = 0.715, p-value = 2.9e-07

> shapiro.test(golub[2302,])

        Shapiro-Wilk normality test

data:  golub[2302, ]
W = 0.7537, p-value = 1.355e-06
```

⇨ Since both test gives p-valu less than 0.05, we reject the null hypothesis. Thus we conclude that these tests do not follow normality and so t-test cannot be used here.

6 e) Use a nonparametric test to check (the alternative hypothesis) if the *median* difference between the expression values of GRO3 gene and the expression values of MYC gene is less than zero

Here we use Wilcox test

```
> wilcox.test (x= GRO3.data, y= MYC.data, paired=T, alternative="less")

        Wilcoxon signed rank test with continuity
        correction

data:  GRO3.data and MYC.data
V = 107, p-value = 0.04208
alternative hypothesis: true location shift is less than 0
```

⇨ P value = 0.04208 , we reject the null hypothesis and accept the alternate hypothesis that the difference is less than zero

6 **f)** Calculate a nonparametric 95% one-sided upper confidence interval for the *median* difference between the expression values of GRO3 gene and of MYC gene

```
> data.diff<-abs(golub[2715,]-golub[2302,])
> n<-length(data.diff)
> nboot<-1000
> boot.xbar<-rep(NA, nboot)
> for(i in 1:nboot) {
+   data.star <- data.diff[sample(1:n,replace=TRUE)]
+   boot.xbar[i]<-median(data.star)
+ }
> quantile(boot.xbar,c(0.95))
     95%
0.795765
```

⇨ 95% one sided upper CI for the median difference between expression values of bothe the genes is -Infinity , 0.795765

Solutions to Midterm Module

6g) Calculate a nonparametric bootstrap 95% one-sided upper confidence interval for the *mean* difference between the expression values of GRO3 gene and of MYC gene.

- ⇨ Non parametric bootstrap 95% one-sisde upper CI for median difference between the expression values of the genes is –Infinity, 1.071662

```
> data.diff<-abs(golub[2715,]-golub[2302,])
> n<-length(data.diff)
> nboot<-1000
> t.boot = rep(NA,nboot)
> for(i in 1:nboot){
+   data.star<-data.diff[sample(1:n,replace=TRUE)]
+   t.boot[i]= mean(data.star)
+ }
> quantile(t.boot,c(0.95))
     95%
1.071662
```

Problem 7 (15 points)

On the Golub et al. (1999) data set, complete the following:

a) Find the row number of the "HPCA Hippocalcin" gene.

b) Find the proportion among ALL patients that the "HPCA Hippocalcin" gene is negatively expressed (expression value<0).

c) We want to show that "HPCA Hippocalcin" gene is negatively expressed in at least half of the *population* of the ALL patients. State the null hypothesis and the alternative hypothesis. Carry out the appropriate test.

d) Find a 95% confidence interval for the difference of proportions in the ALL group versus in the AML group of patients with negatively expressed "HPCA Hippocalcin" gene.

Solutions:

7**a)** Find the row number of the "HPCA Hippocalcin" gene.

```
> # Finding the roe index through grep
>
> grep("HPCA Hippocalcin",golub.gnames[,2])
[1] 118
```

- ⇨ The row number of HPCA Hippocalcin is 118

Solutions to Midterm Module

7**b)** Find the proportion among ALL patients that the "HPCA Hippocalcin" gene is negatively expressed (expression value<0).

```
> HPCA.data = golub[118, gol.fac=="ALL"]
> mean(HPCA.data<0)
[1] 0.5925926
```

⇨ Proportion among ALL patients that the HPCA Hippocalcin gene is negatively expressed is 0.5925926

7**c)** We want to show that "HPCA Hippocalcin" gene is negatively expressed in at least half of the *population* of the ALL patients. State the null hypothesis and the alternative hypothesis. Carry out the appropriate test.

$H_0 : P_{ALL} = ½ ; H_A: P_{ALL} > ½$

```
> p.all<-sum(golub[118,gol.fac=="ALL"]<0)
> binom.test(x=p.all,n=27,p= 0.5, alternative="greater")

        Exact binomial test

data:  p.all and 27
number of successes = 16, number of trials = 27,
p-value = 0.221
alternative hypothesis: true probability of success is greater than 0.5
95 percent confidence interval:
 0.4170687 1.0000000
sample estimates:
probability of success
             0.5925926
```

⇨ As the pvalue is 0.221 , we accept Null Hypothesis

7d) Find a 95% confidence interval for the difference of proportions in the ALL group versus in the AML group of patients with negatively expressed "HPCA Hippocalcin" gene.

```
> # getting the row index for HPCA
> grep("HPCA Hippocalcin",golub.gnames[,2])
[1] 118
> # getting the data
> x.ALL <- golub[118,gol.fac=="ALL"]
> nALL <- length(x.ALL)
> x.AML<- golub[118,gol.fac=="AML"]
> nAML <- length(x.AML)
> nboot<-1000
> boot.diff <- rep(NA,nboot)
> for (i in 1:nboot) {
+   data.ALL <- x.ALL[sample(1:nALL,replace=TRUE)]
+   data.AML <- x.AML[sample(1:nAML,replace=TRUE)]
+   data.diff <- data.ALL-data.AML
+   boot.diff[i] <- mean(data.diff)
+ }
```

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```
There were 50 or more warnings (use warnings() to see the first 50)
> quantile(boot.diff,c(0.025,0.975))
      2.5%      97.5%
-0.4796049  0.3626952
```

- ⇨ The 95% CI for the difference of proportions in the ALL group versus in the AML group of patients with negatively expressed “HPCA Hippocalcin” gene is -0.4796049, 0.3626952

Solutions to Midterm Module