Assignment 4

Ex 1

```
angles <- read.table("angles.txt")
angles <- as.vector(angles$x)</pre>
```

K estimation by MLE numerical optimization from previous exercise:

```
dsink <- function(x, k = 1, lg = FALSE) {
    sinintegral <- integrate(function(x) sin(x) ^ k, lower = 0, upper = pi)$value
    if (lg == FALSE) {
        return(sin(x) ^ k / sinintegral)
    }
    else{
        return(log(sin(x) ^ k / sinintegral))
    }
}
minusll <- function(k, xvals) {
    return(-sum(dsink(xvals, k, lg = TRUE)))
}
k_est <- optimize(f = minusll, xvals = angles, interval = c(0, 100))$minimum</pre>
```

Ex 1.1 Build a 99% confidence interval for k based on the data in angles.txt, how you can estimate the standard error?

$$z_{\alpha/2} = F^{-1}(1 - (\alpha/2))$$

$$C_n = (a, b) = \left(\bar{X} - \frac{\sigma}{\sqrt{n}}z_{\alpha/2}, \bar{X} + \frac{\sigma}{\sqrt{n}}z_{\alpha/2}\right)$$

$$SEM = \frac{\sigma}{\sqrt{n}}$$

First we find $SEM(\hat{k})$ by bootstrap:

```
vect_k_est_bt <- replicate(1000, expr = {
   angles_bt <- sample(angles, size = length(angles), replace = TRUE)
   optimize(f = minusll, xvals = angles_bt, interval = c(0, 100))$minimum
})
se_est <- sd(vect_k_est_bt)
se_est</pre>
```

[1] 0.5402932

Than we calculate the 99% confidence interval for the parameter k:

```
alpha <- 0.01
z <- qnorm(1 - alpha/2)
a <- k_est - se_est * z
b <- k_est + se_est * z
paste("99% Confidence Interval for k: ( a =", a, ", b= ", b, ")")

## [1] "99% Confidence Interval for k: ( a = 10.0086904579238 , b= 12.7920963516759 )"

We can also calculate the percentile confidence interval:

quantile(vect_k_est_bt, probs = c(alpha/2, 1 - alpha/2))

## 0.5% 99.5%
## 10.20796 12.91283</pre>
```

Ex 1.2 Test if k is larger than 10 at a confidence level alpha equeal to 0.05.

One side Wald test $H_0 = \theta \le 10$

```
k0 <- 10
alpha <- 0.05
z <- qnorm(1 - alpha)
w <- (k_est - k0) / se_est  # w > Z TRUE, so we reject Ho and we think theta > 10
w > z  # (we can assume that because it is a 1 side test)
```

[1] TRUE

$$H_0 = \theta \le 10$$
$$H_1 = \theta > 10$$

Since w > Z we reject the null hyphotesis, so with 95% confidence we think that k > 10.

The approximate p-value is:

```
pval <- 1 - pnorm(w)
pval</pre>
```

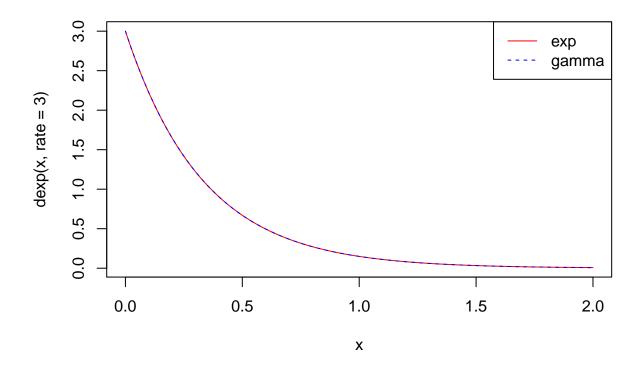
[1] 0.004772181

Ex 2

```
spikes <- read.table("neuronspikes.txt")
spikes <- spikes$V1</pre>
```

2.1 The exponential distribution is a special case of the gamma distribution when the shape parameter is equal to 1. Check this fact graphically in R.

```
curve(dexp(x, rate = 3), col = "red", from = 0, to = 2)
curve(dgamma(x, rate = 3, shape = 1), col = "blue", lty = 2, add = TRUE)
legend("topright", legend = c("exp", "gamma"), col = c("red", "blue"), lty = c(1, 2))
```



2.2 Since the exponential model is nested in the gamma model we can perform the likelihood ratio test to select between the two models.

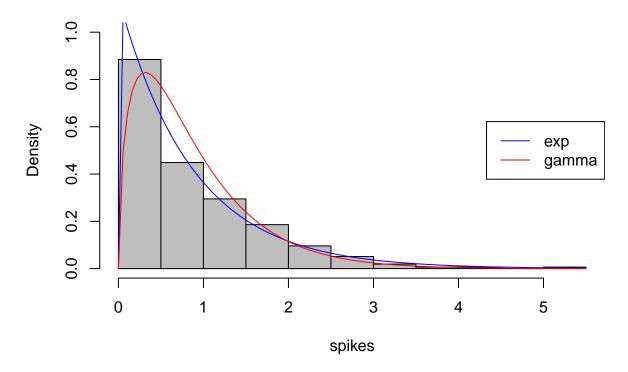
LRT to test whether the parameter rich model is significantly better than the simpler model.

 H_0 = the model M1 is sufficient do describe the data.

We can plot the densities of the exp and gamma distributions together with the spikes:

```
hist(spikes, freq = FALSE, col = "gray", ylim = c(0,1))
curve(dexp(x, rate = exp_mle_rate), col = "blue", add = TRUE)
curve(dgamma(x, shape = gamma_mle_shape, rate = gamma_mle_rate), col = "red", add = TRUE)
legend("right", c("exp", "gamma"), col = c("blue", "red"), lty = 1)
```

Histogram of spikes



Under the null hypothesis assumption: $\lambda(X_1, \dots, X_n) = -2\log(q(X)) \approx \chi^2_{d-d_0}$.

We can now calculate λ :

```
 LR\_lambda <- 2*(gamma\_mle\_value - exp\_mle\_value) \# lambda = 2*(ll\_large.m - ll\_small.m) \\ LR\_lambda \# bigger is the LR\_lambda and more convinient is to use the less restricted model
```

[1] 33.07526

LR test statistic is 33.07 (distributed chi_squared), with 1 degree of freedom.

Now we compare λ with the upper quantile of the chi squared distribution with $d-d_0$ degrees of freedom:

```
alpha = 0.05
LR_lambda > qchisq(1-alpha, df = 1) # not sure about this
```

[1] TRUE

Since $\lambda(X_1, \dots, X_n) > \chi^2_{d-d_0:\alpha}$ I reject H_0 . <- (NOT SURE HERE)

The p_value =
$$1-F_{\chi_{d-d_0}}^2$$
 ($\lambda(X_1,\ldots,X_n)$) (in our case $d-d_0=2-1=1$) pvalue <- 1 - pchisq(LR_lambda, df = 1) pvalue

[1] 8.86598e-09

P-value is really low (p-value < alpha?) so we reject the null hypothesis.

Thus we can state that it is preferable to use the gamma model to describe the data.

Ex 3.

Ex 3.1 Find the MLE for the exponential, gamma, inverse Gaussian and log_normal model.

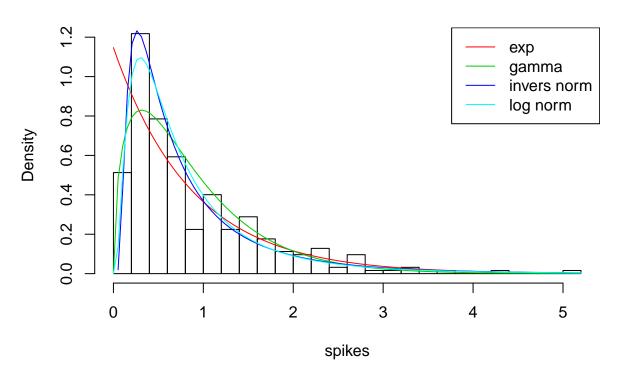
```
Mll exponential:
mll_exp <- function(par, xvals){</pre>
  return(-sum(dexp(xvals, rate = par, log = TRUE)))
\exp_{mle} \leftarrow \operatorname{optimize}(f = mll_exp, interval = c(0,100), xvals = spikes)
exp_mle_par <- exp_mle$minimum</pre>
exp_mle_value <- -exp_mle$objective</pre>
                                                      # convert from -sum(logll) to +sum(logll)
exp_mle_value
## [1] -269.2388
Mll gamma:
mll_gamma <- function(par, xvals){</pre>
  return(-sum(dgamma(xvals, shape = par[1], rate = par[2], log = TRUE)))
gamma_mle \leftarrow optim(f = mll_gamma, par = c(1, 1), xvals = spikes)
gamma_mle_par <- gamma_mle$par</pre>
gamma_mle_value <- -gamma_mle$value</pre>
gamma_mle_value
## [1] -252.7012
Mll inverse Gaussian:
dinvnorm <- function(x, mu, lambda, lg = FALSE){</pre>
  if(lg == TRUE){
    return(log(sqrt(lambda/(2*pi*(x^3)))*exp(-lambda*((x-mu)^2)/(2*(mu^2)*x))))
    }
  else{
    return(sqrt(lambda/(2*pi*(x^3)))*exp(-lambda*((x-mu)^2)/(2*(mu^2)*x)))
}
mll invnorm <- function(par, xvals){</pre>
  return(-sum(dinvnorm(xvals, mu = par[1], lambda = par[2], lg = TRUE)))
invnorm_mle <- optim(par = c(1, 1), fn = mll_invnorm, xvals = spikes)
invnorm mle par <- invnorm mle$par</pre>
invnorm_mle_value <- -invnorm_mle$value</pre>
invnorm_mle_value
## [1] -235.4785
Mll log normal:
mll_lnorm <- function(par, xvals){</pre>
  return(-sum(dlnorm(xvals, meanlog = par[1], sdlog = par[2], log = TRUE)))
}
lnorm_ml <- optim(par = c(1, 1), fn = mll_lnorm, xvals = spikes)</pre>
lnorm_ml_par <- lnorm_ml$par</pre>
lnorm_ml_value <- -lnorm_ml$value</pre>
lnorm_ml_value
```

[1] -240.3783

We now plot the densities of the models on top of the data.

```
hist(spikes, freq = FALSE, breaks = 30, ylim = c(0,1.2))
curve(dexp
          (x, rate = exp_mle_par), col = 2, add = TRUE)
curve(dgamma
          (x, shape = gamma_mle_par[1], rate = gamma_mle_par[2]), col = 3, add = TRUE)
curve(dinvnorm
          (x, mu = invnorm_mle$par[1], lambda = invnorm_mle$par[2]), col = 4, add = TRUE)
curve(dlnorm
          (x, meanlog = lnorm_ml_par[1], sdlog = lnorm_ml_par[2]), col = 5, add = TRUE)
legend("topright", legend = c("exp", "gamma", "invers norm", "log norm"),
          col = c(2,3,4,5), lty = 1)
```

Histogram of spikes



Ex.3.2 Perform model selection using AIC and BIC.

```
k = 1
AIC_exp <- -2 * exp_mle_value + 2 * k
BIC_exp <- -2 * exp_mle_value + k * log(length(spikes))
AIC_exp
## [1] 540.4776
BIC_exp
## [1] 544.2206</pre>
```

```
AIC_gamma <- -2 * gamma_mle_value + 2 * k
BIC_gamma <- -2 * gamma_mle_value + k * log(length(spikes))
AIC_gamma
## [1] 509.4023
BIC_gamma
## [1] 516.8883
AIC_invnorm <- -2 * invnorm_mle_value + 2 * k
BIC_invnorm <- -2 * invnorm_mle_value + k * log(length(spikes))
AIC_invnorm
## [1] 474.957
BIC_invnorm
## [1] 482.443
AIC_lnorm <- -2 * lnorm_ml_value + 2 * k
BIC_lnorm <- -2 * lnorm_ml_value + k * log(length(spikes))
AIC_lnorm
## [1] 484.7566
BIC_lnorm
## [1] 492.2426
```

We choose the model with the smallest AIC or BIC, the inverse normal distribution fit best our data.

Now we do the same using functions

First I need a list for each model with the loglikelihood value and parameters, then I need a list of all models

```
exp <- list(
   value = exp_mle_value,
   par = exp_mle_par
)

gamma <- list(
   value = gamma_mle_value,
   par = gamma_mle_par
)

invnorm <- list(
   value = invnorm_mle_value,
   par = invnorm_mle_par
)

lognorm <- list(
   value = lnorm_ml_value,
   par = lnorm_ml_value,
   par = lnorm_ml_par
)</pre>
candidates <- list( exp = exp, gamma = gamma, invnorm = invnorm, lognorm = lognorm)
```

Now we can write the functions for AIC and BIC and apply them to the list of models (candidates)

```
aic <- function(model){</pre>
  return(-2 * model$value + 2 * length(model$par))
bic <- function(model){</pre>
  return(-2* model$value + length(model$par) * log(length(spikes)))
scores <- data.frame(</pre>
 AIC = sapply(X = candidates, FUN = aic),
 BIC = sapply(candidates, bic)
)
scores
##
                 AIC
                          BIC
           540.4776 544.2206
## exp
           509.4023 516.8883
## gamma
## invnorm 474.9570 482.4430
## lognorm 484.7566 492.2426
```

Ex.4

Ex 4.1 Estimate the standard error of the MLE estimator of μ for the log_normal distribution applied to the ramp spike time data.

```
ramp_spikes <- read.csv("cell_types.csv", na.strings = "")</pre>
ramp_spikes <- ramp_spikes$ef__peak_t_ramp</pre>
ramp_spikes <- ramp_spikes[!is.na(ramp_spikes)]</pre>
Mll log_normal distribution and MLE:
mll_lnormal <- function(par, xvals){</pre>
  return(-sum(dlnorm(xvals, meanlog = par[1], sdlog = par[2], log = TRUE)))
mu_lnorm_est <- optim(f = mll_lnormal, par = c(1, 1), xvals = ramp_spikes)$par[1]</pre>
mu_lnorm_est
## [1] 1.668835
Calculate SE(\hat{\log \mu}):
vect_lnorm_par_est_bt <- replicate(1000, expr = {</pre>
  ramp_spikes_bt <- sample(ramp_spikes, size = length(ramp_spikes), replace = TRUE)</pre>
  optim(par = c(1, 1), f = mll_lnormal, xvals = ramp_spikes_bt)$par
})
se_mu_lnorm_est <- sd(vect_lnorm_par_est_bt[1,])</pre>
se_mu_lnorm_est
## [1] 0.01272791
```

Ex 4.2 Obtain a 95% confidence interval for the parameter μ (try the different methods).

```
alpha <- 0.05
```

```
1° method:
z \leftarrow qnorm(1 - alpha/2)
a <- mu_lnorm_est - se_mu_lnorm_est * z
b <- mu_lnorm_est + se_mu_lnorm_est * z</pre>
paste("95% Confidence Interval for k: ( a =", a, ", b= ", b, ")")
## [1] "95% Confidence Interval for k: ( a = 1.64388908806877 , b = 1.6937815647182 )"
2° method (percentile confidence intervals):
quantile(vect_lnorm_par_est_bt[1,], probs = c(alpha/2, 1 - alpha / 2))
       2.5%
               97.5%
## 1.644098 1.693755
Ex 4.3 Obtain again a 95% confidence interval for the parameter μ using only
the human cells.
ramp_spikes <- read.csv("cell_types.csv")# It's faster to reload the data than change all the names
m <- ramp_spikes$donor_species == "Homo Sapiens"</pre>
ramp_spikes_human <- na.omit(ramp_spikes$ef__peak_t_ramp[m])</pre>
sum(is.na(ramp_spikes_human))
## [1] O
Find MLE for human cells:
mu_lnorm_est_human <- optim(f = mll_lnormal, par = c(1, 1), xvals = ramp_spikes_human)$par[1]</pre>
Find SEM:
vect_lnorm_par_est_bt_human <- replicate(1000, expr = {</pre>
 ramp spikes bt <- sample(ramp spikes human, size = length(ramp spikes human), replace = TRUE)
  optim(par = c(1, 1), f = mll_lnormal, xvals = ramp_spikes_bt)$par
})
se_mu_lnorm_est_human <- sd(vect_lnorm_par_est_bt_human[1,])</pre>
se_mu_lnorm_est_human
## [1] 0.03467046
Find confidence interval:
alpha <- 0.05
z \leftarrow qnorm(1 - alpha/2)
a <- mu_lnorm_est_human - se_mu_lnorm_est_human * z
b <- mu_lnorm_est_human + se_mu_lnorm_est_human * z
paste("95% Confidence Interval for k: ( a =", a, ", b= ", b, ")")
## [1] "95% Confidence Interval for k: ( a = 1.78434369585193 , b= 1.92024941777163 )"
2° method (percentile confidence intervals):
quantile(vect_lnorm_par_est_bt_human[1,], probs = c(alpha/2, 1 - alpha / 2))
       2.5%
               97.5%
## 1.787580 1.919534
```

Ex 5.

Ex 5.1 Transform the ramp spike time using the logarithm as we did in Week 3 and then perform a two sample t_test between the human and mouse cells.

```
m = ramp_spikes$donor_species == "Mus musculus"
ramp_spikes_mouse <- na.omit(ramp_spikes$ef__peak_t_ramp[m])</pre>
sum(is.na(ramp_spikes_mouse))
## [1] 0
ramp_spikes_human_log <- log(ramp_spikes_human)</pre>
ramp_spikes_mouse_log <- log(ramp_spikes_mouse)</pre>
t.test(ramp spikes human log, ramp spikes mouse log)
##
##
    Welch Two Sample t-test
##
## data: ramp_spikes_human_log and ramp_spikes_mouse_log
## t = 5.9063, df = 529.61, p-value = 6.26e-09
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## 0.1495649 0.2986374
## sample estimates:
## mean of x mean of y
## 1.852376 1.628275
H_0: \mu_h = \mu_m
H_1: \mu_h \neq \mu_m
p_value < \alpha, we reject H_0.
```

We think that the 2 means are significantly different with a confidence of 95% (actually at a level 0.001 from Gherardo solution).

Basic t_{test} (var.equal = T) works only with samples that have homogeneous variance but by default the var.equal is set to FALSE and so we can use it with sample that have different variance.

Ex 5.2 Perform directly a Wald test to check if $\mu h = \mu m$ where μh and μm are the mean_log parameters of the log_normal distributions for the human and mouse cells.

$$w = \frac{|\bar{x}_h - \bar{x}_m|}{\sqrt{\frac{s_h^2}{n_h} + \frac{s_m^2}{n_m}}}$$

```
alpha <- 0.05
Zquantile <- qnorm(1 - alpha/2)

w <- abs(mean(ramp_spikes_human_log) - mean(ramp_spikes_mouse_log)) / (
    sqrt(
        (var(ramp_spikes_human_log)^2 / length(ramp_spikes_human_log)) +
              (var(ramp_spikes_mouse_log)^2/length(ramp_spikes_mouse_log))
        )

w <= Zquantile  # Ho: mean_human = mean_mouse, since Z (or W) > Z, I reject Ho.
```

Repeat 5.2 from Gherardo solution

Various calculation to obtain the stadard error of the difference of the means

Since we assume that $\mathbb{V}(X_i) = \mathbb{V}(Y_i) = \sigma^2$, we can write

$$se(\delta) = \sigma \sqrt{\frac{m+n}{mn}}$$

and an estimator of $se(\delta)$ is

$$\hat{se}(\delta) = \hat{\sigma}\sqrt{\frac{m+n}{mn}}$$

where $\hat{\sigma}$ is the empirical standard deviation of the joined sample.

```
n <- length(ramp_spikes_mouse_log) ## mouse sample size
m <- length(ramp_spikes_human_log) ## human sample size
sigma_est <- sd(c(ramp_spikes_mouse_log, ramp_spikes_human_log))## empirical sd joined sample
se_delta_est <- sigma_est * sqrt((n + m)/ (n * m))</pre>
```

Calculate delta and the p-value

p-value =
$$1 - 2F_Z(|\delta|/\hat{se}(\delta)) = 2F_Z(-|\delta|/\hat{se}(\delta))$$

```
delta <- mean(ramp_spikes_mouse_log) - mean(ramp_spikes_human_log)
pvalue <- 1 - 2 * pnorm( abs(delta) / se_delta_est )
pvalue

## [1] -1
pvalue <- 2 * pnorm( - abs(delta) / se_delta_est ) # why it's not the same? use this one
pvalue</pre>
```

[1] 1.086408e-11

Also the Wald test obtain a very small p-value and thus a similar result to the t-test.

Ex 6.

Ex 6.1 Simulate two groups of i.i.d. data following two normal distributions.

```
m = 20
n = 40
mu1 = 2
```

```
mu2 = 2.5
sigma = 4
x = rnorm(m, mean = mu1, sd = sigma)
y = rnorm(n, mean = mu2, sd = sigma)
```

Ex 6.2 Compute the p_value of the two_sample t_test with equal variance.

T-Test

```
t <- t.test(x, y, var.equal = TRUE)
t$p.value</pre>
```

[1] 0.3204236

if p_value > α , we can't reject the H_0 : $\xi 1 = \xi 2$, but the result of the p-value in this case change from one sample generated to an other.

Ex 6.3

Compute the Wald test for $H_0: \xi 1 = \xi 2$

Wald-Test

```
alpha <- 0.05
delta <- mean(x) - mean(y)

Z <- qnorm(1 - alpha/2)

w <- abs(delta / (
    sqrt( (var(x)^2 / length(x)) + (var(y)^2/length(y)) ) ) # <- ERROR!!
)

w <= Z  # the SE of delta found in this way it's not correct</pre>
```

```
## [1] TRUE
```

```
p_value_Wtest = 2 * pnorm(-abs(w))
p_value_Wtest
```

[1] 0.7724048

The Wald t-test use the $\delta = \bar{X} - \bar{Y}$ statistic. Where $se(\delta) = \sigma \sqrt{\frac{m+n}{mn}}$

Estimate SE of delta analytically (from the formula above obtained in 5.2)

```
delta <- mean(x) - mean(y)
se_delta <- sigma * sqrt( (m+n) / (m*n))
w <- list(
    w = delta / se_delta,
    p.value = 2 * pnorm(-abs(delta) / se_delta)
)
w$p.value</pre>
```

[1] 0.4176629

Estimate SE of delta by bootstraping

```
vect_norm_meandiff_bt <- replicate(10000, expr = {
   x_bt <- sample(x, size = length(x), replace = TRUE)
   y_bt <- sample(y, size = length(y), replace = TRUE)
   mean(x_bt)-mean(y_bt)
})
se_delta_bt <- sd(vect_norm_meandiff_bt)

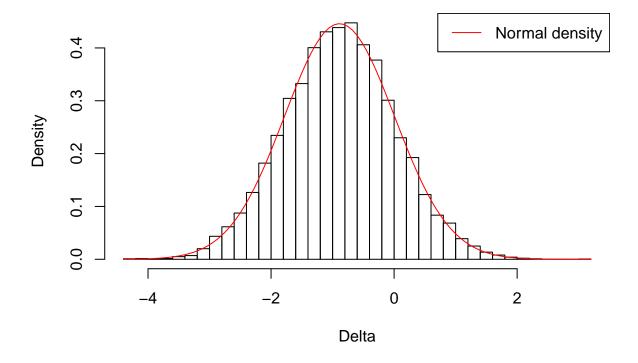
p_value.bt <- 2 * pnorm( - abs(delta) / se_delta_bt)
p_value.bt</pre>
```

[1] 0.3210421

Prove that the mean difference is Gaussian distributed

```
hist(vect_norm_meandiff_bt, freq = FALSE, breaks = 50,
    main = "Distribution of Delta by bootstrapping",xlab = "Delta")
curve(dnorm(x, mean = delta, sd = se_delta_bt), add = TRUE, col = "red")
legend("topright", legend = "Normal density", col = "red", lty = 1)
```

Distribution of Delta by bootstrapping



It is visually possible to observe that $\delta = \bar{X} - \bar{Y}$ is Gaussian distributed.

Ex 6.4

Perform the likelihood ratio test for $H_0: \xi 1 = \xi 2$.

LRT-Test

[1] 0.4176629

Ex 6.5 Compare the results obtained in the different tests, in particular report the different p_values.

```
tests <- list(
  wald = w,
  t.test = t,
  LRT = LRT
)
sapply(tests, function(x) return(x$p.value))
## wald t.test LRT</pre>
```

wald t.test LRT ## 0.4176629 0.3204236 0.4176629

For all the test performed the p-value is always larger than α and so we don't reject the H_0 .

Now we can try with more sample size.

```
m = 2000
n = 4000
mu1 = 2
mu2= 2.5
sigma = 4
x = rnorm(m, mu1, sigma)
y = rnorm(n, mu2, sigma)
```

1) T-Test

```
t <- t.test(x, y, var.queal = TRUE)
t$p.value</pre>
```

[1] 3.56235e-06

2) Wald-Test

Estimate SE_delta by bootstrap

```
delta_bt <- replicate(10000, expr = {
  x_bt <- sample(x, size = length(x), replace = TRUE)
  y_bt <- sample(y, size = length(y), replace = TRUE)
  mean(x_bt) - mean(y_bt)</pre>
```

```
})
se_delta_bt <- sd(delta_bt)</pre>
```

Calculate w and the p-value

```
delta = mean(x) - mean(y)
w <- list(
  w = delta / se_delta_bt,
  p.value = 2 * pnorm( -abs(delta) / se_delta_bt)
)
w$p.value</pre>
```

[1] 3.626292e-06

3) LRT-Test

[1] 2.83525e-06

Conclusions

```
tests <- list(
  t.test = t,
  wald = w,
  LRT = LRT
)
sapply(tests, function(x) return(x$p.value))</pre>
```

```
## t.test wald LRT
## 3.562350e-06 3.626292e-06 2.835250e-06
```

With larger sample size the p-values from all tests are really low, thus we reject Ho. It become evident that $\mu_1 \neq \mu_2$