

Assignment 3

1 A Trigonometric Density

Ex 1.0 How can you compute the normalization of C_k ?

$$f(x|k) = C_k \sin(x)^k$$
$$C_k = \frac{f(x|k)}{\sin(x)^k}$$

We can use this equation to calculate the value of C_k . But to solve this equation, we need to find the value of $f(x|k)$ first.

We know that $f(x|k)$ is proportional to the probability density of $\sin(x)^k$, which just means $f(x|k)$ is a probability of $\sin(x)^k$. In order to calculate the probability of something, we just need to divide it by the total number of possibilities, which in this case is the area under the curve $\sin(x)^k$. Therefore:

$$f(x|k) = \frac{\sin(x)^k}{\int_0^\pi \sin(x)^k dx}$$

We can substitute this value into our previous equation for C_k to get:

$$C_k = \frac{\frac{\sin(x)^k}{\int_0^\pi \sin(x)^k dx}}{\sin(x)^k}$$
$$C_k = \frac{1}{\int_0^\pi \sin(x)^k dx}$$

Ex 1.1 The model is parametric? Which are the parameters of the model?

Yes, the model is parametric. It has one parameter which is k .

Ex 1.2 Write the minus log-likelihood function of the model and implement it in an R function.

The minus log likelihood function is:

$$-\ell(k) = -\sum_{i=1}^n \log \frac{\sin(X_i)^k}{\int_0^\pi \sin(x)^k dx}$$

The R implementation of this minus log likelihood function:

```
dSinK <- function(x, k = 1, lg = FALSE) {  
  #returns a vector of sin(x)^k or log(sin(x)^k)  
  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))
  }
}

dSinKMLL <- function(k, xvals) {
  return(-sum(dSinK(xvals, k, lg=TRUE)))
}

```

Ex 1.3 Use numerical optimization method to find the maximum likelihood estimator.

```
optimize(f = dSinKMLL, xvals = angles, interval = c(0, 50))
```

```

## $minimum
## [1] 11.40039
##
## $objective
## [1] 158.3675

```

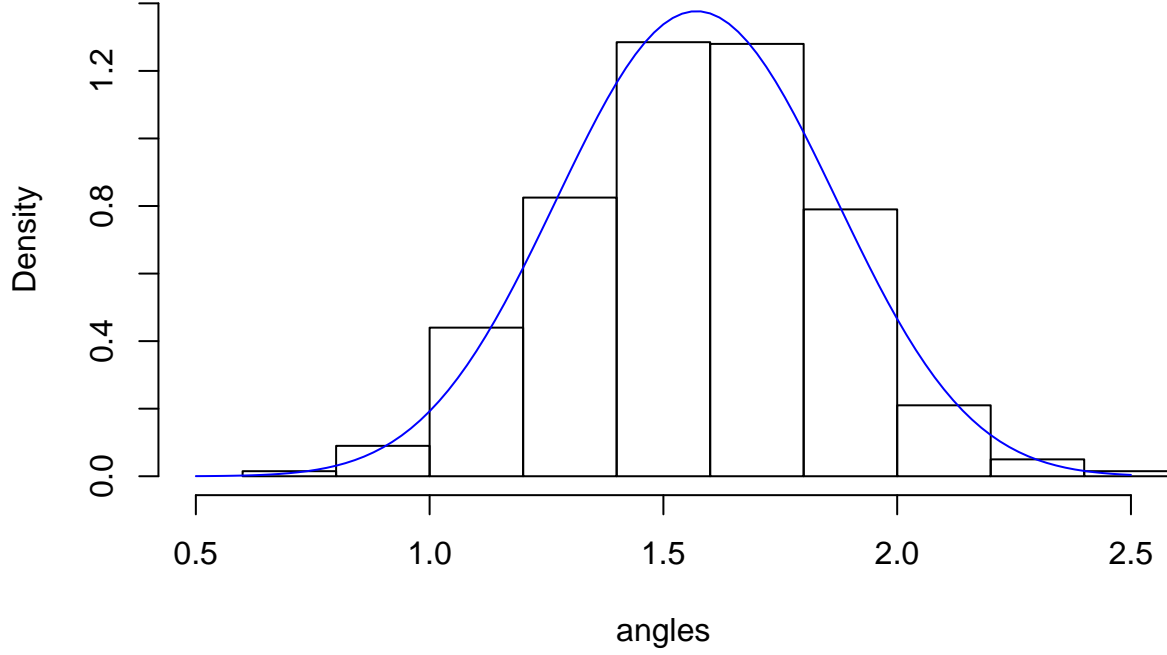
Ex 1.4 Plot the histogram of the data and the density corresponding to the MLE.

```

hist(
  angles,
  xlim = c(0.5, 2.5),
  ylim = c(0, 1.4),
  probability = TRUE
)
minK <- optimize(f = dSinKMLL, xvals = angles, interval = c(0, 50))$minimum
curve(dSinK(x, k = minK), add = TRUE, col = "blue")

```

Histogram of angles



2 A case study of neuronal data

Ex 2.1 If we assume the ISI observations are i.i.d. following an exponential distribution with parameter λ . Compute the maximum likelihood estimate of λ .

If we assume the ISI data follows an exponential distribution with parameter λ , then $\ell(\lambda)$ is given by the following equation:

$$\ell(\lambda) = n \log(\lambda) - \lambda \sum_{i=1}^n X_i$$

The first derivative of $\ell(\lambda)$ is given by the following equation:

$$\ell'(\lambda) = \frac{n}{\lambda} - \sum_{i=1}^n X_i$$

We know that the maximum value of λ will occur when $\ell'(\lambda) = 0$. Therefore:

$$\frac{n}{\lambda} - \sum_{i=1}^n X_i = 0$$

$$\frac{n}{\lambda} = \sum_{i=1}^n X_i$$

$$\lambda = \frac{n}{\sum_{i=1}^n X_i}$$

$$\lambda = \frac{1}{\bar{X}}$$

```
ISImean <- mean(isidata)
lambda <- 1/ISImean
```

```
## [1] "Lambda = 1.14689142797908"
```

Ex 2.2 Assume now that the ISI observations are i.i.d. following a gamma distribution with parameters α (shape) and β (rate), find the MLE estimates of the parameters α and β .

```
gammaMLH <- function(parameters, xvals){
  return(-sum(dgamma(xvals, shape = parameters[1], rate = parameters[2], log = TRUE)))
}

parametersGamma <- optim(par = c(1, 1), fn = gammaMLH, xvals = isidata)$par
```

```
## [1] "Alpha = 1.56231848686039"
```

```
## [1] "Beta = 1.79165490720006"
```

Ex 2.3 Try to find the method of moments estimator of α and β . The method of moments can be used to find the first estimation to initialize the MLE iterative algorithm.

We know that:

$$E(X) = \frac{\alpha}{\beta} \text{ and } V(X) = \frac{\alpha}{\beta^2}$$

Therefore:

$$V(X) = \frac{\alpha}{\beta} \times \frac{1}{\beta}$$

$$V(X) = E(X) \times \frac{1}{\beta}$$

$$\beta = E(X)/V(X)$$

We can calculate the value of α by substituting this value of β into the equation for $E(X)$:

$$\alpha = E(X) \times \beta$$

```
beta_estimator <- mean(isidata)/var(isidata)
```

```
## [1] 1.472556
```

```
alpha_estimator <- mean(isidata)*beta_estimator
```

```
## [1] 1.283954
```

Ex 3

Ex 3.1 Write (analytically) the formula for the log-likelihood given n i.i.d. observations.

$$f(x|\mu, \lambda) = \frac{\lambda}{2\pi x^3} \exp\left(\frac{-\lambda(x - \mu)^2}{2\mu^2 x}\right)$$

$$\mathcal{L}_n(\mu, \lambda) = \prod_{i=1}^n \left(\frac{\lambda}{2\pi X_i^3}\right)^{\frac{1}{2}} \exp\left(\frac{-\lambda(x - \mu)^2}{2\mu^2 x}\right)$$

$$\ell_n(\mu, \lambda) = \sum_{i=1}^n \ln\left(\frac{\lambda}{2\pi X_i^3}\right)^{\frac{1}{2}} + \sum_{i=1}^n \ln\left(\exp\left(\frac{-\lambda(x - \mu)^2}{2\mu^2 x}\right)\right)$$

$$\ell_n(\mu, \lambda) = \sum_{i=1}^n \ln \lambda^{\frac{1}{2}} - \sum_{i=1}^n \ln 2\pi X_i^3 + \sum_{i=1}^n \frac{-\lambda(x - \mu)^2}{2\mu^2 x}$$

$$\ell_n(\mu, \lambda) = \frac{n}{2} \ln \lambda - \sum_{i=1}^n \ln 2\pi X_i^3 + \frac{\lambda}{2} \sum_{i=1}^n \frac{(X_i - \mu)^2}{\mu^2 X_i}$$

Ex 3.2 Try to derive the formula for the maximum likelihood estimators for μ and λ

Ex 3.3 Apply the MLE estimators in the previous step to the experimental ISI data, that is calculate the theoretical estimates of μ and λ for the ISI data.

Ex3.4 Find the maximum likelihood estimators using numerical methods.

```
dInvNorm <- function(x, mu, lambda, lg = FALSE){
  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)))
  }
}

invNormMLH <- function(parameters, xvals){
  return(-sum(dInvNorm(xvals, mu=parameters[1], lambda = parameters[2], lg = TRUE)))
}

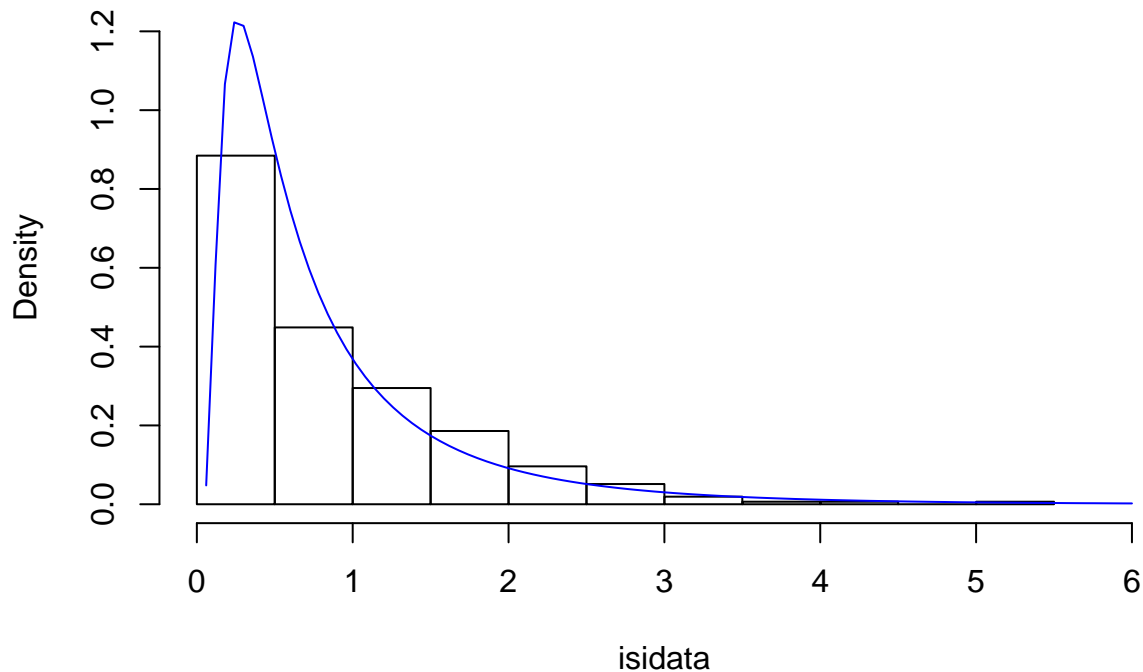
parametersinvNorm <- optim(par = c(1, 1), fn = invNormMLH, xvals = isidata)$par

## [1] "Mu = 0.871873219725603"
## [1] "Lambda = 0.867973616707968"
```

Ex 3.5 Plot the estimated inverse Gaussian density on top of the histogram of the ISI data and with the kernel density estimation.

```
hist(
  isidata,
  xlim = c(0, 6),
  ylim = c(0, 1.2),
  probability = TRUE
)
curve(dInvNorm(x, parametersinvNorm[1], parametersinvNorm[2]), col = "blue", add = TRUE)
```

Histogram of isidata



3 Brain cell dataset

Ex 4.1 Find numerically the MLE estimates of the parameters of the log-normal distribution for the ramp spike time observations.

```
dlnormMLL <- function(parameters, xvals){  
  return(-sum(dlnorm(xvals, meanlog = parameters[1], sdlog = parameters[2], log = TRUE)))  
}
```

```
parametersDlnorm <- optim(par = c(1, 1), fn = dlnormMLL, xvals = rampSpike)$par
```

```
## [1] "Meanlog = 1.66883532639348"
```

```
## [1] "SDlog = 0.605661842011454"
```

Ex 4.2 Transform the ramp spike time observations using the logarithm and then obtain the MLE of the parameters for a Gaussian distribution using the transformed data. Check that the results you obtain are equal to the MLE estimates obtained numerically in point 4.1.

```
logRampSpike <- log(rampSpike)
```

```
dnormMLL <- function(parameters, xvals){  
  return(-sum(dnorm(xvals, mean = parameters[1], sd = parameters[2], log = TRUE)))  
}
```

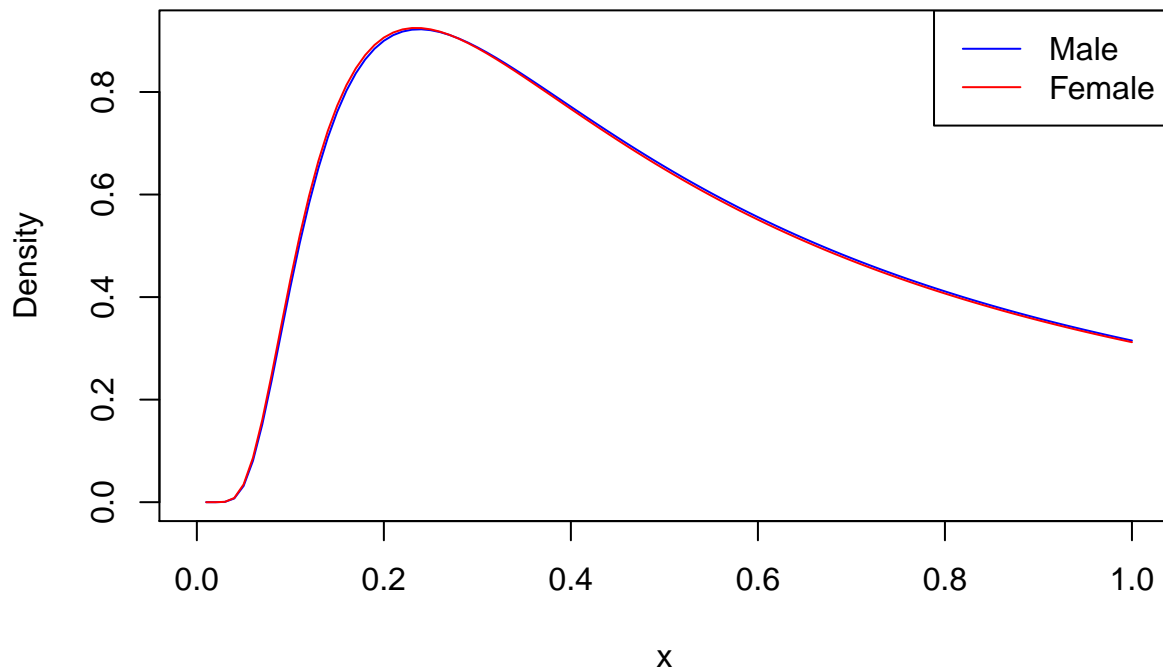
```
parametersDnorm <- optim(par = c(1, 1), fn = dnormMLL, xvals = logRampSpike)$par
```

```
## [1] "Mean = 1.66895647611618"
## [1] "SD = 0.605623564290239"
```

Ex 4.3 Find now the MLE estimates for the parameters of the log-normal distribution using only the male human observations and the female human observations. Plot the two obtained log-normal densities in the same plot.

```
parametersDlnormMale <- optim(par = c(1, 1), fn = dlnormMLL,
                             xvals = maleRampSpike)$par
parametersDlnormFemale <- optim(par = c(1, 1), fn = dlnormMLL,
                                xvals = femaleRampSpike)$par

curve(dlnorm(x, parametersDlnormMale[1], parametersDlnormMale[2]),
      col = "blue", ylab = "Density")
curve(dlnorm(x, parametersDlnormFemale[1], parametersDlnormFemale[2]),
      col = "red", add = TRUE)
legend("topright", legend = c("Male", "Female"), col = c("blue", "red"), lty = c(1, 1))
```



4 Molecular evolution, Jukes-Cantor model

Ex 5.1

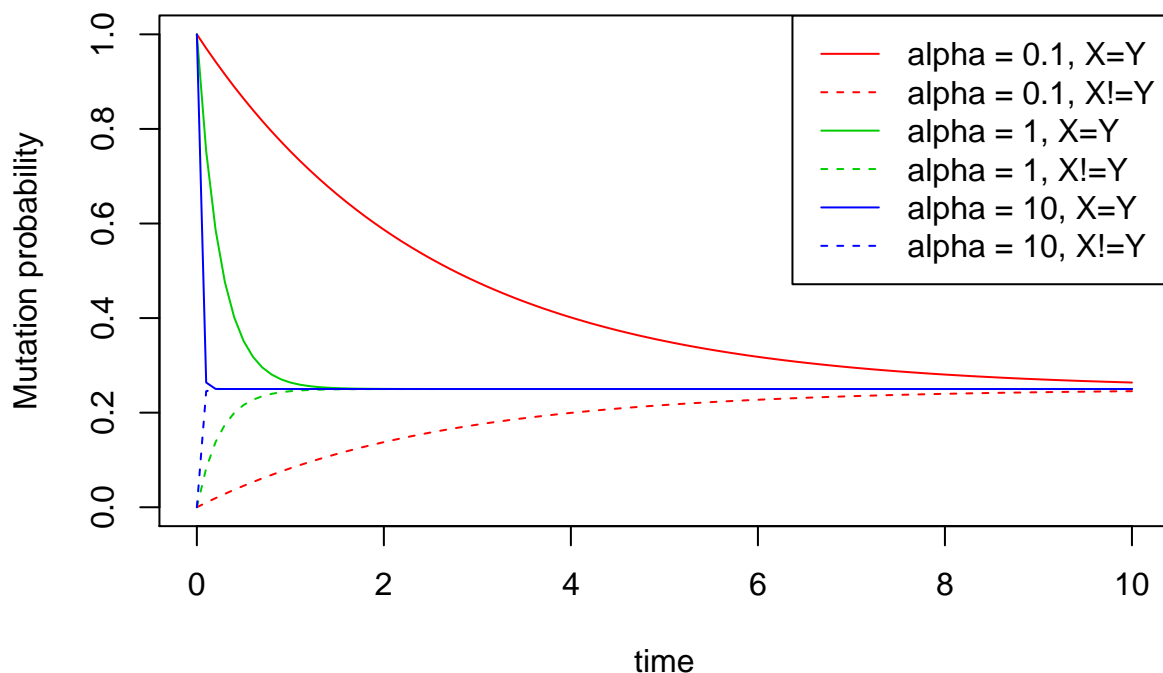
```

JKprob <- function(X, Y, alpha, t=1000){
  if(X==Y){
    return(0.25+0.75*exp(-4*alpha*t))
  }
  else{
    return(0.25-0.25*exp(-4*alpha*t))
  }
}

plot(
  1, type = "n", xlab = "time", xlim = c(0, 10), ylim = c(0, 1),
  ylab = "Mutation probability",
  main = "Behavior of Jukes-Cantor model"
)
for (i in 1:1) {
  curve(
    JKprob(X = "A", Y = "A", alpha = 10 ^ i, t=x),
    from = 0, to = 10, add = TRUE, col = i + 3, lty = 1
  )
  curve(
    JKprob(X = "A", Y = "C", alpha = 10 ^ i, t=x),
    from = 0, to = 10, add = TRUE, col = i + 3, lty = 2
  )
}
legend(
  "topright", col = rep(2:4, each=2), lty = rep(1:2, 3),
  legend = c(
    "alpha = 0.1, X=Y",
    "alpha = 0.1, X!=Y",
    "alpha = 1, X=Y",
    "alpha = 1, X!=Y",
    "alpha = 10, X=Y",
    "alpha = 10, X!=Y"
  )
)

```


Behavior of Jukes–Cantor model



Ex 5.2 Write the log-likelihood function for the observations as a function of α .

Our observations are n pairs of i.i.d nucleotides:

$$(X_i, Y_i), \dots, (X_n, Y_n)$$

Therefore our likelihood function should be:

$$\mathcal{L}_n(\alpha) = \prod_{i=1}^n P(X = X_i, Y = Y_i)$$

We know that the joint probability of observing $(X = x; Y = y)$ is:

$$P(X = x, Y = y) = P(Y = y|X = x)P(X = x)$$

And we assume all nucleotides have equal marginal probabilities, such that:

$$P(X = x) = 0.25 \quad x \in \{A, T, C, G\}$$

Therefore our likelihood function becomes:

$$\mathcal{L}_n(\alpha) = \prod_{i=1}^n P(Y = Y_i|X = X_i)P(X = x)$$

$$\mathcal{L}_n(\alpha) = \prod_{i=1}^n 0.25P(Y = Y_i|X = X_i)$$

The Jukes-Cantor model tells us:

$$P(Y = y|X = x) = \begin{cases} 0.25 + 0.75\exp(-4\alpha t), & \text{if } x = y \\ 0.25 - 0.25\exp(-4\alpha t), & \text{if } x \neq y \end{cases}$$

Since the Jukes-Cantor model only depends on whether $x = y$ or not, let n_1 be the number of times $X_i = Y_i$ in our data and n_2 be the number of times $X_i \neq Y_i$ in our data. Therefore our likelihood function becomes:

$$\begin{aligned} \mathcal{L}_n(\alpha) &= (0.25(0.25 + 0.75\exp(-4\alpha t)))^{n_1} (0.25(0.25 - 0.25\exp(-4\alpha t)))^{n_2} \\ \ell_n(\alpha) &= \log((0.25(0.25 + 0.75\exp(-4\alpha t)))^{n_1} (0.25(0.25 - 0.25\exp(-4\alpha t)))^{n_2}) \\ \ell_n(\alpha) &= \log(0.25(0.25 + 0.75\exp(-4\alpha t)))^{n_1} + \log(0.25(0.25 - 0.25\exp(-4\alpha t)))^{n_2} \\ \ell_n(\alpha) &= n_1 \log(0.25(0.25 + 0.75\exp(-4\alpha t))) + n_2 \log(0.25(0.25 - 0.25\exp(-4\alpha t))) \end{aligned}$$

Ex 5.3 Try to find the theoretical maximum likelihood estimator for α .

Ex 5.4 Try to implement the Jukes-Cantor model in R:

```
#Implement probability function
distJK <- function(pair, alpha){
  A <- sapply(JK_pairs,function(x) x[1]) #select first element of each vector inside list
  B <- sapply(JK_pairs,function(x) x[2]) #select second element (list of letters)
  n <- length(pair)
  n1 <- sum(A == B)
  n2 <- n - n1
  match <- n1*log(JKprob(X="X", Y="X", alpha=alpha)*0.25)
  mismatch <- n2*log(JKprob(X="X", Y="Y", alpha=alpha)*0.25)
  return(match+mismatch)
}

#Implement sampling procedure
simulate_JKpair <- function(start="A", alpha=1e-5, t = 1000){
  mutations <- rpois(1, lambda = 4*alpha*t)
  if(mutations == 0){
    end <- start
    return(c(start, end))
  }
  else {
    for (i in 1:mutations){
      end <- sample(c("A", "C", "T", "G"), size = 1)
    }
  }
  return(c(start, end))
}

JK_pairs <- list()
for (i in 1:1000){
  JK_pairs[[i]] <- simulate_JKpair(t=1000)
}

#Minus log likelihood function
distJKMLL <- function(alpha, xvals){
  return(-sum(distJK(xvals, alpha)))
}
```

#Solving numerically

```
optimize(f = distJKMLL, xvals = JK_pairs, interval = c(-100, 100))
```

```
## Warning in log(JKprob(X = "X", Y = "Y", alpha = alpha) * 0.25): NaNs produced
```

```
## Warning in optimize(f = distJKMLL, xvals = JK_pairs, interval = c(-100, : NA/Inf  
## replaced by maximum positive value
```

```
## Warning in log(JKprob(X = "X", Y = "Y", alpha = alpha) * 0.25): NaNs produced
```

```
## Warning in optimize(f = distJKMLL, xvals = JK_pairs, interval = c(-100, : NA/Inf  
## replaced by maximum positive value
```

```
## $minimum
```

```
## [1] 23.60665
```

```
##
```

```
## $objective
```

```
## [1] 2772.589
```