

Tests for local alignments and DNA shape

Uploadings

Load libraries

```
#library(Biostrings)
library(ggplot2)
library(DNASHapeR)
projpath <- "/home/davidfm/Projects/UBMI-IFC/EnhaProm/"
```

Load functions and libraries

```
setwd(projpath)
source("scripts/genome-functions.R")
```

DNA shape metrics

```
#shape_promoters <- getShape("datasets/testing/promoters_train_positive.fasta", shapeType= c
#getShape("datasets/testing/promoters_train_positive.fasta",
#      shapeType= c("Stretch", "Tilt", "Buckle", "Shear"))
#getShape("datasets/testing/promoters_train_positive.fasta")
#getShape("datasets/testing/promoters_train_positive.fasta", parse=FALSE)
# setwd(paste0(projpath, "liltests/"))
setwd(projpath)
shape_seqs <- getShape("datasets/GB-Testing/10seqs.fasta")
```

Reading the input sequence.....
Reading the input sequence.....
Reading the input sequence.....
Reading the input sequence.....
Reading the input sequence.....

Parsing files.....

Record length: 505

Warning in rbind(`1` = c(NA, NA, NA, NA, NA, NA, NA, 4.67, 4.92, 4.63, 4.92, :
number of columns of result is not a multiple of vector length (arg 1)

Record length: 504

Warning in rbind(`1` = c(NA, NA, NA, NA, NA, NA, NA, 36.61, 31.5, 36.01, 34.17, :
number of columns of result is not a multiple of vector length (arg 1)

Record length: 505

Warning in rbind(`1` = c(NA, NA, NA, NA, NA, NA, NA, -2.4, -6.1, -4.81, :
number of columns of result is not a multiple of vector length (arg 1)

Record length: 504

Warning in rbind(`1` = c(NA, NA, NA, NA, NA, NA, NA, -1.63, -2.51, -2.33, -1.19, :
number of columns of result is not a multiple of vector length (arg 1)

Record length: 505

Warning in rbind(`1` = c(NA, NA, NA, NA, NA, NA, NA, -6.16, -7.26, -5.59, :
number of columns of result is not a multiple of vector length (arg 1)

Done

```

# Change matrix rows into list of vectors
ss_mgw <- t(shape_seqs$MGW)
small_ <- t(shape_seqs$MGW[c(3,5,8),200:300])
#           ^If not transposed, this becomes a mess
# ss_mgw[c(1:10,(nrow(ss_mgw)-10):nrow(ss_mgw)),1:3]
split_factor1 <- rep(1:ncol(ss_mgw), each = nrow(ss_mgw))
split_factor2 <- rep(1:ncol(small_), each = nrow(small_))

ss_mgw_list <- split(ss_mgw, split_factor1)
ss_mgw_list <- lapply(ss_mgw_list, na.omit)
small_list <- split(small_, split_factor2)
# ^There are no NAs in this list since no 'border' columns are considered
any(is.na(small_))

```

[1] FALSE

```

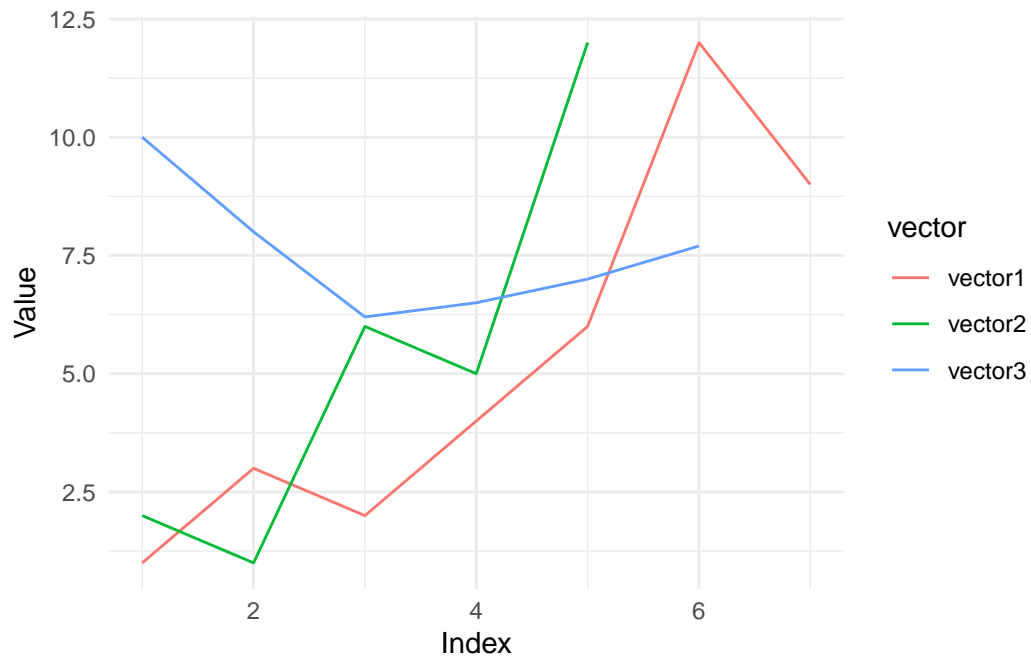
# Plot list of vectors
linesplot <- function(vector_list) {
# Create a data frame to hold the data
  df <- do.call(rbind, lapply(vector_list,
                             function(x) data.frame(x = seq_along(x), y = x)))
  df$vector <- rep(names(vector_list), sapply(vector_list, length))

  # Create the plot
  ggplot(df, aes(x = x, y = y, color = vector)) +
    geom_line() +
    labs(x = "Index", y = "Value") +
    theme_minimal()
}

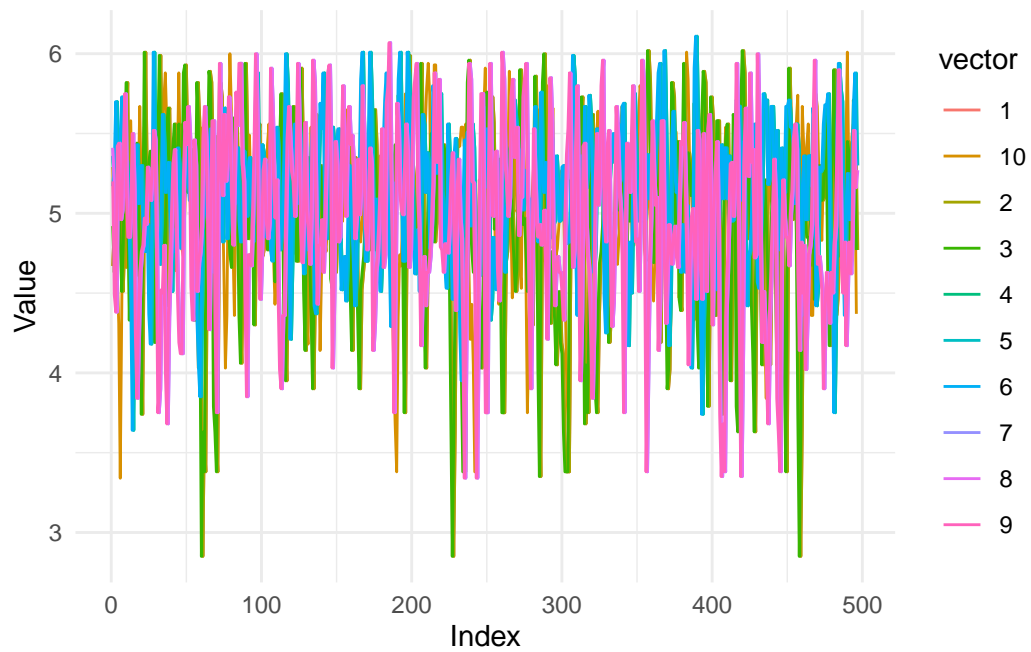
# Sample data: a list of vectors
vector_list <- list(
  vector1 = c(1, 3, 2, 4, 6, 12, 9),
  vector2 = c(2, 1, 6, 5, 12),
  vector3 = c(10, 8, 6.2, 6.5, 7, 7.7)
)

linesplot(vector_list)

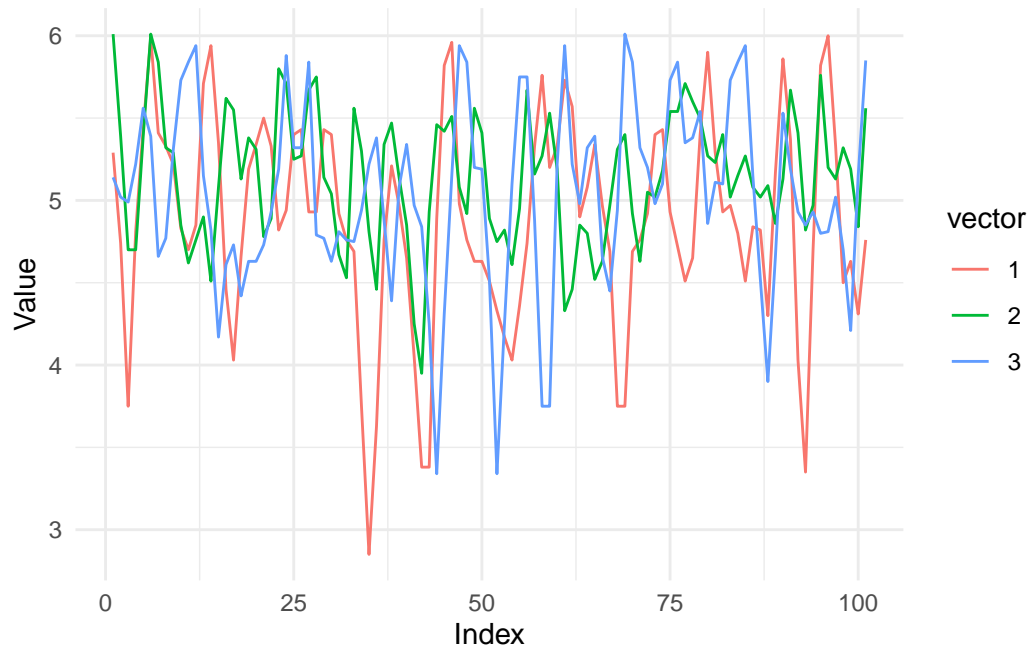
```



```
linesplot(ss_mgw_list)
```



```
linesplot(small__list)
```



Regressions

```
## Shape data as dataframe per sequence
seqshape_df <- function(seqshape) {
  # Normalization
  #: norm_val <- max(c(max(seqshape), abs(min(seqshape))))
  #: norm_seqshape <- seqshape / norm_val
  norm_seqshape <- 2 * (seqshape - min(seqshape)) / (max(seqshape) - min(seqshape)) - 1

  # Positions in 'relative' values
  rel_positions <- seq_along(seqshape) / 100

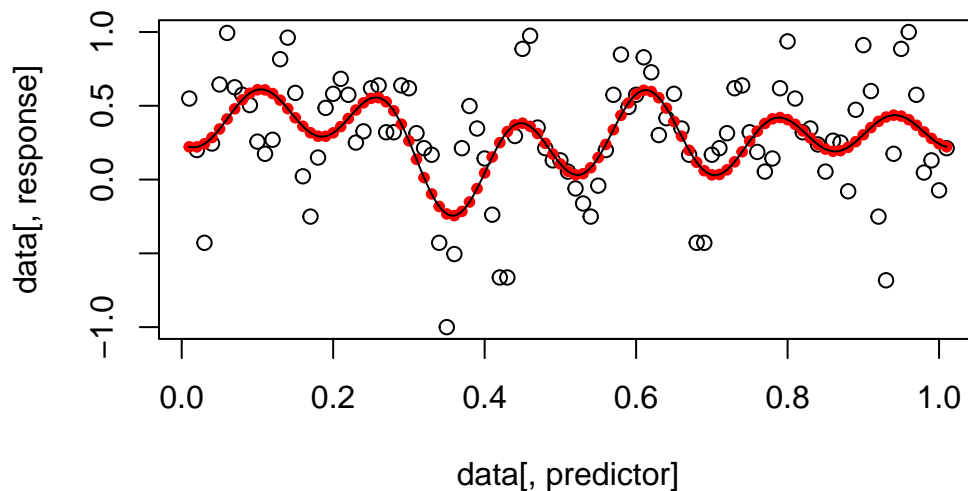
  return(data.frame(mgw_values = norm_seqshape,
                    positions = rel_positions))
}
```

```
# Example shape data
sshape3 <- shape_seqs$MGW[3,200:300]
sshape5 <- shape_seqs$MGW[5,200:300]
sshape8 <- shape_seqs$MGW[8,200:300]

trunc_fourier(seqshape_df(sshape3), "mgw_values", "positions",
              n_peaks=7, aem_option=1, bottomtop=TRUE,
              silent=TRUE, check_again=TRUE, only_coefficients=FALSE)
```

```

      1      2 3      4 5      6 7 8 9      10 11      12 13
l_coefs 0 0.1007206 0 0.1217824 0 -0.08472715 0 0 0 0.08941141 0 -0.197114 0
s_coefs 0 0.0000000 0 0.5000000 0 0.25000000 0 0 0 0.40000000 0 0.300000 0
      14
l_coefs 0
s_coefs 0
```



```
Call:
lm(formula = as.formula(f_i), data = data)
```

```
Coefficients:
```

```

              (Intercept)          cos(pi * ((2 * positions)))
              0.29007              0.10072
cos(pi * ((4 * positions) - 0.5)) cos(pi * ((6 * positions) - 0.25))
              0.12178              -0.08473
cos(pi * ((10 * positions) - 0.4)) cos(pi * ((12 * positions) - 0.3))
              0.08941              -0.19711

```

```

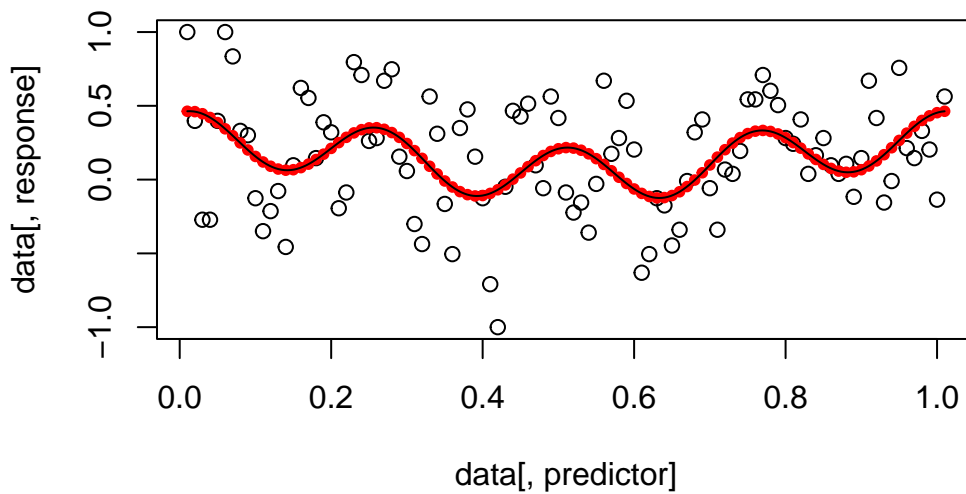
trunc_fourier(seqshape_df(sshape5), "mgw_values", "positions",
              n_peaks=7, aem_option=1, bottomtop=TRUE,
              silent=TRUE, check_again=TRUE, only_coefficients=FALSE)

```

```

      1          2 3 4 5 6 7          8 9 10 11 12 13 14
l_coefs 0 0.1237253 0 0 0 0 0 0.1848824 0 0 0 0 0 0
s_coefs 0 0.0500000 0 0 0 0 0 0.1000000 0 0 0 0 0 0

```



```

Call:
lm(formula = as.formula(f_i), data = data)

```

```

Coefficients:
              (Intercept)  cos(pi * ((2 * positions) - 0.05))

```

```

                                0.1555                                0.1237
cos(pi * ((8 * positions) - 0.1))
                                0.1849

```

```

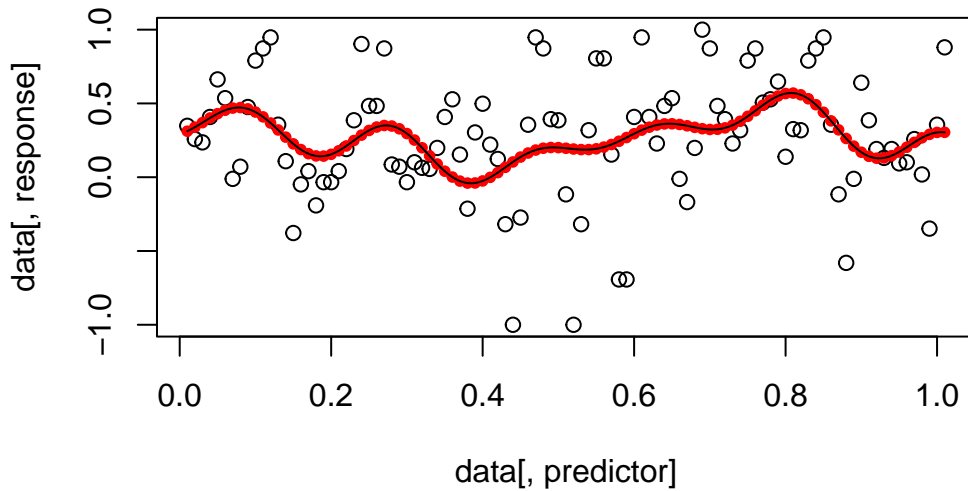
trunc_fourier(seqshape_df(sshape8), "mgw_values", "positions",
              n_peaks=7, aem_option=1, bottomtop=TRUE,
              silent=TRUE, check_again=TRUE, only_coefficients=FALSE)

```

```

      1          2          3 4 5 6 7          8 9 10          11 12 13 14
l_coefs 0 -0.05255758 0.1358541 0 0 0 0 0.07942362 0 0 -0.08769285 0 0 0
s_coefs 0  0.50000000 0.3000000 0 0 0 0 0.30000000 0 0  0.05000000 0 0 0

```



```

Call:
lm(formula = as.formula(f_i), data = data)

```

```

Coefficients:
      (Intercept)      cos(pi * ((2 * positions) - 0.5))
           0.25014                -0.05256
cos(pi * ((3 * positions) - 0.3))      cos(pi * ((8 * positions) - 0.3))
           0.13585                0.07942

```



```
testseq1 <- paste0("TTCTCCTGCCTTAGCCTCCCAAGTCACTGGGATTACAGGTGCCACCACCATACCAGGCTAA",
  "TTTTTGTATTTTTAGTGGAGATGCGGTTTACCATGTTGGCCGGGCCAGTCTCGAACTCCTGACGTC",
  "AAGTGATCTTCCCGCCTCGACTCCTGATATCAAGTGATCTTCCCGCCTCGGCCTCCAGAGTGCTGA",
  "GATTACAGACGTGAACCCATGCCTGGCCAGGAATTTTGTTTTATAGGAAGGCTTTCTACTAATGGAA",
  "TTCCTGGCCTTGAGAGGATGTTACTTTAGAAGGAAAGGATTTTTTGTATTAAAAAGGTAAGATTCC",
  "TGGATTCTTATTGGACTGTTGTCTCTGTTATGAGTAATCCATCTTTAGTCATTACCACTAGGGTTG",
  "TATTTAATTAAGTCTGAGTTATTTTATGGTGATTTTGTTTGTTTTGTTTTGTTTTACCGAATTTT",
  "GTTCTCATTGCCGTGGCTTGAGGGCAATGACGTGAT") # Pasted so the output don't overflow
testseq2 <- "CAAGCTTGTGCAGTGTTGCTGTTCTATCTCGGCTCACTGCAAGCTGTTACGCCATGTTCTGTT"
#sort(sapply(ls()[grep("seq", ls())], function(x) object.size(get(x))))
```

(This was practically already done) This functions measures all the spaces in between a given ‘kmer’, the produced data can either be represented ‘as-is’ or in terms of position relative to sequence length.

```
[1] 0 5 18 115 121 147 152 178 184 355 470
[1] 2 15 112 118 144 149 175 181 352 467 500
InterSpaces:
lengths: 2 10 94 3 23 2 23 3 168 112 30
positions: 1 10 65 116.5 132.5 148 163.5 179.5 268 411 485
```

9

```

9      168      268.0
10     112      411.0
11      30      485.0

```

```
get_interspaces(testseq1, k = 3, kmer = "CTC", relative = TRUE, print = TRUE)
```

```

[1]  0  5 18 115 121 147 152 178 184 355 470
[1]  2 15 112 118 144 149 175 181 352 467 500
InterSpaces:
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97

```

	lengths	positions
1	0.004	0.002
2	0.020	0.020
3	0.188	0.130
4	0.006	0.233
5	0.046	0.265
6	0.004	0.296
7	0.046	0.327
8	0.006	0.359
9	0.336	0.536
10	0.224	0.822
11	0.060	0.970

Kmer-Interspaces

(This function was already done and moved to ‘trash-code’ since it wasn’t of use at the moment. Its’ only modification was moving interspaces’ computation to an individual function an adding the ‘acc_peaks’ (“accentuate peaks”) and ‘rel’ (“relative”) paramters). This function used the previous one and adjusts the data to many trigonometric linear models from which it chooses the ‘best’ one.

```
kmer_interspace_polynome(testseq1, kmer="CTG", aem_option=5, acc_peaks=TRUE)
```

```

[1]  0  8 29 124 155 195 221 269 332 348 357 413
[1]  5 26 121 152 192 218 266 329 345 354 410 500
InterSpaces:
lengths: 0.01 0.036 0.184 0.056 0.074 0.046 0.09 0.12 0.026 0.012 0.106 0.174
positions: 0.005 0.034 0.15 0.276 0.347 0.413 0.487 0.598 0.677 0.702 0.767 0.913

```

Best Case chosen: 7 - 1

Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + sin(2 * pi * spc_pos) +  
    cos(4 * pi * spc_pos) + sin(4 * pi * spc_pos) + cos(6 * pi *  
    spc_pos) + sin(6 * pi * spc_pos) + cos(8 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	sin(2 * pi * spc_pos)
0.0137238	0.0079268	-0.0017201
cos(4 * pi * spc_pos)	sin(4 * pi * spc_pos)	cos(6 * pi * spc_pos)
-0.0019572	-0.0005418	-0.0119401
sin(6 * pi * spc_pos)	cos(8 * pi * spc_pos)	
-0.0043036	-0.0078595	

```
kmer_interspace_polynome(testseq1, kmer="CTG", aem_option=7, acc_peaks=TRUE)
```

```
[1] 0 8 29 124 155 195 221 269 332 348 357 413
```

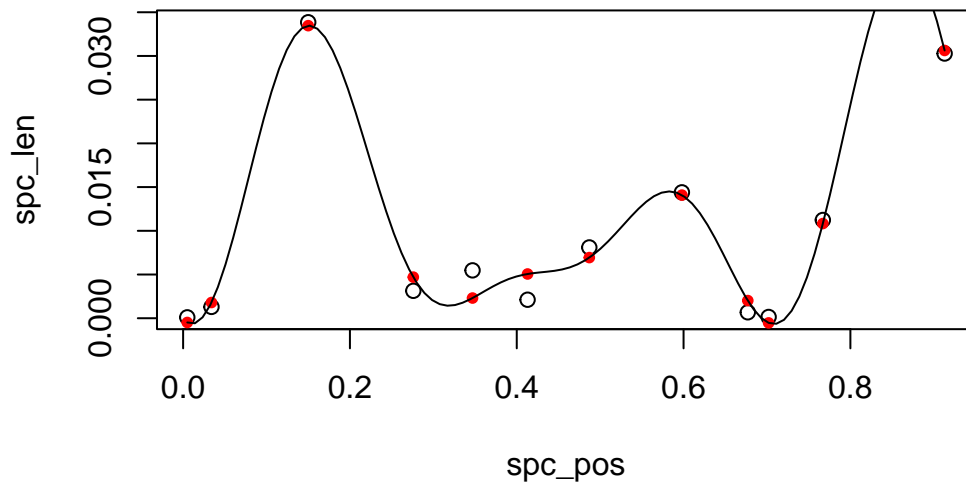
```
[1] 5 26 121 152 192 218 266 329 345 354 410 500
```

InterSpaces:

```
lengths: 0.01 0.036 0.184 0.056 0.074 0.046 0.09 0.12 0.026 0.012 0.106 0.174
```

```
positions: 0.005 0.034 0.15 0.276 0.347 0.413 0.487 0.598 0.677 0.702 0.767 0.913
```

Best Case chosen: 7 - 1



Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + sin(2 * pi * spc_pos) +
    cos(4 * pi * spc_pos) + sin(4 * pi * spc_pos) + cos(6 * pi *
    spc_pos) + sin(6 * pi * spc_pos) + cos(8 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	sin(2 * pi * spc_pos)
0.0137238	0.0079268	-0.0017201
cos(4 * pi * spc_pos)	sin(4 * pi * spc_pos)	cos(6 * pi * spc_pos)
-0.0019572	-0.0005418	-0.0119401
sin(6 * pi * spc_pos)	cos(8 * pi * spc_pos)	
-0.0043036	-0.0078595	

```
kmer_interspace_polynome(testseq1, kmer="CTC", aem_option=7, acc_peaks=TRUE)
```

```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

```
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
```

```
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97
```

Best Case chosen: 4 - 1

Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + sin(2 * pi * spc_pos) +  
    cos(4 * pi * spc_pos) + sin(4 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	sin(2 * pi * spc_pos)
0.05025	-0.04161	-0.04964
cos(4 * pi * spc_pos)	sin(4 * pi * spc_pos)	
-0.00581	0.03897	

```
kmer_interspace_polynome(testseq1, kmer="CTC", aem_option=8, acc_peaks=TRUE)
```

```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

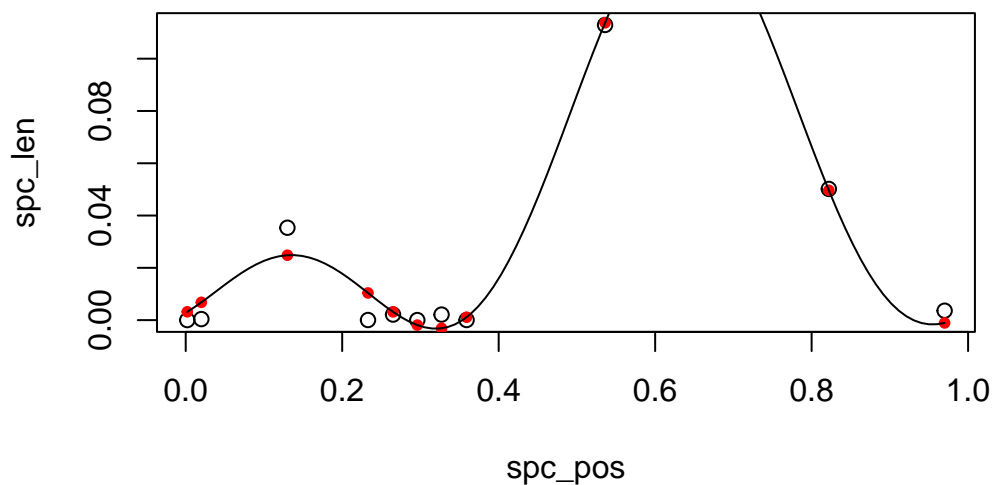
```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

```
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
```

```
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97
```

Best Case chosen: 4 - 1



Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + sin(2 * pi * spc_pos) +  
    cos(4 * pi * spc_pos) + sin(4 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	sin(2 * pi * spc_pos)
0.05025	-0.04161	-0.04964
cos(4 * pi * spc_pos)	sin(4 * pi * spc_pos)	
-0.00581	0.03897	

At a certain point I wanted to visualize the process of model selection so I added the parameter 'silent' (Since the output is really long, we won't evaluate the following cell)

```
kmer_interspace_polynome(testseq1, kmer="CTC", aem_option=7, acc_peaks=TRUE, silent=FALSE)  
kmer_interspace_polynome(testseq1, kmer="CTC", aem_option=8, acc_peaks=TRUE, silent=FALSE)
```

To visualize this in a plot I added the parameter 'aem_graph' ('AEM' standing for 'Adjust-Error Metric')

```
kmer_interspace_polynome(testseq1, kmer="CTC", silent=TRUE, aem_option=5, acc_peaks=TRUE, aem_graph=TRUE)
```

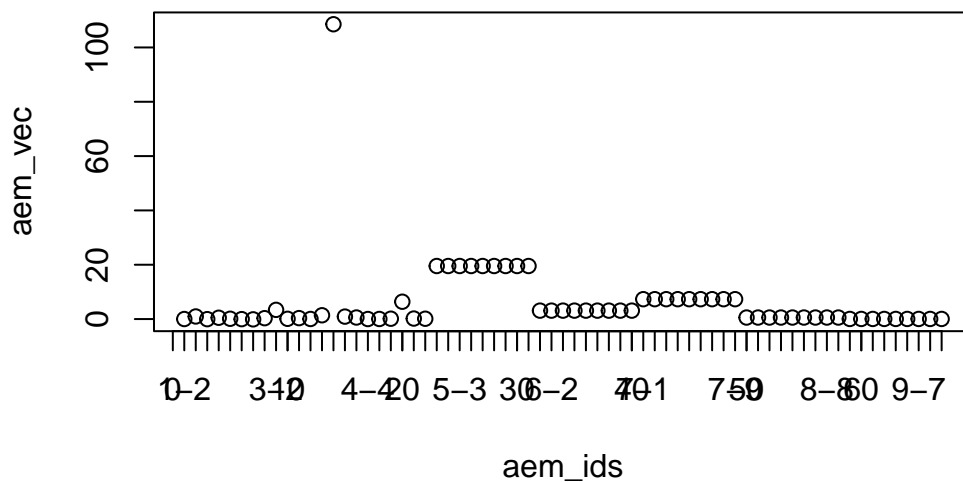
```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

```
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
```

```
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97
```



Best Case chosen: 4 - 1

Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + sin(2 * pi * spc_pos) +
    cos(4 * pi * spc_pos) + sin(4 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	sin(2 * pi * spc_pos)
0.05025	-0.04161	-0.04964
cos(4 * pi * spc_pos)	sin(4 * pi * spc_pos)	
-0.00581	0.03897	

```
kmer_interspace_polynome(testseq1, kmer="CTC", silent=TRUE, aem_option=7, acc_peaks=TRUE, aer
```

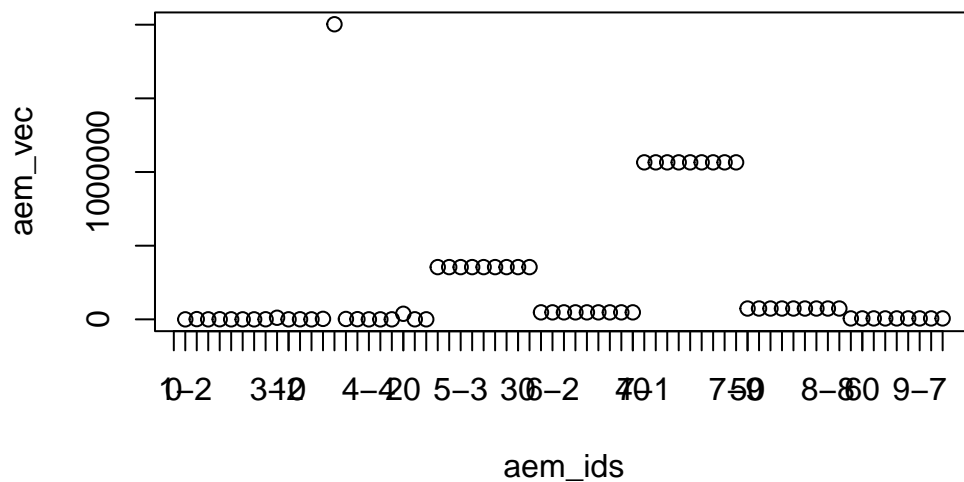
```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

```
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
```

```
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97
```



Best Case chosen: 4 - 1

Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + sin(2 * pi * spc_pos) +
    cos(4 * pi * spc_pos) + sin(4 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	sin(2 * pi * spc_pos)
0.05025	-0.04161	-0.04964
cos(4 * pi * spc_pos)	sin(4 * pi * spc_pos)	
-0.00581	0.03897	

```
kmer_interspace_polynome(testseq1, kmer="CTC", silent=TRUE, aem_option=8, acc_peaks=TRUE, aer
```

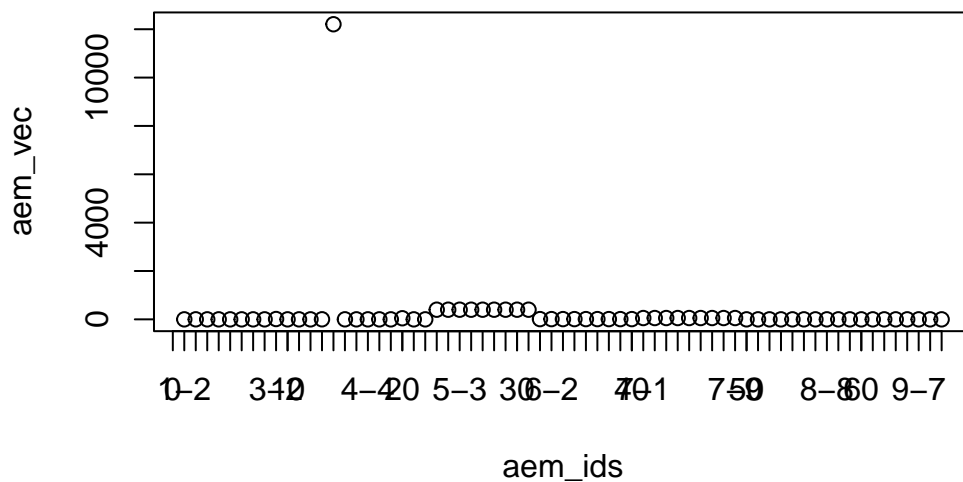
```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

```
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
```

```
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97
```

Best Case chosen: 4 - 1

Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + sin(2 * pi * spc_pos) +
    cos(4 * pi * spc_pos) + sin(4 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	sin(2 * pi * spc_pos)
0.05025	-0.04161	-0.04964
cos(4 * pi * spc_pos)	sin(4 * pi * spc_pos)	
-0.00581	0.03897	

In case I wanted to watch a specific trigonometric case, I added the 'fixed' parameter:

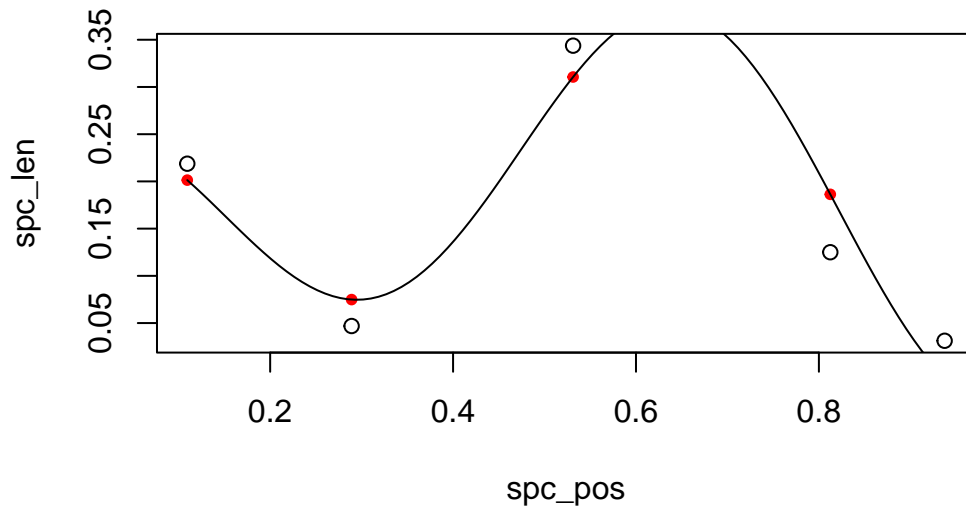
```
kmer_interspace_polynome(testseq2, kmer="GTT", silent=TRUE, fixed=TRUE, case=2, subcase=10)
```

```
[1] 0 17 23 48 59 64
```

```
[1] 14 20 45 56 61 64
```

InterSpaces:

```
lengths: 0.21875 0.046875 0.34375 0.125 0.03125
positions: 0.109375 0.2890625 0.53125 0.8125 0.9375
```



Call:

```
lm(formula = spc_len ~ cos(2 * pi * spc_pos) + cos(3 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(2 * pi * spc_pos)	cos(3 * pi * spc_pos)
0.18878	-0.08092	0.14612

```
kmer_interspace_polynome(testseq2, kmer="GTT", silent=TRUE, fixed=TRUE, case=2, subcase=8)
```

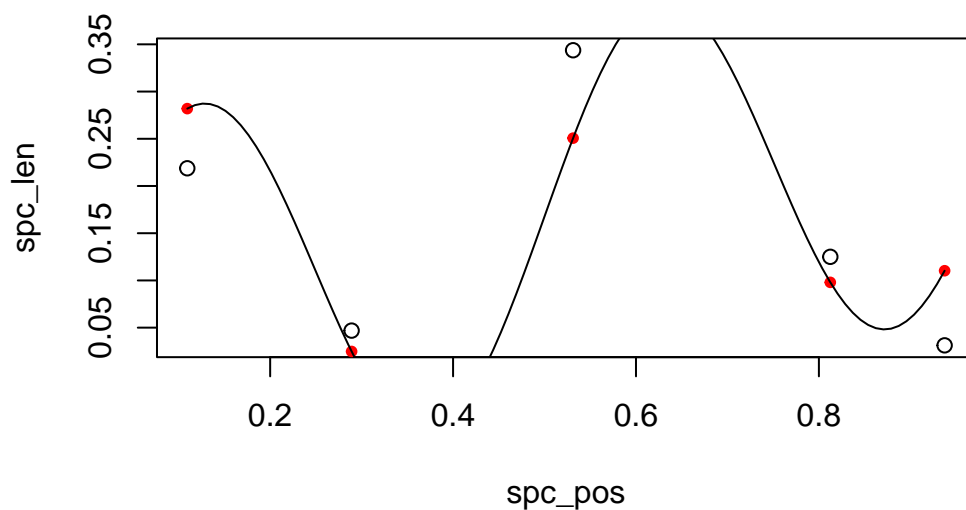
```
[1] 0 17 23 48 59 64
```

```
[1] 14 20 45 56 61 64
```

InterSpaces:

```
lengths: 0.21875 0.046875 0.34375 0.125 0.03125
```

```
positions: 0.109375 0.2890625 0.53125 0.8125 0.9375
```



Call:

```
lm(formula = spc_len ~ cos(1 * pi * spc_pos) + sin(4 * pi * spc_pos))
```

Coefficients:

(Intercept)	cos(1 * pi * spc_pos)	sin(4 * pi * spc_pos)
0.16772	-0.08245	0.19561

I also got the curiosity to apply Kernel Density Estimation to the data, so I added the parameters 'kdesmooth' and 'bw' (for "bandwidth"):

```
kmer_interspace_polynome(testseq1, kmer="CTC", silent=TRUE, kdesmooth=TRUE, bw = 0.2)
```

```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

```
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
```

```
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97
```

Loading required package: scales

Attaching package: 'scales'

The following object is masked from 'package:datawizard':

rescale

[1] 0.2

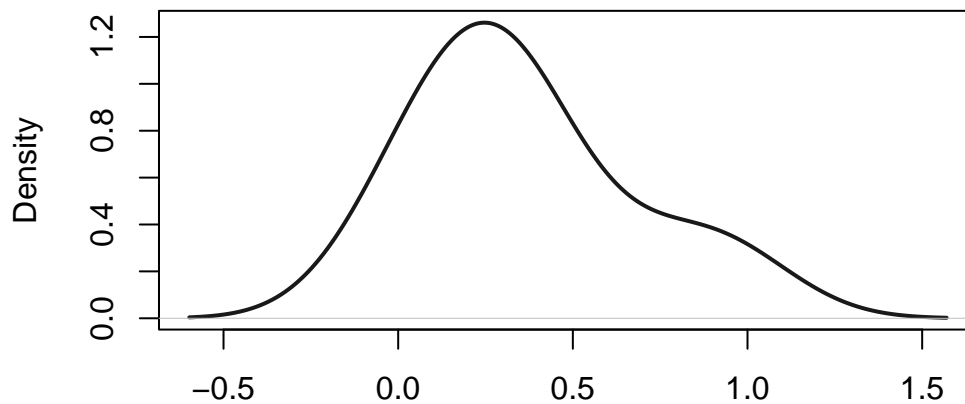
Call:

density.default(x = spc_pos, bw = bw, kernel = "gaussian")

Data: spc_pos (11 obs.); Bandwidth 'bw' = 0.2

x	y
Min. :-0.598	Min. :0.002206
1st Qu.: -0.056	1st Qu.:0.077116
Median : 0.486	Median :0.374828
Mean : 0.486	Mean :0.460642
3rd Qu.: 1.028	3rd Qu.:0.770248
Max. : 1.570	Max. :1.261022

density(x = spc_pos, bw = bw, kernel = "gaussian")



N = 11 Bandwidth = 0.2

```
[1] "finished"
```

```
kmer_interspace_polynome(testseq1, kmer="CTC", silent=TRUE, kdesmooth=TRUE, bw = 0.1)
```

```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06

positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97

```
[1] 0.1
```

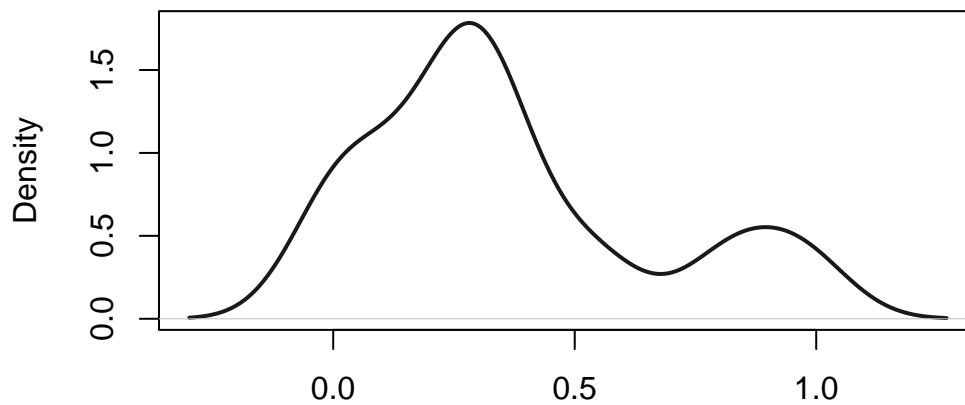
Call:

```
density.default(x = spc_pos, bw = bw, kernel = "gaussian")
```

Data: spc_pos (11 obs.); Bandwidth 'bw' = 0.1

x	y
Min. :-0.298	Min. :0.00409
1st Qu.: 0.094	1st Qu.:0.27074
Median : 0.486	Median :0.48539
Mean : 0.486	Mean :0.63694
3rd Qu.: 0.878	3rd Qu.:1.02560
Max. : 1.270	Max. :1.78358

density(x = spc_pos, bw = bw, kernel = "gaussian")



N = 11 Bandwidth = 0.1

```
[1] "finished"
```

```
kmer_interspace_polynome(testseq1, kmer="CTC", silent=TRUE, kdesmooth=TRUE, bw = 0.05)
```

```
[1] 0 5 18 115 121 147 152 178 184 355 470
```

```
[1] 2 15 112 118 144 149 175 181 352 467 500
```

InterSpaces:

```
lengths: 0.004 0.02 0.188 0.006 0.046 0.004 0.046 0.006 0.336 0.224 0.06
```

```
positions: 0.002 0.02 0.13 0.233 0.265 0.296 0.327 0.359 0.536 0.822 0.97
```

```
[1] 0.05
```

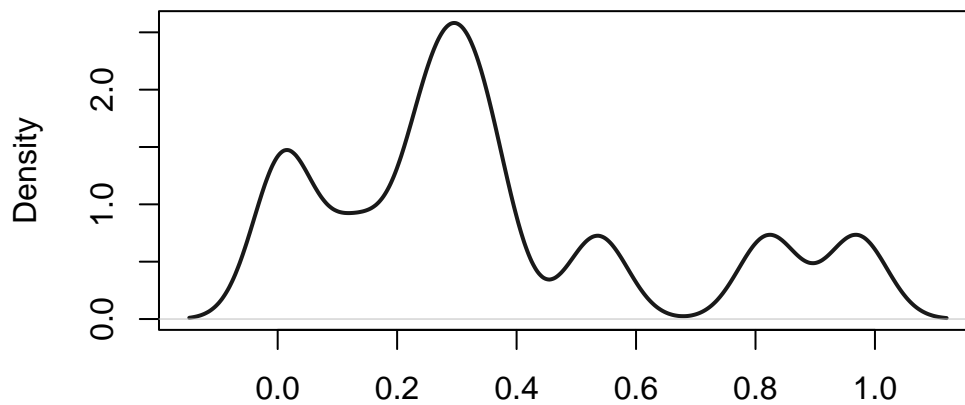
Call:

```
density.default(x = spc_pos, bw = bw, kernel = "gaussian")
```

Data: spc_pos (11 obs.); Bandwidth 'bw' = 0.05

x	y
Min. :-0.148	Min. :0.00818
1st Qu.: 0.169	1st Qu.:0.32513
Median : 0.486	Median :0.63738
Mean : 0.486	Mean :0.78767
3rd Qu.: 0.803	3rd Qu.:1.05675
Max. : 1.120	Max. :2.58171

density(x = spc_pos, bw = bw, kernel = "gaussian")



N = 11 Bandwidth = 0.05

```
[1] "finished"
```

```
#kmer_interspace_polynome(windows=testseq1, kmer="CTC", silent=TRUE, aem_option=7, rel = FALSE)
```