LTMG - GCR track (LTMG->biclustering analysis)

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Analysis

We will have a data namely "Yan" for the example of LTMG - GCR (biclustering) pipeline. Basically, we may need the following steps for this analysis

(i) a standard data loading function

```
data0 <- log(as.matrix(read.delim("Yan_expression_RPKM.txt", row.names = 1)))</pre>
```

(ii) running LTMG -> a standard output of LTMG parameters

Select genes

Genes with non-zero expression in more than 5 samples in data0

```
selected.genes <- which(rowSums(data0 > 0) > 5)
print(head(selected.genes))
## RPS11 ELMO2 CREB3L1 PNMA1 TMEM216 LOC653712
```

```
## RPS11 ELM02 CREB3L1 PNMA1 TMEM216 LOC653712
## 2 3 4 5 7 8
```

Run LTMG for the selected genes

LTMG -> output list(N: number of peaks; a 3N matrix: A, U, S; If Zcut (If 0 expression is more than 5, Zcut); Iteration number, upper limit 1000)

```
library(LTMGSCA)
for (gene in head(selected.genes, 3)) {
  for (k in 1:5) {
    print(SeparateKRpkmNew(x = data0[gene, ], n = 100, q = 0, k = k, err = 1e-10))
  }
}
```

```
## p mean sd
## [1,] 1 7.802228 0.04416125
## p mean sd
## Late_blastocyst.2_Cell.7 0.5189909 7.632955 0.5688547
## X4.cell_embryo.1_Cell.4 0.4810091 7.872066 0.5948461
## p mean sd
## X2.cell_embryo.1_Cell.2 0.1210234 7.083230 0.1913294
## Late_blastocyst.3_Cell.5 0.7937210 7.768004 0.5549263
## X4.cell_embryo.3_Cell.2 0.0852556 8.505077 0.1026225
## p mean sd
## Late_blastocyst.2_Cell.4 0.006933978 7.788798 0.36486339
```

```
## Morulae.1 Cell.8
                            0.448993364 7.267528 0.35678557
                            0.480661380 8.095959 0.44529688
## Morulae.2 Cell.3
## X4.cell embryo.3 Cell.1 0.063411278 8.507573 0.09591338
##
                                      р
                                            mean
                                                        sd
## Oocyte.1
                            0.005328433 7.727174 0.3884293
## Late blastocyst.2 Cell.7 0.356379577 7.199494 0.3289284
## Late blastocyst.3 Cell.5 0.309216553 7.755904 0.3974516
## X4.cell_embryo.1_Cell.4   0.322192465   8.343583   0.3577630
## X8.cell_embryo.1_Cell.1 0.006882971 7.925339 0.4211202
##
         p mean sd
## [1,] NaN NaN NaN
##
                                   р
## X8.cell_embryo.2_Cell.4 0.3138683 -2.385534 2.460532
## X8.cell_embryo.1_Cell.1 0.6861317 2.645441 1.280540
                                           mean
                                    р
## Late_blastocyst.2_Cell.1 0.2726636 -2.943190 1.0155455
## X8.cell_embryo.3_Cell.1 0.4874510 1.851239 0.8095599
## X4.cell_embryo.1_Cell.2  0.2398854  4.123094  0.1710736
                                   р
                                          mean
## X8.cell embryo.2 Cell.6 0.2722165 -2.584755 0.8242646
## X8.cell_embryo.2_Cell.7 0.2930781 1.687644 0.7978886
## X8.cell_embryo.2_Cell.3 0.1945976 2.090904 0.7665579
## X2.cell_embryo.3_Cell.1 0.2401079 4.123058 0.1711315
                                    p
                                           mean
## Morulae.1 Cell.2
                           0.27343650 -2.346844 0.7156853
## X8.cell_embryo.2_Cell.4 0.22096460 1.561465 0.7070268
## X8.cell_embryo.3_Cell.1 0.16654932 1.775654 0.7409112
## X8.cell_embryo.1_Cell.1 0.09679837 2.609410 0.5179847
## X4.cell_embryo.2_Cell.4 0.24225121 4.122422 0.1716394
       р
                    mean
                                sd
## [1,] 1 -1.154028e+138 0.6502746
##
                                                       sd
                                           mean
                                   р
                           0.8524664 -1.4311960 1.4985531
## X8.cell_embryo.1_Cell.2 0.1475336  0.9262817 0.9096018
                                             mean
                                     p
## X4.cell embryo.2 Cell.3 0.70557942 -1.2865546 0.4785381776
## Late blastocyst.2 Cell.3 0.27219997 0.7239671 0.5938110246
## X4.cell_embryo.3_Cell.3  0.02222061  2.7078834  0.0005667612
##
                                            mean
                                    p
## Zygote.2
                           0.72496505 -1.2936882 0.4602185469
## X2.cell embryo.2 Cell.1 0.11346035 0.4516975 0.2993225110
## X8.cell_embryo.1_Cell.4 0.13935362
                                      1.0987104 0.4882202184
## X4.cell embryo.1 Cell.2 0.02222099
                                       2.7078834 0.0005667612
##
                                             mean
                                     p
## Zygote.2
                            0.69349422 -1.3076762 0.4388586900
## Zygote.1
                            0.06286983
                                       0.1033333 0.7265148824
## Late_blastocyst.2_Cell.3 0.08060027
                                        0.4484580 0.3466538911
## X8.cell_embryo.1_Cell.2 0.14081500
                                       1.0348833 0.5179808674
## X4.cell_embryo.3_Cell.4 0.02222069 2.7078834 0.0005667612
```

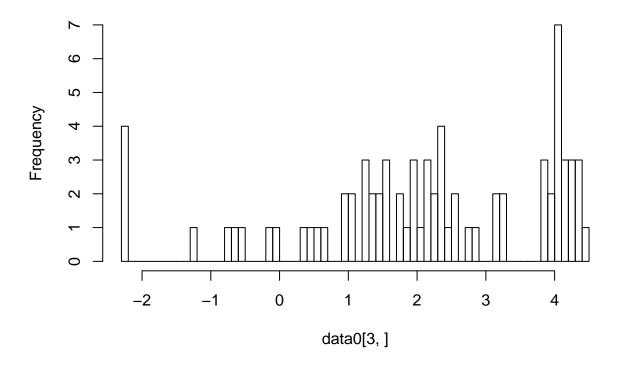
Here we have the BIC functions:

```
BIC_f_zcut <- function(y, rrr, Zcut) {</pre>
  n <- length(y)</pre>
  nparams <- nrow(rrr) * 3</pre>
  w <- rrr[, 1]
  u <- rrr[, 2]
  sig <- rrr[, 3]
  cc <- c()
  y0 \leftarrow y[which(y \ge Zcut)]
  y1 <- y[which(y < Zcut)]
  y1 <- y1 * 0 + Zcut
  for (i in 1:nrow(rrr)) {
    c0 <- dnorm(y0, u[i], sig[i]) * w[i]</pre>
    c1 <- (1 - pnorm(y1, u[i], sig[i])) * w[i]
    c \leftarrow c(c0, c1)
    cc <- rbind(cc, c)
  }
  d <- apply(cc, 2, sum)</pre>
  e <- sum(log(d))
  f <- e * 2 - nparams * log(n)
  return (f)
BIC_f_zcut2 <- function(y, rrr, Zcut) {</pre>
  n <- length(y)
  nparams <- nrow(rrr) * 3</pre>
  w <- rrr[, 1]
  u <- rrr[, 2]
  sig <- rrr[, 3]
  y0 \leftarrow y[which(y \ge Zcut)]
  cc <- c()
  for (i in 1:nrow(rrr)) {
    c <- dnorm(y0, u[i], sig[i]) * w[i]</pre>
    cc <- rbind(cc, c)</pre>
  d <- apply(cc, 2, sum)</pre>
  e \leftarrow sum(log(d))
  f \leftarrow e * 2 - nparams * log(n)
  return (f)
We can now get f value using BIC_f_zcut2().
for (k in 1:5) {
  rrr <- SeparateKRpkmNew(x = data0[selected.genes[1], ], n = 100, q = 0, k = k, err = 1e-10)
  print(BIC_f_zcut2(y = data0[selected.genes[1], ], rrr, 0))
}
## [1] -16016.58
## [1] -188.4811
## [1] -195.0944
## [1] -208.8539
## [1] -223.8346
```

We are only print while k != 2.

```
GetBestK <- function(x, n, q, err = 1e-10){</pre>
  best.bic <- -Inf</pre>
  best.k <- 0
  best.result \leftarrow c(0, 0, 0)
  for (k in 1:7) {
    rrr <- SeparateKRpkmNew(x = x, n = n, q = q, k = k, err = err)
    bic <- BIC_f_zcut2(y = x, rrr, q)</pre>
    if(is.nan(bic)) {
      bic <- -Inf
    }
    if (bic >= best.bic) {
      best.bic <- bic</pre>
      best.k <- k
      best.result <- rrr</pre>
    } else {
      return(list(k = best.k, bic = best.bic, result = best.result))
    }
  }
  return(list(k = 0, bic = 0, result = c(0, 0, 0)))
for (gene in head(selected.genes, 30)) {
  best <- GetBestK(x = data0[gene, ], n = 100, q = 0, err = 1e-10)
  if (best[1] != 2) {
    print(gene)
  }
}
## [1] 3
## [1] 4
## [1] 42
This is the 3rd one:
best <- GetBestK(x = data0[3, ], n = 100, q = 0, err = 1e-10)
print(best)
## $k
## [1] 3
##
## $bic
## [1] -247.7207
##
## $result
                                             mean
## Late_blastocyst.2_Cell.1 0.2726636 -2.943190 1.0155455
## X8.cell_embryo.3_Cell.1 0.4874510 1.851239 0.8095599
## X4.cell_embryo.1_Cell.2  0.2398854  4.123094  0.1710736
hist(data0[3,], breaks = 60)
```

Histogram of data0[3,]



(iii) LTMG -> discretization

We have the following functions ready for this step: $calculate_prob_sep_Zcut$, $discretization_method_1_LLR_mean$, and $Build_R_matrix$.

```
calculate_prob_sep_Zcut <- function(data1, Zcut, a, u, sig) {</pre>
  cc <- matrix(0, length(a), length(data1))</pre>
  colnames(cc) <- names(data1)</pre>
  for (i in 1:length(a)) {
    c <- a[i] / sig[i] * exp(-(data1 - u[i]) ^ 2 / (2 * sig[i] ^ 2))
    cc[i, ] <- c
  cut_p <- rep(0, length(a))</pre>
  for (i in 1:length(a)) {
    cut_p[i] <- a[i] * pnorm(Zcut, u[i], sig[i])</pre>
  }
  for (i in 1:ncol(cc)) {
    if (data1[i] < Zcut) {</pre>
      cc[, i] <- cut_p
    }
  }
  cc[which(is.na(cc) == 1)] \leftarrow 0
  return(cc)
}
```

```
discretization_method_1_LLR_mean <- function(y, aaa, ccc, LLR_cut = 2) {</pre>
  K <- 1 / LLR_cut + 1</pre>
  if (nrow(aaa) == 1) {
    print("Only one class")
    return(y)
  } else {
    discretized_y <- rep(0, length(y))</pre>
    for (i in 1:ncol(ccc)) {
      11 \leftarrow which(ccc[, i] = max(ccc[, i]))[1]
      if ((max(ccc[, i])/sum(ccc[, i])) > (1/K)) {
        discretized_y[i] <- 11</pre>
      }
    }
    blocks <- c()
    st_c <- 1
    end_c <- 1
    st_c_v \leftarrow y[order(y)[1]]
    end_c_v <- y[order(y)[1]]
    label_c <- discretized_y[order(y)[1]]</pre>
    for (i in 2:length(order(y))) {
      if (discretized_y[order(y)[i]] == discretized_y[order(y)[i - 1]]) {
        end_c <- i
        end_c_v <- y[order(y)[i]]</pre>
        if (i == length(order(y))) {
          end c \leftarrow i
          end_c_v <- y[order(y)[i]]</pre>
          blocks <- rbind(blocks, c(st_c, end_c, st_c_v, end_c_v, label_c))</pre>
        }
      } else {
        blocks <- rbind(blocks, c(st_c, end_c, st_c_v, end_c_v,
          label_c))
        label_c <- discretized_y[order(y)[i]]</pre>
        st_c <- i
        end_c \leftarrow i
        st_c_v <- y[order(y)[i]]
        end_c_v <- y[order(y)[i]]</pre>
        if (i == length(order(y))) {
          end_c <- i
          end_c_v <- y[order(y)[i]]</pre>
          blocks <- rbind(blocks, c(st_c, end_c, st_c_v, end_c_v, label_c))</pre>
        }
      }
    if (nrow(blocks) > 1) {
      for (i in 1:nrow(blocks)) {
        if (blocks[i, 5] != 0) {
          tg_i <- blocks[i, 5]
          if (!((blocks[i, 3] <= aaa[tg_i, 2]) & (blocks[i, 4] >= aaa[tg_i, 2]))) {
          blocks[i, 5] <- 0
          }
        }
      for (i in 1:nrow(blocks)) {
```

```
discretized_y[order(y)[blocks[i, 1]:blocks[i, 2]]] <- blocks[i, 5]</pre>
      }
    }
    return(discretized_y)
  }
Build_R_matrix <- function(cc, Zcut0, U, Gname) {</pre>
  tg_s <- intersect(which(U > Zcut0), unique(cc))
  dd <- c()
  nc \leftarrow c()
  if (length(tg_s) > 0) {
    for (i in 1:length(tg_s)) {
      nc <- c(nc, paste(Gname, tg_s[i], sep = "__"))</pre>
      ccc <- (cc == tg_s[i]) * 1
      dd <- rbind(dd, ccc)
  }
  rownames(dd) <- nc
  return(dd)
}
```

best\$result is a K*3 matrix with 1st, 2nd and 3rd columns are the A, U, S of the gene x is the normalized expression level

```
i <- 4
x <- data0[i, ]
Zcut0 <- 0
best <- GetBestK(x = x, n = 1000, q = Zcut0, err = 1e-10)

pp <- calculate_prob_sep_Zcut(x, Zcut0, best$result[, 1], best$result[, 2], best$result[, 3])
cc <- discretization_method_1_LLR_mean(x, best$result, pp, LLR_cut = 0.1)
dd <- Build_R_matrix(cc, Zcut0, best$result[, 2], rownames(data0)[i])

print(x)</pre>
```

```
##
                     Oocyte.1
                                                Oocyte.2
##
                    0.000000
                                               0.3534698
##
                     Oocyte.3
                                                Zygote.1
##
                    0.6657760
                                               0.5905606
##
                     Zygote.2
                                                Zygote.3
                                              -0.3133418
##
                    0.3611648
##
     X2.cell_embryo.1_Cell.1
                                X2.cell_embryo.1_Cell.2
##
                    0.4643627
                                               0.2342813
##
     X2.cell_embryo.2_Cell.1
                                X2.cell_embryo.2_Cell.2
##
                    0.6339278
                                               0.3708737
##
     X2.cell_embryo.3_Cell.1
                                X2.cell_embryo.3_Cell.2
##
                   -0.3523984
                                              -0.7052198
##
     X4.cell_embryo.1_Cell.1
                                X4.cell_embryo.1_Cell.2
##
                         -Inf
                                               1.5526559
##
     X4.cell_embryo.1_Cell.3
                                X4.cell_embryo.1_Cell.4
##
                         -Inf
                                                    -Inf
##
     X4.cell_embryo.2_Cell.1
                                X4.cell_embryo.2_Cell.2
                  -1.3586792
                                              -0.2943711
##
##
     X4.cell_embryo.2_Cell.3
                                X4.cell_embryo.2_Cell.4
```

```
##
                    0.4491630
                                               1.0217312
##
                                X4.cell_embryo.3_Cell.2
     X4.cell_embryo.3_Cell.1
                    1.1177611
##
                                               0.9250522
##
                                X4.cell_embryo.3_Cell.4
     X4.cell_embryo.3_Cell.3
##
                    1.4548872
                                               1.6122340
##
     X8.cell embryo.1 Cell.1
                                X8.cell embryo.1 Cell.2
##
                   -0.7635696
                                               1.0328285
##
     X8.cell_embryo.1_Cell.3
                                X8.cell_embryo.1_Cell.4
##
                    0.6559644
                                               0.9266370
##
     X8.cell_embryo.2_Cell.1
                                X8.cell_embryo.2_Cell.2
##
                         -Inf
                                                    -Inf
##
                                X8.cell_embryo.2_Cell.4
     X8.cell_embryo.2_Cell.3
##
                         -Inf
##
     X8.cell_embryo.2_Cell.5
                                X8.cell_embryo.2_Cell.6
##
                         -Inf
##
     X8.cell_embryo.2_Cell.7
                                X8.cell_embryo.2_Cell.8
##
                         -Inf
##
     X8.cell_embryo.3_Cell.1
                                X8.cell_embryo.3_Cell.2
##
                         -Inf
##
     X8.cell_embryo.3_Cell.3
                                X8.cell embryo.3 Cell.4
##
                         -Inf
##
     X8.cell_embryo.3_Cell.5
                                X8.cell_embryo.3_Cell.6
##
                         -Inf
##
                                X8.cell embryo.3 Cell.8
     X8.cell_embryo.3_Cell.7
##
                         -Inf
                                               1.7516317
##
            Morulae.1_Cell.1
                                        Morulae.1_Cell.2
##
                         -Inf
                                                    -Inf
                                        Morulae.1_Cell.4
##
            Morulae.1_Cell.3
##
                                              -0.2930297
                         -Inf
##
            Morulae.1_Cell.5
                                        Morulae.1_Cell.6
##
                         -Inf
##
            Morulae.1_Cell.7
                                        Morulae.1_Cell.8
##
                         -Inf
##
            Morulae.2_Cell.1
                                        Morulae.2_Cell.2
##
                         -Inf
                                                    -Inf
##
            Morulae.2 Cell.3
                                        Morulae.2 Cell.4
##
##
            Morulae.2_Cell.5
                                        Morulae.2_Cell.6
##
                                              -0.9702191
##
            Morulae.2_Cell.7
                                        Morulae.2_Cell.8
                  -0.9597203
##
    Late_blastocyst.1_Cell.1
                               Late_blastocyst.1_Cell.2
##
                         -Inf
##
    Late_blastocyst.1_Cell.3
                               Late_blastocyst.1_Cell.4
##
                         -Inf
##
    Late_blastocyst.1_Cell.5
                               Late_blastocyst.1_Cell.6
##
                         -Inf
                               Late_blastocyst.1_Cell.8
##
    Late_blastocyst.1_Cell.7
##
                         -Inf
                                                    -Inf
##
    Late_blastocyst.1_Cell.9 Late_blastocyst.1_Cell.10
##
                         -Inf
   Late_blastocyst.1_Cell.11 Late_blastocyst.1_Cell.12
##
##
                         -Inf
    Late_blastocyst.2_Cell.1 Late_blastocyst.2_Cell.2
```

```
##
                  -0.3495575
                                             1.6981811
##
   Late_blastocyst.2_Cell.3 Late_blastocyst.2_Cell.4
##
                   0.6714127
##
   Late_blastocyst.2_Cell.5
                              Late_blastocyst.2_Cell.6
##
                        -Inf
                                                  -Tnf
##
   Late_blastocyst.2_Cell.7
                              Late blastocyst.2 Cell.8
##
                        -Inf
##
   Late_blastocyst.2_Cell.9 Late_blastocyst.2_Cell.10
##
                        -Inf
                                                   -Inf
##
   Late_blastocyst.3_Cell.1
                              Late_blastocyst.3_Cell.2
##
                        -Inf
                                                  -Inf
##
   Late_blastocyst.3_Cell.3
                              Late_blastocyst.3_Cell.4
##
                        -Inf
                                                  -Inf
##
    Late_blastocyst.3_Cell.5
                              Late_blastocyst.3_Cell.6
##
                   2.7084501
##
    Late_blastocyst.3_Cell.7
                              Late_blastocyst.3_Cell.8
##
                        -Inf
                                             2.7073166
print(pp)
          Oocyte.1
                      Oocyte.2
                                   Oocyte.3
                                                Zygote.1
   [1,] 0.02453824 0.001542643 0.0000750863 0.0001633965
   [2,] 0.22504345 0.382762784 0.4578324387 0.4495556219
  Zygote.3 X2.cell_embryo.1_Cell.1
          Zygote.2
##
   [1,] 0.00144129 0.70151041
                                        0.0005612054
   [2,] 0.38571522 0.03192687
                                         0.4208080150
   [3,] 0.00000000 0.00000000
                                         0.000000000
##
        X2.cell_embryo.1_Cell.2 X2.cell_embryo.2_Cell.1
## [1,]
                    0.004237879
                                           0.0001047639
## [2,]
                    0.332717460
                                           0.4551859299
##
  [3,]
                    0.00000000
                                           0.000000000
##
        X2.cell_embryo.2_Cell.2 X2.cell_embryo.3_Cell.1
  [1,]
##
                    0.001322238
                                             0.70151041
##
  [2,]
                    0.389380992
                                             0.03192687
## [3,]
                    0.00000000
                                             0.00000000
##
        X2.cell_embryo.3_Cell.2 X4.cell_embryo.1_Cell.1
## [1,]
                     0.70151041
                                             0.70151041
## [2,]
                     0.03192687
                                             0.03192687
  [3,]
                     0.00000000
                                             0.0000000
##
        X4.cell_embryo.1_Cell.2 X4.cell_embryo.1_Cell.3
## [1,]
                   7.305006e-10
                                             0.70151041
## [2,]
                   1.725700e-01
                                             0.03192687
## [3,]
                   0.000000e+00
                                             0.00000000
##
        X4.cell embryo.1 Cell.4 X4.cell embryo.2 Cell.1
## [1,]
                     0.70151041
                                             0.70151041
## [2,]
                     0.03192687
                                             0.03192687
  [3,]
##
                     0.0000000
                                             0.0000000
##
        X4.cell_embryo.2_Cell.2 X4.cell_embryo.2_Cell.3
## [1,]
                     0.70151041
                                           0.0006472473
## [2,]
                     0.03192687
                                           0.4162216657
## [3,]
                                           0.000000000
                     0.00000000
##
        X4.cell_embryo.2_Cell.4 X4.cell_embryo.3_Cell.1
## [1,]
                  1.236439e-06
                                           3.619440e-07
## [2,]
                   4.028836e-01
                                           3.663466e-01
```

```
## [3,]
                    0.000000e+00
                                             0.000000e+00
##
        X4.cell_embryo.3_Cell.2 X4.cell_embryo.3_Cell.3
## [1,]
                   4.044036e-06
                                             3.230622e-09
## [2,]
                    4.319703e-01
                                             2.140125e-01
##
   [3,]
                    0.000000e+00
                                             0.000000e+00
##
        X4.cell embryo.3 Cell.4 X8.cell embryo.1 Cell.1
                    2.876387e-10
## [1,]
                                               0.70151041
## [2,]
                    1.493903e-01
                                               0.03192687
## [3,]
                    0.000000e+00
                                               0.0000000
##
        X8.cell_embryo.1_Cell.2 X8.cell_embryo.1_Cell.3
   [1,]
                    1.075611e-06
                                             8.325015e-05
   [2,]
                    3.990062e-01
                                             4.571534e-01
##
   [3,]
                    0.000000e+00
##
                                             0.000000e+00
##
        X8.cell_embryo.1_Cell.4 X8.cell_embryo.2_Cell.1
## [1,]
                   3.967901e-06
                                               0.70151041
## [2,]
                    4.315677e-01
                                               0.03192687
## [3,]
                   0.000000e+00
                                               0.0000000
##
        X8.cell_embryo.2_Cell.2 X8.cell_embryo.2_Cell.3
## [1,]
                      0.70151041
                                               0.70151041
##
   [2,]
                      0.03192687
                                               0.03192687
##
   [3,]
                      0.00000000
                                               0.00000000
##
        X8.cell_embryo.2_Cell.4 X8.cell_embryo.2_Cell.5
## [1,]
                      0.70151041
                                               0.70151041
  [2,]
##
                      0.03192687
                                               0.03192687
## [3,]
                      0.0000000
                                               0.00000000
        X8.cell_embryo.2_Cell.6 X8.cell_embryo.2_Cell.7
##
   [1,]
                      0.70151041
                                               0.70151041
   [2,]
##
                      0.03192687
                                               0.03192687
## [3,]
                      0.0000000
                                               0.0000000
##
        X8.cell_embryo.2_Cell.8 X8.cell_embryo.3_Cell.1
## [1,]
                      0.70151041
                                               0.70151041
## [2,]
                      0.03192687
                                               0.03192687
   [3,]
##
                      0.0000000
                                               0.0000000
##
        X8.cell_embryo.3_Cell.2 X8.cell_embryo.3_Cell.3
##
   [1,]
                      0.70151041
                                               0.70151041
##
   [2,]
                      0.03192687
                                               0.03192687
##
   [3,]
                      0.0000000
                                               0.0000000
##
        X8.cell_embryo.3_Cell.4 X8.cell_embryo.3_Cell.5
## [1,]
                      0.70151041
                                               0.70151041
## [2,]
                      0.03192687
                                               0.03192687
## [3,]
                      0.0000000
                                               0.0000000
##
        X8.cell_embryo.3_Cell.6 X8.cell_embryo.3_Cell.7
## [1,]
                      0.70151041
                                               0.70151041
## [2,]
                      0.03192687
                                               0.03192687
## [3,]
                      0.0000000
                                               0.0000000
##
        X8.cell_embryo.3_Cell.8 Morulae.1_Cell.1
## [1,]
                    3.008084e-11
                                        0.70151041
## [2,]
                    1.025517e-01
                                        0.03192687
                                       0.00000000
##
   [3,]
                   0.000000e+00
##
        Morulae.1_Cell.2 Morulae.1_Cell.3 Morulae.1_Cell.4
## [1,]
              0.70151041
                                0.70151041
                                                  0.70151041
## [2,]
              0.03192687
                                0.03192687
                                                  0.03192687
## [3,]
              0.00000000
                                0.0000000
                                                  0.0000000
##
        Morulae.1 Cell.5 Morulae.1 Cell.6 Morulae.1 Cell.7
```

```
## [1,]
              0.70151041
                                0.70151041
                                                  0.70151041
## [2,]
              0.03192687
                                0.03192687
                                                  0.03192687
##
  [3,]
              0.00000000
                                0.0000000
                                                  0.0000000
##
        Morulae.1_Cell.8 Morulae.2_Cell.1 Morulae.2_Cell.2
##
  [1,]
              0.70151041
                                0.70151041
                                                  0.70151041
  [2,]
              0.03192687
                                0.03192687
                                                  0.03192687
##
## [3.]
              0.0000000
                                0.0000000
                                                  0.0000000
##
        Morulae.2 Cell.3 Morulae.2 Cell.4 Morulae.2 Cell.5
## [1,]
              0.70151041
                                0.70151041
                                                  0.70151041
   [2,]
##
              0.03192687
                                0.03192687
                                                  0.03192687
   [3,]
              0.0000000
                                0.0000000
                                                  0.0000000
        Morulae.2_Cell.6 Morulae.2_Cell.7 Morulae.2_Cell.8
##
##
  [1,]
              0.70151041
                                0.70151041
                                                  0.70151041
## [2,]
              0.03192687
                                0.03192687
                                                  0.03192687
## [3,]
              0.0000000
                                0.0000000
                                                  0.0000000
##
        Late_blastocyst.1_Cell.1 Late_blastocyst.1_Cell.2
## [1,]
                       0.70151041
                                                 0.70151041
## [2,]
                       0.03192687
                                                 0.03192687
                                                 0.0000000
##
   [3.]
                       0.00000000
##
        Late blastocyst.1 Cell.3 Late blastocyst.1 Cell.4
## [1,]
                       0.70151041
                                                 0.70151041
## [2,]
                       0.03192687
                                                 0.03192687
## [3,]
                       0.00000000
                                                 0.00000000
##
        Late blastocyst.1 Cell.5 Late blastocyst.1 Cell.6
                                                 0.70151041
##
   [1,]
                      0.70151041
  [2,]
                       0.03192687
                                                 0.03192687
## [3,]
                       0.00000000
                                                 0.00000000
##
        Late_blastocyst.1_Cell.7 Late_blastocyst.1_Cell.8
## [1,]
                       0.70151041
                                                 0.70151041
## [2,]
                       0.03192687
                                                 0.03192687
## [3,]
                       0.0000000
                                                 0.00000000
##
        Late_blastocyst.1_Cell.9 Late_blastocyst.1_Cell.10
## [1,]
                       0.70151041
                                                  0.70151041
## [2,]
                       0.03192687
                                                  0.03192687
##
   [3,]
                       0.0000000
                                                  0.0000000
##
        Late_blastocyst.1_Cell.11 Late_blastocyst.1_Cell.12
## [1,]
                        0.70151041
                                                   0.70151041
## [2,]
                        0.03192687
                                                   0.03192687
## [3,]
                        0.0000000
                                                   0.0000000
##
        Late_blastocyst.2_Cell.1 Late_blastocyst.2_Cell.2
   [1,]
                       0.70151041
                                               7.241376e-11
##
  [2,]
                       0.03192687
                                               1.192267e-01
   [3.]
                       0.0000000
##
                                               0.000000e+00
##
        Late_blastocyst.2_Cell.3 Late_blastocyst.2_Cell.4
## [1,]
                    7.074638e-05
                                                 0.70151041
## [2,]
                    4.581673e-01
                                                 0.03192687
##
   [3,]
                    0.000000e+00
                                                 0.00000000
##
        Late_blastocyst.2_Cell.5 Late_blastocyst.2_Cell.6
## [1,]
                       0.70151041
                                                 0.70151041
   [2,]
##
                       0.03192687
                                                 0.03192687
##
   [3,]
                       0.0000000
                                                 0.0000000
##
        Late blastocyst.2 Cell.7 Late blastocyst.2 Cell.8
## [1,]
                      0.70151041
                                                 0.70151041
## [2,]
                       0.03192687
                                                 0.03192687
```

```
0.00000000
                                              0.0000000
## [3,]
##
       Late_blastocyst.2_Cell.9 Late_blastocyst.2_Cell.10
                     0.70151041
## [1,]
                                               0.70151041
## [2,]
                     0.03192687
                                               0.03192687
## [3,]
                     0.00000000
                                               0.0000000
##
       Late_blastocyst.3_Cell.1 Late_blastocyst.3_Cell.2
## [1,]
                     0.70151041
                                              0.70151041
                     0.03192687
## [2,]
                                              0.03192687
## [3,]
                     0.00000000
                                              0.00000000
##
       Late_blastocyst.3_Cell.3 Late_blastocyst.3_Cell.4
  [1,]
                     0.70151041
                                              0.70151041
## [2,]
                     0.03192687
                                              0.03192687
## [3,]
                     0.00000000
                                              0.00000000
##
       Late_blastocyst.3_Cell.5 Late_blastocyst.3_Cell.6
## [1,]
                   3.029268e-19
                                              0.70151041
## [2,]
                   1.793851e-03
                                              0.03192687
## [3,]
                   2.377976e+01
                                              0.0000000
##
       Late_blastocyst.3_Cell.7 Late_blastocyst.3_Cell.8
                                            3.105414e-19
                     0.70151041
## [1,]
## [2,]
                     0.03192687
                                            1.805197e-03
## [3,]
                     0.0000000
                                            2.377974e+01
print(cc)
  [1] 2 2 2 2 2 1 2 2 2 2 1 1 1 2 1 1 1 1 2 2 2 2 2 2 1 2 2 2
## [85] 1 1 3 1 1 3
print(dd)
             [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9]
  CREB3L1__2
                1
                     1
                          1
                               1
                                    1
                                         0
                                                   1
  CREB3L1__3
                0
                     0
                          0
                               0
                                    0
                                         0
                                              0
                                                   0
                                                       0
             [,10] [,11] [,12] [,13] [,14] [,15] [,16] [,17]
##
  CREB3L1__2
                             0
                                   0
                                               0
                                                    0
##
                 1
                       0
                                         1
##
  CREB3L1__3
                 0
                       0
                             0
                                   0
                                         0
                                               0
                                                     0
                                                          0
##
             [,18] [,19] [,20] [,21] [,22]
                                          [,23]
                                                [,24]
  CREB3L1__2
                 0
                                   1
                                         1
                                               1
                                                     1
                       1
                             1
##
   CREB3L1__3
                 0
                       0
                             0
                                   0
                                         0
                                               0
                                                     0
##
             [,26] [,27] [,28] [,29] [,30] [,31] [,32]
                                                      [.33]
                                   0
                                               0
                                                     0
  CREB3L1 2
                 1
                       1
                             1
                                         0
                 0
                       0
                             0
                                   0
                                         0
                                               0
                                                    0
##
  CREB3L1 3
                                                           0
##
              [,34] [,35] [,36] [,37] [,38] [,39] [,40]
##
  CREB3L1__2
                 Λ
                       Λ
                             0
                                   0
                                         Λ
                                               0
                                                     0
                                                           0
  CREB3L1__3
                 0
                       0
                             0
                                   0
                                         0
                                               0
                                                     0
             [,42] [,43] [,44] [,45] [,46] [,47] [,48]
##
                                   0
                                         0
                                               0
##
  CREB3L1_2
                       0
                             1
                                                    0
  CREB3L1__3
                 0
                       0
                             0
                                   0
                                         0
                                               0
              [,50] [,51] [,52] [,53] [,54] [,55] [,56]
  CREB3L1__2
                             0
                                   0
                                               0
                                                    0
##
                 0
                       0
                                         0
                                                          0
##
  CREB3L1__3
                 0
                       0
                             0
                                   0
                                         0
                                               0
                                                     0
                                                          0
             [,58] [,59] [,60] [,61] [,62] [,63] [,64] [,65]
##
```

0

0

0

0

0

0

0

CREB3L1 2

CREB3L1__3

0

0

0

0

0

0

0

0

```
[,66] [,67] [,68] [,69] [,70] [,71] [,72] [,73]
## CREB3L1__2
                         0
                                0
                                      0
                                             0
                                                   0
                                                         0
                   0
   CREB3L1__3
                   0
                                0
                                      0
                                             0
                                                   0
                                                         0
                                                                0
               [,74] [,75] [,76] [,77] [,78] [,79] [,80]
##
                                                            [,81]
##
   CREB3L1__2
                         1
                                0
                                      0
                                             0
                                                   0
                         0
                                0
                                      0
                                             0
                                                   0
                                                         0
                                                                0
   CREB3L1 3
                   0
##
               [,82] [,83] [,84] [,85] [,86] [,87]
                                                     [,88]
## CREB3L1
            2
                         0
                                0
                                      0
                                             0
                                                   0
                                                         0
## CREB3L1__3
                   0
                         0
                                0
                                      0
                                             0
                                                   1
                                                                0
               [,90]
##
## CREB3L1__2
                   0
## CREB3L1__3
                   1
i <- 5
x <- data0[i, ]
Zcut0 <- 0
best <- GetBestK(x = x, n = 1000, q = Zcut0, err = 1e-10)
pp <- calculate_prob_sep_Zcut(x, Zcut0, best$result[, 1], best$result[, 2], best$result[, 3])
cc <- discretization_method_1_LLR_mean(x, best$result, pp, LLR_cut = 0.1)</pre>
dd <- Build_R_matrix(cc, Zcut0, best$result[, 2], rownames(data0)[i])</pre>
print(x)
##
                                                 Oocyte.2
                     Oocyte.1
##
                                                0.2949059
                   -0.3871342
##
                     Oocyte.3
                                                 Zygote.1
##
                    0.7537718
                                                1.7446679
##
                     Zygote.2
                                                 Zygote.3
##
                    1.5871923
                                                1.7313015
##
     X2.cell_embryo.1_Cell.1
                                 X2.cell_embryo.1_Cell.2
##
                    1.4611699
                                                1.4011830
##
     X2.cell_embryo.2_Cell.1
                                 X2.cell_embryo.2_Cell.2
##
                    1.4731599
                                                1.5475625
##
     X2.cell_embryo.3_Cell.1
                                 X2.cell_embryo.3_Cell.2
##
                    1.0501221
                                                0.8742180
##
     X4.cell_embryo.1_Cell.1
                                 X4.cell_embryo.1_Cell.2
##
                    1.4060970
                                               -1.8325815
##
     X4.cell_embryo.1_Cell.3
                                 X4.cell_embryo.1_Cell.4
##
                    0.1856493
##
                                 X4.cell_embryo.2_Cell.2
     X4.cell_embryo.2_Cell.1
##
                    1.1413524
                                                     -Inf
##
     X4.cell_embryo.2_Cell.3
                                 X4.cell_embryo.2_Cell.4
##
                    2.3799164
                                               -0.9288695
##
     X4.cell_embryo.3_Cell.1
                                 X4.cell_embryo.3_Cell.2
##
                    1.5411591
                                                1.7523254
##
     X4.cell_embryo.3_Cell.3
                                 X4.cell_embryo.3_Cell.4
##
                    1.5091755
                                                1.7288197
##
     X8.cell_embryo.1_Cell.1
                                 X8.cell_embryo.1_Cell.2
##
                    3.5036336
                                                3.6047095
##
     X8.cell_embryo.1_Cell.3
                                 X8.cell_embryo.1_Cell.4
##
                    2.8523237
                                                3.7815954
##
     X8.cell_embryo.2_Cell.1
                                 X8.cell_embryo.2_Cell.2
##
                    2.7822296
                                                1.7838953
##
     X8.cell_embryo.2_Cell.3
                                 X8.cell_embryo.2_Cell.4
```

```
##
                    2.0550208
                                                3.6057967
##
     X8.cell_embryo.2_Cell.5
                                 X8.cell_embryo.2_Cell.6
                                               2.2490788
##
                    2.8845213
##
     X8.cell_embryo.2_Cell.7
                                 X8.cell_embryo.2_Cell.8
##
                    2.2758304
                                                2.9764475
##
     X8.cell embryo.3 Cell.1
                                 X8.cell embryo.3 Cell.2
##
                    3.2518463
                                                3.4940196
##
     X8.cell_embryo.3_Cell.3
                                 X8.cell_embryo.3_Cell.4
##
                    4.0421210
                                                3.8096580
##
     X8.cell_embryo.3_Cell.5
                                 X8.cell_embryo.3_Cell.6
##
                    3.6084554
                                                2.3880286
##
     X8.cell_embryo.3_Cell.7
                                 X8.cell_embryo.3_Cell.8
##
                    2.9516759
                                                4.0716217
##
            Morulae.1_Cell.1
                                        Morulae.1_Cell.2
##
                    3.9599366
                                               3.4106195
##
            Morulae.1_Cell.3
                                        Morulae.1_Cell.4
##
                   -0.1086994
                                               3.2040464
##
            Morulae.1 Cell.5
                                        Morulae.1 Cell.6
##
                    3.0037004
                                                4.1114475
##
            Morulae.1 Cell.7
                                        Morulae.1 Cell.8
##
                    3.7993021
                                              -0.8141855
##
                                        Morulae.2 Cell.2
            Morulae.2 Cell.1
##
                    3.0061775
                                                4.1204670
##
            Morulae.2 Cell.3
                                        Morulae.2 Cell.4
##
                    3.9427656
                                               3.4452781
##
            Morulae.2 Cell.5
                                        Morulae.2_Cell.6
##
                    3.0906333
                                                3.1098642
##
            Morulae.2_Cell.7
                                        Morulae.2_Cell.8
##
                    3.8282935
                                               4.1413236
##
    Late_blastocyst.1_Cell.1
                               Late_blastocyst.1_Cell.2
##
                    0.3133498
                                                2.3487050
##
    Late_blastocyst.1_Cell.3
                               {\tt Late\_blastocyst.1\_Cell.4}
##
                    3.4520489
                                                2.5867861
##
    Late_blastocyst.1_Cell.5
                                Late_blastocyst.1_Cell.6
##
                    4.2983325
                                                3.2938349
##
    Late_blastocyst.1_Cell.7
                               Late_blastocyst.1_Cell.8
##
                    2.2683042
                                               1.4092782
##
    Late_blastocyst.1_Cell.9 Late_blastocyst.1_Cell.10
##
                         -Inf
                                                3.0728322
##
   Late_blastocyst.1_Cell.11 Late_blastocyst.1_Cell.12
##
                    1.8878269
                                                2.3270826
##
    Late_blastocyst.2_Cell.1
                               Late_blastocyst.2_Cell.2
##
                    2.2086040
                                                2.9670756
##
                                Late_blastocyst.2_Cell.4
    Late_blastocyst.2_Cell.3
##
                    3.2008340
                                              -0.3768777
##
    Late_blastocyst.2_Cell.5
                                Late_blastocyst.2_Cell.6
                   -0.2256467
##
                                                2.8136107
##
    Late_blastocyst.2_Cell.7
                                Late_blastocyst.2_Cell.8
##
                   -0.8462984
                                                2.6758713
##
    Late_blastocyst.2_Cell.9 Late_blastocyst.2_Cell.10
##
                    1.4768204
                                                2.1813210
##
    Late_blastocyst.3_Cell.1
                               Late blastocyst.3 Cell.2
##
                    2.0725428
                                                1.3790180
    Late_blastocyst.3_Cell.3 Late_blastocyst.3_Cell.4
```

```
##
                    2.3051817
                                               2.4216118
##
    Late_blastocyst.3_Cell.5
                              Late_blastocyst.3_Cell.6
##
                   3.4375293
                                              -1.9661129
    Late_blastocyst.3_Cell.7
##
                               Late_blastocyst.3_Cell.8
##
                  -0.9314044
                                               1.9226415
print(pp)
##
           Oocyte.1
                      Oocyte.2
                                  Oocyte.3
                                              Zygote.1
  [1,] 0.142058828 0.10099843 0.08286467 0.04255067
   [2,] 0.002148516 0.03887417 0.11327751 0.52103074
##
          Zygote.2
                     Zygote.3 X2.cell_embryo.1_Cell.1
## [1,] 0.04835016 0.04302846
                                             0.05323813
  [2,] 0.43916973 0.51406614
                                             0.37563368
##
        X2.cell_embryo.1_Cell.2 X2.cell_embryo.2_Cell.1
## [1,]
                        0.055632
                                               0.05276456
## [2,]
                        0.346590
                                               0.38154475
##
        X2.cell_embryo.2_Cell.2 X2.cell_embryo.3_Cell.1
   [1,]
##
                      0.04986525
                                               0.07025561
   [2,]
##
                      0.41889125
                                               0.20003396
##
        X2.cell_embryo.3_Cell.2 X4.cell_embryo.1_Cell.1
## [1,]
                      0.07776154
                                               0.05543441
##
   [2,]
                      0.14438931
                                               0.34893383
##
        X4.cell_embryo.1_Cell.2 X4.cell_embryo.1_Cell.3
## [1,]
                    0.142058828
                                               0.10478288
##
  [2,]
                    0.002148516
                                               0.02913153
##
        X4.cell_embryo.1_Cell.4 X4.cell_embryo.2_Cell.1
## [1,]
                    0.142058828
                                               0.06638278
## [2,]
                    0.002148516
                                               0.23375092
##
        X4.cell embryo.2 Cell.2 X4.cell embryo.2 Cell.3
## [1,]
                    0.142058828
                                               0.02336931
##
   [2,]
                    0.002148516
                                               0.78888868
##
        X4.cell_embryo.2_Cell.4 X4.cell_embryo.3_Cell.1
##
   [1,]
                    0.142058828
                                               0.05011202
                    0.002148516
##
   [2,]
                                               0.41563682
        X4.cell_embryo.3_Cell.2 X4.cell_embryo.3_Cell.3
##
## [1,]
                      0.04227821
                                               0.05135246
##
   [2,]
                      0.52501705
                                               0.39948877
##
        X4.cell_embryo.3_Cell.4 X8.cell_embryo.1_Cell.1
##
  [1,]
                      0.04311748
                                              0.005825674
##
   [2,]
                      0.51277225
                                              0.559069231
##
        X8.cell_embryo.1_Cell.2 X8.cell_embryo.1_Cell.3
## [1,]
                      0.00503651
                                               0.01371725
## [2,]
                      0.50662638
                                               0.80729450
##
        X8.cell embryo.1 Cell.4 X8.cell embryo.2 Cell.1
## [1,]
                    0.003872077
                                               0.01491548
## [2,]
                    0.415124284
                                               0.81700745
##
        X8.cell_embryo.2_Cell.2 X8.cell_embryo.2_Cell.3
##
   [1,]
                      0.04116475
                                               0.03228834
##
   [2,]
                      0.54141032
                                               0.67416070
##
        X8.cell_embryo.2_Cell.4 X8.cell_embryo.2_Cell.5
## [1,]
                    0.005028538
                                               0.01319236
##
   [2,]
                    0.506059230
                                               0.80143059
##
        X8.cell_embryo.2_Cell.6 X8.cell_embryo.2_Cell.7
## [1,]
                      0.02673139
                                                0.0260188
```

```
## [2,]
                      0.75083533
                                                0.7596164
##
        X8.cell_embryo.2_Cell.8 X8.cell_embryo.3_Cell.1
## [1,]
                      0.0117793
                                              0.008248957
## [2,]
                       0.7800521
                                              0.680740316
##
        X8.cell_embryo.3_Cell.2 X8.cell_embryo.3_Cell.3
                    0.005905847
                                              0.002579446
## [1,]
## [2,]
                    0.564004259
                                              0.290916028
##
        X8.cell embryo.3 Cell.4 X8.cell embryo.3 Cell.5
## [1,]
                    0.003710332
                                              0.005009086
   [2,]
##
                    0.400950808
                                              0.504672239
##
        X8.cell_embryo.3_Cell.6 X8.cell_embryo.3_Cell.7
   [1,]
                      0.02317101
##
                                               0.01214783
##
   [2,]
                      0.79082419
                                               0.78646959
##
        X8.cell_embryo.3_Cell.8 Morulae.1_Cell.1
## [1,]
                    0.002459978
                                      0.002939261
##
   [2,]
                    0.278135320
                                      0.328057092
##
        Morulae.1_Cell.2 Morulae.1_Cell.3 Morulae.1_Cell.4
##
  [1,]
             0.006640721
                               0.142058828
                                                 0.008791032
                                                 0.701170601
   [2.]
             0.606114778
                               0.002148516
##
##
        Morulae.1 Cell.5 Morulae.1 Cell.6 Morulae.1 Cell.7
                               0.002306365
## [1,]
              0.01138407
                                                 0.003769333
  [2,]
                               0.261373546
                                                 0.406164587
              0.77245475
        Morulae.1_Cell.8 Morulae.2_Cell.1 Morulae.2_Cell.2
##
                                0.01134867
## [1.]
             0.142058828
                                                 0.002272763
  [2,]
##
             0.002148516
                                0.77173688
                                                 0.257658019
        Morulae.2 Cell.3 Morulae.2 Cell.4 Morulae.2 Cell.5
   [1,]
               0.0030197
                               0.006326611
                                                  0.01019296
##
##
   [2,]
               0.3360840
                               0.588788281
                                                  0.74466823
        Morulae.2_Cell.6 Morulae.2_Cell.7 Morulae.2_Cell.8
##
## [1,]
               0.0099434
                               0.003606151
                                                 0.002196698
##
   [2,]
               0.7378356
                               0.391621125
                                                 0.249182691
##
        Late_blastocyst.1_Cell.1 Late_blastocyst.1_Cell.2
## [1,]
                      0.10033384
                                                 0.02414328
   [2,]
                       0.04076196
##
                                                 0.78096288
##
        Late_blastocyst.1_Cell.3 Late_blastocyst.1_Cell.4
## [1,]
                      0.006266712
                                                 0.01867651
##
  [2,]
                      0.585372106
                                                 0.82113503
##
        Late_blastocyst.1_Cell.5 Late_blastocyst.1_Cell.6
## [1,]
                      0.001692224
                                                0.007795538
   [2,]
##
                      0.190788203
                                                0.661922969
##
        Late blastocyst.1 Cell.7 Late blastocyst.1 Cell.8
## [1,]
                      0.02621797
                                                 0.05530664
##
   [2,]
                       0.75719541
                                                 0.35045467
##
        Late_blastocyst.1_Cell.9 Late_blastocyst.1_Cell.10
## [1,]
                      0.142058828
                                                   0.0104284
## [2,]
                                                   0.7507792
                      0.002148516
##
        Late_blastocyst.1_Cell.11 Late_blastocyst.1_Cell.12
## [1,]
                        0.03761386
                                                   0.02468975
                        0.59449805
##
   [2,]
                                                   0.77503573
##
        Late_blastocyst.2_Cell.1 Late_blastocyst.2_Cell.2
## [1,]
                      0.02783421
                                                 0.01191768
## [2,]
                      0.73664808
                                                 0.78253551
##
        Late_blastocyst.2_Cell.3 Late_blastocyst.2_Cell.4
## [1,]
                      0.008828473
                                                0.142058828
```

```
## [2,]
                  0.702502598
                                        0.002148516
##
      Late_blastocyst.2_Cell.5 Late_blastocyst.2_Cell.6
## [1,]
                  0.142058828
                                        0.01436952
## [2,]
                  0.002148516
                                        0.81318328
##
      Late_blastocyst.2_Cell.7 Late_blastocyst.2_Cell.8
## [1,]
                  0.142058828
                                        0.01688368
## [2,]
                  0.002148516
                                        0.82349604
      Late_blastocyst.2_Cell.9 Late_blastocyst.2_Cell.10
##
## [1,]
                   0.05262032
                                         0.02859434
## [2,]
                   0.38335586
                                         0.72650345
      Late_blastocyst.3_Cell.1 Late_blastocyst.3_Cell.2
## [1,]
                   0.03175874
                                        0.05652637
## [2,]
                   0.68189923
                                        0.33610218
##
      Late_blastocyst.3_Cell.3 Late_blastocyst.3_Cell.4
## [1,]
                   0.02525186
                                        0.02236261
## [2,]
                   0.76867837
                                        0.79827767
##
      Late_blastocyst.3_Cell.5 Late_blastocyst.3_Cell.6
## [1,]
                  0.006395745
                                       0.142058828
## [2,]
                  0.592685944
                                       0.002148516
##
      Late_blastocyst.3_Cell.7 Late_blastocyst.3_Cell.8
## [1,]
                  0.142058828
                                        0.03646491
## [2,]
                  0.002148516
                                        0.61180664
print(cc)
## [57] 2 2 2 2 1 2 2 2 2 2 2 2 2 2 2 2 2 2 1 1 2 1 2 2 2 2 2
## [85] 2 2 2 1 1 2
print(dd)
          [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9] [,10]
## PNMA1__2
           0
               0 1 1 1 1
                                        1 1
                                    1
          [,11] [,12] [,13] [,14] [,15] [,16] [,17] [,18]
## PNMA1__2
            1 1 1
                            0
                                 0
                                       0
                                            1
##
          [,19] [,20] [,21] [,22] [,23] [,24] [,25] [,26]
## PNMA1__2
                  0 1
                            1
                                  1
                                       1
                                            1
          [,27] [,28] [,29] [,30] [,31] [,32] [,33] [,34]
## PNMA1__2
                  1
                       1 1
                                 1
                                       1
                                            1
          [,35] [,36] [,37] [,38] [,39] [,40] [,41] [,42]
## PNMA1 2
            1
                 1
                      1
                            1
                                 1
                                       1
                                            1
          [,43] [,44] [,45] [,46] [,47] [,48] [,49] [,50]
##
## PNMA1__2
            1 1 1 1
                                 0
                                       1
                                            1
##
          [,51] [,52] [,53] [,54] [,55] [,56] [,57] [,58]
## PNMA1__2
                  0
                       1
                            1
                                  1
                                       1
          [,59] [,60] [,61] [,62] [,63] [,64] [,65] [,66]
##
## PNMA1 2
             1
                  1
                       0
                            1
                                 1
                                       1
                                            1 1
          [,67] [,68] [,69] [,70] [,71] [,72] [,73] [,74]
## PNMA1__2
             1
                  1
                       0 1
                                 1
                                       1
                                            1 1
          [,75] [,76] [,77] [,78] [,79] [,80] [,81] [,82]
##
## PNMA1__2
             1
                  0
                       0 1
                                  0
                                       1
                                            1 1
          [,83] [,84] [,85] [,86] [,87] [,88] [,89] [,90]
## PNMA1 2 1 1 1 1
                                 1
                                    0
```

(iv) directly apply qubic from the QUBIC package

We are trying save the result to a file first.

```
WriteQubicInput <- function(file.name, data0, genes, q = 0, err = 1e-10) {
  cat("o", colnames(data0), "\n", file = file.name)
  for (i in genes) {
    cat(i, colnames(data0), "\n", file = "progress")
    x <- data0[i, ]
    Zcut0 <- q
    best <- GetBestK(x = x, n = 1000, q = Zcut0, err = 1e-10)
    if (best$k == 0) {
      next
    }
    pp <- calculate_prob_sep_Zcut(x, Zcut0, best$result[, 1], best$result[, 2], best$result[, 3])</pre>
    cc <- discretization_method_1_LLR_mean(x, best$result, pp, LLR_cut = 0.1)</pre>
    dd <- Build_R_matrix(cc, Zcut0, best$result[, 2], rownames(data0)[i])</pre>
    write.table(dd, file = file.name, col.names = FALSE, append = TRUE, quote = FALSE)
  }
}
system.time(WriteQubicInput("qubic_input_head", data0, head(selected.genes)))
##
      user system elapsed
##
      2.75
              0.00
                       2.93
system.time(WriteQubicInput("qubic_input_head30", data0, head(selected.genes, 30)))
##
      user system elapsed
##
      9.22
              0.06
                       9.66
This may be slow...
print(length(selected.genes))
## [1] 14542
qubic.file = "qubic_input"
if (!file.exists(qubic.file)) {
  WriteQubicInput(qubic.file, data0, selected.genes)
}
It is the time to read all the data back.
qubic.input <- as.matrix(read.table(qubic.file, row.names = 1, header = TRUE))</pre>
Run QUBIC(Zhang et al. 2017), need several minute.
library(QUBIC)
if (!file.exists("res.RData")) {
 res <- qubiclust_d(qubic.input)</pre>
  save(res, file="res.RData")
} else {
  load("res.RData")
save(res, file="res.RData")
```

(v) results summary

```
res
##
## An object of class Biclust
##
## call:
   NULL
##
##
## Number of Clusters found: 100
## First 5 Cluster sizes:
##
                       BC 1 BC 2 BC 3 BC 4 BC 5
## Number of Rows:
                        934
                            931
                                  921
                                        959
## Number of Columns:
                         73
                              73
                                   73
                                         70
biclust::summary(res)
##
## An object of class Biclust
##
## call:
##
   NULL
##
## Number of Clusters found: 100
##
##
  Cluster sizes:
##
                       BC 1 BC 2 BC 3 BC 4 BC 5 BC 6 BC 7 BC 8
## Number of Rows:
                        934
                                        959 941
                            931
                                  921
                                                  911
                                                        909
  Number of Columns:
                         73
                                         70
                                                   73
                              73
                                   73
                                              71
                                                         73
                                                              75
##
                       BC 9 BC 10 BC 11 BC 12 BC 13 BC 14 BC 15
## Number of Rows:
                        882
                              917
                                     902
## Number of Columns:
                         75
                               72
                                      73
                                            68
                                                  74
                                                         75
                                                               75
                       BC 16 BC 17 BC 18 BC 19 BC 20 BC 21
## Number of Rows:
                         894
                               892
                                      891
                                            910
                                                  897
                                                         907
## Number of Columns:
                          73
                                73
                                       73
                                             71
                                                   72
##
                       BC 22 BC 23 BC 24 BC 25 BC 26 BC 27
## Number of Rows:
                         870
                               870
                                      905
                                            866
                                                  850
## Number of Columns:
                          74
                                74
                                       71
                                             74
                                                   75
                       BC 28 BC 29 BC 30 BC 31 BC 32 BC 33
## Number of Rows:
                         846
                               845
                                      832
                                            832
                                                  832
                                                         832
## Number of Columns:
                          75
                                74
                                       75
                                             75
                                                   75
                                                          75
##
                       BC 34 BC 35 BC 36 BC 37 BC 38 BC 39
## Number of Rows:
                         831
                               831
                                            831
                                                  831
                                      831
                                                         831
## Number of Columns:
                          75
                                75
                                       75
                                             75
                                                    75
##
                       BC 40 BC 41 BC 42 BC 43 BC 44 BC 45
## Number of Rows:
                         831
                               838
                                      826
                                            826
                                                  826
                                                         826
## Number of Columns:
                          75
                                74
                                       75
                                             75
                                                   75
                                                          75
                       BC 46 BC 47 BC 48 BC 49 BC 50 BC 51
## Number of Rows:
                         832
                               831
                                      863
                                            808
                                                  814
## Number of Columns:
                          74
                                74
                                       71
                                             75
                                                   73
                                                          75
                       BC 52 BC 53 BC 54 BC 55 BC 56 BC 57
## Number of Rows:
                         792
                               792
                                      792
                                            792
                                                  792
                                                         792
## Number of Columns:
                                             75
                          75
                                75
                                       75
                                                   75
                                                          75
```

```
##
                        BC 58 BC 59 BC 60 BC 61 BC 62 BC 63
## Number of Rows:
                          792
                                792
                                       792
                                              792
                                                    792
                                                           792
  Number of Columns:
                           75
                                  75
                                        75
                                               75
                                                     75
                                                            75
##
                       BC 64 BC 65 BC 66 BC 67 BC 68 BC 69
##
  Number of Rows:
                          792
                                792
                                       792
                                              792
                                                    792
                                                           792
##
  Number of Columns:
                                 75
                                        75
                                               75
                                                     75
                           75
                                                            75
##
                        BC 70 BC 71 BC 72 BC 73 BC 74 BC 75
                                              792
                                                    792
## Number of Rows:
                          792
                                792
                                       792
                                                           792
##
   Number of Columns:
                           75
                                  75
                                        75
                                               75
                                                     75
                                                            75
##
                        BC 76 BC 77 BC 78 BC 79 BC 80 BC 81
##
  Number of Rows:
                          792
                                792
                                       792
                                              792
                                                    792
                                                           792
##
   Number of Columns:
                           75
                                  75
                                        75
                                               75
                                                     75
                                                            75
                        BC 82 BC 83 BC 84 BC 85 BC 86 BC 87
##
                                792
                                                    792
                          792
                                       792
   Number of Rows:
                                              792
                                                           792
##
   Number of Columns:
                           75
                                  75
                                        75
                                               75
                                                     75
                                                            75
##
                        BC 88 BC 89 BC 90 BC 91 BC 92 BC 93
                          792
                                792
                                       792
                                              791
                                                    792
                                                           792
##
  Number of Rows:
   Number of Columns:
                           75
                                  75
                                        75
                                               75
                                                     74
                                                            74
##
                        BC 94 BC 95 BC 96 BC 97 BC 98 BC 99
##
  Number of Rows:
                          792
                                792
                                       739
                                              725
                                                    699
                                                           683
  Number of Columns:
##
                           74
                                 74
                                        77
                                               76
                                                     78
                                                            77
##
                        BC 100
## Number of Rows:
                           668
## Number of Columns:
                            78
```

References

Zhang, Yu, Juan Xie, Jinyu Yang, Anne Fennell, Chi Zhang, and Qin Ma. 2017. "QUBIC: A Bioconductor Package for Qualitative Biclustering Analysis of Gene Co- Expression Data." *Bioinformatics* 33 (3): 450–52. https://doi.org/10.1093/bioinformatics/btw635.