Package ‘QUBIC’

May 30, 2024

**Type**  Package

**Title**  An R package for qualitative biclustering in support of gene
co-expression analyses

**Description**  The core function of this R package is to provide the
implementation of the well-cited and well-reviewed QUBIC algorithm, aiming to
deliver an effective and efficient biclustering capability. This package also
includes the following related functions: (i) a qualitative representation
of the input gene expression data, through a well-designed discretization way
considering the underlying data property, which can be directly used in other
biclustering programs; (ii) visualization of identified biclusters using heatmap
in support of overall expression pattern analysis; (iii) bicluster-based
co-expression network elucidation and visualization, where different correlation
coefficient scores between a pair of genes are provided; and (iv) a generalize
output format of biclusters and corresponding network can be freely downloaded
so that a user can easily do following comprehensive functional enrichment
analysis (e.g. DAVID) and advanced network visualization (e.g. Cytoscape).

**VignetteBuilder**  knitr

**biocViews**  StatisticalMethod, Microarray, DifferentialExpression,
MultipleComparison, Clustering, Visualization, GeneExpression,
Network

**Version**  1.32.0

**License**  CC BY-NC-ND 4.0 + file LICENSE

**Depends**  R (>= 3.1), biclust

**Imports**  Rcpp (>= 0.11.0), methods, Matrix

**LinkingTo**  Rcpp, RcppArmadillo

**Suggests**  QUBICdata, qgraph, fields, knitr, rmarkdown

**SystemRequirements**  C++11, Rtools (>= 3.1)

**Enhances**  RColorBrewer

**URL**  http://github.com/zy26/QUBIC

**BugReports**  http://github.com/zy26/QUBIC/issues

**git_url**  https://git.bioconductor.org/packages/QUBIC
BCQU-class

Class BCQU.

Description

Class BCQU define a QUalitative BIClustering calculator.

See Also

BCQU qudiscretize qunetwork qunet2xml biclust

QUBIC

QUBIC: A Qualitative Biclustering Algorithm for Analyses of Gene Expression Data

Description

QUBIC is a biclustering package, with source code upgrading from C code to C++ code. The updated source code can avoid memory allocation error and is much efficient than the original one. Based on our preliminary analysis, it can save 40% running time on a plant microarray data. Whenever using this package, please cite as Yu Zhang, Juan Xie, Jinyu Yang, Anne Fennell, Chi Zhang, Qin Ma; QUBIC: a bioconductor package for qualitative biclustering analysis of gene co-expression data. Bioinformatics, 2017; 33 (3): 450-452. doi: 10.1093/bioinformatics/btw635

BCQUD performs a QUalitative BIClustering for a discret matrix.
Usage

### S4 method for signature 'matrix,BCQU'
```r
biclust(x, method = BCQU(),
  r = 1, q = 0.06,
  c = 0.95, o = 100, f = 1,
  k = max(ncol(x) %% 20, 2),
  type = 'default', P = FALSE, C = FALSE, verbose = TRUE,
  weight = NULL, seedbicluster = NULL)
```

### S4 method for signature 'matrix,BCQUD'
```r
biclust(x, method = BCQUD(),
  c = 0.95, o = 100, f = 1,
  k = max(ncol(x) %% 20, 2),
  type = 'default', P = FALSE, C = FALSE, verbose = TRUE,
  weight = NULL, seedbicluster = NULL)
```

### qubiclust_d(x, c = 0.95, o = 100, f = 1,
```r
c = max(ncol(x) %% 20, 2),
  type = 'default', P = FALSE, C = FALSE, verbose = TRUE,
  weight = NULL, seedbicluster = NULL)
```

### qubiclust(x, r = 1L, q = 0.06, c = 0.95, o = 100, f = 1,
```r
c = max(ncol(x) %% 20, 2),
  type = 'default', P = FALSE, C = FALSE, verbose = TRUE,
  weight = NULL, seedbicluster = NULL)
```

Arguments

- **x**
  the input data matrix, which could be the normalized gene expression matrix or its qualitative representation from Qdiscretization or other discretization ways. (for example: a qualitative representation of gene expression data)
  For BCQU(), the data matrix should be real
  For BCQUD(), the data matrix should be discretized as integer. Zeros in the matrix will be treated as non-relevant value.

- **r**
  Affect the granularity of the biclusters. The range of possible ranks. A user can start with a small value of r (the default value is 1 so the corresponding data matrix consists of values '1', '-1' and '0'), evaluate the results, and then use larger values (should not be larger than half of the number of the columns) to look for fine structures within the identified biclusters.

- **q**
  Affect the granularity of the biclusters. The percentage of the regulating conditions for each gene. The choice of q’s value depends on the specific application goals; that is if the goal is to find genes that are responsive to local regulators, we should use a relatively small q-value; otherwise we may want to consider larger q-values. The default value of q is 0.06 in QUBIC (this value is selected based on the optimal biclustering results on simulated data).

- **c**
  The required consistency level of a bicluster. The default value of c is 0.95

- **o**
  The number of output biclusters. o’s default value is 100.
Control parameter, to control the level of overlaps between to-be-identified biclusters. The filter cut-off for data post-processing. For overlaps among to-be-identified biclusters. Its default value is set to 1 to ensure that no two reported biclusters overlap more than f.

k

The minimum column width of the block, minimum \( \max(ncol(x) \div 20, 2) \) columns.

type

The constrain type. If type is omitted or type='default', the original objective function in QUBIC will be used, which is to maximize the minimal value of numbers of rows and columns. If type='area', the program tries to identify the bicluster with the maximal value of number of rows multiplied by number of columns. Other types are reserved for future use.

P

The flag to enlarge current bicluster using a p-value contrain, which is defined based on its significance of expression consistency comparing to some simulated submatrix. Default: FALSE.

C

The flag to set the lower bound of the condition number in a bicluster as 5% of the total condition number in the input data. Only suggested to use when the input data has a few conditions (e.g. less than 20). Default: FALSE.

verbose

If 'TRUE', prints extra information on progress.

weight

Alternative weight matrix provided by user, will append to default weight. o, f, k, P, type, C will be ignored if using this parameter.

seedbicluster

Seed provided by user, normally should be a result of function biclust.

method

BCQU() or BCQUD(), to perform QUBIC algorithm

Details

For a given representing matrix of a microarray data set, we construct a weighted graph G with genes represented as vertices, edges connecting every pair of genes, and the weight of each edge being the similarity level between the two corresponding (entire) rows. Clearly, the higher a weight, the more similar two corresponding rows are. Intuitively, genes in a bicluster should induce a heavier subgraph of G because under a subset of the conditions, these genes have highly similar expression patterns that should make the weight of each involved edge heavier, comparing to the edges in the background. But it should be noted that some heavy subgraph may not necessarily correspond to a bicluster, i.e. genes from a heavy subgraph may not necessarily have similar expression patterns because different edges in a subgraph may have heavier weights under completely different subsets of conditions. It should also be noted that recognizing all heavy subgraphs in a weighted graph itself is computationally intractable because identification of maximum cliques in a graph is a special case of this, and the maximum clique problem is a well known intractable problem (NP-hard). So in our solution, we do not directly solve the problem of finding heavy subgraphs in a graph. Instead, we built our biclustering algorithm based on this graph representation of a microarray gene expression data, and tackle the biclustering problem as follows. We find all feasible biclusters (I,J) in the given data set such that \( \min(|I|, |J|) \) is as large as possible, where I and J are subsets of genes and conditions, respectively.

Value

Returns an Biclust object, which contains bicluster candidates
**Functions**

- **BCQU**: Performs a QUalitative BIClustering.
- **BCQUd**: Performs a QUalitative BIClustering for a discret matrix.
- **qubiclust_d**: Performs a QUalitative BIClustering for a discret matrix.
- **qubiclust**: Performs a QUalitative BIClustering.

**References**

Yu Zhang, Juan Xie, Jinyu Yang, Anne Fennell, Chi Zhang, Qin Ma: QUBIC: a bioconductor package for qualitative biclustering analysis of gene co-expression data. *Bioinformatics*, 2017; 33 (3): 450-452.

**See Also**

- **BCQU-class**
- **qudiscretize**
- **qunetwork**
- **qunet2xml**
- **biclust**

**Examples**

```r
# Random matrix with one embedded bicluster
test <- matrix(rnorm(5000), 100, 50)
test[11:20, 11:20] <- rnorm(100, 3, 0.3)
res <- biclust::biclust(test, method = BCQU())
summary(res)
show(res)
names(attributes(res))

# Not run:
# Load microarray matrix
data(BicatYeast)

# Display number of column and row of BicatYeast
ncol(BicatYeast)
nrow(BicatYeast)

# Bicluster on microarray matrix
system.time(res <- biclust::biclust(BicatYeast, method = BCQU()))

# Show bicluster info
res
# Show the first bicluster
biclust::bicluster(BicatYeast, res, 1)

# Get the 4th bicluster
bic4 <- biclust::bicluster(BicatYeast, res, 4)[[1]]

# or
bic4 <- biclust::bicluster(BicatYeast, res)[[4]]

# Show rownames of the 4th bicluster
rownames(bic4)

# Show colnames of the 4th bicluster
colnames(bic4)
```
```r
# Bicluster on selected of genes
data(EisenYeast)
"YGR218W", "YGL041C", "YOR202W", "YCR005C")
# same result as res <- biclust::biclust(EisenYeast[1:10,], method=BCQU())
res <- biclust::biclust(EisenYeast[genes, ], method = BCQU())
res
```

```r
# Get bicluster by row name = 249364_at
biclust::bicluster(BicatYeast, res, which(res@RowxNumber[which(rownames(BicatYeast) == "249364_at"), ]))
```

```r
# Get bicluster by col name = cold_roots_6h
biclust::bicluster(BicatYeast, res, which(res@NumberxCol[, which(colnames(BicatYeast) == "cold_roots_6h")]))
```

```r
# Draw a single bicluster using drawHeatmap {bicust}
data(BicatYeast)
res <- biclust::biclust(BicatYeast, BCQU(), verbose = FALSE)
# Draw heatmap of the first cluster
biclust::drawHeatmap(BicatYeast, res, 1)
```

```r
# Draw a single bicluster using heatmap {stats}
data(BicatYeast)
res <- biclust::biclust(BicatYeast, BCQU(), verbose = FALSE)
bic10 <- biclust::bicluster(BicatYeast, res, 10)[[1]]

# Draw heatmap of the 10th cluster using heatmap {stats}
heatmap(as.matrix(t(bic10)), Rowv = NA, Colv = NA, scale = 'none')

# Draw heatmap of the 10th cluster using plot_heatmap {phyloseq}
if (requireNamespace('phyloseq'))
  phyloseq::plot_heatmap(otu_table(bic10, taxa_are_rows = TRUE))
```

```r
# Draw a single bicluster with original data background and color options
```
qudiscretize

Create a qualitative discrete matrix for a given gene expression matrix

Description

qudiscretize delivers a discrete matrix. It is useful if we just want to get a discretized matrix.

Usage

qudiscretize(x, r = 1L, q = 0.06)
Arguments

\( x \)
the input data matrix, which could be the normalized gene expression matrix or its qualitative representation from \texttt{Qdiscretization} or other discretization ways. (for example: a qualitative representation of gene expression data)
For \texttt{BCQU()}, the data matrix should be real
For \texttt{BCQU()}, the data matrix should be discretized as integer. Zeros in the matrix will be treated as non-relevant value.

\( r \)
Affect the granularity of the biclusters. The range of possible ranks. A user can start with a small value of \( r \) (the default value is 1 so the corresponding data matrix consists of values '1', '-1' and '0'), evaluate the results, and then use larger values (should not be larger than half of the number of the columns) to look for fine structures within the identified biclusters.

\( q \)
Affect the granularity of the biclusters. The percentage of the regulating conditions for each gene. The choice of \( q \)'s value depends on the specific application goals; that is if the goal is to find genes that are responsive to local regulators, we should use a relatively small \( q \)-value; otherwise we may want to consider larger \( q \)-values. The default value of \( q \) is 0.06 in \texttt{QUBIC} (this value is selected based on the optimal biclustering results on simulated data).

Details

\texttt{qudiscretize} convert a given gene expression matrix to a discrete matrix. It’s implemented in C++, providing a increase in speed over the C equivalent.

Value

A qualitative discrete matrix

See Also

\texttt{QUBIC discretize}

Examples

# Qualitative discretize yeast microarray data
data(BicatYeast)
qudiscretize(BicatYeast[1:7, 1:5])

\begin{verbatim}
quheatmap
\end{verbatim}

\textit{Visualization of identified biclusters}

Description

This function can visualize the identified biclusters using heatmap in support of overall expression pattern analysis, either for a single bicluster or two biclusters.
Usage

quheatmap(x, bicResult, number = 1, showlabel = FALSE, col = c("#313695", "#4575B4", "#74ADD1", "#ABD9E9", "#E0F3F8", "#FFFFFF", "#FFEE00", "#FEE090", "#FDAE61", "#F46D43", "#D73027", "#A50026"), ...)

Arguments

x
The data matrix
bicResult
biclust::BiclustResult object
number
which bicluster to be plotted
showlabel
If TRUE, show the xlabel and ylabel
col
default: c("#313695", "#4575B4", "#74ADD1", "#ABD9E9", "#E0F3F8", "#FFFFFF", "#FFEE00", "#FEE090", "#FDAE61", "#F46D43", "#D73027", "#A50026")
...
Additional options in fields::image.plot

See Also

qunet2xml QUBIC heatmapBC

Examples

# Load microarray matrix
data(BicatYeast)
res <- biclust::biclust(BicatYeast, method=BCQU(), verbose = FALSE)
# Draw heatmap for the 2th identified bicluster
par(mar = c(5, 4, 3, 5) + 0.1, mgp = c(0, 1, 0), cex.lab = 1.1, cex.axis = 0.5, cex.main = 1.1)
quheatmap(x = BicatYeast, res, number = 2, showlabel = TRUE)
# Draw heatmap for the 2th and 3th identified biclusters.
par(mar = c(5, 5, 5, 5), cex.lab = 1.1, cex.axis = 0.5, cex.main = 1.1)
quheatmap(x = BicatYeast, res, number = c(2, 3), showlabel = TRUE)

qunet2xml

Convert network to XGMML

Description

This function can convert the constructed co-expression networks into XGMML format, which can be used to do further network analysis in Cytoscape, Biomax and JNets.

Usage

qunet2xml(net, minimum = 0.6,
         color = cbind(grDevices::rainbow(length(net[[2]]) - 1), "gray"))
qunetwork

Construction and visualization of co-expression network

Description

This function can automatically create co-expression networks along with their visualization based on identified biclusters in QUBIC. Three correlation methods, Pearson, Kendall and Spearman, are available for a user, facilitating different preferences in practical usage.

Usage

qunetwork(x, BicRes, number = 1:BicRes@Number, groups = c(number[[1]]), method = c("pearson", "kendall", "spearman"))

Arguments

- x: The data matrix
- BicRes: biclust::BiclustResult object
- number: Which bicluster to be plotted
- groups: An object that indicates which nodes belong together.
- method: A character string indicating which correlation coefficient (or covariance) is to be computed. One of 'pearson' (default), 'kendall', or 'spearman', can be abbreviated.

Value

Text of XGMML

See Also

qunetwork QUBIC

Examples

# Load microarray matrix
data(BicatYeast)
res <- biclust::biclust(BicatYeast[1:50, ], method=BCQU(), verbose = FALSE)
# Get all biclusters
net <- qunetwork(BicatYeast[1:50, ], res, group = c(4, 13), method = 'spearman')
# Save the network to a XGMML file
sink('tempnetworkresult.gr')
qunet2xml(net, minimum = 0.6, color = cbind(grDevices::rainbow(length(net[[2]]) - 1), 'gray'))
sink()
# You can use Cytoscape, Biomax or JNets open file named tempnetworkresult.gr
showinfo

Value

a list contains a weights matrix and groupinfo

See Also

qunet2xml QUBIC cor

Examples

# Load microarray matrix
data(BicatYeast)
res <- biclust::biclust(BicatYeast[1:50, ], method=BCQU(), verbose = FALSE)
# Constructing the networks for the 4th and 13th identified biclusters.
net <- qunetwork(BicatYeast[1:50, ], res, number = c(4, 13), group = c(4, 13), method = 'spearman')
## Not run:
if (requireNamespace('qgraph'))
  qgraph::qgraph(net[[1]], groups = net[[2]], layout = 'spring', minimum = 0.6,
  color = cbind(rainbow(length(net[[2]]) - 1), 'gray'), edge.label = FALSE)

## End(Not run)
## Not run:
#Load microarray matrix
data(BicatYeast)
res <- biclust::biclust(BicatYeast[1:50, ], method=BCQU(), verbose = FALSE)
# Constructing the networks for the 4th and 13th identified biclusters,
# using the whole network as a background.
net <- qunetwork(BicatYeast[1:50, ], res, group = c(4, 13), method = 'spearman')
if (requireNamespace('qgraph'))
  qgraph::qgraph(net[[1]], groups = net[[2]], layout = 'spring', minimum = 0.6,
  color = cbind(rainbow(length(net[[2]]) - 1), 'gray'), edge.label = FALSE)

## End(Not run)

showinfo  Show report of biclusters

Description

This function can make a report for biclusters.

Usage

showinfo(matrix, bic)

Arguments

matrix  microarray matrix
bic  array of biclusters
Value

Text of report

See Also

QUBIC

Examples

# Load microarray matrix
data(BicatYeast)
matrix <- BicatYeast[1:50, ];
res1 <- biclust::biclust(matrix, method=BCQU(), verbose = FALSE)
res2 <- biclust::biclust(matrix, method=BCCC())
res3 <- biclust::biclust(matrix, method=BCBimax())
# Show the report
showinfo(matrix, c(res1, res2, res3))

showinfo
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