

rqubic

March 24, 2012

QUBICBiclusterSet-class

Class "QUBICBiclusterSet"

Description

Object representing a set of biclusters identified by the QUBIC algorithm. The class structure inherits the `Biclust` class in the `biclust` package.

Objects from the Class

Created by functions parsing the output files of QUBIC command line tool, or functions calling QUBIC algorithm implementations in R.

Not intended to be created manually by end-users. However, interested users are invited to review the source code or use the `showClass` method to view the construction of the class.

Slots

See the class structure of `Biclust`. The slots `Parameter` and `Info` have been filled with lists relevant to the QUBIC algorithm, and all items should be accessed by S4-methods to make sure the consistency.

Methods

Svalue `signature(object = "QUBICBiclusterSet", index = "missing")`: Return S values of QUBIC biclusters as a vector

Svalue `signature(object = "QUBICBiclusterSet", index = "numeric")`: S values of specified bicluster(s) are returned. Index is one or a vector of integers. Non-integers will be coerced.

[`signature(x = "QUBICBiclusterSet", i = "ANY", j = "missing", drop = "missing")`: Returning a subset of the current QUBICBiclusterSet.

parameter `signature(object = "Biclust", index = "character")`: return an input parameter specified by the parameter name

parameter `signature(object = "Biclust", index = "missing")`: return a list of input parameters used by the biclustering algorithm, for example QUBIC

info signature(object = "Biclust", index = "ANY"): return information of the biclusters. For end-users, specific information accessors should be preferred, for example [features](#), [conditions](#) and `Svalue`

info signature(object = "Biclust", index = "missing"): return all information of the biclusters in a list. For end-users, specific information accessors should be preferred, for example [features](#), [conditions](#) and `Svalue`

show signature(object = "QUBICBiclusterSet"): showing method

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

References

Guojun Li, Qin Ma, Haibao Tang, Andrew H. Paternson and Ying Xu (2009) *QUBIC: a qualitative biclustering algorithm for analyses of gene expression data*. Nucleic Acids Research, 37:e101

See Also

[Biclust](#) is the basic block accomodating biclusters identified by the QUBIC algorithm.

Examples

```
showClass("QUBICBiclusterSet")
```

quantileDiscretize *Discretize expression matrix for qualitative biclustering*

Description

Performs recursive quantilizations on gene expression data across samples, to `quantileDiscretize` gene expression matrix. The quantile parameter `q` determines the estimated proportion of differentially expressed genes ($2q$ as for both up- and down-regulaton). The rank parameter `r` determines how many discrete levels should differentially expressed genes (or outliers) have. See details below.

Usage

```
quantileDiscretize(x, ...)
```

Arguments

`x` It can be an object of the `eSet` class or inheriting it. The most commonly used form is an `linkS4class{ExpressionSet}` class. Alternatively, it can be a numeric matrix.

`...` Currently, the `...` accepts two parameter: `q` and `rank`, explained below.

- `q` Estimated proportion of conditions where gene is up- or down-regulated, value between (0, 0.5), default value is set to 0.06. By specifying `q` one estimates that in $2q$ of all conditions, the expression value of a gene is considered as outlier.

- `rankRanks` (levels) of outliers, a positive integer, default is 1L. By default, all conditions get one label for each gene in $-1, 0, 1$, representing down expression, not changing and high expression respectively. In case $rank > 1$, the outliers are further divided into $rank$ levels by applying recursive quantilization with equal intervals.

Details

Parameter `q` corresponds to the command line option `-q` in the QUBIC command line tool, and the `rank` option corresponds to `-r`.

For each gene, the algorithm applies quantile discretization first to divide conditions into negative (lower), un-changed and positive (higher) expressions. Negative and positive expressed conditions are considered as *outliers*. For outliers in each direction, the algorithm tries to further quantileDiscretize the expression values in case $rank > 1$.

This second discretization step is performed by dividing the sorted outliers into $rank$ tandom groups with equal conditions. A label is assigned to each of these tandom groups, in the following order:

$$-1, -2, \dots, -rank$$

for outliers with negative expression, from the *most negative group* to the *least negative group* (not the other way around!).

Similarly, for positive outliers, labels in the order of

$$rank, rank - 1, \dots, 1$$

are assigned to tandom groups from the *least positive group* to the *most positive group*.

That is, signs of labels indicate the direction of gene expression change, and the absolute value represents the quantileDiscretized $rank$ in the outliers.

Value

An object of the same class as the input parameter, with the `exprs` slot replaced by the quantileDiscretized matrix, which is a matrix of integer.

Note

Note that the resulting discrete matrix of this implementation can be slightly different from the one used by the QUBIC command line tool.

The main reason for this is the internal data type: while QUBIC uses `float` to represent expression matrix, we use `double` to represent the matrix.

It has the advantages of interfacing to R, having higher precision and avoiding errors caused by floating presentation. It is implemented with potential larger costs of memory, however for test data sets (for example the ALL dataset with more than 120 samples and 12000 genes) the peak memory use (<100M) as well as the execution time (CPU time 0.028s) are well under control.

The differentially is especially often observed when there are many tied values. These cases however are very rare cases and we assume they will not affect the results to a large extent.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

References

Li et al. (2009) *QUBIC: a qualitative biclustering algorithm for analyses of gene expression data* Nucleic Acids Research 37:e101

See Also

[parseQubicChars](#) parses the quantileDiscretized matrix by the QUBIC command line tool into a data frame.

Examples

```
data(sample.ExpressionSet, package="Biobase")
sample.disc <- quantileDiscretize(sample.ExpressionSet)
exprs(sample.disc)[1:6, 1:6]

## Equivalent to pass a numeric matrix
sample.mat.disc <- quantileDiscretize(exprs(sample.ExpressionSet))
sample.mat.disc[1:6, 1:6]
## Not run: identical(exprs(sample.disc), sample.mat.disc)

## with multiple ranks
sample.rank3 <- quantileDiscretize(sample.ExpressionSet, rank=3)
exprs(sample.rank3)[1:6, 1:6]
```

eSetDimName

Get dimname from an eSet object

Description

This function is implemented to automatically validate and choose feature (sample) names from the user input. This function is exported for the purpose of easing other Bioconductor developers performing the similar job, and is not tended to be called by end-user directly.

Usage

```
eSetDimName(eset, input, type = c("feature", "sample"))
```

Arguments

| | |
|-------|---|
| eset | An object of eSet class, mostly an ExpressionSet class. |
| input | The user input, see details below |
| type | Either ‘feature’ or ‘sample’, indicating which dimension should be determined |

Details

The input can be one of the following three possibilities:

- Missing. Depending on the type, the results of calling [featureNames](#) (“feature”) or [sampleNames](#) (“sample”) on the `eset` object will be returned.
- A character string of length 1. Depending on the type, it is first to be matched to the column names of either [fData](#) or [pData](#) results of the `eset` object. If found, the values in that column are returned (coerced to characters if necessary). If not found, the function stops by raising an error.

- A character vector of the length equal to one of the two dimensions of the *eset*. In this scenario, the function only validates the equality of the length, coerces the input into characters, and return them.

If none of the scenarios above was met, the function stops by raising an error.

Value

A vector of characters, the length of which determined by the dimension of the input object.

Note

A special case arises if one of the dimensions of the *eset* object is 1: In this case, the input value is interpreted as the new name and returned. No column name match will take place in this case.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

See Also

[sampleNames](#), [featureNames](#), [fData](#), [pData](#)

[writeQubicInputFile](#) calls the function.

Examples

```
data(sample.ExpressionSet)
sub.eset <- sample.ExpressionSet[1:3, 1:3]

## usage one:
eSetDimName(sub.eset, type="feature")
eSetDimName(sub.eset, type="sample")

## usage two
## "sex" is one column in the pData(sub.eset)
eSetDimName(sub.eset, input="sex", type="sample")
## Not run: eSetDimName(sub.eset, input="foo", type="sample")

## usage three
eSetDimName(sub.eset, input=paste("Sample", 1:3), type="sample")
## Not run: eSetDimName(sub.eset, input=paste("Sample", 1:4),
type="sample")
## End(Not run)

## special case: dim equals to one
eSetDimName(sub.eset[,1], input="foo", type="sample")
```

Description

Generic function `features` and `conditions`, as well as auxillary count functions, are implemented for `QUBICBiclusterSet` objects.

They can be used in one of the following forms:

1. Used on a `QUBICBiclusterSet`, and without specifying `index`, `features` or `conditions` returns the unique and ordered features or conditions involved in at least one bicluster, and `featureCount` or `conditionCount` returns the length of respective vectors. To get the feature/condition numbers in each bicluster of the set, use `BCfeatureCount/BCconditionCount`.
2. Used on a `QUBICBiclusterSet` and provided `index` (indices), the features/conditions or their counts are returned for specified biclusters.

In addition, `featureNames` and `sampleNames` are of the same implementation as `features` and `conditions`.

Methods

`signature(object = "QUBICBicluster")` Information about all the biclusters.

`signature(object = "QUBICBiclusterSet", index = "missing")` Information about all the biclusters in the set.

`signature(object = "QUBICBiclusterSet", index = "ANY")` Information about selected biclusters in the set, the `index` can be integers or logical variables for subsetting.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

References

Guojun Li, Qin Ma, Haibao Tang, Andrew H. Paternson and Ying Xu (2009) *QUBIC: a qualitative biclustering algorithm for analyses of gene expression data*. *Nucleic Acids Research*, 37:e101

See Also

Methods are also documented in `QUBICBiclusterSet`.

Examples

```
example.file <- system.file("extdata", "sampleExpressionSet.blocks", package="rqubic")

example.block <- parseQubicBlocks(example.file)

head(features(example.block))
featureCount(example.block)
head(conditions(example.block))
conditionCount(example.block)

BCfeatureCount(example.block)
```

```

BCfeatures(example.block) [1:2]
BCconditionCount(example.block)
BCconditions(example.block) [1:2]

head(featureNames(example.block))
head(sampleNames(example.block))

```

```
generateSeeds-methods
```

Generate seeds for biclustering

Description

`generateSeeds` takes either matrix or an `ExpressionSet` object to generate seeds. Seeds are defined as pairs of genes (edges) which share coincident expression levels in samples. The higher the coincidence, the higher the score of the seeds will be. The seeds are generated by subsequent comparing each pair of genes. When all seeds have been produced, they are sorted by the coincidence scores and returned as an object. See the details section for notes on implementation.

Methods

In the `rqubic` package, `generateSeeds` currently supports two data types: `ExpressionSet` (an inherited type of `eSet`, or numeric matrix).

Both methods requires in addition a parameter, `minColWidth`, specifying the minimum number of conditions shared by the two genes of each seed. Its default value is 2. When this default value is used, the minimum coincidence score is defined as $\max(2, ncol/20)$, where `ncol` represents the number of conditions. When a non-default value is provided, the value is used to select seeds.

`signature(object = "eSet")` An object representing expression data. Note that the `exprs` must be a matrix of integers, otherwise the method warns and coerces the storage mode of matrix into integer.

`signature(object = "matrix")` A matrix of integers. In case filled by non-integers, the method warns and coerces the storage mode into integer

Details

The function compares all pairs of genes, namely all edges of a complete graph composed by genes. The weight of each edge is defined as the number of samples, in which two genes have the same expression level. This weight, also known as the *coincidence score*, reflects the co-regulation relationship between two genes.

The seed is chosen by picking edges with higher scores than the minimum score, provided by the `minColWidth` parameter (default: 2).

To implement such a selection algorithm, a *Fibonacci heap* is constructed in the C codes. Its size is predefined as a constant, which should be reduced in case the gene number is too large to run the algorithm. A new seed, which was selected by having a higher coincidence score than the minimum, is inserted to the heap. And dependent on whether the heap is full or not, it is either inserted by squeezing the minimum seed out, or put into the heap directly.

Once the heap is filled by examining all pairs of genes, it is dumped into an array of edge pointers, with decreasingly ordered edge pointers by their scores. This array is captured as an external pointer, attached as an attribute of an `rqubicSeeds` object.

An `rqubicSeeds` object holds an integer, which records the height of the heap. It has (besides the class identifier) two attributes: one for the external pointer, and the other one for the threshold of the coincidence score.

Note

In the `rqubic` implementation, the variable `arr_c[i][j]` holds the level symbols (-1, 0, 1 in the default case), whereas in the `QUBIC` implementation, this variable holds the index of level symbols, and the level symbols are saved in the global variable `symbols`.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

Examples

```
data(sample.ExpressionSet, package="Biobase")
sample.disc <- quantileDiscretize(sample.ExpressionSet)
sample.seeds <- generateSeeds(sample.disc)
sample.seeds

## with higher threshold of incidence score
sample.seeds.higher <- generateSeeds(sample.disc, minColWidth=5)
sample.seeds.higher
```

parseQubicBlocks *Parse QUBIC Command Line Tool Output Files*

Description

These functions parse output files of the `QUBIC` command line tool developed by Ma et al.

Usage

```
parseQubicRules(filename)
parseQubicChars(file, check.names=FALSE, ...)
parseQubicBlocks(filename)
```

Arguments

| | |
|--------------------------|---|
| <code>filename</code> | Input filename |
| <code>file</code> | Input filename |
| <code>check.names</code> | logical, should the column names be checked? |
| <code>...</code> | other parameters passed to the <code>read.csv</code> function |

Details

Parse `QUBIC` Command Line Tool Output Files

Value

`parseQubicRules` and `parseQubicChars` both return a data frame.
`parseQubicBlocks` returns an instance of `QUBICBiClusterSet` class.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

References

<http://csbl.bmb.uga.edu/~maqin/bicluster/>

Examples

```
getRqubicFile <- function(filename) system.file("extdata", filename, package="rqubic")

## parse QUBIC rules
rule.file <- getRqubicFile("sampleExpressionSet.rules")
rqubic.sample.rule <- parseQubicRules(rule.file)

## parse QUBIC chars
chars.file <- getRqubicFile("sampleExpressionSet.chars")
rqubic.sample.chars <- parseQubicChars(chars.file)

## parse QUBIC blocks
block.file <- getRqubicFile("sampleExpressionSet.blocks")
rqubic.sample.data <- parseQubicBlocks(block.file)
```

quBicluster

Qualitative Biclustering

Description

The function takes seeds and quantileDiscretized ExpressionSet as input, biclusters the data and returns an object holding biclusters. Users may control the report number of clusters, tolerance of incoherent genes (or conditions), as well as the filtering of redundant clusters.

Usage

```
quBicluster(seeds, eset, report.no = 100L, tolerance = 0.95, filter.proportion =
```

Arguments

| | |
|-------------------|--|
| seeds | An object of the S3-class <code>rqubicSeeds</code> , representing seeds generated from the quantileDiscretized expression data |
| eset | Discretized expression data |
| report.no | Number of biclusters that should be reported. Detected biclusters are ranked by the S-score, which is defined by the product of gene counts and sample counts. They are ordered and the top ones are reported. |
| tolerance | Percentage of tolerated incoherent samples, 0.95 by default |
| filter.proportion | Proportion of a cluster, over which the cluster is considered as redundant. Each bicluster is compared to all better ranking biclusters, and the overlapping proportion is measured by the proportion of the product of overlapping samples and overlapping genes, to the product samples and genes. If the proportion is larger than the given threshold, the block will be considered redundant and therefore not reported. Setting the threshold to 1 (default) does not perform any filtering. |

Details

The function calls a C routine to perform the biclustering. Currently the routine returns blocks with fewer samples specified by the minimum column number, due to the set of tolerance values. This might be changed in the fewer versions.

Value

An object of the `QUBICBiclusterSet-class`, holding all biclusters.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

References

Li et al. (2009) *QUBIC: a qualitative biclustering algorithm for analyses of gene expression data* Nucleic Acids Research 37:e101

See Also

`quantileDiscretize` and `generateSeeds`

Examples

```
data(sample.ExpressionSet)
rqubic.example.discret <- quantileDiscretize(sample.ExpressionSet, rank=2L)

rqubic.example.sel.seeds <- generateSeeds(rqubic.example.discret, minColWidth=2L)

rqubic.example.blocks <- quBicluster(rqubic.example.sel.seeds,
  rqubic.example.discret,
  report.no=200L,
  filter.proportion=0.1)

## print features in each bicluster
BCfeatures(rqubic.example.blocks)
```

rqubic-package

Qualitative biclustering algorithm for expression data analysis

Description

QUBIC is a qualitative biclustering algorithm for high-throughput expression data analysis. `rqubic` package implements this algorithm in R, partly with the codes contributed by Haibao Tang and Qin Ma (version 0.23 released without any limitation).

The `rqubic` package also provides parsers for the command line tool of `qubic` written in C.

Details

Package: rqubic
 Type: Package
 Version: 1.5
 Date: 2011-04-11
 License: LGPL-2
 LazyLoad: yes

Part of the source code in C is modified from the source code of the QUBIC command line tool (in C) provided by Haibao Tang and Qin Ma <maqin@csbl.bmb.uga.edu>, downloaded from <http://csbl.bmb.uga.edu/~maqin/bicluster/> on 01.03.2011, version 0.23.

Source code of QUBIC also uses open-source data structure library codes. See the README file included in the QUBIC command line tool source.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>, Laura Badi and Martin Ebeling Maintainer: Jitao David Zhang <jitao_david.zhang@roche.com>

References

Li et al. (2009) *QUBIC: a qualitative biclustering algorithm for analyses of gene expression data* Nucleic Acids Research 37:e101

```
writeQubicInputFile
```

Write an ExpressionSet object into the file format required by the QUBIC command line tool

Description

The QUBIC command line tool (developed by Ma et al.) requires a tab-limited data matrix as input file, with some special requirements (see details below). This function takes an object of ExpressionSet and outputs the file.

Usage

```
writeQubicInputFile(x, file = "", featureNames, sampleNames)
```

Arguments

| | |
|--------------|---|
| x | An object inheriting the <code>eSet</code> class, most commonly an <code>ExpressionSet</code> object, representing expression data of features across samples. |
| file | Filename to output, or a connection to write to (e.g. <code>stdout()</code>). |
| featureNames | Specifies the feature names. It can be left blank, in which case the result of calling <code>featureNames</code> on <code>x</code> will be used. Alternatively, it can be one character string, specifying which column in the <code>fData</code> should be used. The third possibility, it can be a vector of characters, with the same length as features in the object. In the last option, all other types will be converted to characters. |

`sampleNames` Specifies the sample names. It can be left blank, in which case the result of calling `sampleNames` on `x` will be used. Alternatively, it can be one character string, specifying which column in the `pData` should be used. The third possibility, it can be a vector of characters, with the same length as features in the object. In the last option, all other types will be converted to characters.

Details

The description of the data format can be checked by running the QUBIC tool in the command line mode, with the option `-h` (for *help*). A special requirement, which makes it different from the results of the `write.table` function in R, is that before the sample names (column names), an “o” must be added.

Value

No visible value will be returned, the function is called for its side effect.

Author(s)

Jitao David Zhang <jitao_david.zhang@roche.com>

See Also

`eSetDimName`, `write.table`

Examples

```
tmpfile <- tempfile()
data(sample.ExpressionSet)
sub.eset <- sample.ExpressionSet[1:3, 1:3]

## write to standard output
writeQubicInputFile(sub.eset)

## write to a temporary file
writeQubicInputFile(sub.eset, tmpfile)
head(readLines(tmpfile))

## specify names with one column name in fData/pData
writeQubicInputFile(sub.eset, file="", sampleNames="sex")

## alternatively specify names manually
writeQubicInputFile(sub.eset, file="", sampleNames=paste("Sample", 1:3))
```

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