Package 'iBBiG'

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Type Package

Title Iterative Binary Biclustering of Genesets

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Depends biclust

Imports stats4,xtable,ade4

Suggests methods

Description iBBiG is a bi-clustering algorithm which is optimizes for binary data analysis. We apply it to meta-gene set analysis of large numbers of gene expression datasets. The iterative algorithm extracts groups of phenotypes from multiple studies that are associated with similar gene sets. iBBiG does not require prior knowledge of the number or scale of clusters and allows discovery of clusters with diverse sizes

Reference Gusenleitner D, Howe EA, Bentink S, Quackenbush J, Culhane AC. iBBiG: Iterative Binary Bi-clustering of Gene Sets. Bioinformatics. In Press

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URL <http://bcb.dfci.harvard.edu/~aedin/publications/>

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Contents

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iBBiG-package   *iBBiG performs bi-clustering of binary matrices*

Description

iBBiG is a bi-clustering algorithm, optimized for module discovery in sparse noisy binary genomics data. We designed iBBiG to have high specificity and thereby minimize the false positive rate when discovering new classes; the iterative approach employed in iBBiG is able to discover weak signals, even if they are potentially masked by stronger ones.

Details

Package:	iBBiG
Type:	Package
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License:	Free Artistic
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The main functions is iBBiG. This is the biclustering algorithm.

Author(s)

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References

Daniel Gusenleitner, Eleanor A Howe, Stefan Bentink, John Quackenbush and Aedin C Culhane iBBiG: Iterative Binary Bi-clustering of Gene Sets Bioinformatics. In review.

See Also

Also see biclust ~~

Examples

```
#create simulated datasets
binMat<-makeArtificial()
binMat
plot(binMat)
res<- try(iBBiG(binMat@Seeddata, nModules=10))
plot(res)
res


## Subset a cluster

res[4]
res[1:2]


## As iBBiG extends the class Biclust can use Biclust functions on it
## View the rows and columns of an iBBiG object

## Create a list of matrices, one for each cluster
Modules<-bicluster(res@Seeddata, res)
length(Modules)
lapply(Modules, dim)


# Or extract a list of a specific cluster
M1<-bicluster(res@Seeddata, res, 1)
dim(M1[[1]])
str(M1)
M1[[1]][1:5,1:3]
```

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iBBiG   *Iterative Binary Bi-Clustering for GeneSets*

Description

iBBiG is a bi-clustering algorithm which is optimized for clustering binary data resulting from discretized p-values of genomic analyses

Usage

```
iBBiG(binaryMatrix, nModules, alpha = 0.3, pop_size = 100, mutation = 0.08, stagnation = 50, selection_p
```

Arguments

binaryMatrix   Matrix. A binary or logical matrix.

nModules   Numeric. The number of expected modules. As iBBiG is optimized to find a
                miminal number, nModules can be a larger than expected value

alpha   Numeric, weighting factor, that will balances the tradeoff between specificity
                    and sensitivity. Default 0.3. Simulated studies indicate range 0.3-0.5 is appro-
                    priate

pop_size   Numeric. Default 100. Population size establishes the genetic diversity of solu-
                    tions in Genetic Algorithm. Simulated studies show that it has marginal effect
                    on performance.

mutation   Numeric. Default 0.08. Mutation rate of GA. Simulated studies show that it has
                    little effect on performance.

stagnation   Numeric. Default is stop criterion of 50 iterations of stagnation. Simulated
                    studies show that it has little effect on performance.

selection_pressure
                    Numeric. Default is 1.2. Selection pressure for parent selection. Simulated
                    studies show that it has little effect on performance

max_sp   Numeric. Default is 15. Simulated studies show that it has little effect on per-
                    formance

success_ratio   Numeric. Deafult 0.6. Success ratio determines how many children have to
                    outperform at least one of their parents. Simulated studies show that it has little
                    effect on performance

Details

iBBiG is a bi-clustering algorithm, optimized for module discovery in sparse noisy binary genomics
data. We designed iBBiG to have high specificity and thereby minimize the false positive rate when
discovering new classes; the iterative approach employed in iBBiG is able to discover weak sig-
nals, even if they are potentially masked by stronger ones. For a compairions with global clustering
approaches (K-means, hierarchical cluster analysis) and bi-clustering approaches (Bimax, FABIA,
COALESCE) see our manuscript Gusenleitner et al., 2012. An advantage of iBBiG relative to other
methods is that it does not require a priori knowledge of the true number of clusters. Following the
application of iBBiG, the number of true clusters can be estimated from the weighted cluster scores
and RowScorexNumber of the extracted modules. In some cases, we observed that a module may
represent the residue or remaining signal of a stronger, previously extracted module. This residue
remains because iBBiG only removes information from the data matrix that is actually used for the
entropy based score in a module. However, we do not consider these residual modules to be a short-
coming of the method as their existence facilitates discovery of the true overlap between modules
and, further, these modules can be easily detected by looking at the overlap of clinical covariates
and gene sets.\ Although iBBiG includes several parameters, we have shown that most impact only
computation time, and do not effect cluster discovery. The only parameter that had an impact on
cluster discovery was alpha, which is a weighting factor that balances the cost of increasing cluster
size (number of rows) against cluster homogeneity. In generating small homogeneous clusters, one
might miss information. Conversely, large hetergeneous clusters may contain more false positives.
Although alpha does not regulate the number of clusters, decreasing stringency, by increasing alpha
values may produce greater numbers of clusters. As a results the alpha parameter is useful in adjust-
ing the sensitivity-specificity ratio. Alpha has a range 0.1-1 where 0.1 will generate fewer, smaller
homogeneous clusters whereas 0.9 is less stringent and results in more hetergeneous clusters (with
greater potential for false positives). Increasing alpha will generate more clusters of greater size,
with potentially greater specificity at the expense of decreased sensitivity. Following tests on sim-
ulated data we recommended alpha values between 0.3-0.5 (Gusenleitner et al., 2012). The default
alpha is 0.3

Value

Returns an object with class iBBiG, which extents the class Biclust.

Seeddata	Input binaryMatrix
RowScorexNumber	
	Matrix. Score for each signature (row) in each cluster. Matrix with dimensions, Number of Rows in Seeddata x Number of clusters
Clusterscores	Vector. Score for each cluster. It has length equal to the number of clusters.
Parameters	List of Input Parameters (if provided)
RowxNumber	Binary or Logical Matrix with dimensions, Number of Rows in Seeddata x Number of clusters, where 1 represents cluster membership
NumberxCol	Binary or Logical Matrix with dimensions, Number of clusters x Number of Columns in Seeddata ,where 1 represents cluster membership
Number	Numeric. Number of modules(clusters)
info	list. which is a general contained for other information.

Author(s)

Aedin Culhane, Daniel Gusenleitner

References

Daniel Gusenleitner, Eleanor A Howe, Stefan Bentink, John Quackenbush and Aedin C Culhane iBBiG: Iterative Binary Bi-clustering of Gene Sets Bioinformatics. In review.

See Also

Further functions for viewing and clustering binaray data are available in the package biclust. We have written iBBiG and its classes so that it is compatible with biclust, and the class iBBiG inherits Biclust-class.

Examples

```
binMat<-makeArtificial()
plot(binMat)
res<- iBBiG(binMat@Seeddata, nModules=10)
plot(res)
res
analyzeClust(res,binMat)
```

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iBBiG-class   *Class* "iBBiG"

Description

Class to contain and describe result of iBBiG Anlaysis

Objects from the Class

Objects can be created by calls of the form new("iBBiG", ...).

Slots

Seeddata: Input binaryMatrix

RowScorexNumber: Matrix. Score for each signature (row) in each cluster. Matrix with dimensions, Number of Rows in Seeddata x Number of clusters

Clusterscores: Vector. Score for each cluster. It has length equal to the number of clusters

Parameters: List of Input Parameters (if provided)

RowxNumber: Binary or Logical Matrix with dimensions, Number of Rows in Seeddata x Number of clusters, where 1 represents cluster membership

NumberxCol: Binary or Logical Matrix with dimensions, Number of clusters x Number of Columns in Seeddata ,where 1 represents cluster membership

Number: Numeric. Number of modules(clusters)

info: list. which is a general contained for other information.

Extends

Class "Biclust", directly.

Methods

RowScorexNumber signature(x = "iBBiG"): Returns the row scores fore each cluster.

Clusterscores signature(x = "iBBiG"): Returns the overall score for each cluster.

Seeddata signature(x = "iBBiG"): Returns the original binary matrix, the clustering is based on.

Parameters signature(x = "iBBiG"): Returns parameter sets, inhereted from biclust.

RowxNumber signature(x = "iBBiG"): Returns a logical matrix indicating, which rows are included in each bicluster.

NumberxCol signature(x = "iBBiG"): Returns a logical matrix indicating, which columns are included in each bicluster.

Number signature(x = "iBBiG"): Returns the number of biclusters contained in the iBBiG object.

info `signature(x = "iBBiG")`: Returns additional information on the particular iBBiG object, inhereted from biclust.

plot `signature(x = "iBBiG")`: Plot the iBBiG clustering.

show `signature(object = "iBBiG")`: Shows the Biclusters.

summary `signature(object = "iBBiG")`: Summary of found bi-clusters.

[`signature(object = "iBBiG")`: ...

JIdist `signature(object = "iBBiG")`: ...

analyzeClust `signature(object = "iBBiG")`: ...

Author(s)

Aedin Culhane, Daniel Gusenleitner

References

Daniel Gusenleitner, Eleanor A Howe, Stefan Bentink, John Quackenbush and Aedin C Culhane iBBiG: Iterative Binary Bi-clustering of Gene Sets Bioinformatics. In review.

See Also

Further functions for viewing and clustering binary data are available in the package biclust. We have written iBBiG and its classes so that it is compatible with biclust, and the class iBBiG inherits Biclust-class.

Examples

```
showClass("iBBiG")


#create simulated datasets
binMat<-makeArtificial()
binMat

## Create a binary matrix of 400 rows v 400 cols
## Its created as a Biclust object, so its easier to visualize
plot(binMat)

## Perform biclustering analysis on the binary matrix
res<- iBBiG(binMat@Seeddata, nModules=8)
res
plot(res)

## Compare 2 iBBiG or Biclust results
analyzeClust(res, binMat)

## Subset a cluster

res[4]
res[1:2]
```

```
## As iBBiG extends the class Biclust can use Biclust functions on it
## View the rows and columns of an iBBiG object

## Create a list of matrices, one for each cluster
Modules<-bicluster(res@Seeddata, res)
length(Modules)
lapply(Modules, dim)

# Or extract a list of a specific cluster
M1<-bicluster(res@Seeddata, res, 1)
dim(M1[[1]])
str(M1)
M1[[1]][1:5,1:3]
```

---

makeArtificial   *Create a 400x400 simulated binary matrix for testing iBBiG and other*
                                binary biclustering methods

Description

Create a binary matrix of 400 rows x 400 columns, where 1 is a positive association. This matrix is
seeded with 7 modules of various size and with various levels of noise as described by Gusenleitner
et al.,

Usage

```
makeArtificial(nRow = 400, nCol = 400, noise = 0.1, verbose = TRUE, dM = makeSimDesignMat(verbose = verbo
```

Arguments

nRow	Numeric nRow number of rows
nCol	Numeric nRow number of columns
noise	Numeric. Value between 0-1. Default is 10 percent random noise (1) introduced into the spare binary matrix
verbose	Verbose output. Default is TRUE
dM	A design matrix specifying where the columns are. The function makeSimDesignMat create the matrix which specifies the design matrix
seed	Integer, passed to function set.seed() the random-number generator function, so that the artical simulated data is reproduced. If you wish to generate a random simulated data set use seed=NULL

Details

See Guesnleitner et al, for more information

Value

Output is a class of Biclust.

Author(s)

Aedin Culhane, Daniel Gusenleitner

References

Daniel Gusenleitner, Eleanor A Howe, Stefan Bentink, John Quackenbush and Aedin C Culhane iBBiG: Iterative Binary Bi-clustering of Gene Sets Bioinformatics. In review.

See Also

Further functions for viewing and clustering binaray data are available in the package biclust. We have written iBBiG and its classes so that it is compatible with biclust, and the class iBBiG inherits Biclust-class.

Examples

```
##---- Should be DIRECTLY executable !! ----
##-- ==>  Define data, use random,
##--or do  help(data=index)  for the standard data sets.

## The function is currently defined as
arti<-makeArtificial()
plot(arti)
```

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