

Package ‘ADaM’

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Type Package

Title Adaptive Daisy Model

Version 0.1.0

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Description The ADaM package implements a semi-supervised algorithm for computing a fuzzy-intersection of non-fuzzy sets by adaptively determining the minimal number of sets to which an element should belong in order to be a member of the fuzzy-intersection (the membership threshold). This threshold maximises the deviance from expectation of the cardinality of the resulting fuzzy-intersection, as well as the coverage of predefined elements. This method can be used to identify the minimal number of cell lines from a given tissue in which the inactivation of a gene (for example via CRISPR-Cas9 targeting) should exert a reduction of viability (or fitness effect) in order for that gene to be considered a core-fitness essential gene for the tissue under consideration. This method is used to discriminate between core-fitness and context-specific essential genes in a study describing a large scale genome-wide CRISPR-Cas9 pooled drop-out screening (Behan FM & Iorio F & Picco G et al., Prioritisation of cancer therapeutic targets using CRISPR-Cas9 screens. Nature, In press).

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LazyData true

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ADAM.generateNullModel

Generate null profile of number of fitness genes across fixed numbers of cell lines and cumulative sums.

Description

This function randomly perturbs the binary dependency matrix to generate a null distribution of profiles of fitness genes across fixed number of cell lines, and corresponding null distribution of cumulative sums.

Usage

```
ADAM.generateNullModel(depMat, ntrials=100, display=TRUE)
```

Arguments

depMat	Binary dependency matrix, rows are genes and columns are samples. 1 in position $\text{depMat}[i,j]$ indicates that inactivation of the i th gene exerts a significant loss of fitness in the j th sample, 0 otherwise.
ntrials	Integer, default =100. How many times to randomly perturb dependency matrix to generate the null distributions.
display	Boolean, default is TRUE. Should bar plots of the null profiles be plotted

Details

For a number of trials specified in (ntrials) the inputted binary dependency matrix is randomised, keeping its column marginal sums. The profiles of fitness genes across fixed number of cell lines, and corresponding cumulative sums, are returned for each random perturbation.

Value

A list with the following two matrices

nullProf	Matrix of number of fitness genes for fixed number of cell lines from. Each row of matrix corresponds to a random trial.
nullCumSum	Matrix of profile of cumulative number of fitness genes in fixed number of cell lines. Each row of matrix is one random trial.

Author(s)

F. Iorio

Examples

```
data(exampleDepMat)
pprofile <- ADAM.generateNullModel(depMat = exampleDepMat, ntrials=100)
```

ADAM.panessprofile	<i>Calculate profile of number of fitness genes across fixed numbers of cell lines and cumulative sums.</i>
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Description

This function calculates the numbers (and cumulative numbers) of genes whose inactivation exerts a fitness effect in n cell lines, varying n from 1 to the number of cell lines in the dataset in input.

Usage

```
ADAM.panessprofile(depMat,
  display=TRUE,
  main_suffix='fitness genes in at least 1 cell line',
  xlab='n. dependent cell lines')
```

Arguments

depMat	Binary dependency matrix, rows are genes and columns are samples. 1 in position <code>depMat[i,j]</code> indicates that inactivation of the <code>gene</code> exerts a significant loss of fitness in the <code>sample</code> , 0 otherwise.
display	Boolean, default is TRUE. Should bar plots of the dependency profiles be plotted
main_suffix	If <code>display=TRUE</code> , title suffix to give to plot of number of genes depleted in a given number of cell lines, default is 'genes depleted in at least 1 cell line'
xlab	If <code>display=TRUE</code> , label to give to x-axis of the plots, default is 'n. cell lines'

Value

A list with the following two named vectors:

panessprof	Number of genes that are depleted for a number of cell lines
CUMsums	Cumulative number of genes depleted in at least x cell lines

Author(s)

F. Iorio

Examples

```
data(exampleDepMat)
pprofile <- ADAM.panessprofile(depMat = exampleDepMat)
```

exampleDepMat	<i>Example dependency matrix data object</i>
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Description

A binary matrix summarising the fitness effect status (1 = cellular fitness reduced upon gene inactivation via CRISPR-Cas9 targeting) of all the genes (at a genome scale) across 32 human colorectal cancer cell lines, derived from [1].

Usage

```
data("exampleDepMat")
```

Format

The format is: `num [1:17995, 1:32] 0 0 0 0 0 0 0 0 0 ... - attr(*, "dimnames")=List of 2 ..$: chr [1:17995] "A1BG" "A1CF" "A2M" "A2ML1"$: chr [1:32] "Cell_line_1" "Cell_line_2" "Cell_line_3" "Cell_line_4" ...`

References

[1] Behan FM & Iorio F & Picco G et al., *Prioritisation of cancer therapeutic targets using CRISPR-Cas9 screens*. **Nature**, In press.

Examples

```
data(exampleDepMat)
head(exampleDepMat)
```

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