

Package ‘pathprint’

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Type Package

Title Pathway fingerprinting for analysis of gene expression arrays

Description Algorithms to convert a gene expression array provided as an expression table or a GEO reference to a 'pathway fingerprint', a vector of discrete ternary scores representing high (1), low(-1) or insignificant (0) expression in a suite of pathways.

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consensusDistance	<i>Calculate a distribution of distances from a consensus fingerprint</i>
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Description

Calculates the distance from a consensus for a series of pathway fingerprints, accounting only for significantly high or low (-1 or 1) pathways in the consensus

Usage

```
consensusDistance(consensus, fingerprintframe)
```

Arguments

consensus	consensus fingerprint
fingerprintframe	dataframe of sample fingerprints from which the distance will be calculated

Details

The consensus fingerprint can be calculated using [consensusFingerprint](#) or alternatively can be a single fingerprint vector

Value

A dataframe with rows corresponding to each sample contained in the fingerprintframe with the following columns

distance	Manhattan distance of sample from the consensus fingerprint, scaled by the maximum possible distance
pvalue	p-value representing the probability that the samples are not phenotypically matched. N.B. this is only valid when the fingerprint frame represents a sufficiently broad coverage of phenotypes, e.g. the GEO corpus. This p-value is based on an assumption that the distances are normally distributed

Author(s)

Gabriel Altschuler

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[consensusFingerprint](#)

Examples

```
require(pathprintGEOdata)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)

ds = c("chipframe", "genesets",
       "pathprint.Hs.gs", "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

# free up space by removing the geo_sum_data object
remove(geo_sum_data)

# Extract common GSMs since we only loaded part of the geo_sum_data object
common_GSMs <- intersect(pluripotents.frame$GSM, colnames(GEO.fingerprint.matrix))

# search for pluripotent arrays
# create consensus fingerprint for pluripotent samples
pluripotent.consensus <- consensusFingerprint(
  GEO.fingerprint.matrix[,common_GSMs], threshold=0.9)

# calculate distance from the pluripotent consensus
geo.pluripotentDistance <- consensusDistance(
  pluripotent.consensus, GEO.fingerprint.matrix)

# plot histograms
par(mfcol = c(2,1), mar = c(0, 4, 4, 2))
geo.pluripotentDistance.hist <- hist(geo.pluripotentDistance[, "distance"],
  nclass = 50, xlim = c(0,1), main = "Distance from pluripotent consensus")
par(mar = c(7, 4, 4, 2))
hist(geo.pluripotentDistance[pluripotents.frame$GSM, "distance"],
  breaks = geo.pluripotentDistance.hist$breaks, xlim = c(0,1),
  main = "", xlab = "above: all GEO, below: curated pluripotent samples")
```

Description

Produces a pathway fingerprint that represents the consensus of a series of pathway fingerprints, according to a user-defined threshold

Usage

```
consensusFingerprint(fingerprintframe, threshold)
```

Arguments

fingerprintframe	matrix of fingerprints from which the consensus will be calculated
threshold	threshold value (between 0 and 1)

Details

For each pathway the mean fingerprint score, m , is calculated, and the consensus defined as
+1 if $m > \text{threshold}$
-1 if $m < \text{threshold}$
0 otherwise

Value

Vector of consensus pathway fingerprint scores with names corresponding to pathways

Author(s)

Gabriel Altschuler

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[consensusDistance](#)

Examples

```
require(pathprintGEOdata)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)

ds = c("chipframe", "genesets", "pathprint.Hs.gs",
      "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])
```

```

# free up space by removing the geo_sum_data object
remove(geo_sum_data)

# Extract common GSMs since we only loaded part of the geo_sum_data object
common_GSMs <- intersect(pluripotents.frame$GSM,colnames(GEO.fingerprint.matrix))

# search for pluripotent arrays
# load fingerprint matrix and pluripotent reference

# create consensus fingerprint
pluripotent.consensus<-consensusFingerprint(
  GEO.fingerprint.matrix[,common_GSMs], threshold=0.9)

# calculate distance from the pluripotent consensus
geo.pluripotentDistance<-consensusDistance(pluripotent.consensus,
  GEO.fingerprint.matrix)

# plot histograms
par(mfcol = c(2,1), mar = c(0, 4, 4, 2))
geo.pluripotentDistance.hist<-hist(geo.pluripotentDistance[, "distance"],
  nclass = 50, xlim = c(0,1), main = "Distance from pluripotent consensus")
par(mar = c(7, 4, 4, 2))
hist(geo.pluripotentDistance[pluripotents.frame$GSM, "distance"],
  breaks = geo.pluripotentDistance.hist$breaks, xlim = c(0,1),
  main = "", xlab = "above: all GEO, below: curated pluripotent samples")

```

customCDFAnn

Map probes to Entrez Gene IDs

Description

Annotates an expression array with entrez gene IDs, averaging to resolve redundancies

Usage

```
customCDFAnn(data, ann)
```

Arguments

data	expression dataframe
ann	annotation dataframe

Details

Maps array probes to a unique list of Entrez Gene IDs. The mean expression value is used for multiple probes mapping to the same gene.

Value

Returns a dataframe with a column for each column of the input data and rownames as unique entrez IDs.

Author(s)

Gabriel Altschuler

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[single.chip.enrichment](#)

Examples

```
require(pathprintGEOdata)

# load ALL dataset
require(ALL)
data(ALL)
annotation(ALL)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)

ds = c("chipframe", "genesets", "pathprint.Hs.gs",
      "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

# free up space by removing the geo_sum_data object
remove(geo_sum_data)

# The chip used was the Affymetrix Human Genome U95 Version 2 Array
# The corresponding GEO ID is GPL8300

# Extract portion of the expression matrix
ALL.exprs<-exprs(ALL)
ALL.exprs.sub<-ALL.exprs[,1:5]

# Annotate with Entrez Gene IDs,
ALL.exprs.sub.entrez<-customCDFAnn(ALL.exprs.sub, chipframe$GPL8300$ann)
head(ALL.exprs.sub.entrez)
```

diffPathways

Detect differentially activated pathways between fingerprints

Description

A function to return pathways consistently differentially expressed between two groups of pathway fingerprints

Usage

```
diffPathways(fingerprints, fac, threshold)
```

Arguments

fingerprints	matrix of fingerprints, the number of columns should correspond to the length of fac
fac	vector of characters or factors, in an order corresponding to the order of columns in the fingerprint matrix. Contains two levels, denoting the groups to be compared.
threshold	numeric, between 0 and 2 - the threshold at which to assign an average difference in pathway usage.

Details

The vector of factors must contain only two levels (or two unique values for a character vector).

Value

Returns a list of the rownames (i.e. pathways for the pathway fingerprint) corresponding to the rows for which the difference in the means between the two groups is greater than the threshold value. For a ternary fingerprint (-1,0,1), setting the threshold between 0.5 and 1 ensures that rownames are selected that differ across the majority of the arrays in the two groups. with values closer to 1 representing higher stringency. This can break down and allow false positives in the case where one group contains a significant but minority number of +1 and the other -1s.

Author(s)

Gabriel Altschuler

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[exprs2fingerprint](#), [consensusDistance](#), [consensusFingerprint](#)

Examples

```
require(pathprintGEOdata)

# Use ALL dataset as an example

require(ALL)
data(ALL)
annotation(ALL)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)
```

```

ds = c("chipframe", "genesets", "pathprint.Hs.gs",
      "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

# free up space by removing the geo_sum_data object
remove(geo_sum_data)

# The chip used was the Affymetrix Human Genome U95 Version 2 Array
# The corresponding GEO ID is GPL8300

# Analyze patients with ALL1/AF4 and BCR/ABL translocations
ALL.eset <- ALL[, ALL$mol.biol %in% c("BCR/ABL", "ALL1/AF4")]
ALL.exprs<-exprs(ALL.eset)

patient.type<-as.character(ALL$mol.biol[
  ALL$mol.biol %in% c("BCR/ABL", "ALL1/AF4")])

# Process fingerprints
ALL.fingerprint<-exprs2fingerprint(exprs = ALL.exprs,
  platform = "GPL8300",
  species = "human",
  progressBar = TRUE
)

color.map <- function(mol.biol) {
  if (mol.biol=="ALL1/AF4") "#00FF00" else "#FF00FF"
}
patientcolors <- sapply(ALL$mol.biol[
  ALL$mol.biol %in% c("BCR/ABL", "ALL1/AF4")],
  function(x){
    if (x == "ALL1/AF4") "#00FF00" else "#FF00FF"
  })

# define differentially activated pathways between the two groups
signif.pathways<-diffPathways(ALL.fingerprint,
  fac = patient.type,
  threshold = 0.6)

# draw heatmap
heatmap(ALL.fingerprint[signif.pathways,],
  ColSideColors = patientcolors,
  col = c("blue", "white", "red"),
  scale = "none", mar = c(10,20),
  cexRow = 0.75)
title(sub = "Pathways differentially activated in patients
with ALL1/AF4 (green) and BCR/ABL(purple) translocations",
  cex.sub = 0.75)

```


Description

The function converts the gene expression values to a ternary matrix of pathway expression values, (-1,0,1) corresponding to (low, background, high). This is based on applying a pre-calculated threshold to pathway enrichment scores.

Usage

```
exprs2fingerprint(exprs, platform, species, progressBar = TRUE)
```

Arguments

exprs	matrix containing a probe expression table, can be one or more columns
platform	microarray platform GEO ID
species	character string to define the species of the experiment, see details.
progressBar	logical. If TRUE, a progress bar is displayed while the script is running

Details

exprs should be a matrix or dataframe of the expression values, with rownames containing probe names and colnames the experiment IDs. Platforms should be of the type listed in GEO (e.g. "GPL570"). Species can be full latin names

"Homo sapiens", "Mus musculus", "Rattus norvegicus", "Danio rerio", "Drosophila melanogaster", "Caenorhabditis elegans".

or corresponding common-use names

"human", "mouse", "rat", "zebrafish", "drosophila", "C.elegans".

The array is first annotated with Entrez Gene IDs using annotations contained in the pathprintGEO-Data package. Pathway expression scores are calculated by the mean-squared rank of the gene expression and normalized against the appropriate distribution for the given platform in the GEO corpus. There is a progressBar to track the script, can be set to FALSE for (possibly) marginally faster running

Value

Returns a dataframe containing the pathway fingerprint for each of column in the expression table. Rownames correspond to pathways and colnames to the experiment IDs.

Author(s)

Gabriel Altschuler

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[consensusFingerprint](#), [single.chip.enrichment](#), [customCDFAnn](#), [thresholdFingerprint](#)

Examples

```

require(pathprintGEOData)

# Use ALL dataset as an example
require(ALL)
data(ALL)
annotation(ALL)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)

ds = c("chipframe", "genesets", "pathprint.Hs.gs",
      "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

# free up space by removing the geo_sum_data object
remove(geo_sum_data)

# The chip used was the Affymetrix Human Genome U95 Version 2 Array
# The corresponding GEO ID is GPL8300

# Extract portion of the expression matrix and process fingerprints
ALL.First5.fingerprint<-exprs2fingerprint(exprs = ALL[1:5],
    platform = "GPL8300",
    species = "human",
    progressBar = TRUE
)
head(ALL.First5.fingerprint)

```

genesets

Names of genesets used in pathprint

Description

An index to the genesets used in pathprint for each species, referenced by common and latin name

Usage

```
genesets
```

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

Examples

```
data("genesets")
genesets
```

pathprint

Pathway fingerprinting for analysis of gene expression arrays

Description

Algorithms to convert a gene expression array provided as an expression table to a 'pathway fingerprint'. The pathway fingerprint provides an unbiased, consistent annotation of expression data as a molecular phenotype, represented by activation status in 633 pathways. This is a vector of discrete ternary scores to represent high (1), low(-1) or insignificant (0) expression in a suite of pathways. Systematic definition of these functional relationships provides a tool for searching a pathway activation map of gene expression spanning species and technologies.

Details

Package: pathprint
Type: Package
Version: 2.0.0
Date: 2018-04-15
License: GPL

Author(s)

Gabriel Altschuler, Sokratis Kariotis
Maintainer: Sokratis Kariotis <s.kariotis@sheffield.ac.uk>

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[exprs2fingerprint](#), [consensusFingerprint](#), [consensusDistance](#)

Examples

```
require(pathprintGEOData)

# Use fingerprints to analyze the ALL dataset
require(ALL)
data(ALL)
annotation(ALL)
library(SummarizedExperiment)
```

```

# load the data use
data(SummarizedExperimentGEO)

ds = c("chipframe", "genesets", "pathprint.Hs.gs",
      "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

# free up space by removing the geo_sum_data object
remove(geo_sum_data)

# The chip used was the Affymetrix Human Genome U95 Version 2 Array
# The corresponding GEO ID is GPL8300

# Extract portion of the expression matrix
ALL.exprs<-exprs(ALL)
ALL.exprs.sub<-ALL.exprs[,1:5]

# Process fingerprints
ALL.fingerprint<-exprs2fingerprint(exprs = ALL.exprs.sub,
  platform = "GPL8300",
  species = "human",
  progressBar = TRUE
)

head(ALL.fingerprint)

####
# Construct consensus fingerprint based on pluripotent records
# Use this consensus to find similar arrays

# Extract common GSMs since we only loaded part of the geo_sum_data object
common_GSMs <- intersect(pluripotents.frame$GSM, colnames(GEO.fingerprint.matrix))

pluripotent.consensus<-consensusFingerprint(
  GEO.fingerprint.matrix[,common_GSMs], threshold=0.9)

# calculate distance from the pluripotent consensus
geo.pluripotentDistance<-consensusDistance(
  pluripotent.consensus, GEO.fingerprint.matrix)

# plot histograms
par(mfcol = c(2,1), mar = c(0, 4, 4, 2))
geo.pluripotentDistance.hist<-hist(geo.pluripotentDistance[, "distance"],
  nclass = 50, xlim = c(0,1), main = "Distance from pluripotent consensus")

par(mar = c(7, 4, 4, 2))
hist(geo.pluripotentDistance[pluripotents.frame$GSM, "distance"],
  breaks = geo.pluripotentDistance.hist$breaks, xlim = c(0,1),
  main = "", xlab = "above: all GEO, below: pluripotent samples")

```

pathprint.Ce.gs *Pathprint genesets - C. elegans*

Description

Pathways and genesets used by pathprint for *C. elegans* arrays, referenced by Entrez Gene ID

Usage

```
pathprint.Ce.gs
```

Details

Gene sets were inferred by homology from the human genesets, [pathprint.Hs.gs](#), using the HomoloGene database, www.ncbi.nlm.nih.gov/homologene

Source

O. Hofmann

References

Sayers et al. Database resources of the National Center for Biotechnology Information. *Nucleic Acids Research* (2011) vol. 39 (Database issue) pp. D38-51
Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

Examples

```
data("pathprint.Ce.gs")  
pathprint.Ce.gs[grep("ZN175_7728", names(pathprint.Ce.gs))]
```

pathprint.Dm.gs *Pathprint genesets - D. melanogaster*

Description

Pathways and genesets used by pathprint for *D. melanogaster* arrays, referenced by Entrez Gene ID

Usage

```
pathprint.Dm.gs
```

Details

Gene sets were inferred by homology from the human genesets, [pathprint.Hs.gs](#), using the HomoloGene database, www.ncbi.nlm.nih.gov/homologene

Source

O. Hofmann

References

Sayers et al. Database resources of the National Center for Biotechnology Information. *Nucleic Acids Research* (2011) vol. 39 (Database issue) pp. D38-51

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

Examples

```
data("pathprint.Dm.gs")
pathprint.Dm.gs[grep("ZN175_7728", names(pathprint.Dm.gs))]
```

pathprint.Dr.gs	<i>Pathprint genesets - D. rerio</i>
-----------------	--------------------------------------

Description

Pathways and genesets used by pathprint for *D. rerio* arrays, referenced by Entrez Gene ID

Usage

```
pathprint.Dr.gs
```

Details

Gene sets were inferred by homology from the human genesets, [pathprint.Hs.gs](#), using the HomoloGene database, www.ncbi.nlm.nih.gov/homologene

Source

O. Hofmann

References

Sayers et al. Database resources of the National Center for Biotechnology Information. *Nucleic Acids Research* (2011) vol. 39 (Database issue) pp. D38-51

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

Examples

```
data("pathprint.Dr.gs")
pathprint.Dr.gs[grep("ZN175_7728", names(pathprint.Dr.gs))]
```

pathprint.Hs.gs *Pathprint genesets - H. sapiens*

Description

Pathways and genesets used by pathprint for *H.sapiens* arrays, referenced by Entrez Gene ID

Usage

```
pathprint.Hs.gs
```

Source

O. Hofmann

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

Examples

```
data("pathprint.Hs.gs")
pathprint.Hs.gs[grep("ZN175_7728", names(pathprint.Hs.gs))]
```

pathprint.Mm.gs *Pathprint genesets - M. musculus*

Description

Pathways and genesets used by pathprint for *M. musculus* arrays, referenced by Entrez Gene ID

Usage

```
pathprint.Mm.gs
```

Details

Gene sets were inferred by homology from the human genesets, [pathprint.Hs.gs](#), using the HomoloGene database, www.ncbi.nlm.nih.gov/homologene

Source

O. Hofmann

References

Sayers et al. Database resources of the National Center for Biotechnology Information. Nucleic Acids Research (2011) vol. 39 (Database issue) pp. D38-51
Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." Genome Med 5(7): 68.

Examples

```
data("pathprint.Mm.gs")  
pathprint.Mm.gs[grep("ZN175_7728", names(pathprint.Mm.gs))]
```

pathprint.Rn.gs	<i>Pathprint genesets - R. norvegicus</i>
-----------------	---

Description

Pathways and genesets used by pathprint for *R. norvegicus* arrays, referenced by Entrez Gene ID

Usage

```
pathprint.Rn.gs
```

Details

Gene sets were inferred by homology from the human genesets, [pathprint.Hs.gs](#), using the HomoloGene database, www.ncbi.nlm.nih.gov/homologene

Source

O. Hofmann

References

Sayers et al. Database resources of the National Center for Biotechnology Information. Nucleic Acids Research (2011) vol. 39 (Database issue) pp. D38-51
Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." Genome Med 5(7): 68.

Examples

```
data("pathprint.Rn.gs")  
pathprint.Rn.gs[grep("ZN175_7728", names(pathprint.Rn.gs))]
```

platform.thresholds *Pathway fingerprint threshold values*

Description

Ternary threshold values for conversion of continuous geneset enrichment scores to discrete Pathway Fingerprint scores - high (1), mid (0), low (-1) for each geneset and platform covered by the Pathway Fingerprint.

Usage

```
platform.thresholds
```

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

Examples

```
require(pathprintGEOdata)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)
data("platform.thresholds")

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

head(platform.thresholds[[1]])
```

pluripotents.frame *Manually curated list of pluripotent arrays*

Description

A manually compiled list of pluripotent arrays (induced pluripotent cells and embryonic stem cells) together with their GEO IDs and descriptions

Usage

```
pluripotents.frame
```

Format

A data frame with 278 observations on the following 5 variables.

GSM GEO sample ID

GSE GEO series ID

GPL GEO platform ID

source GEO description - Source

Characteristics GEO description - Characteristic

Source

<http://www.ncbi.nlm.nih.gov/geo/>

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[consensusDistance](#), [consensusFingerprint](#)

Examples

```
require(pathprintGEOdata)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)

ds = c("chipframe", "genesets", "pathprint.Hs.gs",
       "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

# Extract common GSMs since we only loaded part of the geo_sum_data object
common_GSMs <- intersect(pluripotents.frame$GSM, colnames(GEO.fingerprint.matrix))

# free up space by removing the geo_sum_data object
remove(geo_sum_data)

head(pluripotents.frame)

# Use pathway fingerprints to search for
# additional pluripotent arrays across GEO
# create consensus pluripotent fingerprint
pluripotent.consensus<-consensusFingerprint(
  GEO.fingerprint.matrix[,common_GSMs], threshold=0.9)

# calculate distance from the pluripotent consensus
```

```

geo.pluripotentDistance<-consensusDistance(
  pluripotent.consensus, GEO.fingerprint.matrix)

# plot histograms
par(mfcol = c(2,1), mar = c(0, 4, 4, 2))
geo.pluripotentDistance.hist<-hist(geo.pluripotentDistance[, "distance"],
  nclass = 50, xlim = c(0,1), main = "Distance from pluripotent consensus")
par(mar = c(7, 4, 4, 2))
hist(geo.pluripotentDistance[pluripotents.frame$GSM, "distance"],
  breaks = geo.pluripotentDistance.hist$breaks, xlim = c(0,1),
  main = "", xlab = "above: all GEO, below: pluripotent samples")

```

single.chip.enrichment

Calculate enrichment of a list of genesets in an array

Description

Function to assess enrichment of gene sets in an array or matrix of arrays using various summary statistics

Usage

```

single.chip.enrichment(exprs,
  geneset,
  transformation = "rank",
  statistic = "mean",
  normalizedScore = FALSE,
  progressBar = TRUE)

```

Arguments

exprs	An expression matrix, rownames correspond to gene ids used in the list of genesets
geneset	list of pathways or genesets over which to assess statistic
transformation	Initial transformation applied to each column of exprs, can be one of "rank", "squared.rank" or "log.rank"
statistic	Summary statistic to be applied, either "mean" or "median"
normalizedScore	Logical. If statistic = "mean" and normalizedScore = TRUE, option to calculate a parametric significance score based on the expected distribution of scores. Other summary statistics currently not supported
progressBar	Logical. Shows progress of script, good to check running okay, set to FALSE for possible faster running

Details

This is the worker function for `exprs2fingerprint`, in conjunction with an `exprs` based on Entrez Gene IDs and the standard pathprint genesets e.g. [pathprint.Hs.gs](#). The (un-normalized) results are passed onto `thresholdFingerprint` to produce the Pathway Fingerprint scores

Value

Matrix containing pathway enrichment scores for each sample in the `exprs` input matrix. Rownames are genesets and colnames are the columns of the `exprs` matrix.

Author(s)

Gabriel Altschuler

References

Altschuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[exprs2fingerprint](#)

Examples

```
require(pathprintGEOdata)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)

# Compare continuous pathway enrichment values to Pathway Fingerprint scores

# Use ALL dataset as an example

require(ALL)
data(ALL)
annotation(ALL)

ds = c("chipframe", "pathprint.Hs.gs", "genesets", "platform.thresholds")
data(list = ds)

# The chip used was the Affymetrix Human Genome U95 Version 2 Array
# The corresponding GEO ID is GPL8300

# Analyze patients with ALL1/AF4 and BCR/ABL translocations
ALL.eset <- ALL[, ALL$mol.biol %in% c("BCR/ABL", "ALL1/AF4")]
ALL.exprs <- exprs(ALL.eset)

patient.type <- as.character(ALL$mol.biol[
  ALL$mol.biol %in% c("BCR/ABL", "ALL1/AF4")])

# Process fingerprints
ALL.fingerprint <- exprs2fingerprint(exprs = ALL.exprs,
  platform = "GPL8300",
  species = "human",
  progressBar = TRUE
)

color.map <- function(mol.biol) {
```

```

    if (mol.biol=="ALL1/AF4") "#00FF00" else "#FF00FF"
  }
patientcolors <- sapply(ALL$mol.biol[
  ALL$mol.biol %in% c("BCR/ABL", "ALL1/AF4")],
  function(x){
    if (x == "ALL1/AF4") "#00FF00" else "#FF00FF"
  })

# define list of differentially activated pathways between the two groups
signif.pathways<-diffPathways(ALL.fingerprint,
  fac = patient.type,
  threshold = 0.6)

# draw heatmap
heatmap(ALL.fingerprint[signif.pathways,],
  ColSideColors = patientcolors,
  col = c("blue", "white", "red"),
  scale = "none", mar = c(10,20),
  cexRow = 0.75)
title(sub = "Pathways differentially activated in patients
  with ALL1/AF4 (green) and BCR/ABL(purple) translocations",
  cex.sub = 0.75)

#####
# Compare to continuous values
ALL.exprs.entrez <- customCDFAnn(ALL.exprs, chipframe$GPL8300$ann)
ALL.enrichment <- single.chip.enrichment(exprs = ALL.exprs.entrez,
  geneset = pathprint.Hs.gs,
  transformation = "squared.rank",
  statistic = "mean",
  normalizedScore = FALSE,
  progressBar = TRUE
)

heatmap(ALL.enrichment[signif.pathways,],
  ColSideColors = patientcolors,
  col = colorRampPalette(c("blue", "white", "red"))(100),
  scale = "row", mar = c(10,20),
  cexRow = 0.75)
title(sub = "Continuous pathway enrichment scores for patients
  with ALL1/AF4 (green) and BCR/ABL(purple) translocations",
  cex.sub = 0.75)

```

thresholdFingerprint *Apply threshold values to produce a Pathway Fingerprint*

Description

Function to produce ternary threshold values, Pathway Fingerprint scores, from continuous geneset enrichment values. Returns ternary scores for each pathway, high (1), mid (0), low (-1)

Usage

```
thresholdFingerprint(SCE, platform)
```

Arguments

SCE Pathway enrichment matrix from [single.chip.enrichment](#)
 platform GEO platform ID for array used

Details

The thresholds have been pre-calculated and optimized against a panel of tissue samples (see ref).

Value

Matrix containing ternary scores for each sample in the SCE input matrix. Rownames are genesets and colnames are the columns of the SCE matrix.

Author(s)

Gabriel Altshuler

References

Altshuler, G. M., O. Hofmann, I. Kalatskaya, R. Payne, S. J. Ho Sui, U. Saxena, A. V. Krivtsov, S. A. Armstrong, T. Cai, L. Stein and W. A. Hide (2013). "Pathprinting: An integrative approach to understand the functional basis of disease." *Genome Med* 5(7): 68.

See Also

[exprs2fingerprint](#), [platform.thresholds](#)

Examples

```
require(pathprintGEOData)
library(SummarizedExperiment)

# load the data
data(SummarizedExperimentGEO)

# Comparing workflows

# 1. Pathway Fingerprint scores from exprs2fingerprint

# Use ALL dataset as an example

require(ALL)
data(ALL)
annotation(ALL)

ds = c("chipframe", "genesets", "pathprint.Hs.gs",
       "platform.thresholds", "pluripotents.frame")
data(list = ds)

# extract part of the GEO.fingerprint.matrix and GEO.metadata.matrix
GEO.fingerprint.matrix = assays(geo_sum_data[,300000:350000])$fingerprint
GEO.metadata.matrix = colData(geo_sum_data[,300000:350000])

# free up space by removing the geo_sum_data object
remove(geo_sum_data)
```

```
# The chip used was the Affymetrix Human Genome U95 Version 2 Array
# The corresponding GEO ID is GPL8300

# Analyze patients with ALL1/AF4 and BCR/ABL translocations
ALL.eset <- ALL[,1:5]
ALL.exprs<-exprs(ALL.eset)
# Process fingerprints
ALL.fingerprint<-exprs2fingerprint(exprs = ALL.exprs,
  platform = "GPL8300",
  species = "human",
  progressBar = TRUE
)

# 2. Thresholded pathway enrichment values

# Annotate
ALL.exprs.entrez <- customCDFAnn(ALL.exprs, chipframe$GPL8300$ann)

# Pathway enrichment
ALL.enrichment <- single.chip.enrichment(exprs = ALL.exprs.entrez,
  geneset = pathprint.Hs.gs,
  transformation = "squared.rank",
  statistic = "mean",
  normalizedScore = FALSE,
  progressBar = TRUE
)

# Threshold
ALL.enrichment.threshold <- thresholdFingerprint(
  ALL.enrichment, "GPL8300")

# Compare 1. and 2.
all.equal(ALL.enrichment.threshold, ALL.fingerprint)
```

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