Package ‘genomicInstability’

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**Imports** mixtools, SummarizedExperiment  

**Description**  
This package contain functions to run genomic instability analysis (GIA) from scRNA-Seq data.  
GIA estimates the association between gene expression and genomic location of the coding genes.  
It uses the aREA algorithm to quantify the enrichment of sets of contiguous genes (loci-blocks) on the gene expression profiles and estimates the Genomic Instability Score (GIS) for each analyzed cell.

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Description

This package contains functions to run genomic instability analysis (GIA) from scRNA-Seq data. GIA estimates the association between gene expression and genomic location of the coding genes. It uses the aREA algorithm to quantify the enrichment of sets of contiguous genes (loci-blocks) on the gene expression profiles and estimates the Genomic Instability Score (GIS) for each analyzed cell.

Details

The basic functionality of this package can be performed by inferCNV(), to infer the enrichment of loci-blocks on gene expression; genomicInstabilityScore(), to estimate the genomic instability for each of the cells in the scRNASeq dataset; giLikelihood(), to estimate the relative likelihood for each cell to be normal (low genomic instability) or tumor (high genomic instability); plot() and giDensityPlot() to plot the scores per loci-block and the distribution of the genomic instability score, respectively.

Author(s)

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geneLength

See Also

[inferCNV()] for estimating loci-block enrichment, [genomicInstabilityScore()] for estimating the genomic instability of each cell in the dataset, [giLikelihood()] for estimating the relative likelihood for the cells to be normal or neoplastic, [plot.inferCNV() and [giDensityPlot() to plot the results.

geneLength

*Average length of human and mouse known genes*

Description

A dataset containing the average length for known mouse and human genes

Usage

geneLength

Format

Vector of integers indicating the average length in bp for each gene, indicated with EntrezIDs as name argument. To access this data use:

- data(hg38) Human
- data(mm10) Mouse

genePosition

*Chromosomal coordinate of human and mouse known genes*

Description

A dataset containing the chromosomal coordinate for known human and mouse genes

Usage

genePosition

Format

data.frame with 2 columns: Chromosome and Coordinate. To access this data use:

- data(hg38) Human
- data(mm10) Mouse
generateChromosomeGeneSet

Topological gene sets

Description

This function generates a list of sets of k genes encoded by neighbor loci

Usage

generateChromosomeGeneSet(species = c("human", "mouse"), k = 100, skip = 25)

Arguments

- species: Character string indicating the species, either human or mouse
- k: Integer indicating the number of genes per set
- skip: Integer indicating the displacement of the window for selecting the k genes

Value

List of topologically-close gene sets

Examples

chrom_set <- generateChromosomeGeneSet('human')
length(chrom_set)
chrom_set[seq_len(2)]

genomicInstabilityScore

Genomic Instability Analysis

Description

This function computes the genomic instability for an object of class inferCNV

Usage

genomicInstabilityScore(cnv, likelihood = FALSE)

Arguments

- cnv: Object of class inferCNV generated by inferCNV() function
- likelihood: Logical, whether the genomic instability likelihood should be estimated
Value

Object of class inferCNV with updated slots for gis and gisnull

See Also

[inferCNV()] to infer the enrichment of loci-blocks in the gene expression data.

Examples

```r
eh <- ExperimentHub::ExperimentHub()
dset <- eh["EH5419"]
tpm_matrix <- SummarizedExperiment::assays(dset)$TPM
set.seed(1)
tpm_matrix <- tpm_matrix[, sample(ncol(tpm_matrix), 500)]
cnv <- inferCNV(tpm_matrix)
cnv <- genomicInstabilityScore(cnv)
plot(density(cnv$gis))
```

---

Description

This function plot the genomic instability distribution, gaussian fits and null distribution if available

Usage

```r
giDensityPlot(inferCNV, legend = c("topleft", "top", "topright", "none"), ...)
```

Arguments

- `inferCNV`: Object of class inferCNV
- `legend`: Character string indicating the location of the legend. none to not include it
- `...`: Additional parameters for plot()

Value

None, a figure is created in the default output device

See Also

[giLikelihood()] to estimate the relative likelihood, [genomicInstabilityScore()] to estimate the genomic instability score for each cell in the dataset, and [inferCNV()] to infer the enrichment of loci-blocks in the gene expression data.
Examples

```r
eh <- ExperimentHub::ExperimentHub()
dset <- eh["EH5419"]

TPM <- SummarizedExperiment::assays(dset)$TPM

set.seed(1)

tpm_matrix <- tpm_matrix[, sample(ncol(tpm_matrix), 500)]
cnv <- inferCNV(tpm_matrix)
cnv <- genomicInstabilityScore(cnv)
cnv <- giLikelihood(cnv, distros=c(3, 3), tumor=2:3)
giDensityPlot(cnv)
```

---

**giLikelihood**  
*Genomic instability likelihood*

### Description
This function computes the genomic instability likelihood

### Usage

```r
giLikelihood(  
inferCNV,  
recompute = TRUE,  
distros = c(1, 3),  
tumor = NULL,  
normal = NULL  
)
```

### Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td><code>inferCNV</code></td>
<td>InferCNV-class object</td>
</tr>
<tr>
<td><code>recompute</code></td>
<td>Logical, whether the model fits should be re-computed</td>
</tr>
<tr>
<td><code>distros</code></td>
<td>Vector of 2 integers indicating the minimum and maximum number of Gaussian</td>
</tr>
<tr>
<td></td>
<td>models to fit</td>
</tr>
<tr>
<td><code>tumor</code></td>
<td>Optional vector of integers indicating the Gaussians considered as tumors</td>
</tr>
<tr>
<td><code>normal</code></td>
<td>Optional vector of integers indicating the Gaussians considered as normal.</td>
</tr>
<tr>
<td></td>
<td>This is only useful when no null model has been provided for the analysis</td>
</tr>
</tbody>
</table>

### Value
Updated inferCNV-class object with gi_likelihood slot

### See Also

[genomicInstabilityScore()] to estimate the genomic instability score for each cell in the dataset, and [inferCNV()] to infer the enrichment of loci-blocks in the gene expression data.
inferCNV

Inference of CNV from expression data

Description

This function estimates the CNV score based on expression data.

Usage

inferCNV(
  expmat,
  nullmat = NULL,
  species = c("human", "mouse"),
  k = 100,
  skip = 25,
  min_geneset = 10,
  verbose = TRUE
)

Arguments

expmat       Matrix of gene expression profiles or signatures with genes *(entrezID)* in rows and samples in columns
nullmat      Optional matrix with same number of rows as expmat to be used as null model
species      Character string indicating the species, either human or mouse
k            Integer indicating the number of genes per set
skip         Integer indicating the displacement of the window for selecting the k genes
min_geneset  Integer indicating the minimum size for the genesets
verbose      Logical, whether progress should be reported

Value

Object of class inferCNV, which is a list containing matrix of nes, and parameters (param), including species, window (k) and skip

Examples

eh <- ExperimentHub::ExperimentHub()
dset <- eh[["EH5419"]]

tpm_matrix <- SummarizedExperiment::assays(dset)$TPM

set.seed(1)

tpm_matrix <- tpm_matrix[, sample(ncol(tpm_matrix), 500)]

cnv <- inferCNV(tpm_matrix)

cnv <- genomicInstabilityScore(cnv)

cnv <- giLikelihood(cnv, distros=c(3, 3), tumor=2:3)

print(cnv$gi_fit)

plot(density(cnv$gi_likelihood, from=0, to=1))
Examples

```r
eh <- ExperimentHub::ExperimentHub()
dset <- eh[["EH5419"]]
tpm_matrix <- SummarizedExperiment::assays(dset)$TPM
set.seed(1)
tpm_matrix <- tpm_matrix[, sample(ncol(tpm_matrix), 500)]
cnv <- inferCNV(tpm_matrix)
class(cnv)
names(cnv)
cnv$nes[1:5, 1:3]
```

plot.inferCNV

Plot chromosome map

Description

This function generates a chromosomes map plot for the inferred CNVs

Usage

```r
## S3 method for class 'inferCNV'
plot(x, output = NULL, threshold = 0.2, gamma = 1.5, resolution = 150, ...)
```

Arguments

- `x` Object of class inferCNV
- `output` Optional output PDF file name (with extension)
- `threshold` Likelihood threshold for identifying genomically inestable cells/samples, 0 disables this filter
- `gamma` Number indicating the gamma transformation for the colors
- `resolution` Integer indicating the ppi for the png and jpg output files
- `...` Additional parameters for plot

Value

Nothing, a plot is generated in the default output devise

See Also

- [giLikelihood()] to estimate the relative likelihood, [genomicInstabilityScore()] to estimate the genomic instability score for each cell in the dataset, and [inferCNV()] to infer the enrichment of loci-blocks in the gene expression data.
Examples

```r
eh <- ExperimentHub::ExperimentHub()
dset <- eh[["EH5419"]]
 TPM_matrix <- SummarizedExperiment::assays(dset)$TPM
 set.seed(1)
 TPM_matrix <- TPM_matrix[, sample(ncol(TPM_matrix), 500)]
cnv <- inferCNV(TPM_matrix)
cnv <- genomicInstabilityScore(cnv)
cnv <- giLikelihood(cnv, distros=c(3, 3), tumor=2:3)
plot(cnv, output='test.png')```

```
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