Package ‘Statial’

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Type Package

Title A package to identify changes in cell state relative to spatial associations

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Imports BiocParallel, spatstat.geom, concaveman, data.table, spatstat.explore, dplyr, tidyr, SingleCellExperiment, tibble, stringr, tidyselect, ggplot2, methods, stats, SummarizedExperiment, S4Vectors, plotly, purrr, ranger, magrittr, limma, SpatialExperiment

Suggests BiocStyle, knitr, testthat (>= 3.0.0), ClassifyR, spicyR, ggsurvfit, lisaClust, survival

Description Statial is a suite of functions for identifying changes in cell state. The functionality provided by Statial provides robust quantification of cell type localisation which are invariant to changes in tissue structure. In addition to this Statial uncovers changes in marker expression associated with varying levels of localisation. These features can be used to explore how the structure and function of different cell types may be altered by the agents they are surrounded with.

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RoxygenNote 7.2.3

Config/testthat/edition 3

URL https://sydneybiox.github.io/Statial
    https://github.com/SydneyBioX/Statial/issues

BugReports https://github.com/SydneyBioX/Statial/issues

git_url https://git.bioconductor.org/packages/Statial
calcContamination

Description

Calculate the level of marker contamination of each cell

Calculates contamination scores using a random forest classification
Usage

calcContamination(
  cells, 
  markers = NULL, 
  num.trees = 100, 
  verbose = FALSE, 
  missingReplacement = 0, 
  assay = "intensities", 
  cellType = "cellType", 
  redDimName = "contaminations"
)

Arguments

cells A SingleCellExperiment or SpatialExperiment with a cellType column as well as marker intensity information corresponding to each cell.
markers A vector of markers that proxy a cell’s state. If NULL, all markers will be used.
num.trees Number of trees to be used in the random forest classifier
verbose A logical indicating whether information about the final random forest model should be outputted.
missingReplacement A default value to replace missing marker intensities for classification.
assay The assay in the SingleCellExperiment object that contains the desired marker expressions.
cellType The name of the column in colData that stores the cell types.
redDimName The redDimName to store the output in the sce.

Examples

data("kerenSCE")

singleCellDataDistancesContam <- calcContamination(
  kerenSCE
)

calcStateChanges

First layer wrapper function to build linear models measuring state changes

Description

Builds linear models measuring marker based state changes in a cell type based on the proximity or abundance of another cell type. The function provides the option to build robust and mixed linear model variants.
calcStateChanges

Usage

calcStateChanges(
cells,
  marker = NULL,
  from = NULL,
  to = NULL,
  image = NULL,
  type = "distances",
  assay = 1,
  cellType = "cellType",
  imageID = "imageID",
  contamination = NULL,
  minCells = 20,
  verbose = FALSE,
  timeout = 10,
  nCores = 1
)

Arguments

cells A dataframe with a imageID, cellType, and marker intensity column along with covariates (e.g. distance or abundance of the nearest cell type) to model cell state changes

marker A vector of markers that proxy a cell’s state. If NULL, all markers will be used.

from A vector of cell types to use as the primary cells. If NULL, all cell types will be used.

to A vector of cell types to use as the interacting cells. If NULL, all cell types will be used.

image A vector of images to filter to. If null all images will be used.

type What type of state change. This value should be in reduced dimensions.

assay The assay in the SingleCellExperiment object that contains the marker expressions.

cellType The column in colData that stores the cell types.

imageID The column in colData that stores the image ids.

contamination If TRUE, use the contamination scores that have previously been calculate. Otherwise a name of which reduced dimension contains the scores.

minCells The minimum number of cells required to fit a model.

verbose A logical indicating if messages should be printed

timeout A maximum time allowed to build each model. Setting this may be important when building rlm mixed linear models

nCores Number of cores for parallel processing
**distanceCalculator**

*Calculate pairwise distance between cell types*

**Description**

Calculates the euclidean distance from each cell to the nearest cell of each type for a single image.

**Usage**

distanceCalculator(data, maxDist = 200, distFun = "min")

**Arguments**

- `data`: the single cell data of interest.
- `maxDist`: Maximum distance between pairs of points to be counted as close pairs.
- `distFun`: How to merge duplicate entries.

---

**getAbundances**

*Wrapper to calculate imhomogenous K function between a cell and surrounding types on each image*

**Description**

Calculate the imhomogenous K function (a measure of cell type abundance) for each cell to other cell types.
Usage

getAbundances(
  cells,
  r = 200,
  distFun = "abundance",
  redDimName = "abundances",
  cellType = "cellType",
  imageID = "imageID",
  spatialCoords = c("x", "y"),
  nCores = 1
)

Arguments

cells A dataframe with a cellType column as well as x and y spatial coordinates. The dataframe must contain a imageID column and cellID (unique cell identifier's) column as well

r Radius to include in that calculation of pairwise abundance (K-function) between cells (can be a numeric or vector of radii)
distFun What distance function to use.
redDimName Name of the reduced dimension to store in sce.
cellType The name of the column in colData that stores the cell types.
imageID The name of the column in colData that Stores the image ids.
spatialCoords The names of the columns in colData that store the spatial coordinates.
nCores Number of cores for parallel processing

Examples

library(dplyr)
data("kerenSCE")

singleCellDataCounts <- getAbundances(kerenSCE,
  r = 200,
)

getDistances Wrapper to calculate pairwise distance between cell types by image

Description

Calculates the euclidean distance from each cell to the nearest cell of each type
Usage

generateDistances(
    cells,
    maxDist = NULL,
    imageID = "imageID",
    spatialCoords = c("x", "y"),
    cellType = "cellType",
    redDimName = "distances",
    distFun = "min",
    nCores = 1
)

Arguments

cells A dataframe with a cellType column as well as x and y spatial coordinates. The
dataframe must contain a imageID column and cellID (unique cell identifier's) column as well
maxDist The maximum distance considered.
imageID The name of the colData column that stores in the image ID.
spatialCoords The columns that store the spatial coordinates.
cellType The name of the colData column that stores the cell types.
redDimName The name of the reduced dimension to store the distances in.
distFun What distance function to use. Can be min or abundance.
nCores Number of cores for parallel processing.

Examples

data("kerenSCE")

kerenSCE <- generateDistances(kerenSCE,
    maxDist = 200
)

description

Extract the average expression for all markers for each cell type in
each region defined by lisaClust

description

Takes a SingleCellExperiment and outputs a dataframe in a convenient format for cross validation
Usage

getMarkerMeans(
  data,
  imageID = NULL,
  cellType = NULL,
  region = NULL,
  markers = NULL,
  assay = 1,
  replaceVal = 0
)

Arguments

data A SingleCellExperiment object with intensities data in the assays slot and regions information in colData generated by lisaClust.
imageID The colData column that stores the image IDs.
cellType The colData column that store the cell types.
region The colData column that stores the regions.
markers A string vector of markers that proxy a cell’s state. If NULL, all markers will be used.
assay Which assay do you want to use for the expression data.
replaceVal A value to replace missing values with.

Examples

data(kerenSCE)

kerenSCE <- kerenSCE[,kerenSCE$imageID %in% c("5","6")]
regionSCE <- lisaClust::lisaClust(kerenSCE, k = 5)
lisaClustOutput <- getMarkerMeans(regionSCE)

---

isKontextual Test whether an object is a kontextualResult

Description

Test whether an object is a kontextualResult

Usage

isKontextual(kontextualResult)
**kerenKontextual**

**Arguments**

- kontextualResult
  - a object to test

**Examples**

```r
data = data.frame()
if(!isKontextual(data)) print("Not a kontextualResult")
```

---

**kernenKontextual**

*Kontextual results from kerenSCE*

**Description**

This is a kontextual results data.frame created using Kontextual on the kerenSCE dataset.

**Usage**

```r
data(kernenKontextual)
```

**Format**

- kernenKontextual a kontextual results object.

---

**kernenSCE**

*MIBI-TOF Breast cancer intensities*

**Description**

This is a single MIBI-TOF data of breast cancer from patient 6 of the Keren et al 2018 dataset.

**Usage**

```r
data(kernenSCE)
```

**Format**

- kernenSCE a SingleCellExperiment object

**References**

kontextCurve

Evaluation of Kontextual over a range of radii.

Description

This function obtains 'Kondtional' values over a range of radii, standard deviations for each value can be obtained using permutation for significance testing. To obtain estimates for standard deviations specify 'se = TRUE'.

Usage

kontextCurve(
  cells,
  from,
  to,
  parent,
  image = NULL,
  rs = seq(10, 100, 10),
  inhom = FALSE,
  edge = FALSE,
  se = FALSE,
  nSim = 20,
  cores = 1,
  imageID = "imageID",
  cellType = "cellType",
  ...
)

Arguments

cells  A single image from a SingleCellExperiment object
from   The first cell type to be evaluated in the pairwise relationship.
to     The second cell type to be evaluated in the pairwise relationship.
parent The parent population of the from cell type (must include from cell type).
image  A vector of images to subset the results to. If NULL we default to all images.
rs      A vector of radii to evaluate kontextual over.
inom    A logical value indicating whether to perform an inhomogeneous L function.
edge    A logical value indicating whether to perform edge correction.
se      A logical value to indicate if the standard deviation of kontextual should be calculated to construct error bars.
nSim    Number of randomisations to perform using relabelKontextual, which will be used to calculated the SE.
cores   Number of cores for parallel processing.
imageID The column in colData that stores the image ids.
The column in colData that stores the cell types.

Any arguments passed into Kontextual.

Value

A data frame of original L values and Kontextual values evaluated over a range of radii.

Examples

data("kerenSCE")

kerenImage6 = kerenSCE[, kerenSCE$imageID == "6"]

rsDf <- kontextCurve(
cells = kerenSCE,
from = "CD4_Cell",
to = "Keratin_Tumour",
parent = c("CD4_Cell", "Macrophages"),
rs = seq(10, 510, 100),
cores = 2
)

kontextPlot(rsDf)

Description

This function takes outputs from rsCurve and plots them in ggplot. If standard deviation is estimated in rsCurve, then confidence intervals will be constructed based on the standard deviation. If the confidence interval overlaps with 0, then the relationship is insignificant for that radius.

Usage

kontextPlot(rsDf)

Arguments

rsDf A data frame from kontextCurve.

Value

A ggplotly object showing the original and kontextual L function values over a range of radii.
Examples

```r
data("kerenSCE")

kerenImage6 = kerenSCE[, kerenSCE$imageID == "6"]

rsDf <- kontextCurve(
  cells = kerenImage6,
  from = "p53",
  to = "Immune",
  parent = c("p53", "Keratin+Tumour"),
  rs = seq(10, 510, 100),
  cores = 2
)

kontextPlot(rsDf)
```

**Description**

Kontextual identifies the relationship between two cell types which are conditional on the spatial behaviour of a 3rd cell population, for a particular radius (r).

**Usage**

```r
Kontextual(
  cells,
  r,
  parentDf = NULL,
  from = NULL,
  to = NULL,
  parent = NULL,
  image = NULL,
  inhom = FALSE,
  edgeCorrect = TRUE,
  window = "convex",
  window.length = NA,
  weightQuantile = 0.8,
  includeZeroCells = TRUE,
  includeOriginal = TRUE,
  spatialCoords = c("x", "y"),
  cellType = "cellType",
  imageID = "imageID",
  cores = 1
)
```
**Arguments**

- **cells**: A `SingleCellExperiment`, `SpatialExperiment` or a list of data.frames containing columns specifying the imageID, cellType, and x and y spatial coordinates.
- **r**: Radii to evaluated pairwise relationships between from and to cells.
- **parentDf**: A data frame from `parentCombinations`
- **from**: The first cell type to be evaluated in the pairwise relationship.
- **to**: The second cell type to be evaluated in the pairwise relationship.
- **parent**: The parent population of the from cell type (must include from cell type).
- **image**: A vector of images to subset the results to. If NULL we default to all images.
- **inhom**: A logical value indicating whether to account for inhomogeneity.
- **edgeCorrect**: A logical value indicating whether to perform edge correction.
- **window**: Type of window for data, either 'square', 'convex' or 'concave', passed into `makeWindow`.
- **window.length**: A tuning parameter for controlling the level of concavity when estimating concave windows. Passed into `makeWindow`.
- **weightQuantile**: A decimal value indicating what quantile of parent density used to weight the 'from' cells.
- **includeZeroCells**: A logical value indicating whether to include cells with zero counts in the pairwise association calculation.
- **includeOriginal**: A logical value to return the original L function values along with the kontextual values.
- **spatialCoords**: The columns which contain the x and y spatial coordinates.
- **cellType**: The column which contains the cell types.
- **imageID**: The column which contains image identifiers.
- **cores**: Number of cores for parallel processing.

**Value**

A `kontextualResult` object

**Examples**

```r
# Load data
data("kerenSCE")

CD4_Kontextual <- Kontextual(
cells = kerenSCE,
r = 50,
from = "Macrophages",
to = "Keratin_Tumour",
parent = c("Macrophages", "CD4_Cell"),
image = "6"
)```
**makeWindow**

*Creates a window for a PPP object*

**Description**

This function creates a window for a `spatstat::ppp` object, the type of window can be specified using the `window` argument.

**Usage**

```r
makeWindow(data, window = "square", window.length = NULL)
```

**Arguments**

- `data` A single image data frame from a SingleCellExperiment object or PPP object.
- `window` The shape of window around the regions, can be ‘square’, ‘convex’ or ‘concave’
- `window.length` A tuning parameter for controlling the level of concavity when estimating concave windows.

**Value**

Creates an `owin` class, representing the observation window for the image.

**Examples**

```r
data <- data.frame(x = rnorm(10), y = rnorm(10))
ow <- makeWindow(data, window = "square")

spatstat.geom::ppp(x = data$x, y = data$y, window = ow)
```
**parentCombinations**

Create all combinations of cell type relationships from a list of parents

**Description**

This function takes in named vectors of all the parent populations in the dataset, and creates a data frame containing all pairwise cell relationships, this data frame can be inputed into the ‘parentDf’ argument in ‘Kontextual’.

**Usage**

parentCombinations(all, ...)

**Arguments**

- **all**: A list of all the ‘to’ cell types Kontextual is evaluated over
- **...**: Vectors of each parent population

**Value**

A data frame containing all pairwise cell relationships and their corresponding parent

**Examples**

```r
tcells <- c("CD4", "CD8")
tissue <- c("epithelial", "stromal")
allCells <- c("tumour", tissue, tcells)
parentCombinations(all = allCells, tcells, tissue)
```

---

**plotStateChanges**

Visualise Cell-Cell Marker Relationships

**Description**

Helper functions to visualise OLS model fits for image based state models

**Usage**

plotStateChanges(
  cells,
  image,
  from,          
  to,
  marker,
```
type = "distances",
assay = 1,
cellType = "cellType",
imageID = "imageID",
spatialCoords = c("x", "y"),
size = 1,
shape = 19,
interactive = FALSE,
plotModelFit = FALSE,
method = "lm"
)

**Arguments**

- **cells**: A SingleCellExperiment that has had distances already calculated.
- **image**: An image to subset to.
- **from**: A character indicating the name of the cell type (from the cellType column) whose cell state is being investigated in
- **to**: A character indicating the name of the cell type (from the cellType column) who may be influencing the cell state of another cell type
- **marker**: The marker of interest.
- **type**: The name of the reduced dimension to use for the x-axis.
- **assay**: Name of the assay that stores the marker expression.
- **cellType**: The name of the column in colData that stores the cell types.
- **imageID**: The name of the column in colData that stores the image ids.
- **spatialCoords**: The names of the columns in colData that store the spatial coordinates.
- **size**: Aesthetic numerical variable determining the size of the displayed cells
- **shape**: Aesthetic variable determining the shape grouping of the displayed cells
- **interactive**: Logical indicating if the output visualisation should be interactive (plotly)
- **plotModelFit**: Logical indicating if fitted values should be plotted or actual intensities for marker specified. The default is to plot actual intensities
- **method**: The method to build the model with. Currently the only option is "lm". However, capabilities may be expanded in the future

**Details**

- **image**,

**Examples**

```r
library(dplyr)
data("kerenSCE")

kerenSCE <- getDistances(kerenSCE)
```
p <- plotStateChanges(
  cells = kerenSCE,
  type = "distances",
  image = "6",
  from = "Keratin_Tumour",
  to = "Macrophages",
  marker = "p53",
  size = 1,
  shape = 19,
  interactive = FALSE,
  plotModelFit = FALSE,
  method = "lm"
)

p

prepMatrix

Convert Kontextual or state changes result to a matrix for classification

Description

Convert Kontextual or state changes result to a matrix for classification

Usage

prepMatrix(result, replaceVal = 0, column = NULL, test = NULL)

Arguments

result a kontextual or state changes result data.frame.
replaceVal value which NAs are replaced with.
column The column which contains the scores that you want to select.
test A column containing which will be the column names of the expanded matrix.

Examples

data("kerenSCE")

CD4_Kontextual <- Kontextual(
  cells = kerenSCE,
  r = 50,
  from = "Macrophages",
  to = "Keratin_Tumour",
  parent = c("Macrophages", "CD4_Cell"),
  image = "6"
)
relabellKontextual

Cell permutation for Kontextual

Description

Function which randomises specified cells in an image and calculates the ‘Kontextual’ value. This can be used to estimate the null distribution, of the parent cell population for significance testing. This function relabels all specified cells within a single image, to estimate the null distribution of cell population specified.

Usage

relabellKontextual(
  cells,  
nSim = 1,  
r,  
from,  
to,  
parent,  
image = NULL,  
returnImages = FALSE,  
inhom = TRUE,  
edge = FALSE,  
cores = 1,  
spatialCoords = c("x", "y"),  
cellType = "cellType",  
imageID = "imageID",  
...  
)

relabel(image, labels = NULL)

Arguments

cells A single image data frame from a SingleCellExperiment object

nSim Number of randomisations which will be calculated.

r Radius to evaluated pairwise relationships between from and to cells.

from The first cell type to be evaluated in the pairwise relationship.

to The second cell type to be evaluated in the pairwise relationship.

parent The parent population of the from cell type (must include from cell type).

image A single image from a Single Cell Experiment object.
relabelKontextual

returnImages  A logical value to indicate whether the function should return the randomised images along with the Kontextual values.
inhom  A logical value indicating whether to account for inhomogeneity.
edge  A logical value indicating whether to perform edge correction.
cores  Number of cores for parallel processing.
spatialCoords  A character vector containing the names of the two spatial dimensions in the data. Defaults to c("x", "y").
cellType  The name of the cell type field in the data. Defaults to "cellType".
imageID  The name of the image ID field in the data. Defaults to "imageID".
...  Any arguments passed into Kontextual
labels  A vector of CellTypes labels to be permuted. If NULL, all cell labels will be randomised.

Value

A data frame containing Kontextual value for each randomised image. If `returnImages = TRUE` function will return a list with Kontextual values and the randomised images.
A data frame containing all pairwise cell relationships and their corresponding parent

Examples

data("kerenSCE")

kerenImage6 = kerenSCE[, kerenSCE$imageID == "6"]

relabelResult <- relabelKontextual(
  cells = kerenImage6,
  nSim = 5,
  r = 250,
  from = "CD4_Cell",
  to = "Keratin_Tumour",
  parent = c("CD4_Cell", "Macrophages"),
  cores = 2
)

data("kerenSCE")

kerenImage6 = kerenSCE[, kerenSCE$imageID == "6"]

kerenImage6 <- kerenImage6 |> SingleCellExperiment::colData() |> data.frame()

# Permute CD8 T cells and T cell labels in the image
relabeledImage <- relabel(kerenImage6, labels = c("p53", "Keratin+Tumour"))
plot(relabeledImage)
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