

# Package ‘smoppix’

September 19, 2025

**Type** Package

**Title** Analyze Single Molecule Spatial Omics Data Using the Probabilistic Index

**Version** 1.1.6

**Description** Test for univariate and bivariate spatial patterns in spatial omics data with single-molecule resolution. The tests implemented allow for analysis of nested designs and are automatically calibrated to different biological specimens. Tests for aggregation, colocalization, gradients and vicinity to cell edge or centroid are provided.

**License** GPL-2

**Encoding** UTF-8

**Imports** spatstat.geom(>= 3.2.0), spatstat.random, methods, BiocParallel, SummarizedExperiment, SpatialExperiment, scam, Rdpack, stats, utils, extra(>= 1.0.11), spatstat.model, openxlsx

**Suggests** testthat, rmarkdown, knitr, DropletUtils, polyCub, RImageJROI, sp, ape, htmltools, funkycells, glmnet, doParallel

**RdMacros** Rdpack

**RoxygenNote** 7.3.2

**biocViews** Transcriptomics, Spatial, SingleCell

**Depends** R (>= 4.5.0)

**VignetteBuilder** knitr

**BugReports** <https://github.com/sthawinke/smoppix/issues>

**URL** <https://github.com/sthawinke/smoppix>

**LinkingTo** Rcpp

**git\_url** <https://git.bioconductor.org/packages/smoppix>

**git\_branch** devel

**git\_last\_commit** 37202d7

**git\_last\_commit\_date** 2025-09-12

**Repository** Bioconductor 3.22

**Date/Publication** 2025-09-18

**Author** Stijn Hawinkel [cre, aut] (ORCID:  
<<https://orcid.org/0000-0002-4501-5180>>)

**Maintainer** Stijn Hawinkel <[stijn.hawinkel@psb.ugent.be](mailto:stijn.hawinkel@psb.ugent.be)>

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---

|                |                                                                             |
|----------------|-----------------------------------------------------------------------------|
| <i>addCell</i> | <i>Add cell boundaries and event-wise cell identifiers to a hyperframe.</i> |
|----------------|-----------------------------------------------------------------------------|

---

## Description

Add the list of the cells and their centroids in the hyperframe, check in which cell each event lies and add a cell marker.

## Usage

```
addCell(
  hypFrame,
  owins,
  cellTypes = NULL,
  findOverlappingOwins = FALSE,
  warnOut = TRUE,
  coords = c("x", "y"),
  verbose = TRUE,
  addCellMarkers = TRUE,
  overwriteCells = FALSE,
  ...
)
```

## Arguments

|                             |                                                                                                                                                                                                                                      |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>hypFrame</i>             | A hyperframe                                                                                                                                                                                                                         |
| <i>owins</i>                | A list containing a list of owins per point pattern. The length of the list must match the length of the hyperframe, and the names must match. Also lists of geojson objects, coordinate matrices or rois are accepted, see details. |
| <i>cellTypes</i>            | A dataframe of cell types and other cell-associated covariates. If supplied, it must contain a variable 'cell' that is matched with the names of the owins                                                                           |
| <i>findOverlappingOwins</i> | a boolean, should windows be checked for overlap? Can be computationally intensive.                                                                                                                                                  |
| <i>warnOut</i>              | a boolean, should warning be issued when points are not contained in window?                                                                                                                                                         |
| <i>coords</i>               | The names of the coordinates, if the windows are given as sets of coordinates.                                                                                                                                                       |
| <i>verbose</i>              | A boolean, should verbose output be printed?                                                                                                                                                                                         |
| <i>addCellMarkers</i>       | A boolean, should cell identities be added? Set this to FALSE if cell identifiers are already present in the data, and you only want to add windows and centroids.                                                                   |
| <i>overwriteCells</i>       | A boolean, should cells already present in hyperframe be overwritten?                                                                                                                                                                |
| <i>...</i>                  | Further arguments passed onto <a href="#">convertToOwins</a>                                                                                                                                                                         |

## Details

First the different cells are checked for overlap per point pattern if 'findOverlappingOwins' is TRUE. If no overlap is found, each event is assigned the cell that it falls into. Events not belonging to any cell will trigger a warning and be assigned 'NA'. Cell types and other variables are added to the marks if applicable. This function employs multithreading through the BiocParallel package. If this leads to excessive memory usage and crashes, try serial processing by setting register(SerialParam()). Different formats of windows are allowed, if the corresponding packages are installed. A dataframe of coordinates or a list of spatstat.geom owins is always allowed, as the necessary packages are required by smoppix. A 'SpatialPolygonsDataFrame' object is allowed if the 'polycub' package is installed, and a list of 'ijroi' object or a single 'ijzip' object if the 'RImageJROI' package is installed.

## Value

The hyperframe with cell labels added in the marks of the point patterns

## Note

By default, overlap between windows is not checked. Events are assigned to the first window they fall in. If you are not sure of the quality of the segmentation, do check your input or set checkOverlap to TRUE, even when this make take time.

## See Also

[buildHyperFrame](#), [convertToOwins](#)

## Examples

```
library(spatstat.random)
set.seed(54321)
n <- 1e3 # number of molecules
ng <- 25 # number of genes
nfov <- 3 # Number of fields of view
conditions <- 3
# sample xy-coordinates in [0, 1]
x <- runif(n)
y <- runif(n)
# assign each molecule to some gene-cell pair
gs <- paste0("gene", seq(ng))
gene <- sample(gs, n, TRUE)
fov <- sample(nfov, n, TRUE)
condition <- sample(conditions, n, TRUE)
# construct data.frame of molecule coordinates
df <- data.frame(gene, x, y, fov, "condition" = condition)
# A list of point patterns
listPPP <- tapply(seq(nrow(df)), df$fov, function(i) {
  ppp(x = df$x[i], y = df$y[i], marks = df[i, "gene", drop = FALSE])
}, simplify = FALSE)
# Regions of interest (roi): Diamond in the center plus four triangles
w1 <- owin(poly = list(x = c(0, .5, 1, .5), y = c(.5, 0, .5, 1)))
w2 <- owin(poly = list(x = c(0, 0, .5), y = c(.5, 0, 0)))
w3 <- owin(poly = list(x = c(0, 0, .5), y = c(1, 0.5, 1)))
w4 <- owin(poly = list(x = c(1, 1, .5), y = c(0.5, 1, 1)))
w5 <- owin(poly = list(x = c(1, 1, .5), y = c(0, 0.5, 0)))
hypFrame <- buildHyperFrame(df,
```

```

    coordVars = c("x", "y"),
    imageVars = c("condition", "fov")
  )
  nDesignFactors <- length(unique(hypFrame$image))
  wList <- lapply(seq_len(nDesignFactors), function(x) {
    list("w1" = w1, "w2" = w2, "w3" = w3, "w4" = w4, "w5" = w5)
  })
  names(wList) <- rownames(hypFrame) # Matching names is necessary
  hypFrame2 <- addCell(hypFrame, wList)

```

---

addDesign

*Add design variables to hyperframe*


---

### Description

Add design variables to hyperframe

### Usage

```
addDesign(hypFrame, desMat, designVec)
```

### Arguments

|           |                   |
|-----------|-------------------|
| hypFrame  | The hyperframe    |
| desMat    | The design matrix |
| designVec | The design vector |

### Value

The hyperframe with design variables added

---

addNuclei

*Add nuclei to a hyperframe*


---

### Description

Add the nuclei identifiers to a hyperframe already containing cells.

### Usage

```

addNuclei(
  hypFrame,
  nucleiList,
  checkSubset = TRUE,
  verbose = TRUE,
  coords = c("x", "y"),
  overwriteNuclei = FALSE,
  ...
)

```

## Arguments

|                 |                                                                                                                                                                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| hypFrame        | A hyperframe                                                                                                                                                                                                                                       |
| nucleiList      | A list containing a list of owin per point pattern. The length of the list must match the length of the hyperframe, and the names must match. Also lists of geojson objects, coordinate matrices or rois are accepted, see <a href="#">addCell</a> |
| checkSubset     | A boolean, should be checked whether nuclei are encompassed by cells?                                                                                                                                                                              |
| verbose         | A boolean, should verbose output be printed?                                                                                                                                                                                                       |
| coords          | The names of the coordinates, if the nuclei are given as sets of coordinates.                                                                                                                                                                      |
| overwriteNuclei | A boolean, should existing nuclei be replaced?                                                                                                                                                                                                     |
| ...             | Further arguments passed onto <a href="#">convertToOwins</a>                                                                                                                                                                                       |

## Details

The nuclei names must match the cell names already present, all other nuclei are dropped. A warning is issued when nuclei are not encompassed by their cell.

## Value

The hyperframe with nuclei added as entry

## See Also

[addCell](#), [convertToOwins](#)

## Examples

```
library(spatstat.random)
set.seed(54321)
n <- 1e3 # number of molecules
ng <- 25 # number of genes
nfov <- 3 # Number of fields of view
conditions <- 3
# sample xy-coordinates in [0, 1]
x <- runif(n)
y <- runif(n)
# assign each molecule to some gene-cell pair
gs <- paste0("gene", seq(ng))
gene <- sample(gs, n, TRUE)
fov <- sample(nfov, n, TRUE)
condition <- sample(conditions, n, TRUE)
# construct data.frame of molecule coordinates
df <- data.frame(gene, x, y, fov, "condition" = condition)
# A list of point patterns
listPPP <- tapply(seq(nrow(df)), df$fov, function(i) {
  ppp(x = df$x[i], y = df$y[i], marks = df[i, "gene", drop = FALSE])
}, simplify = FALSE)
# Regions of interest (roi): Diamond in the center plus four triangles
w1 <- owin(poly = list(x = c(0, .5, 1, .5), y = c(.5, 0, .5, 1)))
w2 <- owin(poly = list(x = c(0, 0, .5), y = c(.5, 0, 0)))
w3 <- owin(poly = list(x = c(0, 0, .5), y = c(1, 0.5, 1)))
w4 <- owin(poly = list(x = c(1, 1, .5), y = c(0.5, 1, 1)))
w5 <- owin(poly = list(x = c(1, 1, .5), y = c(0, 0.5, 0)))
```

```

hypFrame <- buildHyperFrame(df,
  coordVars = c("x", "y"),
  imageVars = c("condition", "fov")
)
nDesignFactors <- length(unique(hypFrame$image))
wList <- lapply(seq_len(nDesignFactors), function(x) {
  list("w1" = w1, "w2" = w2, "w3" = w3, "w4" = w4, "w5" = w5)
})
names(wList) <- rownames(hypFrame) # Matching names is necessary
hypFrame2 <- addCell(hypFrame, wList)
# The nuclei
n1 <- owin(poly = list(x = c(0.2, .4, 0.8, .4), y = c(.4, .2, .4, .8)))
n2 <- owin(poly = list(x = c(0.1, 0.1, .4), y = c(.4, .1, .1)))
n3 <- owin(poly = list(x = c(0.1, 0.1, .4), y = c(1, .75, 1)))
n4 <- owin(poly = list(x = c(1, 1, .6), y = c(.7, .9, .9)))
n5 <- owin(poly = list(x = c(.95, .95, .7), y = c(.1, .4, .1)))
nList <- lapply(seq_len(nDesignFactors), function(x) {
  list("w1" = n1, "w2" = n2, "w3" = n3, "w4" = n4, "w5" = n5)
})
names(nList) <- rownames(hypFrame) # Matching names is necessary
hypFrame3 <- addNuclei(hypFrame2, nList)

```

addTabObs

*Add tables with gene counts to the hyperframe, presort by gene and x-ccordinate and add design varibales*

## Description

Add tables with gene counts to the hyperframe, presort by gene and x-ccordinate and add design varibales

## Usage

```
addTabObs(hypFrame)
```

## Arguments

hypFrame      The hyperframe

## Value

The hyperframe with tabObs added

---

|                |                                                                            |
|----------------|----------------------------------------------------------------------------|
| buildDataFrame | <i>Extract a data frame for a certain gene and PI from a fitted object</i> |
|----------------|----------------------------------------------------------------------------|

---

## Description

Based on a fitted object, a dataframe with results for a certain feature and PI is built, e.g. in preparation for linear modelling.

## Usage

```
buildDataFrame(
  obj,
  gene,
  pi = c("nn", "nnPair", "edge", "centroid", "nnCell", "nnPairCell"),
  piMat,
  pppDf,
  prepMat,
  prepTab,
  prepCells
)
```

## Arguments

|                             |                                                                                                                                                                                               |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| obj                         | A results object. For distances to fixed objects, the result of a call to <a href="#">estPis</a> ; for nearest neighbour distances, the result of a call to <a href="#">addWeightFunction</a> |
| gene                        | A character string indicating the desired gene or gene pair (genes separated by double hyphens)                                                                                               |
| pi                          | character string indicating the desired PI                                                                                                                                                    |
| piMat                       | A data frame. Will be constructed if not provided, for internal use.                                                                                                                          |
| pppDf                       | Dataframe of point pattern-wise variables. It is precalculated in <code>fitLMMsSingle</code> for speed, but will be newly constructed when not provided.                                      |
| prepMat, prepTab, prepCells | Preconstructed objects to save computation time, for internal use                                                                                                                             |

## Value

A dataframe with estimated PIs and covariates

## See Also

[addWeightFunction](#)

## Examples

```
example(addWeightFunction, "smoppix")
dfUniNN <- buildDataFrame(yangObj, gene = "SmVND2", pi = "nn")
# Example analysis with linear mixed model
library(lmerTest)
mixedMod <- lmer(pi ~ 0.5 ~ day + (1 | root),
  weight = weight, data = dfUniNN,
  contrasts = list("day" = "contr.sum")
)
```



```
)
summary(mixedMod)
# Evidence for aggregation
```

---

|              |                                                  |
|--------------|--------------------------------------------------|
| buildFormula | <i>Build a formula from different components</i> |
|--------------|--------------------------------------------------|

---

## Description

Build a formula from different components

## Usage

```
buildFormula(Formula, fixedVars, randomVars, outcome = "pi - 0.5")
```

## Arguments

|                       |                                                               |
|-----------------------|---------------------------------------------------------------|
| Formula               | A formula. If not supplied or equals NULL, will be overridden |
| fixedVars, randomVars | Character vectors with fixed and random variables             |
| outcome               | A character vector describing the outcome                     |

## Details

Random intercepts are assumed for the random effects, if more complicated designs are used, do supply your own formula.

## Value

A formula

## See Also

[fitLMMs,formula](#)

---

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| buildHyperFrame | <i>Build a hyperframe containing all point patterns of an experiment.</i> |
|-----------------|---------------------------------------------------------------------------|

---

## Description

Build a spatstat hyperframe with point patterns and metadata. Matrices, dataframe, lists and SpatialExperiment inputs are accepted.

**Usage**

```

buildHyperFrame(x, ...)

## S4 method for signature 'data.frame'
buildHyperFrame(
  x,
  coordVars,
  imageIdentifier = imageVars,
  imageVars,
  pointVars = setdiff(names(x), c(imageVars, imageIdentifier, coordVars, featureName)),
  featureName = "gene",
  ...
)

## S4 method for signature 'matrix'
buildHyperFrame(
  x,
  imageVars,
  imageIdentifier = imageVars,
  covariates,
  featureName = "gene",
  ...
)

## S4 method for signature 'list'
buildHyperFrame(
  x,
  coordVars = c("x", "y"),
  covariates = NULL,
  idVar = NULL,
  featureName = "gene",
  ...
)

## S4 method for signature 'SpatialExperiment'
buildHyperFrame(x, imageVars, pointVars, imageIdentifier = imageVars, ...)

```

**Arguments**

|                              |                                                                                                       |
|------------------------------|-------------------------------------------------------------------------------------------------------|
| <code>x</code>               | the input object, see <code>methods('buildHyperFrame')</code>                                         |
| <code>...</code>             | additional constructor arguments                                                                      |
| <code>coordVars</code>       | Names of coordinates                                                                                  |
| <code>imageIdentifier</code> | A character vector of variables whose unique combinations define the separate point patterns (images) |
| <code>imageVars</code>       | Covariates belonging to the point patterns                                                            |
| <code>pointVars</code>       | Names of event-wise covariates such as gene or cell for each single point                             |
| <code>featureName</code>     | The name of the feature identifier for the molecules.                                                 |
| <code>covariates</code>      | A matrix or dataframe of covariates                                                                   |
| <code>idVar</code>           | An optional id variable present in covariates, that is matched with the names of covariates           |

list                    A list of matrices or of point patterns of class 'spatstat.geom::ppp'

### Value

An object of class 'hyperframe' from the 'spatstat.geom' package

### See Also

[hyperframe](#)

### Examples

```
data(Yang)
hypYang <- buildHyperFrame(Yang,
  coordVars = c("x", "y"),
  imageVars = c("day", "root", "section")
)
```

---

|                   |                                                                  |
|-------------------|------------------------------------------------------------------|
| calcIndividualPIs | <i>Calculate individual PI entries of a single point pattern</i> |
|-------------------|------------------------------------------------------------------|

---

### Description

Calculate individual PI entries of a single point pattern

### Usage

```
calcIndividualPIs(
  p,
  tabObs,
  pis,
  pSubLeft,
  owins,
  centroids,
  null,
  features,
  ecdfAll,
  ecdfsCell,
  loopFun,
  minDiff,
  minObsNN
)
```

### Arguments

|                  |                                                                         |
|------------------|-------------------------------------------------------------------------|
| p                | The point pattern                                                       |
| tabObs           | A table of observed gene frequencies                                    |
| pis              | The PIs to be estimated or for which weighting functions is to be added |
| pSubLeft         | The subsampled overall point pattern returned by subSampleP             |
| owins, centroids | The list of windows corresponding to cells, and their centroids         |

|                    |                                                                                                                                                                                                               |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| null               | A character vector, indicating how the null distribution is defined. See details.                                                                                                                             |
| features           | A character vector, for which features should the probabilistic indices be calculated?                                                                                                                        |
| ecdfAll, ecdfsCell | Empirical cumulative distribution functions of all events and of cells within the cell, under the null                                                                                                        |
| loopFun            | The function to use to loop over the features. Defaults to bplapply except when looping over features within cells                                                                                            |
| minDiff            | An integer, the minimum number of events from other genes needed for calculation of background distribution of distances. Matters mainly for within-cell calculations: cells with too few events are skipped. |
| minObsNN           | An integer, the minimum number of events required for a gene to be analysed. See details.                                                                                                                     |

### Details

For the single-feature nearest neighbour distances, the PI is average over the point pattern

### Value

A list containing PI entries per feature

### See Also

[estPis](#), [calcNNPI](#)

---

|          |                                                                                                                                  |
|----------|----------------------------------------------------------------------------------------------------------------------------------|
| calcNNPI | <i>Estimate the PI for the nearest neighbour distances, given a set of ranks, using the negative hypergeometric distribution</i> |
|----------|----------------------------------------------------------------------------------------------------------------------------------|

---

### Description

Estimate the PI for the nearest neighbour distances, given a set of ranks, using the negative hypergeometric distribution

### Usage

```
calcNNPI(Ranks, n, m, ties, r = 1)
```

### Arguments

|       |                                                                                                                                             |
|-------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Ranks | The (approximate) ranks, number of times observed distance is larger                                                                        |
| n     | the total number of observed distances minus the number of distances under consideration (the number of failures or black balls in the urn) |
| m     | the number of observed distances (successes or white balls in the urn)                                                                      |
| ties  | The number of times the observed distance is equal to a null distance, of the same length as Ranks                                          |
| r     | The rank of distances considered, r=1 is nearest neighbour distance                                                                         |

**Details**

Ties are counted half to match the definition of the PI.

**Value**

A vector of evaluations of the negative hypergeometric distribution function

**See Also**

[pnhyper](#), [calcIndividualPIs](#)

---

|                  |                                                                                                        |
|------------------|--------------------------------------------------------------------------------------------------------|
| calcWindowDistPI | <i>Estimate the PI for the distance to a fixed object of interest, such as a cell wall or centroid</i> |
|------------------|--------------------------------------------------------------------------------------------------------|

---

**Description**

Estimate the PI for the distance to a fixed object of interest, such as a cell wall or centroid

**Usage**

```
calcWindowDistPI(pSub, owins, centroids, ecdfAll, pi)
```

**Arguments**

|                  |                                                                 |
|------------------|-----------------------------------------------------------------|
| pSub             | The subset point pattern containing only a single gene          |
| owins, centroids | The list of windows corresponding to cells, and their centroids |
| ecdfAll          | the cumulative distribution function under the null             |
| pi               | The type of PI to calculate                                     |

**Details**

Analysis of the distance to the border was introduced by (Joyner et al. 2013) in the form of the B-function. The independent evaluations of the B-functions under the null hypothesis represented by *ecdfAll* per cell are here returned as realizations of the probabilistic index.

**Value**

A list of vectors of estimated probabilistic indices per event

**References**

Joyner M, Ross C, Seier E (2013). "Distance to the border in spatial point patterns." *Spat. Stat.*, **6**, 24 - 40. ISSN 2211-6753, doi:[10.1016/j.spasta.2013.05.002](https://doi.org/10.1016/j.spasta.2013.05.002).

**See Also**

[addCell](#), [estPis](#)

---

|               |                                 |
|---------------|---------------------------------|
| centerNumeric | <i>Center numeric variables</i> |
|---------------|---------------------------------|

---

**Description**

Center numeric variables

**Usage**

```
centerNumeric(x)
```

**Arguments**

|   |                                                          |
|---|----------------------------------------------------------|
| x | The dataframe whose numeric variables are being centered |
|---|----------------------------------------------------------|

**Value**

The adapted dataframe

---

|               |                                                    |
|---------------|----------------------------------------------------|
| checkFeatures | <i>Check if features are present in hyperframe</i> |
|---------------|----------------------------------------------------|

---

**Description**

Check if features are present in hyperframe

**Usage**

```
checkFeatures(hypFrame, features)
```

**Arguments**

|          |                                                                                        |
|----------|----------------------------------------------------------------------------------------|
| hypFrame | A hyperframe                                                                           |
| features | A character vector, for which features should the probabilistic indices be calculated? |

**Value**

Throws error when features not found

---

|         |                                                             |
|---------|-------------------------------------------------------------|
| checkPi | <i>Check if the required PI's are present in the object</i> |
|---------|-------------------------------------------------------------|

---

**Description**

Check if the required PI's are present in the object

**Usage**

```
checkPi(x, pi)
```

**Arguments**

|    |                                                           |
|----|-----------------------------------------------------------|
| x  | The result of the PI calculation, or a weighting function |
| pi | A character string indicating the desired PI              |

**Value**

Throws an error when the PIs are not found, otherwise returns invisible

---

|                     |                                             |
|---------------------|---------------------------------------------|
| constructDesignVars | <i>Check for or construct design matrix</i> |
|---------------------|---------------------------------------------|

---

**Description**

Run checks on design variables, or construct them as vector them if missing

**Usage**

```
constructDesignVars(designVars, lowestLevelVar, allCell, resList)
```

**Arguments**

|                |                                                 |
|----------------|-------------------------------------------------|
| designVars     | The initial design variables                    |
| lowestLevelVar | Variable indicating the lowest level of nesting |
| allCell        | A boolean, are all PIs cell-related?            |
| resList        | The results list                                |

**Value**

A vector of design variables

**See Also**

[buildDataFrame](#)

---

|                |                                                     |
|----------------|-----------------------------------------------------|
| convertToOwins | <i>Convert windows to spatstat.geom owin format</i> |
|----------------|-----------------------------------------------------|

---

### Description

Convert a list of windows in different possible formats to owin, for addition to a hyperframe.

### Usage

```
convertToOwins(windows, namePPP, coords, ...)
```

### Arguments

|         |                                                                                |
|---------|--------------------------------------------------------------------------------|
| windows | The list of windows. See <a href="#">addCell</a> for accepted formats.         |
| namePPP | the name of the point pattern, will be added to the cell names                 |
| coords  | The names of the coordinates, if the windows are given as sets of coordinates. |
| ...     | passed onto as.owin                                                            |

### Details

Order of traversal of polygons may differ between data types. Where applicable, different orders are tried before throwing an error.

### Value

A list of owin

### See Also

[addCell](#), [as.owin](#)

---

|                  |                                                                         |
|------------------|-------------------------------------------------------------------------|
| crossdistWrapper | <i>A wrapper for C-functions calculating cross-distance matrix fast</i> |
|------------------|-------------------------------------------------------------------------|

---

### Description

A wrapper for C-functions calculating cross-distance matrix fast

### Usage

```
crossdistWrapper(x, y)
```

### Arguments

|      |                                                                               |
|------|-------------------------------------------------------------------------------|
| x, y | the matrices or point patterns between which to calculate the cross distances |
|------|-------------------------------------------------------------------------------|

### Value

a matrix of cross distances



Eng

*Spatial transcriptomics data of mouse fibroblast cells***Description**

Single-molecule spatial transcriptomics seqFISH+ data containing measurements of 10,000 genes in NIH/3T3 mouse fibroblast cells by (Eng et al. 2019). Molecule locations, gene identity and design variables are included, a subset of eight most expressed genes is included in the package, and the dataset was subsampled to 100,000 observations for memory reasons. In addition, a list of regions of interest (rois) is given describing the cell boundaries.

**Usage**

```
data(Eng)
```

**Format**

1. **Eng** A data frame with variables
  - x,y** Molecule coordinates
  - gene** Character vector with gene identities
  - experiment,fov** Design variables
2. **EngRois** A list of lists of regions of interest (ROIs): the cell boundaries

**Source**

[doi:10.1038/s415860191049y](https://doi.org/10.1038/s415860191049y)

**References**

Eng CL, Lawson M, Zhu Q, Dries R, Koulana N, Takei Y, Yun J, Cronin C, Karp C, Yuan G, Cai L (2019). "Transcriptome-scale super-resolved imaging in tissues by RNA seqFISH+." *Nature*, **568**(7751), 235 - 239. ISSN 1476-4687, [doi:10.1038/s415860191049y](https://doi.org/10.1038/s415860191049y).

estGradients

*Estimate gradients over multiple point patterns, and test for significance*

**Description**

estGradients() estimate gradients on all single-molecule point patterns of a hyperframe. estGradientsSingle() is the workhorse function for a single point pattern. getPvaluesGradient() extracts the p-values of the fits.

**Usage**

```

estGradients(
  hypFrame,
  gradients = c("overall", if (!is.null(hypFrame$owins)) "cell"),
  fixedEffects = NULL,
  randomEffects = NULL,
  verbose = FALSE,
  features = getFeatures(hypFrame),
  silent = TRUE,
  loopFun = "bplapply",
  ...
)

estGradientsSingle(
  hypFrame,
  gradients,
  fixedForm,
  randomForm,
  fixedFormSimple,
  effects = NULL,
  ...
)

getPValuesGradient(res, gradient, method = "BH")

```

**Arguments**

|                                        |                                                                                                                         |
|----------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| hypFrame                               | A hyperframe                                                                                                            |
| gradients                              | The gradients types to be estimated: "overall" or within cell ("cell")                                                  |
| fixedEffects, randomEffects            | Character vectors of fixed and random effects present in the hyperframe, modifying the baseline intensity. See details. |
| verbose                                | A boolean, whether to report on progress of the fitting process.                                                        |
| features                               | A character vector, for which features should the gradients indices be calculated?                                      |
| silent                                 | A boolean, should error messages from spatstat.model::mppm be printed?                                                  |
| loopFun                                | The function to use to loop over the features.                                                                          |
| ...                                    | Passed onto fitGradient                                                                                                 |
| fixedForm, randomForm, fixedFormSimple | Formulae for fixed effects, random effects and fixed effects without slopes respectively                                |
| effects                                | Character vector of fixed and random effects                                                                            |
| res                                    | The fitted gradients                                                                                                    |
| gradient                               | The gradient to be extracted, a character vector equal to "overall" or "cell".                                          |
| method                                 | Method of multiplicity correction, see <a href="#">p.adjust</a> . Defaults to Benjamini-Hochberg.                       |

**Details**

The test for existence of a gradient revolves around interaction terms between x and y coordinates and image identifiers. If this interactions are significant, this implies existence of gradients in the

different point patterns, albeit with different directions. Yet be aware that a gradient that is significant for a computer may look very different from the human perspective; many spatial patterns can be captured by a gradient to some extent. Baseline intensity corrections for every image or cell are included by default. The fixed and random effects modify the baseline intensity of the point pattern, not the gradient! Random effects can lead to problems with fitting and are dissuaded.

## Value

For `estGradients()`, a list with the estimated gradients

For `estGradientsSingle()`, a list containing

|                      |                           |
|----------------------|---------------------------|
| <code>overall</code> | Overall gradients         |
| <code>cell</code>    | Gradients within the cell |

For `getPvaluesGradient()`, a vector of p-values

## Note

Fitting Poisson point processes is computation-intensive.

## See Also

[fitGradient](#)

## Examples

```
# Overall Gradients
data(Yang)
hypYang <- buildHyperFrame(Yang,
  coordVars = c("x", "y"),
  imageVars = c("day", "root", "section")
)
yangGrads <- estGradients(hypYang[seq_len(2), ],
  features = getFeatures(hypYang)[1],
  fixedEffects = "day", randomEffects = "root")
# Gradients within cell
data(Eng)
hypEng <- buildHyperFrame(Eng[Eng$fov %in% c(1,2), ],
  coordVars = c("x", "y"),
  imageVars = c("fov", "experiment")
) #Subset for speed
hypEng <- addCell(hypEng, EngRois[rownames(hypEng)], verbose = FALSE)
# Limit number of cells and genes for computational reasons
engGrads <- estGradients(hypEng[seq_len(2), ],
  features = feat <- getFeatures(hypEng)[1])
pVals <- getPvaluesGradient(engGrads, "cell")
```

---

|        |                                                                                                                           |
|--------|---------------------------------------------------------------------------------------------------------------------------|
| estPis | <i>Estimate probabilistic indices for single-molecule localization patterns, and add the variance weighting function.</i> |
|--------|---------------------------------------------------------------------------------------------------------------------------|

---

## Description

Estimate different probabilistic indices for localization on all point patterns of a hyperframe, and integrate the results in the same hyperframe. `estPisSingle()` is the workhorse function for a single point pattern.

`addWeightFunction()` adds a weighting function based on the data to the object by modeling variance as a non-increasing spline as a function of the number of events.

## Usage

```
estPis(
  hypFrame,
  pis = c("nn", "nnPair", "edge", "centroid", "nnCell", "nnPairCell"),
  verbose = TRUE,
  null = c("background", "CSR"),
  nPointsAll = switch(null, background = 50000, CSR = 2000),
  nPointsAllWithinCell = switch(null, background = 5000, CSR = 1000),
  nPointsAllWin = 10000,
  minDiff = 20,
  minObsNN = 1L,
  features = getFeatures(hypFrame),
  ...
)

estPisSingle(
  p,
  pis,
  null,
  tabObs,
  oWins = NULL,
  centroids = NULL,
  window = p$window,
  loopFun = "bplapply",
  features,
  nPointsAll,
  nPointsAllWithinCell,
  nPointsAllWin,
  minDiff,
  minObsNN
)

addWeightFunction(
  resList,
  pis = resList$pis,
  designVars,
  lowestLevelVar,
```

```

    maxObs = 1e+05,
    maxFeatures = 1000,
    minNumVar = 3,
    ...
)

```

## Arguments

|                                  |                                                                                                                                                                                                                                                             |
|----------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| hypFrame                         | A hyperframe                                                                                                                                                                                                                                                |
| pis                              | The PIs to be estimated or for which weighting functions is to be added                                                                                                                                                                                     |
| verbose                          | A boolean, whether to report on progress of the fitting process.                                                                                                                                                                                            |
| null                             | A character vector, indicating how the null distribution is defined. See details.                                                                                                                                                                           |
| nPointsAll, nPointsAllWithinCell | How many points to subsample or simulate to calculate the overall nearest neighbour distance distribution under the null hypothesis. The second argument (nPointsAllWithinCell) applies to within cell calculations, where a lower number usually suffices. |
| nPointsAllWin                    | How many points to subsample or simulate to calculate distance to cell edge or centroid distribution                                                                                                                                                        |
| minDiff                          | An integer, the minimum number of events from other genes needed for calculation of background distribution of distances. Matters mainly for within-cell calculations: cells with too few events are skipped.                                               |
| minObsNN                         | An integer, the minimum number of events required for a gene to be analysed. See details.                                                                                                                                                                   |
| features                         | A character vector, for which features should the probabilistic indices be calculated?                                                                                                                                                                      |
| ...                              | Additional arguments passed on to the <a href="#">scam</a> function, fitting the spline                                                                                                                                                                     |
| p                                | The point pattern                                                                                                                                                                                                                                           |
| tabObs                           | A table of observed gene frequencies                                                                                                                                                                                                                        |
| owins, centroids                 | The list of windows corresponding to cells, and their centroids                                                                                                                                                                                             |
| window                           | An window of class owin, in which events can occur                                                                                                                                                                                                          |
| loopFun                          | The function to use to loop over the features. Defaults to bplapply except when looping over features within cells                                                                                                                                          |
| resList                          | A results list, from a call to estPis().                                                                                                                                                                                                                    |
| designVars                       | A character vector containing all design factors (both fixed and random), that are also present as variables in hypFrame.                                                                                                                                   |
| lowestLevelVar                   | The design variable at the lowest level of nesting, often separating technical replicates. The conditional variance is calculated within the groups of PIs defined by this variable.                                                                        |
| maxObs, maxFeatures              | The maximum number of observations respectively features for fitting the weighting function. See details.                                                                                                                                                   |
| minNumVar                        | The minimum number of observations needed to calculate a variance. Groups with fewer replicates are ignored.                                                                                                                                                |

## Details

The null distribution used to calculate the PIs can be either 'background' or 'null'. For 'background', the observed distributions of all genes is used. Alternatively, for null = 'CSR', Monte-Carlo simulation under complete spatial randomness is performed within the given window to find the null distribution of the distance under study. See (Hawinkel et al. 2025) for precise definition of the PI.

The 'nn' prefix indicates that nearest neighbour distances are being used, either univariately or bivariate. The suffix 'Pair' indicates that bivariate probabilistic indices, testing for co- and antio-calization are being used. 'edge' and 'centroid' calculate the distance to the edge respectively the centroid of the windows added using the [addCell](#) function. The suffix 'Cell' indicates that nearest neighbour distances are being calculated within cells only.

It can be useful to set the minObsNN higher than the default of 5 for calculations within cells when the number of events is low, not to waste computation time on gene (pairs) with very variable PI estimates.

Provide either 'designVars' or 'lowestLevelVar'. The 'designVars' are usually the same as the regressors in the linear model. In case 'lowestLevelVar' is provided, the design variables are set to all imageVars in the hypFrame object except lowestLevelVar. When the PI is calculated on the cell level ("nnCell" or "nnPairCell"), the cell is always the lowest nesting level, and inputs to 'designVars' or 'lowestLevelVar' will be ignored for these PIs. The registered parallel backend will be used for fitting the trends of the different PIs. For computational and memory reasons, for large datasets the trend fitting is restricted to a random subset of the data through the maxObs and maxFeatures parameters.

## Value

For `estPis()`, the hyperframe with the estimated PIs present in it

For `estPisSingle()`, a list of data frames with estimated PIs per gene and/or gene pair:

|                              |                                            |
|------------------------------|--------------------------------------------|
| <code>pointDists</code>      | PIs for pointwise distances overall        |
| <code>windowDists</code>     | PIs for distances to cell wall or centroid |
| <code>withinCellDists</code> | PIs for pointwise distances within cell    |

For `addWeightFunction()`, the input object 'resList' with a slot 'Wfs' added containing the weighting functions.

## See Also

[buildDataFrame](#), [estPis](#)

## Examples

```
data(Yang)
hypYang <- buildHyperFrame(Yang,
  coordVars = c("x", "y"),
  imageVars = c("day", "root", "section")
)
yangPims <- estPis(hypYang[c(seq_len(4), seq(27, 29)), ], pis = "nn",
  nPointsAll = 4e2)
# Univariate nearest neighbour distances
yangObj <- addWeightFunction(yangPims, designVars = c("day", "root"))
# Add the weight functions
yangObj <- addWeightFunction(yangPims, lowestLevelVar = "section",
```

```
pi = "nn")
# Alternative formulation with 'lowestLevelVar'
```

---

|                    |                                               |
|--------------------|-----------------------------------------------|
| evalWeightFunction | <i>Evaluate a variance weighting function</i> |
|--------------------|-----------------------------------------------|

---

### Description

Evaluate the variance weighting function to return unnormalized weights

### Usage

```
evalWeightFunction(wf, newdata)
```

### Arguments

|         |                            |
|---------|----------------------------|
| wf      | The weighting function     |
| newdata | A data frame with new data |

### Value

A vector of weights, so the inverse of predicted variances, unnormalized

### See Also

[predict.scam](#), [addWeightFunction](#)

### Examples

```
data(Yang)
hypYang <- buildHyperFrame(Yang, coordVars = c("x", "y"),
  imageVars = c("day", "root", "section"))
yangPims <- estPis(hypYang, pis = "nn",
  features = getFeatures(hypYang)[12:19], nPointsAll = 5e2)
# First Build the weighting function
yangObj <- addWeightFunction(yangPims, designVars = c("day", "root"))
evalWeightFunction(yangObj$Wfs$nn, newdata = data.frame("NP" = 2))
```

---

|                |                                                                             |
|----------------|-----------------------------------------------------------------------------|
| extractResults | <i>Extract results from a list of fitted LMMs. For internal use mainly.</i> |
|----------------|-----------------------------------------------------------------------------|

---

### Description

Extract results from a list of fitted LMMs. For internal use mainly.

### Usage

```
extractResults(models, hypFrame, fixedVars = NULL, method = "BH")
```

**Arguments**

|           |                                                          |
|-----------|----------------------------------------------------------|
| models    | The models                                               |
| hypFrame  | The original hyperframe                                  |
| fixedVars | The fixed effects for which the effect is to be reported |
| method    | Multiplicity correction method passed onto p.adjust      |

**Value**

A list of matrices, all containing estimate, standard error, p-value and adjusted p-value

**See Also**

[fitLMMs](#), [p.adjust](#)

---

|               |                                                                                                    |
|---------------|----------------------------------------------------------------------------------------------------|
| findEcdfsCell | <i>Construct empirical cumulative distribution functions (ecdfs) for distances within the cell</i> |
|---------------|----------------------------------------------------------------------------------------------------|

---

**Description**

The distance distribution under the null hypothesis of complete spatial randomness (CSR) within the cell is the same for all genes. This function precalculates this distribution using Monte-Carlo simulation under CSR, and summarizes it in an ecdf object

**Usage**

```
findEcdfsCell(p, owin, nPointsAllWin, centroids, null, pis, loopFun)
```

**Arguments**

|                 |                                                                                                                    |
|-----------------|--------------------------------------------------------------------------------------------------------------------|
| p               | The point pattern                                                                                                  |
| owin, centroids | The list of windows corresponding to cells, and their centroids                                                    |
| nPointsAllWin   | How many points to subsample or simulate to calculate distance to cell edge or centroid distribution               |
| null            | A character vector, indicating how the null distribution is defined. See details of <a href="#">estPis</a> .       |
| pis             | The PIs to be estimated or for which weighting functions is to be added                                            |
| loopFun         | The function to use to loop over the features. Defaults to bplapply except when looping over features within cells |

**Value**

The list of ecdf functions

**See Also**

[ecdf](#)



---

|             |                                             |
|-------------|---------------------------------------------|
| findOverlap | <i>Find overlap between list of windows</i> |
|-------------|---------------------------------------------|

---

### Description

The function seeks overlap between the list of windows supplied, and throws an error when found or returns the id's when found.

### Usage

```
findOverlap(owins, centroids = NULL, returnIds = FALSE, numCentroids = 30)
```

### Arguments

|              |                                                                                                            |
|--------------|------------------------------------------------------------------------------------------------------------|
| owins        | the list of windows                                                                                        |
| centroids    | The centroids of the windows                                                                               |
| returnIds    | A boolean, should the indices of the overlap be returned? If FALSE an error is thrown at the first overlap |
| numCentroids | An integer, the number of cells with closest centroids to consider looking for overlap                     |

### Value

Throws an error when overlap found, otherwise returns invisible. When returnIds=TRUE, the indices of overlapping windows are returned.

### Examples

```
library(spatstat.geom)
owins <- replicate(10, owin(
  xrange = runif(1) + c(0, 0.2),
  yrange = runif(1) + c(0, 0.1)
), simplify = FALSE)
idOverlap <- findOverlap(owins, returnIds = TRUE)
```

---

|             |                                                                        |
|-------------|------------------------------------------------------------------------|
| fitGradient | <i>Test for presence of gradient in a hyperframe of point patterns</i> |
|-------------|------------------------------------------------------------------------|

---

### Description

A Poisson process is fitted to the data assuming exponential relationship with intensity of the interaction between x and y variables and image identifier. This is compared to a model without this interaction to test for the significance of the gradient.

Usage

```
fitGradient(  
  hypFrame,  
  fixedForm,  
  randomForm,  
  fixedFormSimple,  
  returnModel = FALSE,  
  silent,  
  ...  
)
```

Arguments

|                                        |                                                                                                           |
|----------------------------------------|-----------------------------------------------------------------------------------------------------------|
| hypFrame                               | the hyperframe                                                                                            |
| fixedForm, randomForm, fixedFormSimple | Formulae for fixed effects, random effects and fixed effects without slopes respectively                  |
| returnModel                            | A boolean, should the entire model be returned? Otherwise the p-value and coefficient vector are returned |
| silent                                 | A boolean, should error messages from spatstat.model::mppm be printed?                                    |
| ...                                    | passed onto <a href="#">mppm</a>                                                                          |

Value

A list contraining

|      |                                        |
|------|----------------------------------------|
| pVal | The p-value for existence of gradients |
| coef | The model coefficients                 |

or a mppm model when returnModel is true

See Also

[estGradients](#)

---

|         |                                                                                    |
|---------|------------------------------------------------------------------------------------|
| fitLMMs | <i>Fit linear (mixed) models for all probabilistic indices (PIs) and all genes</i> |
|---------|------------------------------------------------------------------------------------|

---

Description

The PI is used as outcome variable in a linear (mixed) model, with design variables as regressors. Separate models are fitted for every combination of gene and PI. fitLMMsSingle() is the workhorse function for a single point pattern, fitSingleLmmModel() for a single feature in a single point pattern.

getResults() extracts effect size estimates, standard errors and adjusted p-values for a certain parameter from a linear model.

**Usage**

```

fitLMMs(
  obj,
  pis = obj$pis,
  fixedVars = NULL,
  randomVars = NULL,
  verbose = TRUE,
  returnModels = FALSE,
  Formula = NULL,
  randomNested = TRUE,
  features = getEstFeatures(obj),
  ...
)

fitLMMsSingle(
  obj,
  pi,
  fixedVars,
  randomVars,
  verbose,
  returnModels,
  Formula,
  randomNested,
  features
)

getResults(obj, pi, parameter)

```

**Arguments**

|                           |                                                                                               |
|---------------------------|-----------------------------------------------------------------------------------------------|
| <code>obj</code>          | The result object                                                                             |
| <code>pis</code>          | Optional, the pis required. Defaults to all pis in the object                                 |
| <code>fixedVars</code>    | Names of fixed effects                                                                        |
| <code>randomVars</code>   | Names of random variables                                                                     |
| <code>verbose</code>      | A boolean, should the formula be printed?                                                     |
| <code>returnModels</code> | a boolean: should the full models be returned? Otherwise only summary statistics are returned |
| <code>Formula</code>      | A formula; if not supplied it will be constructed from the fixed and random variables         |
| <code>randomNested</code> | A boolean, indicating if random effects are nested within point patterns. See details.        |
| <code>features</code>     | The features for which to fit linear mixed models. Defaults to all features in the object     |
| <code>...</code>          | Passed onto <code>fitLMMsSingle</code>                                                        |
| <code>pi</code>           | The desired PI                                                                                |
| <code>parameter</code>    | The desired parameter                                                                         |

## Details

Genes or gene pairs with insufficient observations will be silently omitted. When `randomVars` is provided as a vector, independent random intercepts are fitted for them by default. Providing them separated by ``\`` or ``:`` as in the lmer formulas is also allowed to reflect nesting structure, but the safest is to construct the formula yourself and pass it onto `fitLMMs`.

It is by default assumed that random effects are nested within the point patterns. This means for instance that cells with the same name but from different point patterns are assigned to different random effects. Set `'randomNested'` to `FALSE` to override this behaviour.

## Value

For `fitLMMs()`, a list of fitted objects

For `fitLMMsSingle()`, a list of test results, if requested also the linear models are returned

For `getResults()`, the matrix with results, with p-values in ascending order

|          |                                         |
|----------|-----------------------------------------|
| Estimate | The estimated PI                        |
| se       | The corresponding standard error        |
| pVal     | The p-value                             |
| pAdj     | The Benjamini-Hochberg adjusted p-value |

## See Also

[buildDataFrame](#)

## Examples

```
example(addWeightFunction, "smoppix")
lmmModels <- fitLMMs(yangObj, fixedVars = "day", randomVars = "root")
res <- getResults(lmmModels, "nn", "Intercept") #Extract the results
head(res)
```

---

fitPiModel

*Fit a linear model for an individual gene and PI combination*

---

## Description

Fit a linear model for an individual gene and PI combination

## Usage

```
fitPiModel(Formula, dff, contrasts, Control, MM, Weight = NULL)
```

## Arguments

|           |                                                                                       |
|-----------|---------------------------------------------------------------------------------------|
| Formula   | A formula; if not supplied it will be constructed from the fixed and random variables |
| dff       | The dataframe                                                                         |
| contrasts | The contrasts to be used, see <a href="#">model.matrix</a>                            |
| Control   | Control parameters                                                                    |
| MM        | A boolean, should a mixed model be tried                                              |
| Weight    | A weight variable                                                                     |

**Value**

A fitted model

**See Also**

[fitLMMsSingle](#)

---

|                   |                                                                          |
|-------------------|--------------------------------------------------------------------------|
| fitSingleLmmModel | <i>Take an existing frame, add outcome and weight and fit lmer model</i> |
|-------------------|--------------------------------------------------------------------------|

---

**Description**

Take an existing frame, add outcome and weight and fit lmer model

**Usage**

```
fitSingleLmmModel(ff, y, Control, Terms, modMat, MM, Assign, weights = NULL)
```

**Arguments**

|               |                                          |
|---------------|------------------------------------------|
| ff            | The prepared frame                       |
| y             | outcome vector                           |
| Control       | Control parameters                       |
| modMat        | Design matrix of the fixed effects model |
| MM            | A boolean, should a mixed model be tried |
| Assign, Terms | Added to fitted fixed effects model      |
| weights       | weights vector                           |

**Value**

A fitted lmer model

---

|              |                                                               |
|--------------|---------------------------------------------------------------|
| getCoordsMat | <i>Extract coordinates from a point pattern or data frame</i> |
|--------------|---------------------------------------------------------------|

---

**Description**

Extract coordinates from a point pattern or data frame

**Usage**

```
getCoordsMat(x)
```

**Arguments**

|   |                                        |
|---|----------------------------------------|
| x | the point pattern, dataframe or matrix |
|---|----------------------------------------|

**Value**

the matrix of coordinates

---

|               |                                                                                                                        |
|---------------|------------------------------------------------------------------------------------------------------------------------|
| getDesignVars | <i>getDesignVars() returns all design variables, both at the level of the point pattern and the level of the event</i> |
|---------------|------------------------------------------------------------------------------------------------------------------------|

---

### Description

getDesignVars() returns all design variables, both at the level of the point pattern and the level of the event

getPPVars() extract variables related to point patterns

getEventVars() extracts variables related to events, e.g. the cell (the marks)

### Usage

```
getDesignVars(x)
```

```
getPPVars(
  x,
  exclude = c("tabObs", "centroids", "owins", "ppp", "pimRes", "image", "nuclei")
)
```

```
getEventVars(x, exclude = c("x", "y", "z"))
```

### Arguments

|         |                                      |
|---------|--------------------------------------|
| x       | The results list, output from estPis |
| exclude | variables to exclude                 |

### Details

getDesignVars() returns all design variables, [getPPVars](#) returns design variables related to the different images and [getEventVars](#) returns design variables related to the individual events

### Value

A vector of design variables

---

|            |                                                   |
|------------|---------------------------------------------------|
| getElement | <i>Extract en element from a matrix or vector</i> |
|------------|---------------------------------------------------|

---

### Description

Extract en element from a matrix or vector

### Usage

```
getElement(x, e)
```

**Arguments**

|   |                            |
|---|----------------------------|
| x | the matrix or vector       |
| e | The column or element name |

**Value**

The desired element

---

|             |                                                                                             |
|-------------|---------------------------------------------------------------------------------------------|
| getFeatures | <i>Extract all unique features from an object, or the ones for which PIs were estimated</i> |
|-------------|---------------------------------------------------------------------------------------------|

---

**Description**

Extract all unique features from an object, or the ones for which PIs were estimated

**Usage**

```
getFeatures(x)
```

**Arguments**

|   |                                                        |
|---|--------------------------------------------------------|
| x | A hyperframe or a results list containing a hyperframe |
|---|--------------------------------------------------------|

**Value**

A vector of features

**Examples**

```
data(Yang)
hypYang <- buildHyperFrame(Yang,
  coordVars = c("x", "y"),
  imageVars = c("day", "root", "section")
)
head(getFeatures(hypYang))
```

---

|       |                                                               |
|-------|---------------------------------------------------------------|
| getGp | <i>Helper function to get gene pair from a vector or list</i> |
|-------|---------------------------------------------------------------|

---

**Description**

When provided with argument "geneA-geneB", looks for this gene pair as well as for "geneB-geneA" in the provided object.

**Usage**

```
getGp(x, gp, drop = TRUE, Collapse = "--", notFoundReturn = NULL)
```

**Arguments**

|                |                                                                 |
|----------------|-----------------------------------------------------------------|
| x              | The object in which to look                                     |
| gp             | A character string describing the gene pair                     |
| drop           | A boolean, should matrix attributes be dropped in [] subsetting |
| Collapse       | The character separating the gene pair                          |
| notFoundReturn | value to return if element is not found                         |

**Value**

The element sought

**Examples**

```
mat <- t(cbind(
  "gene1--gene2" = c(1, 2),
  "gene1--gene3" = c(2, 3)
))
getGp(mat, "gene3--gene1")
```

---

|             |                               |
|-------------|-------------------------------|
| getHypFrame | <i>Extract the hyperframe</i> |
|-------------|-------------------------------|

---

**Description**

Extract the hyperframe

**Usage**

```
getHypFrame(x)
```

**Arguments**

|   |                                        |
|---|----------------------------------------|
| x | The hyperframe, or list containing one |
|---|----------------------------------------|

**Value**

the hyperframe



---

|                 |                                           |
|-----------------|-------------------------------------------|
| getPiAndWeights | <i>Build a matrix with pi and weights</i> |
|-----------------|-------------------------------------------|

---

**Description**

Build a matrix with pi and weights

**Usage**

```
getPiAndWeights(obj, gene, pi, piMat, prepMat, prepTab)
```

**Arguments**

|                  |                                                                                                                                                                                               |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| obj              | A results object. For distances to fixed objects, the result of a call to <a href="#">estPis</a> ; for nearest neighbour distances, the result of a call to <a href="#">addWeightFunction</a> |
| gene             | A character string indicating the desired gene or gene pair (genes separated by double hyphens)                                                                                               |
| pi               | character string indicating the desired PI                                                                                                                                                    |
| piMat            | A data frame. Will be constructed if not provided, for internal use.                                                                                                                          |
| prepMat, prepTab | Preconstructed objects to avoid looping over genes. For internal use mainly                                                                                                                   |

**Value**

A matrix of two columns: pi estimate and weights

---

|              |                                                                                       |
|--------------|---------------------------------------------------------------------------------------|
| lm_from_wfit | <i>Add compoments to a result from lm.wfit to make it a minimally valid lm object</i> |
|--------------|---------------------------------------------------------------------------------------|

---

**Description**

Add compoments to a result from lm.wfit to make it a minimally valid lm object

**Usage**

```
lm_from_wfit(obj, y, Terms, Assign)
```

**Arguments**

|               |                      |
|---------------|----------------------|
| obj           | The lm.wfit() result |
| y             | the outcome variable |
| Terms, Assign | Added to the object  |

**Value**

A object of class lm

---

|                     |                                                                  |
|---------------------|------------------------------------------------------------------|
| loadBalanceBplapply | <i>Parallel processing with BiocParallel with load balancing</i> |
|---------------------|------------------------------------------------------------------|

---

### Description

The vector to iterate over (iterator) is split into as many parts as there are cores available, such that each core gets an equal load and overhead is minimized. The registered backend is then used by default to multithread using [bplapply](#).

### Usage

```
loadBalanceBplapply(
  iterator,
  func,
  loopFun = if (bpparam()$workers == 1) "lapply" else "bplapply"
)
```

### Arguments

|          |                                                                  |
|----------|------------------------------------------------------------------|
| iterator | The vector to iterate over                                       |
| func     | The function to apply to each element                            |
| loopFun  | The looping function, can also be 'lapply' for serial processing |

### Value

A list with the same length as iterator

### Examples

```
library(BiocParallel)
loadBalanceBplapply(LETTERS, length)
```

---

|               |                                                                     |
|---------------|---------------------------------------------------------------------|
| makeDesignVar | <i>Make design variable by combining different design variables</i> |
|---------------|---------------------------------------------------------------------|

---

### Description

Make design variable by combining different design variables

### Usage

```
makeDesignVar(x, designVars, sep = "_")
```

### Arguments

|            |                                       |
|------------|---------------------------------------|
| x          | the design matrix                     |
| designVars | the design variables to be combined   |
| sep        | The string to separate the components |

**Value**

a vector of design levels

---

makePairs

*An aux function to build gene pairs*


---

**Description**

An aux function to build gene pairs

**Usage**

```
makePairs(genes)
```

**Arguments**

genes                      The genes to be combined

**Value**

A character vector of gene pairs

**Examples**

```
genes <- paste0("gene", seq_len(4))
makePairs(genes)
```

---

named.contr.sum

*A version of contr.sum that retains names, a bit controversial but also clearer*


---

**Description**

A version of contr.sum that retains names, a bit controversial but also clearer

**Usage**

```
named.contr.sum(x, ...)
```

**Arguments**

x, ...                      passed on to contr.sum

**Value**

The matrix of contrasts

**Note**

After <https://stackoverflow.com/questions/24515892/r-how-to-contrast-code-factors-and-retain-meaningful-labels-in-output-summary>

---

|            |                                                                                   |
|------------|-----------------------------------------------------------------------------------|
| nestRandom | <i>Nest random effects within fixed variables, in case the names are the same</i> |
|------------|-----------------------------------------------------------------------------------|

---

### Description

Nest random effects within fixed variables, in case the names are the same

### Usage

```
nestRandom(df, randomVars, fixedVars)
```

### Arguments

|            |                      |
|------------|----------------------|
| df         | The dataframe        |
| randomVars | The random variables |
| fixedVars  | The fixed variables  |

### Value

The dataframe with adapted randomVars

---

|           |                                                             |
|-----------|-------------------------------------------------------------|
| plotCells | <i>Plot the n cells with highest abundance of a feature</i> |
|-----------|-------------------------------------------------------------|

---

### Description

After testing for within-cell patterns, it may be useful to look at the cells with the most events for certain genes. These are plotted here, but the spatial location of the cells in the point pattern is lost! The choice and ranking of cells is one of decreasing gene (pair) expression.

### Usage

```
plotCells(
  obj,
  features = getFeatures(obj)[seq_len(3)],
  nCells = 100,
  Cex = 1.5,
  borderColVar = NULL,
  borderCols = rev(palette()),
  Mar = c(0.5, 0.1, 0.75, 0.1),
  warnPosition = TRUE,
  summaryFun = "min",
  plotNuclei = !is.null(getHypFrame(obj)$nuclei),
  nucCol = "lightblue",
  ...
)
```

**Arguments**

|              |                                                                                                                                                                                                                                          |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| obj          | A hyperframe, or an object containing one                                                                                                                                                                                                |
| features     | The features to be plotted, a character vector                                                                                                                                                                                           |
| nCells       | An integer, the number of cells to be plotted                                                                                                                                                                                            |
| Cex          | The point expansion factor                                                                                                                                                                                                               |
| borderColVar | The variable to colour borders of the cell                                                                                                                                                                                               |
| borderCols   | Colour palette for the borders                                                                                                                                                                                                           |
| Mar          | the margins                                                                                                                                                                                                                              |
| warnPosition | A boolean, should a warning be printed on the image that cells are not in their original location?                                                                                                                                       |
| summaryFun   | A function to summarize the gene-cell table in case multiple genes are plotted, to determine which cells are plotted. Choose "min" for cells with the highest minimum, or "sum" for highest total expression of the combination of genes |
| plotNuclei   | A boolean, should nuclei be added?                                                                                                                                                                                                       |
| nucCol       | A character string, the colour in which the nucleus' boundary is plotted                                                                                                                                                                 |
| ...          | Additional arguments, currently ignored                                                                                                                                                                                                  |

**Value**

Plots cells with highest expression to the plotting window, returns invisible

**Examples**

```
example(addCell, "smoppix")
plotCells(hypFrame2, "gene1")
plotCells(hypFrame2, "gene1", borderColVar = "condition", nCells = 10)
```

---

plotExplore

---

*Plot a hyperframe with chosen features highlighted*


---

**Description**

All points of the hyperframe are plotted in grey, with a subset of features highlighted in colour. A selection of point patterns is plotted that fit in the window, by default the first six. This function is meant for exploratory purposes as well as for visual confirmation of findings.

**Usage**

```
plotExplore(
  hypFrame,
  features = getFeatures(hypFrame)[seq_len(6)],
  ppps,
  numPps,
  maxPlot = 1e+05,
  Cex = 1,
  plotWindows = !is.null(hypFrame$owins),
  plotPoints = TRUE,
  plotNuclei = !is.null(hypFrame$nuclei),
```

```

piEsts = NULL,
Xlim = NULL,
Ylim = NULL,
Cex.main = 1.1,
Mar = c(0.5, 0.1, 0.9, 0.1),
titleVar = NULL,
piColourCell = NULL,
palCols = c("blue", "yellow"),
nucCol = "lightblue",
border = NULL,
CexLegend = 1.4,
CexLegendMain = 1.7,
Nrow,
Cols
)

```

### Arguments

|                          |                                                                                            |
|--------------------------|--------------------------------------------------------------------------------------------|
| hypFrame                 | The hyperframe                                                                             |
| features                 | A small number of features to be highlighted. Defaults to the first 5.                     |
| ppps                     | The rownames or indices of the point patterns to be plotted. Defaults to maximum 99.       |
| numPps                   | The number of point patterns with highest expression to be shown. Ignored is pps is given. |
| maxPlot                  | The maximum number of events plotted per point pattern                                     |
| Cex, Cex.main            | Point and title expansion factors, respectively                                            |
| plotWindows              | A boolean, should windows be plotted too?                                                  |
| plotPoints               | A boolean, should the molecules be plotted as points?                                      |
| plotNuclei               | A boolean, should the nuclei be plotted?                                                   |
| piEsts                   | Set of PI estimates, returned by estPis                                                    |
| Xlim, Ylim               | plotting limits                                                                            |
| Mar                      | the margins                                                                                |
| titleVar                 | Image variable to be added to the title                                                    |
| piColourCell             | PI by which to colour the cell                                                             |
| palCols                  | Two extremes of the colour palette for colouring the cells                                 |
| nucCol                   | The colour for the nucleus window                                                          |
| border                   | Passed on to plot.owin, and further to graphics::polygon                                   |
| CexLegend, CexLegendMain | Expansion factor for the legend and its title respectively                                 |
| Nrow                     | Number of rows of the facet plot. Will be calculated if missing.                           |
| Cols                     | colours vector named by features. If missing a default palette is used                     |

### Details

When cell-specific PIs are calculated ("nnCell", "nnCellPair", "edge", "centroid"), the cells can be coloured by them to investigate their spatial distribution, for instance those discovered through Moran's I statistic. The colour palette is taken from the output of palette(), so set that one to change the colour scheme.

**Value**

Plots a facet of point patterns to output

**Note**

palCols sets the pseudo-continuous scale to colour cells.

**Examples**

```
example(buildHyperFrame, "smoppix")
plotExplore(hypYang)
plotExplore(hypYang, titleVar = "day")
plotExplore(hypYang, features = c("SmRBRb", "SmTMO5b", "SmWER--SmAHK4f"))
```

---

plotTopResults

---

*Plot the most significant findings for a certain PI*


---

**Description**

Extract the most significant features for a certain PI and direction of effect, and plot them using an appropriate function: either [plotExplore](#) or [plotCells](#)

**Usage**

```
plotTopResults(
  hypFrame,
  results,
  pi,
  effect = "Intercept",
  what = if (pi %in% c("nn", "nnCell")) {
    "aggregated"
  } else if (pi %in%
    c("nnPair", "nnPairCell")) {
    "colocalized"
  } else if (pi %in% c("edge",
    "centroid")) {
    "close"
  },
  sigLevel = 0.05,
  numFeats = 2,
  piThreshold = switch(effect, Intercept = 0.5, 0),
  effectParameter = NULL,
  ...
)
```

**Arguments**

|          |                                                        |
|----------|--------------------------------------------------------|
| hypFrame | The hyperframe with the data                           |
| results  | The results frame                                      |
| pi       | A character string, specifying the probabilistic index |

|                 |                                                                                    |
|-----------------|------------------------------------------------------------------------------------|
| effect          | The name of the effect                                                             |
| what            | Which features should be detected? Can be abbreviated, see details.                |
| sigLevel        | The significance level                                                             |
| numFeats        | The number of features to plot                                                     |
| piThreshold     | The threshold for PI, a minimum effect size                                        |
| effectParameter | A character string, indicating which parameter to look for when effect is provided |
| ...             | passed onto plotting functions plotCells or plotExplore                            |

### Details

The "what" argument indicates if features far from or close to cell wall or centroid should be shown for pi "edge" or "centroid", aggregated or regular features for "nn" and "nnCell" and colocalized or antilocalized features for "nnPair" and "nnPairCell". Partial matching is allowed. Defaults to small probabilistic indices: proximity, aggregation and colocalization. For fixed effects, provide the name of the parameter, in combination with what. For instance, what = "regular", effect = "Var1" and effectParameter = "level1" will return features more regular at level1 of the variable than at baseline.

### Value

A plot from plotCells or plotExplore, throws an error when no features meet the criteria

### See Also

[plotCells](#), [plotExplore](#), [fitLMMs](#)

### Examples

```
example(fitLMMs, "smoppix")
plotTopResults(hypYang, lmmModels, "nn")
#For the sake of illustration, set high significance level, as example dataset is small
plotTopResults(hypYang, lmmModels, "nn",
  effect = "day", what = "reg",
  effectParameter = "day0", sigLevel = 1-1e-10)
```

---

plotWf

*Plot the variance weighting function*

---

### Description

The observation weights are plotted as a function of number of events. For a univariate PI, this is a line plot, for a bivariate PI this is a scatterplot of majority gene as a function of minority gene, with the weight represented as a colour scale. The minority respectively majority gene are the genes in the gene pair with least and most events

### Usage

```
plotWf(obj, pi = obj$pis[1])
```



**Arguments**

obj                    The result of a call to [addWeightFunction](#)  
 pi                    The PI for which to plot the weighting function

**Value**

For univariate PI, returns a line plot; for bivariate PI a ggplot object

**Examples**

```
example(addWeightFunction, "smoppix")
plotWf(yangObj, "nn")
```

---

|          |                                             |
|----------|---------------------------------------------|
| selfName | <i>Name a character vector after itself</i> |
|----------|---------------------------------------------|

---

**Description**

Name a character vector after itself

**Usage**

```
selfName(x)
```

**Arguments**

x                    The vector to be names

**Value**

the named vector

**Examples**

```
selfName(LETTERS[1:5])
```

---

|         |                                                                                          |
|---------|------------------------------------------------------------------------------------------|
| smoppix | <i>smoppix: Analyze Single Molecule Spatial Omics Data Using the Probabilistic Index</i> |
|---------|------------------------------------------------------------------------------------------|

---

**Description**

Test for univariate and bivariate spatial patterns in spatial omics data with single-molecule resolution. The tests implemented allow for analysis of nested designs and are automatically calibrated to different biological specimens. Tests for aggregation, colocalization, gradients and vicinity to cell edge or centroid are provided.

**Author(s)**

**Maintainer:** Stijn Hawinkel <stijn.hawinkel@psb.ugent.be> ([ORCID](#))

**See Also**

Useful links:

- <https://github.com/sthawinke/smoppix>
- Report bugs at <https://github.com/sthawinke/smoppix/issues>

---

|        |                                          |
|--------|------------------------------------------|
| sortGp | <i>Sort feature pairs alphabetically</i> |
|--------|------------------------------------------|

---

**Description**

Sort feature pairs alphabetically

**Usage**

```
sortGp(featurePairs)
```

**Arguments**

featurePairs    The feature pairs to be sorted

**Value**

A character vector of the same length as the features, with pairs sorted

---

|             |                                                      |
|-------------|------------------------------------------------------|
| splitWindow | <i>Split a number of plots into rows and columns</i> |
|-------------|------------------------------------------------------|

---

**Description**

Split a number of plots into rows and columns

**Usage**

```
splitWindow(x)
```

**Arguments**

x                      The number of plots

**Value**

A vector of length 2 with required number of rows and columns

---

`subSampleP`*Subsample a point pattern when it is too large*

---

**Description**

Subsample a point pattern when it is too large

**Usage**

```
subSampleP(p, nSims, returnId = FALSE)
```

**Arguments**

|                       |                                                               |
|-----------------------|---------------------------------------------------------------|
| <code>p</code>        | The point pattern                                             |
| <code>nSims</code>    | The maximum size                                              |
| <code>returnId</code> | A boolean, should the id of the sampled elements be returned? |

**Value**

A point pattern, subsampled if necessary

---

`sund`*Helper function to spit gene pairs*

---

**Description**

Helper function to spit gene pairs

**Usage**

```
sund(x, sep = "--")
```

**Arguments**

|                  |                             |
|------------------|-----------------------------|
| <code>x</code>   | character string            |
| <code>sep</code> | The character used to split |

**Value**

The split string

**Examples**

```
GenePair <- "gene1--gene2"  
sund(GenePair)
```

---

writeToXlsx

*Write effect sizes and p-values results to excel worksheet*


---

## Description

The results of the linear models are written to an excel spreadsheet with different tabs for every sign (PI smaller than or larger than 0.5) of every PI, sorted by increasing p-value.

## Usage

```
writeToXlsx(obj, file, overwrite = FALSE, digits = 3, sigLevel = 0.05)
```

## Arguments

|           |                                                                                                                                                                                 |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| obj       | The results of linear model fitting                                                                                                                                             |
| file      | The file to write the results to                                                                                                                                                |
| overwrite | A boolean, should the file be overwritten if it exists already?                                                                                                                 |
| digits    | An integer, the number of significant digits to retain for the PI, raw and adjusted p-values                                                                                    |
| sigLevel  | The significance level threshold to use for the adjusted p-values, only features exceeding the threshold are written to the file. Set this parameter to 1 to write all features |

## Details

If no feature exceeds the significance threshold for a certain pi and parameter combination, an empty tab is created. For fixed effects, a single tab is written for PI differences of any sign. The "baseline" tabs indicate the overall patterns, the other tabs are named after the fixed effects and indicate departure from this baseline depending on this fixed effect

## Value

Returns invisible with a message when writing operation successful, otherwise throws an error.

## See Also

[createWorkbook](#), [writeData](#), [addWorksheet](#), [saveWorkbook](#)

## Examples

```
example(fitLMMs, "smoppix")
writeToXlsx(lmmModels, "tmpFile.xlsx")
file.remove("tmpFile.xlsx")
```

---

Yang*Spatial transcriptomics data of Selaginella moellendorffii roots*

---

**Description**

Single-molecule spatial transcriptomics smFISH data of *Selaginella moellendorffii* roots of a replicated experiment by (Yang et al. 2023). Molecule locations, gene identity and design variables are included. Only a subset of the data, consisting of roots 1-3 and sections 1-5 is included in the package for computational and memory reasons. The data are in table format to illustrate conversion to [hyperframe](#) using [buildHyperFrame](#).

**Usage**

```
data(Yang)
```

**Format**

A data matrix

**x,y** Molecule coordinates

**gene** Character vector with gene identities

**root,section,day** Design variables

**Source**

[doi:10.1016/j.cub.2023.08.030](https://doi.org/10.1016/j.cub.2023.08.030)

**References**

Yang X, Poelmans W, Grones C, Lakehal A, Pevernagie J, Bel MV, Njo M, Xu L, Nelissen H, Rybel BD, Motte H, Beeckman T (2023). “Spatial transcriptomics of a lycophyte root sheds light on root evolution.” *Curr. Biol.*, **33**(19), 4069 - 4084. ISSN 0960-9822, [doi:10.1016/j.cub.2023.08.030](https://doi.org/10.1016/j.cub.2023.08.030).

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