# Package 'spaSim'

September 19, 2024

Title Spatial point data simulator for tissue images

```
Version 1.7.0
Date 2023-05-22
Description A suite of functions for simulating spatial patterns of cells in
      tissue images. Output images are multitype point data in SingleCellExperiment
      format. Each point represents a cell, with its 2D locations and cell type.
      Potential cell patterns include background cells, tumour/immune cell clusters,
      immune rings, and blood/lymphatic vessels.
License Artistic-2.0
URL https://trigosteam.github.io/spaSim/
BugReports https://support.bioconductor.org/t/spaSim
biocViews StatisticalMethod, Spatial, BiomedicalInformatics
Encoding UTF-8
Roxygen list(markdown = TRUE)
RoxygenNote 7.2.2
Imports ggplot2, methods, stats, dplyr, spatstat.geom,
      spatstat.random, SpatialExperiment, SummarizedExperiment, RANN
Depends R (>= 4.2.0)
LazyData true
Suggests RefManageR, BiocStyle, knitr, testthat (>= 3.0.0),
      sessioninfo, rmarkdown, markdown
Config/testthat/edition 3
VignetteBuilder knitr
git_url https://git.bioconductor.org/packages/spaSim
git_branch devel
git_last_commit ddcef2b
git_last_commit_date 2024-04-30
Repository Bioconductor 3.20
Date/Publication 2024-09-18
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```

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# **Description**

A data frame containing 4915 background cells on 2000 by 2000 size window

# Usage

bg1

# **Format**

A data frame with 4915 rows (cells) and 3 columns:

**Cell.X.Position** X coordinate **Cell.Y.Position** Y coordinate

Cell.Type cell type

# Description

Format a data frame object into a SpatialExperiment class object where the count assay is empty.

# Usage

 $format\_spe(df)$ 

#### **Arguments**

df

A data frame where each row contains information about a cell. The columns of the data frame will become the colData of the SpatialExperiment object.

#### Value

An SPE object

```
multiple_background_images
```

Simulate multiple background images (mixed cell types)

# Description

Generate a set of background images with different proportions of mixed cell types all at once. The default values for the arguments give an example of multiple image simulation which enable an automatic multiple image simulation without the specification of any argument.

## Usage

```
multiple_background_images(
  bg_sample = bg1,
  idents = c("Tumour", "Immune", "Others"),
  props = list(rep(0.1, 9), seq(0, 0.4, 0.05), seq(0.9, 0.5, -0.05)),
  plot_image = TRUE,
  plot_colours = NULL
)
```

# Arguments

bg\_sample A data frame or SpatialExperiment class object with locations of points rep-

resenting background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords() of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions". By

default use the internal bg1 background image.

idents String Vector. Names of the cell types to generate.

props List. Each element is a vector of proportions of the corresponding cell type. The

length of the vector is how many images to generate. All vectors should be of

the same length, also equal to the number of images.

plot\_image Boolean. Whether plot the simulated images or not. Default is TRUE.

plot\_colours String Vector. If plot\_image is TRUE, this param is the corresponding colours

for the idents arg. Default is NULL, the predefined colour vector would be

used for plotting.

# Value

A list of SPE objects

#### See Also

multiple\_images\_with\_clusters for simulating multiple images with clusters, and multiple\_images\_with\_immune for simulating multiple images with immune rings.

Other simulate multiple images functions: multiple\_images\_with\_clusters(), multiple\_images\_with\_immune\_ri

# **Examples**

```
idents <- c("Tumour","Immune","Others")
prop1 <- rep(0.1,9)
prop2 <- seq(0, 0.4, 0.05)
prop3 <- seq(0.9,0.5,-0.05)
set.seed(610)
bg_image_list <- multiple_background_images(bg_sample = bg1,
idents = idents, props = list(prop1, prop2, prop3), plot_image = FALSE)</pre>
```

multiple\_images\_with\_clusters

Simulate multiple images with clusters

# Description

Generate a set of images with different cluster properties. Trying out the default parameters is recommended for understanding this function. The default values for the arguments give an example of multiple image simulation which enable an automatic multiple image simulation without the specification of any argument.

# Usage

```
multiple_images_with_clusters(
   bg_sample = bg1,
   cluster_shape = 2,
   prop_infiltration = 0.1,
   cluster_size = seq(200, 1000, 100),
   cluster_loc_x = 0,
   cluster_loc_y = 0,
   plot_image = TRUE,
   plot_categories = NULL,
   plot_colours = NULL
)
```

## **Arguments**

bg\_sample

A data frame or SpatialExperiment class object with locations of points representing background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords() of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions". By default use the internal bg1 background image.

cluster\_shape

Number. Choose from one of the following pre-designed shapes (1 or 2 for tumour cluster or 3 for immune cluster). The pre-designed shape contains information of the cell names of the cluster, the infiltration cell types, the proportions of infiltration, the cluster size, and the cluster centre locations. In order

to simulate a set of images, use the arguments below to specify the ranges of the properties. The predefined cell types can not be changed, while users can change them manually after the simulation.

#### prop\_infiltration

Numeric Vector. The degree of infiltration. If numeric, all simulated images have the same infiltration degree. If vector, images with a range of different infiltration proportions will be simulated.

cluster\_size Numeric Vector. The size of the cluster. If numeric, all simulated images have the same cluster size. If vector, images with a range of different cluster sizes

will be simulated. The size should not exceed the limit of the image sides.

cluster\_loc\_x Numeric or Vector. The X location of the cluster center offset. If numeric, all simulated images have the same center X location. If vector, images with a

range of different center locations will be simulated.

cluster\_loc\_y Numeric or Vector of the same length of cluster\_loc\_x. The Y location of the

cluster center offset.

plot\_image Boolean Whether plot the simulated images or not.Default is TRUE.

plot\_categories

String Vector specifying the order of the cell categories to be plotted. Default is NULL - the cell categories under the "Cell.Type" column would be used for

plotting.

 $\verb|plot_colours| String Vector specifying the order of the colours that correspond to the \verb|plot_categories| \\$ 

arg. Default is NULL - the predefined colour vector would be used for plotting.

#### Value

A list of SPE objects

# See Also

multiple\_background\_images for simulating multiple mixed background images, and multiple\_images\_with\_immur for simulating multiple images with immune rings.

Other simulate multiple images functions: multiple\_background\_images(), multiple\_images\_with\_immune\_rings

# **Examples**

```
set.seed(610)
cluster_image_list <- multiple_images_with_clusters(bg_sample=bg1,
cluster_shape=2, prop_infiltration=0.1, cluster_size = seq(200,1000,100),
cluster_loc_x = 0, cluster_loc_y = 0, plot_image = TRUE)</pre>
```

```
multiple_images_with_immune_rings
```

Simulate multiple images with immune rings

# Description

Generate a set of images with different immune ring properties. The default values for the arguments give an example of multiple image simulation which enable an automatic multiple image simulation without the specification of any argument.

#### **Usage**

```
multiple_images_with_immune_rings(
  bg_sample = bg1,
  cluster_size = 200,
  ring_shape = 1,
  prop_infiltration = 0,
  ring_width = seq(50, 100, 10),
  cluster_loc_x = 0,
  cluster_loc_y = 0,
  prop_ring_infiltration = seq(0, 0.2, 0.05),
  plot_image = TRUE,
  plot_categories = NULL,
  plot_colours = NULL
)
```

#### **Arguments**

bg\_sample

A data frame or SpatialExperiment class object with locations of points representing background cells. Further cell types will be simulated based on this background sample. The data frame or the spatialCoords() of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions". By default use the internal bg1 background image.

cluster\_size

Numeric Vector. The size of the cluster. If numeric, all simulated images have the same cluster size. If vector, images with a range of different cluster sizes will be simulated. The size should not exceed the limit of the image sides.

ring\_shape

Number. Choose from one of the following pre-designed shapes (1,2 or 3). The pre-designed shape contains information of the cell names of the cluster, the infiltration cell types, the proportions of infiltration, the cluster size, the ring width, the proportions of infiltrated cells into immune rings and the cluster centre locations. In order to simulate a set of images, use the arguments below to specify the ranges of the properties. The predefined cell types can not be changed, while users can change them manually after the simulation.

prop\_infiltration

Numeric Vector. The degree of infiltration. If numeric, all simulated images have the same infiltration degree. If vector, images with a range of different infiltration proportions will be simulated.

ring\_width

Numeric Vector. The width of the immune ring. If numeric, all simulated images have the same ring width. If vector, images with a range of different ring widths will be simulated.

cluster\_loc\_x

Numeric or Vector. The X location of the cluster center offset. If numeric, all simulated images have the same center X location. If vector, images with a range of different center locations will be simulated.

cluster\_loc\_y

Numeric or Vector of the same length of cluster\_loc\_x. The Y location of the cluster center offset.

prop\_ring\_infiltration

Numeric or Vector. The degree of tumour infiltration in the region of immune rings.

plot\_image

Boolean Whether plot the simulated images or not. Default is TRUE.

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```
plot_categories
```

String Vector specifying the order of the cell cateories to be plotted. Default is NULL - the cell categories under the "Cell.Type" column would be used for plotting.

plot\_colours

String Vector specifying the order of the colours that correspond to the plot\_categories arg. Default is NULL - the predefined colour vector would be used for plotting.

#### Value

A list of spe objects

#### See Also

multiple\_background\_images for simulating multiple mixed background images, and multiple\_images\_with\_clust for simulating multiple images with clusters.

Other simulate multiple images functions: multiple\_background\_images(), multiple\_images\_with\_clusters()

## **Examples**

```
set.seed(610)
ring_image_list <- multiple_images_with_immune_rings(bg_sample = bg1,
ring_shape = 1, prop_infiltration = 0, ring_width = seq(50,100,10),
cluster_size = 200, cluster_loc_x = 0, cluster_loc_y = 0,
prop_ring_infiltration = seq(0, 0.2,0.05), plot_image = TRUE)</pre>
```

plot\_cells

plot\_cells

# **Description**

Produces a scatter plot of the cells in the tissue. Cells are coloured categorically by Cell.Type column. Cell categories not specified will be coloured "lightgrey" and labled "Unspecified".

# Usage

```
plot_cells(
   spe_object,
   categories_of_interest = NULL,
   colour_vector = NULL,
   feature_colname = "Cell.Type"
)
```

# **Arguments**

feature\_colname

String specifying the column the cell categories belong to.

#### Value

A plot is returned

# Description

Simulate cell locations. The 2D locations of the cells are simulated and plotted in a rectangular window. Users can specify the window size, cell number and the minimum distance between two cells. All cells have the same cell type, specified by the "Cell.Type" param.

# Usage

```
simulate_background_cells(
    n_cells,
    width,
    height,
    method = "Hardcore",
    min_d,
    oversampling_rate = 1.2,
    jitter = 0.3,
    Cell.Type = "Others",
    plot_image = TRUE
)
```

## **Arguments**

n_cells Numeric. Number of cells to simulate in the background
--

width, height Numeric. The width and height of the image.

method String. The distribution model for the background cells. Options are "Hardcore"

for tumour tissues and "Even" for normal tissues. Default is "Hardcore".

min\_d (OPTIONAL) Numeric. Use when method is "Hardcore". The minimum dis-

tance between two cells.

oversampling\_rate

(OPTIONAL) Numeric. Use when method is "Hardcore". The multiplier for oversampling. Without oversampling, the simulation deletes cells that are within min\_d from each other, resulting in a less total number of cells than n\_cells. Default is 1.2 (this should be set based on n\_cells and min\_d; should always

be larger than 1).

jitter (OPTIONAL) Numeric. Use when method is "Even". The uniform distribution

parameter to generate the jitter distance for each cell from the vertices of the

hexagon.

Cell. Type (OPTIONAL) String. The name of the background cell type. Default is "Others"

since there shouldn't be any identity of the background cells.

plot\_image (OPTIONAL) Boolean. Default is TRUE.

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#### **Details**

There are two options for the background cell distribution model. 1) Hardcore model for tumour tissues. This model uses rHardcore spatstat.random. Since rHardcore deletes cells that are within the distance of min\_d to another cell, resulting in fewer cell specified by users, we here introduce parameter oversampling\_rate to generate more cells than specified. 2) Normal tissues use an evenly-spaced model where the cells are distributed approximately according to the vertices of a hexagon. The function accomplishes this by generating cells on a hexagonal grid and individually applying a bounded uniform random jitter. In our algorithm, jitter is the parameter to define the uniform distribution of the jitter of the cells from the hexagon vertices. If there is a reference image, jitter can be estimated by comparing the average minimum distance between cells of the simulated image and the reference image. If without a reference image, We suggest 0.3 as the default value of jitter as this gives a sensible outcome.

#### Value

A data frame of the simulated background image

#### See Also

```
simulate_mixing for mixed background simulation, simulate_clusters for cluster simulation, simulate_immune_rings/simulate_double_rings for immune ring simulation, and simulate_stripes for vessel simulation.
```

```
Other simulate pattern functions: simulate_clusters(), simulate_double_rings(), simulate_immune_rings(), simulate_mixing(), simulate_stripes()
```

## **Examples**

simulate\_clusters

Simulate clusters

#### **Description**

Based on an existing background image, simulate clusters of cells where the same type of cells aggregate. The default values for the arguments give an example of cluster simulation which enable an automatic simulation of clusters without the specification of any argument.

# Usage

```
simulate_clusters(
  bg_sample = bg1,
  n_clusters = 2,
  bg_type = "Others",
  cluster_properties = list(C1 = list(name_of_cluster_cell = "Tumour", size = 300, shape
```

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```
= "Oval", centre_loc = data.frame(x = 500, y = 500), infiltration_types =
    c("Immune1", "Others"), infiltration_proportions = c(0.1, 0.05)), C2 =
    list(name_of_cluster_cell = "Immune1", size = 500, shape = "Irregular", centre_loc =
    data.frame(x = 1500, y = 500), infiltration_types = c("Immune2", "Others"),
    infiltration_proportions = c(0.1, 0.05))),
    plot_image = TRUE,
    plot_categories = NULL,
    plot_colours = NULL
)
```

#### Arguments

bg\_sample (OPTIONAL) A data frame or SpatialExperiment class object with locations

of points representing background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords() of

the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions".

By default use the internal bg1 background image.

n\_clusters Numeric. Number of clusters. This must match the length(cluster\_properties).

bg\_type (OPTIONAL) String. The name of the background cell type if the background

sample does not have a "Cell.Type" column. By default is "Others".

cluster\_properties

List of properties of the clusters. See examples for the format of this arg.

plot\_image Boolean. Whether the simulated image is plotted.

plot\_categories

String Vector specifying the order of the cell categories to be plotted. Default is NULL - the cell categories under the "Cell.Type" column would be used for

plotting.

plot\_colours String Vector specifying the order of the colours that correspond to the plot\_categories

arg. Default is NULL - the predefined colour vector would be used for plotting.

## Value

A data.frame of the simulated image

# See Also

simulate\_background\_cells for all cell simulation, simulate\_mixing for mixed background simulation, simulate\_immune\_rings/simulate\_double\_rings for immune ring simulation, and simulate\_stripes for vessel simulation.

Other simulate pattern functions: simulate\_background\_cells(), simulate\_double\_rings(), simulate\_immune\_rings(), simulate\_mixing(), simulate\_stripes()

#### **Examples**

```
set.seed(610)
cluster_image <- simulate_clusters(bg_sample = bg1,
n_clusters=2, cluster_properties=list(C1=list(name_of_cluster_cell="Tumour",
size=300, shape="0val", centre_loc=data.frame("x"=500, "y"=500),
infiltration_types=c("Immune1", "Others"), infiltration_proportions=c(0.1, 0.05)),
C2=list(name_of_cluster_cell="Immune1", size=500, shape="Irregular",
centre_loc=data.frame("x"=1500,"y"=500), infiltration_types=c("Immune2", "Others"),
infiltration_proportions=c(0.1, 0.05))))</pre>
```

simulate\_double\_rings Simulate double immune rings

## **Description**

Based on an existing background image, simulate double rings of immune cells that surround tumour clusters. The inner ring is the internal margin of a tumour cluster. The outer ring is the external tumour margin. The tumour clusters and the double immune rings are simulated at the same time. The default values for the arguments give an example of double ring simulation which enable an automatic simulation of double rings without the specification of any argument.

#### Usage

```
simulate_double_rings(
  bg_sample = bg1,
 bg_type = "Others",
 n_dr = 2,
 dr_properties = list(D1 = list(name_of_cluster_cell = "Tumour", size = 300, shape =
    "Circle", centre_loc = data.frame(x = 1000, y = 1000), infiltration_types =
  c("Immune1", "Immune2", "Others"), infiltration_proportions = c(0.15, 0.05, 0.05),
    name_of_ring_cell = "Immune1", immune_ring_width = 150,
  immune_ring_infiltration_types = c("Others"), immune_ring_infiltration_proportions =
    c(0.15), name_of_double_ring_cell = "Immune2", double_ring_width = 100,
  double_ring_infiltration_types = c("Others"), double_ring_infiltration_proportions =
    c(0.15)),
    D2 = list(name_of_cluster_cell = "Tumour", size = 300, shape =
    "Oval", centre_loc = data.frame(x = 1200, y = 1200), infiltration_types =
  c("Immune1", "Immune2", "Others"), infiltration_proportions = c(0.15, 0.05, 0.05),
    name_of_ring_cell = "Immune1", immune_ring_width = 150,
  immune_ring_infiltration_types = c("Others"), immune_ring_infiltration_proportions =
    c(0.15), name_of_double_ring_cell = "Immune2", double_ring_width = 100,
  double_ring_infiltration_types = c("Others"), double_ring_infiltration_proportions =
    c(0.15)),
  plot_image = TRUE,
 plot_categories = NULL,
 plot_colours = NULL
```

# **Arguments**

bg_sample	(OPTIONAL) A data frame or SpatialExperiment class object with locations of points representing background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords() of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions". By default use the internal bg1 background image.
bg_type	(OPTIONAL) String The name of the background cell type. By default is "Others".
n_dr	Number of double immune rings. This must match the length(dr_properties).
dr_properties	List of properties of the double immune rings. Please refer to the examples for the structure of dr_properties.

```
plot_image Boolean. Whether the simulated image is plotted.

plot_categories

String Vector specifying the order of the cell categories to be plotted. Default is NULL - the cell categories under the "Cell.Type" column would be used for plotting.

plot_colours

String Vector specifying the order of the colours that correspond to the plot_categories arg. Default is NULL - the predefined colour vector would be used for plotting.
```

#### Value

A data.frame of the simulated image

#### See Also

simulate\_background\_cells for all cell simulation, simulate\_mixing for mixed background simulation, simulate\_clusters for cluster simulation, simulate\_immune\_rings for single immune ring simulation, and simulate\_stripes for vessel simulation.

Other simulate pattern functions: simulate\_background\_cells(), simulate\_clusters(), simulate\_immune\_rings simulate\_mixing(), simulate\_stripes()

## **Examples**

```
# manually define the properties of the immune ring
dr_properties <- list(D1 = list(name_of_cluster_cell = "Tumour", size = 300,</pre>
shape = "Circle",centre_loc = data.frame("x" = 1000, "y" = 1000),infiltration_types
= c("Immune1", "Immune2", "Others"), infiltration_proportions = <math>c(0.15, 0.05, 0.05),
name_of_ring_cell = "Immune1",immune_ring_width = 150,immune_ring_infiltration_types
= c("Others"),immune_ring_infiltration_proportions = c(0.15),name_of_double_ring_cell
= "Immune2", double_ring_width = 100, double_ring_infiltration_types = c("Others"),
double_ring_infiltration_proportions = c(0.15)),
D2 = list(name_of_cluster_cell = "Tumour", size = 300, shape = "Oval", centre_loc
= data.frame("x" = 1200, "y" = 1200), infiltration_types = c("Immune1", "Immune2", "Others"),
infiltration\_proportions = c(0.15, 0.05, 0.05), name\_of\_ring\_cell = "Immune1", other infiltration\_proportions = c(0.15, 0.05, 0.05), name\_of\_ring\_cell = "Immune1", other infiltration\_proportions = c(0.15, 0.05, 0.05), name\_of\_ring\_cell = "Immune1", other infiltration\_proportions = c(0.15, 0.05, 0.05), name\_of\_ring\_cell = "Immune1", other infiltration\_proportions = c(0.15, 0.05), other infiltration\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_proportion\_propo
immune_ring_width = 150,immune_ring_infiltration_types = c("Others"),
immune\_ring\_infiltration\_proportions = c(0.15), name\_of\_double\_ring\_cell = "Immune2",
double_ring_width = 100,double_ring_infiltration_types = c("Others"),
double_ring_infiltration_proportions = c(0.15))
double_ring_image <- simulate_double_rings(bg_sample = bg1,</pre>
n_dr = 2, dr_properties = dr_properties)
```

```
simulate_immune_rings simulate_immune_rings
```

#### **Description**

Based on an existing background image, simulate rings of immune cells that surround tumour clusters. The tumour clusters and immune rings are simulated at the same time. The default values for the arguments give an example of immune ring simulation which enable an automatic simulation of immune rings without the specification of any argument.

#### Usage

```
simulate_immune_rings(
 bg_sample = bg1,
 bg_type = "Others",
 n_{ir} = 2,
 ir_properties = list(I1 = list(name_of_cluster_cell = "Tumour", size = 600, shape =
    "Circle", centre_loc = data.frame(x = 930, y = 1000), infiltration_types =
  c("Immune1", "Immune2", "Others"), infiltration_proportions = <math>c(0.15, 0.05, 0.05),
    name_of_ring_cell = "Immune1", immune_ring_width = 150,
  immune_ring_infiltration_types = c("Others"), immune_ring_infiltration_proportions =
  c(0.15)), I2 = list(name_of_cluster_cell = "Tumour", size = 500, shape = "Oval",
   centre_loc = data.frame(x = 1330, y = 1100), infiltration_types = c("Immune1",
    "Immune2", "Others"), infiltration_proportions = c(0.15, 0.05, 0.05),
    name_of_ring_cell = "Immune1", immune_ring_width = 150,
  immune_ring_infiltration_types = c("Others"), immune_ring_infiltration_proportions =
    c(0.15)),
  plot_image = TRUE,
 plot_categories = NULL,
 plot_colours = NULL
)
```

#### **Arguments**

bg_sample	(OPTIONAL) A data frame or SpatialExperiment class object with locations of points representing background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords() of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions". By default use the internal bg1 background image.			
bg_type	(OPTIONAL) String The name of the background cell type. By default is "Others".			
n_ir	Number of immune rings. This must match the arg length(ir_properties).			
ir_properties	List of properties of the immune rings. Please refer to the examples for the structure of ir_properties.			
plot_image	Boolean. Whether the simulated image is plotted.			
plot_categories				
	String Vector specifying the order of the cell categories to be plotted. Default is NULL - the cell categories under the "Cell.Type" column would be used for plotting.			
plot_colours	String Vector specifying the order of the colours that correspond to the plot_categories arg. Default is NULL - the predefined colour vector would be used for plotting.			

#### Value

A data.frame of the simulated image

# See Also

simulate\_background\_cells for all cell simulation, simulate\_mixing for mixed background simulation, simulate\_clusters for cluster simulation, simulate\_double\_rings for double immune ring simulation, and simulate\_stripes for vessel simulation.

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Other simulate pattern functions: simulate\_background\_cells(), simulate\_clusters(), simulate\_double\_rings simulate\_mixing(), simulate\_stripes()

#### **Examples**

```
set.seed(610)
# manually define the properties of the immune ring
ir_properties <- list(I1=list(name_of_cluster_cell="Tumour", size=600,
shape="Circle",centre_loc=data.frame("x"=930, "y"=1000),
infiltration_types=c("Immune1", "Immune2", "Others"), infiltration_proportions
=c(0.15, 0.05, 0.05), name_of_ring_cell="Immune1", immune_ring_width=150,
immune_ring_infiltration_types=c("Others"), immune_ring_infiltration_proportions=c(0.15)),
I2=list(name_of_cluster_cell="Tumour", size=500, shape="Oval",
centre_loc=data.frame("x"=1330, "y"=1100), infiltration_types=c("Immune1", "Immune2", "Others"),
infiltration_proportions=c(0.15, 0.05, 0.05), name_of_ring_cell="Immune1",
immune_ring_width=150, immune_ring_infiltration_types=c("Others"),
immune_ring_infiltration_proportions=c(0.15)))
# simulate immune rings (`n_ir` should match the length of `ir_properties`)
immune_ring_image <- simulate_immune_rings(bg_sample=bg1,
n_ir=2, ir_properties=ir_properties)</pre>
```

simulate\_mixing

Simulate mixed background image

#### **Description**

Based on an existing background image, simulate mixed cell types with specified cell types and proportions. The default values for the arguments give an example of mixed cell type simulation which enable an automatic simulation of mixed cell types without the specification of any argument.

# Usage

```
simulate_mixing(
  bg_sample = bg1,
  idents = c("Tumour", "Immune", "Others"),
  props = c(0.2, 0.4, 0.4),
  plot_image = TRUE,
  plot_colours = NULL
)
```

#### **Arguments**

bg_sample	(OPTIONAL) A data frame or SpatialExperiment class object with locations of points representing background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords() of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions". By default use the internal bg1 background image.
idents	String Vector of the mixed cell types.
props	Numeric Vector of the proportions of the mixed cell types.
plot_image	Boolean. Whether the simulated image is plotted.
plot colours	String Vector specifying the order of the colours that correspond to the idents

arg. Default is NULL - the predefined colour vector would be used for plotting..

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#### Value

A data.frame of the simulated image

#### See Also

simulate\_background\_cells for all cell simulation, simulate\_clusters for cluster simulation, simulate\_immune\_rings/simulate\_double\_rings for immune ring simulation, and simulate\_stripes for vessel simulation.

Other simulate pattern functions: simulate\_background\_cells(), simulate\_clusters(), simulate\_double\_rings simulate\_immune\_rings(), simulate\_stripes()

#### **Examples**

```
set.seed(610)
mix_background <- simulate_mixing(bg_sample=bg1,
idents=c("Tumour","Immune", "Others"), props=c(0.2, 0.4, 0.4),
plot_image=TRUE)</pre>
```

simulate\_stripes

simulate\_stripes

## **Description**

Based on an existing background image, simulate stripes of cells representing vessels. The cell types and widths of the stripes can be specified. The locations of the stripes are randomly simulated. Please refer to the examples to check what properties of the stripes can be specified. The default values for the arguments give an example of vessel simulation which enable an automatic simulation of vessels without the specification of any argument.

# Usage

```
simulate_stripes(
  bg_sample = bg1,
  n_stripe_type = 2,
  stripe_properties = list(S1 = list(number_of_stripes = 1, name_of_stripe_cell =
    "Others", width_of_stripe = 80, infiltration_types = c("Immune"),
    infiltration_proportions = c(0.08)), S2 = list(number_of_stripes = 1,
    name_of_stripe_cell = "Others", width_of_stripe = 80, infiltration_types =
    c("Immune"), infiltration_proportions = c(0.08))),
    plot_image = TRUE,
    plot_categories = NULL,
    plot_colours = NULL
)
```

# **Arguments**

bg\_sample

(OPTIONAL) A data frame or SpatialExperiment class object with locations of points representing background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords() of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions". By default use the internal bg1 background image.

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n\_stripe\_type Number of stripe types. Should be the same as length(stripe\_properties.

stripe\_properties

List of the properties of the stripes. See examples for the format of the properties. Please refer to the examples for the structure of stripe\_properties.

plot\_image Boolean. Whether the simulated image is plotted. Default is TRUE.

plot\_categories

String Vector specifying the order of the cell categories to be plotted. Default is NULL - the cell categories under the "Cell.Type" column would be used for plotting.

plot\_colours String Vector specifying the order of the colours that correspond to the plot\_categories arg. Default is NULL - the predefined colour vector would be used for plotting.

#### Value

A data.frame of the simulated image

#### See Also

simulate\_background\_cells for all cell simulation, simulate\_mixing for mixed background simulation, simulate\_clusters for cluster simulation, and simulate\_immune\_rings/simulate\_double\_rings for immune ring simulation

Other simulate pattern functions: simulate\_background\_cells(), simulate\_clusters(), simulate\_double\_rings simulate\_immune\_rings(), simulate\_mixing()

#### **Examples**

```
stripe_properties <- list(</pre>
S1 = list(
  number_of_stripes = 1,
  name_of_stripe_cell = "Others",
 width_of_stripe = 80,
  infiltration_types = c("Immune"),
  infiltration\_proportions = c(0.08)
), S2 = list(
  number_of_stripes = 1,
  name_of_stripe_cell = "Others",
  width_of_stripe = 80,
  infiltration_types = c("Immune"),
  infiltration\_proportions = c(0.08)))
set.seed(610)
stripe_image <- simulate_stripes(bg_sample = bg1, n_stripe_type=2,</pre>
stripe_properties = stripe_properties, plot_image = TRUE)
```

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# **Description**

Tissue Image Simulator (TIS) integrates the basic simulation functions in spaSim, including simulating (mixed) background image, clusters, immune rings, double immune rings and stripes. The patterns are simulated on separate layers sequentially (e.g. immune rings are simulated after/on top of background cells). And each layer is also plot sequentially.

Pattern properties (e.g. properties\_of\_clusters) contain the properties of a pattern in the format of list where each element is one pattern. These properties need to be manually defined. Details about the format of the properties see the examples in simulate\_clusters simulate\_immune\_rings simulate\_double\_rings simulate\_stripes

## Usage

```
TIS(
  bg_sample = NULL,
  n_{cells} = NULL,
  width = NULL,
  height = NULL,
  bg_method = NULL,
  min_d = NULL,
  oversampling_rate = 1.2,
  jitter = 0.3,
  names_of_bg_cells = NULL,
  proportions_of_bg_cells = NULL,
  n_clusters = NULL,
  properties_of_clusters = NULL,
  n_immune_rings = NULL,
  properties_of_immune_rings = NULL,
  n_double_rings = NULL,
  properties_of_double_rings = NULL,
  n_stripe_type = NULL,
  properties_of_stripes = NULL,
  image_name = NULL,
  plot_image = FALSE,
  plot_categories = NULL,
  plot_colours = NULL
```

# **Arguments**

bg_sample	(OPTIONAL) A data frame or SpatialExperiment class object with locations of points representing background cells. Further cell types will be simulated based on this background sample. The data.frame or the spatialCoords of the SPE object should have colnames including "Cell.X.Positions" and "Cell.Y.Positions".
	By default use the internal bg1 background image.
n_cells	(OPTIONAL) Number of background cells to simulate. Only when bg_sample is NULL.
width	(OPTIONAL) Number The width of the image.
height	(OPTIONAL) Number The height of the image.
bg_method	(OPTIONAL) String specifying the distribution of the background cells. Choose from "Hardcore" and "Even".
min_d	(OPTIONAL) Number The minimum distance between two cells.

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oversampling\_rate

(OPTIONAL) Numeric. The multiplier for oversampling. Without oversampling, the simulation deletes cells that are within min\_d from each other, resulting in a less total number of cells than n\_cells. Default is 1.2 (this should be set based on n\_cells and min\_d; should always be larger than 1).

jitter

(OPTIONAL) Numeric. Use when method is "Even". The uniform distribution parameter to generate the jitter distance for each cell from the vertices of the hexagon.

names\_of\_bg\_cells

(OPTIONAL) Vector The cell types of the background cells. If NULL, the background cells are of one type.

proportions\_of\_bg\_cells

(OPTIONAL) Vector The corresponding proportion of each cell type in the background cells.

 $\label{eq:nclusters} \mbox{n\_clusters} \quad \mbox{(OPTIONAL) Number of cell clusters. If NULL, no clusters to simulate.} \\ \mbox{properties\_of\_clusters}$ 

(OPTIONAL) List of parameters to define the clusters.

 $\label{eq:n_immune_rings} \textbf{(OPTIONAL) Number of immune rings. If NULL, no immune rings to simulate.} \\ \textbf{properties\_of\_immune\_rings}$ 

(OPTIONAL) List of parameters to define the immune rings.

n\_double\_rings (OPTIONAL) Number of double immune rings. If NULL, no double rings to simulate.

properties\_of\_double\_rings

(OPTIONAL) List of parameters to define the double immune rings.

 $\label{eq:n_stripe_type} \textbf{(OPTIONAL) Number of stripe (vessel) types. If NULL, no stripes to simulate.} \\ \textbf{properties\_of\_stripes}$ 

(OPTIONAL) List of parameters to define the stripes.

image\_name (OPTIONAL) String to name the output tissue image.

plot\_image Boolean. Whether the simulated image is plotted.

plot\_categories

String Vector specifying the order of the cell categories to be plotted. Default is NULL - the cell categories under the "Cell.Type" column would be used for plotting.

plot\_colours

String Vector specifying the order of the colours that correspond to the plot\_categories arg. Default is NULL - the predefined colour vector would be used for plotting.

#### Value

An spe object of the simulated image

#### **Examples**

```
set.seed(610)
double_ring_image <- TIS(bg_sample=bg1, n_clusters=1,
properties_of_clusters=list(C1=list( name_of_cluster_cell="Tumour",
size=300, shape="Oval", centre_loc=data.frame("x"=500, "y"=500),
infiltration_types=c("Immune1", "Others"), infiltration_proportions=c(0.1, 0.05))),
plot_image=TRUE)</pre>
```

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