

Package ‘SpaTalk’

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Title Infer Cell-Cell Communication for Spatial Transcriptomics

Version 1.0

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Description This package can infer cell-cell communication for spatial transcriptomics.

License GPL (>= 3)

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scales, scatterpie, pheatmap, corrplot, circlize, ggraph,
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VignetteBuilder knitr

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Author Xin Shao [aut, cre] (<<https://orcid.org/0000-0002-1928-3878>>)

Maintainer Xin Shao <xin_shao@zju.edu.cn>

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createSpaTalk	<i>SpaTalk object</i>
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Description

create SpaTalk object using spatial transcriptomics data.

Usage

```
createSpaTalk(st_data, st_meta, species, if_st_is_sc, spot_max_cell)
```

Arguments

st_data	A matrix containing counts of spatial transcriptomics, each column representing a spot or a cell, each row representing a gene.
st_meta	A data.frame containing coordinate of spatial transcriptomics with three columns, namely 'spot', 'x', 'y' for spot-based spatial transcriptomics data or 'cell', 'x', 'y' for single-cell spatial transcriptomics data.
species	A character meaning species of the spatial transcriptomics data. 'Human' or 'Mouse'.
if_st_is_sc	A logical meaning if it is single-cell spatial transcriptomics data. TRUE is FALSE.
spot_max_cell	A integer meaning max cell number for each plot to predict. If if_st_sc is FALSE, please determine the spot_max_cell.

Value

SpaTalk object

dec_cci	<i>Decomposing cell-cell communications for spatial transcriptomics data</i>
---------	--

Description

Identify the cell-cell communications for single-cell or spot-based spatial transcriptomics data with proximal ligand-receptor-target interactions.

Usage

```
dec_cci(
  object,
  celltype_sender,
  celltype_receiver,
  n_neighbor = 10,
  min_pairs = 5,
  min_pairs_ratio = 0,
  per_num = 1000,
  pvalue = 0.05,
  co_exp_ratio = 0.1
)
```

Arguments

object	SpaTalk object after find_lr_path .
celltype_sender	Name of celltype_sender.
celltype_receiver	Name of celltype_receiver.
n_neighbor	Number of neighbor cells to select as the proximal cell-cell pair. Default is 10.
min_pairs	Min proximal cell-cell pairs between for sending and receiving cell types. Default is 5.
min_pairs_ratio	Min proximal cell-cell pairs ratio between for sending and receiving cell types. Default is 0.
per_num	Number of repeat times for permutation test. Default is 1000.
pvalue	Include the significantly proximal LR pairs with this cutoff of p value from permutation test. Default is 0.05.
co_exp_ratio	Min cell ratio in receiving cells with co-expressed source and target genes for predicting the downstream pathway activity.

Value

SpaTalk object containing the inferred LR pairs and pathways.

dec_cci_all	<i>Decomposing cell-cell communications for spatial transcriptomics data</i>
-------------	--

Description

Identify the all cell-cell communications for single-cell or spot-based spatial transcriptomics data with proximal ligand-receptor-target interactions.

Usage

```
dec_cci_all(
  object,
  n_neighbor = 10,
  min_pairs = 5,
  min_pairs_ratio = 0,
  per_num = 1000,
  pvalue = 0.05,
  co_exp_ratio = 0.1
)
```

Arguments

object	SpaTalk object after find_lr_path .
n_neighbor	Number of neighbor cells to select as the proximal cell-cell pair. Default is 10.
min_pairs	Min proximal cell-cell pairs between for sending and receiving cell types. Default is 5.
min_pairs_ratio	Min proximal cell-cell pairs ratio between for sending and receiving cell types. Default is 0.
per_num	Number of repeat times for permutation test. Default is 1000.
pvalue	Include the significantly proximal LR pairs with this cutoff of p value from permutation test. Default is 0.05.
co_exp_ratio	Min cell ratio in receiving cells with co-expressed source and target genes for predicting the downstream pathway activity.

Value

SpaTalk object containing the inferred LR pairs and pathways.

dec_celltype

*Decomposing cell type for spatial transcriptomics data***Description**

Identify the cellular composition for single-cell or spot-based spatial transcriptomics data with non-negative regression.

Usage

```
dec_celltype(
  object,
  sc_data,
  sc_celltype,
  min_percent = 0.5,
  min_nFeatures = 10,
  if_use_normalize_data = T,
  if_use_hvg = F,
  if_use_all_cores = T,
  iter_num = 1000
)
```

Arguments

object	SpaTalk object generated from createSpaTalk .
sc_data	A matrix containing counts of single-cell RNA-seq data as the reference, each column representing a cell, each row representing a gene.
sc_celltype	A character containing the cell type of the reference single-cell RNA-seq data.
min_percent	Min percent to predict new cell type for single-cell st_data or predict new cell for spot-based st_data. Default is 0.5.
min_nFeatures	Min number of expressed features/genes for each spot/cell in st_data. Default is 10.
if_use_normalize_data	Whether to use normalized st_data and sc_data with Seurat normalization. Default is TRUE. set it FALSE when the st_data and sc_data are already normalized matrix with other methods.
if_use_hvg	Whether to use highly variable genes for non-negative regression. Default is FALSE.
if_use_all_cores	Whether to use all CPU cores. Default is TRUE.
iter_num	Number of iteration to generate the single-cell data for spot-based data. Default is 1000.

Value

SpaTalk object containing the decomposing results.

demo_geneinfo	<i>Demo data of geneinfo</i>
---------------	------------------------------

Description

Demo data of geneinfo

Usage

```
demo_geneinfo()
```

Details

geneinfo used in `dec_celltype` must be a `data.frame` object with three columns, namely 'symbol', 'synonyms', 'species'.

Examples

```
geneinfo_demo <- demo_geneinfo()
```

demo_lrpairs	<i>Demo data of lrpairs</i>
--------------	-----------------------------

Description

Demo data of lrpairs

Usage

```
demo_lrpairs()
```

Details

lrpairs used in `dec_cci` must be a `data.frame` object with three columns, namely 'ligand', 'receptor', 'species'.

Value

A `data.frame`.

Examples

```
lrpairs_demo <- demo_lrpairs()
```

demo_pathways	<i>Demo data of pathways</i>
---------------	------------------------------

Description

Demo data of pathways

Usage

```
demo_pathways()
```

Details

pathways used in [dec_cci](#) must be a data.frame object with seven columns, namely 'src', 'dest', 'pathway', 'source', 'type', 'src_tf', 'dest_tf', 'species'.

Value

A data.frame.

Examples

```
pathways_demo <- demo_pathways()
```

demo_sc_data	<i>Demo data of sc_data</i>
--------------	-----------------------------

Description

Demo data of sc_data.

Usage

```
demo_sc_data()
```

Details

sc_data used in [dec_celltype](#) must be a matrix object, each column representing a cell, each row representing a gene.

Value

A matrix.

Examples

```
sc_data_demo <- demo_sc_data()
```

demo_st_data	<i>Demo data of st_data</i>
--------------	-----------------------------

Description

Demo data of st_data.

Usage

```
demo_st_data()
```

Details

st_data used in [dec_celltype](#) must be a matrix object, each column representing a spot, each row representing a gene.

Value

A matrix.

Examples

```
st_data_demo <- demo_st_data()
```

demo_st_meta	<i>Demo data of st_meta</i>
--------------	-----------------------------

Description

Demo data of st_meta

Usage

```
demo_st_meta()
```

Details

st_meta used in [dec_celltype](#) must be a data.frame object with three columns, namely 'spot', 'x', 'y' for spot-based spatial transcriptomics data.

Value

A data.frame.

Examples

```
st_meta_demo <- demo_st_meta()
```

demo_st_sc_data	<i>Demo data of single-cell st_data</i>
-----------------	---

Description

Demo data of single-cell st_data.

Usage

```
demo_st_sc_data()
```

Details

st_data used in `dec_celltype` must be a matrix object, each column representing a cell, each row representing a gene.

Value

A matrix.

Examples

```
st_data_demo <- demo_st_sc_data()
```

demo_st_sc_meta	<i>Demo data of st_sc_meta</i>
-----------------	--------------------------------

Description

Demo data of st_sc_meta

Usage

```
demo_st_sc_meta()
```

Details

st_sc_meta used in `dec_celltype` must be a data.frame object with three columns, namely 'cell', 'x', 'y' for single-cell spatial transcriptomics data.

Value

A data.frame.

Examples

```
st_sc_meta_demo <- demo_st_sc_meta()
```

find_lr_path	<i>Find lrpairs and pathways</i>
--------------	----------------------------------

Description

Find lrpairs and pathways with receptors having downstream targets and transcriptional factors.

Usage

```
find_lr_path(object, lrpairs, pathways, max_hop = NULL)
```

Arguments

object	SpaTalk object generated from dec_celltype .
lrpairs	A data.frame of the system data containing ligand-receptor pairs of 'Human' and 'Mouse' from CellTalkDB.
pathways	A data.frame of the system data containing gene-gene interactions and pathways from KEGG and Reactome as well as the information of transcriptional factors.
max_hop	Max hop from the receptor to the downstream target transcriptional factor to find for receiving cells. Default is 3 for human and 4 for mouse.

Value

SpaTalk object containing the filtered lrpairs and pathways.

geneinfo	<i>geneinfo</i>
----------	-----------------

Description

Gene symbols of 'Human' and 'Mouse' updated on June 30, 2021 for revising count matrix.

Usage

```
geneinfo
```

Format

An object of class `data.frame` with 250934 rows and 3 columns.

Source

<https://www.ncbi.nlm.nih.gov/gene>

generate_spot	<i>Generate pseudo spot st_data</i>
---------------	-------------------------------------

Description

Generate pseudo spot st_data with single-cell st_data

Usage

```
generate_spot(st_data, st_meta, x_min, x_res, x_max, y_min, y_res, y_max)
```

Arguments

st_data	A matrix containing counts of spatial transcriptomics, each column representing a cell, each row representing a gene.
st_meta	A data.frame containing coordinate of spatial transcriptomics with three columns, 'cell', 'x', 'y', and celltype.
x_min	Min value of x axis.
x_res	Resolution of x coordinate.
x_max	Max value of x axis.
y_min	Min value of y axis.
y_res	Resolution of y coordinate.
y_max	Max value of y axis.

Value

A list of spot st_data and st_meta

get_lr_path	<i>Get LR and downstream pathways</i>
-------------	---------------------------------------

Description

Get LR and downstream pathways and get p value of receptor-related pathways with LR-target genes by the Fisher-exact test.

Usage

```
get_lr_path(
  object,
  celltype_sender,
  celltype_receiver,
  ligand,
  receptor,
  min_gene_num = 5
)
```

Arguments

object SpaTalk object generated from [dec_cci](#).
 celltype_sender Name of celltype_sender.
 celltype_receiver Name of celltype_receiver.
 ligand Name of ligand from celltype_sender.
 receptor Name of receptor from celltype_receiver.
 min_gene_num Min genes number for each pathway.

Value

A list containing two data.frame. One is LR and downstream pathways, another is the p value of receptor-related pathways with LR-target genes.

lrpairs	<i>lrpairs</i>
---------	----------------

Description

Ligand-receptor pairs of 'Human' and 'Mouse' containing 3398 human and 2033 mouse pairs.

Usage

lrpairs

Format

An object of class data.frame with 5431 rows and 3 columns.

Source

<http://tcm.zju.edu.cn/celltalkdb/>

pathways	<i>pathways</i>
----------	-----------------

Description

KEGG pathways and Reactomes of 'Human' and 'Mouse' for intra-cellular genes and transcription factors.

Usage

pathways

Format

An object of class data.frame with 669197 rows and 8 columns.

Source

<https://www.genome.jp/kegg/pathway.html>
<https://reactome.org/>
<http://bioinfo.life.hust.edu.cn/AnimalTFDB/#!/>

plot_ccdist	<i>Plot cell-cell distribution</i>
-------------	------------------------------------

Description

Point plot with spatial distribution of celltype_sender and celltype_receiver

Usage

```
plot_ccdist(
  object,
  celltype_sender,
  celltype_receiver,
  color = NULL,
  size = 1,
  if_plot_others = T,
  if_plot_density = T,
  if_plot_edge = T,
  arrow_length = 0.05,
  plot_cells = NULL
)
```

Arguments

object	SpaTalk object generated from dec_celltype .
celltype_sender	Name of celltype_sender.
celltype_receiver	Name of celltype_receiver.
color	Color for celltype_sender, celltype_receiver, and others. Three values.
size	Point size. Default is 1.
if_plot_others	Whether to plot others. Default is TRUE.
if_plot_density	Whether to plot marginal density plots. Default is TRUE.
if_plot_edge	Whether to plot edge between neighbors. Default is TRUE.
arrow_length	Arrow length.
plot_cells	Which cells to plot. Default is all cells. Input a character vector of cell names to plot.

plot_cci_lrpairs	<i>Plot LR pairs</i>
------------------	----------------------

Description

Heatmap with LR pairs of celltype_sender and celltype_receiver

Usage

```
plot_cci_lrpairs(
  object,
  celltype_sender,
  celltype_receiver,
  top_lrpairs = 20,
  color = NULL,
  border_color = "black",
  type = NULL,
  fontsize_number = 1,
  number_color = "black"
)
```

Arguments

object	SpaTalk object generated from dec_cci .
celltype_sender	Name of celltype_sender.
celltype_receiver	Name of celltype_receiver.
top_lrpairs	Number of top lrpairs for plotting. Default is 20.
color	Color for the cells in heatmap.
border_color	color of cell borders on heatmap, use NA if no border should be drawn.
type	Set 'sig' to plot significant LR pairs or set 'number' to plot the number of spatial LR interactions.
fontsize_number	fontsize of the numbers displayed in cells.
number_color	color of the text.

plot_lrpair	<i>Plot LR pair</i>
-------------	---------------------

Description

Point plot with LR pair from celltype_sender to celltype_receiver

Usage

```
plot_lrpair(
  object,
  celltype_sender,
  celltype_receiver,
  ligand,
  receptor,
  color = NULL,
  size = 1,
  if_plot_density = T,
  if_plot_edge = T,
  arrow_length = 0.05,
  plot_cells = NULL
)
```

Arguments

object	SpaTalk object generated from dec_celltype .
celltype_sender	Name of celltype_sender.
celltype_receiver	Name of celltype_receiver.
ligand	Name of ligand from celltype_sender.
receptor	Name of receptor from celltype_receiver.
color	Color for ligand, receptor, and others. Three values.
size	Point size. Default is 1.
if_plot_density	Whether to plot marginal density plots. Default is TRUE.
if_plot_edge	Whether to plot edge between neighbors. Default is TRUE.
arrow_length	Arrow length.
plot_cells	Which cells to plot. Default is all cells. Input a character vector of cell names to plot.

plot_lrpair_vln	<i>Plot spatial distance of LR pair with vlnplot</i>
-----------------	--

Description

Violin plot spatial distance of LR pair between expressed senders and receivers and between expressed cell-cell pairs.

Usage

```
plot_lrpair_vln(
  object,
  celltype_sender,
  celltype_receiver,
  ligand,
```

```
receptor,  
vln_color = NULL,  
if_plot_boxplot = T,  
box_width = 0.2  
)
```

Arguments

object	SpaTalk object generated from dec_celltype .
celltype_sender	Name of celltype_sender.
celltype_receiver	Name of celltype_receiver.
ligand	Name of ligand from celltype_sender.
receptor	Name of receptor from celltype_receiver.
vln_color	Color for violins. Two values.
if_plot_boxplot	Whether to plot boxplot. Default is TRUE.
box_width	Box width. Default is 0.2.

plot_lr_path	<i>Plot LR and downstream pathways</i>
--------------	--

Description

Plot network with LR and downstream pathways

Usage

```
plot_lr_path(  
  object,  
  celltype_sender,  
  celltype_receiver,  
  ligand,  
  receptor,  
  color = NULL,  
  size = 5,  
  arrow_length = 0.1  
)
```

Arguments

object	SpaTalk object generated from dec_cci .
celltype_sender	Name of celltype_sender.
celltype_receiver	Name of celltype_receiver.
ligand	Name of ligand from celltype_sender.
receptor	Name of receptor from celltype_receiver.

color	Color for points Two values.
size	Size of points.
arrow_length	Arrow length.

plot_path2gene	<i>River plot of significantly activated pathways and related downstream genes of receptors.</i>
----------------	--

Description

River plot of significantly activated pathways and related downstream genes of receptors.

Usage

```
plot_path2gene(
  object,
  celltype_sender,
  celltype_receiver,
  ligand,
  receptor,
  min_gene_num = 5,
  pvalue = 0.5,
  color = NULL,
  color_flow = "blue"
)
```

Arguments

object	SpaTalk object generated from dec_cci .
celltype_sender	Name of celltype_sender.
celltype_receiver	Name of celltype_receiver.
ligand	Name of ligand from celltype_sender.
receptor	Name of receptor from celltype_receiver.
min_gene_num	Min genes number for each pathway.
pvalue	P value of the Fisher-exact test.
color	Color of pathways and genes. Two values.
color_flow	Color of the flow.

plot_st_celltype	<i>Plot spatial distribution of a single cell type</i>
------------------	--

Description

Ponit plot with spatial distribution of a single predicted cell type for transcriptomics data

Usage

```
plot_st_celltype(
  object,
  celltype,
  size = 1,
  color_celltype = "blue",
  color_others = "grey"
)
```

Arguments

object	SpaTalk object generated from dec_celltype .
celltype	Name of cell type in the sc_celltype.
size	Point size. Default is 1.
color_celltype	Color for the celltype of interest.
color_others	Color for the others.

plot_st_celltype_all	<i>Plot spatial distribution of all cell types</i>
----------------------	--

Description

Plot spatial distribution of all predicted cell types for transcriptomics data

Usage

```
plot_st_celltype_all(object, size = 1, color = NULL)
```

Arguments

object	SpaTalk object generated from dec_celltype .
size	Point size. Default is 1.
color	Color for all predicted cell types.

plot_st_celltype_density

Plot spatial density of a single cell type

Description

Plot spatial density of a single predicted cell type for transcriptomics data

Usage

```
plot_st_celltype_density(
  object,
  celltype,
  type,
  if_plot_point = T,
  point_color = NULL,
  point_size = 1,
  color_low = "grey",
  color_mid = NULL,
  color_high = "blue",
  color_midpoint = NULL,
  size = 1
)
```

Arguments

object	SpaTalk object generated from dec_celltype .
celltype	Name of cell type in the sc_celltype.
type	Select 'contour' or 'raster'.
if_plot_point	Whether to plot points when type is 'contour'.
point_color	Point color.
point_size	Point size. Default is 1.
color_low	Color for the lowest value.
color_mid	Color for the middle value for using scale_color_gradient2. Default is NULL.
color_high	Color for the highest value.
color_midpoint	Value for the middle scale. Default is NULL.
size	Line size when type is 'contour'. Default is 1.

plot_st_celltype_percent

Plot spatial distribution of a single cell type percent

Description

Plot spatial distribution of a single predicted cell type percent for transcriptomics data

Usage

```
plot_st_celltype_percent(
  object,
  celltype,
  size = 1,
  color_low = NULL,
  color_mid = NULL,
  color_high = NULL,
  color_midpoint = NULL
)
```

Arguments

object	SpaTalk object generated from dec_celltype .
celltype	Name of cell type in the sc_celltype.
size	Point size. Default is 1.
color_low	Color for the lowest value.
color_mid	Color for the middle value for using scale_color_gradient2. Default is NULL.
color_high	Color for the highest value.
color_midpoint	Value for the middle scale. Default is NULL.

plot_st_cor_heatmap

Plot heatmap of correlation between marker genes and cell types

Description

Plot heatmap of correlation between the expression of marker genes and the predicted score of cell types among all spatial cells or spots.

Usage

```
plot_st_cor_heatmap(
  object,
  marker_genes,
  celltypes,
  color_low = NULL,
  color_mid = NULL,
  color_high = NULL,
```

```

    scale = "none",
    if_show_top = T,
    top_direction = "row",
    border_color = NA
  )

```

Arguments

object	SpaTalk object generated from dec_celltype .
marker_genes	A character containing the known marker genes to plot, provide at least two marker genes of interest.
celltypes	A character containing name of cell type in the sc_celltype. Default is to plot all cell types.
color_low	Color for the lowest value.
color_mid	Color for the middle value for using scale_color_gradient2. Default is NULL.
color_high	Color for the highest value.
scale	Character indicating if the values should be centered and scaled in either the row direction or the column direction, or none. Corresponding values are 'row', 'column' and 'none'.
if_show_top	Whether to plot a symbol to the highest value across rows or columns. Default is TRUE.
top_direction	Direction to identify the highest value, select 'row' or 'column'.
border_color	Color of the cell border. Default is 'NA'.

plot_st_gene	<i>Plot spatial distribution of gene</i>
--------------	--

Description

Point plot with spatial distribution of a gene for transcriptomics data

Usage

```

plot_st_gene(
  object,
  gene,
  size = 1,
  color_low = "grey",
  color_mid = NULL,
  color_high = "blue",
  color_midpoint = NULL,
  if_use_newmeta = T,
  celltype = NULL,
  if_plot_others = T
)

```

Arguments

object	SpaTalk object generated from dec_celltype .
gene	Symbol of gene, e.g., 'AKT1'.
size	Point size. Default is 1.
color_low	Color for the lowest value.
color_mid	Color for the middle value for using <code>scale_color_gradient2</code> . Default is NULL.
color_high	Color for the highest value.
color_midpoint	Value for the middle scale. Default is NULL.
if_use_newmeta	Whether to use newmeta o plot the spatial distribution of gene after dec_celltype for spot-based data. Default is TRUE.
celltype	gene in which celltype to plot. Default is NULL. Set <code>Nif_use_newmeta</code> TRUE when using this parameter.
if_plot_others	Whether to plot other cells when to use defined celltype.

Details

Please set `if_use_newmeta` as FALSE to plot the spatial distribution of gene before [dec_celltype](#) for spot-based data.

plot_st_pie	<i>Plot spatial transcriptomics data</i>
-------------	--

Description

Plot scatterpie for spatial transcriptomics data

Usage

```
plot_st_pie(object, pie_scale = 1, xy_ratio = 1, color = NULL)
```

Arguments

object	SpaTalk object generated from dec_celltype .
pie_scale	Scale of each pie to plot. Default is 1.
xy_ratio	Ratio of y and x coordinates. Default is 1.
color	Filled of colors for pie plot, length of color must be equal to the number of unique cell types in <code>sc_celltype</code> .

plot_st_pie_generate *Plot spatial transcriptomics data*

Description

Plot scatterpie for spot-based ST data

Usage

```
plot_st_pie_generate(st_meta, pie_scale = 1, xy_ratio = 1, color = NULL)
```

Arguments

st_meta	st_meta generated from generate_spot
pie_scale	Scale of each pie to plot. Default is 1.
xy_ratio	Ratio of y and x coordinates. Default is 1.
color	Filled of colors for pie plot, length of color must be equal to the number of unique cell types in sc_celltype.

rev_gene *Pre-processing step: revising gene symbols*

Description

Revise genes according to NCBI Gene symbols updated in June 30, 2021 for count matrix, user-custom lrpairs data.frame, and user-custom pathways data.frame.

Usage

```
rev_gene(data = NULL, data_type = NULL, species = NULL, geneinfo = NULL)
```

Arguments

data	A matrix containing count data each column representing a spot or a cell, each row representing a gene; Or a data.frame containing ligand-receptor pairs; Or a data.frame containing gene-gene interactions and pathways from KEGG and Reactome as well as the information of transcriptional factors.
data_type	A character to define the type of data, select 'count' for the data matrix, 'lrpairs' for the data.frame containing lrpairs, 'pathways' for the data.frame containing pathways.
species	Species of the data. 'Human' or 'Mouse'.
geneinfo	A data.frame of the system data containing gene symbols of 'Human' and 'Mouse' updated on June 30, 2021 for revising count matrix.

Value

A new matrix or data.frame.

SpaTalk

Definition of 'SpaTalk' class

Description

An S4 class containing the data, meta, and results of inferred cell type compositions, LR pairs, and pathways.

Slots

`data` A list containing the raw and normalized data.

`meta` A list containing the raw and new meta data.

`para` A list containing the parameters.

`coef` A matrix containing the results of deconvolution.

`cellpair` A list containing the cell-cell pairs based on the spatial distance.

`dist` A matrix containing the Euclidean distance among cells.

`lrpair` A data frame containing the inferred LR pairs.

`tf` A data frame containing the TFs of receptors.

`lr_path` A list containing the lrpairs and pathways.

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