

Package ‘mistyR’

February 20, 2025

Type Package

Title Multiview Intercellular SpaTial modeling framework

Version 1.15.0

Description mistyR is an implementation of the Multiview Intercellular SpaTial modeling framework (MISTy). MISTy is an explainable machine learning framework for knowledge extraction and analysis of single-cell, highly multiplexed, spatially resolved data. MISTy facilitates an in-depth understanding of marker interactions by profiling the intra- and intercellular relationships. MISTy is a flexible framework able to process a custom number of views. Each of these views can describe a different spatial context, i.e., define a relationship among the observed expressions of the markers, such as intracellular regulation or paracrine regulation, but also, the views can also capture cell-type specific relationships, capture relations between functional footprints or focus on relations between different anatomical regions. Each MISTy view is considered as a potential source of variability in the measured marker expressions. Each MISTy view is then analyzed for its contribution to the total expression of each marker and is explained in terms of the interactions with other measurements that led to the observed contribution.

URL <https://saezlab.github.io/mistyR/>

BugReports <https://github.com/saezlab/mistyR/issues>

biocViews Software, BiomedicalInformatics, CellBiology, SystemsBiology, Regression, DecisionTree, SingleCell, Spatial

Depends R (>= 4.0)

License GPL-3

Encoding UTF-8

VignetteBuilder knitr

Imports assertthat, caret, deldir, digest, distances, dplyr (>= 1.1.0), filelock, furrr (>= 0.2.0), ggplot2, methods, purrr, ranger, readr (>= 2.0.0), ridge, rlang, rlist, R.utils, stats, stringr, tibble, tidyr, tidyselect (>= 1.2.0), utils, withr

Suggests BiocStyle, covr, earth, future, igraph ($\geq 1.2.7$), iml, kernlab, knitr, MASS, rmarkdown, RSNNS, testthat ($\geq 3.0.0$), xgboost

RoxygenNote 7.2.3

Config/testthat/edition 3

git_url <https://git.bioconductor.org/packages/mistyR>

git_branch devel

git_last_commit 89f8c5d

git_last_commit_date 2024-10-29

Repository Bioconductor 3.21

Date/Publication 2025-02-19

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Contents

| | |
|--|----|
| add_juxtaview | 3 |
| add_paraview | 4 |
| add_views | 6 |
| clear_cache | 7 |
| collect_results | 8 |
| create_initial_view | 9 |
| create_view | 10 |
| extract_signature | 11 |
| filter_views | 12 |
| plot_contrast_heatmap | 14 |
| plot_contrast_results | 15 |
| plot_improvement_stats | 16 |
| plot_interaction_communities | 17 |
| plot_interaction_heatmap | 18 |
| plot_view_contributions | 19 |
| reexports | 20 |
| remove_views | 21 |
| rename_view | 22 |
| run_misty | 23 |
| select_markers | 25 |
| synthetic | 26 |

| | |
|--------------|-----------|
| Index | 27 |
|--------------|-----------|

| | |
|---------------|---|
| add_juxtaview | <i>Generate and add a juxtaview to the current view composition</i> |
|---------------|---|

Description

The juxtaview captures the expression of all markers within the immediate neighborhood of a spatial unit.

Usage

```
add_juxtaview(  
  current.views,  
  positions,  
  neighbor.thr = 15,  
  prefix = "",  
  cached = FALSE,  
  verbose = TRUE  
)
```

Arguments

| | |
|----------------------------|---|
| <code>current.views</code> | the current view composition. |
| <code>positions</code> | a data.frame, tibble or a matrix with named coordinates in columns and rows for each spatial unit ordered as in the intraview. |
| <code>neighbor.thr</code> | a threshold value used to indicate the largest distance between two spatial units that can be considered as neighboring. |
| <code>prefix</code> | a prefix to add to the column names. |
| <code>cached</code> | a logical indicating whether to cache the calculated view after the first calculation and to reuse a previously cached view if it already exists for this sample. |
| <code>verbose</code> | a logical controlling the verbosity of the output of the function during execution. |

Details

The neighborhood of each spatial unit is estimated by constructing a graph by 2D Delaunay triangulation following by removal of edges with length larger than `neighbor.thr`. For each spatial unit the juxtaview contains the sum of expressions across its estimated neighbors for each marker.

Value

A mistyR view composition with added juxtaview.

See Also

[create_initial_view\(\)](#) for starting a view composition with an intraview only.

Other view composition functions: [add_paraview\(\)](#), [add_views\(\)](#), [create_initial_view\(\)](#), [create_view\(\)](#), [remove_views\(\)](#)

Examples

```
# Create a view composition of an intraview and a juxtaview.

library(dplyr)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))
# get the coordinates for each cell
pos <- synthetic[[1]] %>% select(row, col)

# compose
misty.views <- create_initial_view(expr) %>% add_juxtaview(pos, neighbor.thr = 1.5)

# preview
str(misty.views[["juxtaview.1.5"]])
```

add_paraview

Generate and add a paraview to the current view composition

Description

The paraview captures the expression of all markers in the broader tissue structure.

Usage

```
add_paraview(
  current.views,
  positions,
  l,
  zoi = 0,
  family = c("gaussian", "exponential", "linear", "constant"),
  approx = 1,
  nn = NULL,
  prefix = "",
  cached = FALSE,
  verbose = TRUE
)
```

Arguments

`current.views` the current view composition.

`positions` a data.frame, tibble or a matrix with named coordinates in columns and rows for each spatial unit ordered as in the intraview.

`l` effective radius of influence of expression in the broader tissue structure.

`zoi` spatial units with distance smaller than the zone of indifference will not be taken into account when generating the paraview.

| | |
|---------|---|
| family | the family <i>f</i> functions used to generate weights. (see Details) |
| approx | rank of the Nyström approximation matrix. (see Details) |
| nn | the number of spatial units to be used for approximating the paraview using a fast nearest neighbor search. (see Details) |
| prefix | a prefix to add to the column names. |
| cached | a logical indicating whether to cache the calculated view after the first calculation and to reuse a previously cached view if it already exists for this sample. |
| verbose | a logical controlling the verbosity of the output of the function during execution. |

Details

The paraview is generated by weighted sum of the expression of all spatial units for each marker. The weights for each spatial unit *i* are dependent on the family which can be one of "gaussian", "exponential", "linear" or "constant".

If "gaussian" the weights are calculated based on the distance to the spatial unit *j* and the parameter *l* using the radial basis function

$$w_{ij} = e^{-\frac{d_{ij}^2}{l^2}}$$

The parameter *l* here denotes the "effective" radius of influence.

If "exponential" the weights are calculated based on the distance to the spatial unit *j* and the parameter *l* using the exponential function

$$w_{ij} = e^{-\frac{d_{ij}}{l}}$$

The parameter *l* here denotes signaling length. For more information consult Oyler-Yaniv et. al. Immunity 46(4) 2017.

If "linear" the weights are calculated based on the distance to the spatial unit *j* and the parameter *l* using the linear function

$$w_{ij} = 1 - d(i, j)/l$$

The parameter *l* here denotes the intersect of the linear function. For distances larger than *l* the weight is equal to 0.

If "constant" the weights are always 1. The parameter *l* here denotes the number of nearest neighbors to take into account if *nn* is not defined.

Since the generation of the paraview requires the calculation of pairwise distances of all spatial units it can take a significant amount of computation time. The parameters *approx* and *nn* can be set to speed up the calculation by approximation. The approximation can be achieved by using the Nyström low-rank approximation method or by limiting the calculation of the paraview to a number of nearest neighbors around each spatial unit.

If the value of *approx* is between 0 and 1 it will be interpreted as fraction of the number of spatial units. Discrete values above 1 will be interpreted as the size of the approximation block. The number of nearest neighbors *nn* around each spatial unit are determined using a fast nearest neighbor search.

If both *approx* and *nn* have non-null values, *nn* has priority and an approximation based on fast nearest neighbor search will be used to generate the paraview.

Value

A mistyR view composition with added paraview with parameter 1.

See Also

[create_initial_view\(\)](#) for starting a view composition with an intraview only.

Other view composition functions: [add_juxtaview\(\)](#), [add_views\(\)](#), [create_initial_view\(\)](#), [create_view\(\)](#), [remove_views\(\)](#)

Examples

```
# Create a view composition of an intraview and a paraview with radius 10.

library(dplyr)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))
# get the coordinates for each cell
pos <- synthetic[[1]] %>% select(row, col)

# compose
misty.views <- create_initial_view(expr) %>% add_paraview(pos, l = 10)

# preview
str(misty.views[["paraview.10"]])
```

add_views

Add custom views to the current view composition

Description

Add one or more custom views to the current view composition.

Usage

```
add_views(current.views, new.views)
```

Arguments

`current.views` the current view composition.

`new.views` a view or a list of views created with [create_view\(\)](#) or otherwise.

Value

A mistyR view composition containing an union of views from `current.views` and `new.views`.

See Also

[create_initial_view\(\)](#) for starting a view composition, with an intraview, [create_view\(\)](#) for creating a custom view.

Other view composition functions: [add_juxtaview\(\)](#), [add_paraview\(\)](#), [create_initial_view\(\)](#), [create_view\(\)](#), [remove_views\(\)](#)

Examples

```
# create random views
view1 <- data.frame(marker1 = rnorm(100, 10, 2), marker2 = rnorm(100, 15, 3))
view2 <- data.frame(marker1 = rnorm(100, 10, 5), marker2 = rnorm(100, 15, 5))

misty.views <- create_initial_view(view1)

new.view <- create_view("dummyname", view2, "dname")
add_views(misty.views, new.view)

misty.views %>% add_views(create_view("dummyname", view2, "dname"))
```

clear_cache

Clear cached objects

Description

Purge the cache or clear the cached objects for a single sample.

Usage

```
clear_cache(id = NULL)
```

Arguments

`id` the unique id of the sample.

Details

The cached objects are removed from disk and cannot be retrieved. Whenever possible specifying an `id` is recommended. If `id = NULL` all contents of the folder `‘.misty.temp’` will be removed.

Value

None (NULL)

Examples

```
clear_cache("b98ad35f4e671871cba35f2155228612")

clear_cache()
```

| | |
|-----------------|--------------------------------------|
| collect_results | <i>Collect and aggregate results</i> |
|-----------------|--------------------------------------|

Description

Collect and aggregate performance, contribution and importance estimations of a set of raw results produced by `run_misty()`.

Usage

```
collect_results(folders)
```

Arguments

`folders` Paths to folders containing the raw results from `run_misty()`.

Value

List of collected performance, contributions and importances per sample, performance and contribution statistics and aggregated importances.

improvements Long format tibble with measurements of performance for each *target* and each *sample*. Available performance measures are RMSE and variance explained (R2) for a model containing only an intrinsic view (*intra.RMSE*, *intra.R2*), model with all views (*multi.RMSE*, *multi.R2*), gain of RMSE and gain of variance explained of multi-view model over the intrinsic model where *gain.RMSE* is the relative decrease of RMSE in percent, while *gain.R2* is the absolute increase of variance explained in percent. Each *value* represents the mean performance across folds (k-fold cross-validation). The p values of a one sided t-test of improvement of performance (*p.RMSE*, *p.R2*) are also available as a measure.

improvements.stats Long format tibble with summary statistics (mean, standard deviation and coefficient of variation) for all performance measures for each target over all samples.

contributions Long format tibble with the values of the coefficients for each *view* in the meta-model, for each *target* and each *sample*. The p values for the coefficient for each view, under the null hypothesis of zero contribution to the meta model are also available.

contributions.stats Long format tibble with summary statistics for all views per target over all samples. Including mean coefficient value, fraction of contribution, mean and standard deviation of p values.

importances List of view-specific predictor-target importance tables per sample. The importances in each table are standardized per target and weighted by the quantile of the coefficient for the target in that view. Columns other than *Predictor* represent target markers.

importances.aggregated A list of aggregated view-specific predictor-target importance tables. Aggregation is reducing by mean over all samples.

See Also

`run_misty()` to train models and generate results.

Examples

```
# Train and collect results for 3 samples in synthetic

library(dplyr)
library(purrr)

data("synthetic")

misty.results <- synthetic[seq_len(3)] %>%
  imap_chr(~ create_initial_view(.x %>% select(-c(row, col, type))) %>%
    add_paraview(.x %>% select(row, col), l = 10) %>%
    run_misty(paste0("results/", .y))) %>%
  collect_results()
str(misty.results)
```

create_initial_view **Start here:** *create a basic view composition with an intraview*

Description

This function is the first one to be called when building a mistyR workflow, starting from view composition. The initial view describes the intraview of the sample.

Usage

```
create_initial_view(data, unique.id = NULL)
```

Arguments

| | |
|-----------|--|
| data | A data.frame or a tibble containing expression information for all markers of interest (in named columns) for each spatial unit (in rows). |
| unique.id | A character vector. Identifier of the current sample. If not provided (unique.id = NULL) then an id is automatically generated by calculating the md5 hash of table. |

Value

An initial mistyR view composition containing an *intraview* list item named described with abbreviation "intra" and *data* as provided in *data* and a *misty.uniqueid* list item containing the provided or automatically calculated *unique.id*. A cache folder for the sample will be automatically created in the working directory as a subfolder of `‘.misty.temp/’` with the same name as *unique.id*.

See Also

Other view composition functions: [add_juxtaview\(\)](#), [add_paraview\(\)](#), [add_views\(\)](#), [create_view\(\)](#), [remove_views\(\)](#)

Examples

```
# Create an intrinsic view from the first sample in the dataset synthetic.

library(dplyr)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))

create_initial_view(expr)
```

| | |
|-------------|-----------------------------|
| create_view | <i>Create a custom view</i> |
|-------------|-----------------------------|

Description

Create a custom view from a `data.frame` or a `tibble`.

Usage

```
create_view(name, data, abbrev = name)
```

Arguments

| | |
|--------|--|
| name | Name of the view. A character vector. |
| data | A <code>data.frame</code> or a <code>tibble</code> with named variables in columns and rows for each spatial unit ordered as in the <code>intraview</code> . |
| abbrev | Abbreviated name. A character vector. |

Details

Creating a custom view does not add it to the current view composition.

Value

A new `mistyR` view. A list with a single named item described by the provided abbreviation and `data` containing the provided data.

See Also

[add_views\(\)](#) for adding created views to a view composition.

Other view composition functions: [add_juxtaview\(\)](#), [add_paraview\(\)](#), [add_views\(\)](#), [create_initial_view\(\)](#), [remove_views\(\)](#)

Examples

```

# Create a view from the mean expression of the 10 nearest neighbors of
# each cell.

library(dplyr)
library(purrr)
library(distances)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))
# get the coordinates for each cell
pos <- synthetic[[1]] %>% select(row, col)

# find the 10 nearest neighbors
neighbors <- nearest_neighbor_search(distances(as.matrix(pos)), k = 11)[-1, ]

# calculate the mean expression of the nearest neighbors for all markers
# for each cell in expr
nnexpr <- seq_len(nrow(expr)) %>%
  map_dfr(~ expr %>%
    slice(neighbors[, .x]) %>%
    colMeans())

create_view("nearest", nnexpr, "nn")

```

| | |
|-------------------|--|
| extract_signature | <i>Extract signatures from the results</i> |
|-------------------|--|

Description

Signature is a representation of each sample in the space of mistyR results.

Usage

```

extract_signature(
  misty.results,
  type = c("performance", "contribution", "importance"),
  trim = -Inf,
  trim.measure = c("gain.R2", "multi.R2", "intra.R2", "gain.RMSE", "multi.RMSE",
    "intra.RMSE")
)

```

Arguments

`misty.results` a results list generated by `collect_results()`.

`type` type of signature to extract from the results.

| | |
|--------------|--|
| trim | display targets with performance value above (if R2 or gain) or below (otherwise) this value only. |
| trim.measure | the measure used for trimming. |

Details

The performance signature of each sample is a concatenation of the estimated values of variance explained using only the intraview, the variance explained by the multiview model and the gain in variance explained for each marker. The performance signature vector for each sample available in `misty.results` is of length `markers · 3`.

The contribution signature of each sample is a concatenation of the estimated fraction of contribution of each view for each marker. The contribution signature vector for each sample available in `misty.results` is of length `markers · views`.

The importance signature of each sample is a concatenation of the estimated and weighted importances for each predictor-target marker pair from all views. The importance signature vector for each sample available in `misty.results` is of length `markers2 · views`.

Value

A table with one row per sample from `misty.results` representing its signature.

See Also

[collect_results\(\)](#) to generate a results list from raw results.

Examples

```
library(dplyr)

misty.results <-
  list.files("results", full.names = TRUE) %>% collect_results()

extract_signature(misty.results, "performance")
```

filter_views

Filter spatial units

Description

Select, remove (or duplicate) rows from all views in a composition by their row locations or according to conditions based on a specific view.

Usage

```
filter_views(current.views, rows, view = "intraview", ...)
```

Arguments

| | |
|---------------|---|
| current.views | the current view composition. |
| rows | row (integer) location; positive values to keep (duplicate) and/or negative to remove. |
| view | the name of the view to be used for filtering. |
| ... | logical expressions defined in terms of the variables in view passed on to <code>dplyr::filter()</code> . |

Details

The values in rows have priority over the other parameters. If rows doesn't contain integer values then filtering is performed based on the view specified in view and expressions (...) returning logical values defined in terms of the variables in view.

Value

A mistyR view composition with filtered spatial units from all views.

See Also

[<data-masking>](#).

Other view manipulation functions: [rename_view\(\)](#), [select_markers\(\)](#)

Examples

```
# Create a view composition with an intraview and filter

library(dplyr)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))

# compose
misty.views <- create_initial_view(expr)

# select only the first 10 spatial units and preview
misty.views %>%
  filter_views(1:10) %>%
  str()

# select only the units where the expression of ligA is larger than 0.5
# and preview
misty.views %>%
  filter_views(NA, "intraview", ligA > 0.5) %>%
  str()
```

plot_contrast_heatmap *Plot heatmap of local contrast between two views*

Description

The heatmap shows the interactions that are present and have importance above a cutoff value in the to.view but but not in the from.view.

Usage

```
plot_contrast_heatmap(  
  misty.results,  
  from.view,  
  to.view,  
  cutoff = 1,  
  trim = -Inf,  
  trim.measure = c("gain.R2", "multi.R2", "intra.R2", "gain.RMSE", "multi.RMSE",  
                  "intra.RMSE")  
)
```

Arguments

`misty.results` a results list generated by `collect_results()`.

`from.view, to.view` abbreviated name of the view.

`cutoff` importance threshold. Importances below this value will be colored white in the heatmap and considered as not relevant.

`trim` display targets with performance value above (if R2 or gain) or below (otherwise) this value only.

`trim.measure` the measure used for trimming.

Value

The `misty.results` list (invisibly).

See Also

`collect_results()` to generate a results list from raw results.

Other plotting functions: `plot_contrast_results()`, `plot_improvement_stats()`, `plot_interaction_communities()`, `plot_interaction_heatmap()`, `plot_view_contributions()`

Examples

```

all.samples <- list.dirs("results", recursive = FALSE)

misty.results <- collect_results(all.samples)

misty.results %>%
  plot_contrast_heatmap("intra", "para.10")

misty.results %>%
  plot_contrast_heatmap("intra", "para.10", cutoff = 0.5)

```

plot_contrast_results *Plot heatmap of contrast between two result lists*

Description

Plot interexperiment contrast of views.

Usage

```

plot_contrast_results(
  misty.results.from,
  misty.results.to,
  views = NULL,
  cutoff.from = 1,
  cutoff.to = 1,
  trim = -Inf,
  trim.measure = c("gain.R2", "multi.R2", "intra.R2", "gain.RMSE", "multi.RMSE",
    "intra.RMSE")
)

```

Arguments

`misty.results.from`, `misty.results.to`
a results list generated by `collect_results()`.

`views`
one or more abbreviated names of views.

`cutoff.from`, `cutoff.to`
importance thresholds respective to the result lists.

`trim`
display targets with performance value above (if R2 or gain) or below (otherwise) this value only.

`trim.measure`
the measure used for trimming.

Details

The heatmaps show the interactions that are present and have importance above a `cutoff.to` value in the views of `misty.results.to` but not present or have importance below `cutoff.from` in the views of `misty.results.from`.

Value

The `misty.results` from list (invisibly).

See Also

[collect_results\(\)](#) to generate a results list from raw results.

Other plotting functions: [plot_contrast_heatmap\(\)](#), [plot_improvement_stats\(\)](#), [plot_interaction_communities\(\)](#), [plot_interaction_heatmap\(\)](#), [plot_view_contributions\(\)](#)

Examples

```
# if for example the available samples come from different grades of tumors

grade1.results <- collect_results(c("results/synthetic1", "results/synthetic2"))
grade3.results <- collect_results("results/synthetic10")

# highlight interactions present in grade 1 tumors but not in grade 3 tumors
# in the paraview

grade3.results %>% plot_contrast_results(grade1.results, views = "para.10")

# see the loss of interactions in all views with lower sensitivity

plot_contrast_results(grade3.results, grade1.results, cutoff.from = 0.75, cutoff.to = 0.5)
```

plot_improvement_stats

Plot observed performance and improvement per target

Description

Generates a plot of the mean (+- standard deviation) of the performance value per target across all samples from the results.

Usage

```
plot_improvement_stats(
  misty.results,
  measure = c("gain.R2", "multi.R2", "intra.R2", "gain.RMSE", "multi.RMSE", "intra.RMSE"),
  trim = -Inf
)
```

Arguments

`misty.results` a results list generated by [collect_results\(\)](#).

`measure` performance measure to be plotted (See [collect_results\(\)](#)).

`trim` display targets with performance value above (if R2 or gain) or below (otherwise) this value only.

Value

The `misty.results` list (invisibly).

See Also

[collect_results\(\)](#) to generate a results list from raw results.

Other plotting functions: [plot_contrast_heatmap\(\)](#), [plot_contrast_results\(\)](#), [plot_interaction_communities\(\)](#), [plot_interaction_heatmap\(\)](#), [plot_view_contributions\(\)](#)

Examples

```
all.samples <- list.dirs("results", recursive = FALSE)

collect_results(all.samples) %>% plot_improvement_stats()

misty.results <- collect_results(all.samples)
misty.results %>% plot_improvement_stats(measure = "gain.RMSE")
misty.results %>% plot_improvement_stats(measure = "intra.R2")
```

plot_interaction_communities

Plot marker interaction communities

Description

Identify and plot a graph of marker interaction communities.

Usage

```
plot_interaction_communities(misty.results, view, cutoff = 1)
```

Arguments

| | |
|----------------------------|---|
| <code>misty.results</code> | a results list generated by collect_results() . |
| <code>view</code> | abbreviated name of the view. |
| <code>cutoff</code> | importance threshold. Importances below this value will be colored white in the heatmap and considered as not relevant. |

Details

The communities are identified using the Louvain algorithm. Communities can be extracted only from views that have the same predictor and target markers.

Value

The `misty.results` list (invisibly).

See Also

`collect_results()` to generate a results list from raw results.

Other plotting functions: `plot_contrast_heatmap()`, `plot_contrast_results()`, `plot_improvement_stats()`, `plot_interaction_heatmap()`, `plot_view_contributions()`

Examples

```
all.samples <- list.dirs("results", recursive = FALSE)

misty.results <- collect_results(all.samples)

misty.results %>%
  plot_interaction_communities("intra") %>%
  plot_interaction_communities("para.10")

misty.results %>%
  plot_interaction_communities("para.10", cutoff = 0.5)
```

plot_interaction_heatmap

Plot importance heatmap for a view

Description

Generate a heatmap with importances of predictor-target interaction.

Usage

```
plot_interaction_heatmap(
  misty.results,
  view,
  cutoff = 1,
  trim = -Inf,
  trim.measure = c("gain.R2", "multi.R2", "intra.R2", "gain.RMSE", "multi.RMSE",
    "intra.RMSE"),
  clean = FALSE
)
```

Arguments

| | |
|----------------------------|---|
| <code>misty.results</code> | a results list generated by <code>collect_results()</code> . |
| <code>view</code> | abbreviated name of the view. |
| <code>cutoff</code> | importance threshold. Importances below this value will be colored white in the heatmap and considered as not relevant. |
| <code>trim</code> | display targets with performance value above (if R2 or gain) or below (otherwise) this value only. |

trim.measure the measure used for trimming.
 clean a logical indicating whether to remove rows and columns with all importances are below cutoff from the heatmap.

Value

The misty.results list (invisibly).

See Also

[collect_results\(\)](#) to generate a results list from raw results.

Other plotting functions: [plot_contrast_heatmap\(\)](#), [plot_contrast_results\(\)](#), [plot_improvement_stats\(\)](#), [plot_interaction_communities\(\)](#), [plot_view_contributions\(\)](#)

Examples

```
all.samples <- list.dirs("results", recursive = FALSE)

collect_results(all.samples) %>%
  plot_interaction_heatmap("intra") %>%
  plot_interaction_heatmap("para.10", cutoff = 0.5)
```

plot_view_contributions

Plot view contributions per target

Description

Generate a stacked barplot of the average view contribution fraction per target across all samples from the results.

Usage

```
plot_view_contributions(
  misty.results,
  trim = -Inf,
  trim.measure = c("gain.R2", "multi.R2", "intra.R2", "gain.RMSE", "multi.RMSE",
    "intra.RMSE")
)
```

Arguments

misty.results a results list generated by [collect_results\(\)](#).
 trim display targets with performance value above (if R2 or gain) or below (otherwise) this value only.
 trim.measure the measure used for trimming.

Value

The `misty.results` list (invisibly).

See Also

[collect_results\(\)](#) to generate a results list from raw results.

Other plotting functions: [plot_contrast_heatmap\(\)](#), [plot_contrast_results\(\)](#), [plot_improvement_stats\(\)](#), [plot_interaction_communities\(\)](#), [plot_interaction_heatmap\(\)](#)

Examples

```
all.samples <- list.dirs("results", recursive = FALSE)

collect_results(all.samples) %>% plot_view_contributions()
```

reexports

Objects exported from other packages

Description

These objects are imported from other packages. Follow the links below to see their documentation.

dplyr [%>%](#)

Examples

```
# Create a view composition of an intraview and a paraview with radius 10 then
# run MISTy for a single sample.

library(dplyr)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))
# get the coordinates for each cell
pos <- synthetic[[1]] %>% select(row, col)

# compose
misty.views <- create_initial_view(expr) %>% add_paraview(pos, l = 10)

# run with default parameters
run_misty(misty.views)
```

| | |
|--------------|---|
| remove_views | <i>Remove views from the current view composition</i> |
|--------------|---|

Description

Remove one or more views from the view composition.

Usage

```
remove_views(current.views, view.names)
```

Arguments

`current.views` the current view composition.
`view.names` the names of one or more views to be removed.

Details

The intraview and the unique id cannot be removed with this function.

Value

A mistyR view composition with `view.names` views removed.

See Also

Other view composition functions: [add_juxtaview\(\)](#), [add_paraview\(\)](#), [add_views\(\)](#), [create_initial_view\(\)](#), [create_view\(\)](#)

Examples

```
library(dplyr)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))
# get the coordinates for each cell
pos <- synthetic[[1]] %>% select(row, col)

# compose
misty.views <- create_initial_view(expr) %>%
  add_juxtaview(pos, neighbor.thr = 1.5) %>%
  add_paraview(pos, l = 10)

# preview
str(misty.views)

# remove juxtaview and preview
misty.views %>%
```

```

remove_views("juxtaview.1.5") %>%
  str()

# remove juxtaview and paraview and preview
misty.views %>%
  remove_views(c("juxtaview.1.5", "paraview.10")) %>%
  str()

```

rename_view
Rename view in a view composition

Description

Rename view in a view composition

Usage

```
rename_view(current.views, old.name, new.name, new.abbrev = new.name)
```

Arguments

`current.views` the current view composition.
`old.name` old name of the view.
`new.name` new name of the view.
`new.abbrev` new abbreviated name.

Value

A mistyR view composition with a renamed view.

See Also

Other view manipulation functions: [filter_views\(\)](#), [select_markers\(\)](#)

Examples

```

view1 <- data.frame(marker1 = rnorm(100, 10, 2), marker2 = rnorm(100, 15, 3))
view2 <- data.frame(marker1 = rnorm(100, 10, 5), marker2 = rnorm(100, 15, 5))

misty.views <- create_initial_view(view1) %>%
  add_views(create_view("originalname", view2, "on"))
str(misty.views)

# rename and preview
misty.views %>%
  rename_view("originalname", "renamed", "rn") %>%
  str()

```

run_misty

*Train MISTy models***Description**

Trains multi-view models for all target markers, estimates the performance, the contributions of the view specific models and the importance of predictor markers for each target marker.

Usage

```
run_misty(
  views,
  results.folder = "results",
  seed = 42,
  target.subset = NULL,
  bypass.intra = FALSE,
  cv.folds = 10,
  cached = FALSE,
  append = FALSE,
  model.function = random_forest_model,
  ...
)
```

Arguments

| | |
|----------------|---|
| views | view composition. |
| results.folder | path to the top level folder to store raw results. |
| seed | seed used for random sampling to ensure reproducibility. |
| target.subset | subset of targets to train models for. If NULL, models will be trained for markers in the intraview. |
| bypass.intra | a logical indicating whether to train a baseline model using the intraview data (see Details). |
| cv.folds | number of cross-validation folds to consider for estimating the performance of the multi-view models |
| cached | a logical indicating whether to cache the trained models and to reuse previously cached ones if they already exist for this sample. |
| append | a logical indicating whether to append the performance and coefficient files in the results.folder. Consider setting to TRUE when rerunning a workflow with different target.subset parameters. |
| model.function | a function which is used to model each view, default model is random_forest_model. Other models included in mistyR are gradient_boosting_model, bagged_mars_model, mars_model, linear_model, svm_model, mlp_model |
| ... | all additional parameters are passed to the chosen ML model for training the view-specific models |

Details

If `bypass.intra` is set to `TRUE` all variable in the intraview the intraview data will be treated as targets only. The baseline intraview model in this case is a trivial model that predicts the average of each target. If the intraview has only one variable this switch is automatically set to `TRUE`.

Default model to train the view-specific views is a Random Forest model based on `ranger()` – `run_misty(views, model.function = random_forest_model)`

The following parameters are the default configuration: `num.trees = 100`, `importance = "impurity"`, `num.threads = 1`, `seed = seed`.

Gradient boosting is an alternative to model each view using gradient boosting. The algorithm is based on `xgb.train()` – `run_misty(views, model.function = gradient_boosting_model)`

The following parameters are the default configuration: `booster = "gbtree"`, `rounds = 10`, `objective = "reg:squarederror"`. Set `booster` to `"gblinear"` for linear boosting.

Bagged MARS is an alternative to model each view using bagged MARS, (multivariate adaptive spline regression models) trained with bootstrap aggregation samples. The algorithm is based on `earth()` – `run_misty(views, model.function = bagged_mars_model)`

The following parameters are the default configuration: `degree = 2`. Furthermore 50 base learners are used by default (pass `n.bags` as parameter via `...` to change this value).

MARS is an alternative to model each view using multivariate adaptive spline regression model. The algorithm is based on `earth()` – `run_misty(views, model.function = mars_model)`

The following parameters are the default configuration: `degree = 2`.

Linear model is an alternative to model each view using a simple linear model. The algorithm is based on `lm()` – `run_misty(views, model.function = linear_model)`

SVM is an alternative to model each view using a support vector machines. The algorithm is based on `ksvm()` – `run_misty(views, model.function = svm_model)`

The following parameters are the default configuration: `kernel = "vanilladot"` (linear kernel), `C = 1`, `type = "eps-svr"`.

MLP is an alternative to model each view using a multi-layer perceptron. The alogorithm is based on `mlp()` – `run_misty(views, model.function = mlp_model)`

The following parameters are the default configuration: `size = c(10)` (meaning we have 1 hidden layer with 10 units).

Value

Path to the results folder that can be passed to `collect_results()`.

See Also

`create_initial_view()` for starting a view composition.

Examples

```
# Create a view composition of an intraview and a paraview with radius 10 then
# run MISTy for a single sample.

library(dplyr)
```



```
# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))
# get the coordinates for each cell
pos <- synthetic[[1]] %>% select(row, col)

# compose
misty.views <- create_initial_view(expr) %>% add_paraview(pos, l = 10)

# run with default parameters
run_misty(misty.views)
```

| | |
|----------------|---|
| select_markers | <i>Select a subset of markers in a view</i> |
|----------------|---|

Description

Select a subset of markers in a view

Usage

```
select_markers(current.views, view = "intraview", ...)
```

Arguments

`current.views` the current view composition.
`view` the name of the view to select markers for.
`...` one or more [select](#) expressions `dplyr::select()` for the specified view.

Value

A mistyR view composition with selected markers in view.

See Also

[<tidy-select>](#).
Other view manipulation functions: [filter_views\(\)](#), [rename_view\(\)](#)

Examples

```
# Create a view composition with an intraview and select

library(dplyr)

# get the expression data
data("synthetic")
expr <- synthetic[[1]] %>% select(-c(row, col, type))
```

```
# compose
misty.views <- create_initial_view(expr)

# select markers from the intraview not starting with lig and preview
misty.views %>%
  select_markers("intraview", !starts_with("lig")) %>%
  str()
```

synthetic

Synthetic benchmark data for mistyR

Description

Data generated from 10 random layouts of four cell types and empty space on 100-by-100 grid by simulating a two-dimensional cellular automata model that focuses on signaling events. Cell growth, division, motility and death are neglected. The intracellular processes involve two layers, first the ligand activation of signaling hubs and ligand production/secretion regulated by proteins. The model simulates the production, diffusion, degradation and interactions of 11 molecular species. Ligands are produced in each cell-type based on the activity level of their production nodes and then freely diffuse, degrade or interact with other cells on the grid. Other molecular species involved in signaling are localised in the intracellular space and their activity depends on ligand binding and intracellular wiring.

Usage

```
data("synthetic")
```

Format

A named list of length 10. Each list item is a tibble that corresponds to a simulation of one random layout with information about each cell in rows described by the following 14 variables:

row, col location of the cell on the grid

ligA, ligB, ligC, ligD expression of ligands

protE, protF expression of intracellular proteins

prodA, prodB, prodC, prodD expression of regulatory proteins

type cell type id

Source

https://github.com/saezlab/misty_pipelines/

Index

- * **datasets**
 - synthetic, [26](#)
- * **internal**
 - reexports, [20](#)
- * **plotting functions**
 - plot_contrast_heatmap, [14](#)
 - plot_contrast_results, [15](#)
 - plot_improvement_stats, [16](#)
 - plot_interaction_communities, [17](#)
 - plot_interaction_heatmap, [18](#)
 - plot_view_contributions, [19](#)
- * **view composition functions**
 - add_juxtview, [3](#)
 - add_paraview, [4](#)
 - add_views, [6](#)
 - create_initial_view, [9](#)
 - create_view, [10](#)
 - remove_views, [21](#)
- * **view manipulation functions**
 - filter_views, [12](#)
 - rename_view, [22](#)
 - select_markers, [25](#)
 - ..., [13](#)
 - %>% (reexports), [20](#)
 - %>%, [20](#)
- add_juxtview, [3](#), [6](#), [7](#), [9](#), [10](#), [21](#)
- add_paraview, [3](#), [4](#), [7](#), [9](#), [10](#), [21](#)
- add_views, [3](#), [6](#), [6](#), [9](#), [10](#), [21](#)
- clear_cache, [7](#)
- collect_results, [8](#), [11](#), [12](#), [14–20](#), [24](#)
- create_initial_view, [3](#), [6](#), [7](#), [9](#), [10](#), [21](#), [24](#)
- create_view, [3](#), [6](#), [7](#), [9](#), [10](#), [21](#)
- dplyr::filter, [13](#)
- dplyr::select, [25](#)
- earth, [24](#)
- extract_signature, [11](#)
- filter_views, [12](#), [22](#), [25](#)
- ksvm, [24](#)
- lm, [24](#)
- mlp, [24](#)
- plot_contrast_heatmap, [14](#), [16–20](#)
- plot_contrast_results, [14](#), [15](#), [17–20](#)
- plot_improvement_stats, [14](#), [16](#), [16](#), [18–20](#)
- plot_interaction_communities, [14](#), [16](#), [17](#), [17](#), [19](#), [20](#)
- plot_interaction_heatmap, [14](#), [16–18](#), [18](#), [20](#)
- plot_view_contributions, [14](#), [16–19](#), [19](#)
- ranger, [24](#)
- reexports, [20](#)
- remove_views, [3](#), [6](#), [7](#), [9](#), [10](#), [21](#)
- rename_view, [13](#), [22](#), [25](#)
- run_misty, [8](#), [23](#)
- select, [25](#)
- select_markers, [13](#), [22](#), [25](#)
- synthetic, [26](#)
- xgb.train, [24](#)