## Package 'longmixr'

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Title Longitudinal Consensus Clustering with 'flexmix'

Version 1.0.0

**Description** An adaption of the consensus clustering approach from 'ConsensusClusterPlus' for longitudinal data. The longitudinal data is clustered with flexible mixture models from 'flexmix', while the consensus matrices are hierarchically clustered as in 'ConsensusClusterPlus'. By using the flexibility from 'flexmix' and 'FactoMineR', one can use mixed data types for the clustering.

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**Encoding** UTF-8

LazyData true

RoxygenNote 7.1.1

URL https://cellmapslab.github.io/longmixr/

BugReports https://github.com/cellmapslab/longmixr/issues

**Depends** R (>= 3.5.0)

#### biocViews

- Imports checkmate, ConsensusClusterPlus, graphics, grDevices, flexmix, StatMatch, stats, utils
- Suggests testthat (>= 3.0.0), knitr, rmarkdown, dplyr, tidyr, ggplot2, ggalluvial, FactoMineR, factoextra, lme4, purrr

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VignetteBuilder knitr

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crosssectional\_consensus\_cluster

Cross-sectional clustering with categorical variables

#### Description

This function uses the ConsensusClusterPlus function from the package with the same name with defaults for clustering data with categorical variables. As the distance function, the Gower distance is used.

#### Usage

```
crosssectional_consensus_cluster(
  data,
  reps = 1000,
  finalLinkage = "ward.D2",
   innerLinkage = "ward.D2",
   ...
)
```

#### Arguments

data	a matrix or data.frame containing variables that should be used for computing the distance. This argument is passed to StatMatch::gower.dist
reps	number of repetitions, same as in ConsensusClusterPlus
finalLinkage	linkage method for final clustering, same as in ConsensusClusterPlussame as in ConsensusClusterPlus
innerLinkage	linkage method for clustering steps, same as in ConsensusClusterPlus
	other arguments passed to ConsensusClusterPlus, attention: the d argument can <b>not</b> be set as it is directly computed by crosssectional_consensus_cluster

#### Details

data can take all input data types that gower.dist can handle, i.e. numeric, character/factor, ordered and logical.

#### Value

The output is produced by ConsensusClusterPlus

#### Examples

fake\_questionnaire\_data

Fake questionnaire data

#### Description

A simulated data set containing observations of 100 individuals at four time points. The data was simulated in two groups (50 individuals each) and contains two questionnaires with five items each, one questionnaire with five continuous variables and one additional cross-sectional continuous variable. In this data set the group variable from the simulation is included. You typically don't have this group variable in your data.

#### Usage

fake\_questionnaire\_data

#### Format

A data frame with 400 rows and 20 variables:

**ID** patient ID

visit time point of the observation

group to which simulated group the observation belongs to

age\_visit\_1 age of the patient at time point 1

**single\_continuous\_variable** a cross-sectional continuous variable, i.e. there is only one unique value per individual

questionnaire\_A\_1 the first item of questionnaire A with categories 1 to 5

questionnaire\_A\_2 the second item of questionnaire A with categories 1 to 5 questionnaire\_A\_3 the third item of questionnaire A with categories 1 to 5 questionnaire\_A\_4 the fourth item of questionnaire A with categories 1 to 5 questionnaire\_A\_5 the fifth item of questionnaire A with categories 1 to 5 questionnaire\_B\_1 the first item of questionnaire B with categories 1 to 5 questionnaire\_B\_2 the second item of questionnaire B with categories 1 to 5 questionnaire\_B\_3 the third item of questionnaire B with categories 1 to 5 questionnaire\_B\_3 the third item of questionnaire B with categories 1 to 5 questionnaire\_B\_4 the fourth item of questionnaire B with categories 1 to 5 questionnaire\_B\_5 the fifth item of questionnaire B with categories 1 to 5 questionnaire\_C\_1 the first continuous variable of questionnaire C questionnaire\_C\_3 the third continuous variable of questionnaire C questionnaire\_C\_4 the fourth continuous variable of questionnaire C questionnaire\_C\_5 the fifth continuous variable of questionnaire C

#### Source

simulated data

#### Description

This functions extracts the cluster assignments from an lcc object. One can specify which for which number of clusters the assignments should be returned.

#### Usage

```
get_clusters(cluster_solution, number_clusters = NULL)
```

#### Arguments

```
cluster_solution
```

an lcc object

number\_clusters

default is NULL to return all assignments. Otherwise specify a numeric vector with the number of clusters for which the assignments should be returned, e.g. 2:4

#### Value

a data.frame with an ID column (the name of the ID column was specified by the user when calling the longitudinal\_consensus\_cluster) function and one column with cluster assignments for every specified number of clusters. Only the assignments included in number\_clusters are returned in the form of columns with the names assignment\_num\_clus\_x

#### Examples

```
# not run
set.seed(5)
test_data <- data.frame(patient_id = rep(1:10, each = 4),</pre>
visit = rep(1:4, 10),
var_1 = c(rnorm(20, -1), rnorm(20, 3)) +
rep(seq(from = 0, to = 1.5, length.out = 4), 10),
var_2 = c(rnorm(20, 0.5, 1.5), rnorm(20, -2, 0.3)) +
rep(seq(from = 1.5, to = 0, length.out = 4), 10))
model_list <- list(flexmix::FLXMRmgcv(as.formula("var_1 ~ .")),</pre>
flexmix::FLXMRmgcv(as.formula("var_2 ~ .")))
clustering <- longitudinal_consensus_cluster(</pre>
data = test_data,
id_column = "patient_id",
max_k = 2,
reps = 3,
model_list = model_list,
flexmix_formula = as.formula("~s(visit, k = 4) | patient_id"))
cluster_assignments <- get_clusters(clustering, number_clusters = 2)</pre>
# end not run
```

longitudinal\_consensus\_cluster

Longitudinal consensus clustering with flexmix

#### Description

This function performs longitudinal clustering with flexmix. To get robust results, the data is subsampled and the clustering is performed on this subsample. The results are combined in a consensus matrix and a final hierarchical clustering step performed on this matrix. In this, it follows the approach from the ConsensusClusterPlus package.

#### Usage

```
longitudinal_consensus_cluster(
  data = NULL,
  id_column = NULL,
  max_k = 3,
  reps = 10,
  p_item = 0.8,
  model_list = NULL,
```

```
flexmix_formula = as.formula("~s(visit, k = 4) | patient_id"),
title = "untitled_consensus_cluster",
final_linkage = c("average", "ward.D", "ward.D2", "single", "complete", "mcquitty",
    "median", "centroid"),
seed = 3794,
verbose = FALSE
```

#### Arguments

)

data	a data.frame with one or several observations per subject. It needs to contain one column that specifies to which subject the entry (row) belongs to. This ID column is specified in id_column. Otherwise, there are no restrictions on the column names, as the model is specified in flexmix_formula.
id_column	name (character vector) of the ID column in data to identify all observations of one subject
max_k	maximum number of clusters, default is 3
reps	number of repetitions, default is 10
p_item	fraction of samples contained in subsampled sample, default is 0.8
<pre>model_list flexmix_formula</pre>	either one flexmix driver or a list of flexmix drivers of class FLXMR
	a formula object that describes the flexmix model relative to the formula in the flexmix drivers (the dot in the flexmix drivers is replaced, see the example). That means that you usually only specify the right-hand side of the formula here. However, this is not enforced or checked to give you more flexibility over the flexmix interface
title	name of the clustering; used if writeTable = TRUE
final_linkage	<pre>linkage used for the last hierarchical clustering step on the consensus matrix; has to be average,ward.D,ward.D2,single,complete,mcquitty,median or centroid. The default is average</pre>
seed	seed for reproducibility
verbose	boolean if status messages should be displayed. Default is FALSE

#### Details

The data types longitudinal\_consensus\_cluster can handle depends on how the flexmix models are set up, in principle all data types are supported for which there is a flexmix driver with the desired outcome variable.

If you follow the dimension reduction approach outlined in vignette("Example clustering analysis", package = "longmixr"), the input data types depend on what FAMD from the FactoMineR package can handle. FAMD accepts numeric variables and treats all other variables as factor variables which it can handle as well.

#### Value

An object (list) of class lcc with length maxk. The first entry general\_information contains the entries:

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```
plot.lcc
```

consensus_matrices	a list of all consensus matrices (for all specified clusters)
cluster_assignments	a data.frame with an ID column named after id_column and a column for every specified number
call	the call/all arguments how longitudinal_consensus_cluster was called

The other entries correspond to the number of specified clusters (e.g. the second entry corresponds to 2 specified clusters) and each contains a list with the following entries:

consensus_matrix	the consensus matrix
consensus_tree	the result of the hierarchical clustering on the consensus matrix
consensus_class	the resulting class for every observation
found_flexmix_clusters	a vector of the actual found number of clusters by flexmix (which can deviate from the specifie

#### Examples

```
set.seed(5)
test_data <- data.frame(patient_id = rep(1:10, each = 4),</pre>
visit = rep(1:4, 10),
var_1 = c(rnorm(20, -1), rnorm(20, 3)) +
rep(seq(from = 0, to = 1.5, length.out = 4), 10),
var_2 = c(rnorm(20, 0.5, 1.5), rnorm(20, -2, 0.3)) +
rep(seq(from = 1.5, to = 0, length.out = 4), 10))
model_list <- list(flexmix::FLXMRmgcv(as.formula("var_1 ~ .")),</pre>
flexmix::FLXMRmgcv(as.formula("var_2 ~ .")))
clustering <- longitudinal_consensus_cluster(</pre>
data = test_data,
id_column = "patient_id",
max_k = 2,
reps = 3,
model_list = model_list,
flexmix_formula = as.formula("~s(visit, k = 4) | patient_id"))
# not run
# plot(clustering)
# end not run
```

```
plot.lcc
```

Plot a longitudinal consensus clustering

#### Description

Plot a longitudinal consensus clustering

#### Usage

```
## S3 method for class 'lcc'
plot(x, color_palette = NULL, ...)
```

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#### Arguments

Х	<pre>lcc object (output from longitudinal_consensus_cluster)</pre>
color_palette	optional character vector of colors for consensus matrix
	additional parameters for plotting; currently not used

#### Value

Plots the following plots:

consensus matrix legend	the legend for the following consensus matrix plots
consensus matrix plot	for every specified number of clusters, a heatmap of the consensus matrix and the result of the fin
consensus CDF	a line plot of the CDFs for all different specified numbers of clusters
Delta area	elbow plot of the difference in the CDFs between the different numbers of clusters
tracking plot	cluster assignment of the subjects throughout the different cluster solutions
item-consensus	for every item (subject), calculate the average consensus value with all items that are assigned to
cluster-consensus	every bar represents the average pair-wise item-consensus within one consensus cluster

```
test_clustering_methods
```

Try out different linkage methods

#### Description

In the final step, the consensus clustering performs a hierarchical clustering step on the consensus cluster. This function tries out different linkage methods and returns the corresponding clusterings. The outputs can be plotted like the results from longitudinal\_consensus\_cluster.

#### Usage

```
test_clustering_methods(
  results,
  use_methods = c("average", "ward.D", "ward.D2", "single", "complete", "mcquitty",
        "median", "centroid")
)
```

#### Arguments

results	clustering result of class lcc
use_methods	character vector of one or several items of average, ward.D, ward.D2, single,
	complete, mcquitty, median or centroid

#### Value

a list of elements, each element of class lcc. The entries are named after the used linkage method.

#### Examples

```
set.seed(5)
test_data <- data.frame(patient_id = rep(1:10, each = 4),</pre>
visit = rep(1:4, 10),
var_1 = c(rnorm(20, -1), rnorm(20, 3)) +
rep(seq(from = 0, to = 1.5, length.out = 4), 10),
var_2 = c(rnorm(20, 0.5, 1.5), rnorm(20, -2, 0.3)) +
rep(seq(from = 1.5, to = 0, length.out = 4), 10))
model_list <- list(flexmix::FLXMRmgcv(as.formula("var_1 ~ .")),</pre>
flexmix::FLXMRmgcv(as.formula("var_2 ~ .")))
clustering <- longitudinal_consensus_cluster(</pre>
data = test_data,
id_column = "patient_id",
max_k = 2,
reps = 3,
model_list = model_list,
flexmix_formula = as.formula("~s(visit, k = 4) | patient_id"))
clustering_linkage <- test_clustering_methods(results = clustering,</pre>
use_methods = c("average", "single"))
# not run
# plot(clustering_linkage[["single"]])
# end not run
```

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