Package 'LACE'

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Title Longitudinal Analysis of Cancer Evolution (LACE)

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Depends R (>= 3.6.0)

Imports graphics, grDevices, igraph, parallel, RColorBrewer, Rfast,
stats, utils

Suggests BiocGenerics, BiocStyle, testthat, knitr

Name LACE: an R package for the inference of longitudinal cancer
evolution models

Description LACE is an algorithmic framework that processes single-cell somatic mutation profiles from cancer samples collected at different time points and in distinct experimental settings, to produce longitudinal models of cancer evolution. The approach solves a Boolean Matrix Factorization problem with phylogenetic constraints, by maximizing a weighed likelihood function computed on multiple time points.

Encoding UTF-8

LazyData TRUE

License file LICENSE

URL https://github.com/BIMIB-DISCo/LACE

BugReports https://github.com/BIMIB-DISCo/LACE

biocViews BiomedicalInformatics

RoxygenNote 7.0.2

VignetteBuilder knitr

NeedsCompilation no

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`data` *mutation data from Rambow, Florian, et al. "Toward minimal residual disease-directed therapy in melanoma." Cell 174.4 (2018): 843-855.*

Description

mutation data from Rambow, Florian, et al. "Toward minimal residual disease-directed therapy in melanoma." Cell 174.4 (2018): 843-855.

Usage

```
data(data)
```

Format

list of mutation data for four time points

Value

list of mutational data for a total of 475 single cells

Source

Rambow, Florian, et al. "Toward minimal residual disease-directed therapy in melanoma." Cell 174.4 (2018): 843-855.

`inference` *results obtained with the function LACE on the provided input data from Rambow, Florian, et al. "Toward minimal residual disease-directed therapy in melanoma." Cell 174.4 (2018): 843-855.*

Description

results obtained with the function LACE on the provided input data from Rambow, Florian, et al. "Toward minimal residual disease-directed therapy in melanoma." Cell 174.4 (2018): 843-855.

Usage

```
data(inference)
```

Format

results obtained with the function LACE on the provided input data

Value

results obtained with the function LACE on the provided input data

`LACE` *LACE*

Description

Perform inference of the maximum likelihood clonal tree from longitudinal data.

Usage

```
LACE(
  D,
  lik_w = NULL,
  alpha = NULL,
  beta = NULL,
  initialization = NULL,
  keep_equivalent = TRUE,
  check_indistinguishable = TRUE,
  num_rs = 50,
  num_iter = 10000,
  n_try_bs = 500,
  learning_rate = 1,
  marginalize = FALSE,
  num_processes = Inf,
  seed = NULL,
  verbose = TRUE,
  log_file = ""
)
```

Arguments

`D` Mutation data from multiple experiments for a list of driver genes.

`lik_w` Weight for each data point. If not provided, weights to correct for sample sizes are used.

`alpha` False positive error rate provided as list of elements; if a vector of alpha (and beta) is provided, the inference is performed for multiple values and the solution at maximum-likelihood is returned.

`beta` False negative error rate provided as list of elements; if a vector of beta (and alpha) is provided, the inference is performed for multiple values and the solution at maximum-likelihood is returned.

`initialization` Starting point of the mcmc; if not provided, a random starting point is used.

`keep_equivalent`
Boolean. Shall I return results (B and C) at equivalent likelihood with the best returned solution?

`check_indistinguishable`
Boolean. Shall I remove any indistinguishable event from input data prior inference?

`num_rs` Number of restarts during mcmc inference.

`num_iter` Maximum number of mcmc steps to be performed during the inference.

`n_try_bs` Number of steps without change in likelihood of best solution after which to stop the mcmc.

`learning_rate` Parameter to tune the probability of accepting solutions at lower values during mcmc. Value of learning_rate = 1 (default), set a probability proportional to the difference in likelihood; values of learning_rate greater than 1 inclease the chance of accepting solutions at lower likelihood during mcmc while values lower than 1 decrease such probability.

`marginalize` Boolean. Shall I marginalize C when computing likelihood?

`num_processes` Number of processes to be used during parallel execution. To execute in single process mode, this parameter needs to be set to either NA or NULL.

`seed` Seed for reproducibility.

`verbose` Boolean. Shall I print to screen information messages during the execution?

`log_file` log file where to print outputs when using parallel. If parallel execution is disabled, this parameter is ignored.

Value

A list of 9 elements: B, C, clones_prevalence, relative_likelihoods, joint_likelihood, clones_summary and error_rates. Here, B returns the maximum likelihood longitudinal clonal tree, C the attachment of cells to clones, corrected_genotypes the corrected genotypes and clones_prevalence clones' prevalence; relative_likelihoods and joint_likelihood are respectively the likelihood of the solutions at each individual time points and the joint likelihood; clones_summary provide a summary of association of mutations to clones. In equivalent_solutions, solutions (B and C) with likelihood equivalent to the best solution are returned. Finally error_rates provides the best values of alpha and beta among the considered ones.

Examples

```
data(data)
inference = LACE(D = data,
                 lik_w = c(0.2308772,0.2554386,0.2701754,0.2435088),
                 alpha = list(c(0.10,0.05,0.05,0.05)),
                 beta = list(c(0.10,0.05,0.05,0.05)),
                 keep_equivalent = FALSE,
                 num_rs = 5,
                 num_iter = 10,
                 n_try_bs = 5,
                 num_processes = NA,
                 seed = 12345,
                 verbose = FALSE)
```

`longitudinal.tree.plot` *longitudinal.tree.plot*

Description

Plot a longitudinal tree inferred by LACE.

Usage

```
longitudinal.tree.plot(
  inference,
  labels = "mutations",
  clone_labels = NULL,
  label.cex = 1,
  iter_max = 100,
  size = 500,
  size2 = NULL,
  tk_plot = FALSE,
  tp_mark = TRUE,
  tp_mark_alpha = 0.5,
  legend = TRUE,
  legend_position = "topleft",
  legend_cex = 0.8
)
```

Arguments

`inference` Results of the inference by LACE.

`labels` Specify which type of label should be placed on the tree; options are, "mutations": parental edges are labeled with the acquired mutation between the two nodes (genotypes); "clones": nodes (genotypes) are labeled with their last acquired mutation; "both": either nodes and edges are labeled as specified above; "none": no labels will show on the longitudinal tree.

`clone_labels` Character vector that specifies the name of the nodes (genotypes). If it is NULL (default), nodes will be labeled as specified by "label" parameter.

`label.cex` Specify the size of the labels.

`iter_max` Maximum number of iteration to be used to remove intersecting edges.

`size` Specify size of the nodes. The final area is proportional with the node prevalence.

`size2` Specify the size of the second dimension of the nodes. If NULL (default), it is set equal to "size".

`tk_plot` If TRUE, uses tkplot function from igraph library to plot an interactive tree. Default is FALSE.

`tp_mark` If TRUE (defaul) the function draws different colored area under the nodes in different time points.

`tp_mark_alpha` Specify the alpha value of the area drawed when tp_mark = TRUE.

`legend` If TRUE (default) a legend will be displayed on the plot.

`legend_position`
Specify the legend position.

`legend_cex` Specify size of the legend text.

Examples

```
data(inference)
clone_labels = c("ARPC2","RPL5","PRAME","COL1A2","CCT8","HNRNPC")
longitudinal.tree.plot(inference = inference,
                       labels = "clones",
                       clone_labels = clone_labels,
                       legend_position = "topright")
```

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