Package ‘cardelino’

May 3, 2024

Type Package
Title Clone Identification from Single Cell Data
Version 1.6.0
Description Methods to infer clonal tree configuration for a population of cells using single-cell RNA-seq data (scRNA-seq), and possibly other data modalities. Methods are also provided to assign cells to inferred clones and explore differences in gene expression between clones. These methods can flexibly integrate information from imperfect clonal trees inferred based on bulk exome-seq data, and sparse variant alleles expressed in scRNA-seq data. A flexible beta-binomial error model that accounts for stochastic dropout events as well as systematic allelic imbalance is used.
License GPL-3
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BugReports https://github.com/single-cell-genetics/cardelino/issues
Depends R (>= 4.2), stats
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Contents

assign_cells_to_clones .................................................. 3
assign_scores ............................................................ 4
A_clone ................................................................. 4
A_germline ............................................................. 5
binaryPRC ............................................................... 6
binaryROC ............................................................... 7
Clone ID ................................................................. 8
colMatch ............................................................... 11
Config_all ............................................................. 12
devianceIC ............................................................. 12
donor_read_simulator .................................................... 13
D_clone ................................................................. 14
D_germline ............................................................ 14
D_input ................................................................. 15
get_logLik ............................................................. 16
get_snp_matrices ......................................................... 16
get_tree ............................................................... 17
Geweke_Z ............................................................. 18
heatmap.theme .......................................................... 19
heat_matrix .......................................................... 19
load_cellSNP_vcf ....................................................... 20
load_GT_vcf .......................................................... 21
mixBinom .............................................................. 22
mtx_to_df ............................................................ 23
multiPRC .............................................................. 23
plot_config_diffs ......................................................... 24
plot_tree .............................................................. 25
predMixBinom .......................................................... 26
prob_heatmap .......................................................... 26
pub.theme ............................................................ 27
read_vcf ............................................................... 28
rowArgmax .............................................................. 29
rowMax ............................................................... 29
sample_seq_depth ........................................................ 30
sample_tree_SNV ......................................................... 31
sim_read_count ........................................................ 31
**assign_cells_to_clones**

Assign cells to clones from cardelino results

**Description**

Assign cells to clones from cardelino results

**Usage**

```r
assign_cells_to_clones(prob_mat, threshold = 0.5)
```

**Arguments**

- `prob_mat`: numeric matrix (cells x clones) of clone posterior probabilities as output by `clone_id`
- `threshold`: numeric(1), posterior probability threshold for cell-clone assignment: if posterior probability is above threshold, assign cell to clone, otherwise leave cell "unassigned"

**Value**

a `data.frame` with cell ID, assigned clone label and maximum posterior probability across clones.

**Author(s)**

Davis McCarthy

**Examples**

```r
data(example_donor)
assignments <- clone_id(A_clone, D_clone, Config = tree$Z, inference = "EM")
df <- assign_cells_to_clones(assignments$prob)
head(df)
table(df$clone)
```
**assign_scores**  
*Scoring the simulation in assignment of singlets and doublets*

**Description**
Scoring the simulation in assignment of singlets and doublets

**Usage**
```r
assign_scores(prob, I_sim, cutoff = seq(0, 1, 0.001))
```

**Arguments**
- `prob`  Probability matrix for each cell to each component
- `I_sim`  The true identity of assignment from simulation
- `cutoff`  A list of cutoffs from 0 to 1

**Value**
A list with components: `df_sg`, the recall/precision data.frame calculated by `multiPRC()`, `AUC_sg`, the AUC calculated by `multiPRC()`, `df_db`, the recall/precision data.frame calculated by `binaryPRC()` and `AUC_db` the AUC calculated by `binaryPRC()`. Note that `multiPRC()` is run on a multiclass version of the problem and `binaryPRC` is run on a binarised version of the problem.

**A_clone**  
*A matrix of read numbers of alternative alleles for clone ID*

**Description**
This matrix contains read numbers of alternative alleles for 34 somatic variants across 428 cells, from one example scRNA-seq sample

**Usage**
```r
eexample_donor
```

**Format**
a matrix of float

**Value**
NULL, but makes available a matrix
**A_germline**

**Author(s)**
Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**
A fibroblast sample from HipSci project

---

| A_germline | A matrix of read numbers of alternative alleles |

**Description**
This matrix contains read numbers of alternative alleles for 34 germline variants (near the somatic variants) across 428 cells, from one example scRNA-seq sample

**Usage**
example_donor

**Format**
a matrix of float

**Value**
NULL, but makes available a matrix

**Author(s)**
Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**
A fibroblast sample from HipSci project
Description

Precision-recall curve for binary label prediction

Usage

binaryPRC(
  scores,
  labels,
  cutoff = NULL,
  cut_direction = ">=",
  add_cut1 = FALSE,
  empty_precision = 1
)

Arguments

scores          Prediction score for each sample
labels          True labels for each sample, e.g., from simulation
cutoff          A vector of cutoffs; if NULL use all unique scores
cut_direction   A string to compare with cutoff: >=, >, <=, <
add_cut1        Logical value; if True, manually add a cutoff of 1
empty_precision Float value for default precision if no any recall

Value

A data.frame containing recall and precision values at various cutoffs.

Examples

scores <- 1:10
labels <- c(0, 0, 0, 1, 0, 1, 0, 1, 1, 1)
binaryPRC(scores, labels)

# Extra arguments.
binaryPRC(scores, labels, cutoff = seq(1, 10, by = 2))
binaryPRC(scores, labels, cut_direction = ">")
binaryPRC(scores, labels, add_cut1 = TRUE)
binaryROC

**Description**

ROC curve for binary label prediction

**Usage**

```r
binaryROC(
  scores,
  labels,
  cutoff = NULL,
  cut_direction = ">=",
  add_cut1 = TRUE,
  cutoff_point = 0.9
)
```

**Arguments**

- `scores`: Prediction score for each sample
- `labels`: True labels for each sample, e.g., from simulation
- `cutoff`: A vector of cutoffs; if NULL use all unique scores
- `cut_direction`: A string to compare with cutoff: `>=`, `>`, `<=`, `<`
- `add_cut1`: Logical value; if True, manually add a cutoff of 1
- `cutoff_point`: Numeric value; additional cutoff value

**Value**

A data.frame containing AUC and AUPRC at various cutoffs.

**Examples**

```r
scores <- 1:10
labels <- c(0, 0, 0, 1, 0, 1, 0, 1, 1, 1)
binaryROC(scores, labels)

# Extra arguments.
binaryROC(scores, labels, cutoff = seq(1, 10, by = 2))
binaryROC(scores, labels, cut_direction = ">")
binaryROC(scores, labels, add_cut1 = TRUE)
```
Clone ID  

_Infer clonal identity of single cells_

Description

Infer clonal identity of single cells

Assign cells to clones using an EM algorithm

Assign cells to clones using a Gibbs sampling algorithm

Usage

```r
clone_id(
  A,
  D,
  Config = NULL,
  n_clone = NULL,
  Psi = NULL,
  relax_Config = TRUE,
  relax_rate_fixed = NULL,
  inference = "sampling",
  n_chain = 1,
  n_proc = 1,
  verbose = TRUE,
  ...
)
```

```r
clone_id_EM(
  A,
  D,
  Config,
  Psi = NULL,
  min_iter = 10,
  max_iter = 1000,
  logLik_threshold = 1e-05,
  verbose = TRUE
)
```

```r
clone_id_Gibbs(
  A,
  D,
  Config,
  Psi = NULL,
  relax_Config = TRUE,
  relax_rate_fixed = NULL,
  relax_rate_prior = c(1, 9),
  keep_base_clone = TRUE,
```
prior0 = c(0.2, 99.8),
prior1 = c(0.45, 0.55),
min_iter = 5000,
max_iter = 20000,
buin_frac = 0.5,
wise = "variant",
relabel = FALSE,
verbose = TRUE
}

Arguments

A

variant x cell matrix of integers; number of alternative allele reads in variant i cell j

D

variant x cell matrix of integers; number of total reads covering variant i cell j

Config

variant x clone matrix of binary values. The clone-variant configuration, which encodes the phylogenetic tree structure. This is the output Z of Canopy

n_clone

integer(1), the number of clone to reconstruct. This is in use only if Config is NULL

Psi

A vector of float. The fractions of each clone, output P of Canopy

relax_Config

logical(1), If TRUE, relaxing the Clone Configuration by changing it from fixed value to act as a prior Config with a relax rate.

relax_rate_fixed

numeric(1), If the value is between 0 to 1, the relax rate will be set as a fix value during updating clone Config. If NULL, the relax rate will be learned automatically with relax_rate_prior.

inference

character(1), the method to use for inference, either "sampling" to use Gibbs sampling (default) or "EM" to use expectation-maximization (faster)

n_chain

integer(1), the number of chains to run, which will be averaged as an output result

n_proc

integer(1), the number of processors to use. This parallel computing can largely reduce time when using multiple chains

verbose

logical(1), should the function output verbose information as it runs?

... arguments passed to clone_id_Gibbs or clone_id_EM (as appropriate)

min_iter

A integer. The minimum number of iterations in the Gibbs sampling. The real iteration may be longer until the convergence.

max_iter

A integer. The maximum number of iterations in the Gibbs sampling, even haven’t passed the convergence diagnosis

logLik_threshold

A float. The threshold of logLikelihood increase for detecting convergence.

relax_rate_prior

numeric(2), the two parameters of beta prior distribution of the relax rate for relaxing the clone Configuration. This mode is used when relax_relax is NULL.
keep_base_clone
bool(1), if TRUE, keep the base clone of Config to its input values when relax mode is used.

prior0 numeric(2), alpha and beta parameters for the Beta prior distribution on the inferred false positive rate.

prior1 numeric(2), alpha and beta parameters for the Beta prior distribution on the inferred (1 - false negative) rate.

buin_frac numeric(1), the fraction of chain as burn-in period

wise A string, the wise of parameters for theta1: global, variant, element.

relabel bool(1), if TRUE, relabel the samples of both Config and prob during the Gibbs sampling.

Details
The two Bernoulli components correspond to false positive and false negative rates. The two binomial components correspond to the read distributions with and without the mutation present.

Value
If inference method is "EM", a list containing theta, a vector of two floats denoting the parameters of the two components of the base model, i.e., mean of Bernoulli or binomial model given variant exists or not; prob, the matrix of posterior probabilities of each cell belonging to each clone with fitted parameters; and logLik, the log likelihood of the final parameters.

If inference method is "sampling", a list containing: theta0, the mean of sampled false positive parameter values; theta1 the mean of sampled (1 - false negative rate) parameter values; theta0_all, all sampled false positive parameter values; theta1_all, all sampled (1 - false negative rate) parameter values; element; logLik_all, log-likelihood for model for all sampled parameter sets; prob_all; prob, matrix with mean of sampled cell-clone assignment posterior probabilities (the key output of the model); prob_variant.

a list containing theta, a vector of two floats denoting the binomial rates given variant exists or not; prob, the matrix of posterior probabilities of each cell belonging to each clone with fitted parameters, and logLik, the log likelihood of the final parameters.

Author(s)
Yuanhua Huang and Davis McCarthy
Yuanhua Huang

Examples
```
data(example_donor)
assignments <- clone_id(A_clone, D_clone,
    Config = tree$Z,
    min_iter = 800, max_iter = 1200
)
prob_heatmap(assignments$prob)

assignments_EM <- clone_id(A_clone, D_clone,
```
**colMatch**

Column match between two matrices by minimum mean absolute difference

**Description**

Column match between two matrices by minimum mean absolute difference

**Usage**

```r
colMatch(A, B, force = FALSE)
```

**Arguments**

- **A**
  - The first matrix which will be matched
- **B**
  - The second matrix, the return index will be used on
- **force**
  - `bool(1)`, If TRUE, force traversing all permutations of B to find the optimised match to A with computing cost of O(n!). Otherwise, use greedy search with computing cost of O(n^2).

**Value**

`idx`, the column index of B to be matched to A

**Examples**

```r
matA <- matrix(sample(seq(12)), nrow = 3)
col_idx <- sample(4)
matB <- matA[, col_idx]
colMatch(matB, matA)
```
**Config_all**

*A list of tree configuration*

**Description**
This list of tree configuration between 3 clones to 10 clones, each element is a list with all possible tree matrix.

**Usage**

```r
cfg_all
```

**Format**
a list of list of matrix

**Value**
NULL, but makes available a list

**Author(s)**
Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**
PASTRI Python package

---

**devianceIC**

*Deviance Information Criterion for cardelino model*

**Description**
Deviance Information Criterion for cardelino model.

**Usage**

```r
devianceIC(logLik_all, logLik_post)
```

**Arguments**

- **logLik_all**
  A vector of numeric; the log likelihood of posterior sample, i.e., posterior samples of deviance.

- **logLik_post**
  numeric(1); the log likelihood of mean posterior parameters, i.e., deviance of posterior means.
**donor_read_simulator**

**Value**

DIC, a float of deviance information criterion

**Author(s)**

Yuanhua Huang

---

**donor_read_simulator**  
*Reads simulator for donor identification*

---

**Description**

Reads simulator for donor identification

**Usage**

```r
donor_read_simulator(
  GT,
  D_seed,
  sample_variants = FALSE,
  donor_size = NULL,
  beta_shapes = NULL,
  n_cell = 5000,
  doublet_rate = NULL
)
```

**Arguments**

- **GT**: Variant-by-donor matrix for genotypes
- **D_seed**: Variant-by-cell matrix for read coverage for generating depth, which be row sample and column sample both with replacement
- **sample_variants**: logical(1), if TRUE, sample variants with replacement to the same size, otherwise not
- **donor_size**: Vector of float for the fractions of each donor; default NULL means uniform
- **beta_shapes**: A 3-by-2 matrix of beta parameters for genotypes: 0, 1, and 2; default NULL means matrix(c(0.2, 0.5, 99.8, 99.8, 0.5, 0.2), nrow = 3)
- **n_cell**: An integer for number of total cells
- **doublet_rate**: A float from 0 to 1 for doublet rate; default NULL means rate n_cell / 100000

**Value**

A list of various components of the simulated dataset.
### D_clone

**Description**
This matrix contains sequencing depths for 34 somatic variants across 428 cells, from one example scRNA-seq sample.

**Usage**
example_donor

**Format**
a matrix of float

**Value**
NULL, but makes available a matrix

**Author(s)**
Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**
A fibroblast sample from HipSci project

---

### D_germline

**Description**
This matrix contains sequencing depths for 34 germline variants (near the somatic variants) across 428 cells, from one example scRNA-seq sample.

**Usage**
example_donor

**Format**
a matrix of float

**Value**
NULL, but makes available a matrix
**D_input**

**Author(s)**

Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**

A fibroblast sample from HipSci project

---

**D_input**

*A matrix of sequencing depths*

---

**Description**

This matrix contains sequencing depths for 439 somatic variants across 151 cells, from one particular scRNA-seq sample, can be used to generate sequencing depths

**Usage**

`simulation_input`

**Format**

a matrix of float

**Value**

NULL, but makes available a matrix

**Author(s)**

Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**

A fibroblast sample from HipSci project
get_logLik

Log likelihood of clone_id model It returns $P(A, D \mid C, I, \theta_0, \theta_1)$

Description
Log likelihood of clone_id model It returns $P(A, D \mid C, I, \theta_0, \theta_1)$

Usage
get_logLik(A1, B1, Config, Assign, theta0, theta1)

Arguments
A1 variant x cell matrix of integers; number of alternative allele reads in variant i cell j
B1 variant x cell matrix of integers; number of reference allele reads in variant i cell j
Config variant x clone matrix of float values. The clone-variant configuration probability, averaged by posterior samples
Assign cells x clone matrix of float values. The cell-clone assignment probability, averaged by posterior samples
theta0 the binomial rate for alternative allele from config = 0
theta1 the binomial rate for alternative allele from config = 1

Value
logLik, a float of log likelihood

Author(s)
Yuanhua Huang

get_snp_matrices

Get SNP data matrices from VCF object(s)

Description
Get SNP data matrices from VCF object(s)

Usage
get_snp_matrices(vcf_cell, vcf_donor = NULL, verbose = TRUE, donors = NULL)
get_tree

Arguments

vcf_cell a CollapsedVCF object containing variant data for cells
vcf_donor an optional CollapsedVCF object containing genotype data for donors
verbose logical(1), should the function output verbose information as it runs?
donors optional character vector providing a set of donors to use, by subsetting the donors present in the donor_vcf_file; if NULL (default) then all donors present in VCF will be used.

Value

a list containing A, a matrix of integers. Number of alteration reads in SNP i cell j. D, a matrix of integers. Number of reads depth in SNP i cell j. R, a matrix of integers. Number of reference reads in SNP i cell j. GT_cells, a matrix of integers for genotypes. The cell-SNP configuration. GT_donors, a matrix of integers for genotypes. The donor-SNP configuration.

Examples

vcf_cell <- read_vcf(system.file("extdata", "cells.donorid.vcf.gz", package = "cardelino"))
vcf_donor <- read_vcf(system.file("extdata", "donors.donorid.vcf.gz", package = "cardelino"))
snp_data <- get_snp_matrices(vcf_cell, vcf_donor)

get_tree

Get a clonal tree from a configuration matrix

Description

Get a clonal tree from a configuration matrix

Usage

get_tree(Config, P = NULL, strictness = "lax")

Arguments

Config variant x clone matrix of binary values. The clone-variant configuration, which encodes the phylogenetic tree structure. This is the output Z of Canopy
P a one-column numeric matrix encoding the (observed or estimated) prevalence (or frequency) of each clone
strictness character(1), a character string defining the strictness of the function if there are all-zero rows in the Config matrix. If "lax" then the function silently drops all-zero rows and proceeds. If "warn" then the function warns of dropping all-zero rows and proceeds. If "error" then the function throws an error if all-zero rows are detected.
Details

Output tree may be nonsensical if the input Config matrix does not define a coherent tree structure.

Value

An object of class "phylo" describing the tree structure. The output object also contains an element "sna" defining the clustering of variants onto the branches of the tree, and if P is non-null it also contains VAF (variant allele frequency), CCF (cell clone fraction) and clone prevalence values (computed from the supplied P argument).

Author(s)

Davis McCarthy

Examples

```r
Configk3 <- matrix(c(
  rep(0, 15), rep(1, 8), rep(0, 7), rep(1, 5), rep(0, 3),
  rep(1, 7)
), ncol = 3)
tree_k3 <- get_tree(Config = Configk3, P = matrix(rep(1 / 3, 3), ncol = 1))
plot_tree(tree_k3)
```

Geweke_Z

Geweke diagnostic for MCMC sampling.

Description

Geweke diagnostic for MCMC sampling.

Usage

```r
Geweke_Z(X, first = 0.1, last = 0.5)
```

Arguments

- `X`: A matrix of MCMC samples for N samples per K variables
- `first`: A float between 0 and 1. The initial region of MCMC chain.
- `last`: A float between 0 and 1. The final region of MCMC chain.

Value

`Z`, a vector of absolute value of Z scores for each variable. When |Z| <= 2, the sampling could be taken as converged.

Author(s)

Yuanhua Huang
**heatmap.theme**

*The theme of heatmaps for prob_heatmap and sites_heatmap*

**Description**

The theme of heatmaps for prob_heatmap and sites_heatmap

**Usage**

```r
heatmap.theme(legend.position = "bottom", size = 12)
```

**Arguments**

- `legend.position` character, describes where to place legend on plot (passed to `theme_gray`)
- `size` numeric, base font size for plot (passed to `theme_gray`)

**Value**

A ggplot theme based on `theme_gray`

---

**heat_matrix**

*Plot heatmap from a matrix*

**Description**

Plot heatmap from a matrix

**Usage**

```r
heat_matrix(mat, base_size = 12, digits = 2, show_value = FALSE)
```

**Arguments**

- `mat` A matrix to show, column by x-axis and row by y-axis
- `base_size` Numeric value for the base size in `theme_bw`
- `digits` Integer value for the number of digits to show
- `show_value` Logical value for showing the value for each element or not

**Value**

A ggplot heatmap visualization of the passed matrix.
Examples

```r
mat <- matrix(rnorm(9), ncol = 3, nrow = 3) + diag(rnorm(3, 2, 0.1))
rownames(mat) <- paste0("sample_", letters[1:3])
colnames(mat) <- paste0("var_", 1:3)
heat_matrix(mat)

# Additional arguments.
heat_matrix(mat, base_size = 6)
heat_matrix(mat, show_value = TRUE)
heat_matrix(mat, show_value = TRUE, digits = 4)
```

---

**load_cellSNP_vcf**

Load sparse matrices A and D from cellSNP VCF file with filtering SNPs

**Description**

Load sparse matrices A and D from cellSNP VCF file with filtering SNPs

**Usage**

```r
load_cellSNP_vcf(
  vcf_file,
  min_count = 0,
  min_MAF = 0,
  max_other_allele = NULL,
  rowname_format = "full",
  keep_GL = FALSE
)
```

**Arguments**

- **vcf_file**: character(1), path to VCF file generated from cellSNP
- **min_count**: minimum count across all cells, e.g., 20
- **min_MAF**: minimum minor allele fraction, e.g., 0.1
- **max_other_allele**: maximum ratio of other alleles comparing to REF and ALT alleles; for cellSNP vcf, we recommend 0.05
- **rowname_format**: the format of rowname: NULL is the default from vcfR, short is CHROM_POS, and full is CHROM_POS_REF_ALT
- **keep_GL**: logical(1), if TRUE, check if GL (genotype probability) exists it will be returned

**Value**

A list with elements the matrices A and D and GL, the genotype probability. If keep_GL is false the GL element will be an empty list.
load_GT_vcf

Examples

```r
vcf_file <- system.file("extdata", "cellSNP.cells.vcf.gz", 
    package = "cardelino"
)
input_data <- load_cellSNP_vcf(vcf_file)
```
# mixBinom

**EM algorithm for estimating binomial mixture model**

## Description

EM algorithm for estimating binomial mixture model

## Usage

```r
mixBinom(
  k,
  n,
  n_components = 2,
  p_init = NULL,
  learn_p = TRUE,
  min_iter = 10,
  max_iter = 1000,
  logLik_threshold = 1e-05
)
```

## Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>k</code></td>
<td>A vector of integers. number of success</td>
</tr>
<tr>
<td><code>n</code></td>
<td>A vector of integers. number of trials</td>
</tr>
<tr>
<td><code>n_components</code></td>
<td>A number. number of components</td>
</tr>
<tr>
<td><code>p_init</code></td>
<td>A vector of floats with length <code>n_components</code>, the initial value of <code>p</code></td>
</tr>
<tr>
<td><code>learn_p</code></td>
<td>bool(1) or a vector of bool, whether learn each <code>p</code></td>
</tr>
<tr>
<td><code>min_iter</code></td>
<td>integer(1). number of minimum iterations</td>
</tr>
<tr>
<td><code>max_iter</code></td>
<td>integer(1). number of maximum iterations</td>
</tr>
<tr>
<td><code>logLik_threshold</code></td>
<td>A float. The threshold of logLikelihood increase for detecting convergence</td>
</tr>
</tbody>
</table>

## Value

A list containing `p`, a vector of floats between 0 and 1 giving the estimated success probability for each component, `psi`, estimated fraction of each component in the mixture, and `prob`, the matrix of fitted probabilities of each observation belonging to each component.

## Examples

```r
n1 <- array(sample(1:30, 50, replace = TRUE))
n2 <- array(sample(1:30, 200, replace = TRUE))
k1 <- apply(n1, 1, rbinom, n = 1, p = 0.5)
k2 <- apply(n2, 1, rbinom, n = 1, p = 0.01)
RV <- mixBinom(c(k1, k2), c(n1, n2))
```
** mtx_to_df **

* Convert a matrix to data frame *

** Description **

Convert a matrix to data frame

** Usage **

```r
mtx_to_df(X)
```

** Arguments **

- `X` A matrix of values

** Value **

A data.frame version of the passed matrix.

** Examples **

```r
mtx_to_df(matrix(seq(12), nrow = 3))
```

---

** multiPRC **

* Precision-recall curve for multi-class prediction *

** Description **

Precision-recall curve for multi-class prediction

** Usage **

```r
multiPRC(
    prob_mat,
    simu_mat,
    marginal_mode = "best",
    cutoff = NULL,
    multiLabel.rm = TRUE,
    add_cut1 = FALSE
)
```
Arguments

- **prob_mat**  
  Probability matrix for each cell to each component

- **simu_mat**  
  The true identity of assignment from simulation

- **marginal_mode**  
  A string for the mode to marginalize the column: best, second, or delta

- **cutoff**  
  A list of cutoff; if NULL use all unique scores

- **multiLabel.rm**  
  Logical value; if True, remove the samples with multiple labels

- **add_cut1**  
  Logical value; if True, manually add a cutoff of 1

Value

A list with two components: df, a data.frame containing precision and recall values at various cutoffs and AUC, the overall AUC.

---

**plot_config_diffs**  
*Define a publication-style plot theme*

Description

Define a publication-style plot theme

Usage

```
plot_config_diffs(Config1, Config2, show_variant_names = FALSE)
```

Arguments

- **Config1**  
  variant by clone matrix defining the first clonal structure

- **Config2**  
  variant by clone matrix defining the second clonal structure

- **show_variant_names**  
  logical(1), should the variant names (rownames of Config matrices) be shown on the plot? Default is FALSE.

Value

a ggplot heatmap style plot showing the differences between the two Config matrices, specifically the differences Config1 - Config2.

Examples

```
Config1 <- matrix(c(
  rep(0, 15), rep(1, 8), rep(0, 7),
  rep(1, 5), rep(0, 3), rep(1, 7)
), ncol = 3)
Config2 <- matrix(c(
  rep(0, 15), rep(1, 8), rep(1, 7),
  rep(0, 5), rep(1, 3), rep(1, 7)
)
plot_tree

Plot a phylogenetic tree

Description

Plot a phylogenetic tree

Usage

plot_tree(tree, orient = "h")

Arguments

tree  A phylogenetic tree object of class "phylo"
orient A string for the orientation of the tree: "v" (vertical) or "h" (horizontal)

Details

This function plots a phylogenetic tree from an object of class "phylo", as produced, for example, by the Canopy package.

Value

a ggtree object

Author(s)

Davis McCarthy and Yuanhua Huang

References

This function makes use of the ggtree package:

Examples

data(example_donor)
plot_tree(tree, orient = "v")
**predMixBinom**  
*Predicted probability from learned binomial mixture model*

**Description**

Predicted probability from learned binomial mixture model

**Usage**

```r
predMixBinom(k, n, p, psi)
```

**Arguments**

- `k`: A vector of integers. number of success
- `n`: A vector of integers. number of trials
- `p`: A vector of binomial success probabilities
- `psi`: A float between 0 and 1. fraction of each component

**Value**

A list with two components: `prob`, a matrix representing the probability of each of the passed values coming from each component of the mixture and `logLik`, the total log-likelihood of the new samples.

**Examples**

```r
n1 <- array(sample(1:30, 50, replace = TRUE))
n2 <- array(sample(1:30, 200, replace = TRUE))
k1 <- apply(n1, 1, rbinom, n = 1, p = 0.5)
k2 <- apply(n2, 1, rbinom, n = 1, p = 0.01)
RV <- mixBinom(c(k1, k2), c(n1, n2))
RV_pred <- predMixBinom(3, 10, RV$p, RV$psi)
```

---

**prob_heatmap**  
*Plot a heatmap for probability of clone assignment*

**Description**

Plot a heatmap for probability of clone assignment

**Usage**

```r
prob_heatmap(prob_mat, threshold = 0.5, mode = "best", cell_idx = NULL)
```
Arguments

- **prob_mat**: A matrix (M x K), the probability of cell j to clone k
- **threshold**: A float value, the threshold for assignable cells
- **mode**: A string, the method for defining scores for filtering cells: best and delta. best: highest probability of a cell to K clones, delta: the difference between the best and second.
- **cell_idx**: A vector the indices of the input cells. If NULL, order by the probability of each clone

Value

a ggplot object

Examples

```r
data(example_donor)
assignments <- clone_id(A_clone, D_clone, Config = tree$Z, inference = "EM")
fig <- prob_heatmap(assignments$prob)
```

---

### pub.theme

*Define a publication-style plot theme*

**Description**

Define a publication-style plot theme

**Usage**

```r
pub.theme(size = 12)
```

**Arguments**

- **size**: numeric, base font size for adapted ggplot2 theme

**Details**

This theme modifies the `theme_classic` theme in ggplot2.

**Value**

a ggplot theme based on theme_classic
Examples

```r
library(ggplot2)
x <- sample(10)
y <- x + runif(10) - 0.5
df <- data.frame(x = x, y = y)
fig <- ggplot(df, aes(x = x, y = y)) +
  geom_point() +
  pub.theme()
```

---

**read_vcf**  
*Read a VCF file into R session*

**Description**

Read a VCF file into R session

**Usage**

```r
read_vcf(
  vcf_file,  
  genome = "GRCh37",  
  seq_levels_style = "Ensembl",  
  verbose = TRUE
)
```

**Arguments**

- `vcf_file` character(1), path to VCF file to read into R session as a `CollapsedVCF` object
- `genome` character(1), string indicating the genome build used in the VCF file(s) (default: "GRCh37")
- `seq_levels_style` character(1), string passed to `seqlevelsStyle` the style to use for chromosome/contig names (default: "Ensembl")
- `verbose` logical(1), should messages be printed as function runs?

**Value**

a vcf object

**Examples**

```r
vcf <- read_vcf(system.file("extdata", "cells.donorid.vcf.gz",  
                           package = "cardelino"))
```
**rowArgmax**

*Column index of the maximum value for each row in a matrix*

---

**Description**

Column index of the maximum value for each row in a matrix

**Usage**

\[ \text{rowArgmax}(X) \]

**Arguments**

- **X**: A matrix of floats.

**Value**

A vector of the index of column for each row. Note, when multiple columns have the same value, only the earliest column will be returned.

**Examples**

```r
matA <- matrix(sample(seq(12)), nrow = 3)
rowArgmax(matA)
```

---

**rowMax**

*Maximum value for each row in a matrix*

---

**Description**

Maximum value for each row in a matrix

**Usage**

\[ \text{rowMax}(X, \text{mode} = \text{"best"}) \]

**Arguments**

- **X**: A matrix of floats.
- **mode**: A string, the method for defining scores for filtering cells: best, second and delta. best: highest value for each row, similarly for the second. delta is the difference between the best and the second.

**Value**

A vector of the collapsed value for each row, depending on the mode used.
sample_seq_depth

Update matrix D with manually selected missing rate

Description

Given missing rate, the NA will be generated first. For none NA element, sequencing depth with uniformly sampled from D, row wisely. Namely, the depth is variant specific.

Usage

```r
sample_seq_depth(D, n_cells = NULL, n_sites = NULL, missing_rate = NULL)
```

Arguments

- `D`: A matrix (N variants x M cells), the original sequencing coverage, NA means missing
- `n_cells`: A integer, the number of the cells to generate
- `n_sites`: A integer, the number of variants to generate
- `missing_rate`: A float value, if NULL, use the same missing rate as D

Value

A n_sites by n_cells matrix sampled from input D.

Examples

```r
data(simulation_input)
D1 <- sample_seq_depth(D_input,
  n_cells = 500, n_sites = 50,
  missing_rate = 0.85
)
```
**sample_tree_SNV**

Down sample number of SNVs in the tree

**Description**

Down sample number of SNVs in the tree

**Usage**

```r
sample_tree_SNV(tree, n_SNV = NULL)
```

**Arguments**

- `tree`: A tree object from Canopy
- `n_SNV`: An integer, the number of SNVs to keep in the output tree

**Value**

A phylo tree with down sampled variants

**Examples**

```r
data(simulation_input)
tree_lite <- sample_tree_SNV(tree_4clone, n_SNV = 10)
```

**sim_read_count**

Synthetic reads generator for genetic variants

**Description**

There are following steps to generate the simulated reads counts for variants in single cells: 1) given the clonal genotype and the clonal prevalence, the genotypes (i.e., the clone) of cells will be generated following a multinomial distribution. Note, one cell may contain variants from two clones when it is a doublet. 2) given the distribution of reads coverage, e.g., a matrix of read coverage from real data, (variant specific), the total reads of each variant will be generated by random sampling. Note, the missing rate is governed by this matrix. 3) the allelic frequency of each variant will be generated by following a beta distribution with parameters of mean and variance. 4) Given the genotype of a cell, if the mutation exists in a cell, the alteration read counts will be generated by a binomial distribution, parameterized the allelic frequency, sampled from step 3. 5) Given the genotype of a cell, if the mutation does not exist in a cell, the alteration read counts will be generated by a binomial distribution, parameterized by the technical error rate.
Usage

```r
sim_read_count(
    Config,
    D,
    Psi = NULL,
    means = c(0.002, 0.45),
    vars = c(100, 1),
    wise0 = "element",
    wise1 = "variant",
    cell_num = 300,
    permute_D = FALSE,
    sample_cell = TRUE,
    doublet = 0
)
```

Arguments

- **Config**: A matrix of binary values. The clone-variant configuration, which encodes the phylogenetic tree structure, and the genotype of each clone.
- **D**: A matrix of integers. Sequencing depth for N variants across x cells (ideally >100 cells). NA means 0 here.
- **Psi**: A vector of float. The fractions of each clone. If NULL, set a uniform distribution.
- **means**: A vector of two floats. The mean theta_1 (false positive rate) and the mean theta_2 (true positive rate).
- **vars**: A vector of two floats. The variance of theta_1 and theta_2.
- **wise0**: A string, the beta-binomial parameter specificity for theta0: global, variant, element.
- **wise1**: A string, the beta-binomial parameter specificity for theta1: global, variant, element.
- **cell_num**: A integer. The number of cells to generate.
- **permute_D**: A Boolean value. If True permute variants in D.
- **sample_cell**: A Boolean value. If True and M > ncol(D), sample cells.
- **doublet**: A float between 0 and 1, the rate of doublets

Value

A list containing:
- `A_sim`, a matrix for alteration reads,
- `A_sim`, a matrix for total reads,
- `I_sim`, a matrix for clonal label,
- `H_sim`, a matrix for genotype,
- `theta0`, a matrix of expected false positive rate,
- `theta1`, a matrix of expected true positive rate,
- `theta0_binom`, theta0 as binomial parameter,
- `theta1_binom`, theta0 as binomial parameter, and
- `is_doublet`, a vector of Boolean value if a cell is a doublet.
Examples

data(simulation_input)
D2 <- sample_seq_depth(D_input, n_cells = 500, n_sites = nrow(tree_4clone$Z))
simu <- sim_read_count(tree_4clone$Z, D2, Psi = NULL, cell_num = 500)

---

tree

A tree object

---

Description

This tree object contains clonal tree information, inferred from bulk exome-seq data

Usage

eexample_donor

Format

a tree object

Value

NULL, but makes available a tree object

Author(s)

Yuanhua Huang, Davis McCarthy, 2018-06-25

Source

A fibroblast sample from HipSci project

---

tree_3clone

A tree object

---

Description

This tree object with 3 clones contains clonal tree information, inferred from bulk exome-seq data

Usage

simulation_input

Format

a tree object
**Value**

NULL, but makes a tree object available

**Author(s)**

Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**

A fibroblast sample from HipSci project

---

**Description**

This tree object with 4 clones contains clonal tree information, inferred from bulk exome-seq data

**Usage**

simulation_input

**Format**

a tree object

**Value**

NULL, but makes a tree object available

**Author(s)**

Yuanhua Huang, Davis McCarthy, 2018-06-25

**Source**

A fibroblast sample from HipSci project
tree_5clone

A tree object

Description
This tree object with 5 clones contains clonal tree information, inferred from bulk exome-seq data

Usage
simulation_input

Format
a tree object

Value
NULL, but makes available a tree object

Author(s)
Yuanhua Huang, Davis McCarthy, 2018-06-25

Source
A fibroblast sample from HipSci project

vc_heatmap
Plot a variant-cell heatmap for cell clonal assignment

Description
Plot a variant-cell heatmap for cell clonal assignment

Usage
vc_heatmap(mat, prob, Config, show_legend = FALSE)

Arguments
mat A matrix for heatmap: N variants x M cells. row and column will be sorted automatically.
prob A matrix of probability of clonal assignment: M cells x K clones
Config A binary matrix of clonal Configuration: N variants x K clones
show_legend A bool value: if TRUE, show the legend
Value

- a pheatmap object
- a ggplot object

References

This function makes use of the pheatmap packages

Examples

data(example_donor)
assignments <- clone_id(A_clone, D_clone, Config = tree$Z)
fig <- vc_heatmap(assignments$prob_variant, assignments$prob, tree$Z)
Index

<table>
<thead>
<tr>
<th>Function</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A_clone</td>
<td>4</td>
</tr>
<tr>
<td>A_germline</td>
<td>5</td>
</tr>
<tr>
<td>assign_cells_to_clones</td>
<td>3</td>
</tr>
<tr>
<td>assign_scores</td>
<td>4</td>
</tr>
<tr>
<td>binaryPRC</td>
<td>6</td>
</tr>
<tr>
<td>binaryROC</td>
<td>7</td>
</tr>
<tr>
<td>Clone ID</td>
<td>8</td>
</tr>
<tr>
<td>clone_id</td>
<td>3</td>
</tr>
<tr>
<td>clone_id (Clone ID)</td>
<td>8</td>
</tr>
<tr>
<td>clone_id_EM</td>
<td>9</td>
</tr>
<tr>
<td>clone_id_EM (Clone ID)</td>
<td>8</td>
</tr>
<tr>
<td>clone_id_Gibbs</td>
<td>9</td>
</tr>
<tr>
<td>clone_id_Gibbs (Clone ID)</td>
<td>8</td>
</tr>
<tr>
<td>CollapsedVCF</td>
<td>17, 28</td>
</tr>
<tr>
<td>colMatch</td>
<td>11</td>
</tr>
<tr>
<td>Config_all</td>
<td>12</td>
</tr>
<tr>
<td>D_clone</td>
<td>14</td>
</tr>
<tr>
<td>D_germline</td>
<td>14</td>
</tr>
<tr>
<td>D_input</td>
<td>15</td>
</tr>
<tr>
<td>devianceIC</td>
<td>12</td>
</tr>
<tr>
<td>donor_read_simulator</td>
<td>13</td>
</tr>
<tr>
<td>get_loglik</td>
<td>16</td>
</tr>
<tr>
<td>get.snp_matrices</td>
<td>16</td>
</tr>
<tr>
<td>get.tree</td>
<td>17</td>
</tr>
<tr>
<td>Geweke_Z</td>
<td>18</td>
</tr>
<tr>
<td>ggtree</td>
<td>25</td>
</tr>
<tr>
<td>heat_matrix</td>
<td>19</td>
</tr>
<tr>
<td>heatmap. theme</td>
<td>19</td>
</tr>
<tr>
<td>load_cellSNP_vcf</td>
<td>20</td>
</tr>
<tr>
<td>load_GT_vcf</td>
<td>21</td>
</tr>
<tr>
<td>mixBinom</td>
<td>22</td>
</tr>
<tr>
<td>mtx_to_df</td>
<td>23</td>
</tr>
<tr>
<td>multiPRC</td>
<td>23</td>
</tr>
<tr>
<td>pheatmap</td>
<td>26</td>
</tr>
<tr>
<td>plot_config_diffs</td>
<td>24</td>
</tr>
<tr>
<td>plot_tree</td>
<td>25</td>
</tr>
<tr>
<td>predMixBinom</td>
<td>26</td>
</tr>
<tr>
<td>prob_heatmap</td>
<td>26</td>
</tr>
<tr>
<td>pub.theme</td>
<td>27</td>
</tr>
<tr>
<td>read_vcf</td>
<td>28</td>
</tr>
<tr>
<td>rowArgmax</td>
<td>29</td>
</tr>
<tr>
<td>rowMax</td>
<td>29</td>
</tr>
<tr>
<td>sample_seq_depth</td>
<td>30</td>
</tr>
<tr>
<td>sample_tree_SNV</td>
<td>31</td>
</tr>
<tr>
<td>seqlevelsStyle</td>
<td>28</td>
</tr>
<tr>
<td>sim_read_count</td>
<td>31</td>
</tr>
<tr>
<td>theme_classic</td>
<td>27</td>
</tr>
<tr>
<td>theme_gray</td>
<td>19</td>
</tr>
<tr>
<td>tree</td>
<td>33</td>
</tr>
<tr>
<td>tree_3clone</td>
<td>33</td>
</tr>
<tr>
<td>tree_4clone</td>
<td>34</td>
</tr>
<tr>
<td>tree_5clone</td>
<td>35</td>
</tr>
<tr>
<td>vc_heatmap</td>
<td>35</td>
</tr>
</tbody>
</table>