

Package ‘DCLEAR’

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Title Distance Based Cell Lineage Reconstruction

Author Il-Youp Kwak [aut, cre],
Wuming Gong [aut]

Maintainer Il-Youp Kwak <ikwak2@cau.ac.kr>

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Suggests knitr, rmarkdown, markdown

Description R codes for distance based cell lineage reconstruction. Our methods won both sub-challenges 2 and 3 of the Allen Institute Cell Lineage Reconstruction DREAM Challenge in 2020. The challenge paper is Gong et al. (2021) <[doi:10.1016/j.cels.2021.05.008](https://doi.org/10.1016/j.cels.2021.05.008)>.

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`as_igraph`

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`as_igraph`

Generic function for as_igraph

Description

Generic function for `as_igraph`

Usage

```
as_igraph(x, ...)
```

Arguments

<code>x</code>	a phylo object
<code>...</code>	additional parameters

`as_igraph`, phylo-method

as_igraph

Description

Convert an phylo object to an igraph object, while keeping the weight (in contrast to `igraph::as.igraph`)

Usage

```
## S4 method for signature 'phylo'  
as_igraph(x)
```

Arguments

<code>x</code>	a phylo object
----------------	----------------

Value

an igraph object

as_lineage_tree *Generic function for as_lineage_tree*

Description

Generic function for as_lineage_tree

Usage

```
as_lineage_tree(x, y, config, ...)
```

Arguments

x	a phyDat object
y	a phylo object
config	a lineage_tree_config object
...	additional parameters

as_lineage_tree,phyDat,phylo,lineage_tree_config-method
as_lineage_tree

Description

Convert a phylo object and a phyDat object to a lineage_tree object

Usage

```
## S4 method for signature 'phyDat,phylo,lineage_tree_config'  
as_lineage_tree(x, y, config, ...)
```

Arguments

x	a phyDat object
y	a phylo object
config	a lineage_tree_config object
...	additional parameters

Value

a lineage_tree object

as_phylo	<i>Generic function for as_phylo</i>
----------	--------------------------------------

Description

Generic function for as_phylo

Usage

```
as_phylo(x, ...)
```

Arguments

x	a graph object
...	additional parameters

as_phylo, igraph-method	<i>as_phylo</i>
-------------------------	-----------------

Description

Convert an igraph object to a phylo object

Usage

```
## S4 method for signature 'igraph'
as_phylo(x)
```

Arguments

x	an igraph object
---	------------------

Value

a phylo object or a igraph object

DCLEAR	<i>DCLEAR: A package for DCLEAR: Distance based Cell LinEAge Re- construction</i>
--------	---

Description

Distance based methods for inferring lineage trees from single cell data

dist_kmer_replacement_inference

Core function of computing kmer replacement distance

Description

Compute the sequence distance matrix using inferred kmer replacement matrix

Usage

```
dist_kmer_replacement_inference(x, kmer_summary, k = 2)
```

Arguments

x	input data in phyDat format
kmer_summary	a kmer_summary object
k	k-mers (default k=2)

Value

a dist object

Author(s)

Wuming Gong (gongx030@umn.edu)

dist_replacement

Generic function for dist_replacement

Description

Generic function for dist_replacement

Usage

```
dist_replacement(x, kmer_summary, k, ...)
```

Arguments

x	a sequence object
kmer_summary	a kmer_summary object
k	k-mer length
...	additional parameters

dist_replacement, phyDat, kmer_summary, integer-method
Compute the kmer replacement distance

Description

Compute the kmer replacement distance between sequences

Usage

```
## S4 method for signature 'phyDat,kmer_summary,integer'  
dist_replacement(x, kmer_summary, k = 2, ...)
```

Arguments

x	input data in phyDat format
kmer_summary	a kmer_summary object
k	k-mer length
...	other arguments passed to substr_kmer

Value

a dist object

Author(s)

Wuming Gong (gongx030@umn.edu)

dist_replacement, phyDat, missing, integer-method
Compute the kmer replacement distance

Description

Compute the kmer replacement distance between sequences

Usage

```
## S4 method for signature 'phyDat,missing,integer'  
dist_replacement(x, kmer_summary, k = 2L, ...)
```

Arguments

x	input data in phyDat format
kmer_summary	a kmer_summary object
k	k-mer length
...	other arguments passed to substr_kmer

Value

a dist object

Author(s)

Wuming Gong (gongx030@umn.edu)

`dist_weighted_hamming` *Generic function for dist_weighted_hamming*

Description

Generic function for `dist_weighted_hamming`

Usage

```
dist_weighted_hamming(x, wVec, ...)
```

Arguments

x	a sequence object
wVec	weight vector
...	additional parameters

`dist_weighted_hamming, phyDat, numeric-method`
dist_weighted_hamming

Description

implementation of weighted hamming algorithm

Usage

```
## S4 method for signature 'phyDat,numeric'
dist_weighted_hamming(x, wVec, dropout = FALSE)
```

Arguments

x	Sequence object of 'phyDat' type.
wVec	Weight vector for the calculation of weighted hamming distance
dropout	Different weighting strategy is taken to consider interval dropout with dropout = 'TRUE'. Default is, dropout = 'FALSE'.

Value

Calculated distance matrix of input sequences. The result is a 'dist' class object.

Author(s)

Il-Youp Kwak

Examples

```

library(DCLEAR)
library(phangorn)
library(ape)

set.seed(1)
mu_d1 = c( 30, 20, 10, 5, 5, 1, 0.01, 0.001)
mu_d1 = mu_d1/sum(mu_d1)
simn = 10 # number of cell samples
m = 10 ## number of targets
sD = sim_seqdata(sim_n = simn, m = m, mu_d = 0.03,
                 d = 12, n_s = length(mu_d1), outcome_prob = mu_d1, p_d = 0.005 )
## RF score with hamming distance
D_hm = dist.hamming(sD$seqs)
tree_hm = NJ(D_hm)
RF.dist(tree_hm, sD$tree, normalize = TRUE)

## RF score with weighted hamming
InfoW = -log(mu_d1)
InfoW[1:2] = 1
InfoW[3:7] = 4.5
D_wh = dist_weighted_hamming(sD$seqs, InfoW, dropout = FALSE)
tree_wh = NJ(D_wh)
RF.dist(tree_wh, sD$tree, normalize = TRUE)

## RF score with weighted hamming, considering dropout situation
nfoW = -log(mu_d1)
InfoW[1] = 1
InfoW[2] = 12
InfoW[3:7] = 3
D_wh2 = dist_weighted_hamming(sD$seqs, InfoW, dropout = TRUE)
tree_wh2 = NJ(D_wh2)
RF.dist(tree_wh2, sD$tree, normalize = TRUE)

```

downsample *Generic function for downsample*

Description

Generic function for downsample

Usage

```
downsample(x, ...)
```

Arguments

x a data object
... additional parameters

downsample,igraph-method
downsample

Description

Sample a lineage tree

Usage

```
## S4 method for signature 'igraph'  
downsample(x, n = 10L, ...)
```

Arguments

x a igraph object
n number of leaves (tips) in the down-sampled tree
... additional parameters

Value

a phylo object

downsample,lineage_tree-method
downsample

Description

Sample a lineage tree

Usage

```
## S4 method for signature 'lineage_tree'  
downsample(x, n = 10L, ...)
```

Arguments

x	a lineage_tree object
n	number of leaves (tips) in the down-sampled tree
...	additional parameters

Value

a lineage_tree object

get_distance_prior *get_distance_prior*

Description

prior distribution of distance

Usage

```
get_distance_prior(x)
```

Arguments

x	a kmer_summary object
---	-----------------------

Value

a probabilistic vector of the distribution of nodal distances

Author(s)

Wuming Gong (gongx030@umn.edu)

<code>get_leaves</code>	<i>Generic function for <code>get_leaves</code></i>
-------------------------	---

Description

Generic function for `get_leaves`

Usage

```
get_leaves(x, ...)
```

Arguments

<code>x</code>	a <code>lineage_tree</code> object
<code>...</code>	additional parameters

<code>get_leaves,lineage_tree-method</code>
<i>get_leaves</i>

Description

Get the leaf sequences

Usage

```
## S4 method for signature 'lineage_tree'  
get_leaves(x, ...)
```

Arguments

<code>x</code>	a <code>lineage_tree</code> object
<code>...</code>	additional parameters

Value

a `phyDat` object

get_node_names *get_node_names*

Description

Convenient function for get node names

Usage

```
get_node_names(x)
```

Arguments

x node id

Value

node names

Author(s)

Wuming Gong (gongx030@umn.edu)

get_replacement_probability
get_replacement_probability

Description

Compute $p(A, B|d)$, the conditional probability of seeing a replacement of from kmer A to B or vice versa

Usage

```
get_replacement_probability(x)
```

Arguments

x a kmer_summary object

Value

an 3D probabilistic array (kmers by kmers by distances)

Author(s)

Wuming Gong (gongx030@umn.edu)

```
get_transition_probability  
    get_transition_probability
```

Description

Compute $p(A, X|B, Y, d)$, the conditional probability of seeing a replacement from A to B given the previous replacement B from Y at nodal distance d

Usage

```
get_transition_probability(x)
```

Arguments

x a kmer_summary object

Value

an 3D probabilistic array (kmers by kmers by distances)

Author(s)

Wuming Gong (gongx030@umn.edu)

```
lineages                    Lineage data
```

Description

Lineage data

Usage

```
data(lineages)
```

Format

An object of class list of length 100.

Examples

```
data(lineages)
```

positional_mutation_prob
positional_mutation_prob

Description

Convenient function for get node names

Usage

positional_mutation_prob(x, config)

Arguments

x a phyDat object
config a lineage_tree_config object

Value

a positional mutation probability matrix

process_sequence *Generic function for process_sequence*

Description

Generic function for process_sequence

Usage

process_sequence(x, ...)

Arguments

x a sequence object
... additional parameters

process_sequence, phyDat-method
Process sequences

Description

Process sequences

Usage

```
## S4 method for signature 'phyDat'  
process_sequence(x, division = 16L)
```

Arguments

x input data in phyDat format
division cell divisions (default: 16L)

Value

a 'lineage_tree_config' object

Author(s)

Wuming Gong (gongx030@umn.edu)

prune *Generic function for prune*

Description

Generic function for prune

Usage

```
prune(x, ...)
```

Arguments

x a lineage_tree object
... additional parameters

```
prune,igraph-method  prune
```

Description

Trim a full lineage tree into phylogenetic tree

Usage

```
## S4 method for signature 'igraph'
prune(x, weighted = TRUE, ...)
```

Arguments

x	an igraph object
weighted	whether or not keep the edge weight (default: TRUE)
...	additional parameters

Value

an igraph object

```
prune,lineage_tree-method
      prune
```

Description

Trim a full lineage tree into phylogenetic tree

Usage

```
## S4 method for signature 'lineage_tree'
prune(x, ...)
```

Arguments

x	a lineage_tree object
...	additional parameters passed to as_phylo()

Value

a lineage_tree object

random_tree	<i>random_tree</i>
-------------	--------------------

Description

Simulate a random lineage tree

Usage

```
random_tree(n_samples, division = 16L)
```

Arguments

n_samples	number of samples to simulate
division	number of cell division

Value

a data frame

Author(s)

Wuming Gong (gongx030@umn.edu)

rbind,phyDat-method	<i>rbind</i>
---------------------	--------------

Description

Concatenate multiple phyDat objects

Usage

```
## S4 method for signature 'phyDat'  
rbind(..., deparse.level = 1)
```

Arguments

...	a list of phyDat objects
deparse.level	see definition in generic rbind

Value

a phyDat object

sample_outcome_prob	<i>sample_outcome_prob</i>
---------------------	----------------------------

Description

Sampling outcome probability based on a gamma distribution

Usage

```
sample_outcome_prob(config, num_states = 20L, shape = 0.1, scale = 2)
```

Arguments

config	a lineage_tree_config object
num_states	number of states used in simulation.
shape	shape parameter in gamma distribution
scale	scale parameter in gamma distribution

Value

a probability vector for each alphabet

Author(s)

Wuming Gong (gongx030@umn.edu)

simulate	<i>Generic function for simulate</i>
----------	--------------------------------------

Description

Generic function for simulate

Usage

```
simulate(config, x, ...)
```

Arguments

config	a lineage_tree_config object
x	a sequence object
...	additional parameters

simulate,lineage_tree_config,missing-method
simulate

Description

Simulate a cell lineage tree Adoped from https://github.com/elifesciences-publications/CRISPR_recorders_sims/blob/master

Usage

```
## S4 method for signature 'lineage_tree_config,missing'  
simulate(config, x, n_samples = 200, ...)
```

Arguments

config	simulation configuration; a lineage_tree_config object
x	missing
n_samples	number of samples to simulate
...	additional parameters

Value

a lineage_tree object

Author(s)

Wuming Gong (gongx030@umn.edu)

simulate,lineage_tree_config,phyDat-method
simulate

Description

Simulate a cell lineage tree based on a set of sequences

Usage

```
## S4 method for signature 'lineage_tree_config,phyDat'  
simulate(config, x, n_samples = 200L, ...)
```

Arguments

config	simulation configuration; a lineage_tree_config object
x	a sequence object
n_samples	number of samples to simulate
...	additional parameters

Value

a lineage_tree object

Author(s)

Wuming Gong (gongx030@umn.edu)

simulate_core	<i>simulate_core</i>
---------------	----------------------

Description

Simulate a cell lineage tree Adoped from https://github.com/elifesciences-publications/CRISPR_recorders_sims/blob/master/

Usage

```
simulate_core(config, mp = NULL, n_samples = 200L, ...)
```

Arguments

config	simulation configuration; a lineage_tree_config object
mp	site specific mutation probability
n_samples	number of samples to simulate
...	additional parameters

`sim_seqdata`*sim_seqdata*

Description

Generate single cell barcode data set with tree shaped lineage information

Usage

```
sim_seqdata(  
  sim_n = 200,  
  m = 200,  
  mu_d = 0.03,  
  d = 15,  
  n_s = 23,  
  outcome_prob = NULL,  
  p_d = 0.003  
)
```

Arguments

<code>sim_n</code>	Number of cell samples to simulate.
<code>m</code>	Number of targets.
<code>mu_d</code>	Mutation rate. (a scalar or a vector)
<code>d</code>	Number of cell divisions.
<code>n_s</code>	Number of possible outcome states
<code>outcome_prob</code>	Outcome probability vector (default is NULL)
<code>p_d</code>	Dropout probability

Value

The result is a list containing two objects, 'seqs' and 'tree'. The 'seqs' is 'phyDat' object of 'sim_n' number of simulated barcodes corresponding to each cell, and The 'tree' is a 'phylo' object, a ground truth tree structure for the simulated data.

Author(s)

Il-Youp Kwak

Examples

```
library(DCLEAR)  
library(phangorn)  
library(ape)
```

```

set.seed(1)
mu_d1 = c( 30, 20, 10, 5, 5, 1, 0.01, 0.001)
mu_d1 = mu_d1/sum(mu_d1)
simn = 10 # number of cell samples
m = 10 ## number of targets
sD = sim_seqdata(sim_n = simn, m = m, mu_d = 0.03,
                 d = 12, n_s = length(mu_d1), outcome_prob = mu_d1, p_d = 0.005 )
## RF score with hamming distance
D_hm = dist.hamming(sD$seqs)
tree_hm = NJ(D_hm)
RF.dist(tree_hm, sD$tree, normalize = TRUE)

## RF score with weighted hamming
InfoW = -log(mu_d1)
InfoW[1:2] = 1
InfoW[3:7] = 4.5
D_wh = dist_weighted_hamming(sD$seqs, InfoW, dropout=FALSE)
tree_wh = NJ(D_wh)
RF.dist(tree_wh, sD$tree, normalize = TRUE)

## RF score with weighted hamming, cosidering dropout situation
nfoW = -log(mu_d1)
InfoW[1] = 1
InfoW[2] = 12
InfoW[3:7] = 3
D_wh2 = dist_weighted_hamming(sD$seqs, InfoW, dropout = TRUE)
tree_wh2= NJ(D_wh2)
RF.dist(tree_wh2, sD$tree, normalize = TRUE)

```

substr_kmer

Generic function for substr_kmer

Description

Generic function for substr_kmer

Usage

```
substr_kmer(x, ...)
```

Arguments

x	a kmer object
...	additional parameters

substr_kmer, kmer_summary-method
Subsetting a kmer_summary object

Description

Summarize the short k-mer summary from the long k-mer summary

Usage

```
## S4 method for signature 'kmer_summary'  
substr_kmer(x, k = 2)
```

Arguments

x	a kmer_summary object
k	k-mer length(default: 2)

Value

a new kmer_summary object

Author(s)

Wuming Gong (gongx030@umn.edu)

subtract *Generic function for subtract*

Description

Generic function for subtract

Usage

```
subtract(x, y, ...)
```

Arguments

x	a lineage_tree object
y	a lineage_tree object
...	additional parameters

subtract,lineage_tree,lineage_tree-method
subtract

Description

Subtract a subtree from a large tree

Usage

```
## S4 method for signature 'lineage_tree,lineage_tree'  
subtract(x, y, ...)
```

Arguments

x	a lineage_tree object
y	a lineage_tree object
...	additional parameters

Value

a lineage_tree object

subtree *Generic function for subtree*

Description

Generic function for subtree

Usage

```
subtree(x, ...)
```

Arguments

x	a lineage_tree object
...	additional parameters

subtree,lineage_tree-method
subtree

Description

Extract a subtree with specific leaves

Usage

```
## S4 method for signature 'lineage_tree'  
subtree(x, leaves = NULL, ...)
```

Arguments

x	a lineage_tree object
leaves	leaves of the extracted tree
...	additional parameters

Value

a lineage_tree object

subtree,phylo-method *subtree*

Description

Extract a subtree with specific leaves

Usage

```
## S4 method for signature 'phylo'  
subtree(x, leaves = NULL, ...)
```

Arguments

x	a phylo object
leaves	leaves of the extracted tree
...	additional parameters

Value

a phylo object

summarize_kmer	<i>Generic function for summarize_kmer</i>
----------------	--

Description

Generic function for summarize_kmer

Usage

```
summarize_kmer(x, ...)
```

Arguments

x	a sequence object
...	additional parameters

summarize_kmer, phyDat-method	<i>summarize_kmer</i>
-------------------------------	-----------------------

Description

Summarize kmer distributions with input sequences

Usage

```
## S4 method for signature 'phyDat'
summarize_kmer(
  x,
  division = 16L,
  k = 2,
  reps = 20L,
  n_samples = 200L,
  n_nodes = 100L,
  n_targets
)
```

Arguments

x	input data as a phyDat object
division	number of cell division
k	k-mer (default = 2)
reps	number of simulated trees
n_samples	number of samples to simulate

n_nodes	number of nodes to sample (including both leaves and interval nodes)
n_targets	sequence length. If this argument is missing, the length of the input sequences will be used.

Value

a kmer_summary object

Author(s)

Wuming Gong (gongx030@umn.edu)

summarize_kmer_core	<i>summarize_kmer_core</i>
---------------------	----------------------------

Description

Summarize kmer distributions (core function)

Usage

```
summarize_kmer_core(
  k = 2,
  reps = 20L,
  n_samples = 200L,
  n_nodes = 100L,
  config = NULL
)
```

Arguments

k	k-mer (default = 2)
reps	number of simulated trees
n_samples	number of samples to simulate
n_nodes	number of nodes to sample (including both leaves and interval nodes)
config	lineage tree configuration (a lineage_tree_config object)

Value

a kmer_summary object

Author(s)

Wuming Gong (gongx030@umn.edu)

 WH

 WH

Description

implementation of weighted hamming algorithm

Usage

```
WH(x, InfoW, dropout = FALSE)
```

Arguments

x	Sequence object of 'phyDat' type.
InfoW	Weight vector for the calculation of weighted hamming distance
dropout	Different weighting strategy is taken to consider interval dropout with dropout = 'TRUE'. Default is, dropout = 'FALSE'.

Value

Calculated distance matrix of input sequences. The result is a 'dist' class object.

Author(s)

Il-Youp Kwak

Examples

```
set.seed(1)
library(phangorn)
mu_d1 = c( 30, 20, 10, 5, 5, 1, 0.01, 0.001)
mu_d1 = mu_d1/sum(mu_d1)
simn = 10 # number of cell samples
m = 10 ## number of targets
sD = sim_seqdata(sim_n = simn, m = m, mu_d = 0.03,
                 d = 12, n_s = length(mu_d1), outcome_prob = mu_d1, p_d = 0.005 )

## RF score with hamming distance
D_h = dist.hamming(sD$seqs)
tree_h= NJ(D_h)
RF.dist(tree_h, sD$tree, normalize = TRUE)

## RF score with weighted hamming
InfoW = -log(mu_d1)
InfoW[1:2] = 1
InfoW[3:7] = 4.5

D_wh = WH(sD$seqs, InfoW)
```

```

tree_wh= NJ(D_wh)
RF.dist(tree_wh, sD$tree, normalize = TRUE)

## RF score with weighted hamming, considering dropout situation
nfoW = -log(mu_d1)
InfoW[1] = 1
InfoW[2] = 12
InfoW[3:7] = 3

D_wh2 = WH(sD$seqs, InfoW, dropout=TRUE)
tree_wh2= NJ(D_wh2)
RF.dist(tree_wh2, sD$tree, normalize = TRUE)

```

WH_train

Train weights for WH

Description

Train weights for WH and output weight vector

Usage

```
WH_train(X, loc0 = 2, locDropout = 1, locMissing = FALSE)
```

Arguments

X	a list of k number of input data, X[[1]] ... X[[k]]. The ith data have sequence information as phyDat format in X[[i]][[1]], and tree information in X[[i]][[2]] as phylo format.
loc0	weight location of initial state
locDropout	weight location of dropout state
locMissing	weight location of missing state, FALSE if there is no missing values

Value

a weight vector

Author(s)

Il-Youp Kwak (ikwak2@cau.ac.kr)

WH_train_fit	<i>Train weights for WH, and output distance object</i>
--------------	---

Description

Train weights for WH using the given data, and fit the distance matrix for a input sequence.

Usage

```
WH_train_fit(x, X)
```

Arguments

x	input data in phyDat format
X	a list of k number of input data, X[[1]] ... X[[k]]. The ith data have sequence information as phyDat format in X[[i]][[1]], and tree information in X[[i]][[2]] as phylo format.

Value

a dist object

Author(s)

Il-Youp Kwak (ikwak2@cau.ac.kr)

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