

# Package ‘CIMICE’

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**Type** Package

**Title** CIMICE-R: (Markov) Chain Method to Infer Cancer Evolution

**Version** 1.17.0

**Description** CIMICE is a tool in the field of tumor phylogenetics and its goal is to build a Markov Chain (called Cancer Progression Markov Chain, CPMC) in order to model tumor subtypes evolution. The input of CIMICE is a Mutational Matrix, so a boolean matrix representing altered genes in a collection of samples. These samples are assumed to be obtained with single-cell DNA analysis techniques and the tool is specifically written to use the peculiarities of this data for the CMPC construction.

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---

*annotate\_mutational\_matrix*  
*Add samples and genes names to a mutational matrix*

---

### Description

Given M mutational matrix, add samples as row names, and genes as column names. If there are repetitions in row names, these are solved by adding a sequential identifier to the names.

### Usage

```
annotate_mutational_matrix(M, samples, genes)
```

### Arguments

M	mutational matrix
samples	list of sample names
genes	list of gene names

### Value

N with the set row and column names

### Examples

```
require(Matrix)
genes <- c("A", "B", "C")
samples <- c("S1", "S2", "S2")
M <- Matrix(c(0,0,1,0,0,1,0,1,1), ncol=3, sparse=TRUE, byrow = TRUE)

annotate_mutational_matrix(M, samples, genes)
```

---

binary\_radix\_sort      *Radix sort for a binary matrix*

---

**Description**

Sort the rows of a binary matrix in ascending order

**Usage**

```
binary_radix_sort(mat)
```

**Arguments**

mat                    a binary matrix (of 0 and 1)

**Value**

the sorted matrix

**Examples**

```
require(Matrix)
m <- Matrix(c(1,1,0,1,0,0,0,1,1), sparse = TRUE, ncol = 3)
binary_radix_sort(m)
```

---

build\_subset\_graph      *Remove transitive edges and prepare graph*

---

**Description**

Create a graph from the "build\_topology\_subset" edge list, so that it respects the subset relation, omitting the transitive edges.

**Usage**

```
build_subset_graph(edges, labels)
```

**Arguments**

edges                    edge list, built from "build\_topology\_subset"  
labels                    list of node labels, to be paired with the graph

**Value**

a graph with the subset topology, omitting transitive edges

**Examples**

```
require(dplyr)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
edges <- build_topology_subset(samples)
g <- build_subset_graph(edges, labels)
```

---

build\_topology\_subset *Compute subset relation as edge list*

---

**Description**

Create an edge list  $E$  representing the 'subset' relation for binary strings so that:

$$(A, B) \in E \iff \text{forall}(i) : A[i] - > B[i]$$

**Usage**

```
build_topology_subset(samples)
```

**Arguments**

samples            input dataset (mutational matrix) as matrix

**Value**

the computed edge list

**Examples**

```
require(dplyr)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
build_topology_subset(samples)
```

---

chunk_reader	<i>Gradually read a file from disk</i>
--------------	--

---

**Description**

This function creates a reader to read a text file in batches (or chunks). It can be used for very large files that cannot fit in RAM.

**Usage**

```
chunk_reader(file_path)
```

**Arguments**

file\_path      path to large file

**Value**

a list-object containing the function ‘read’ to read lines from the given file, and ‘close’ to close the connection to the file stream.

**Examples**

```
# open connection to file
reader <- chunk_reader(
  system.file("extdata", "paac_jhu_2014_500.maf", package = "CIMICE", mustWork = TRUE)
)

while(TRUE){
  # read a chunk
  chunk <- reader$read(10)
  if(length(chunk) == 0){
    break
  }
  # --- process chunk ---
}
# close connection
reader$close()
```

---

CIMICE	<i>CIMICE Package</i>
--------	-----------------------

---

**Description**

R implementation of the CIMICE tool. CIMICE is a tool in the field of tumor phylogenetics and its goal is to build a Markov Chain (called Cancer Progression Markov Chain, CPMC) in order to model tumor subtypes evolution. The input of CIMICE is a Mutational Matrix, so a boolean matrix representing altered genes in a collection of samples. These samples are assumed to be obtained with single-cell DNA analysis techniques and the tool is specifically written to use the peculiarities of this data for the CMPC construction. See <https://github.com/redsnic/tumorEvolutionWithMarkovChains/tree/master/> for the original Java version of this tool.

**Details**

CIMICE-R: (Markov) Chain Method to Infer Cancer Evolution

**Author(s)**

Nicolò Rossi <olocin.issor@gmail.com>

---

compact_dataset	<i>Compact dataset rows</i>
-----------------	-----------------------------

---

**Description**

Count duplicate rows and compact the dataset (mutational). The column 'freq' will contain the counts for each row.

**Usage**

```
compact_dataset(mutmatrix)
```

**Arguments**

mutmatrix      input dataset (mutational matrix)

**Value**

a list with matrix (the compacted dataset (mutational matrix)), counts (frequencies of genotypes) and row\_names (comma separated string of sample IDs) fields

**Examples**

```
compact_dataset(example_dataset())
```

---

computeDWNW	<i>Down weights computation</i>
-------------	---------------------------------

---

**Description**

Computes the Down weights formula using a Dinamic Programming approach (starting call), see vignettes for further explanation.

**Usage**

```
computeDWNW(g, freqs, no.of.children, A, normUpWeights)
```

**Arguments**

**g** graph (a Directed Acyclic Graph)  
**freqs** observed genotype frequencies  
**no.of.children** number of children for each node  
**A** adjacency matrix of G  
**normUpWeights** normalized up weights as computed by normalizeUPW

**Value**

a vector containing the Up weights for each edge

**Examples**

```

require(dplyr)
require(igraph)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
g <- graph_non_transitive_subset_topology(samples, labels)
# prepare adj matrix
A <- as.matrix(as_adj(g))
# pre-compute exiting edges from each node
no.of.children <- get_no_of_children(A,g)
upWeights <- computeUPW(g, freqs, no.of.children, A)
normUpWeights <- normalizeUPW(g, freqs, no.of.children, A, upWeights)
computeDWNW(g, freqs, no.of.children, A, normUpWeights)

```

---

computeDWNW\_aux

*Down weights computation (aux)*


---

**Description**

Computes the Down weights formula using a Dinamic Programming approach (recursion), see vignettes for further explanation.

**Usage**

```
computeDWNW_aux(g, edge, freqs, no.of.children, A, normUpWeights)
```

**Arguments**

**g** graph (a Directed Acyclic Graph)  
**edge** the currently considered edge  
**freqs** observed genotype frequencies  
**no.of.children** number of children for each node  
**A** adjacency matrix of G  
**normUpWeights** normalized up weights as computed by normalizeUPW

**Value**

a vector containing the Up weights for each edge

---

computeUPW	<i>Up weights computation</i>
------------	-------------------------------

---

**Description**

Computes the up weights formula using a Dinamic Programming approach (starting call), see vignettes for further explanation.

**Usage**

```
computeUPW(g, freqs, no.of.children, A)
```

**Arguments**

<code>g</code>	graph (a Directed Acyclic Graph)
<code>freqs</code>	observed genotype frequencies
<code>no.of.children</code>	number of children for each node
<code>A</code>	adjacency matrix of G

**Value**

a vector containing the Up weights for each edge

**Examples**

```
require(dplyr)
require(igraph)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
g <- graph_non_transitive_subset_topology(samples, labels)
# prepare adj matrix
A <- as.matrix(as_adj(g))
# pre-compute exiting edges from each node
no.of.children <- get_no_of_children(A,g)
computeUPW(g, freqs, no.of.children, A)
```

---

computeUPW_aux	<i>Up weights computation (aux)</i>
----------------	-------------------------------------

---

**Description**

Computes the up weights formula using a Dinamic Programming approach (recursion), see vignettes for further explanation.

**Usage**

```
computeUPW_aux(g, edge, freqs, no.of.children, A)
```

**Arguments**

g	graph (a Directed Acyclic Graph)
edge	the currently considered edge
freqs	observed genotype frequencies
no.of.children	number of children for each node
A	adjacency matrix of G

**Value**

a vector containing the Up weights for each edge

---

compute_weights_default	<i>Compute default weights</i>
-------------------------	--------------------------------

---

**Description**

This procedure computes the weights for edges of a graph accordingly to CIMICE specification. (See vignettes for further explanations)

**Usage**

```
compute_weights_default(g, freqs)
```

**Arguments**

g	a graph (must be a DAG with no transitive edges)
freqs	observed frequencies of genotypes

**Value**

a graph with the computed weights

**Examples**

```
require(dplyr)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
g <- graph_non_transitive_subset_topology(samples, labels)
compute_weights_default(g, freqs)
```

---

`corrplot_from_mutational_matrix`*Correlation plot from mutational matrix*

---

**Description**

Prepare correlation plot based on a mutational matrix

**Usage**

```
corrplot_from_mutational_matrix(mutmatrix)
```

**Arguments**

`mutmatrix`      input dataset

**Value**

the computed correlation plot

**Examples**

```
corrplot_from_mutational_matrix(example_dataset())
```

---

`corrplot_genes`*Gene based correlation plot*

---

**Description**

Prepare a correlation plot computed from genes' perspective using a mutational matrix

**Usage**

```
corrplot_genes(mutmatrix)
```

**Arguments**

`mutmatrix`      input dataset (mutational matrix)

**Value**

the computed correlation plot

**Examples**

```
corrplot_genes(example_dataset())
```

---

corrplot\_samples      *Sample based correlation plot*

---

**Description**

Prepare a correlation plot computed from samples' perspective using a mutational matrix

**Usage**

```
corrplot_samples(mutmatrix)
```

**Arguments**

mutmatrix      input dataset (mutational matrix)

**Value**

the computed correlation plot

**Examples**

```
corrplot_samples(example_dataset())
```

---

dataset\_preprocessing      *Run CIMICE preprocessing*

---

**Description**

executes the preprocessing steps of CIMICE

**Usage**

```
dataset_preprocessing(dataset)
```

**Arguments**

dataset      a mutational matrix as a (sparse) matrix

**Details**

Preprocessing steps:

- 1) dataset is compacted
- 2) genotype frequencies are computed
- 3) labels are prepared

**Value**

a list containing the mutational matrix ("samples"), the mutational frequencies of the genotypes ("freqs"), the node labels ("labels") and finally the gene names ("genes")

**Examples**

```
require(dplyr)
example_dataset() %>% dataset_preprocessing
```

---

dataset\_preprocessing\_population

*Run CIMICE preprocessing for population format dataset*

---

**Description**

executes the preprocessing steps of CIMICE

**Usage**

```
dataset_preprocessing_population(compactDataset)
```

**Arguments**

compactDataset

a list (matrix: a mutational matrix, counts: number of samples with given genotype). "counts" is normalized automatically.

**Details**

Preprocessing steps:

- 1) genotype frequencies are computed
- 2) labels are prepared

**Value**

a list containing the mutational matrix ("samples"), the mutational frequencies of the genotypes ("freqs"), the node labels ("labels") and finally the gene names ("genes")

**Examples**

```
require(dplyr)
example_dataset_withFreqs() %>% dataset_preprocessing_population
```

draw\_ggraph *ggplot graph output*

---

**Description**

Draws the output graph using ggplot

**Usage**

```
draw_ggraph(out, digits = 4, ...)
```

**Arguments**

out	the output object of CIMICE (es, from quick run)
digits	precision for edges' weights
...	other arguments for format_labels

**Value**

ggraph object representing g as described

**Examples**

```
draw_ggraph(quick_run(example_dataset()))
```

---

draw\_networkD3 *NetworkD3 graph output*

---

**Description**

Draws the output graph using networkD3

**Usage**

```
draw_networkD3(out, ...)
```

**Arguments**

out	the output object of CIMICE (es, from quick run)
...	other arguments for format_labels

**Value**

networkD3 object representing g as described

**Examples**

```
draw_networkD3(quick_run(example_dataset()))
```

---

draw_visNetwork	<i>VisNetwork graph output (default)</i>
-----------------	--

---

**Description**

Draws the output graph using VisNetwork

**Usage**

```
draw_visNetwork(out, ...)
```

**Arguments**

out	the output object of CIMICE (es, from quick run)
...	other arguments for format_labels

**Value**

visNetwork object representing g as described

**Examples**

```
draw_visNetwork(quick_run(example_dataset()))
```

---

example_dataset	<i>Creates a simple example dataset</i>
-----------------	---

---

**Description**

Creates a simple example dataset

**Usage**

```
example_dataset()
```

**Value**

a simple mutational matrix

**Examples**

```
example_dataset()
```

---

```
example_dataset_withFreqs
```

*Creates a simple example dataset with frequency column*

---

### Description

Creates a simple example dataset with frequency column

### Usage

```
example_dataset_withFreqs()
```

### Value

a simple mutational matrix

### Examples

```
example_dataset_withFreqs()
```

---

```
finalize_generator
```

*Finalize generator normalizing edge weights*

---

### Description

Checks if a generator can be normalized so that it actually is a Markov Chain

### Usage

```
finalize_generator(generator)
```

### Arguments

generator      a generator

### Value

A generator with edge weights that respect DTMC definition

### Examples

```
require(dplyr)
```

```
example_dataset() %>%
  make_generator_stub() %>%
  set_generator_edges(
    list(
      "D", "A, D", 1 ,
      "A", "A, D", 1 ,
      "A, D", "A, C, D", 1 ,
```

```

    "A, D", "A, B, D", 1 ,
    "Clonal", "D", 1 ,
    "Clonal", "A", 1 ,
    "D", "D", 1 ,
    "A", "A", 1 ,
    "A, D", "A, D", 1 ,
    "A, C, D", "A, C, D", 1 ,
    "A, B, D", "A, B, D", 1 ,
    "Clonal", "Clonal", 1
  )) %>%
  finalize_generator

```

---

fix\_clonal\_genotype    *Manage Clonal genotype in data*

---

## Description

Fix the absence of the clonal genotype in the data (if needed)

## Usage

```
fix_clonal_genotype(samples, freqs, labels, matching_samples)
```

## Arguments

samples	input dataset (mutational matrix) as matrix
freqs	genotype frequencies (in the rows' order)
labels	list of gene names (in the columns' order)
matching_samples	list of sample names matching each genotype

## Value

a named list containing the fixed "samples", "freqs" and "labels"

## Examples

```

require(dplyr)

# compact
compactDataset <- compact_dataset(example_dataset())
samples <- compactDataset$matrix

# save genes' names
genes <- colnames(compactDataset$matrix)

# keep the information on frequencies for further analysis
freqs <- compactDataset$counts/sum(compactDataset$counts)

# prepare node labels listing the mutated genes for each node
labels <- prepare_labels(samples, genes)
if( is.null(compactDataset$row_names) ){

```

```

    compactedDataset$row_names <- rownames(compactedDataset$matrix)
  }
  matching_samples <- compactedDataset$row_names
  # matching_samples
  matching_samples

  # fix Clonal genotype absence, if needed
  fix <- fix_clonal_genotype(samples, freqs, labels, matching_samples)

```

---

format_labels	<i>Format labels for output object</i>
---------------	--

---

### Description

Prepare labels based on multiple identifiers so that they do not exceed a certain size (if they do, a simple number is used)

### Usage

```
format_labels(labels, max_col = 3, max_row = 3)
```

### Arguments

labels	a character vector of the labels to manage
max_col	maximum number of identifiers in a single row for a label
max_row	maximum number of rows of identifiers in a label

### Value

the updated labels

### Examples

```
format_labels(c("A, B", "C, D, E"))
```

---

gene_mutations_hist	<i>Histogram of genes' frequencies</i>
---------------------	--

---

### Description

Create the histogram of the genes' mutational frequencies

### Usage

```
gene_mutations_hist(mutmatrix, binwidth = 1)
```

**Arguments**

mutmatrix      input dataset (mutational matrix)  
binwidth        binwidth parameter for the histogram (as in ggplot)

**Value**

the newly created histogram

**Examples**

```
gene_mutations_hist(example_dataset(), binwidth = 10)
```

---

get_no_of_children	<i>Get number of children</i>
--------------------	-------------------------------

---

**Description**

Compute number of children for each node given an adj matrix

**Usage**

```
get_no_of_children(A, g)
```

**Arguments**

A                Adjacency matrix of the graph g  
g                a graph

**Value**

a vector containing the number of children for each node in g

**Examples**

```
require(dplyr)
require(igraph)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
g <- graph_non_transitive_subset_topology(samples, labels)
A <- as_adj(g)
get_no_of_children(A, g)
```

---

```
graph_non_transitive_subset_topology
```

*Default preparation of graph topology*

---

**Description**

By default, CIMICE computes the relation between genotypes using the subset relation. For the following steps it is also important that the transitive edges are removed.

**Usage**

```
graph_non_transitive_subset_topology(samples, labels)
```

**Arguments**

samples	mutational matrix
labels	genotype labels

**Value**

a graph with the wanted topology

**Examples**

```
require(dplyr)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
graph_non_transitive_subset_topology(samples, labels)
```

---

```
make_dataset
```

*Dataset line by line construction: initialization*

---

**Description**

Initialize a dataset for "line by line" creation

**Usage**

```
make_dataset(...)
```

**Arguments**

...	gene names (do not use '"', the input is automatically converted to strings)
-----	--

**Value**

a mutational matrix without samples structured as (sparse) matrix

**Examples**

```
make_dataset(APC,P53,KRAS)
```

---

```
make_generator_stub     Create a stub for a generator
```

---

**Description**

Create a generator topology directly from a dataset. The topology will follow the subset relation.

**Usage**

```
make_generator_stub(dataset)
```

**Arguments**

dataset                A compacted CIMICE dataset

**Value**

a generator, with weight = 0 for all the edges

**Examples**

```
make_generator_stub(example_dataset())
```

---

```
make_labels             Helper function to create labels
```

---

**Description**

This function helps creating labels for nodes with different information

**Usage**

```
make_labels(out, mode = "samplesIDs", max_col = 3, max_row = 3)
```

**Arguments**

out                    the output object of CIMICE (es, from quick run)

mode                   which labels to print: samplesIDs (matching samples), sequentialIDs (just a sequential numer), geneIDs (genotype)

max\_col                identifiers are represented in a max\_col times max\_row grid (if the number of IDs exceeds, a the sequentialID number is used instead)

max\_row                identifiers are represented in a max\_col times max\_row grid (if the number of IDs exceeds, a the sequentialID number is used instead)

**Value**

the requested labels

**Examples**

```
make_labels(quick_run(example_dataset()))
```

---

normalizeDWNW

*Down weights normalization*

---

**Description**

Normalizes Down weights so that the sum of weights of edges exiting a node is 1

**Usage**

```
normalizeDWNW(g, freqs, no.of.children, A, downWeights)
```

**Arguments**

g	graph (a Directed Acyclic Graph)
freqs	observed genotype frequencies
no.of.children	number of children for each node
A	adjacency matrix of G
downWeights	Down weights as computed by computeDWNW

**Value**

a vector containing the normalized Down weights for each edge

**Examples**

```
require(dplyr)
require(igraph)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
g <- graph_non_transitive_subset_topology(samples, labels)
# prepare adj matrix
A <- as.matrix(as_adj(g))
# pre-compute exiting edges from each node
no.of.children <- get_no_of_children(A,g)
upWeights <- computeUPW(g, freqs, no.of.children, A)
normUpWeights <- normalizeUPW(g, freqs, no.of.children, A, upWeights)
downWeights <- computeDWNW(g, freqs, no.of.children, A, normUpWeights)
normalizeUPW(g, freqs, no.of.children, A, downWeights)
```

---

normalizeUPW	<i>Up weights normalization</i>
--------------	---------------------------------

---

**Description**

Normalizes up weights so that the sum of weights of edges entering in a node is 1

**Usage**

```
normalizeUPW(g, freqs, no.of.children, A, upWeights)
```

**Arguments**

g	graph (a Directed Acyclic Graph)
freqs	observed genotype frequencies
no.of.children	number of children for each node
A	adjacency matrix of G
upWeights	Up weights as computed by computeUPW

**Value**

a vector containing the normalized Up weights for each edge

**Examples**

```
require(dplyr)
require(igraph)
preproc <- example_dataset() %>% dataset_preprocessing
samples <- preproc[["samples"]]
freqs <- preproc[["freqs"]]
labels <- preproc[["labels"]]
genes <- preproc[["genes"]]
g <- graph_non_transitive_subset_topology(samples, labels)
# prepare adj matrix
A <- as.matrix(as_adj(g))
# pre-compute exiting edges from each node
no.of.children <- get_no_of_children(A,g)
upWeights <- computeUPW(g, freqs, no.of.children, A)
normalizeUPW(g, freqs, no.of.children, A, upWeights)
```

---

perturb_dataset	<i>Perturbate a boolean matrix</i>
-----------------	------------------------------------

---

**Description**

Given a boolean matrix, randomly add False Positives (FP), False Negatives (FN) and Missing data following user defined rates. In the final matrix, missing data is represented by the value 3.

**Usage**

```
perturb_dataset(dataset, FP_rate = 0, FN_rate = 0, MIS_rate = 0)
```

**Arguments**

dataset	a matrix/sparse matrix
FP_rate	False Positive rate
FN_rate	False Negative rate
MIS_rate	Missing Data rate

**Details**

Note that CIMICE does not support dataset with missing data natively, so using MIS\_rate != 0 will then require some pre-processing.

**Value**

the new, perturbed, matrix

**Examples**

```
require(dplyr)

example_dataset() %>%
  make_generator_stub() %>%
  set_generator_edges(
    list(
      "D", "A, D", 1 ,
      "A", "A, D", 1 ,
      "A, D", "A, C, D", 1 ,
      "A, D", "A, B, D", 1 ,
      "Clonal", "D", 1 ,
      "Clonal", "A", 1 ,
      "D", "D", 1 ,
      "A", "A", 1 ,
      "A, D", "A, D", 1 ,
      "A, C, D", "A, C, D", 1 ,
      "A, B, D", "A, B, D", 1 ,
      "Clonal", "Clonal", 1
    )
  ) %>%
  finalize_generator %>%
  simulate_generator(3, 10) %>%
  perturb_dataset(FP_rate = 0.01, FN_rate = 0.1, MIS_rate = 0.12)
```

---

plot\_generator

*Plot a generator*

---

**Description**

Simple ggraph interface to draw a generator

**Usage**

```
plot_generator(generator)
```

**Arguments**

generator          a generator

**Value**

a basic plot of this generator

**Examples**

```
require(dplyr)

example_dataset() %>%
  make_generator_stub() %>%
  set_generator_edges(
    list(
      "D", "A, D", 1 ,
      "A", "A, D", 1 ,
      "A, D", "A, C, D", 1 ,
      "A, D", "A, B, D", 1 ,
      "Clonal", "D", 1 ,
      "Clonal", "A", 1 ,
      "D", "D", 1 ,
      "A", "A", 1 ,
      "A, D", "A, D", 1 ,
      "A, C, D", "A, C, D", 1 ,
      "A, B, D", "A, B, D", 1 ,
      "Clonal", "Clonal", 1
    )
  ) %>%
  finalize_generator %>%
  plot_generator
```

---

```
prepare_generator_edge_set_command
```

*Prepare a command to add edge weights to a generator*

---

**Description**

Prints a string in the form of the command that sets weights for all the edges of this generator.

**Usage**

```
prepare_generator_edge_set_command(generator, by = "labels")
```

**Arguments**

generator          a generator  
 by                  "labels" or "samples" to use gene labels or sample labels as references for edge identifiers.

**Value**

NULL (the string with the function calls is printed on the stdout)

**Examples**

```
require(dplyr)
example_dataset() %>%
  make_generator_stub() %>%
  prepare_generator_edge_set_command()
```

---

prepare_labels	<i>Prepare node labels based on genotypes</i>
----------------	---

---

**Description**

Prepare node labels so that each node is labelled with a comma separated list of the altered genes representing its associated genotype.

**Usage**

```
prepare_labels(samples, genes)
```

**Arguments**

samples	input dataset (mutational matrix) as matrix
genes	list of gene names (in the columns' order)

**Details**

Note that after this procedure the user is expected also to run `fix_clonal_genotype` to also add the clonal genotype to the mutational matrix if it is not present.

**Value**

the computed edge list

**Examples**

```
require(dplyr)

# compact
compactDataset <- compact_dataset(example_dataset())
samples <- compactDataset$matrix

# save genes' names
genes <- colnames(compactDataset$matrix)

# keep the information on frequencies for further analysis
freqs <- compactDataset$counts/sum(compactDataset$counts)

# prepare node labels listing the mutated genes for each node
labels <- prepare_labels(samples, genes)
```

---

quick_run	<i>Run CIMICE defaults</i>
-----------	----------------------------

---

**Description**

This function executes CIMICE analysis on a dataset using default settings.

**Usage**

```
quick_run(dataset, mode = "CAPRI")
```

**Arguments**

dataset	a mutational matrix as a (sparse) matrix
mode	indicates the used input format. Must be either "CAPRI" or "CAPRIpop"

**Value**

a list object representing the graph computed by CIMICE with the structure ‘list(topology = g, weights = W, labels = labels, freqs=freqs)’

**Examples**

```
quick_run(example_dataset())
```

---

read	<i>Read a "CAPRI" file</i>
------	----------------------------

---

**Description**

Read a "CAPRI" formatted file, as read\_CAPRI

**Usage**

```
read(filepath)
```

**Arguments**

filepath	path to file
----------	--------------

**Value**

the described mutational matrix as a (sparse) matrix

**Examples**

```
read(system.file("extdata", "example.CAPRI", package = "CIMICE", mustWork = TRUE))
```

---

read_CAPRI	<i>Read a "CAPRI" file</i>
------------	----------------------------

---

**Description**

Read a "CAPRI" formatted file from the file system

**Usage**

```
read_CAPRI(filepath)
```

**Arguments**

filepath          path to file

**Value**

the described mutational matrix as a (sparse) matrix

**Examples**

```
#            "pathToDataset/myDataset.CAPRI"  
read_CAPRI(system.file("extdata", "example.CAPRI", package = "CIMICE", mustWork = TRUE))
```

---

read_CAPRIpop	<i>Read a "CAPRIpop" file</i>
---------------	-------------------------------

---

**Description**

Read a "CAPRIpop" formatted file from the file system

**Usage**

```
read_CAPRIpop(filepath)
```

**Arguments**

filepath          path to file

**Value**

a list containing the described mutational matrix as a (sparse) matrix and a list of the frequency of the genotypes

**Examples**

```
#            "pathToDataset/myDataset.CAPRI"  
read_CAPRI(system.file("extdata", "example.CAPRIpop", package = "CIMICE", mustWork = TRUE))
```

---

read\_CAPRIpop\_string    *Read "CAPRIpop" file from a string*

---

**Description**

Read a "CAPRIpop" formatted file, from a text string

**Usage**

```
read_CAPRIpop_string(txt)
```

**Arguments**

txt                    string in valid "CAPRIpop" format

**Value**

the described mutational matrix as a (sparse) matrix

**Examples**

```
read_CAPRIpop_string("
s\\g A B C D freqs
S1 0 0 0 1 0.1
S2 1 0 0 0 0.1
S3 1 0 0 0 0.2
S4 1 0 0 1 0.3
S5 1 1 0 1 0.05
S6 1 1 0 1 0.1
S7 1 0 1 1 0.05
S8 1 1 0 1 0.01
")
```

---

read\_CAPRI\_string        *Read "CAPRI" file from a string*

---

**Description**

Read a "CAPRI" formatted file, from a text string

**Usage**

```
read_CAPRI_string(txt)
```

**Arguments**

txt                    string in valid "CAPRI" format

**Value**

the described mutational matrix as a (sparse) matrix

**Examples**

```
read_CAPRI_string("
s\\g A B C D
S1 0 0 0 1
S2 1 0 0 0
S3 1 0 0 0
S4 1 0 0 1
S5 1 1 0 1
S6 1 1 0 1
S7 1 0 1 1
S8 1 1 0 1
")
```

---

read\_MAF

*Create mutational matrix from MAF file*

---

**Description**

Read a MAF (Mutation Annotation Format) file and create a Mutational Matrix combining gene and sample IDs.

**Usage**

```
read_MAF(path, ...)
```

**Arguments**

path	path to MAF file
...	other maftools::mutCountMatrix arguments

**Value**

the mutational (sparse) matrix associated to the MAF file

**Examples**

```
read_MAF(system.file("extdata", "paac_jhu_2014_500.maf", package = "CIMICE", mustWork = TRUE))
```

---

read_matrix	<i>Read dataset from an R matrix</i>
-------------	--------------------------------------

---

**Description**

also converts that matrix to a sparse matrix

**Usage**

```
read_matrix(mat)
```

**Arguments**

mat                    a boolean mutational matrix

**Value**

the sparse mutational matrix to be used as CIMICE's input

**Examples**

```
m <- matrix(c(0,0,1,1,0,1,1,1,1), ncol=3)
colnames(m) <- c("A", "B", "C")
rownames(m) <- c("S1", "S2", "S3")
read_matrix(m)
```

---

remove_transitive_edges	<i>Remove transitive edges from an edgelist</i>
-------------------------	---

---

**Description**

Remove transitive edges from an edgelist. This procedure is temporary to cover a bug in 'relations' package.

**Usage**

```
remove_transitive_edges(E)
```

**Arguments**

E                    edge list, built from "build\_topology\_subset"

**Value**

a new edgelist without transitive edges (as a N\*2 matrix)

**Examples**

```
l <- list(c(1,2),c(2,3), c(1,3))
remove_transitive_edges(l)
```

---

sample\_mutations\_hist *Histogram of samples' frequencies*

---

**Description**

Create the histogram of the samples' mutational frequencies

**Usage**

```
sample_mutations_hist(mutmatrix, binwidth = 1)
```

**Arguments**

mutmatrix	input dataset (mutational matrix)
binwidth	binwidth parameter for the histogram (as in ggplot)

**Value**

the newly created histogram

**Examples**

```
sample_mutations_hist(example_dataset(), binwidth = 10)
```

---

select\_genes\_on\_mutations  
*Filter dataset by genes' mutation count*

---

**Description**

Dataset filtering on genes, based on their mutation count

**Usage**

```
select_genes_on_mutations(mutmatrix, n, desc = TRUE)
```

**Arguments**

mutmatrix	input dataset (mutational matrix) to be reduced
n	number of genes to be kept
desc	TRUE: select the n least mutated genes, FALSE: select the n most mutated genes

**Value**

the modified dataset (mutational matrix)

**Examples**

```
# keep information on the 100 most mutated genes
select_genes_on_mutations(example_dataset(), 5)
# keep information on the 100 least mutated genes
select_genes_on_mutations(example_dataset(), 5, desc = FALSE)
```

---

```
select_samples_on_mutations
      Filter dataset by samples' mutation count
```

---

**Description**

Dataset filtering on samples, based on their mutation count

**Usage**

```
select_samples_on_mutations(mutmatrix, n, desc = TRUE)
```

**Arguments**

mutmatrix	input dataset (mutational matrix) to be reduced
n	number of samples to be kept
desc	T: select the n least mutated samples, F: select the n most mutated samples

**Value**

the modified dataset (mutational matrix)

**Examples**

```
require(dplyr)
# keep information on the 5 most mutated samples
select_samples_on_mutations(example_dataset(), 5)
# keep information on the 5 least mutated samples
select_samples_on_mutations(example_dataset(), 5, desc = FALSE)
# combine selections
select_samples_on_mutations(example_dataset(), 5, desc = FALSE) %>%
  select_genes_on_mutations(5)
```

---

set\_generator\_edges    *Add edge weights to a generator*

---

### Description

Add edge weights to a generator

### Usage

```
set_generator_edges(generator, f_t_w_list, by = "labels")
```

### Arguments

generator	a generator
f_t_w_list	a list of triplets (from, to, list), the triplets must not be nested in the list. For example list("A","B",0.3, "B", "C", 0.2) is a valid input.
by	"labels" or "samples" to use gene labels or sample labels as references for edge identifiers.

### Value

the generator with the modified edges (invalid edges are ignored)

### Examples

```
require(dplyr)

example_dataset() %>%
  make_generator_stub() %>%
  set_generator_edges(
    list(
      "D", "A, D", 1 ,
      "A", "A, D", 1 ,
      "A, D", "A, C, D", 1 ,
      "A, D", "A, B, D", 1 ,
      "Clonal", "D", 1 ,
      "Clonal", "A", 1 ,
      "D", "D", 1 ,
      "A", "A", 1 ,
      "A, D", "A, D", 1 ,
      "A, C, D", "A, C, D", 1 ,
      "A, B, D", "A, B, D", 1 ,
      "Clonal", "Clonal", 1
    )
  )
```

---

simulate\_generator      *Create datasets from generators*

---

### Description

Simulate the DTMC associated to the generator to create a dataset that reflects the genotypes of 'times' cells, sampled after 'time\_ticks' passages.

### Usage

```
simulate_generator(
  generator,
  time_ticks,
  times,
  starting_label = "Clonal",
  by = "labels",
  mode = "full"
)
```

### Arguments

generator	a generator
time_ticks	number of steps (updates) of the DTMC associated to the generato
times	number of sumlated cells
starting_label	node from which to start the simulation
by	"labels" or "samples" to use gene labels or sample labels as references to identify the 'starting_label's node
mode	"full" to generate a matrix with 'times' genotypes, "compacted" to *efficiently* create an already compacted dataset (a dataset showing the genotypes and their respective frequencies)

### Value

the simulated dataset

### Examples

```
require(dplyr)

example_dataset() %>%
  make_generator_stub() %>%
  set_generator_edges(
    list(
      "D", "A, D", 1 ,
      "A", "A, D", 1 ,
      "A, D", "A, C, D", 1 ,
      "A, D", "A, B, D", 1 ,
      "Clonal", "D", 1 ,
      "Clonal", "A", 1 ,
      "D", "D", 1 ,
      "A", "A", 1 ,
    )
  )
```

```

    "A, D", "A, D", 1 ,
    "A, C, D", "A, C, D", 1 ,
    "A, B, D", "A, B, D", 1 ,
    "Clonal", "Clonal", 1
  )) %>%
  finalize_generator %>%
  simulate_generator(3, 10)

```

---

to\_dot

*Dot graph output*


---

### Description

Represents this graph in dot format (a textual output format)

### Usage

```
to_dot(out, ...)
```

### Arguments

out	the output object of CIMICE (es, from quick run)
...	other arguments for format_labels

### Value

a string representing the graph in dot format

### Examples

```
to_dot(quick_run(example_dataset()))
```

---

update\_df

*Dataset line by line construction: add a sample*


---

### Description

Add a sample (a row) to an existing dataset. This procedure is meant to be used with the "

### Usage

```
update_df(mutmatrix, sampleName, ...)
```

### Arguments

mutmatrix	an existing (sparse) matrix (mutational matrix)
sampleName	the row (sample) name
...	sample's genotype (0/1 numbers)

**Value**

the modified (sparse) matrix (mutational matrix)

**Examples**

```
require(dplyr)
make_dataset(APC,P53,KRAS) %>%
  update_df("S1", 1, 0, 1) %>%
  update_df("S2", 1, 1, 1)
```

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