# Package 'MitoHEAR'

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Title Quantification of Mitochondrial DNA Heteroplasmy
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<b>Description</b> Allows the estimation and downstream statistical analysis of the mitochondrial DNA Heteroplasmy calculated from single-cell datasets <a href="https://github.com/ScialdoneLab/MitoHEAR/tree/master">https://github.com/ScialdoneLab/MitoHEAR/tree/master</a> .
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```

choose\_features\_clustering

#### **Description**

choose\_features\_clustering

### Usage

```
choose_features_clustering(
  heteroplasmy_matrix,
  allele_matrix,
  cluster,
  top_pos,
  deepSplit_param,
  minClusterSize_param,
  min_value_vector,
  threshold = 0.2,
  index,
  max_frac = 0.7
)
```

#### **Arguments**

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

allele\_matrix Fourth element returned by get\_heteroplasmy.

cluster Vector specifying a partition of the samples.

top\_pos Numeric value. Number of bases sorted with decreasing values of distance vari-

ance (see section *Details* below) among samples. If *relevant\_bases*=NULL, then the bases for performing hierarchical clustering are the ones whose relative variance (variance of the base divided sum of variance among *top\_pos* bases) is

above min\_value.

deepSplit\_param

Integer value between 0 and 4 for the deepSplit parameter of the function cutree-

Hybrid. See section Details below.

minClusterSize\_param

Integer value specifying the minClusterSize parameter of the function cutreeHy-

brid. See section Details below.

min\_value\_vector

Numeric vector. For each value in the vector, the function  $clustering\_angular\_distance$ 

is run with parameter min\_value equal to one element of the vector min\_value\_vector.

threshold Numeric value. If a base has heteroplasmy greater or equal to threshold in more

than max\_frac of cells, then the base is not considered for down stream analysis.

index Fifth element returned by *get\_heteroplasmy*.

max\_frac Numeric value.If a base has heteroplasmy greater or equal to *threshold* in more

than max\_frac of cells, then the base is not considered for down stream analysis.

### Value

Clustree plot returned by function *clustree* from package *clustree*.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

https://cran.r-project.org/package=clustree

clustering\_angular\_distance

clustering\_angular\_distance

### **Description**

For each pair of samples and for each base, an angular distance matrix is computed based on the four allele frequencies. Then only the angular distances corresponding to the relevant\_bases are kept. If relevant bases is NULL, then only the angular distances corresponding to the bases with relative distance variance among samples above *min\_value* are kept. Finally the distance between each pair of samples is defined as the euclidean distance of the angular distances corresponding to the bases that pass the previous filtering step. On this final distance matrix, a hierarchical clustering approach is performed using the function *cutreeHybrid* of the package *dynamicTreeCut*.

### Usage

```
clustering_angular_distance(
  heteroplasmy_matrix,
  allele_matrix,
  cluster,
  top_pos,
  deepSplit_param,
  minClusterSize_param,
  threshold = 0.2,
  min_value,
  index,
  relevant_bases = NULL,
  max_frac = 0.7
)
```

### Arguments

top\_pos

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

allele\_matrix Fourth element returned by get\_heteroplasmy.

cluster Vector specifying a partition of the samples.

Numeric value. Number of bases sorted with decreasing values of distance variance (see section *Details* below) among samples. If *relevant\_bases*=NULL, then the bases for performing hierarchical clustering are the ones whose relative variance (variance of the base divided sum of variance among *top\_pos* bases) is

above min\_value.

deepSplit\_param

Integer value between 0 and 4 for the *deepSplit* parameter of the function *cutree-Hybrid*. See section *Details* below.

minClusterSize\_param

Integer value specifying the *minClusterSize* parameter of the function *cutreeHy*-

brid. See section Details below.

threshold Numeric value. If a base has heteroplasmy greater or equal to threshold in more

than max\_frac of cells, then the base is not considered for down stream analysis.

min\_value Numeric value. If *relevant\_bases*=NULL, then the bases for performing hier-

archical clustering are the ones whose relative variance (variance of the base

divided sum of variance among *top\_pos* bases) is above *min\_value*.

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index Fifth element returned by *get\_heteroplasmy*.

relevant\_bases Character vector of bases to consider as features for performing hierarchical

clustering on samples.Default=NULL.

max\_frac Numeric value.If a base has heteroplasmy greater or equal to threshold in more

than max\_frac of cells, then the base is not considered for down stream analysis.

### Value

It returns a list with 4 elements:

classification Dataframe with two columns and n\_row equal to n\_row in heteroplasmy\_matrix.

The first column is the old cluster annotation provided by cluster. The second columns is the new cluster annotation obtained with hierarchical clustering on

distance matrix based on heteroplasmy values.

dist\_ang\_matrix

Distance matrix based on heteroplasmy values as defined in the section *Details* 

top\_bases\_dist Vector of bases used for hierarchical clustering. If relevant\_bases is not NULL,

then top\_bases\_dist=NULL

common\_idx Vector of indices of samples for which hierarchical clustering is performed. If

index is NULL, then common\_idx=NULL

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

https://www.rdocumentation.org/packages/dynamicTreeCut/versions/1.63-1/topics/cutreeHybrid

detect\_insertion detect\_insertion

#### **Description**

detect\_insertion

### Usage

detect\_insertion(ref\_sequence, different\_sequence, length\_comparison = 10)

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### **Arguments**

reference. different\_sequence

Character vector whose elements are the bases of a DNA sequence different

from the reference.

length\_comparison

Integer number. Number of bases to consider for the comparison between the two DNA sequences in order to detect and remove insertions in the non-reference sequence.

### Value

Character vector of the different\_sequence with length equal to ref\_sequence, after having removed the insertions.

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

dpt\_test

dpt\_test

### **Description**

dpt\_test

### Usage

```
dpt_test(heteroplasmy_matrix, time, index = NULL, method = "GAM")
```

#### **Arguments**

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

time Vector of diffusion pseudo time.
index index returned by get\_heteroplasmy.

method Character name denoting the method to choose for assigning an adjusted p value

to each of the bases. Can be one of GAM, pearson and spearman. GAM: For each base, a GAM fit with formula  $z \sim lo(t)$  is performed between the heteroplasmy values (z) and the time (t). The p value from the table "Anova for Parametric Effects" is then assigned to the base. pearson, spearman: for each base, a pearson or spearman correlation test is performed between the heteroplasmy values and the time . The p value obtained from the test is then assigned to the base. In all the three possible methods, all the p values are then corrected with

the method FDR.

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### Value

A data frame with 2 columns and number of rows equal to n\_col in *heteroplasmy\_matrix*. In the first column there are the names of the bases while in the second column there are the adjusted p value.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

https://www.rdocumentation.org/packages/gam/versions/1.20/topics/gam

filter\_bases

filter\_bases

### Description

filter\_bases

### Usage

```
filter_bases(heteroplasmy_matrix, min_heteroplasmy, min_cells, index = NULL)
```

### **Arguments**

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

 ${\tt min\_heteroplasmy}$ 

Numeric value.

min\_cells Numeric value.

index Fifth element returned by *get\_heteroplasmy*.

### Value

Character vector of bases that have an heteroplasmy greater than *min\_heteroplasmy* in more than *min\_cells*.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

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get\_distribution

get\_distribution

### Description

```
get_distribution
```

### Usage

```
get_distribution(heteroplasmy_matrix, FUNCTION, index = NULL)
```

### **Arguments**

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

FUNCTION A character specifying the function to be applied on each column of *matrix*. The

possible values are: mean,max,min,median and sum.

index index returned by *get\_heteroplasmy*.

### Value

It returns a numeric vector with length equal to n\_col of *matrix* where each element contains the result of the operation defined by *FUNCTION*.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

get\_heteroplasmy

get\_heteroplasmy

### Description

It is one of the two main functions of the **MitoHEAR** package (together with *get\_raw\_counts\_allele*). It computes the allele frequencies and the heteroplasmy matrix starting from the counts matrix obtained with *get\_raw\_counts\_allele*.

### Usage

```
get_heteroplasmy(
  raw_counts_allele,
  name_position_allele,
  name_position,
  number_reads,
  number_positions,
  filtering = 1,
  my.clusters = NULL
)
```

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#### **Arguments**

raw\_counts\_allele

A raw counts matrix obtained from get\_raw\_counts\_allele.

name\_position\_allele

A character vector with elements specifying the genomic coordinate of the base and the allele (obtained from *get\_raw\_counts\_allele*).

name\_position A character vector with elements specifying the genomic coordinate of the base

(obtained from get\_raw\_counts\_allele).

base covered by the sample.

number\_positions

Integer specifying the minimumnumber of bases that must be covered by the sample (with counts>number\_reads), in order to keep the sample for down-

stream analysis.

filtering Numeric value equal to 1 or 2. If 1 then only the bases that are covered by all

the samples are kept for the downstream analysis. If 2 then all the bases that are covered by more than 50% of the the samples in each cluster (specified by

my.clusters) are kept for the down-stream analysis. Default is 1.

my.clusters Character vector specifying a partition of the samples. It is only used when

filtering is equal to 2. Default is NULL

### **Details**

Starting from *raw counts allele matrix*, the function performed two consequentially filtering steps. The first one is on the samples, keeping only the ones that cover a number of bases above number\_positions. The second one is on the bases, defined by the parameter filtering. The heteroplasmy for each sample-base pair is computed as I-max(f), where f are the frequencies of the four alleles.

#### Value

It returns a list with 5 elements:

sum\_matrix A matrix (n\_row=number of sample, n\_col=number of bases) with the counts

for each sample/base, for all the initial samples and bases included in the raw

counts allele matrix.

sum\_matrix\_qc A matrix (n\_row=number of sample, n\_col=number of bases) with the counts for

each sample/base, for all the samples and bases that pass the two consequentially

filtering steps.

heteroplasmy\_matrix

A matrix with the same dimension of *sum\_matrix\_qc* where each entry (i,j) is

the heteroplasmy for sample i in base j.

allele\_matrix A matrix (n\_row=number of sample, n\_col=4\*number of bases) with allele fre-

quencies, for all the samples and bases that pass the two consequentially filtering

steps.

index Indices of the samples that cover a base, for all bases and samples that pass the

two consequentially filtering steps; if all the samples cover all the bases, then

index is NULL

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

#### **Examples**

```
# Two samples and two bases whose reference allele is A and C.
# The two samples have 100 reads in the reference allele and 0 in all the others.
sample1_A <- c(100, 0, 0, 0)
names_A <- rep("1_A", length(sample1_A))</pre>
sample1_C <- c(100, 0, 0, 0)
names_C <- rep("2_C", length(sample1_C))</pre>
allele <- c("A", "C", "T", "G")
names_A_allele <- paste(names_A, allele, sep = " ")</pre>
names_C_allele <- paste(names_C, allele, sep = " ")</pre>
sample1 <- c(sample1_A, sample1_C)</pre>
sample2_A \leftarrow c(100, 0, 0, 0)
sample2_C <- c(100, 0, 0, 0)
sample2 <- c(sample2_A, sample2_C)</pre>
test_allele <- matrix(c(sample1, sample2), byrow = TRUE, ncol = 8, nrow = 2)</pre>
colnames(test_allele) <- c(names_A_allele, names_C_allele)</pre>
row.names(test_allele) <- c("sample1", "sample2")</pre>
name_position_allele_test <- c(names_A_allele, names_C_allele)</pre>
name_position_test <- c(names_A, names_C)</pre>
test <- get_heteroplasmy(test_allele, name_position_allele_test, name_position_test, 50, 1, 1)
```

```
get_raw_counts_allele get_raw_counts_allele
```

### Description

It is one the two main function of the **MitoHEAR** package (together with *get\_heteroplasmy*). The function allows to obtain a matrix of counts (n\_row = number of sample, n\_col= 4\*number of bases) of the four alleles in each base, for every sample. It takes as input a vector of sorted bam files (one bam file for each sample) and a fasta file for the genomic region of interest. It is based on the *pileup* function of the package Rsamtools.

#### Usage

```
get_raw_counts_allele(bam_input, path_fasta, cell_names, cores_number = 1)
```

### **Arguments**

bam_input	Character vector of sorted bam files (full path). Each sample is defined by one bam file. For each bam file it is needed also the index bam file (.bai) at the same path.
path_fasta	Character string with full path to the fasta file of the genomic region of interest.
cell_names	Character vector of sample names.
cores_number	Number of cores to use.

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#### Value

A list with three elements:

matrix\_allele\_counts

Matrix of counts (n\_row = number of sample, n\_col= 4\*number of bases) of the four alleles in each base, for every sample. The row names is equal to cell\_names.

name\_position\_allele

Character vector with length equal to n\_col of matrix\_allele\_counts. Each element specifies the coordinate of genomic position for a base and the allele.

name\_position

Character vector with length equal to n\_col of matrix\_allele\_counts. Each element specifies the coordinate of genomic position for a base.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

#### See Also

https://www.rdocumentation.org/packages/Rsamtools/versions/1.24.0/topics/pileup

### Description

```
get_wilcox_test
```

### Usage

```
get_wilcox_test(heteroplasmy_matrix, cluster, label_1, label_2, index = NULL)
```

#### Arguments

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

cluster Vector specifying a partition of the samples.

label\_1 Character name of a first label included in cluster. It denotes the first group used

for the Wilcoxon test

label\_2 Character name of a second label included in cluster and different from label\_1.

it denotes the second group used for the Wilcoxon test.

index Fifth element returned by *get\_heteroplasmy*.

### Value

It returns a numeric vector of length equal to n\_row in matrix. Each element stands for a base and it contains the adjusted p-value (FDR), obtained in unpaired two-samples Wilcoxon test from the comparison of the heteroplasmy between the label\_1 and label\_2 group.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

#### See Also

https://www.rdocumentation.org/packages/stats/versions/3.6.2/topics/wilcox.test

```
plot_allele_frequency
```

### **Description**

```
plot_allele_frequency
```

### Usage

```
plot_allele_frequency(
   position,
   heteroplasmy_matrix,
   allele_matrix,
   cluster,
   names_allele_qc,
   names_position_qc,
   size_text,
   index
)
```

### **Arguments**

```
position Character name of the base to plot.
```

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

allele\_matrix Fourth element returned by *get\_heteroplasmy*. cluster Vector specifying a partition of the samples.

names\_allele\_qc

Character vector with length equal to n\_col of allele\_matrix. Each element spec-

ifies the name of the base and the allele.

names\_position\_qc

Character vector with length equal to n\_col of allele\_matrix. Each element spec-

ifies the name of the base.

size\_text Character specifying the size of the text for gridExtra function grid.arrange)

index Fifth element returned by *get\_heteroplasmy*.

### Value

grid.arrange plot of allele frequencies of a specific base across samples divided according to cluster.

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### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

```
https://cran.r-project.org/package=gridExtra
```

```
plot_base_coverage
```

### **Description**

```
plot_base_coverage
```

### Usage

```
plot_base_coverage(
   sum_matrix,
   sum_matrix_qc,
   selected_cells,
   interactive = FALSE,
   text_size = 10
)
```

### **Arguments**

```
sum_matrix First element returned by the function <code>get_heteroplasmy</code>.

sum_matrix_qc Second element returned by the function <code>get_heteroplasmy</code>.

selected_cells Character vector with cells used fro plotting the coverage.

interactive Logical. If TRUE an interactive plot is produced.

text_size Character specifying the size of the text for ggplot2.
```

### Value

```
ggplot2 object (if interactive=FALSE) or plotly object (if interactive=TRUE).
```

#### Author(s)

```
Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>
```

### See Also

```
https://plotly.com/r/
```

plot\_cells\_coverage

plot\_batch plot\_batch

### **Description**

plot\_batch

### Usage

plot\_batch(position, heteroplasmy\_matrix, batch, cluster, text\_size, index)

### **Arguments**

position Character name of the base to plot.

heteroplasmy\_matrix

Third element returned by get\_heteroplasmy.

batch Vector of batch names, with length equal to n\_row of heteroplasmy\_matrix.

cluster Vector specifying a partition of the samples.

text\_size Character specifying the size of the text for ggplot2.

index Fifth element returned by *get\_heteroplasmy*.

### Value

ggplot2 object of the heteroplasmy level of a specific base across samples divided according to batch.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

plot\_cells\_coverage plot\_cells\_coverage

### Description

plot\_cells\_coverage

### Usage

plot\_cells\_coverage(sum\_matrix, cells\_selected, cluster, interactive = FALSE)

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### **Arguments**

sum\_matrix First element returned by the function *get\_heteroplasmy*.

cells\_selected Character vector of cells for which the coverage is computed.

cluster Character vector with partition information for cells specified in cells\_selected

interactive Logical. If TRUE an interactive plot is produced.

#### Value

```
ggplot2 object (if interactive=FALSE) or plotly object (if interactive=TRUE).
```

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

```
https://plotly.com/r/
```

plot\_condition

plot\_condition

### **Description**

```
plot_condition
```

### Usage

```
plot_condition(
   distribution_1,
   distribution_2,
   label_1,
   label_2,
   name_x,
   name_y,
   name_title
)
```

### **Arguments**

### Value

ggplot2 boxplot of the quantities specified by *distribution\_1* and *distribution\_2*, separated by the conditions denoted by *label\_1* and *label\_2*.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### Description

```
plot_coordinate_cluster
```

### Usage

```
plot_coordinate_cluster(coordinate_dm, cluster)
```

### **Arguments**

coordinate\_dm Dataframe whit samples on the rows and coordinates names on the columns.

cluster Vector specifying a partition of the samples.

#### Value

ggplot2 object.

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

```
plot\_coordinate\_heteroplasmy\\ plot\_coordinate\_heteroplasmy
```

### Description

plot\_coordinate\_heteroplasmy

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### Usage

```
plot_coordinate_heteroplasmy(
  coordinate_dm,
  heteroplasmy_matrix,
  index,
  name_base
)
```

### Arguments

coordinate\_dm Dataframe whit samples on the rows and coordinates names on the columns. heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

index Fifth element returned by *get\_heteroplasmy*.

name\_base Character name specifying the base.

#### Value

ggplot2 object.

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

```
plot_correlation_bases
```

plot correlation bases

### **Description**

```
plot_correlation_bases
```

### Usage

```
plot_correlation_bases(bases_vector, index, heteroplasmy_matrix)
```

### Arguments

bases\_vector Character vector specifying the bases for which the spearman correlation across

samples is computed.

index Fifth element returned by *get\_heteroplasmy*.

heteroplasmy\_matrix

Third element returned by get\_heteroplasmy.

### Value

Heatmap plot produced by function *Heatmap* from package *ComplexHeatmap*.

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### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

https://www.rdocumentation.org/packages/ComplexHeatmap/versions/1.10.2/topics/Heatmap

plot\_distance\_matrix plot\_distance\_matrix

### **Description**

plot\_distance\_matrix

### Usage

```
plot_distance_matrix(dist_ang_matrix, cluster)
```

### **Arguments**

dist\_ang\_matrix

Distance matrix obtained from  $clustering\_angular\_distance$  (second element of

the output).

cluster

Vector. Can be one of the two partitions returned by function clustering\_angular\_distance

(first element of the output).

### Value

Heatmap plot produced by function *Heatmap* from package *ComplexHeatmap*.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

https://www.rdocumentation.org/packages/ComplexHeatmap/versions/1.10.2/topics/Heatmap

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plot\_distribution plot\_distribution

### **Description**

plot\_distribution

### Usage

```
plot_distribution(quantity_counts_cell, name_x, name_title)
```

### **Arguments**

quantity\_counts\_cell

Vector returned by get\_distribution

name\_x Character name specifying the xlab argument in *ggplot2*.

name\_title Character name specifying the ggtitle argument in *ggplot2*.

#### Value

ggplot2 density plot of the vector quantity\_counts\_cell.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### Description

plot\_dpt

### Usage

```
plot_dpt(position, heteroplasmy_matrix, cluster, time, gam_fit_result, index)
```

### **Arguments**

position Character name of the base to plot.

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

cluster Vector specifying a partition of the samples.

time Vector of diffusion pseudo time, with length equal to n\_row of heteroplasmy\_matrix.

gam\_fit\_result Data frame returned by dpt\_test.

index Fifth element returned by *get\_heteroplasmy*.

#### Value

ggplot2 object of the heteroplasmy level of a specific base across samples and the GAM fitted curve. The title shows the adjusted p value (FDR) for the position obtained from *get\_heteroplasmy*.

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

#### See Also

```
https://cran.r-project.org/package=gam
```

```
plot_genome_coverage
```

### **Description**

```
plot_genome_coverage
```

### Usage

```
plot_genome_coverage(biomart_file, path_fasta, chr_name, heteroplasmy_matrix)
```

### Arguments

biomart_file	Character string with full	path to the txt file dov	wnloaded from l	BioMart https:
--------------	----------------------------	--------------------------	-----------------	----------------

 $\label{lowing_constraint} $$/\text{m.ensembl.org/info/data/biomart/index.html}$. It must have the following five columns: Gene. stable. ID, Gene. name, Gene. start..bp., Gene. end..bp.,$ 

Chromosome.scaffold.name

path\_fasta Character string with full path to the fasta file of the genomic region of interest.

It should be the same file used in *get\_raw\_counts\_allele*.

chr\_name Character specifying the name of the chromosome of interest. It must be one of

the names in the *Chromosome.scaffold.name* column from the *biomart\_file*.

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

#### Value

KaryoPlot object as returned by *plotKaryotype* function from package *karyoploteR*.

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

http://bioconductor.org/packages/release/bioc/html/karyoploteR.html

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plot\_heatmap

plot\_heatmap

### **Description**

```
plot_heatmap
```

### Usage

```
plot_heatmap(
   new_classification,
   old_classification,
   dist_ang_matrix,
   cluster_columns = FALSE,
   cluster_rows = TRUE,
   name_legend
)
```

### **Arguments**

new\_classification

Character vector. Second column of the dataframe returned by function *cluster-ing\_angular\_distance* (first element of the output).

old\_classification

Character vector. First column of the dataframe returned by function *cluster-ing\_angular\_distance* (first element of the output).

dist\_ang\_matrix

Distance matrix obtained from *clustering\_angular\_distance* (second element of the output).

cluster\_columns

Logical. Parameter for cluster\_columns argument of the function *Heatmap* in

the package ComplexHeatmap

cluster\_rows Logical. Parameter for cluster\_rows argument of the function *Heatmap*name\_legend Character value.Parameter for name argument of the function *Heatmap* 

#### Value

Heatmap plot produced by function *Heatmap* from package *ComplexHeatmap*.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

#### See Also

https://www.rdocumentation.org/packages/ComplexHeatmap/versions/1.10.2/topics/Heatmap

plot\_heteroplasmy

plot\_heteroplasmy

### **Description**

```
plot_heteroplasmy
```

### Usage

```
plot_heteroplasmy(position, heteroplasmy_matrix, cluster, index)
```

### **Arguments**

```
position Character name of the base to plot.
```

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

cluster Vector specifying a partition of the samples. index Fifth element returned by *get\_heteroplasmy*.

#### Value

ggplot2 object of the heteroplasmy level of a specific base across samples divided according to cluster.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

```
plot\_heteroplasmy\_variability \\ plot\_heteroplasmy\_variability
```

### **Description**

```
plot_heteroplasmy_variability
```

### Usage

```
plot_heteroplasmy_variability(
  heteroplasmy_matrix,
  cluster,
  threshold = 0.1,
  frac = FALSE,
  index
)
```

plot\_spider\_chart 23

### **Arguments**

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

cluster Vector specifying a partition of the samples.

threshold Numeric value.

frac Logical. If FALSE the absolute number of cells that have at least one base with

heteroplasmy above threshold are shown separated by cluster. If TRUE, then

the fraction of cells are shown.

index Fifth element returned by *get\_heteroplasmy*.

#### Value

ggplot2 object.

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### Description

plot\_spider\_chart

#### Usage

```
plot_spider_chart(name_base, cluster, heteroplasmy_matrix, index)
```

### **Arguments**

name\_base Character name specifying the base.

cluster Vector specifying a partition of the samples.

heteroplasmy\_matrix

Third element returned by *get\_heteroplasmy*.

index Fifth element returned by *get\_heteroplasmy*.

### Value

radarchart plot produced by function radarchart from package fmsb.

#### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

#### See Also

https://rdrr.io/cran/fmsb/man/radarchart.html

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vi\_comparison

vi\_comparison We compute the variation of information (VI) between the partition provided by new\_classification and old\_classification. The VI between a random partitions (obtained with re-shuffle from original labels in old\_classification) and old\_classification is also computed. A distribution of VI values from random partitions is built. Finally, from the comparison with this distribution, an empirical p value is given to the VI of the unsupervised cluster analysis.

### **Description**

vi\_comparison We compute the variation of information (VI) between the partition provided by new\_classification and old\_classification. The VI between a random partitions (obtained with re-shuffle from original labels in old\_classification) and old\_classification is also computed. A distribution of VI values from random partitions is built. Finally, from the comparison with this distribution, an empirical p value is given to the VI of the unsupervised cluster analysis.

### Usage

vi\_comparison(old\_classification, new\_classification, number\_iter)

#### Arguments

old\_classification

Character vector. First column of the dataframe returned by function *cluster-ing\_angular\_distance* (first element of the output).

new\_classification

Character vector. Second column of the dataframe returned by function *cluster-ing\_angular\_distance* (first element of the output).

number\_iter

Integer value. Specify how many random partition are generated (starting from re-shuffle of labels in *old\_classification*).

### Value

Numeric value (empirical p value).

### Author(s)

Gabriele Lubatti <gabriele.lubatti@helmholtz-muenchen.de>

### See Also

https://www.rdocumentation.org/packages/mcclust/versions/1.0/topics/vi.dist

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