

Package ‘MouseFM’

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Type Package

Title In-silico methods for genetic finemapping in inbred mice

Version 1.20.1

Description This package provides methods for genetic finemapping in inbred mice by taking advantage of their very high homozygosity rate (>95%).

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BugReports <https://github.com/matmu/MouseFM/issues>

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License GPL-3

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annotate_consequences *Annotate with consequences*

Description

Request variant consequences from Variant Effect Predictor (VEP) via Ensembl Rest Service. Not recommended for large queries.

Usage

```
annotate_consequences(geno, species)
```

Arguments

| | |
|---------|---|
| geno | Data frame or GenomicRanges::GRanges object including columns rsid, ref, alt. |
| species | Species name, e.g. mouse (GRCm38) or human (GRCh38). |

Value

Data frame.

Examples

```

geno = finemap("chr1",
  start = 5000000, end = 6000000,
  strain1 = c("C57BL_6J"), strain2 = c("AKR_J", "A_J", "BALB_cJ")
)

df = annotate_consequences(geno[seq_len(10), ], "mouse")

geno.granges = finemap("chr1",
  start = 5000000, end = 6000000,
  strain1 = c("C57BL_6J"), strain2 = c("AKR_J", "A_J", "BALB_cJ"),
  return_obj = "granges"
)

df2 = annotate_consequences(geno.granges[seq_len(10), ], "mouse")

```

annotate_mouse_genes *Annotate with genes*

Description

Request mouse gene annotations from Ensembl BioMart.

Usage

```

annotate_mouse_genes(
  geno,
  flanking = NULL,
  host = "https://nov2020.archive.ensembl.org",
  biomaRt = "ENSEMBL_MART_ENSEMBL",
  dataset_name = "mmusculus_gene_ensembl"
)

```

Arguments

| | |
|--------------|--|
| geno | Data frame or GenomicRanges::GRanges object including chromosome and genomic position information. |
| flanking | Numeric. Size of the flanking region to include on both sides of each interval. |
| host | Character string. Ensembl host passed to biomaRt::useMart(). If the selected host does not match the reference genome used by MouseFM, another Ensembl archive host should be selected, for example from biomaRt::listEnsemblArchives(). |
| biomaRt | Character string. Name of the BioMart database passed to biomaRt::useMart(). |
| dataset_name | Character string. Name of the BioMart dataset to use. Default is "mmusculus_gene_ensembl". |

Value

Data frame with overlapping gene annotations.

Examples

```
geno = finemap("chr1",
  start = 5000000, end = 6000000,
  strain1 = c("C57BL_6J"), strain2 = c("AKR_J", "A_J", "BALB_cJ")
)

genes = annotate_mouse_genes(geno, 50000)
```

avail_chromosomes *Available chromosomes*

Description

Available mouse chromosomes.

Usage

```
avail_chromosomes()
```

Value

Data frame

Examples

```
avail_chromosomes()
```

avail_consequences *Available consequences*

Description

Available consequence and impact types.

Usage

```
avail_consequences()
```

Value

Data frame.

Examples

```
avail_consequences()$consequence
unique(avail_consequences()$impact)
```

| | |
|---------------|--------------------------|
| avail_strains | <i>Available strains</i> |
|---------------|--------------------------|

Description

There are 37 strains available.

Usage

```
avail_strains()
```

Value

Data frame.

Examples

```
avail_strains()
```

| | |
|-----------------|--|
| backend_request | <i>Send HTTP request to backend server</i> |
|-----------------|--|

Description

Send HTTP request to backend server

Usage

```
backend_request(q, n.tries = 2, method = "GET")
```

Arguments

| | |
|---------|--------------------|
| q | Query string |
| n.tries | Number of tries |
| method | HTTP method to use |

Value

Data frame.

| | |
|------|-----------------------------------|
| comb | <i>Strain combination builder</i> |
|------|-----------------------------------|

Description

Generate strain sets and calculate reduction factors

Usage

```
comb(geno, min_strain_benef = 0.1, max_set_size = 3)
```

Arguments

| | |
|------------------|--|
| geno | Data frame of genotypes for additional strains. |
| min_strain_benef | Minimum reduction factor (min) of a single strain. Default is 0.1. |
| max_set_size | Maximum set of strains. Default is 3. |

Value

Data frame

| | |
|------------|--|
| df2GRanges | <i>Data frame to GenomicRanges::GRanges object</i> |
|------------|--|

Description

Wrapper for GenomicRanges::makeGRangesFromDataFrame().

Usage

```
df2GRanges(
  geno,
  chr_name = "chr",
  start_name = "pos",
  end_name = "pos",
  strand_name = NULL,
  ref_version = ref_genome(),
  seq_lengths = NULL,
  is_circular = FALSE
)
```

Arguments

| | |
|-------------|--|
| geno | Data frame. |
| chr_name | Name of chromosome column. Default is 'chr'. |
| start_name | Name of start position column. Default is 'pos'. |
| end_name | Name of end position column. Default is 'pos'. |
| strand_name | Name of end position column. Default is NULL. |
| ref_version | Reference genome version. Default is 'ref_genome()'. |
| seq_lengths | List of sequence lengths with sequence name as key. Default is NULL. |
| is_circular | Whether genome is circular. Default is FALSE. |

Value

GenomicRanges::GRanges object.

Examples

```

geno = finemap("chr1",
  start = 50000000, end = 60000000,
  strain1 = c("C57BL_6J"), strain2 = c("AKR_J", "A_J", "BALB_cJ")
)

geno$strand = "+"
seq_lengths = stats::setNames(
  as.list(avail_chromosomes())$length,
  avail_chromosomes())$chr
)
geno.granges = df2GRanges(geno,
  strand_name = "strand",
  seq_lengths = seq_lengths
)

```

df_split

Splits data frame df into subsets with maximum n rows

Description

Splits data frame df into subsets with maximum n rows

Usage

```
df_split(df, n)
```

Arguments

| | |
|----|--------------------------------|
| df | Data frame. |
| n | Max number of rows per subset. |

Value

List of data frames.

| | |
|------------------|--|
| ensembl_rest_vep | <i>Request variant consequences from Variant Effect Predictor (VEP) via Ensembl Rest Service</i> |
|------------------|--|

Description

Request variant consequences from Variant Effect Predictor (VEP) via Ensembl Rest Service

Usage

```
ensembl_rest_vep(geno, species)
```

Arguments

| | |
|---------|--|
| geno | Data frame including columns rsid, ref, alt. |
| species | Species name, e.g. mouse or human. |

Value

Data frame.

| | |
|-------|--------------|
| fetch | <i>Fetch</i> |
|-------|--------------|

Description

Fetch homozygous genotypes for a specified chromosomal region in 37 inbred mouse strains.

Usage

```
fetch(
  chr,
  start = NULL,
  end = NULL,
  consequence = NULL,
  impact = NULL,
  return_obj = "dataframe"
)
```

Arguments

| | |
|-------------|---|
| chr | Vector of chromosome names. |
| start | Optional vector of chromosomal start positions of target regions (GRCm38). |
| end | Optional vector of chromosomal end positions of target regions (GRCm38). |
| consequence | Optional vector of consequence types. |
| impact | Optional vector of impact types. |
| return_obj | The user can choose to get the result to be returned as data frame ("dataframe") or as a GenomicRanges::GRanges ("granges") object. Default value is "dataframe". |

Value

Data frame or GenomicRanges::GRanges object containing result data.

Examples

```
geno = fetch("chr7", start = 5000000, end = 6000000)

comment(geno)
```

 finemap

Finemapping of genetic regions

Description

Finemapping of genetic regions in 37 inbred mice by taking advantage of their very high homozygosity rate (>95 chromosomal regions (GRCm38), this method extracts homozygous SNVs for which the allele differs between two sets of strains (e.g. case vs controls) and outputs respective causal SNV/gene candidates.

Usage

```
finemap(
  chr,
  start = NULL,
  end = NULL,
  strain1,
  strain2,
  consequence = NULL,
  impact = NULL,
  thr1 = 0,
  thr2 = 0,
  return_obj = "dataframe"
)
```

Arguments

| | |
|-------------|---|
| chr | Vector of chromosome names. |
| start | Optional vector of chromosomal start positions of target regions (GRCm38). |
| end | Optional vector of chromosomal end positions of target regions (GRCm38). |
| strain1 | First strain set with strains from avail_strains(). |
| strain2 | Second strain set with strains from avail_strains(). |
| consequence | Optional vector of consequence types. |
| impact | Optional vector of impact types. |
| thr1 | Number discordant strains in strain1. Between 0 and length(strain1)-1. 0 by default. |
| thr2 | Number discordant strains in strain2. Between 0 and length(strain2)-1. 0 by default. |
| return_obj | The user can choose to get the result to be returned as data frame ("dataframe") or as a GenomicRanges::GRanges ("granges") object. Default value is "dataframe". |

Value

Data frame or GenomicRanges::GRanges object containing result data.

Examples

```
geno = finemap("chr1",
  start = 5000000, end = 6000000,
  strain1 = c("C57BL_6J"), strain2 = c(
    "129S1_SvImJ", "129S5SvEvBrd",
    "AKR_J"
  )
)

comment(geno)
```

finemap_query

Finemap query builder

Description

Finemap query builder

Usage

```
finemap_query(
  chr,
  start = NULL,
  end = NULL,
  strain1 = NULL,
  strain2 = NULL,
  consequence = NULL,
  impact = NULL,
  thr1 = 0,
  thr2 = 0
)
```

Arguments

| | |
|-------------|--|
| chr | Vector of chromosome names. |
| start | Optional vector of chromosomal start positions of target regions (GRCm38). |
| end | Optional vector of chromosomal end positions of target regions (GRCm38). |
| strain1 | First strain set with strains from avail_strains(). |
| strain2 | Second strain set with strains from avail_strains(). |
| consequence | Optional vector of consequence types. |
| impact | Optional vector of impact types. |
| thr1 | Number discordant strains in strain1. Between 0 and length(strain1)-1. 0 by default. |
| thr2 | Number discordant strains in strain2. Between 0 and length(strain2)-1. 0 by default. |

Value

Query string.

| | |
|--------|--------------------------------|
| getURL | <i>Get backend service url</i> |
|--------|--------------------------------|

Description

Get backend service URL. Default: `http://45.85.146.64:9000/rest/finemap/`

Usage

```
getURL()
```

Value

URL string.

Examples

```
getURL()
```

| | |
|---------|---------------------------------|
| get_top | <i>Best strain combinations</i> |
|---------|---------------------------------|

Description

Get best strain combinations

Usage

```
get_top(red, n_top)
```

Arguments

| | |
|-------|--|
| red | Reduction factors data frame. |
| n_top | Number of combinations to be returned. |

Value

Data frame

Examples

```
l = prio("chr1",
  start = 5000000, end = 6000000,
  strain1 = "C57BL_6J", strain2 = "AKR_J"
)

get_top(l$reduction, 3)
```

GRanges2df

*GenomicRanges::GRanges object to data frame***Description**

Wrapper for `as.data.frame()`.

Usage

```
GRanges2df(granges)
```

Arguments

`granges` `GenomicRanges::GRanges` object

Value

Data frame.

Examples

```
geno.granges = finemap("chr1",
  start = 5000000, end = 6000000,
  strain1 = c("C57BL_6J"), strain2 = c("AKR_J", "A_J", "BALB_cJ"),
  return_obj = "granges"
)

geno = GRanges2df(geno.granges)
```

prio

*Prioritization of inbred mouse strains for refining genetic regions***Description**

This method allows to select strain combinations which best refine a specified genetic region (GRCm38). E.g. if a crossing experiment with two inbred mouse strains 'strain1' and 'strain2' resulted in a QTL, the outputted strain combinations can be used to refine the respective region in further crossing experiments.

Usage

```
prio(
  chr,
  start = NULL,
  end = NULL,
  strain1 = NULL,
  strain2 = NULL,
  consequence = NULL,
  impact = NULL,
  min_strain_benef = 0.1,
  max_set_size = 3,
  return_obj = "dataframe"
)
```

Arguments

| | |
|------------------|--|
| chr | Vector of chromosome names. |
| start | Optional vector of chromosomal start positions of target regions (GRCm38). |
| end | Optional vector of chromosomal end positions of target regions (GRCm38). |
| strain1 | First strain set with strains from avail_strains(). |
| strain2 | Second strain set with strains from avail_strains(). |
| consequence | Optional vector of consequence types. |
| impact | Optional vector of impact types. |
| min_strain_benef | Minimum reduction factor (min) of a single strain. |
| max_set_size | Maximum set of strains. |
| return_obj | The user can choose to get the result to be returned as data frame ("dataframe") or as a GenomicRanges::GRanges ("granges") object. Default value is "data frame". |

Value

Data frame

Examples

```
res = prio("chr1",
  start = 5000000, end = 6000000, strain1 = "C57BL_6J",
  strain2 = "AKR_J"
)

comment(res$genotypes)
```

| | |
|-----------|-------------------------------------|
| reduction | <i>Reduction factor calculation</i> |
|-----------|-------------------------------------|

Description

Generate strain sets and calculate reduction factors

Usage

```
reduction(combs, geno)
```

Arguments

| | |
|-------|---|
| combs | Data frame of strain sets. |
| geno | Data frame of genotypes for additional strains. |

Value

Data frame

| | |
|------------|---------------------------------|
| ref_genome | <i>Reference genome version</i> |
|------------|---------------------------------|

Description

Returns version of reference genome used in package MouseFM.

Usage

```
ref_genome()
```

Value

Vector.

Examples

```
ref_genome()
```

| | |
|--------|--------------------------------|
| setURL | <i>Set backend service url</i> |
|--------|--------------------------------|

Description

Set backend service URL. Default: `http://45.85.146.64:9000/rest/finemap/`

Usage

```
setURL(url)
```

Arguments

`url` URL of backend service. With backslash at the end.

Value

No return value.

Examples

```
setURL("http://45.85.146.64:9000/rest/finemap/")
```

`vis_reduction_factors` *Visualize*

Description

Visualize reduction factors

Usage

```
vis_reduction_factors(geno, red, n_top)
```

Arguments

| | |
|--------------------|--|
| <code>geno</code> | Genotype data frame or <code>GenomicRanges::GRanges</code> object. |
| <code>red</code> | Reduction factor data frame. |
| <code>n_top</code> | Number of combinations to be returned. |

Value

Data frame

Examples

```
l = prio(c("chr1", "chr2"),
  start = c(5000000, 5000000),
  end = c(6000000, 6000000), strain1 = c("C3H_HeH"), strain2 = "AKR_J"
)
```

```
plots = vis_reduction_factors(l$genotypes, l$reduction, 2)
```

```
plots[[1]]
plots[[2]]
```

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