Package 'MouseFM'

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Type Package

Title In-silico methods for genetic finemapping in inbred mice

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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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`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 *Available strains*

Description

There are 37 strains available.

Usage

```
avail_strains()
```

Value

Data frame.

Examples

```
avail_strains()
```

backend_request *Send HTTP request to backend server*

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 *Strain combination builder*

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 *Data frame to GenomicRanges::GRanges object*

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 = 5000000, end = 6000000,
  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` *Request variant consequences from Variant Effect Predictor (VEP) via Ensembl Rest Service*

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` *Fetch*

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 *Get backend service url*

Description

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

Usage

```
getURL()
```

Value

URL string.

Examples

```
getURL()
```

get_top *Best strain combinations*

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 *Reduction factor calculation*

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 *Reference genome version*

Description

Returns version of reference genome used in package MouseFM.

Usage

```
ref_genome()
```

Value

Vector.

Examples

```
ref_genome()
```

setURL *Set backend service url*

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

geno	Genotype data frame or GenomicRanges::GRanges object.
red	Reduction factor data frame.
n_top	Number if 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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