

Package ‘crosshap’

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Type Package

Title Local Haplotype Clustering and Visualization

Version 1.4.0

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Description A local haplotyping visualization toolbox to capture major patterns of co-inheritance between clusters of linked variants, whilst connecting findings to phenotypic and demographic traits across individuals. 'crosshap' enables users to explore and understand genomic variation across a trait-associated region. For an example of successful local haplotype analysis, see Marsh et al. (2022) <[doi:10.1007/s00122-022-04045-8](https://doi.org/10.1007/s00122-022-04045-8)>.

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Suggests covr, knitr, rmarkdown, testthat (>= 3.0.0), umap, vdiff

Depends R (>= 4.00)

URL <https://jacobimarsh.github.io/crosshap/>

BugReports <https://github.com/jacobimarsh/crosshap/issues>

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arith_mode	<i>Mode utility function</i>
------------	------------------------------

Description

Mode utility function

Usage

arith_mode(x)

Arguments

x Input vector

Value

Mode numerical values

 build_bot_halfeyepplot *Bot hap-pheno raincloud plot*

Description

build_bot_halfeyepplot() builds a vertical plot displaying the phenotypic scores for each individual, grouped by haplotype, coloured by metadata variable. Metadata groups can be isolated using the isolate_groups argument. Makes use of the \$Indfile information from haplotype object. It is an internal function called by crosshap_viz(), though can be called separately to build a stand-alone plot.

Usage

```
build_bot_halfeyepplot(
  HapObject,
  epsilon,
  hide_labels = TRUE,
  isolate_group = NA
)
```

Arguments

HapObject	Haplotype object created by run_haplotyping().
epsilon	Epsilon to visualize haplotyping results for.
hide_labels	If TRUE, legend is hidden.
isolate_group	If a Metadata group is provided, all other Metadata groups will be masked from the plot. NOTE: it does change the summary tables or marker group phenotype scores.

Value

A ggplot2 object.

Examples

```
build_bot_halfeyepplot(HapObject, epsilon = 0.6, hide_labels = FALSE)
```

build_left_alleleplot *Left SNP-allele plot*

Description

build_left_alleleplot() builds a horizontal plot displaying mean allelic frequencies (reference/alternate/missing/heterozygous) of all SNP loci, grouped by marker group. Makes use of \$Varfile information from a HapObject created by run_haplotyping(). This is an internal function called by crosshap_viz(), though can be called separately to build a stand-alone plot.

Usage

```
build_left_alleleplot(HapObject, epsilon, hide_labels = TRUE)
```

Arguments

HapObject	Haplotype object created by run_haplotyping().
epsilon	Epsilon matching the haplotype object used for umap_in.
hide_labels	If TRUE, legend is hidden.

Value

A ggplot2 object.

Examples

```
build_left_alleleplot(HapObject, epsilon = 0.6, hide_labels = FALSE)
```

build_left_posplot *Left SNP-position plot*

Description

build_left_alleleplot() builds a horizontal plot displaying the chromosomal position of each SNP locus, grouped by marker group. Makes use of the \$Varfile file from haplotype object. It is an internal function called by crosshap_viz(), though can be called separately to build a stand-alone plot.

Usage

```
build_left_posplot(HapObject, epsilon, hide_labels = TRUE)
```

Arguments

HapObject	Haplotype object created by run_haplotyping().
epsilon	Epsilon matching the haplotype object used for umap_in.
hide_labels	If TRUE, legend is hidden.

Value

A ggplot2 object.

Examples

```
build_left_posplot(HapObject, epsilon = 0.6, hide_labels = FALSE)
```

build_mid_dotplot	<i>Middle MG/hap dot plot</i>
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Description

build_mid_dotplot() builds a central dot plot displaying the relationship between haplotype combinations and the characteristic marker group alleles that define them. Makes use of the \$Hapfile information from a haplotype object. This is an internal function called by crosshap_viz(), though can be called separately to build a stand-alone plot (can be useful when patched to a peripheral plot).

Usage

```
build_mid_dotplot(HapObject, epsilon, hide_labels = FALSE)
```

Arguments

HapObject	Haplotype object created by run_haplotyping
epsilon	Epsilon to visualize haplotyping results for.
hide_labels	If TRUE, legend is hidden.

Value

A ggplot2 object.

Examples

```
build_mid_dotplot(HapObject, epsilon = 0.6, hide_labels = FALSE)
```

```
build_right_clusterplot
```

Right intra-cluster linkage plot

Description

build_right_jitterplot() builds a horizontal plot displaying the mean pairwise R^2 linkage between each SNP and all other SNPs in its marker group, grouped by marker group, coloured by alternate allele frequency. Makes use of the \$Varfile information from haplotyping object. It is an internal function called by crosshap_viz(), though can be called separately to build a stand-alone plot.

Usage

```
build_right_clusterplot(HapObject, epsilon, hide_labels = FALSE)
```

Arguments

HapObject	Haplotype object created by run_haplotyping().
epsilon	Epsilon to visualize haplotyping results for.
hide_labels	If TRUE, legend is hidden.

Value

A ggplot2 object.

Examples

```
build_right_clusterplot(HapObject, epsilon = 0.6, hide_labels = FALSE)
```

```
build_right_phenoplot
```

Right SNP-pheno phenoplot

Description

build_right_phenoplot() builds a horizontal plot displaying the mean difference in phenotype score between individuals with the alternate vs reference alleles for each SNP locus, grouped by marker group, coloured by the alternate allele frequency of each SNP. Makes use of the \$Varfile phenotypic information from haplotyping object. It is an internal function called by crosshap_viz(), though can be called separately to build a stand-alone plot.

Usage

```
build_right_phenoplot(HapObject, epsilon, hide_labels = TRUE)
```

Arguments

HapObject	Haplotype object created by run_haplotyping().
epsilon	Epsilon to visualize haplotyping results for.
hide_labels	If TRUE, legend is hidden.

Value

A ggplot2 object.

Examples

```
build_right_phenoplot(HapObject, epsilon = 0.6, hide_labels = FALSE)
```

build_summary_tables *Hap/MG summary tables*

Description

build_summary_tables() builds summary tables for each haplotype and Marker Group with some of the information shown in the peripheral crosshap plots. It is an internal function called by crosshap_viz(), though can be called separately to build stand-alone grob tables.

Usage

```
build_summary_tables(HapObject, epsilon)
```

Arguments

HapObject	Haplotype object created by run_haplotyping().
epsilon	Epsilon to visualize haplotyping results for.

Value

A list containing two TableGrob objects.

build_top_metaplot	<i>Top metadata-hap bar plot</i>
--------------------	----------------------------------

Description

build_top_metaplot() builds a vertical stacked bar plot displaying the frequency of each haplotype combination, broken down by each categorical metadata variable provided. Makes use of the \$Ind-file information from a haplotype object. This is an internal function called by crosshap_viz(), though can be called separately to build a stand-alone plot

Usage

```
build_top_metaplot(HapObject, epsilon, hide_labels = FALSE)
```

Arguments

HapObject	Haplotype object created by run_haplotyping()
epsilon	Epsilon to visualize haplotyping results for.
hide_labels	If TRUE, legend is hidden.

Value

A ggplot2 object.

Examples

```
build_top_metaplot(HapObject, epsilon = 0.6, hide_labels = FALSE)
```

clustree_viz	<i>Clustering tree</i>
--------------	------------------------

Description

clustree_viz() builds a clustering tree displaying changes in haplotype assignment between individuals or changes in Marker Group assignment for SNPs, across different epsilon values. This function is a 'clustree' wrapper.

Usage

```
clustree_viz(HapObject, type = "MG")
```

Arguments

HapObject	A haplotyping object with a range of results from different epsilons created by run_haplotyping()
type	When type = "hap", nodes represent haplotype populations, when type = "MG", nodes represent marker groups.

Value

A ggplot2 object.

crosshap_viz	<i>Visualize haplotypes</i>
--------------	-----------------------------

Description

crosshap_viz() builds five individual plots using various elements of a HapObject created by run_haplotyping(). The central dotplot displays relationship between clusters of linked SNPs (Marker Groups), and distinct haplotypes present within the population. Vertical plots (top/bottom) visualize individuals and populations, grouped by haplotype. Horizontal plots (left/right) visualize SNP information, grouped by Marker Group cluster.

Usage

```
crosshap_viz(
  HapObject,
  epsilon,
  plot_left = "allele",
  plot_right = "pheno",
  hide_labels = FALSE,
  isolate_group = NA
)
```

Arguments

HapObject	Haplotype object created by run_haplotyping().
epsilon	Epsilon to visualize haplotyping results for.
plot_left	When plot_left = "allele", SNP allele frequency information is displayed, when plot_left = "pos", SNP position information is displayed.
plot_right	When plot_right = "pheno", phenotype associations for SNPs are displayed, when plot_right = "cluster", internal marker group linkage is displayed.
hide_labels	When TRUE, legends from plots are hidden.
isolate_group	If one or more Metadata groups are provided, all other Metadata groups will be masked from the plot. NOTE: it does change the summary tables or marker group phenotype scores.

Value

A patchwork object.

HapObject	<i>Example Haplotype object</i>
-----------	---------------------------------

Description

A haplotyping object created by run_haplotyping() for example cqProt-003 soy data

Usage

HapObject

Format

A haplotype (S3) object containing results needed for haplotype visualization across five epsilon values (0.2,0.4,0.6,0.8,1)

epsilon Epsilon value chosen for haplotyping with DBSCAN

MGmin MGmin value (minPts) chosen for haplotyping with DBSCAN

Hapfile Summary of Marker Groups defining haplotype combinations

Indfile Haplotype assignments for individuals

Varfile Marker Group assignments for SNPs, with additional calculated information

LD	<i>Example LD matrix</i>
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Description

A pairwise R^2 linkage matrix generated by PLINK for example cqProt-003 soy data

Usage

LD

Format

A square matrix read in by read_LD()

`mean_na.rm`*Mean utility function*

Description

Mean utility function

Usage

```
mean_na.rm(x)
```

Arguments

`x` Input vector

Value

Mean numerical values

`metadata`*Example Domestication metadata*

Description

Metadata file with level of domestication for each individual in example cqProt-003 soy data

Usage

```
metadata
```

Format

A two-column tibble read in by `read_metadata()`

Source

<https://doi.org/10.1007/s00122-022-04045-8>

pheno	<i>Example phenotype data</i>
-------	-------------------------------

Description

Seed protein scores for each individual in example cqProt-003 soy data

Usage

```
pheno
```

Format

A two-column tibble read in by read_pheno()

Source

<https://doi.org/10.1007/s00122-022-04045-8>

prepare_hap_umap	<i>UMAP haplotype visualization helper</i>
------------------	--

Description

prepare_hap_umap() builds a large composite ggplot2 object ready for faceting and animation (see vignette) for visualizing SNP alleles (coloured by Marker Group) possessed by individuals with each haplotype. UMAP coordinates for each SNP can be generated using umap::umap(), with the LD matrix generated for run_haplotyping() as input. When fully rendered and faceted, the resultant GIF intuitively visualizes the shared loci within each Marker Group that are constant within each haplotype combination.

Usage

```
prepare_hap_umap(
  umap_in,
  hetmiss_as = "allele",
  HapObject,
  epsilon,
  vcf,
  nsamples = 25
)
```

Arguments

umap_in	UMAP results produced for a haplotype object at a given epsilon.
hetmiss_as	If hetmiss_as = "allele", heterozygous-missing SNPs <code>./.N</code> are recoded as <code>'N/N'</code> , if hetmiss_as = "miss", the site is recoded as missing.
HapObject	Haplotype object created by <code>run_haplotyping()</code> .
epsilon	Epsilon matching the haplotype object used for <code>umap_in</code> .
vcf	Input vcf.
nsamples	Number of times to sample each haplotype group, will directly translate to the number of frames in animation. Should be the same as the <code>nframes</code> passed to <code>gganimate::animate()</code> .

Value

A large ggplot2 object.

pseudo_haps	<i>Identify haplotypes from clustered SNPs</i>
-------------	--

Description

`pseudo_haps()` calls the most common allelic states for each SNP marker group across individuals, before building dummy SNPs for each marker group that mimic the binary vcf format. This is the step which determines the haplotype combinations, and therefore enables several summaries to be returned - as contained in the `$Hapfile` and preliminary `$Indfile` and finalised `$MGfile`, following marker group smoothing. This is an internal function not intended for external use.

Usage

```
pseudo_haps(preMGfile, bin_vcf, minHap, LD, keep_outliers)
```

Arguments

preMGfile	SNP clusters from DBscan.
bin_vcf	Binary VCF for region of interest reformatted by <code>run_haplotyping()</code> .
minHap	Minimum size (nIndividuals) to keep haplotype combinations
LD	LD matrix input.
keep_outliers	When FALSE, marker group smoothing is performed to remove outliers.

Value

Returns intermediate of haplotype object

read_LD	<i>Read LD correlation matrix to tibble</i>
---------	---

Description

If your correlation matrix does not have rownames and column names, a VCF will need to be provided so it can be added with read_LD().

Usage

```
read_LD(LDin, vcf = NULL)
```

Arguments

LDin	Square correlation matrix
vcf	VCF object created by read_vcf() that can be used to assign column names

Value

A tibble.

read_metadata	<i>Read metadata to tibble</i>
---------------	--------------------------------

Description

Requires two column text file without a header (Ind | Metadata)

Usage

```
read_metadata(Metain)
```

Arguments

Metain	Input phenotype file
--------	----------------------

Value

A tibble.

read_pheno	<i>Read phenotype data to tibble</i>
------------	--------------------------------------

Description

Requires two column text file without a header (Ind | Pheno)

Usage

```
read_pheno(Phenoin)
```

Arguments

Phenoin	Input phenotype file
---------	----------------------

Value

A tibble.

read_vcf	<i>Read VCF to tibble</i>
----------	---------------------------

Description

Dashes, '-', in individual names are recoded to '.' for downstream compatability.

Usage

```
read_vcf(VCFin)
```

Arguments

VCFin	Input VCF
-------	-----------

Value

A tibble.

run_haplotyping

*Cluster SNPs and identify haplotypes***Description**

run_haplotyping() performs density-based clustering of SNPs in region of interest to identify Marker Groups. Individuals are classified by haplotype combination based on shared combinations of Marker Group alleles. Returns a haplotyping object (HapObject), which can be used as input to build clustering tree for epsilon optimization using clustree_viz(), and can be visualized with reference to phenotype and metadata using crosshap_viz().

Usage

```
run_haplotyping(
  vcf,
  LD,
  pheno,
  metadata = NULL,
  epsilon = c(0.2, 0.4, 0.6, 0.8, 1),
  MGmin = 30,
  minHap = 9,
  hetmiss_as = "allele",
  het_phenos = FALSE,
  keep_outliers = FALSE
)
```

Arguments

vcf	Input VCF for region of interest.
LD	Pairwise correlation matrix of SNPs in region (e.g. from PLINK).
pheno	Input numeric phenotype data for each individual.
metadata	Metadata input (optional).
epsilon	Epsilon values for clustering SNPs with DBscan.
MGmin	Minimum SNPs in marker groups, MinPts parameter for DBscan.
minHap	Minimum nIndividuals in a haplotype combination.
hetmiss_as	If hetmiss_as = "allele", heterozygous-missing SNPs '.N' are recoded as 'N/N', if hetmiss_as = "miss", the site is recoded as missing.
het_phenos	When FALSE, phenotype associations for SNPs are calculated from reference and alternate allele individuals only, when TRUE, heterozygous individuals are included assuming additive allele effects.
keep_outliers	When FALSE, marker group smoothing is performed to remove outliers.

Value

A comprehensive haplotyping S3 object (HapObject) for each provided epsilon value, needed for clustree_viz() and crosshap_viz().

`run_hdbscan_haplotyping`*Cluster SNPs with HDBSCAN and identify haplotypes*

Description

`run_hdbscan_haplotyping()` performs HDBSCAN clustering of SNPs in region of interest to identify marker groups. Individuals are classified by haplotype combination based on shared combinations of marker group alleles. Returns a comprehensive haplotyping object (`HapObject`), which can be visualized with reference to phenotype and metadata using `crosshap_viz()` (set `epsilon` to 1 as a dummy value).

Usage

```
run_hdbscan_haplotyping(  
  vcf,  
  LD,  
  pheno,  
  MGmin,  
  minHap = 5,  
  hetmiss_as = "allele",  
  metadata = NULL,  
  keep_outliers = FALSE  
)
```

Arguments

<code>vcf</code>	Input VCF for region of interest.
<code>LD</code>	Pairwise correlation matrix of SNPs in region (e.g. from PLINK).
<code>pheno</code>	Input numeric phenotype data for each individual.
<code>MGmin</code>	Minimum SNPs in marker groups, <code>MinPts</code> parameter for DBscan.
<code>minHap</code>	Minimum nIndividuals in a haplotype combination.
<code>hetmiss_as</code>	If <code>hetmiss_as = "allele"</code> , heterozygous-missing SNPs <code>./.N</code> are recoded as <code>'N/N'</code> , if <code>hetmiss_as = "miss"</code> , the site is recoded as missing.
<code>metadata</code>	Metadata input (optional).
<code>keep_outliers</code>	When <code>FALSE</code> , marker group smoothing is performed to remove outliers.

Value

A comprehensive haplotyping S3 object (`HapObject`) for each provided `epsilon` value, needed for `clustree_viz()` and `crosshap_viz()`.

tagphenos	<i>Calculate SNP phenotypic associations</i>
-----------	--

Description

tagphenos() reports the frequency of allele types for each SNP and calculates phenotype associations for the different alleles, before returning this information in a \$Varfile in a HapObject. This is an internal function that is not intended for external use.

Usage

```
tagphenos(MGfile, bin_vcf, pheno, het_phenos = FALSE)
```

Arguments

- | | |
|------------|---|
| MGfile | SNP marker groups clustered using DBscan. |
| bin_vcf | Binary VCF for region of interest reformatted by run_haplotyping(). |
| pheno | Input numeric phenotype data for each individual. |
| het_phenos | When FALSE, phenotype associations for SNPs are calculated from reference and alternate allele individuals only, when TRUE, heterozygous individuals are included assuming additive allele effects. |

Value

Returns intermediate of haplotype object.

vcf	<i>Example VCF</i>
-----	--------------------

Description

A VCF containing SNPs for example cqProt-003 soy data

Usage

```
vcf
```

Format

A VCF read in by read_vcf()

Source

<https://doi.org/10.1007/s00122-022-04045-8>

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