Package 'plinkQC'

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Type Package

Title Genotype Quality Control with 'PLINK'

Version 0.3.2

URL https://meyer-lab-cshl.github.io/plinkQC

BugReports https://github.com/meyer-lab-cshl/plinkQC/issues

Maintainer Hannah Meyer <hannah.v.meyer@gmail.com>

Description Genotyping arrays enable the direct measurement of an individuals genotype at thousands of markers. 'plinkQC' facilitates genotype quality control for genetic association studies as described by Anderson and colleagues (2010) <doi:10.1038/nprot.2010.116>. It makes 'PLINK' basic statistics (e.g. missing genotyping rates per individual, allele frequencies per genetic marker) and relationship functions accessible from 'R' and generates a per-individual and per-marker quality control report. Individuals and markers that fail the quality control can subsequently be removed to generate a new, clean dataset. Removal of individuals based on relationship status is optimised to retain as many individuals as possible in the study.

Depends R (>= 3.6.0)

Imports methods, optparse, data.table (>= 1.11.0), R.utils, ggplot2, ggforce, ggrepel, cowplot, UpSetR, dplyr, igraph (>= 1.2.4), sys

Suggests testthat, knitr, rmarkdown

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SystemRequirements plink (1.9)

Encoding UTF-8

LazyData true

RoxygenNote 7.1.0

VignetteBuilder knitr

NeedsCompilation no

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R topics documented:

`checkPlink` *Check PLINK software access*

Description

checkPlink checks that the PLINK software (https://www.cog-genomics.org/plink/1.9/) can be found from system call.

Usage

```
checkPlink(path2plink = NULL)
```

Arguments

`path2plink`	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by `exec`('plink').

Value

Path to PLINK executable.

check_ancestry *Identification of individuals of divergent ancestry*

Description

Runs and evaluates results of plink –pca on merged genotypes from individuals to be QCed and individuals of reference population of known genotypes. Currently, check ancestry only supports automatic selection of individuals of European descent. It uses information from principal components 1 and 2 returned by plink –pca to find the center of the European reference samples (mean(PC1_europeanRef), mean(PC2_europeanRef). It then computes the maximum Euclidean distance (maxDist) of the European reference samples from this centre. All study samples whose Euclidean distance from the centre falls outside the circle described by the radius r=europeanTh* maxDist are considered non-European and their IDs are returned as failing the ancestry check. `check_ancestry` creates a scatter plot of PC1 versus PC2 colour-coded for samples of the reference populations and the study population.

Usage

```
check_ancestry(
  indir,
  name,
  qcdir = indir,
  prefixMergedDataset,
  europeanTh = 1.5,
  refPopulation = c("CEU", "TSI"),
  refSamples = NULL,
  refColors = NULL,
  refSamplesFile = NULL,
  refColorsFile = NULL,
  refSamplesIID = "IID",
  refSamplesPop = "Pop",
  refColorsColor = "Color",
  refColorsPop = "Pop",
  studyColor = "#2c7bb6",
  legend_labels_per_row = 6,
  run.check_ancestry = TRUE,
  interactive = FALSE,
  verbose = verbose,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] prefix of plink files, i.e. name.bed, name.bim, name.fam.
qcdir	[character] /path/to/directory where prefixMergedDataset.eigenvec results as returned by plink –pca should be saved. Per default qcdir=indir. If run.check_ancestry is FALSE, it is assumed that plink –pca prefixMergedDataset has been run

and qcdir/prefixMergedDataset.eigenvec exists.User needs writing permission to qcdir.

`prefixMergedDataset`
: [character] Prefix of merged dataset (study and reference samples) used in plink –pca, resulting in prefixMergedDataset.eigenvec.

`europeanTh`
: [double] Scaling factor of radius to be drawn around center of European reference samples, with study samples inside this radius considered to be of European descent and samples outside this radius of non-European descent. The radius is computed as the maximum Euclidean distance of European reference samples to the centre of European reference samples.

`refPopulation`
: [vector] Vector with population identifiers of European reference population. Identifiers have to be corresponding to population IDs [refColorsPop] in refColorsfile/refColors.

`refSamples`
: [data.frame] Dataframe with sample identifiers [refSamplesIID] corresponding to IIDs in prefixMergedDataset.eigenvec and population identifier [refSamplesPop] corresponding to population IDs [refColorsPop] in refColorsfile/refColors. Either refSamples or refSamplesFile have to be specified.

`refColors`
: [data.frame, optional] Dataframe with population IDs in column [refColorsPop] and corresponding colour-code for PCA plot in column [refColorsColor]. If not provided and is.null(refColorsFile) default colors are used.

`refSamplesFile`
: [character] /path/to/File/with/reference samples. Needs columns with sample identifiers [refSamplesIID] corresponding to IIDs in prefixMergedDataset.eigenvec and population identifier [refSamplesPop] corresponding to population IDs [refColorsPop] in refColorsfile/refColors.

`refColorsFile`
: [character, optional] /path/to/File/with/Population/Colors containing population IDs in column [refColorsPop] and corresponding colour-code for PCA plot in column [refColorsColor].If not provided and is.null(refColors) default colors for are used.

`refSamplesIID`
: [character] Column name of reference sample IDs in refSamples/refSamplesFile.

`refSamplesPop`
: [character] Column name of reference sample population IDs in refSamples/refSamplesFile.

`refColorsColor`
: [character] Column name of population colors in refColors/refColorsFile

`refColorsPop`
: [character] Column name of reference sample population IDs in refColors/refColorsFile.

`studyColor`
: [character] Colour to be used for study population.

`legend_labels_per_row`
: [integer] Number of population names per row in PCA plot.

`run.check_ancestry`
: [logical] Should plink –pca be run to determine principal components of merged dataset; if FALSE, it is assumed that plink –pca has been run successfully and qcdir/prefixMergedDataset.eigenvec is present; `check_ancestry` will fail with missing file error otherwise.

`interactive`
: [logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_ancestry) via ggplot2::ggsave(p=p_ancestry, other_arguments) or pdf(outfile) print(p_ancestry) dev.off().

`verbose`
: [logical] If TRUE, progress info is printed to standard out.

`path2plink`
: [character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name

of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').

showPlinkOutput

[logical] If TRUE, plink log and error messages are printed to standard out.

Value

Named [list] with i) fail_ancestry, containing a [data.frame] with FID and IID of non-European individuals and ii) p_ancestry, a ggplot2-object 'containing' a scatter plot of PC1 versus PC2 colour-coded for samples of the reference populations and the study population, which can be shown by print(p_ancestry).

Examples

```
## Not run:
indir <- system.file("extdata", package="plinkQC")
name <- "data"
fail_ancestry <- check_ancestry(indir=indir, name=name,
refSamplesFile=paste(indir, "/HapMap_ID2Pop.txt",sep=""),
refColorsFile=paste(indir, "/HapMap_PopColors.txt", sep=""),
prefixMergedDataset="data.HapMapIII", interactive=FALSE,
run.check_ancestry=FALSE)

## End(Not run)
```

---

check_het_and_miss *Identification of individuals with outlying missing genotype or heterozygosity rates*

Description

Runs and evaluates results from plink –missing (missing genotype rates per individual) and plink –het (heterozygosity rates per individual). Non-systematic failures in genotyping and outlying heterozygosity (hz) rates per individual are often proxies for DNA sample quality. Larger than expected heterozygosity can indicate possible DNA contamination. The mean heterozygosity in PLINK is computed as hz_mean = (N-O)/N, where N: number of non-missing genotypes and O:observed number of homozygous genotypes for a given individual. Mean heterozygosity can differ between populations and SNP genotyping panels. Within a population and genotyping panel, a reduced heterozygosity rate can indicate inbreeding - these individuals will then likely be returned by check_relatedness as individuals that fail the relatedness filters. check_het_and_miss creates a scatter plot with the individuals' missingness rates on x-axis and their heterozygosity rates on the y-axis.

Usage

```
check_het_and_miss(
  indir,
  name,
  qcdir = indir,
  imissTh = 0.03,
  hetTh = 3,
```

```
  run.check_het_and_miss = TRUE,
  label = TRUE,
  interactive = FALSE,
  verbose = FALSE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam, name.het and name.imiss.
qcdir	[character] /path/to/directory where name.het as returned by plink –het and name.imiss as returned by plink –missing will be saved. Per default qcdir=indir. If run.check_het_and_miss is FALSE, it is assumed that plink –missing and plink –het have been run and qcdir/name.imiss and qcdir/name.het are present. User needs writing permission to qcdir.
imissTh	[double] Threshold for acceptable missing genotype rate per individual; has to be proportion between (0,1)
hetTh	[double] Threshold for acceptable deviation from mean heterozygosity per individual. Expressed as multiples of standard deviation of heterozygosity (het), i.e. individuals outside mean(het) +/- hetTh*sd(het) will be returned as failing heterozygosity check; has to be larger than 0.
run.check_het_and_miss	[logical] Should plink –missing and plink –het be run to determine genotype missingness and heterozygosity rates; if FALSE, it is assumed that plink –missing and plink –het have been run and qcdir/name.imiss and qcdir/name.het are present; check_het_and_miss will fail with missing file error otherwise.
label	[logical] Set TRUE, to add fail IDs as text labels in scatter plot.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_het_imiss) via ggplot2::ggsave(p=p_het_imiss , other_arguments) or pdf(outfile) print(p_het_imiss) dev.off().
verbose	[logical] If TRUE, progress info is printed to standard out.
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
showPlinkOutput	[logical] If TRUE, plink log and error messages are printed to standard out.

Details

check_het_and_miss wraps around run_check_missingness, run_check_heterozygosity and evaluate_check_het_and_miss. If run.check_het_and_miss is TRUE, run_check_heterozygosity

and run_check_missingness are executed ; otherwise it is assumed that plink –missing and plink –het have been run externally and qcdir/name.het and qcdir/name.imiss exist. check_het_and_miss will fail with missing file error otherwise.

For details on the output data.frame fail_imiss and fail_het, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#imiss and https://www.cog-genomics.org/plink/1.9/formats#het

Value

Named [list] with i) fail_imiss [data.frame] containing FID (Family ID), IID (Within-family ID), MISS_PHENO (Phenotype missing? (Y/N)), N_MISS (Number of missing genotype call(s), not including obligatory missings), N_GENO (Number of potentially valid call(s)), F_MISS (Missing call rate) of individuals failing missing genotype check and ii) fail_het [data.frame] containing FID (Family ID), IID (Within-family ID), O(HOM) (Observed number of homozygotes), E(HOM) (Expected number of homozygotes), N(NM) (Number of non-missing autosomal genotypes), F (Method-of-moments F coefficient estimate) of individuals failing outlying heterozygosity check and iii) p_het_imiss, a ggplot2-object 'containing' a scatter plot with the samples' missingness rates on x-axis and their heterozygosity rates on the y-axis, which can be shown by print(p_het_imiss).

Examples

```
 ## Not run:
indir <- system.file("extdata", package="plinkQC")
name <- "data"
fail_het_miss <- check_het_and_miss(indir=indir, name=name,
run.check_het_and_miss=FALSE, interactive=FALSE)

## End(Not run)
```

---

check_hwe *Identification of SNPs showing a significant deviation from Hardy-Weinberg- equilibrium (HWE)*

Description

Runs and evaluates results from plink –hardy. It calculates the observed and expected heterozygote frequencies for all variants in the individuals that passed the perIndividualQC and computes the deviation of the frequencies from Hardy-Weinberg equilibrium (HWE) by HWE exact test. The p-values of the HWE exact test are displayed as histograms (stratified by all and low p-values), where the hweTh is used to depict the quality control cut-off for SNPs.

Usage

```
check_hwe(
  indir,
  name,
  qcdir = indir,
  hweTh = 1e-05,
  interactive = FALSE,
  path2plink = NULL,
  verbose = FALSE,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
qcdir	[character] /path/to/directory where results will be written to. If perIndividualQC was conducted, this directory should be the same as qcdir specified in perIndividualQC, i.e. it contains name.fail.IDs with IIDs of individuals that failed QC. User needs writing permission to qcdir. Per default, qcdir=indir.
hweTh	[double] Significance threshold for deviation from HWE.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_hwe) via ggplot2::ggsave(p=p_hwe, other_arguments) or pdf(outfile) print(p_hwe) dev.off().
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
verbose	[logical] If TRUE, progress info is printed to standard out and specifically, if TRUE, plink log will be displayed.
showPlinkOutput	[logical] If TRUE, plink log and error messages are printed to standard out.

Details

check_hwe uses plink –remove name.fail.IDs –hardy to calculate the observed and expected heterozygote frequencies per SNP in the individuals that passed the perIndividualQC. It does so without generating a new dataset but simply removes the IDs when calculating the statistics.

For details on the output data.frame fail_hwe, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#hwe.

Value

Named list with i) fail_hwe containing a [data.frame] with CHR (Chromosome code), SNP (Variant identifier), TEST (Type of test: one of 'ALL', 'AFF', 'UNAFF', 'ALL(QT)', 'ALL(NP)'), A1 (Allele 1; usually minor), A2 (Allele 2; usually major), GENO ('/'-separated genotype counts: A1 hom, het, A2 hom), O(HET) (Observed heterozygote frequency E(HET) (Expected heterozygote frequency), P (Hardy-Weinberg equilibrium exact test p-value) for all SNPs that failed the hweTh and ii) p_hwe, a ggplot2-object 'containing' the HWE p-value distribution histogram which can be shown by (print(p_hwe)).

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
name <- "data"
path2plink <- '/path/to/plink'
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
fail_hwe <- check_hwe(indir=indir, qcdir=qcdir, name=name, interactive=FALSE,
```

```
verbose=TRUE, path2plink=path2plink)

## End(Not run)
```

---

check_maf *Identification of SNPs with low minor allele frequency*

Description

Runs and evaluates results from plink –freq. It calculates the minor allele frequencies for all variants in the individuals that passed the perIndividualQC. The minor allele frequency distributions is plotted as a histogram.

Usage

```
check_maf(
  indir,
  name,
  qcdir = indir,
  macTh = 20,
  mafTh = NULL,
  verbose = FALSE,
  interactive = FALSE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
qcdir	[character] /path/to/directory where results will be written to. If perIndividualQC was conducted, this directory should be the same as qcdir specified in perIndividualQC, i.e. it contains name.fail.IDs with IIDs of individuals that failed QC. User needs writing permission to qcdir. Per default, qcdir=indir.
macTh	[double] Threshold for minor allele cut cut-off, if both mafTh and macTh are specified, macTh is used (macTh = mafTh*2*NrSamples).
mafTh	[double] Threshold for minor allele frequency cut-off.
verbose	[logical] If TRUE, progress info is printed to standard out and specifically, if TRUE, plink log will be displayed.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_hwe) via ggplot2::ggsave(p=p_maf, other_arguments) or pdf(outfile) print(p_maf) dev.off().
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').

showPlinkOutput
: [logical] If TRUE, plink log and error messages are printed to standard out.

Details

check_maf uses plink –remove name.fail.IDs –freq to calculate the minor allele frequencies for all variants in the individuals that passed the perIndividualQC. It does so without generating a new dataset but simply removes the IDs when calculating the statistics.

For details on the output data.frame fail_maf, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#frq.

Value

Named list with i) fail_maf containing a [data.frame] with CHR (Chromosome code), SNP (Variant identifier), A1 (Allele 1; usually minor), A2 (Allele 2; usually major), MAF (Allele 1 frequency), NCHROBS (Number of allele observations) for all SNPs that failed the mafTh/macTh and ii) p_maf, a ggplot2-object 'containing' the MAF distribution histogram which can be shown by (print(p_maf)).

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
name <- "data"
path2plink <- '/path/to/plink'
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
fail_maf <- check_maf(indir=indir, qcdir=qcdir, name=name, macTh=15,
interactive=FALSE, verbose=TRUE, path2plink=path2plink)

## End(Not run)
```

---

check_relatedness *Identification of related individuals*

Description

Runs and evaluates results from plink –genome. plink –genome calculates identity by state (IBS) for each pair of individuals based on the average proportion of alleles shared at genotyped SNPs. The degree of recent shared ancestry, i.e. the identity by descent (IBD) can be estimated from the genome-wide IBS. The proportion of IBD between two individuals is returned by plink –genome as PI_HAT. check_relatedness finds pairs of samples whose proportion of IBD is larger than the specified highIBDTh. Subsequently, for pairs of individuals that do not have additional relatives in the dataset, the individual with the greater genotype missingness rate is selected and returned as the individual failing the relatedness check. For more complex family structures, the unrelated individuals per family are selected (e.g. in a parents-offspring trio, the offspring will be marked as fail, while the parents will be kept in the analysis). check_relatedness depicts all pair-wise IBD-estimates as histograms stratified by value of PI_HAT.

Usage

```
check_relatedness(
  indir,
  name,
  qcdir = indir,
  highIBDTh = 0.1875,
  genomebuild = "hg19",
  imissTh = 0.03,
  run.check_relatedness = TRUE,
  interactive = FALSE,
  verbose = FALSE,
  mafThRelatedness = 0.1,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam, name.genome and name.imiss.
qcdir	[character] /path/to/directory to where name.genome as returned by plink –genome will be saved. Per default qcdir=indir. If run.check_relatedness is FALSE, it is assumed that plink –missing and plink –genome have been run and qcdir/name.imiss and qcdir/name.genome exist. User needs writing permission to qcdir.
highIBDTh	[double] Threshold for acceptable proportion of IBD between pair of individuals.
genomebuild	[character] Name of the genome build of the PLINK file annotations, ie mappings in the name.bim file. Will be used to remove high-LD regions based on the coordinates of the respective build. Options are hg18, hg19 and hg38. See @details.
imissTh	[double] Threshold for acceptable missing genotype rate in any individual; has to be proportion between (0,1)
run.check_relatedness	[logical] Should plink –genome be run to determine pairwise IBD of individuals; if FALSE, it is assumed that plink –genome and plink –missing have been run and qcdir/name.imiss and qcdir/name.genome are present; check_relatedness will fail with missing file error otherwise.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_IBD() via ggplot2::ggsave(p=p_IBD, other_arguments) or pdf(outfile) print(p_IBD) dev.off().
verbose	[logical] If TRUE, progress info is printed to standard out.
mafThRelatedness	[double] Threshold of minor allele frequency filter for selecting variants for IBD estimation.
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name

of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').

showPlinkOutput

[logical] If TRUE, plink log and error messages are printed to standard out.

Details

check_relatedness wraps around run_check_relatedness and evaluate_check_relatedness. If run.check_relatedness is TRUE, run_check_relatedness is executed ; otherwise it is assumed that plink –genome has been run externally and qcdir/name.genome exists. check_relatedness will fail with missing file error otherwise.

For details on the output data.frame fail_high_IBD, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#genome.

Value

Named [list] with i) fail_high_IBD containing a [data.frame] of IIDs and FIDs of individuals who fail the IBDTh in columns FID1 and IID1. In addition, the following columns are returned (as originally obtained by plink –genome): FID2 (Family ID for second sample), IID2 (Individual ID for second sample), RT (Relationship type inferred from .fam/.ped file), EZ (IBD sharing expected value, based on just .fam/.ped relationship), Z0 (P(IBD=0)), Z1 (P(IBD=1)), Z2 (P(IBD=2)), PI_HAT (Proportion IBD, i.e. P(IBD=2) + 0.5*P(IBD=1)), PHE (Pairwise phenotypic code (1, 0, -1 = AA, AU, and UU pairs, respectively)), DST (IBS distance, i.e. (IBS2 + 0.5*IBS1) / (IBS0 + IBS1 + IBS2)), PPC (IBS binomial test), RATIO (HETHET : IBS0 SNP ratio (expected value 2)). and ii) failIDs containing a [data.frame] with individual IDs [IID] and family IDs [FID] of individuals failing the highIBDTh iii) p_IBD, a ggplot2-object 'containing' all pair-wise IBD-estimates as histograms stratified by value of PI_HAT, which can be shown by print(p_IBD).

Examples

```
## Not run:
indir <- system.file("extdata", package="plinkQC")
name <- 'data'
relatednessQC <- check_relatedness(indir=indir, name=name, interactive=FALSE,
run.check_relatedness=FALSE)

## End(Not run)
```

---

check_sex *Identification of individuals with discordant sex information*

Description

Runs and evaluates results from plink –check-sex. check_sex returns IIDs for individuals whose SNPSEX != PEDSEX (where the SNPSEX is determined by the heterozygosity rate across X-chromosomal variants). Mismatching SNPSEX and PEDSEX IDs can indicate plating errors, sample-mixup or generally samples with poor genotyping. In the latter case, these IDs are likely to fail other QC steps as well. Optionally, an extra data.frame (externalSex) with sample IDs and sex can be provided to double check if external and PEDSEX data (often processed at different centers) match. If a mismatch between PEDSEX and SNPSEX was detected, while SNPSEX == Sex, PEDSEX of these individuals can optionally be updated (fixMixup=TRUE). check_sex depicts the X-chromosomal heterozygosity (SNPSEX) of the individuals split by their (PEDSEX).

Usage

```
check_sex(
  indir,
  name,
  qcdir = indir,
  maleTh = 0.8,
  femaleTh = 0.2,
  run.check_sex = TRUE,
  externalSex = NULL,
  externalFemale = "F",
  externalMale = "M",
  externalSexSex = "Sex",
  externalSexID = "IID",
  fixMixup = FALSE,
  interactive = FALSE,
  verbose = FALSE,
  label = TRUE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam and name.sexcheck.
qcdir	[character] /path/to/directory to save name.sexcheck as returned by plink –check-sex. Per default qcdir=indir. If run.check_sex is FALSE, it is assumed that plink –check-sex has been run and qcdir/name.sexcheck is present. User needs writing permission to qcdir.
maleTh	[double] Threshold of X-chromosomal heterozygosity rate for males.
femaleTh	[double] Threshold of X-chromosomal heterozygosity rate for females.
run.check_sex	[logical] Should plink –check-sex be run? if set to FALSE, it is assumed that plink –check-sex has been run and qcdir/name.sexcheck is present; check_sex will fail with missing file error otherwise.
externalSex	[data.frame, optional] Dataframe with sample IDs [externalSexID] and sex [externalSexSex] to double check if external and PEDSEX data (often processed at different centers) match.
externalFemale	[integer/character] Identifier for 'female' in externalSex.
externalMale	[integer/character] Identifier for 'male' in externalSex.
externalSexSex	[character] Column identifier for column containing sex information in externalSex.
externalSexID	[character] Column identifier for column containing ID information in externalSex.
fixMixup	[logical] Should PEDSEX of individuals with mismatch between PEDSEX and Sex while Sex==SNPSEX automatically corrected: this will directly change the name.bim/.bed/.fam files!
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_sexcheck)

via ggplot2::ggsave(p=p_sexcheck, other_arguments) or pdf(outfile) print(p_sexcheck) dev.off().

`verbose` [logical] If TRUE, progress info is printed to standard out.

`label` [logical] Set TRUE, to add fail IDs as text labels in scatter plot.

`path2plink` [character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').

`showPlinkOutput` [logical] If TRUE, plink log and error messages are printed to standard out.

Details

check_sex wraps around run_check_sex and evaluate_check_sex. If run.check_sex is TRUE, run_check_sex is executed ; otherwise it is assumed that plink –check-sex has been run externally and qcdir/name.sexcheck exists. check_sex will fail with missing file error otherwise.

For details on the output data.frame fail_sex, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#sexcheck.

Value

Named list with i) fail_sex: [data.frame] with FID, IID, PEDSEX, SNPSEX and Sex (if externalSex was provided) of individuals failing sex check, ii) mixup: dataframe with FID, IID, PEDSEX, SNPSEX and Sex (if externalSex was provided) of individuals whose PEDSEX != Sex and Sex == SNPSEX and iii) p_sexcheck, a ggplot2-object 'containing' a scatter plot of the X-chromosomal heterozygosity (SNPSEX) of the sample split by their (PEDSEX), which can be shown by print(p_sexcheck).

Examples

```
 ## Not run:
indir <- system.file("extdata", package="plinkQC")
name <- "data"
fail_sex <- check_sex(indir=indir, name=name, run.check_sex=FALSE,
interactive=FALSE, verbose=FALSE)

## End(Not run)
```

---

check_snp_missingness *Identification of SNPs with high missingness rate*

Description

Runs and evaluates results from plink –missing –freq. It calculate the rates of missing genotype calls and frequency for all variants in the individuals that passed the perIndividualQC. The SNP missingness rates (stratified by minor allele frequency) are depicted as histograms.

Usage

```
check_snp_missingness(
  indir,
  name,
  qcdir = indir,
  lmissTh = 0.01,
  interactive = FALSE,
  path2plink = NULL,
  verbose = FALSE,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
qcdir	[character] /path/to/directory where results will be written to. If perIndividualQC was conducted, this directory should be the same as qcdir specified in perIndividualQC, i.e. it contains name.fail.IDs with IIDs of individuals that failed QC. User needs writing permission to qcdir. Per default, qcdir=indir.
lmissTh	[double] Threshold for acceptable variant missing rate across samples.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_lmiss) via ggplot2::ggsave(p=p_lmiss, other_arguments) or pdf(outfile) print(p_lmiss) dev.off().
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
verbose	[logical] If TRUE, progress info is printed to standard out and specifically, if TRUE, plink log will be displayed.
showPlinkOutput	[logical] If TRUE, plink log and error messages are printed to standard out.

Details

check_snp_missingness uses plink –remove name.fail.IDs –missing –freq to calculate rates of missing genotype calls and frequency per SNP in the individuals that passed the perIndividualQC. It does so without generating a new dataset but simply removes the IDs when calculating the statistics.

For details on the output data.frame fail_missingness, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#lmiss.

Value

Named list with i) fail_missingness containing a [data.frame] with CHR (Chromosome code), SNP (Variant identifier), CLST (Cluster identifier. Only present with –within/–family), N_MISS

(Number of missing genotype call(s), not counting obligatory missings), N_CLST (Cluster size; does not include nonmales on Ychr; Only present with –within/–family), N_GENO (Number of potentially valid call(s)), F_MISS (Missing call rate) for all SNPs failing the lmissTh and ii) p_lmiss, a ggplot2-object 'containing' the SNP missingness histogram which can be shown by (print(p_lmiss)).

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
name <- "data"
path2plink <- '/path/to/plink'
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
fail_snp_missingness <- check_snp_missingness(qcdir=qcdir, indir=indir,
name=name, interactive=FALSE, verbose=TRUE, path2plink=path2plink)

## End(Not run)
```

---

cleanData *Create plink dataset with individuals and markers passing quality control*

Description

Individuals that fail per-individual QC and markers that fail per-marker QC are removed from indir/name.bim/.bed/.fam and a new, dataset with the remaining individuals and markers is created as qcdir/name.clean.bim/.bed/.fam.

Usage

```
cleanData(
  indir,
  name,
  qcdir = indir,
  filterSex = TRUE,
  filterHeterozygosity = TRUE,
  filterSampleMissingness = TRUE,
  filterAncestry = TRUE,
  filterRelated = TRUE,
  filterSNPMissingness = TRUE,
  lmissTh = 0.01,
  filterHWE = TRUE,
  hweTh = 1e-05,
  filterMAF = TRUE,
  macTh = 20,
  mafTh = NULL,
  path2plink = NULL,
  verbose = FALSE,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
qcdir	[character] /path/to/directory where results will be written to. If perIndividualQC was conducted, this directory should be the same as qcdir specified in perIndividualQC, i.e. it contains name.fail.IDs with IIDs of individuals that failed QC. User needs writing permission to qcdir. Per default, qcdir=indir.
filterSex	[logical] Set to exclude samples that failed the sex check (via check_sex or perIndividualQC). Requires file qcdir/name.fail-sexcheck.IDs (automatically created by perIndividualQC if do.evaluate_check_sex set to TRUE).
filterHeterozygosity	[logical] Set to exclude samples that failed check for outlying heterozygosity rates (via check_het_and_miss or perIndividualQC). Requires file qcdir/name.fail-het.IDs (automatically created by perIndividualQC if do.evaluate_check_het_and_miss set to TRUE).
filterSampleMissingness	[logical] Set to exclude samples that failed check for excessive missing genotype rates (via check_het_and_miss or perIndividualQC). Requires file qcdir/name.fail-imiss.IDs (automatically created by perIndividualQC if do.evaluate_check_het_and_miss set to TRUE).
filterAncestry	[logical] Set to exclude samples that failed ancestry check (via check_ancestry or perIndividualQC). Requires file qcdir/name.fail-ancestry.IDs (automatically created by perIndividualQC if do.check_ancestry set to TRUE).
filterRelated	[logical] Set to exclude samples that failed relatedness check (via check_relatedness or perIndividualQC). Requires file qcdir/name.fail-IBD.IDs (automatically created by perIndividualQC if do.evaluate_check_relatedness set to TRUE).
filterSNPMissingness	[logical] Set to exclude markers that have excessive missing rates across samples (via check_snp_missingness or perMarkerQC). Requires lmissTh to be set.
lmissTh	[double] Threshold for acceptable variant missing rate across samples.
filterHWE	[logical] Set to exclude markers that fail HWE exact test (via check_hwe or perMarkerQC). Requires hweTh to be set.
hweTh	[double] Significance threshold for deviation from HWE.
filterMAF	[logical] Set to exclude markers that fail minor allele frequency or minor allele count threshold (via check_maf or perMarkerQC). Requires mafTh or macTh to be set.
macTh	[double] Threshold for minor allele cut cut-off, if both mafTh and macTh are specified, macTh is used (macTh = mafTh*2*NrSamples).
mafTh	[double] Threshold for minor allele frequency cut-off.
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
verbose	[logical] If TRUE, progress info is printed to standard out.
showPlinkOutput	[logical] If TRUE, plink log and error messages are printed to standard out.

Value

names [list] with i) passIDs, containing a [data.frame] with family [FID] and individual [IID] IDs of samples that pass the QC, ii) failIDs, containing a [data.frame] with family [FID] and individual [IID] IDs of samples that fail the QC.

Examples

```
package.dir <- find.package('plinkQC')
indir <- file.path(package.dir, 'extdata')
qcdir <- tempdir()
name <- "data"
path2plink <- '/path/to/plink'
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
# Run individual QC checks
fail_individuals <- perIndividualQC(indir=indir, qcdir=qcdir, name=name,
refSamplesFile=paste(qcdir, "/HapMap_ID2Pop.txt",sep=""),
refColorsFile=paste(qcdir, "/HapMap_PopColors.txt", sep=""),
prefixMergedDataset="data.HapMapIII", interactive=FALSE, verbose=FALSE)

# Run marker QC checks
fail_markers <- perMarkerQC(indir=indir, qcdir=qcdir, name=name)

# Create new dataset of indiviudals and markers passing QC
ids_all <- cleanData(indir=indir, qcdir=qcdir, name=name, macTh=15,
verbose=TRUE, path2plink=path2plink, filterAncestry=FALSE,
filterRelated=TRUE)

## End(Not run)
```

`evaluate_check_ancestry` *Evaluate results from PLINK PCA on combined study and reference data*

Description

Evaluates and depicts results of plink –pca (via `run_check_ancestry` or externally conducted pca) on merged genotypes from individuals to be QCed and individuals of reference population of known genotypes. Currently, check ancestry only supports automatic selection of individuals of European descent. It uses information from principal components 1 and 2 returned by plink –pca to find the center of the European reference samples (mean(PC1_europeanRef), mean(PC2_europeanRef). It computes the maximum Euclidean distance (maxDist) of the European reference samples from this centre. All study samples whose Euclidean distance from the centre falls outside the circle described by the radius r=europeanTh* maxDist are considered non-European and their IDs are returned as failing the ancestry check. check_ancestry creates a scatter plot of PC1 versus PC2 colour-coded for samples of the reference populations and the study population.

Usage

```
evaluate_check_ancestry(
  indir,
```

```
  name,
  prefixMergedDataset,
  qcdir = indir,
  europeanTh = 1.5,
  refSamples = NULL,
  refColors = NULL,
  refSamplesFile = NULL,
  refColorsFile = NULL,
  refSamplesIID = "IID",
  refSamplesPop = "Pop",
  refColorsColor = "Color",
  refColorsPop = "Pop",
  studyColor = "#2c7bb6",
  refPopulation = c("CEU", "TSI"),
  legend_labels_per_row = 6,
  interactive = FALSE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
prefixMergedDataset	[character] Prefix of merged dataset (study and reference samples) used in plink –pca, resulting in prefixMergedDataset.eigenvec.
qcdir	[character] /path/to/directory/with/QC/results containing prefixMergedDataset.eigenvec results as returned by plink –pca. Per default qcdir=indir.
europeanTh	[double] Scaling factor of radius to be drawn around center of European reference samples, with study samples inside this radius considered to be of European descent and samples outside this radius of non-European descent. The radius is computed as the maximum Euclidean distance of European reference samples to the centre of European reference samples.
refSamples	[data.frame] Dataframe with sample identifiers [refSamplesIID] corresponding to IIDs in prefixMergedDataset.eigenvec and population identifier [refSamplesPop] corresponding to population IDs [refColorsPop] in refColorsfile/refColors. Either refSamples or refSamplesFile have to be specified.
refColors	[data.frame, optional] Dataframe with population IDs in column [refColorsPop] and corresponding colour-code for PCA plot in column [refColorsColor]. If not provided and is.null(refColorsFile) default colors are used.
refSamplesFile	[character] /path/to/File/with/reference samples. Needs columns with sample identifiers [refSamplesIID] corresponding to IIDs in prefixMergedDataset.eigenvec and population identifier [refSamplesPop] corresponding to population IDs [refColorsPop] in refColorsfile/refColors. If both refSamplesFile and refSamples are not NULL, refSamplesFile information is used.
refColorsFile	[character, optional] /path/to/File/with/Population/Colors containing population IDs in column [refColorsPop] and corresponding colour-code for PCA plot in column [refColorsColor].If not provided and is.null(refColors) default colors for are used. If both refColorsFile and refColors are not NULL, refColorsFile information is used.

`refSamplesIID` [character] Column name of reference sample IDs in refSamples/refSamplesFile.

`refSamplesPop` [character] Column name of reference sample population IDs in refSamples/refSamplesFile.

`refColorsColor` [character] Column name of population colors in refColors/refColorsFile

`refColorsPop` [character] Column name of reference sample population IDs in refColors/refColorsFile.

`studyColor` [character] Colour to be used for study population if plot is TRUE.

`refPopulation` [vector] Vector with population identifiers of European reference population. Identifiers have to be corresponding to population IDs [refColorsPop] in refColorsfile/refColors.

`legend_labels_per_row` [integer] Number of population names per row in PCA plot.

`interactive` [logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_ancestry) via ggplot2::ggsave(p=p_ancestry, other_arguments) or pdf(outfile) print(p_ancestry) dev.off().

Details

Both `run_check_ancestry` and `evaluate_check_ancestry` can simply be invoked by `check_ancestry`.

Value

Named [list] with i) fail_ancestry, containing a [data.frame] with FID and IID of non-European individuals and ii) p_ancestry, a ggplot2-object 'containing' a scatter plot of PC1 versus PC2 colour-coded for samples of the reference populations and the study population, which can be shown by print(p_ancestry).

Examples

```
## Not run:
qcdir <- system.file("extdata", package="plinkQC")
name <- "data"
fail_ancestry <- evaluate_check_ancestry(indir=qcdir, name=name,
refSamplesFile=paste(qcdir, "/HapMap_ID2Pop.txt",sep=""),
refColorsFile=paste(qcdir, "/HapMap_PopColors.txt", sep=""),
prefixMergedDataset="data.HapMapIII", interactive=FALSE)

## End(Not run)
```

---

evaluate_check_het_and_miss

Evaluate results from PLINK missing genotype and heterozygosity rate check.

Description

Evaluates and depicts results from plink –missing (missing genotype rates per individual) and plink –het (heterozygosity rates per individual) via `run_check_heterozygosity` and `run_check_missingness` or externally conducted check.) Non-systematic failures in genotyping and outlying heterozygosity (hz) rates per individual are often proxies for DNA sample quality. Larger than expected heterozygosity can indicate possible DNA contamination. The mean heterozygosity in PLINK is computed as

hz_mean = (N-O)/N, where N: number of non-missing genotypes and O:observed number of homozygous genotypes for a given individual. Mean heterozygosity can differ between populations and SNP genotyping panels. Within a population and genotyping panel, a reduced heterozygosity rate can indicate inbreeding - these individuals will then be returned by check_relatedness as individuals that fail the relatedness filters. `evaluate_check_het_and_miss` creates a scatter plot with the individuals' missingness rates on x-axis and their heterozygosity rates on the y-axis.

Usage

```
evaluate_check_het_and_miss(
  qcdir,
  name,
  imissTh = 0.03,
  hetTh = 3,
  label = TRUE,
  interactive = FALSE
)
```

Arguments

`qcdir`	[character] path/to/directory/with/QC/results containing name.imiss and name.het results as returned by plink –missing and plink –het.
`name`	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam, name.het and name.imiss.
`imissTh`	[double] Threshold for acceptable missing genotype rate in any individual; has to be proportion between (0,1)
`hetTh`	[double] Threshold for acceptable deviation from mean heterozygosity in any individual. Expressed as multiples of standard deviation of heterozygosity (het), i.e. individuals outside mean(het) +/- hetTh*sd(het) will be returned as failing heterozygosity check; has to be larger than 0.
`label`	[logical] Set TRUE, to add fail IDs as text labels in scatter plot.
`interactive`	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_het_imiss) via ggplot2::ggsave(p=p_het_imiss , other_arguments) or pdf(outfile) print(p_het_imiss) dev.off().

Details

All, `run_check_heterozygosity`, `run_check_missingness` and `evaluate_check_het_and_miss` can simply be invoked by `check_het_and_miss`.

For details on the output data.frame fail_imiss and fail_het, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#imiss and https://www.cog-genomics.org/plink/1.9/formats#het

Value

named [list] with i) fail_imiss dataframe containing FID (Family ID), IID (Within-family ID), MISS_PHENO (Phenotype missing? (Y/N)), N_MISS (Number of missing genotype call(s), not including obligatory missings), N_GENO (Number of potentially valid call(s)), F_MISS (Missing call rate) of individuals failing missing genotype check and ii) fail_het dataframe containing FID (Family ID), IID (Within-family ID), O(HOM) (Observed number of homozygotes), E(HOM)

(Expected number of homozygotes), N(NM) (Number of non-missing autosomal genotypes), F (Method-of-moments F coefficient estimate) of individuals failing outlying heterozygosity check and iii) p_het_imiss, a ggplot2-object 'containing' a scatter plot with the samples' missingness rates on x-axis and their heterozygosity rates on the y-axis, which can be shown by print(p_het_imiss).

Examples

```
qcdir <- system.file("extdata", package="plinkQC")
name <- "data"
## Not run:
fail_het_miss <- evaluate_check_het_and_miss(qcdir=qcdir, name=name,
interactive=FALSE)

## End(Not run)
```

`evaluate_check_relatedness` *Evaluate results from PLINK IBD estimation.*

Description

Evaluates and depicts results from plink –genome on the LD pruned dataset (via `run_check_relatedness` or externally conducted IBD estimation). plink –genome calculates identity by state (IBS) for each pair of individuals based on the average proportion of alleles shared at genotyped SNPs. The degree of recent shared ancestry, i.e. the identity by descent (IBD) can be estimated from the genome-wide IBS. The proportion of IBD between two individuals is returned by –genome as PI_HAT. `evaluate_check_relatedness` finds pairs of samples whose proportion of IBD is larger than the specified highIBDTh. Subsequently, for pairs of individual that do not have additional relatives in the dataset, the individual with the greater genotype missingness rate is selected and returned as the individual failing the relatedness check. For more complex family structures, the unrelated individuals per family are selected (e.g. in a parents-offspring trio, the offspring will be marked as fail, while the parents will be kept in the analysis). `evaluate_check_relatedness` depicts all pair-wise IBD-estimates as histograms stratified by value of PI_HAT.

Usage

```
evaluate_check_relatedness(
  qcdir,
  name,
  highIBDTh = 0.1875,
  imissTh = 0.03,
  interactive = FALSE,
  verbose = FALSE
)
```

Arguments

`qcdir`	[character] path/to/directory/with/QC/results containing name.imiss and name.genome results as returned by plink –missing and plink –genome.
`name`	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam, name.genome and name.imiss.

highIBDTh	[double] Threshold for acceptable proportion of IBD between pair of individuals.
imissTh	[double] Threshold for acceptable missing genotype rate in any individual; has to be proportion between (0,1)
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_IBD() via ggplot2::ggsave(p=p_IBD, other_arguments) or pdf(outfile) print(p_IBD) dev.off().
verbose	[logical] If TRUE, progress info is printed to standard out.

Details

Both run_check_relatedness and evaluate_check_relatedness can simply be invoked by check_relatedness.

For details on the output data.frame fail_high_IBD, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#genome.

Value

a named [list] with i) fail_high_IBD containing a [data.frame] of IIDs and FIDs of individuals who fail the IBDTh in columns FID1 and IID1. In addition, the following columns are returned (as originally obtained by plink –genome): FID2 (Family ID for second sample), IID2 (Individual ID for second sample), RT (Relationship type inferred from .fam/.ped file), EZ (IBD sharing expected value, based on just .fam/.ped relationship), Z0 (P(IBD=0)), Z1 (P(IBD=1)), Z2 (P(IBD=2)), PI_HAT (Proportion IBD, i.e. P(IBD=2) + 0.5*P(IBD=1)), PHE (Pairwise phenotypic code (1, 0, -1 = AA, AU, and UU pairs, respectively)), DST (IBS distance, i.e. (IBS2 + 0.5*IBS1) / (IBS0 + IBS1 + IBS2)), PPC (IBS binomial test), RATIO (HETHET : IBS0 SNP ratio (expected value 2)). and ii) failIDs containing a [data.frame] with individual IDs [IID] and family IDs [FID] of individuals failing the highIBDTh iii) p_IBD, a ggplot2-object 'containing' all pair-wise IBD-estimates as histograms stratified by value of PI_HAT, which can be shown by print(p_IBD).

Examples

```
qcdir <- system.file("extdata", package="plinkQC")
name <- 'data'
## Not run:
relatednessQC <- evaluate_check_relatedness(qcdir=qcdir, name=name,
interactive=FALSE)

## End(Not run)
```

---

evaluate_check_sex *Evaluate results from PLINK sex check.*

Description

Evaluates and depicts results from plink –check-sex (via run_check_sex or externally conducted sex check). Takes file qcdir/name.sexcheck and returns IIDs for samples whose SNPSEX != PEDSEX (where the SNPSEX is determined by the heterozygosity rate across X-chromosomal variants). Mismatching SNPSEX and PEDSEX IDs can indicate plating errors, sample-mixup or generally samples with poor genotyping. In the latter case, these IDs are likely to fail other QC steps as

well. Optionally, an extra data.frame (externalSex) with sample IDs and sex can be provided to double check if external and PEDSEX data (often processed at different centers) match. If a mismatch between PEDSEX and SNPSEX was detected while SNPSEX == Sex, PEDSEX of these individuals can optionally be updated (fixMixup=TRUE). `evaluate_check_sex` depicts the X-chromosomal heterozygosity (SNPSEX) of the samples split by their (PEDSEX).

Usage

```
evaluate_check_sex(
  qcdir,
  name,
  maleTh = 0.8,
  femaleTh = 0.2,
  externalSex = NULL,
  fixMixup = FALSE,
  indir = qcdir,
  externalFemale = "F",
  externalMale = "M",
  externalSexSex = "Sex",
  externalSexID = "IID",
  verbose = FALSE,
  label = TRUE,
  path2plink = NULL,
  showPlinkOutput = TRUE,
  interactive = FALSE
)
```

Arguments

`qcdir`	[character] /path/to/directory containing name.sexcheck as returned by plink –check-sex.
`name`	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam and name.sexcheck.
`maleTh`	[double] Threshold of X-chromosomal heterozygosity rate for males.
`femaleTh`	[double] Threshold of X-chromosomal heterozygosity rate for females.
`externalSex`	[data.frame, optional] with sample IDs [externalSexID] and sex [externalSexSex] to double check if external and PEDSEX data (often processed at different centers) match.
`fixMixup`	[logical] Should PEDSEX of individuals with mismatch between PEDSEX and Sex, with Sex==SNPSEX automatically corrected: this will directly change the name.bim/.bed/.fam files!
`indir`	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files; only required of fixMixup==TRUE. User needs writing permission to indir.
`externalFemale`	[integer/character] Identifier for 'female' in externalSex.
`externalMale`	[integer/character] Identifier for 'male' in externalSex.
`externalSexSex`	[character] Column identifier for column containing sex information in externalSex.
`externalSexID`	[character] Column identifier for column containing ID information in externalSex.
`verbose`	[logical] If TRUE, progress info is printed to standard out.

label	[logical] Set TRUE, to add fail IDs as text labels in scatter plot.
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
showPlinkOutput	[logical] If TRUE, plink log and error messages are printed to standard out.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_sexcheck) via ggplot2::ggsave(p=p_sexcheck, other_arguments) or pdf(outfile) print(p_sexcheck) dev.off().

Details

Both run_check_sex and evaluate_check_sex can simply be invoked by check_sex.

For details on the output data.frame fail_sex, check the original description on the PLINK output format page: https://www.cog-genomics.org/plink/1.9/formats#sexcheck.

Value

named list with i) fail_sex: dataframe with FID, IID, PEDSEX, SNPSEX and Sex (if externalSex was provided) of individuals failing sex check, ii) mixup: dataframe with FID, IID, PEDSEX, SNPSEX and Sex (if externalSex was provided) of individuals whose PEDSEX != Sex and Sex == SNPSEX and iii) p_sexcheck, a ggplot2-object 'containing' a scatter plot of the X-chromosomal heterozygosity (SNPSEX) of the individuals split by their (PEDSEX), which can be shown by print(p_sexcheck).

Examples

```
qcdir <- system.file("extdata", package="plinkQC")
name <- "data"
## Not run:
fail_sex <- evaluate_check_sex(qcdir=qcdir, name=name, interactive=FALSE,
verbose=FALSE)

## End(Not run)
```

---

overviewPerIndividualQC

Overview of per sample QC

Description

overviewPerIndividualQC depicts results of perIndividualQC as intersection plots (via upset) and returns dataframes indicating which QC checks individuals failed or passed.

Usage

```
overviewPerIndividualQC(results_perIndividualQC, interactive = FALSE)
```

Arguments

results_perIndividualQC	[list] Output of perIndividualQC i.e. named [list] with i) sample_missingness containing a [vector] with sample IIDs failing the selected missingness threshold imissTh, ii) highIBD containing a [vector] with sample IIDs failing the selected relatedness threshold highIBDTh, iii) outlying_heterozygosity containing a [vector] with sample IIDs failing selected the heterozygosity threshold hetTh, iv) mismatched_sex containing a [vector] with the sample IIDs failing the sexcheck based on SNPSEX and selected femaleTh/maleTh, v) ancestry containing a vector with sample IIDs failing the ancestry check based on the selected europeanTh and vi) p_sampleQC, a ggplot2-object 'containing' a sub-paneled plot with the QC-plots of check_sex, check_het_and_miss, check_relatedness and check_ancestry.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_overview) via ggplot2::ggsave(p=p_overview, other_arguments) or pdf(outfile) print(p_overview) dev.off().

Value

Named [list] with i) nr_fail_samples: total number of samples [integer] failing perIndividualQC, ii) fail_QC containing a [data.frame] with samples that failed QC steps (excluding ancestry) with IID, FID, all QC steps applied by perIndividualQC (max=4), with entries=0 if passing the QC and entries=1 if failing that particular QC and iii) fail_QC_and_ancestry containing a [data.frame] with samples that failed ancestry and QC checks with IID, FID, QC_fail and Ancestry_fail, with entries=0 if passing and entries=1 if failing that check, iii) p_overview, a ggplot2-object 'containing' a sub-paneled plot with the QC-plots.

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
name <- "data"
## Not run:
fail_individuals <- perIndividualQC(qcdir=qcdir, indir=indir, name=name,
refSamplesFile=paste(qcdir, "/HapMap_ID2Pop.txt",sep=""),
refColorsFile=paste(qcdir, "/HapMap_PopColors.txt", sep=""),
prefixMergedDataset="data.HapMapIII", interactive=FALSE, verbose=FALSE,
do.run_check_het_and_miss=FALSE, do.run_check_relatedness=FALSE,
do.run_check_sex=FALSE, do.run_check_ancestry=FALSE)

overview <- overviewPerIndividualQC(fail_individuals)

## End(Not run)
```

---

overviewPerMarkerQC *Overview of per marker QC*

Description

overviewPerMarkerQC depicts results of perMarkerQC as an intersection plot (via upset) and returns a dataframe indicating which QC checks were failed or passed.

Usage

```
overviewPerMarkerQC(results_perMarkerQC, interactive = FALSE)
```

Arguments

results_perMarkerQC	[list] Output of perIndividualQC i.e. named [list] with i) fail_list, a named [list] with 1. SNP_missingness, containing SNP IDs failing the missingness threshold lmissTh, 2. hwe, containing SNP IDs failing the HWE exact test threshold hweTh and 3. maf, containing SNPs failing the MAF threshold mafTh/MAC threshold macTh and ii) p_markerQC, a ggplot2-object 'containing' a sub-paneled plot with the QC-plots of check_snp_missingness, check_hwe and check_maf
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_overview) via ggplot2::ggsave(p=p_overview, other_arguments) or pdf(outfile) print(p_overview) dev.off().

Value

Named [list] with i) nr_fail_markers: total number of markers [integer] failing perMarkerQC, ii) fail_QC containing a [data.frame] with markers that failed QC steps: marker rsIDs in rows, columns are all QC steps applied by perMarkerQC (max=3), with entries=0 if passing the QC and entries=1 if failing that particular QC.

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
name <- "data"
path2plink <- '/path/to/plink'
# the following code is not run on package build, as the path2plink on the
# user system is not known.
# All quality control checks
## Not run:
fail_markers <- perMarkerQC(qcdir=qcdir, indir=indir, name=name,
interactive=FALSE, verbose=TRUE, path2plink=path2plink)
overview <- overviewPerMarkerQC(fail_markers)

## End(Not run)
```

---

perIndividualQC *Quality control for all individuals in plink-dataset*

Description

perIndividualQC checks the samples in the plink dataset for their total missingness and heterozygosity rates, the concordance of their assigned sex to their SNP sex, their relatedness to other study individuals and their genetic ancestry.

Usage

```
perIndividualQC(
  indir,
  name,
  qcdir = indir,
  dont.check_sex = FALSE,
  do.run_check_sex = TRUE,
  do.evaluate_check_sex = TRUE,
  maleTh = 0.8,
  femaleTh = 0.2,
  externalSex = NULL,
  externalMale = "M",
  externalSexSex = "Sex",
  externalSexID = "IID",
  externalFemale = "F",
  fixMixup = FALSE,
  dont.check_het_and_miss = FALSE,
  do.run_check_het_and_miss = TRUE,
  do.evaluate_check_het_and_miss = TRUE,
  imissTh = 0.03,
  hetTh = 3,
  dont.check_relatedness = FALSE,
  do.run_check_relatedness = TRUE,
  do.evaluate_check_relatedness = TRUE,
  highIBDTh = 0.1875,
  mafThRelatedness = 0.1,
  genomebuild = "hg19",
  dont.check_ancestry = FALSE,
  do.run_check_ancestry = TRUE,
  do.evaluate_check_ancestry = TRUE,
  prefixMergedDataset,
  europeanTh = 1.5,
  refSamples = NULL,
  refColors = NULL,
  refSamplesFile = NULL,
  refColorsFile = NULL,
  refSamplesIID = "IID",
  refSamplesPop = "Pop",
  refColorsColor = "Color",
  refColorsPop = "Pop",
  studyColor = "#2c7bb6",
  label = TRUE,
  interactive = FALSE,
  verbose = TRUE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.

`name` [character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.

`qcdir` [character] /path/to/directory where results will be saved. Per default, qcdir=indir. If do.evaluate_[analysis] is set to TRUE and do.run_[analysis] is FALSE, `perIndividualQC` expects the analysis-specific plink output files in qcdir i.e. do.check_sex expects name.sexcheck, do.evaluate_check_het_and_miss expects name.het and name.imiss, do.evaluate_check_relatedness expects name.genome and name.imiss and do.evaluate_check_ancestr expects prefixMergeData.eigenvec. If these files are not present `perIndividualQC` will fail with missing file error. Setting do.run_[analysis] TRUE will execute the checks and create the required files. User needs writing permission to qcdir.

`dont.check_sex` [logical] If TRUE, no sex check will be conducted; short for do.run_check_sex=FALSE and do.evaluate_check_sex=FALSE. Takes precedence over do.run_check_sex and do.evaluate_check_sex.

`do.run_check_sex` [logical] If TRUE, run `run_check_sex`

`do.evaluate_check_sex` [logical] If TRUE, run `evaluate_check_sex`

`maleTh` [double] Threshold of X-chromosomal heterozygosity rate for males.

`femaleTh` [double] Threshold of X-chromosomal heterozygosity rate for females.

`externalSex` [data.frame, optional] Dataframe with sample IDs [externalSexID] and sex [externalSexSex] to double check if external and PEDSEX data (often processed at different centers) match.

`externalMale` [integer/character] Identifier for 'male' in externalSex.

`externalSexSex` [character] Column identifier for column containing sex information in externalSex.

`externalSexID` [character] Column identifier for column containing ID information in externalSex.

`externalFemale` [integer/character] Identifier for 'female' in externalSex.

`fixMixup` [logical] Should PEDSEX of individuals with mismatch between PEDSEX and Sex while Sex==SNPSEX automatically corrected: this will directly change the name.bim/.bed/.fam files!

`dont.check_het_and_miss` [logical] If TRUE, no heterozygosity and missingness check will be conducted; short for do.run_check_heterozygosity=FALSE, do.run_check_missingness=FALSE and do.evaluate_check_het_and_miss=FALSE. Takes precedence over do.run_check_heterozygosity, do.run_check_missingness and do.evaluate_check_het_and_miss.

`do.run_check_het_and_miss` [logical] If TRUE, run `run_check_heterozygosity` and `run_check_missingness`

`do.evaluate_check_het_and_miss` [logical] If TRUE, run `evaluate_check_het_and_miss`.

`imissTh` [double] Threshold for acceptable missing genotype rate in any individual; has to be proportion between (0,1)

`hetTh` [double] Threshold for acceptable deviation from mean heterozygosity per individual. Expressed as multiples of standard deviation of heterozygosity (het), i.e. individuals outside mean(het) +/- hetTh*sd(het) will be returned as failing heterozygosity check; has to be larger than 0.

`dont.check_relatedness` [logical] If TRUE, no relatedness check will be conducted; short for do.run_check_relatedness=FALS and do.evaluate_check_relatedness=FALSE. Takes precedence over do.run_check_relatedness and do.evaluate_check_relatedness.

`do.run_check_relatedness`
: [logical] If TRUE, run `run_check_relatedness`.

`do.evaluate_check_relatedness`
: [logical] If TRUE, run `evaluate_check_relatedness`.

`highIBDTh`
: [double] Threshold for acceptable proportion of IBD between pair of individuals.

`mafThRelatedness`
: [double] Threshold of minor allele frequency filter for selecting variants for IBD estimation.

`genomebuild`
: [character] Name of the genome build of the PLINK file annotations, ie mappings in the name.bim file. Will be used to remove high-LD regions based on the coordinates of the respective build. Options are hg18, hg19 and hg38. See @details.

`dont.check_ancestry`
: [logical] If TRUE, no ancestry check will be conducted; short for do.run_check_ancestry=FALSE and do.evaluate_check_ancestry=FALSE. Takes precedence over do.run_check_ancestry and do.evaluate_check_ancestry.

`do.run_check_ancestry`
: [logical] If TRUE, run `run_check_ancestry`.

`do.evaluate_check_ancestry`
: [logical] If TRUE, run `evaluate_check_ancestry`.

`prefixMergedDataset`
: [character] Prefix of merged dataset (study and reference samples) used in plink –pca, resulting in prefixMergedDataset.eigenvec.

`europeanTh`
: [double] Scaling factor of radius to be drawn around center of European reference samples, with study samples inside this radius considered to be of European descent and samples outside this radius of non-European descent. The radius is computed as the maximum Euclidean distance of European reference samples to the centre of European reference samples.

`refSamples`
: [data.frame] Dataframe with sample identifiers [refSamplesIID] corresponding to IIDs in prefixMergedDataset.eigenvec and population identifier [refSamplesPop] corresponding to population IDs [refColorsPop] in refColorsfile/refColors. Either refSamples or refSamplesFile have to be specified.

`refColors`
: [data.frame, optional] Dataframe with population IDs in column [refColorsPop] and corresponding colour-code for PCA plot in column [refColorsColor]. If not provided and is.null(refColorsFile) default colors are used.

`refSamplesFile`
: [character] /path/to/File/with/reference samples. Needs columns with sample identifiers [refSamplesIID] corresponding to IIDs in prefixMergedDataset.eigenvec and population identifier [refSamplesPop] corresponding to population IDs [refColorsPop] in refColorsfile/refColors.

`refColorsFile`
: [character, optional] /path/to/File/with/Population/Colors containing population IDs in column [refColorsPop] and corresponding colour-code for PCA plot in column [refColorsColor].If not provided and is.null(refColors) default colors for are used.

`refSamplesIID`
: [character] Column name of reference sample IDs in refSamples/refSamplesFile.

`refSamplesPop`
: [character] Column name of reference sample population IDs in refSamples/refSamplesFile.

`refColorsColor`
: [character] Column name of population colors in refColors/refColorsFile

`refColorsPop`
: [character] Column name of reference sample population IDs in refColors/refColorsFile.

`studyColor`
: [character] Colour to be used for study population.

`label` [logical] Set TRUE, to add fail IDs as text labels in scatter plot.

`interactive` [logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_sampleQC) via ggplot2::ggsave(p=p_sampleQC, other_arguments) or pdf(outfile) print(p_sampleQC) dev.off(). If TRUE, i) depicts the X-chromosomal heterozygosity (SNPSEX) of the samples split by their PEDSEX (if do.evaluate_check_sex is TRUE), ii) creates a scatter plot with samples' missingness rates on x-axis and their heterozygosity rates on the y-axis (if do.evaluate_check_het_and_miss is TRUE), iii) depicts all pair-wise IBD-estimates as histogram (if do.evaluate_check_relatedness is TRUE) and iv) creates a scatter plot of PC1 versus PC2 color-coded for samples of reference populations and study population (if do.check_ancestry is set to TRUE).

`verbose` [logical] If TRUE, progress info is printed to standard out.

`path2plink` [character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').

`showPlinkOutput` [logical] If TRUE, plink log and error messages are printed to standard out.

Details

perIndividualQC wraps around the individual QC functions check_sex, check_het_and_miss, check_relatedness and check_ancestry. For details on the parameters and outputs, check these function documentations. For detailed output for fail IIDs (instead of simple IID lists), run each function individually.

Value

Named [list] with i) fail_list, a named [list] with 1. sample_missingness containing a [vector] with sample IIDs failing the missingness threshold imissTh, 2. highIBD containing a [vector] with sample IIDs failing the relatedness threshold highIBDTh, 3. outlying_heterozygosity containing a [vector] with sample IIDs failing the heterozygosity threshold hetTh, 4. mismatched_sex containing a [vector] with the sample IIDs failing the sexcheck based on SNPSEX and femaleTh/maleTh and 5. ancestry containing a vector with sample IIDs failing the ancestry check based on europeanTh and ii) p_sampleQC, a ggplot2-object 'containing' a sub-paneled plot with the QC-plots of check_sex, check_het_and_miss, check_relatedness and check_ancestry, which can be shown by print(p_sampleQC). List entries contain NULL if that specific check was not chosen.

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
name <- "data"
# All quality control checks
## Not run:
fail_individuals <- perIndividualQC(indir=indir, qcdir=qcdir, name=name,
refSamplesFile=paste(qcdir, "/HapMap_ID2Pop.txt",sep=""),
refColorsFile=paste(qcdir, "/HapMap_PopColors.txt", sep=""),
prefixMergedDataset="data.HapMapIII", interactive=FALSE, verbose=FALSE,
do.run_check_het_and_miss=FALSE, do.run_check_relatedness=FALSE,
```

```
do.run_check_sex=FALSE, do.run_check_ancestry=FALSE)

# Only check sex and missingness/heterozygosity
fail_sex_het_miss <- perIndividualQC(indir=indir, qcdir=qcdir, name=name,
dont.check_ancestry=TRUE, dont.check_relatedness=TRUE,
interactive=FALSE, verbose=FALSE)

## End(Not run)
```

`perMarkerQC` *Quality control for all markers in plink-dataset*

Description

perMarkerQC checks the markers in the plink dataset for their missingness rates across samples, their deviation from Hardy-Weinberg-Equilibrium (HWE) and their minor allele frequencies (MAF). Per default, it assumes that IDs of individuals that have failed `perIndividualQC` have been written to qcdir/name.fail.IDs and removes these individuals when computing missingness rates, HWE p-values and MAF. If the qcdir/name.fail.IDs file does not exist, a message is written to stdout but the analyses will continue for all samples in the name.fam/name.bed/name.bim dataset. Depicts i) SNP missingness rates (stratified by minor allele frequency) as histograms, ii) p-values of HWE exact test (stratified by all and low p-values) as histograms and iii) the minor allele frequency distribution as a histogram.

Usage

```
perMarkerQC(
  indir,
  qcdir = indir,
  name,
  do.check_snp_missingness = TRUE,
  lmissTh = 0.01,
  do.check_hwe = TRUE,
  hweTh = 1e-05,
  do.check_maf = TRUE,
  macTh = 20,
  mafTh = NULL,
  interactive = FALSE,
  verbose = TRUE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

`indir`	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
`qcdir`	[character] /path/to/directory where results will be written to. If `perIndividualQC` was conducted, this directory should be the same as qcdir specified in `perIndividualQC`, i.e. it contains name.fail.IDs with IIDs of individuals that failed QC. User needs writing permission to qcdir. Per default, qcdir=indir.

name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
do.check_snp_missingness	[logical] If TRUE, run check_snp_missingness.
lmissTh	[double] Threshold for acceptable variant missing rate across samples.
do.check_hwe	[logical] If TRUE, run check_hwe.
hweTh	[double] Significance threshold for deviation from HWE.
do.check_maf	[logical] If TRUE, run check_maf.
macTh	[double] Threshold for minor allele cut cut-off, if both mafTh and macTh are specified, macTh is used (macTh = mafTh*2*NrSamples).
mafTh	[double] Threshold for minor allele frequency cut-off.
interactive	[logical] Should plots be shown interactively? When choosing this option, make sure you have X-forwarding/graphical interface available for interactive plotting. Alternatively, set interactive=FALSE and save the returned plot object (p_marker) via ggplot2::ggsave(p=p_marker, other_arguments) or pdf(outfile) print(p_marker) dev.off().
verbose	[logical] If TRUE, progress info is printed to standard out.
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
showPlinkOutput	[logical] If TRUE, plink log and error messages are printed to standard out.

Details

perMarkerQC wraps around the marker QC functions check_snp_missingness, check_hwe and check_maf. For details on the parameters and outputs, check these function documentations.

Value

Named [list] with i) fail_list, a named [list] with 1. SNP_missingness, containing SNP IDs [vector] failing the missingness threshold lmissTh, 2. hwe, containing SNP IDs [vector] failing the HWE exact test threshold hweTh and 3. maf, containing SNPs Ids [vector] failing the MAF threshold mafTh/MAC threshold macTh and ii) p_markerQC, a ggplot2-object 'containing' a sub-paneled plot with the QC-plots of check_snp_missingness, check_hwe and check_maf, which can be shown by print(p_markerQC). List entries contain NULL if that specific check was not chosen.

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
name <- "data"
path2plink <- '/path/to/plink'
# the following code is not run on package build, as the path2plink on the
# user system is not known.
# All quality control checks
## Not run:
fail_markers <- perMarkerQC(indir=indir, qcdir=qcdir, name=name,
interactive=FALSE, verbose=TRUE, path2plink=path2plink)

## End(Not run)
```

`relatednessFilter` *Remove related individuals while keeping maximum number of individuals*

Description

`relatednessFilter` takes a data.frame with pair-wise relatedness measures of samples and returns pairs of individual IDs that are related as well as a list of suggested individual IDs to remove. `relatednessFilter` finds pairs of samples whose relatedness estimate is larger than the specified relatednessTh. Subsequently, for pairs of individual that do not have additional relatives in the dataset, the individual with the worse otherCriterionMeasure (if provided) or arbitrarily individual 1 of that pair is selected and returned as the individual failing the relatedness check. For more complex family structures, the unrelated individuals per family are selected (e.g. in a simple case of a parents-offspring trio, the offspring will be marked as fail, while the parents will be kept in the analysis). Selection is achieved by constructing subgraphs of clusters of individuals that are related. `relatednessFilter` then finds the maximum independent set of vertices in the subgraphs of related individuals. If all individuals are related (i.e. all maximum independent sets are 0), one individual of that cluster will be kept and all others listed as failIDs.

Usage

```
relatednessFilter(
  relatedness,
  otherCriterion = NULL,
  relatednessTh,
  otherCriterionTh = NULL,
  otherCriterionThDirection = c("gt", "ge", "lt", "le", "eq"),
  relatednessIID1 = "IID1",
  relatednessIID2 = "IID2",
  relatednessFID1 = NULL,
  relatednessFID2 = NULL,
  relatednessRelatedness = "PI_HAT",
  otherCriterionIID = "IID",
  otherCriterionMeasure = NULL,
  verbose = FALSE
)
```

Arguments

`relatedness`	[data.frame] containing pair-wise relatedness estimates (in column [relatednessRelatedness]) for individual 1 (in column [relatednessIID1] and individual 2 (in column [relatednessIID1]). Columns relatednessIID1, relatednessIID2 and relatednessRelatedness have to present, while additional columns such as family IDs can be present. Default column names correspond to column names in output of plink –genome (https://www.cog-genomics.org/plink/1.9/ibd). All original columns for pair-wise highIBDTh fails will be returned in fail_IBD.
`otherCriterion`	[data.frame] containing a QC measure (in column [otherCriterionMeasure]) per individual (in column [otherCriterionIID]). otherCriterionMeasure and otherCriterionIID have to present, while additional columns such as family IDs can be present. IIDs in relatednessIID1 have to be present in otherCriterionIID.

`relatednessTh` [double] Threshold for filtering related individuals. Individuals, whose pair-wise relatedness estimates are greater than this threshold are considered related.

`otherCriterionTh` [double] Threshold for filtering individuals based on otherCriterionMeasure. If related individuals fail this threshold they will automatically be excluded.

`otherCriterionThDirection` [character] Used to determine the direction for failing the otherCriterionTh. If 'gt', individuals whose otherCriterionMeasure > otherCriterionTh will automatically be excluded. For pairs of individuals that have no other related samples in the cohort: if both otherCriterionMeasure < otherCriterionTh, the individual with the larger otherCriterionMeasure will be excluded.

`relatednessIID1` [character] Column name of column containing the IDs of the first individual.

`relatednessIID2` [character] Column name of column containing the IDs of the second individual.

`relatednessFID1` [character, optional] Column name of column containing the family IDs of the first individual; if only relatednessFID1 but not relatednessFID2 provided, or none provided even though present in relatedness, FIDs will not be returned.

`relatednessFID2` [character, optional] Column name of column containing the family IDs of the second individual; if only relatednessFID2 but not relatednessFID1 provided, or none provided even though present in relatedness, FIDs will not be returned.

`relatednessRelatedness` [character] Column name of column containing the relatedness estimate.

`otherCriterionIID` [character] Column name of column containing the individual IDs.

`otherCriterionMeasure` [character] Column name of the column containing the measure of the otherCriterion (for instance SNP missingness rate).

`verbose` [logical] If TRUE, progress info is printed to standard out.

Value

named [list] with i) relatednessFails, a [data.frame] containing the data.frame relatedness after filtering for pairs of individuals in relatednessIID1 and relatednessIID2, that fail the relatedness QC; the data.frame is reordered with the fail individuals in column 1 and their related individuals in column 2 and ii) failIDs, a [data.frame] with the [IID]s (and [FID]s if provided) of the individuals that fail the relatednessTh.

`run_check_ancestry` *Run PLINK principal component analysis*

Description

Run plink –pca to calculate the principal components on merged genotypes of the study and reference dataset.

Usage

```
run_check_ancestry(
  indir,
  prefixMergedDataset,
  qcdir = indir,
  verbose = FALSE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files prefixMergedDataset.bim,prefixM and prefixMergedDataset.bed.
prefixMergedDataset	[character] Prefix of merged study and reference data files, i.e. prefixMergedDataset.bed, prefixMergedDataset.bim, prefixMergedDataset.fam.
qcdir	[character] /path/to/directory to save prefixMergedDataset.eigenvec as returned by plink –pca. User needs writing permission to qcdir. Per default qcdir=indir.
verbose	[logical] If TRUE, progress info is printed to standard out.
path2plink	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
showPlinkOutput	[logical] If TRUE, plink log and error messages are printed to standard out.

Details

Both, run_check_ancestry and its evaluation by evaluate_check_ancestry can simply be invoked by check_ancestry.

Examples

```
indir <- system.file("extdata", package="plinkQC")
qcdir <- tempdir()
prefixMergedDataset <- 'data.HapMapIII'
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
run <- run_check_ancestry(indir=indir, qcdir=qcdir, prefixMergedDataset)

## End(Not run)
```

`run_check_heterozygosity` *Run PLINK heterozygosity rate calculation*

Description

Run plink –het to calculate heterozygosity rates per individual.

Usage

```
run_check_heterozygosity(
  indir,
  name,
  qcdir = indir,
  verbose = FALSE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

`indir`	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
`name`	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
`qcdir`	[character] /path/to/directory to save name.het as returned by plink –het. User needs writing permission to qcdir. Per default qcdir=indir.
`verbose`	[logical] If TRUE, progress info is printed to standard out.
`path2plink`	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
`showPlinkOutput`	[logical] If TRUE, plink log and error messages are printed to standard out.

Details

All, run_check_heterozygosity, run_check_missingness and their evaluation by evaluate_check_het_and_miss can simply be invoked by check_het_and_miss.

Examples

```
indir <- system.file("extdata", package="plinkQC")
name <- 'data'
qcdir <- tempdir()
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
run <- run_check_heterozygosity(indir=indir, qcdir=qcdir, name=name)

## End(Not run)
```

`run_check_missingness` *Run PLINK missingness rate calculation*

Description

Run plink –missing to calculate missing genotype rates per individual.

Usage

```
run_check_missingness(
  indir,
  name,
  qcdir = indir,
  verbose = FALSE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

`indir`	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
`name`	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
`qcdir`	[character] /path/to/directory to save name.imiss as returned by plink –missing. User needs writing permission to qcdir. Per default qcdir=indir.
`verbose`	[logical] If TRUE, progress info is printed to standard out.
`path2plink`	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by `exec`('plink').
`showPlinkOutput`	[logical] If TRUE, plink log and error messages are printed to standard out.

Details

All, `run_check_heterozygosity`, `run_check_missingness` and their evaluation by `evaluate_check_het_and_miss` can simply be invoked by `check_het_and_miss`.

Examples

```
indir <- system.file("extdata", package="plinkQC")
name <- 'data'
qcdir <- tempdir()
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
run <- run_check_missingnessness(indir=indir, qcdir=qcdir, name=name)

## End(Not run)
```

`run_check_relatedness` *Run PLINK IBD estimation*

Description

Run LD pruning on dataset with plink –exclude range highldfile –indep-pairwise 50 5 0.2, where highldfile contains regions of high LD as provided by Anderson et (2010) Nature Protocols. Subsequently, plink –genome is run on the LD pruned, maf-filtered data. plink –genome calculates identity by state (IBS) for each pair of individuals based on the average proportion of alleles shared at genotyped SNPs. The degree of recent shared ancestry,i.e. the identity by descent (IBD) can be estimated from the genome-wide IBS. The proportion of IBD between two individuals is returned by –genome as PI_HAT.

Usage

```
run_check_relatedness(
  indir,
  name,
  qcdir = indir,
  highIBDTh = 0.185,
  mafThRelatedness = 0.1,
  path2plink = NULL,
  genomebuild = "hg19",
  showPlinkOutput = TRUE,
  verbose = FALSE
)
```

Arguments

`indir`	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
`name`	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
`qcdir`	[character] /path/to/directory to save name.genome as returned by plink –genome. User needs writing permission to qcdir. Per default qcdir=indir.
`highIBDTh`	[double] Threshold for acceptable proportion of IBD between pair of individuals; only pairwise relationship estimates larger than this threshold will be recorded.
`mafThRelatedness`	[double] Threshold of minor allele frequency filter for selecting variants for IBD estimation.
`path2plink`	[character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').
`genomebuild`	[character] Name of the genome build of the PLINK file annotations, ie mappings in the name.bim file. Will be used to remove high-LD regions based on the coordinates of the respective build. Options are hg18, hg19 and hg38. See @details.
`showPlinkOutput`	[logical] If TRUE, plink log and error messages are printed to standard out.
`verbose`	[logical] If TRUE, progress info is printed to standard out.

Details

Both run_check_relatedness and its evaluation via evaluate_check_relatedness can simply be invoked by check_relatedness.

The IBD estimation is conducted on LD pruned data and in a first step, high LD regions are excluded. The regions were derived from the high-LD-regions file provided by Anderson et (2010) Nature Protocols. These regions are in NCBI36 (hg18) coordinates and were lifted to GRCh37 (hg19) and GRC38 (hg38) coordinates using the liftOver tool available here: https://genome.ucsc.edu/cgi-bin/hgLiftOver. The 'Minimum ratio of bases that must remap' which was set to 0.5 and the 'Allow multiple output regions' box ticked; for all other parameters, the default options were selected. LiftOver files were generated on July 9,2019. The commands for formatting the files are provided in system.file("extdata", 'liftOver.cmd', package="plinkQC").

Examples

```
indir <- system.file("extdata", package="plinkQC")
name <- 'data'
qcdir <- tempdir()
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
run <- run_check_relatedness(indir=indir, qcdir=qcdir, name=name)

## End(Not run)
```

---

run_check_sex *Run PLINK sexcheck*

Description

Run plink –sexcheck to calculate the heterozygosity rate across X-chromosomal variants.

Usage

```
run_check_sex(
  indir,
  name,
  qcdir = indir,
  verbose = FALSE,
  path2plink = NULL,
  showPlinkOutput = TRUE
)
```

Arguments

indir	[character] /path/to/directory containing the basic PLINK data files name.bim, name.bed, name.fam files.
name	[character] Prefix of PLINK files, i.e. name.bed, name.bim, name.fam.
qcdir	[character] /path/to/directory to save name.sexcheck as returned by plink –check-sex. User needs writing permission to qcdir. Per default qcdir=indir.
verbose	[logical] If TRUE, progress info is printed to standard out.

path2plink [character] Absolute path to PLINK executable (https://www.cog-genomics.org/plink/1.9/) i.e. plink should be accesible as path2plink -h. The full name of the executable should be specified: for windows OS, this means path/plink.exe, for unix platforms this is path/plink. If not provided, assumed that PATH set-up works and PLINK will be found by exec('plink').

showPlinkOutput [logical] If TRUE, plink log and error messages are printed to standard out.

Details

Both run_check_sex and its evaluation evaluate_check_sex can simply be invoked by check_sex.

Examples

```
indir <- system.file("extdata", package="plinkQC")
name <- 'data'
qcdir <- tempdir()
# the following code is not run on package build, as the path2plink on the
# user system is not known.
## Not run:
run <- run_check_sex(indir=indir, qcdir=qcdir, name=name)

## End(Not run)
```

---

testNumerics *Test lists for different properties of numerics*

Description

Test all elements of a list if they are numeric, positive numbers, integers or proportions (range 0-1).

Usage

```
testNumerics(numbers, positives = NULL, integers = NULL, proportions = NULL)
```

Arguments

numbers [list] whose elements are tested for being numeric.

positives [list] whose elements are tested for being positive numbers.

integers [list] whose elements are tested for being integers.

proportions [list] whose elements are tested for being proportions. between 0 and 1.

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