Package: bigsnpr (via r-universe)

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Type Package

Title Analysis of Massive SNP Arrays

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Description Easy-to-use, efficient, flexible and scalable tools for analyzing massive SNP arrays. Privé et al. (2018) <doi:10.1093/bioinformatics/bty185>.

License GPL-3

LazyData TRUE

Language en-US

ByteCompile TRUE

SystemRequirements A few functions from package 'bigsnpr' wrap existing software such as 'PLINK' <www.cog-genomics.org/plink2>. Functions are provided to download these software. Note that these external software might not work for some operating systems (e.g. 'PLINK' might not work on Solaris).

Depends R (>= 3.4), bigstatsr (>= 1.6.2)

Imports bigassertr (>= 0.1.7), bigparallelr, bigsparser (>= 0.6), bigreadr, bigutilsr (>= 0.3.3), data.table (>= 1.12.4), doRNG, foreach, ggplot2, magrittr, Matrix (>= 1.3.0), methods, Rcpp, runonce (>= 0.2.3), stats, vctrs

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BugReports https://github.com/privefl/bigsnpr/issues

NeedsCompilation yes

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`bed-class` *Class bed*

Description

A reference class for storing a pointer to a mapped version of a bed file.

Usage

```
bed(bedfile)
```

Arguments

`bedfile`	Path to file with extension ".bed" to read. You need the corresponding ".bim" and ".fam" in the same directory.

Details

A bed object has many field:

- `$address`: address of the external pointer containing the underlying C++ object, to be used internally as a `XPtr<bed>` in C++ code
- `$extptr`: use `$address` instead
- `$bedfile`: path to the bed file
- `$bimfile`: path to the corresponding bim file
- `$famfile`: path to the corresponding fam file
- `$prefix`: path without extension
- `$nrow`: number of samples in the bed file
- `$ncol`: number of variants in the bed file
- `$map`: data frame read from `$bimfile`
- `$fam`: data frame read from `$famfile`
- `$.map`: use `$map` instead
- `$.fam`: use `$fam` instead
- `$light`: get a lighter version of this object for parallel algorithms to not have to transfer e.g. `$.map`.

Examples

```
bedfile <- system.file("extdata", "example-missing.bed", package = "bigsnpr")
(obj.bed <- bed(bedfile))
```

`bed_clumping` *LD clumping*

Description

For a `bigSNP`:

- `snp_pruning()`: LD pruning. Similar to `"--indep-pairwise (size+1) 1 thr.r2"` in PLINK. **This function is deprecated (see this article).**
- `snp_clumping()` (and `bed_clumping()`): LD clumping. If you do not provide any statistic to rank SNPs, it would use minor allele frequencies (MAFs), making clumping similar to pruning.
- `snp_indLRLDR()`: Get SNP indices of long-range LD regions for the human genome.

Usage

```
bed_clumping(
  obj.bed,
  ind.row = rows_along(obj.bed),
  S = NULL,
  thr.r2 = 0.2,
  size = 100/thr.r2,
  exclude = NULL,
  ncores = 1
)

snp_clumping(
  G,
  infos.chr,
  ind.row = rows_along(G),
  S = NULL,
  thr.r2 = 0.2,
  size = 100/thr.r2,
  infos.pos = NULL,
  is.size.in.bp = NULL,
  exclude = NULL,
  ncores = 1
)

snp_pruning(
  G,
  infos.chr,
  ind.row = rows_along(G),
  size = 49,
  is.size.in.bp = FALSE,
  infos.pos = NULL,
  thr.r2 = 0.2,
  exclude = NULL,
  nploidy = 2,
  ncores = 1
)

snp_indLRLDR(infos.chr, infos.pos, LD.regions = LD.wiki34)
```

Arguments

`obj.bed`	Object of type bed, which is the mapping of some bed file. Use `obj.bed <- bed(bedfile)` to get this object.
`ind.row`	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
`S`	A vector of column statistics which express the importance of each SNP (the more important is the SNP, the greater should be the corresponding statistic).

For example, if S follows the standard normal distribution, and "important" means significantly different from 0, you must use abs(S) instead.
If not specified, MAFs are computed and used.

thr.r2 — Threshold over the squared correlation between two SNPs. Default is 0.2.

size — For one SNP, window size around this SNP to compute correlations. Default is 100 / thr.r2 for clumping (0.2 -> 500; 0.1 -> 1000; 0.5 -> 200). If not providing infos.pos (NULL, the default), this is a window in number of SNPs, otherwise it is a window in kb (physical distance). I recommend that you provide the positions if available.

exclude — Vector of SNP indices to exclude anyway. For example, can be used to exclude long-range LD regions (see Price2008). Another use can be for thresholding with respect to p-values associated with S.

ncores — Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

G — A FBM.code256 (typically <bigSNP>$genotypes).
You shouldn't have missing values. Also, remember to do quality control, e.g. some algorithms in this package won't work if you use SNPs with 0 MAF.

infos.chr — Vector of integers specifying each SNP's chromosome.
Typically <bigSNP>mapchromosome.

infos.pos — Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP.
Typically <bigSNP>mapphysical.pos.

is.size.in.bp — Deprecated.

nploidy — Number of trials, parameter of the binomial distribution. Default is 2, which corresponds to diploidy, such as for the human genome.

LD.regions — A data.frame with columns "Chr", "Start" and "Stop". Default use LD.wiki34.

Value

- snp_clumping() (and bed_clumping()): SNP indices that are **kept**.
- snp_indLRLDR(): SNP indices to be used as (part of) the 'exclude' parameter of snp_clumping().

References

Price AL, Weale ME, Patterson N, et al. Long-Range LD Can Confound Genome Scans in Admixed Populations. Am J Hum Genet. 2008;83(1):132-135. doi:10.1016/j.ajhg.2008.06.005

Examples

```
test <- snp_attachExtdata()
G <- test$genotypes

# clumping (prioritizing higher MAF)
ind.keep <- snp_clumping(G, infos.chr = test$map$chromosome,
                         infos.pos = test$map$physical.pos,
                         thr.r2 = 0.1)
```

```
# keep most of them -> not much LD in this simulated dataset
length(ind.keep) / ncol(G)
```

---

bed_counts *Counts*

Description

Counts the number of 0s, 1s, 2s and NAs by variants in the bed file.

Usage

```
bed_counts(
  obj.bed,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  byrow = FALSE,
  ncores = 1
)
```

Arguments

obj.bed	Object of type bed, which is the mapping of some bed file. Use `obj.bed <- bed(bedfile)` to get this object.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
byrow	Whether to count by individual rather than by variant? Default is FALSE (count by variant).
ncores	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.

Value

A matrix of with 4 rows and `length(ind.col)` columns.

Examples

```
bedfile <- system.file("extdata", "example-missing.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)

bed_counts(obj.bed, ind.col = 1:5)

bed_counts(obj.bed, ind.row = 1:5, byrow = TRUE)
```

bed_cprodVec *Cross-product with a vector*

Description

Cross-product between a "bed" object and a vector.

Missing values are replaced by 0 (after centering), as if they had been imputed using parameter `center`.

Usage

```
bed_cprodVec(
  obj.bed,
  y.row,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  center = rep(0, length(ind.col)),
  scale = rep(1, length(ind.col)),
  ncores = 1
)
```

Arguments

`obj.bed`	Object of type bed, which is the mapping of some bed file. Use `obj.bed <- bed(bedfile)` to get this object.
`y.row`	A vector of same size as `ind.row`.
`ind.row`	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
`ind.col`	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
`center`	Vector of same length of `ind.col` to subtract from columns of `X`.
`scale`	Vector of same length of `ind.col` to divide from columns of `X`.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.

Value

$X^T \cdot y$.

Examples

```
bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)
```

```
y.row <- rep(1, nrow(obj.bed))
str(bed_cprodVec(obj.bed, y.row))
```

---

bed_MAF *Allele frequencies*

Description

Allele frequencies of a bed object.

Usage

```
bed_MAF(
  obj.bed,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  ncores = 1
)
```

Arguments

obj.bed	Object of type bed, which is the mapping of some bed file. Use obj.bed <- bed(bedfile) to get this object.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Value

A data.frame with

- $ac: allele counts,
- $mac: minor allele counts,
- $af: allele frequencies,
- $maf: minor allele frequencies,
- $N: numbers of non-missing values.

Examples

```
bedfile <- system.file("extdata", "example-missing.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)

bed_MAF(obj.bed, ind.col = 1:5)
```

bed_prodVec *Product with a vector*

Description

Product between a "bed" object and a vector.

Missing values are replaced by 0 (after centering), as if they had been imputed using parameter `center`.

Usage

```
bed_prodVec(
  obj.bed,
  y.col,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  center = rep(0, length(ind.col)),
  scale = rep(1, length(ind.col)),
  ncores = 1
)
```

Arguments

`obj.bed`	Object of type bed, which is the mapping of some bed file. Use `obj.bed <- bed(bedfile)` to get this object.
`y.col`	A vector of same size as `ind.col`.
`ind.row`	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
`ind.col`	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
`center`	Vector of same length of `ind.col` to subtract from columns of `X`.
`scale`	Vector of same length of `ind.col` to divide from columns of `X`.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.

Value

$X \cdot y$.

Examples

```
bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)
```

```
y.col <- rep(1, ncol(obj.bed))
str(bed_prodVec(obj.bed, y.col))
```

`bed_projectPCA` *Projecting PCA*

Description

Computing and projecting PCA of reference dataset to a target dataset.

Usage

```
bed_projectPCA(
  obj.bed.ref,
  obj.bed.new,
  k = 10,
  ind.row.new = rows_along(obj.bed.new),
  ind.row.ref = rows_along(obj.bed.ref),
  ind.col.ref = cols_along(obj.bed.ref),
  strand_flip = TRUE,
  join_by_pos = TRUE,
  match.min.prop = 0.5,
  build.new = "hg19",
  build.ref = "hg19",
  liftOver = NULL,
  ...,
  verbose = TRUE,
  ncores = 1
)
```

Arguments

`obj.bed.ref`	Object of type bed, which is the mapping of the bed file of the reference data. Use `obj.bed <- bed(bedfile)` to get this object.
`obj.bed.new`	Object of type bed, which is the mapping of the bed file of the target data. Use `obj.bed <- bed(bedfile)` to get this object.
`k`	Number of principal components to compute and project.
`ind.row.new`	Rows to be used in the target data. Default uses them all.
`ind.row.ref`	Rows to be used in the reference data. Default uses them all.
`ind.col.ref`	Columns to be potentially used in the reference data. Default uses all the ones in common with target data.
`strand_flip`	Whether to try to flip strand? (default is `TRUE`) If so, ambiguous alleles A/T and C/G are removed.
`join_by_pos`	Whether to join by chromosome and position (default), or instead by rsid.

`match.min.prop` Minimum proportion of variants in the smallest data to be matched, otherwise stops with an error. Default is `20%`.

`build.new` Genome build of the target data. Default is `hg19`.

`build.ref` Genome build of the reference data. Default is `hg19`.

`liftOver` Path to liftOver executable. Binaries can be downloaded at https://hgdownload.cse.ucsc.edu/admin/exe/macOSX.x86_64/liftOver for Mac and at https://hgdownload.cse.ucsc.edu/admin/exe/linux.x86_64/liftOver for Linux.

`...` Arguments passed on to `bed_autoSVD`

`fun.scaling` A function with parameters `X` (or `obj.bed`), `ind.row` and `ind.col`, and that returns a data.frame with `$center` and `$scale` for the columns corresponding to `ind.col`, to scale each of their elements such as followed:

$$\frac{X_{i,j} - center_j}{scale_j}.$$

Default uses binomial scaling. You can also provide your own `center` and `scale` by using `bigstatsr::as_scaling_fun()`.

`roll.size` Radius of rolling windows to smooth log-p-values. Default is `50`.

`int.min.size` Minimum number of consecutive outlier variants in order to be reported as long-range LD region. Default is `20`.

`thr.r2` Threshold over the squared correlation between two variants. Default is `0.2`. Use `NA` if you want to skip the clumping step.

`alpha.tukey` Default is `0.1`. The type-I error rate in outlier detection (that is further corrected for multiple testing).

`min.mac` Minimum minor allele count (MAC) for variants to be included. Default is `10`. Can actually be higher because of `min.maf`.

`min.maf` Minimum minor allele frequency (MAF) for variants to be included. Default is `0.02`. Can actually be higher because of `min.mac`.

`max.iter` Maximum number of iterations of outlier detection. Default is `5`.

`size` For one SNP, window size around this SNP to compute correlations. Default is `100 / thr.r2` for clumping (0.2 -> 500; 0.1 -> 1000; 0.5 -> 200). If not providing `infos.pos` (`NULL`, the default), this is a window in number of SNPs, otherwise it is a window in kb (physical distance). I recommend that you provide the positions if available.

`verbose` Output some information on the iterations? Default is `TRUE`.

`ncores` Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.

Value

A list of 3 elements:

- `$obj.svd.ref`: big_SVD object computed from reference data.
- `$simple_proj`: simple projection of new data into space of reference PCA.
- `$OADP_proj`: Online Augmentation, Decomposition, and Procrustes (OADP) projection of new data into space of reference PCA.

`bed_projectSelfPCA` *Projecting PCA*

Description

Projecting PCA using individuals from one dataset to other individuals from the same dataset.

Usage

```
bed_projectSelfPCA(
  obj.svd,
  obj.bed,
  ind.row,
  ind.col = attr(obj.svd, "subset"),
  ncores = 1
)

snp_projectSelfPCA(
  obj.svd,
  G,
  ind.row,
  ind.col = attr(obj.svd, "subset"),
  ncores = 1
)
```

Arguments

`obj.svd`	List with `v`, `d`, `center` and `scale`. Typically the an object of type "big_SVD".
`obj.bed`	Object of type bed, which is the mapping of the bed file of the data containing both the individuals that were used to compute the PCA and the other individuals to be projected.
`ind.row`	Rows (individuals) to be projected.
`ind.col`	Columns that were used for computing PCA. If bed_autoSVD was used, then `attr(obj.svd, "subset")` is automatically used by default. Otherwise (e.g. if bed_randomSVD was used), you have to pass `ind.col`.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.
`G`	The FBM.code256 that was used to compute `obj.svd`.

Value

A list of 3 elements:

- `$obj.svd.ref`: big_SVD object computed from reference data.
- `$simple_proj`: simple projection of new data into space of reference PCA.
- `$OADP_proj`: Online Augmentation, Decomposition, and Procrustes (OADP) projection of new data into space of reference PCA.

bed_randomSVD *Randomized partial SVD*

Description

Partial SVD (or PCA) of a genotype matrix stored as a PLINK (.bed) file.#'

Usage

```
bed_randomSVD(
  obj.bed,
  fun.scaling = bed_scaleBinom,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  k = 10,
  tol = 1e-04,
  verbose = FALSE,
  ncores = 1
)
```

Arguments

obj.bed	Object of type bed, which is the mapping of some bed file. Use obj.bed <- bed(bedfile) to get this object.
fun.scaling	A function with parameters X, ind.row and ind.col, and that returns a data.frame with $center and $scale for the columns corresponding to ind.col, to scale each of their elements such as followed: $$\frac{X_{i,j} - center_j}{scale_j}.$$ Default doesn't use any scaling. You can also provide your own center and scale by using as_scaling_fun().
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
k	Number of singular vectors/values to compute. Default is 10. **This algorithm should be used to compute only a few singular vectors/values.**
tol	Precision parameter of svds. Default is 1e-4.
verbose	Should some progress be printed? Default is FALSE.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Value

A named list (an S3 class "big_SVD") of

- d, the singular values,
- u, the left singular vectors,
- v, the right singular vectors,
- niter, the number of the iteration of the algorithm,
- nops, number of Matrix-Vector multiplications used,
- center, the centering vector,
- scale, the scaling vector.

Note that to obtain the Principal Components, you must use predict on the result. See examples.

Examples

```
bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)

str(bed_randomSVD(obj.bed))
```

---

bed_scaleBinom *Binomial(2, p) scaling*

Description

Binomial(2, p) scaling where p is estimated.

Usage

```
bed_scaleBinom(
  obj.bed,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  ncores = 1
)
```

Arguments

obj.bed	Object of type bed, which is the mapping of some bed file. Use obj.bed <- bed(bedfile) to get this object.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Details

You will probably not use this function as is but as parameter `fun.scaling` of other functions (e.g. `bed_autoSVD` and `bed_randomSVD`).

Value

A data frame with `$center` and `$scale`.

References

This scaling is widely used for SNP arrays. Patterson N, Price AL, Reich D (2006). Population Structure and Eigenanalysis. PLoS Genet 2(12): e190. doi:10.1371/journal.pgen.0020190.

Examples

```
bedfile <- system.file("extdata", "example-missing.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)

str(bed_scaleBinom(obj.bed))

str(bed_randomSVD(obj.bed, bed_scaleBinom))
```

---

bed_tcrossprodSelf *tcrossprod / GRM*

Description

Compute GG^T from a bed object, with possible filtering and scaling of `G`. For example, this can be used to compute GRMs.

Usage

```
bed_tcrossprodSelf(
  obj.bed,
  fun.scaling = bed_scaleBinom,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  block.size = block_size(length(ind.row))
)
```

Arguments

`obj.bed`	Object of type bed, which is the mapping of some bed file. Use `obj.bed <- bed(bedfile)` to get this object.

`fun.scaling` A function with parameters `X` (or `obj.bed`), `ind.row` and `ind.col`, and that returns a data.frame with `$center` and `$scale` for the columns corresponding to `ind.col`, to scale each of their elements such as followed:

$$\frac{X_{i,j} - center_j}{scale_j}.$$

Default uses binomial scaling. You can also provide your own `center` and `scale` by using `bigstatsr::as_scaling_fun()`.

`ind.row` An optional vector of the row indices (individuals) that are used. If not specified, all rows are used.
Don't use negative indices.

`ind.col` An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used.
Don't use negative indices.

`block.size` Maximum number of columns read at once. Default uses block_size.

Value

A temporary FBM, with the following two attributes:

- a numeric vector `center` of column scaling,
- a numeric vector `scale` of column scaling.

Matrix parallelization

Large matrix computations are made block-wise and won't be parallelized in order to not have to reduce the size of these blocks. Instead, you can use the MKL or OpenBLAS in order to accelerate these block matrix computations. You can control the number of cores used by these optimized matrix libraries with `bigparallelr::set_blas_ncores()`.

Examples

```
bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)

K <- bed_tcrossprodSelf(obj.bed)
K[1:4, 1:6] / ncol(obj.bed)
```

---

bigSNP-class *Class bigSNP*

Description

An S3 class for representing information on massive SNP arrays.

Value

A named list with at least 3 slots:

genotypes A FBM.code256 which is a special Filebacked Big Matrix encoded with type `raw` (one byte unsigned integer), representing genotype calls and possibly imputed allele dosages. Rows are individuals and columns are SNPs.

fam A `data.frame` containing some information on the individuals (read from a ".fam" file).

map A `data.frame` giving some information on the variants (read from a ".bim" file).

See Also

snp_readBed

`coef_to_liab` *Liability scale*

Description

Coefficient to convert to the liability scale. E.g. h2_liab = coef * h2_obs.

Usage

```
coef_to_liab(K_pop, K_gwas = 0.5)
```

Arguments

`K_pop`	Prevalence in the population.
`K_gwas`	Prevalence in the GWAS. You should provide this if you used (`n_case + n_control`) as sample size. If using the effective sample size `4 / (1 / n_case + 1 / n_control)` instead, you should keep the default value of `K_gwas = 0.5` as the GWAS case-control ascertainment is already accounted for in the effective sample size.

Value

Scaling coefficient to convert e.g. heritability to the liability scale.

Examples

```
h2 <- 0.2
h2 * coef_to_liab(0.02)
```

download_1000G *Download 1000G*

Description

Download 1000 genomes project (phase 3) data in PLINK bed/bim/fam format, including 2490 (mostly unrelated) individuals and ~1.7M SNPs in common with either HapMap3 or the UK Biobank.

Usage

```
download_1000G(dir, overwrite = FALSE, delete_zip = TRUE)
```

Arguments

dir	The directory where to put the downloaded files.
overwrite	Whether to overwrite files when downloading and unzipping? Default is FALSE.
delete_zip	Whether to delete zip after decompressing the file in it? Default is TRUE.

Value

The path of the downloaded bed file.

download_beagle *Download Beagle 4.1*

Description

Download Beagle 4.1 from https://faculty.washington.edu/browning/beagle/beagle.html

Usage

```
download_beagle(dir = tempdir())
```

Arguments

dir	The directory where to put the Beagle Java Archive. Default is a temporary directory.

Value

The path of the downloaded Beagle Java Archive.

`download_genetic_map` *Download a genetic map*

Description

This function uses linear interpolation, whereas `snp_asGeneticPos()` uses nearest neighbors.

Usage

```
download_genetic_map(
  type = c("hg19_OMNI", "hg19_hapmap", "hg38_price"),
  dir,
  ncores = 1
)

snp_asGeneticPos2(infos.chr, infos.pos, genetic_map)
```

Arguments

`type`	Which genetic map to download.
`dir`	Directory where to download and decompress files.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.
`infos.chr`	Vector of integers specifying each SNP's chromosome. Typically `<bigSNP>$map$chromosome`.
`infos.pos`	Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP. Typically `<bigSNP>$map$physical.pos`.
`genetic_map`	A data frame with 3 columns: `chr`, `pos`, and `pos_cM`. You can get it using `download_genetic_map()`.

Details

The hg19 genetic maps are downloaded from https://github.com/joepickrell/1000-genomes-genetic-maps/ while the hg38 one is downloaded from https://alkesgroup.broadinstitute.org/Eagle/downloads/tables/.

Value

A data frame with 3 columns: `chr`, `pos`, and `pos_cM`.

The new vector of genetic positions.

`download_plink` *Download PLINK*

Description

Download PLINK 1.9 from https://www.cog-genomics.org/plink2.

Download PLINK 2.0 from https://www.cog-genomics.org/plink/2.0/.

Usage

```
download_plink(dir = tempdir(), overwrite = FALSE, verbose = TRUE)

download_plink2(
  dir = tempdir(),
  AVX2 = TRUE,
  ARM = FALSE,
  AMD = FALSE,
  overwrite = FALSE,
  verbose = TRUE
)
```

Arguments

`dir`	The directory where to put the PLINK executable. Default is a temporary directory.
`overwrite`	Whether to overwrite file? Default is `FALSE`.
`verbose`	Whether to output details of downloading. Default is `TRUE`.
`AVX2`	Whether to download the AVX2 version? This is only available for 64 bits architectures. Default is `TRUE`.
`ARM`	Whether to download an ARM version. Default is `FALSE`.
`AMD`	Whether to download an AMD version. Default is `FALSE`.

Value

The path of the downloaded PLINK executable.

LD.wiki34 *Long-range LD regions*

Description

34 long-range Linkage Disequilibrium (LD) regions for the human genome based on this wiki table.

Usage

```
LD.wiki34
```

Format

A data frame with 34 rows (regions) and 4 variables:

- `Chr`: region's chromosome
- `Start`: starting position of the region (in bp)
- `Stop`: stopping position of the region (in bp)
- `ID`: some ID of the region.

same_ref *Determine reference divergence*

Description

Determine reference divergence while accounting for strand flips. **This does not remove ambiguous alleles.**

Usage

```
same_ref(ref1, alt1, ref2, alt2)
```

Arguments

`ref1`	The reference alleles of the first dataset.
`alt1`	The alternative alleles of the first dataset.
`ref2`	The reference alleles of the second dataset.
`alt2`	The alternative alleles of the second dataset.

Value

A logical vector whether the references alleles are the same. Missing values can result from missing values in the inputs or from ambiguous matching (e.g. matching A/C and A/G).

See Also

snp_match()

Examples

```
same_ref(ref1 = c("A", "C", "T", "G", NA),
         alt1 = c("C", "T", "C", "A", "A"),
         ref2 = c("A", "C", "A", "A", "C"),
         alt2 = c("C", "G", "G", "G", "A"))
```

SCT *Stacked C+T (SCT)*

Description

Polygenic Risk Scores for a grid of clumping and thresholding parameters.

Stacking over many Polygenic Risk Scores, corresponding to a grid of many different parameters for clumping and thresholding.

Usage

```
snp_grid_clumping(
  G,
  infos.chr,
  infos.pos,
  lpS,
  ind.row = rows_along(G),
  grid.thr.r2 = c(0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 0.95),
  grid.base.size = c(50, 100, 200, 500),
  infos.imp = rep(1, ncol(G)),
  grid.thr.imp = 1,
  groups = list(cols_along(G)),
  exclude = NULL,
  ncores = 1
)

snp_grid_PRS(
  G,
  all_keep,
  betas,
  lpS,
  n_thr_lpS = 50,
 grid.lpS.thr = 0.9999 * seq_log(max(0.1, min(lpS, na.rm = TRUE)), max(lpS, na.rm =
    TRUE), n_thr_lpS),
  ind.row = rows_along(G),
  backingfile = tempfile(),
  type = c("float", "double"),
```

```
  ncores = 1
)

snp_grid_stacking(
  multi_PRS,
  y.train,
  alphas = c(1, 0.01, 1e-04),
  ncores = 1,
  ...
)
```

Arguments

G	A FBM.code256 (typically <bigSNP>$genotypes). **You shouldn't have missing values.** Also, remember to do quality control, e.g. some algorithms in this package won't work if you use SNPs with 0 MAF.
infos.chr	Vector of integers specifying each SNP's chromosome. Typically <bigSNP>mapchromosome.
infos.pos	Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP. Typically <bigSNP>mapphysical.pos.
lpS	Numeric vector of -log10(p-value) associated with betas.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
grid.thr.r2	Grid of thresholds over the squared correlation between two SNPs for clumping. Default is c(0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 0.95).
grid.base.size	Grid for base window sizes. Sizes are then computed as base.size / thr.r2 (in kb). Default is c(50, 100, 200, 500).
infos.imp	Vector of imputation scores. Default is all 1 if you do not provide it.
grid.thr.imp	Grid of thresholds over infos.imp (default is 1), but you should change it (e.g. c(0.3, 0.6, 0.9, 0.95)) if providing infos.imp.
groups	List of vectors of indices to define your own categories. This could be used e.g. to derive C+T scores using two different GWAS summary statistics, or to include other information such as functional annotations. Default just makes one group with all variants.
exclude	Vector of SNP indices to exclude anyway.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
all_keep	Output of snp_grid_clumping() (indices passing clumping).
betas	Numeric vector of weights (effect sizes from GWAS) associated with each variant (column of G). If alleles are reversed, make sure to multiply corresponding effects by -1.
n_thr_lpS	Length for default grid.lpS.thr. Default is 50.
grid.lpS.thr	Sequence of thresholds to apply on lpS. Default is a grid (of length n_thr_lpS) evenly spaced on a logarithmic scale, i.e. on a log-log scale for p-values.

backingfile	Prefix for backingfiles where to store scores of C+T. As we typically use a large grid, this can result in a large matrix so that we store it on disk. Default uses a temporary file.
type	Type of backingfile values. Either "float" (the default) or "double". Using "float" requires half disk space.
multi_PRS	Output of snp_grid_PRS().
y.train	Vector of phenotypes. If there are two levels (binary 0/1), it uses bigstatsr::big_spLogReg() for stacking, otherwise bigstatsr::big_spLinReg().
alphas	Vector of values for grid-search. See bigstatsr::big_spLogReg(). Default for this function is c(1, 0.01, 0.0001).
...	Other parameters to be passed to bigstatsr::big_spLogReg(). For example, using covar.train, you can add covariates in the model with all C+T scores. You can also use pf.covar if you do not want to penalize these covariates.

Value

snp_grid_PRS(): An FBM (matrix on disk) that stores the C+T scores for all parameters of the grid (and for each chromosome separately). It also stores as attributes the input parameters all_keep, betas, lpS and grid.lpS.thr that are also needed in snp_grid_stacking().

---

seq_log *Sequence, evenly spaced on a logarithmic scale*

Description

Sequence, evenly spaced on a logarithmic scale

Usage

```
seq_log(from, to, length.out)
```

Arguments

from, to	the starting and (maximal) end values of the sequence. Of length 1 unless just from is supplied as an unnamed argument.
length.out	desired length of the sequence. A non-negative number, which for seq and seq.int will be rounded up if fractional.

Value

A sequence of length length.out, evenly spaced on a logarithmic scale between from and to.

Examples

```
seq_log(1, 1000, 4)
seq_log(1, 100, 5)
```

`snp_ancestry_summary` *Estimation of ancestry proportions*

Description

Estimation of ancestry proportions. Make sure to match summary statistics using `snp_match()` (and to reverse frequencies correspondingly).

Usage

```
snp_ancestry_summary(
  freq,
  info_freq_ref,
  projection,
  correction,
  min_cor = 0.4,
  sum_to_one = TRUE
)
```

Arguments

`freq`	Vector of frequencies from which to estimate ancestry proportions.
`info_freq_ref`	A data frame (or matrix) with the set of frequencies to be used as reference (one population per column).
`projection`	Matrix of "loadings" for each variant/PC to be used to project allele frequencies.
`correction`	Coefficients to correct for shrinkage when projecting.
`min_cor`	Minimum correlation between observed and predicted frequencies. Default is 0.4. When correlation is lower, an error is returned. For individual genotypes, this should be larger than 0.6. For allele frequencies, this should be larger than 0.9.
`sum_to_one`	Whether to force ancestry coefficients to sum to 1? Default is `TRUE` (otherwise, the sum can be lower than 1).

Value

Vector of coefficients representing the ancestry proportions. Also (as attributes) `cor_each`, the correlation between input frequencies and each reference frequencies, and `cor_pred`, the correlation between input and predicted frequencies.

Examples

```
## Not run:

# GWAS summary statistics for Epilepsy (supposedly in EUR+EAS+AFR)
gz <- runonce::download_file(
  "http://www.epigad.org/gwas_ilae2018_16loci/all_epilepsy_METAL.gz",
```

```
  dir = "tmp-data")
readLines(gz, n = 3)

library(dplyr)
sumstats <- bigreadr::fread2(
  gz, select = c("CHR", "BP", "Allele2", "Allele1", "Freq1"),
  col.names = c("chr", "pos", "a0", "a1", "freq")
) %>%
  mutate_at(3:4, toupper)
# It is a good idea to filter for similar per-variant N (when available..)

all_freq <- bigreadr::fread2(
  runonce::download_file("https://figshare.com/ndownloader/files/31620968",
                         dir = "tmp-data", fname = "ref_freqs.csv.gz"))
projection <- bigreadr::fread2(
  runonce::download_file("https://figshare.com/ndownloader/files/31620953",
                         dir = "tmp-data", fname = "projection.csv.gz"))

matched <- snp_match(
  mutate(sumstats, chr = as.integer(chr), beta = 1),
  all_freq[1:5],
  return_flip_and_rev = TRUE
) %>%
  mutate(freq = ifelse(`_REV_`, 1 - freq, freq))

res <- snp_ancestry_summary(
  freq = matched$freq,
  info_freq_ref = all_freq[matched$`_NUM_ID_`, -(1:5)],
  projection = projection[matched$`_NUM_ID_`, -(1:5)],
  correction = c(1, 1, 1, 1.008, 1.021, 1.034, 1.052, 1.074, 1.099,
                 1.123, 1.15, 1.195, 1.256, 1.321, 1.382, 1.443)
)

# Some ancestry groups are very close to each other, and should be merged
group <- colnames(all_freq)[-(1:5)]
group[group %in% c("Scandinavia", "United Kingdom", "Ireland")]  <- "Europe (North West)"
group[group %in% c("Europe (South East)", "Europe (North East)")] <- "Europe (East)"

tapply(res, factor(group, unique(group)), sum)

## End(Not run)
```

---

snp_asGeneticPos *Interpolate to genetic positions*

Description

Use genetic maps available at https://github.com/joepickrell/1000-genomes-genetic-maps/ to interpolate physical positions (in bp) to genetic positions (in cM).

Usage

```
snp_asGeneticPos(
  infos.chr,
  infos.pos,
  dir = tempdir(),
  ncores = 1,
  rsid = NULL,
  type = c("OMNI", "hapmap")
)
```

Arguments

infos.chr	Vector of integers specifying each SNP's chromosome. Typically <bigSNP>mapchromosome.
infos.pos	Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP. Typically <bigSNP>mapphysical.pos.
dir	Directory where to download and decompress files. Default is tempdir(). Directly use *uncompressed* files there if already present. You can use R.utils::gunzip() to uncompress local files.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
rsid	If providing rsIDs, the matching is performed using those (instead of positions) and variants not matched are interpolated using spline interpolation of variants that have been matched.
type	Whether to use the genetic maps interpolated from "OMNI" (the default), or from "hapmap".

Value

The new vector of genetic positions.

---

snp_attach *Attach a "bigSNP" from backing files*

Description

Load a bigSNP from backing files into R.

Usage

```
snp_attach(rdsfile)
```

Arguments

rdsfile	The path of the ".rds" which stores the bigSNP object.

Details

This is often just a call to readRDS. But it also checks if you have moved the two (".bk" and ".rds") backing files to another directory.

Value

The `bigSNP` object.

Examples

```
(bedfile <- system.file("extdata", "example.bed", package = "bigsnpr"))

# Reading the bedfile and storing the data in temporary directory
rds <- snp_readBed(bedfile, backingfile = tempfile())

# Loading the data from backing files
test <- snp_attach(rds)

str(test)
dim(G <- test$genotypes)
G[1:8, 1:8]
```

`snp_attachExtdata` *Attach a "bigSNP" for examples and tests*

Description

Attach a "bigSNP" for examples and tests

Usage

```
snp_attachExtdata(bedfile = c("example.bed", "example-missing.bed"))
```

Arguments

`bedfile`	Name of one example bed file. Either • `"example.bed"` (the default), • `"example-missing.bed"`.

Value

The example "bigSNP", filebacked in the "/tmp/" directory.

snp_autoSVD *Truncated SVD while limiting LD*

Description

Fast truncated SVD with initial pruning and that iteratively removes long-range LD regions. Some variants are removing due to the initial clumping, then more and more variants are removed at each iteration. You can access the indices of the remaining variants with `attr(*, "subset")`. If some of the variants removed are contiguous, the regions are reported in `attr(*, "lrldr")`.

Usage

```
snp_autoSVD(
  G,
  infos.chr,
  infos.pos = NULL,
  ind.row = rows_along(G),
  ind.col = cols_along(G),
  fun.scaling = snp_scaleBinom(),
  thr.r2 = 0.2,
  size = 100/thr.r2,
  k = 10,
  roll.size = 50,
  int.min.size = 20,
  alpha.tukey = 0.05,
  min.mac = 10,
  min.maf = 0.02,
  max.iter = 5,
  is.size.in.bp = NULL,
  ncores = 1,
  verbose = TRUE
)

bed_autoSVD(
  obj.bed,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  fun.scaling = bed_scaleBinom,
  thr.r2 = 0.2,
  size = 100/thr.r2,
  k = 10,
  roll.size = 50,
  int.min.size = 20,
  alpha.tukey = 0.05,
  min.mac = 10,
  min.maf = 0.02,
  max.iter = 5,
```

```
  ncores = 1,
  verbose = TRUE
)
```

Arguments

G	A FBM.code256 (typically <bigSNP>$genotypes). **You shouldn't have missing values.** Also, remember to do quality control, e.g. some algorithms in this package won't work if you use SNPs with 0 MAF.
infos.chr	Vector of integers specifying each SNP's chromosome. Typically <bigSNP>mapchromosome.
infos.pos	Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP. Typically <bigSNP>mapphysical.pos.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
fun.scaling	A function with parameters X (or obj.bed), ind.row and ind.col, and that returns a data.frame with $center and $scale for the columns corresponding to ind.col, to scale each of their elements such as followed: $$\frac{X_{i,j} - center_j}{scale_j}.$$ Default uses binomial scaling. You can also provide your own center and scale by using bigstatsr::as_scaling_fun().
thr.r2	Threshold over the squared correlation between two variants. Default is 0.2. Use NA if you want to skip the clumping step.
size	For one SNP, window size around this SNP to compute correlations. Default is 100 / thr.r2 for clumping (0.2 -> 500; 0.1 -> 1000; 0.5 -> 200). If not providing infos.pos (NULL, the default), this is a window in number of SNPs, otherwise it is a window in kb (physical distance). I recommend that you provide the positions if available.
k	Number of singular vectors/values to compute. Default is 10. **This algorithm should be used to compute a few singular vectors/values.**
roll.size	Radius of rolling windows to smooth log-p-values. Default is 50.
int.min.size	Minimum number of consecutive outlier variants in order to be reported as long-range LD region. Default is 20.
alpha.tukey	Default is 0.1. The type-I error rate in outlier detection (that is further corrected for multiple testing).
min.mac	Minimum minor allele count (MAC) for variants to be included. Default is 10. Can actually be higher because of min.maf.

min.maf	Minimum minor allele frequency (MAF) for variants to be included. Default is 0.02. Can actually be higher because of min.mac.
max.iter	Maximum number of iterations of outlier detection. Default is 5.
is.size.in.bp	Deprecated.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
verbose	Output some information on the iterations? Default is TRUE.
obj.bed	Object of type bed, which is the mapping of some bed file. Use obj.bed <- bed(bedfile) to get this object.

Details

If you don't have any information about variants, you can try using

- infos.chr = rep(1, ncol(G)),
- size = ncol(G) (if variants are not sorted),
- roll.size = 0 (if variants are not sorted).

Value

A named list (an S3 class "big_SVD") of

- d, the singular values,
- u, the left singular vectors,
- v, the right singular vectors,
- niter, the number of the iteration of the algorithm,
- nops, number of Matrix-Vector multiplications used,
- center, the centering vector,
- scale, the scaling vector.

Note that to obtain the Principal Components, you must use predict on the result. See examples.

Examples

```
ex <- snp_attachExtdata()
G <- ex$genotypes

obj.svd <- snp_autoSVD(G,
                       infos.chr = ex$map$chromosome,
                       infos.pos = ex$map$physical.position)

str(obj.svd)
```

`snp_beagleImpute` *Imputation*

Description

Imputation using **Beagle** version 4.

Usage

```
snp_beagleImpute(
  beagle.path,
  plink.path,
  bedfile.in,
  bedfile.out = NULL,
  memory.max = 3,
  ncores = 1,
  extra.options = "",
  plink.options = "",
  verbose = TRUE
)
```

Arguments

`beagle.path`	Path to the executable of Beagle v4+.
`plink.path`	Path to the executable of PLINK 1.9.
`bedfile.in`	Path to the input bedfile.
`bedfile.out`	Path to the output bedfile. Default is created by appending `"_impute"` to `prefix.in` (`bedfile.in` without extension).
`memory.max`	Max memory (in GB) to be used. It is internally rounded to be an integer. Default is `3`.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.
`extra.options`	Other options to be passed to Beagle as a string. More options can be found at Beagle's website.
`plink.options`	Other options to be passed to PLINK as a string. More options can be found at `https://www.cog-genomics.org/plink2/filter`.
`verbose`	Whether to show PLINK log? Default is `TRUE`.

Details

Downloads and more information can be found at the following websites

- PLINK,
- Beagle.

Value

The path of the new bedfile.

References

Browning, Brian L., and Sharon R. Browning. "Genotype imputation with millions of reference samples." The American Journal of Human Genetics 98.1 (2016): 116-126.

See Also

download_plink download_beagle

---

snp_cor *Correlation matrix*

Description

Get significant (Pearson) correlations between nearby SNPs of the same chromosome (p-values are computed using a two-sided t-test).

Usage

```
snp_cor(
  Gna,
  ind.row = rows_along(Gna),
  ind.col = cols_along(Gna),
  size = 500,
  alpha = 1,
  thr_r2 = 0,
  fill.diag = TRUE,
  infos.pos = NULL,
  ncores = 1
)

bed_cor(
  obj.bed,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  size = 500,
  alpha = 1,
  thr_r2 = 0,
  fill.diag = TRUE,
  infos.pos = NULL,
  ncores = 1
)
```

Arguments

Gna	A FBM.code256 (typically <bigSNP>$genotypes). You can have missing values in these data.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
size	For one SNP, window size around this SNP to compute correlations. Default is 500. If not providing infos.pos (NULL, the default), this is a window in number of SNPs, otherwise it is a window in kb (physical distance). In case you provide infos.pos in centimorgans (genetic distance), you should divide this by 1000 because it is internally multiplied by 1000 (i.e. use 3 / 1000 for 3 cM).
alpha	Type-I error for testing correlations. Default is 1 (no threshold is applied).
thr_r2	Threshold to apply on squared correlations. Default is 0.
fill.diag	Whether to fill the diagonal with 1s (the default) or to keep it as 0s.
infos.pos	Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP. Typically <bigSNP>mapphysical.pos.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
obj.bed	Object of type bed, which is the mapping of some bed file. Use obj.bed <- bed(bedfile) to get this object.

Value

The (Pearson) correlation matrix. This is a sparse symmetric matrix.

Examples

```
test <- snp_attachExtdata()
G <- test$genotypes

corr <- snp_cor(G, ind.col = 1:1000)
corr[1:10, 1:10]

# Sparsity
length(corr@x) / length(corr)
```

`snp_fastImpute` *Fast imputation*

Description

Fast imputation algorithm based on local XGBoost models.

Usage

```
snp_fastImpute(
  Gna,
  infos.chr,
  alpha = 1e-04,
  size = 200,
  p.train = 0.8,
  n.cor = nrow(Gna),
  seed = NA,
  ncores = 1
)
```

Arguments

`Gna`	A FBM.code256 (typically `<bigSNP>$genotypes`). You can have missing values in these data.
`infos.chr`	Vector of integers specifying each SNP's chromosome. Typically `<bigSNP>$map$chromosome`.
`alpha`	Type-I error for testing correlations. Default is `1e-4`.
`size`	Number of neighbor SNPs to be possibly included in the model imputing this particular SNP. Default is `200`.
`p.train`	Proportion of non missing genotypes that are used for training the imputation model while the rest is used to assess the accuracy of this imputation model. Default is `0.8`.
`n.cor`	Number of rows that are used to estimate correlations. Default uses them all.
`seed`	An integer, for reproducibility. Default doesn't use seeds.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.

Value

An FBM with

- the proportion of missing values by SNP (first row),
- the estimated proportion of imputation errors by SNP (second row).

See Also

`snp_fastImputeSimple()`

Examples

```
## Not run:

fake <- snp_attachExtdata("example-missing.bed")
G <- fake$genotypes
CHR <- fake$map$chromosome
infos <- snp_fastImpute(G, CHR)
infos[, 1:5]

# Still missing values
big_counts(G, ind.col = 1:10)
# You need to change the code of G
# To make this permanent, you need to save (modify) the file on disk
fake$genotypes$code256 <- CODE_IMPUTE_PRED
fake <- snp_save(fake)
big_counts(fake$genotypes, ind.col = 1:10)

# Plot for post-checking
## Here there is no SNP with more than 1% error (estimated)
pvals <- c(0.01, 0.005, 0.002, 0.001); colvals <- 2:5
df <- data.frame(pNA = infos[1, ], pError = infos[2, ])

# base R
plot(subset(df, pNA > 0.001), pch = 20)
idc <- lapply(seq_along(pvals), function(i) {
  curve(pvals[i] / x, from = 0, lwd = 2,
        col = colvals[i], add = TRUE)
})
legend("topright", legend = pvals, title = "p(NA & Error)",
       col = colvals, lty = 1, lwd = 2)

# ggplot2
library(ggplot2)
Reduce(function(p, i) {
  p + stat_function(fun = function(x) pvals[i] / x, color = colvals[i])
}, x = seq_along(pvals), init = ggplot(df, aes(pNA, pError))) +
  geom_point() +
  coord_cartesian(ylim = range(df$pError, na.rm = TRUE)) +
  theme_bigstatsr()

## End(Not run)
```

`snp_fastImputeSimple` *Fast imputation*

Description

Fast imputation via mode, mean, sampling according to allele frequencies, or 0.

Usage

```
snp_fastImputeSimple(
  Gna,
  method = c("mode", "mean0", "mean2", "random"),
  ncores = 1
)
```

Arguments

Gna	A FBM.code256 (typically <bigSNP>$genotypes). You can have missing values in these data.
method	Either "random" (sampling according to allele frequencies), "mean0" (rounded mean), "mean2" (rounded mean to 2 decimal places), "mode" (most frequent call).
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Value

A new FBM.code256 object (same file, but different code).

See Also

snp_fastImpute()

Examples

```
bigsnp <- snp_attachExtdata("example-missing.bed")
G <- bigsnp$genotypes
G[, 2]  # some missing values
G2 <- snp_fastImputeSimple(G)
G2[, 2]  # no missing values anymore
G[, 2]  # imputed, but still returning missing values
G$copy(code = CODE_IMPUTE_PRED)[, 2]  # need to decode imputed values

G$copy(code = c(0, 1, 2, rep(0, 253)))[, 2]  # "imputation" by 0
```

---

snp_fst *Fixation index (Fst)*

Description

Fixation index (Fst), either per variant, or genome-wide

Usage

```
snp_fst(list_df_af, min_maf = 0, overall = FALSE)
```

Arguments

list_df_af	List of data frames with $af (allele frequency per variant) and $N (sample size per variant). Typically, the outputs of bed_MAF(). Each new data frame of the list should correspond to a different population.
min_maf	Minimum MAF threshold (for the average of populations) to be included in the final results. Default is 0 (remove monomorphic variants).
overall	Whether to compute Fst genome-wide (TRUE) or per variant (FALSE, the default).

Value

If overall, then one value, otherwise a value for each variant with missing values for the variants not passing min_maf. This should be equivalent to using '--fst --within' in PLINK.

References

Weir, B. S., & Cockerham, C. C. (1984). Estimating F-statistics for the analysis of population structure. Evolution, 1358-1370.

Examples

```
bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
obj.bed <- bed(bedfile)

pop <- rep(1:3, c(143, 167, 207))
ind_pop <- split(seq_along(pop), pop)
list_df_af <- lapply(ind_pop, function(ind) bed_MAF(obj.bed, ind.row = ind))

snp_fst(list_df_af)
snp_fst(list_df_af[c(1, 2)], overall = TRUE)
snp_fst(list_df_af[c(1, 3)], overall = TRUE)
snp_fst(list_df_af[c(3, 2)], overall = TRUE)
```

---

snp_gc *Genomic Control*

Description

Genomic Control

Usage

```
snp_gc(gwas)
```

Arguments

gwas	A mhtest object with the p-values associated with each SNP. Typically, the output of bigstatsr::big_univLinReg, bigstatsr::big_univLogReg or snp_pcadapt.

Value

A ggplot2 object. You can plot it using the print method. You can modify it as you wish by adding layers. You might want to read this chapter to get more familiar with the package **ggplot2**.

References

Devlin, B., & Roeder, K. (1999). Genomic control for association studies. Biometrics, 55(4), 997-1004.

Examples

```
set.seed(9)

test <- snp_attachExtdata()
G <- test$genotypes
y <- rnorm(nrow(G))

gwas <- big_univLinReg(G, y)

snp_qq(gwas)
gwas_gc <- snp_gc(gwas) # this modifies `attr(gwas_gc, "transfo")`
snp_qq(gwas_gc)

# The next plot should be prettier with a real dataset
snp_manhattan(gwas_gc,
              infos.chr = test$map$chromosome,
              infos.pos = test$map$physical.pos) +
  ggplot2::geom_hline(yintercept = -log10(5e-8), linetype = 2, color = "red")

p <- snp_qq(gwas_gc) +
  ggplot2::aes(text = asPlotlyText(test$map)) +
  ggplot2::labs(subtitle = NULL, x = "Expected -log10(p)", y = "Observed -log10(p)")
## Not run: plotly::ggplotly(p, tooltip = "text")
```

---

snp_getSampleInfos *Get sample information*

Description

Get information of individuals by matching from an external file.

Usage

```
snp_getSampleInfos(
  x,
  df.or.files,
  col.family.ID = 1,
  col.sample.ID = 2,
  col.infos = -c(1, 2),
```

```
  pair.sep = "-_-",
  ...
)
```

Arguments

x	A bigSNP.
df.or.files	Either • A data.frame, • A character vector of file names where to find at the information you want. You should have one column for family IDs and one for sample IDs.
col.family.ID	Index of the column containing the family IDs to match with those of the study. Default is the first one.
col.sample.ID	Index of the column containing the sample IDs to match with those of the study. Default is the second one.
col.infos	Indices of the column containing the information you want. Default is all but the first and the second columns.
pair.sep	Separator used for concatenation of family and sample IDs to make unique IDs for matching between the two datasets. Default is "-_-".
...	Any additional parameter to pass to bigreadr::fread2(). Particularly, option header = FALSE is sometimes needed.

Value

The requested information as a data.frame.

See Also

list.files

Examples

```
test <- snp_attachExtdata()
table(test$fam$family.ID)

# Get populations clusters from external files
files <- system.file("extdata", paste0("cluster", 1:3), package = "bigsnpr")
bigreadr::fread2(files[1])
bigreadr::fread2(files[1], header = FALSE)  # need header option here

infos <- snp_getSampleInfos(test, files, header = FALSE)
table(infos[[1]])
```

snp_lassosum2 *lassosum2*

Description

lassosum2

Usage

```
snp_lassosum2(
  corr,
  df_beta,
  delta = c(0.001, 0.01, 0.1, 1),
  nlambda = 30,
  lambda.min.ratio = 0.01,
  dfmax = 2e+05,
  maxiter = 1000,
  tol = 1e-05,
  ind.corr = cols_along(corr),
  ncores = 1
)
```

Arguments

`corr`	Sparse correlation matrix as an SFBM. If `corr` is a dsCMatrix or a dgCMatrix, you can use `as_SFBM(corr)`.
`df_beta`	A data frame with 3 columns: • `$beta`: effect size estimates • `$beta_se`: standard errors of effect size estimates • `$n_eff`: either GWAS sample size(s) when estimating `beta` for a continuous trait, or in the case of a binary trait, this is `4 / (1 / n_control + 1 / n_case)`; in the case of a meta-analysis, you should sum the effective sample sizes of each study instead of using the total numbers of cases and controls, see doi:10.1016/j.biopsych.2022.05.029; when using a mixed model, the effective sample size needs to be adjusted as well, see doi:10.1016/j.xhgg.2022.100136.
`delta`	Vector of shrinkage parameters to try (L2-regularization). Default is `c(0.001, 0.01, 0.1, 1)`.
`nlambda`	Number of different lambdas to try (L1-regularization). Default is `30`.
`lambda.min.ratio`	Ratio between last and first lambdas to try. Default is `0.01`.
`dfmax`	Maximum number of non-zero effects in the model. Default is `200e3`.
`maxiter`	Maximum number of iterations before convergence. Default is `1000`.
`tol`	Tolerance parameter for assessing convergence. Default is `1e-5`.

ind.corr	Indices to "subset" corr, as if this was run with corr[ind.corr, ind.corr] instead. No subsetting by default.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Value

A matrix of effect sizes, one vector (column) for each row in attr(<res>, "grid_param"). Missing values are returned when strong divergence is detected.

---

snp_ld_scores *LD scores*

Description

LD scores

Usage

```
snp_ld_scores(
  Gna,
  ind.row = rows_along(Gna),
  ind.col = cols_along(Gna),
  size = 500,
  infos.pos = NULL,
  ncores = 1
)

bed_ld_scores(
  obj.bed,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  size = 500,
  infos.pos = NULL,
  ncores = 1
)
```

Arguments

Gna	A FBM.code256 (typically <bigSNP>$genotypes). You can have missing values in these data.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**

size	For one SNP, window size around this SNP to compute correlations. Default is 500. If not providing infos.pos (NULL, the default), this is a window in number of SNPs, otherwise it is a window in kb (physical distance). In case you provide infos.pos in centimorgans (genetic distance), you should divide this by 1000 because it is internally multiplied by 1000 (i.e. use 3 / 1000 for 3 cM).
infos.pos	Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP. Typically <bigSNP>mapphysical.pos.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
obj.bed	Object of type bed, which is the mapping of some bed file. Use obj.bed <- bed(bedfile) to get this object.

Value

A vector of LD scores. For each variant, this is the sum of squared correlations with the neighboring variants (including itself).

Examples

```
test <- snp_attachExtdata()
G <- test$genotypes

(ld <- snp_ld_scores(G, ind.col = 1:1000))
```

---

snp_ldpred2_inf *LDpred2*

Description

LDpred2. Tutorial at https://privefl.github.io/bigsnpr/articles/LDpred2.html.

Usage

```
snp_ldpred2_inf(corr, df_beta, h2)

snp_ldpred2_grid(
  corr,
  df_beta,
  grid_param,
  burn_in = 50,
  num_iter = 100,
  ncores = 1,
  return_sampling_betas = FALSE,
  ind.corr = cols_along(corr)
)
```

```
snp_ldpred2_auto(
  corr,
  df_beta,
  h2_init,
  vec_p_init = 0.1,
  burn_in = 500,
  num_iter = 200,
  sparse = FALSE,
  verbose = FALSE,
  report_step = num_iter + 1L,
  allow_jump_sign = TRUE,
  shrink_corr = 1,
  use_MLE = TRUE,
  p_bounds = c(1e-05, 1),
  alpha_bounds = c(-1.5, 0.5),
  ind.corr = cols_along(corr),
  ncores = 1
)
```

Arguments

`corr`	Sparse correlation matrix as an SFBM. If `corr` is a dsCMatrix or a dgCMatrix, you can use `as_SFBM(corr)`.
`df_beta`	A data frame with 3 columns: • `$beta`: effect size estimates • `$beta_se`: standard errors of effect size estimates • `$n_eff`: either GWAS sample size(s) when estimating `beta` for a continuous trait, or in the case of a binary trait, this is `4 / (1 / n_control + 1 / n_case)`; in the case of a meta-analysis, you should sum the effective sample sizes of each study instead of using the total numbers of cases and controls, see doi:10.1016/j.biopsych.2022.05.029; when using a mixed model, the effective sample size needs to be adjusted as well, see doi:10.1016/j.xhgg.2022.100136.
`h2`	Heritability estimate.
`grid_param`	A data frame with 3 columns as a grid of hyper-parameters: • `$p`: proportion of causal variants • `$h2`: heritability (captured by the variants used) • `$sparse`: boolean, whether a sparse model is sought They can be run in parallel by changing `ncores`.
`burn_in`	Number of burn-in iterations.
`num_iter`	Number of iterations after burn-in.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.
`return_sampling_betas`	Whether to return all sampling betas (after burn-in)? This is useful for assessing the uncertainty of the PRS at the individual level (see doi:10.1101/2020.11.30.403188). Default is `FALSE` (only returns the averaged final vectors of betas). If `TRUE`, only one set of parameters is allowed.

ind.corr	Indices to "subset" corr, as if this was run with corr[ind.corr, ind.corr] instead. No subsetting by default.
h2_init	Heritability estimate for initialization.
vec_p_init	Vector of initial values for p. Default is 0.1.
sparse	In LDpred2-auto, whether to also report a sparse solution by running LDpred2-grid with the estimates of p and h2 from LDpred2-auto, and sparsity enabled. Default is FALSE.
verbose	Whether to print "p // h2" estimates at each iteration. Disabled when parallelism is used.
report_step	Step to report sampling betas (after burn-in and before unscaling). Nothing is reported by default. If using num_iter = 200 and report_step = 20, then 10 vectors of sampling betas are reported (as a sparse matrix with 10 columns).
allow_jump_sign	Whether to allow for effects sizes to change sign in consecutive iterations? Default is TRUE (normal sampling). You can use FALSE to force effects to go through 0 first before changing sign. Setting this parameter to FALSE could be useful to prevent instability (oscillation and ultimately divergence) of the Gibbs sampler. This would also be useful for accelerating convergence of chains with a large initial value for p.
shrink_corr	Shrinkage multiplicative coefficient to apply to off-diagonal elements of the correlation matrix. Default is 1 (unchanged). You can use e.g. 0.95 to add a bit of regularization.
use_MLE	Whether to use maximum likelihood estimation (MLE) to estimate alpha and the variance component (since v1.11.4), or assume that alpha is -1 and estimate the variance of (scaled) effects as h2/(m*p), as it was done in earlier versions of LDpred2-auto (e.g. in v1.10.8). Default is TRUE, which should provide a better model fit, but might also be less robust.
p_bounds	Boundaries for the estimates of p (the polygenicity). Default is c(1e-5, 1). You can use the same value twice to fix p.
alpha_bounds	Boundaries for the estimates of α. Default is c(-1.5, 0.5). You can use the same value twice to fix α.

Details

For reproducibility, set.seed() can be used to ensure that two runs of LDpred2 give the exact same results (since v1.10).

Value

snp_ldpred2_inf: A vector of effects, assuming an infinitesimal model.

snp_ldpred2_grid: A matrix of effect sizes, one vector (column) for each row of grid_param. Missing values are returned when strong divergence is detected. If using return_sampling_betas, each column corresponds to one iteration instead (after burn-in).

snp_ldpred2_auto: A list (over vec_p_init) of lists with

- `$beta_est`: vector of effect sizes (on the allele scale); note that missing values are returned when strong divergence is detected
- `$beta_est_sparse` (only when `sparse = TRUE`): sparse vector of effect sizes
- `$postp_est`: vector of posterior probabilities of being causal
- `$corr_est`, the "imputed" correlations between variants and phenotypes, which can be used for post-QCing variants by comparing those to `with(df_beta, beta / sqrt(n_eff * beta_se^2 + beta^2))`
- `$sample_beta`: sparse matrix of sampling betas (see parameter `report_step`), *not* on the allele scale, for which you need to multiply by `with(df_beta, sqrt(n_eff * beta_se^2 + beta^2))`
- `$path_p_est`: full path of p estimates (including burn-in); useful to check convergence of the iterative algorithm
- `$path_h2_est`: full path of h2 estimates (including burn-in); useful to check convergence of the iterative algorithm
- `$path_alpha_est`: full path of alpha estimates (including burn-in); useful to check convergence of the iterative algorithm
- `$h2_est`: estimate of the (SNP) heritability (also see coef_to_liab)
- `$p_est`: estimate of p, the proportion of causal variants
- `$alpha_est`: estimate of alpha, the parameter controlling the relationship between allele frequencies and expected effect sizes
- `$h2_init` and `$p_init`: input parameters, for convenience

`snp_ldsc` *LD score regression*

Description

LD score regression

Usage

```
snp_ldsc(
  ld_score,
  ld_size,
  chi2,
  sample_size,
  blocks = 200,
  intercept = NULL,
  chi2_thr1 = 30,
  chi2_thr2 = Inf,
  ncores = 1
)

snp_ldsc2(
  corr,
```

```
  df_beta,
  blocks = NULL,
  intercept = 1,
  ncores = 1,
  ind.beta = cols_along(corr),
  chi2_thr1 = 30,
  chi2_thr2 = Inf
)
```

Arguments

ld_score	Vector of LD scores.
ld_size	Number of variants used to compute ld_score.
chi2	Vector of chi-squared statistics.
sample_size	Sample size of GWAS corresponding to chi-squared statistics. Possibly a vector, or just a single value.
blocks	Either a single number specifying the number of blocks, or a vector of integers specifying the block number of each chi2 value. Default is 200 for snp_ldsc(), dividing into 200 blocks of approximately equal size. NULL can also be used to skip estimating standard errors, which is the default for snp_ldsc2().
intercept	You can constrain the intercept to some value (e.g. 1). Default is NULL in snp_ldsc() (the intercept is estimated) and is 1 in snp_ldsc2() (the intercept is fixed to 1). This is equivalent to parameter --intercept-h2.
chi2_thr1	Threshold on chi2 in step 1. Default is 30. This is equivalent to parameter --two-step.
chi2_thr2	Threshold on chi2 in step 2. Default is Inf (none).
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
corr	Sparse correlation matrix. Can also be an SFBM.
df_beta	A data frame with 3 columns: • $beta: effect size estimates • $beta_se: standard errors of effect size estimates • $n_eff: either GWAS sample size(s) when estimating beta for a continuous trait, or in the case of a binary trait, this is 4 / (1 / n_control + 1 / n_case); in the case of a meta-analysis, you should sum the effective sample sizes of each study instead of using the total numbers of cases and controls, see doi:10.1016/j.biopsych.2022.05.029; when using a mixed model, the effective sample size needs to be adjusted as well, see doi:10.1016/j.xhgg.2022.100136.
ind.beta	Indices in corr corresponding to df_beta. Default is all.

Value

Vector of 4 values (or only the first 2 if blocks = NULL):

- [["int"]]: LDSC regression intercept,

- [["int_se"]]: SE of this intercept,
- [["h2"]]: LDSC regression estimate of (SNP) heritability (also see coef_to_liab),
- [["h2_se"]]: SE of this heritability estimate.

Examples

```
bigsnp <- snp_attachExtdata()
G <- bigsnp$genotypes
y <- bigsnp$fam$affection - 1
corr <- snp_cor(G, ind.col = 1:1000)

gwas <- big_univLogReg(G, y, ind.col = 1:1000)
df_beta <- data.frame(beta = gwas$estim, beta_se = gwas$std.err,
                      n_eff = 4 / (1 / sum(y == 0) + 1 / sum(y == 1)))

snp_ldsc2(corr, df_beta)
snp_ldsc2(corr, df_beta, blocks = 20, intercept = NULL)
```

---

snp_ldsplit *Independent LD blocks*

Description

Split a correlation matrix in blocks as independent as possible. This finds the splitting in blocks that minimizes the sum of squared correlation between these blocks (i.e. everything outside these blocks). In case of equivalent splits, it then minimizes the sum of squared sizes of the blocks.

Usage

```
snp_ldsplit(
  corr,
  thr_r2,
  min_size,
  max_size,
  max_K = 500,
  max_r2 = 0.3,
  max_cost = ncol(corr)/200,
  pos_scaled = rep(0, ncol(corr))
)
```

Arguments

corr	Sparse correlation matrix. Usually, the output of snp_cor().
thr_r2	Threshold under which squared correlations are ignored. This is useful to avoid counting noise, which should give clearer patterns of costs vs. number of blocks. It is therefore possible to have a splitting cost of 0. If this parameter is used, then corr can be computed using the same parameter in snp_cor() (to increase the sparsity of the resulting matrix).

min_size	Minimum number of variants in each block. This is used not to have a disproportionate number of small blocks.
max_size	Maximum number of variants in each block. This is used not to have blocks that are too large, e.g. to limit computational and memory requirements of applications that would use these blocks. For some long-range LD regions, it may be needed to allow for large blocks. You can now provide a vector of values to try.
max_K	Maximum number of blocks to consider. All optimal solutions for K from 1 to max_K will be returned. Some of these K might not have any corresponding solution due to the limitations in size of the blocks. For example, splitting 10,000 variants in blocks with at least 500 and at most 2000 variants implies that there are at least 5 and at most 20 blocks. Then, the choice of K depends on the application, but a simple solution is to choose the largest K for which the cost is lower than some threshold. Default is 500.
max_r2	Maximum squared correlation allowed for one pair of variants in two different blocks. This is used to make sure that strong correlations are not discarded and also to speed up the algorithm. Default is 0.3.
max_cost	Maximum cost reported. Default is ncol(corr) / 200.
pos_scaled	Vector of positions. The positions should be scaled so that limits of a block must be separated by a distance of 1 at the maximum. E.g. if the positions are in base pairs (bp), and you want a maximum distance of 10 Mbp, you need to provide the vector of positions divided by 10e6.

Value

Either NULL when no block splitting satisfies the conditions, or a tibble with seven columns:

- $max_size: Input parameter, useful when providing a vector of values to try.
- $n_block: Number of blocks.
- $cost: The sum of squared correlations outside the blocks.
- $cost2: The sum of squared sizes of the blocks.
- $perc_kept: Percentage of initial non-zero values kept within the blocks defined.
- $all_last: Last index of each block.
- $all_size: Sizes of the blocks.
- $block_num: Resulting block numbers for each variant. This is not reported anymore, but can be computed with rep(seq_along(all_size), all_size).

Examples

```
## Not run:

  corr <- readRDS(url("https://www.dropbox.com/s/65u96jf7y32j2mj/spMat.rds?raw=1"))

  # adjust `THR_R2` depending on sample size used to compute corr
  # use e.g. 0.05 for small sample sizes, and 0.01 for large sample sizes
  THR_R2 <- 0.02
  m <- ncol(corr)
  (SEQ <- round(seq_log(m / 30, m / 5, length.out = 10)))
  # replace `min_size` by e.g. 100 for larger data
```

```
(res <- snp_ldsplit(corr, thr_r2 = THR_R2, min_size = 10, max_size = SEQ))

# add the variant block IDs corresponding to each split
res$block_num <- lapply(res$all_size, function(.) rep(seq_along(.), .))

library(ggplot2)
# trade-off cost / number of blocks
qplot(n_block, cost, color = factor(max_size, SEQ), data = res) +
  theme_bw(14) +
  scale_y_log10() +
  theme(legend.position = "top") +
  labs(x = "Number of blocks", color = "Maximum block size",
       y = "Sum of squared correlations outside blocks")

# trade-off cost / number of non-zero values
qplot(perc_kept, cost, color = factor(max_size, SEQ), data = res) +
  theme_bw(14) +
  # scale_y_log10() +
  theme(legend.position = "top") +
  labs(x = "Percentage of non-zero values kept", color = "Maximum block size",
       y = "Sum of squared correlations outside blocks")

# trade-off cost / sum of squared sizes
qplot(cost2, cost, color = factor(max_size, SEQ), data = res) +
  theme_bw(14) +
  scale_y_log10() +
  geom_vline(xintercept = 0)+
  theme(legend.position = "top") +
  labs(x = "Sum of squared blocks", color = "Maximum block size",
       y = "Sum of squared correlations outside blocks")


## Pick one solution and visualize blocks
library(dplyr)
all_ind <- res %>%
  arrange(cost2 * sqrt(5 + cost)) %>%
  print() %>%
  slice(1) %>%
  pull(all_last)

## Transform sparse representation into (i,j,x) triplets
corrT <- as(corr, "dgTMatrix")
upper <- (corrT@i <= corrT@j & corrT@x^2 >= THR_R2)
df <- data.frame(
  i = corrT@i[upper] + 1L,
  j = corrT@j[upper] + 1L,
  r2 = corrT@x[upper]^2
)
df$y <- (df$j - df$i) / 2

ggplot(df) +
  geom_point(aes(i + y, y, alpha = r2)) +
  theme_minimal() +
```

```
    theme(axis.text.y = element_blank(), axis.ticks.y = element_blank(),
          strip.background = element_blank(), strip.text.x = element_blank()) +
    scale_alpha_continuous(range = 0:1) +
    scale_x_continuous(expand = c(0.02, 0.02), minor_breaks = NULL,
                       breaks = head(all_ind[[1]], -1) + 0.5) +
    facet_wrap(~ cut(i + y, 4), scales = "free", ncol = 1) +
    labs(x = "Position", y = NULL)

## End(Not run)
```

---

snp_MAF *MAF*

Description

Minor Allele Frequency.

Usage

```
snp_MAF(
  G,
  ind.row = rows_along(G),
  ind.col = cols_along(G),
  nploidy = 2,
  ncores = 1
)
```

Arguments

G	A FBM.code256 (typically <bigSNP>$genotypes). **You shouldn't have missing values.** Also, remember to do quality control, e.g. some algorithms in this package won't work if you use SNPs with 0 MAF.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
nploidy	Number of trials, parameter of the binomial distribution. Default is 2, which corresponds to diploidy, such as for the human genome.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Value

A vector of MAFs, corresponding to ind.col.

Examples

```
obj.bigsnp <- snp_attachExtdata()
str(maf <- snp_MAF(obj.bigsnp$genotypes))
```

---

snp_manhattan *Manhattan plot*

Description

Creates a manhattan plot.

Usage

```
snp_manhattan(
  gwas,
  infos.chr,
  infos.pos,
  colors = c("black", "grey60"),
  dist.sep.chrs = 1e+07,
  ind.highlight = integer(0),
  col.highlight = "red",
  labels = NULL,
  npoints = NULL,
  coeff = 1
)
```

Arguments

gwas	A `mhtest` object with the p-values associated with each SNP. Typically, the output of bigstatsr::big_univLinReg, bigstatsr::big_univLogReg or snp_pcadapt.
infos.chr	Vector of integers specifying each SNP's chromosome. Typically `<bigSNP>$map$chromosome`.
infos.pos	Vector of integers specifying the physical position on a chromosome (in base pairs) of each SNP. Typically `<bigSNP>$map$physical.pos`.
colors	Colors used for each chromosome (they are recycled). Default is an alternation of black and gray.
dist.sep.chrs	"Physical" distance that separates two chromosomes. Default is 10 Mbp.
ind.highlight	Indices of SNPs you want to highlight (of interest). Default doesn't highlight any SNPs.
col.highlight	Color used for highlighting SNPs. Default uses red.
labels	Labels of the x axis. Default uses the number of the chromosome there are in `infos.chr(sort(unique(infos.chr)))`. This may be useful to restrict the number of labels so that they are not overlapping.

npoints	Number of points to keep (ranked by p-value) in order to get a lighter object (and plot). Default doesn't cut anything. If used, the resulting object will have an attribute called subset giving the indices of the kept points.
coeff	Relative size of text. Default is 1.

Details

If you don't have information of chromosome and position, you should simply use plot instead.

Value

A ggplot2 object. You can plot it using the print method. You can modify it as you wish by adding layers. You might want to read this chapter to get more familiar with the package **ggplot2**.

Examples

```
set.seed(9)

test <- snp_attachExtdata()
G <- test$genotypes
y <- rnorm(nrow(G))

gwas <- big_univLinReg(G, y)

snp_qq(gwas)
gwas_gc <- snp_gc(gwas) # this modifies `attr(gwas_gc, "transfo")`
snp_qq(gwas_gc)

# The next plot should be prettier with a real dataset
snp_manhattan(gwas_gc,
              infos.chr = test$map$chromosome,
              infos.pos = test$map$physical.pos) +
  ggplot2::geom_hline(yintercept = -log10(5e-8), linetype = 2, color = "red")

p <- snp_qq(gwas_gc) +
  ggplot2::aes(text = asPlotlyText(test$map)) +
  ggplot2::labs(subtitle = NULL, x = "Expected -log10(p)", y = "Observed -log10(p)")
## Not run: plotly::ggplotly(p, tooltip = "text")
```

---

snp_match *Match alleles*

Description

Match alleles between summary statistics and SNP information. Match by ("chr", "a0", "a1") and ("pos" or "rsid"), accounting for possible strand flips and reverse reference alleles (opposite effects).

Usage

```
snp_match(
  sumstats,
  info_snp,
  strand_flip = TRUE,
  join_by_pos = TRUE,
  remove_dups = TRUE,
  match.min.prop = 0.2,
  return_flip_and_rev = FALSE
)
```

Arguments

sumstats	A data frame with columns "chr", "pos", "a0", "a1" and "beta".
info_snp	A data frame with columns "chr", "pos", "a0" and "a1".
strand_flip	Whether to try to flip strand? (default is TRUE) If so, ambiguous alleles A/T and C/G are removed.
join_by_pos	Whether to join by chromosome and position (default), or instead by rsid.
remove_dups	Whether to remove duplicates (same physical position)? Default is TRUE.
match.min.prop	Minimum proportion of variants in the smallest data to be matched, otherwise stops with an error. Default is 20%.
return_flip_and_rev	Whether to return internal boolean variables "_FLIP_" (whether the alleles must be flipped: A <–> T & C <–> G, because on the opposite strand) and "_REV_" (whether alleles must be swapped: $a0 <–> $a1, in which case corresponding $beta are multiplied by -1). Default is FALSE.

Value

A single data frame with matched variants. Values in column $beta are multiplied by -1 for variants with alleles reversed (i.e. swapped). New variable "_NUM_ID_.ss" returns the corresponding row indices of the input sumstats (first argument of this function), and "_NUM_ID_" corresponding to the input info_snp (second argument).

See Also

snp_modifyBuild

Examples

```
sumstats <- data.frame(
  chr = 1,
  pos = c(86303, 86331, 162463, 752566, 755890, 758144),
  a0 = c("T", "G", "C", "A", "T", "G"),
  a1 = c("G", "A", "T", "G", "A", "A"),
  beta = c(-1.868, 0.250, -0.671, 2.112, 0.239, 1.272),
  p = c(0.860, 0.346, 0.900, 0.456, 0.776, 0.383)
)
```

```
info_snp <- data.frame(
  id = c("rs2949417", "rs115209712", "rs143399298", "rs3094315", "rs3115858"),
  chr = 1,
  pos = c(86303, 86331, 162463, 752566, 755890),
  a0 = c("T", "A", "G", "A", "T"),
  a1 = c("G", "G", "A", "G", "A")
)

snp_match(sumstats, info_snp)
snp_match(sumstats, info_snp, strand_flip = FALSE)
```

---

snp_MAX3 *MAX3 statistic*

Description

Compute the MAX3 statistic, which tests for three genetic models (additive, recessive and dominant).

Usage

```
snp_MAX3(Gna, y01.train, ind.train = rows_along(Gna), val = c(0, 0.5, 1))
```

Arguments

`Gna`	A FBM.code256 (typically `<bigSNP>$genotypes`). You can have missing values in these data.
`y01.train`	Vector of responses, corresponding to `ind.train`. **Must be only 0s and 1s.**
`ind.train`	An optional vector of the row indices that are used, for the training part. If not specified, all rows are used. **Don't use negative indices.**
`val`	Computing $\max_{x \in val} Z^2_{CATT}(x)$. • Default is `c(0, 0.5, 1)` and corresponds to the *MAX3* statistic. • Only `c(0, 1)` corresponds to *MAX2*. • And only `0.5` corresponds to the Armitage trend test. • Finally, `seq(0, 1, length.out = L)` corresponds to *MAXL*.

Details

P-values associated with returned scores are in fact the minimum of the p-values of each test separately. Thus, they are biased downward.

Value

An object of classes `mhtest` and `data.frame` returning one score by SNP. See `methods(class = "mhtest")`.

References

Zheng, G., Yang, Y., Zhu, X., & Elston, R. (2012). Robust Procedures. Analysis Of Genetic Association Studies, 151-206. doi:10.1007/9781461422457_6.

Examples

```
set.seed(1)

# constructing a fake genotype big.matrix
N <- 50; M <- 1200
fake <- snp_fake(N, M)
G <- fake$genotypes
G[] <- sample(as.raw(0:3), size = length(G), replace = TRUE)
G[1:8, 1:10]

# Specify case/control phenotypes
fake$fam$affection <- rep(1:2, each = N / 2)

# Get MAX3 statistics
y01 <- fake$fam$affection - 1
str(test <- snp_MAX3(fake$genotypes, y01.train = y01))
# p-values are not well calibrated
snp_qq(test)
# genomic control is not of much help
snp_qq(snp_gc(test))

# Armitage trend test (well calibrated because only one test)
test2 <- snp_MAX3(fake$genotypes, y01.train = y01, val = 0.5)
snp_qq(test2)
```

---

snp_modifyBuild *Modify genome build*

Description

Modify the physical position information of a data frame when converting genome build using executable *liftOver*.

Usage

```
snp_modifyBuild(
  info_snp,
  liftOver,
  from = "hg18",
  to = "hg19",
  check_reverse = TRUE,
  local_chain = NULL,
  base_url = "https://hgdownload.soe.ucsc.edu/goldenPath/"
)
```

Arguments

info_snp	A data frame with columns "chr" and "pos".
liftOver	Path to liftOver executable. Binaries can be downloaded at https://hgdownload.cse.ucsc.edu/admin/exe/macOSX.x86_64/liftOver for Mac and at https://hgdownload.cse.ucsc.edu/admin/exe/linux.x86_64/liftOver for Linux.
from	Genome build to convert from. Default is hg18.
to	Genome build to convert to. Default is hg19.
check_reverse	Whether to discard positions for which we cannot go back to initial values by doing 'from -> to -> from'. Default is TRUE.
local_chain	Local chain file (e.g. hg18ToHg19.over.chain.gz) to use instead of downloading one from parameters from and to (the default). You can download one such file from e.g. https://hgdownload.soe.ucsc.edu/goldenPath/hg18/liftOver/. Provide a vector of two when using check_reverse.
base_url	From where to download the chain files. Default is "https://hgdownload.soe.ucsc.edu/goldenPath/ You can also try replacing https by http, and/or soe by cse.

Value

Input data frame info_snp with column "pos" in the new build.

References

Hinrichs, Angela S., et al. "The UCSC genome browser database: update 2006." Nucleic acids research 34.suppl_1 (2006): D590-D598.

---

snp_pcadapt *Outlier detection*

Description

Method to detect genetic markers involved in biological adaptation. This provides a statistical tool for outlier detection based on Principal Component Analysis. This corresponds to the statistic based on mahalanobis distance, as implemented in package **pcadapt**.

Usage

```
snp_pcadapt(
  G,
  U.row,
  ind.row = rows_along(G),
  ind.col = cols_along(G),
  ncores = 1
)

bed_pcadapt(
```

```
  obj.bed,
  U.row,
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  ncores = 1
)
```

Arguments

G	A FBM.code256 (typically <bigSNP>$genotypes). **You shouldn't have missing values.** Also, remember to do quality control, e.g. some algorithms in this package won't work if you use SNPs with 0 MAF.
U.row	Left singular vectors (not scores, $U^T U = I$) corresponding to ind.row.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
obj.bed	Object of type bed, which is the mapping of some bed file. Use obj.bed <- bed(bedfile) to get this object.

Value

An object of classes mhtest and data.frame returning one score by SNP. See methods(class = "mhtest").

References

Luu, K., Bazin, E., & Blum, M. G. (2017). pcadapt: an R package to perform genome scans for selection based on principal component analysis. Molecular ecology resources, 17(1), 67-77.

See Also

snp_manhattan, snp_qq and snp_gc.

Examples

```
test <- snp_attachExtdata()
G <- test$genotypes
obj.svd <- big_SVD(G, fun.scaling = snp_scaleBinom(), k = 10)
plot(obj.svd) # there seems to be 3 "significant" components
pcadapt <- snp_pcadapt(G, obj.svd$u[, 1:3])
snp_qq(pcadapt)
```

`snp_plinkIBDQC` *Identity-by-descent*

Description

Quality Control based on Identity-by-descent (IBD) computed by **PLINK 1.9** using its method-of-moments.

Usage

```
snp_plinkIBDQC(
  plink.path,
  bedfile.in,
  bedfile.out = NULL,
  pi.hat = 0.08,
  ncores = 1,
  pruning.args = c(100, 0.2),
  do.blind.QC = TRUE,
  extra.options = "",
  verbose = TRUE
)
```

Arguments

`plink.path`	Path to the executable of PLINK 1.9.
`bedfile.in`	Path to the input bedfile.
`bedfile.out`	Path to the output bedfile. Default is created by appending `"_norel"` to `prefix.in` (`bedfile.in` without extension).
`pi.hat`	PI_HAT value threshold for individuals (first by pairs) to be excluded. Default is `0.08`.
`ncores`	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.
`pruning.args`	A vector of 2 pruning parameters, respectively the window size (in variant count) and the pairwise r^2 threshold (the step size is fixed to 1). Default is `c(100, 0.2)`.
`do.blind.QC`	Whether to do QC with `pi.hat` without visual inspection. Default is `TRUE`. If `FALSE`, return the `data.frame` of the corresponding ".genome" file without doing QC. One could use `ggplot2::qplot(Z0, Z1, data = mydf, col = RT)` for visual inspection.
`extra.options`	Other options to be passed to PLINK as a string (for the IBD part). More options can be found at https://www.cog-genomics.org/plink/1.9/ibd.
`verbose`	Whether to show PLINK log? Default is `TRUE`.

Value

The path of the new bedfile. If no sample is filter, no new bed/bim/fam files are created and then the path of the input bedfile is returned.

References

Chang, Christopher C, Carson C Chow, Laurent CAM Tellier, Shashaank Vattikuti, Shaun M Purcell, and James J Lee. 2015. *Second-generation PLINK: rising to the challenge of larger and richer datasets.* GigaScience 4 (1): 7. doi:10.1186/s1374201500478.

See Also

download_plink snp_plinkQC snp_plinkKINGQC

Examples

```
## Not run:

bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
plink <- download_plink()

bedfile <- snp_plinkIBDQC(plink, bedfile,
                          bedfile.out = tempfile(fileext = ".bed"),
                          ncores = 2)

df_rel <- snp_plinkIBDQC(plink, bedfile, do.blind.QC = FALSE, ncores = 2)
str(df_rel)

library(ggplot2)
qplot(Z0, Z1, data = df_rel, col = RT)
qplot(y = PI_HAT, data = df_rel) +
  geom_hline(yintercept = 0.2, color = "blue", linetype = 2)
snp_plinkRmSamples(plink, bedfile,
                   bedfile.out = tempfile(fileext = ".bed"),
                   df.or.files = subset(df_rel, PI_HAT > 0.2))

## End(Not run)
```

---

snp_plinkKINGQC *Relationship-based pruning*

Description

Quality Control based on KING-robust kinship estimator. More information can be found at https://www.cog-genomics.org/plink/2.0/distance#king_cutoff.

Usage

```
snp_plinkKINGQC(
  plink2.path,
  bedfile.in,
  bedfile.out = NULL,
  thr.king = 2^-3.5,
```

```
  make.bed = TRUE,
  ncores = 1,
  extra.options = "",
  verbose = TRUE
)
```

Arguments

plink2.path	Path to the executable of PLINK 2.
bedfile.in	Path to the input bedfile.
bedfile.out	Path to the output bedfile. Default is created by appending "_norel" to prefix.in (bedfile.in without extension).
thr.king	Note that KING kinship coefficients are scaled such that duplicate samples have kinship 0.5, not 1. First-degree relations (parent-child, full siblings) correspond to ~0.25, second-degree relations correspond to ~0.125, etc. It is conventional to use a cutoff of ~0.354 (2^-1.5, the geometric mean of 0.5 and 0.25) to screen for monozygotic twins and duplicate samples, ~0.177 (2^-2.5) to remove first-degree relations as well, and ~0.0884 (2^-3.5, **default**) to remove second-degree relations as well, etc.
make.bed	Whether to create new bed/bim/fam files (default). Otherwise, returns a table with coefficients of related pairs.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
extra.options	Other options to be passed to PLINK2 as a string.
verbose	Whether to show PLINK log? Default is TRUE.

Value

See parameter make-bed.

References

Manichaikul, Ani, Josyf C. Mychaleckyj, Stephen S. Rich, Kathy Daly, Michele Sale, and Wei-Min Chen. "Robust relationship inference in genome-wide association studies." Bioinformatics 26, no. 22 (2010): 2867-2873.

See Also

download_plink2 snp_plinkQC

Examples

```
## Not run:

bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
plink2 <- download_plink2(AVX2 = FALSE)

bedfile2 <- snp_plinkKINGQC(plink2, bedfile,
                            bedfile.out = tempfile(fileext = ".bed"),
```

```
                              ncores = 2)

df_rel <- snp_plinkKINGQC(plink2, bedfile, make.bed = FALSE, ncores = 2)
str(df_rel)

## End(Not run)
```

---

snp_plinkQC *Quality Control*

Description

Quality Control (QC) and possible conversion to *bed/bim/fam* files using **PLINK 1.9**.

Usage

```
snp_plinkQC(
  plink.path,
  prefix.in,
  file.type = "--bfile",
  prefix.out = paste0(prefix.in, "_QC"),
  maf = 0.01,
  geno = 0.1,
  mind = 0.1,
  hwe = 1e-50,
  autosome.only = FALSE,
  extra.options = "",
  verbose = TRUE
)
```

Arguments

`plink.path`	Path to the executable of PLINK 1.9.
`prefix.in`	Prefix (path without extension) of the dataset to be QCed.
`file.type`	Type of the dataset to be QCed. Default is `"--bfile"` and corresponds to bed/bim/fam files. You can also use `"--file"` for ped/map files, `"--vcf"` for a VCF file, or `"--gzvcf"` for a gzipped VCF. More information can be found at https://www.cog-genomics.org/plink/1.9/input.
`prefix.out`	Prefix (path without extension) of the bed/bim/fam dataset to be created. Default is created by appending `"_QC"` to `prefix.in`.
`maf`	Minimum Minor Allele Frequency (MAF) for a SNP to be kept. Default is `0.01`.
`geno`	Maximum proportion of missing values for a SNP to be kept. Default is `0.1`.
`mind`	Maximum proportion of missing values for a sample to be kept. Default is `0.1`.
`hwe`	Filters out all variants which have Hardy-Weinberg equilibrium exact test p-value below the provided threshold. Default is `1e-50`.

autosome.only	Whether to exclude all unplaced and non-autosomal variants? Default is FALSE.
extra.options	Other options to be passed to PLINK as a string. More options can be found at https://www.cog-genomics.org/plink2/filter. If using PLINK 2.0, you could e.g. use "--king-cutoff 0.0884" to remove some related samples at the same time of quality controls.
verbose	Whether to show PLINK log? Default is TRUE.

Value

The path of the newly created bedfile.

References

Chang, Christopher C, Carson C Chow, Laurent CAM Tellier, Shashaank Vattikuti, Shaun M Purcell, and James J Lee. 2015. *Second-generation PLINK: rising to the challenge of larger and richer datasets.* GigaScience 4 (1): 7. doi:10.1186/s1374201500478.

See Also

download_plink snp_plinkIBDQC

Examples

```
## Not run:

bedfile <- system.file("extdata", "example.bed", package = "bigsnpr")
prefix  <- sub_bed(bedfile)
plink <- download_plink()
test <- snp_plinkQC(plink.path = plink,
                    prefix.in = prefix,
                    prefix.out = tempfile(),
                    file.type = "--bfile",  # the default (for ".bed")
                    maf = 0.05,
                    geno = 0.05,
                    mind = 0.05,
                    hwe = 1e-10,
                    autosome.only = TRUE)
test

## End(Not run)
```

---

snp_plinkRmSamples *Remove samples*

Description

Create new *bed*/*bim*/*fam* files by removing samples with PLINK.

Usage

```
snp_plinkRmSamples(
  plink.path,
  bedfile.in,
  bedfile.out,
  df.or.files,
  col.family.ID = 1,
  col.sample.ID = 2,
  ...,
  verbose = TRUE
)
```

Arguments

plink.path	Path to the executable of PLINK 1.9.
bedfile.in	Path to the input bedfile.
bedfile.out	Path to the output bedfile.
df.or.files	Either • A data.frame, • A character vector of file names where to find at the information you want. You should have one column for family IDs and one for sample IDs.
col.family.ID	Index of the column containing the family IDs to match with those of the study. Default is the first one.
col.sample.ID	Index of the column containing the sample IDs to match with those of the study. Default is the second one.
...	Any additional parameter to pass to bigreadr::fread2(). Particularly, option header = FALSE is sometimes needed.
verbose	Whether to show PLINK log? Default is TRUE.

Value

The path of the new bedfile.

See Also

download_plink

---

snp_prodBGEN *BGEN matrix product*

Description

Compute a matrix product between BGEN files and a matrix. This removes the need to read an intermediate FBM object with snp_readBGEN() to compute the product. Moreover, when using dosages, they are not rounded to two decimal places anymore.

Usage

```
snp_prodBGEN(
  bgenfiles,
  beta,
  list_snp_id,
  ind_row = NULL,
  bgi_dir = dirname(bgenfiles),
  read_as = c("dosage", "random"),
  block_size = 1000,
  ncores = 1
)
```

Arguments

bgenfiles	Character vector of paths to files with extension ".bgen". The corresponding ".bgen.bgi" index files must exist.
beta	A matrix (or a vector), with rows corresponding to `list_snp_id`.
list_snp_id	List of character vectors of SNP IDs to read, with one vector per BGEN file. Each SNP ID should be in the form `"<chr>_<pos>_<a1>_<a2>"` (e.g. `"1_88169_C_T"` or `"01_88169_C_T"`). If you have one BGEN file only, just wrap your vector of IDs with `list()`. **This function assumes that these IDs are uniquely identifying variants.**
ind_row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.** You can access the sample IDs corresponding to the genotypes from the *.sample* file, and use e.g. `match()` to get indices corresponding to the ones you want.
bgi_dir	Directory of index files. Default is the same as `bgenfiles`.
read_as	How to read BGEN probabilities? Currently implemented: • as dosages (rounded to two decimal places), the default, • as hard calls, randomly sampled based on those probabilities (similar to PLINK option '`--hard-call-threshold random`').
block_size	Maximum size of temporary blocks (in number of variants). Default is `1000`.
ncores	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.

Value

The product `bgen_data[ind_row, 'list_snp_id'] %*% beta`.

See Also

`snp_readBGEN()`

snp_PRS *PRS*

Description

Polygenic Risk Scores with possible clumping and thresholding.

Usage

```
snp_PRS(
  G,
  betas.keep,
  ind.test = rows_along(G),
  ind.keep = cols_along(G),
  same.keep = rep(TRUE, length(ind.keep)),
  lpS.keep = NULL,
  thr.list = 0
)
```

Arguments

G	A FBM.code256 (typically <bigSNP>$genotypes). **You shouldn't have missing values.** Also, remember to do quality control, e.g. some algorithms in this package won't work if you use SNPs with 0 MAF.
betas.keep	Numeric vector of weights associated with each SNP corresponding to ind.keep. You may want to see bigstatsr::big_univLinReg or bigstatsr::big_univLogReg.
ind.test	The individuals on whom to project the scores. Default uses all.
ind.keep	Column (SNP) indices to use (if using clumping, the output of snp_clumping). Default doesn't clump.
same.keep	A logical vector associated with betas.keep whether the reference allele is the same for G. Default is all TRUE (for example when you train the betas on the same dataset). Otherwise, use same_ref.
lpS.keep	Numeric vector of -log10(p-value) associated with betas.keep. Default doesn't use thresholding.
thr.list	Threshold vector on lpS.keep at which SNPs are excluded if they are not significant enough. Default doesn't use thresholding.

Value

A matrix of scores, where rows correspond to ind.test and columns correspond to thr.list.

Examples

```
test <- snp_attachExtdata()
G <- big_copy(test$genotypes, ind.col = 1:1000)
CHR <- test$map$chromosome[1:1000]
POS <- test$map$physical.position[1:1000]
y01 <- test$fam$affection - 1

# PCA -> covariables
obj.svd <- snp_autoSVD(G, infos.chr = CHR, infos.pos = POS)

# train and test set
ind.train <- sort(sample(nrow(G), 400))
ind.test <- setdiff(rows_along(G), ind.train) # 117

# GWAS
gwas.train <- big_univLogReg(G, y01.train = y01[ind.train],
                             ind.train = ind.train,
                             covar.train = obj.svd$u[ind.train, ])
# clumping
ind.keep <- snp_clumping(G, infos.chr = CHR,
                         ind.row = ind.train,
                         S = abs(gwas.train$score))
# -log10(p-values) and thresolding
summary(lpS.keep <- -predict(gwas.train)[ind.keep])
thrs <- seq(0, 4, by = 0.5)
nb.pred <- sapply(thrs, function(thr) sum(lpS.keep > thr))

# PRS
prs <- snp_PRS(G, betas.keep = gwas.train$estim[ind.keep],
               ind.test = ind.test,
               ind.keep = ind.keep,
               lpS.keep = lpS.keep,
               thr.list = thrs)

# AUC as a function of the number of predictors
aucs <- apply(prs, 2, AUC, target = y01[ind.test])
library(ggplot2)
qplot(nb.pred, aucs) +
  geom_line() +
  scale_x_log10(breaks = nb.pred) +
  labs(x = "Number of predictors", y = "AUC") +
  theme_bigstatsr()
```

---

snp_qq *Q-Q plot*

Description

Creates a quantile-quantile plot from p-values from a GWAS study.

Usage

```
snp_qq(gwas, lambdaGC = TRUE, coeff = 1)
```

Arguments

gwas	A mhtest object with the p-values associated with each SNP. Typically, the output of bigstatsr::big_univLinReg, bigstatsr::big_univLogReg or snp_pcadapt.
lambdaGC	Add the Genomic Control coefficient as subtitle to the plot?
coeff	Relative size of text. Default is 1.

Value

A ggplot2 object. You can plot it using the print method. You can modify it as you wish by adding layers. You might want to read this chapter to get more familiar with the package **ggplot2**.

Examples

```
set.seed(9)

test <- snp_attachExtdata()
G <- test$genotypes
y <- rnorm(nrow(G))

gwas <- big_univLinReg(G, y)

snp_qq(gwas)
gwas_gc <- snp_gc(gwas) # this modifies `attr(gwas_gc, "transfo")`
snp_qq(gwas_gc)

# The next plot should be prettier with a real dataset
snp_manhattan(gwas_gc,
              infos.chr = test$map$chromosome,
              infos.pos = test$map$physical.pos) +
  ggplot2::geom_hline(yintercept = -log10(5e-8), linetype = 2, color = "red")

p <- snp_qq(gwas_gc) +
  ggplot2::aes(text = asPlotlyText(test$map)) +
  ggplot2::labs(subtitle = NULL, x = "Expected -log10(p)", y = "Observed -log10(p)")
## Not run: plotly::ggplotly(p, tooltip = "text")
```

---

snp_readBed *Read PLINK files into a "bigSNP"*

Description

Functions to read bed/bim/fam files into a bigSNP.

Usage

```
snp_readBed(bedfile, backingfile = sub_bed(bedfile))

snp_readBed2(
  bedfile,
  backingfile = sub_bed(bedfile),
  ind.row = rows_along(obj.bed),
  ind.col = cols_along(obj.bed),
  ncores = 1
)
```

Arguments

bedfile	Path to file with extension ".bed" to read. You need the corresponding ".bim" and ".fam" in the same directory.
backingfile	The path (without extension) for the backing files for the cache of the bigSNP object. Default takes the bedfile without the ".bed" extension.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.col	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**
ncores	Number of cores used. Default doesn't use parallelism. You may use `bigstatsr::nb_cores()`.

Details

For more information on these formats, please visit PLINK webpage. For other formats, please use PLINK to convert them in bedfiles, which require minimal space to store and are faster to read. For example, to convert from a VCF file, use the `--vcf` option. See snp_plinkQC.

Value

The path to the RDS file that stores the `bigSNP` object. Note that this function creates another file (*.bk*) that stores the values of the Filebacked Big Matrix.
You shouldn't read from PLINK files more than once. Instead, use snp_attach to load the "bigSNP" object in any R session from backing files.

Examples

```
(bedfile <- system.file("extdata", "example.bed", package = "bigsnpr"))

# Reading the bedfile and storing the data in temporary directory
rds <- snp_readBed(bedfile, backingfile = tempfile())

# Loading the data from backing files
test <- snp_attach(rds)
```

```
str(test)
dim(G <- test$genotypes)
G[1:8, 1:8]
```

---

snp_readBGEN *Read BGEN files into a "bigSNP"*

Description

Function to read the UK Biobank BGEN files into a bigSNP.

Usage

```
snp_readBGEN(
  bgenfiles,
  backingfile,
  list_snp_id,
  ind_row = NULL,
  bgi_dir = dirname(bgenfiles),
  read_as = c("dosage", "random"),
  ncores = 1
)
```

Arguments

bgenfiles	Character vector of paths to files with extension ".bgen". The corresponding ".bgen.bgi" index files must exist.
backingfile	The path (without extension) for the backing files (".bk" and ".rds") that are created by this function for storing the bigSNP object.
list_snp_id	List of character vectors of SNP IDs to read, with one vector per BGEN file. Each SNP ID should be in the form "<chr>_<pos>_<a1>_<a2>" (e.g. "1_88169_C_T" or "01_88169_C_T"). If you have one BGEN file only, just wrap your vector of IDs with list(). **This function assumes that these IDs are uniquely identifying variants.**
ind_row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.** You can access the sample IDs corresponding to the genotypes from the *.sample* file, and use e.g. match() to get indices corresponding to the ones you want.
bgi_dir	Directory of index files. Default is the same as bgenfiles.
read_as	How to read BGEN probabilities? Currently implemented: • as dosages (rounded to two decimal places), the default, • as hard calls, randomly sampled based on those probabilities (similar to PLINK option '--hard-call-threshold random').
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Details

For more information on this format, please visit BGEN webpage.

This function is designed to read UK Biobank imputation files. This assumes that variants have been compressed with zlib, that there are only 2 possible alleles, and that each probability is stored on 8 bits. For example, if you use *qctool* to generate your own BGEN files, please make sure you are using options '`-ofiletype bgen_v1.2 -bgen-bits 8 -assume-chromosome`'.

If the format is not the expected one, this will result in an error or even a crash of your R session. Another common source of error is due to corrupted files; e.g. if using UK Biobank files, compare the result of `tools::md5sum()` with the ones at `https://biobank.ndph.ox.ac.uk/ukb/refer.cgi?id=998`.

You can look at some example code from my papers on how to use this function:

- `https://github.com/privefl/paper-infer/blob/main/code/prepare-geno-simu.R`
- `https://github.com/privefl/paper-misspec/blob/main/code/prepare-genotypes.R`

Value

The path to the RDS file `<backingfile>.rds` that stores the `bigSNP` object created by this function. Note that this function creates another file (*.bk*) that stores the values of the FBM (`$genotypes`). The rows corresponds to the order of `ind_row`; the columns to the order of `list_snp_id`. The `$map` component of the `bigSNP` object stores some information on the variants (including allele frequencies and INFO scores computed from the imputation probabilities). However, it does not have a `$fam` component; you should use the individual IDs in the *.sample* file (filtered with `ind_row`) to add external information on the individuals.
You shouldn't read from BGEN files more than once. Instead, use snp_attach to load the "bigSNP" object in any R session from backing files.

`snp_readBGI` *Read variant info from one BGI file*

Description

Read variant info from one BGI file

Usage

```
snp_readBGI(bgifile, snp_id = NULL)
```

Arguments

`bgifile`	Path to one file with extension ".bgi".
`snp_id`	Character vector of SNP IDs. These should be in the form `"<chr>_<pos>_<a1>_<a2>"` (e.g. `"1_88169_C_T"` or `"01_88169_C_T"`). **This function assumes that these IDs are uniquely identifying variants.** Default is `NULL`, and returns information on all variants.

Value

A data frame containing variant information.

`snp_save` *Save modifications*

Description

Save a `bigSNP` after having made some modifications to it. As `bigSNP` is an S3 class, you can add any slot you want to an object of this class, then use `snp_save` to save these modifications in the corresponding ".rds" backing file.

Usage

```
snp_save(x, version = NULL)
```

Arguments

`x`	A bigSNP.
`version`	the workspace format version to use. `NULL` specifies the current default version (3). The only other supported value is 2, the default from R 1.4.0 to R 3.5.0.

Value

The (saved) `bigSNP`.

Examples

```
set.seed(1)

# Reading example
test <- snp_attachExtdata()

# I can add whatever I want to an S3 class
test$map$`p-values` <- runif(nrow(test$map))
str(test$map)

# Reading again
rds <- test$genotypes$rds
test2 <- snp_attach(rds)
str(test2$map) # new slot wasn't saved

# Save it
snp_save(test)

# Reading again
test3 <- snp_attach(rds)
str(test3$map) # it is saved now
```

```
# The complicated code of this function
snp_save
```

`snp_scaleAlpha` *Binomial(n, p) scaling*

Description

Binomial(n, p) scaling where `n` is fixed and `p` is estimated.

Usage

```
snp_scaleAlpha(alpha = -1)

snp_scaleBinom(nploidy = 2)
```

Arguments

`alpha`	Assumes that the average contribution (e.g. heritability) of a SNP of frequency p is proportional to $[2p(1-p)]^{1+\alpha}$. The `center` is then $2p$ and the `scale` is $[2p(1-p)]^{-\alpha/2}$. Default is `-1`.
`nploidy`	Number of trials, parameter of the binomial distribution. Default is `2`, which corresponds to diploidy, such as for the human genome.

Details

You will probably not use this function as is but as the `fun.scaling` parameter of other functions of package `bigstatsr`.

Value

A new **function** that returns a data.frame of two vectors "center" and "scale" which are of the length of `ind.col`.

References

This scaling is widely used for SNP arrays. Patterson N, Price AL, Reich D (2006). Population Structure and Eigenanalysis. PLoS Genet 2(12): e190. doi:10.1371/journal.pgen.0020190.

Examples

```
set.seed(1)

a <- matrix(0, 93, 170)
p <- 0.2
a[] <- rbinom(length(a), 2, p)
X <- add_code256(big_copy(a, type = "raw"), code = c(0, 1, 2, rep(NA, 253)))
```

```
X.svd <- big_SVD(X, fun.scaling = snp_scaleBinom())
str(X.svd)
plot(X.svd$center)
abline(h = 2 * p, col = "red")
plot(X.svd$scale)
abline(h = sqrt(2 * p * (1 - p)), col = "red")
```

---

snp_simuPheno *Simulate phenotypes*

Description

Simulate phenotypes using a linear model. When a prevalence is given, the liability threshold is used to convert liabilities to a binary outcome. The genetic and environmental liabilities are scaled such that the variance of the genetic liability is exactly equal to the requested heritability, and the variance of the total liability is equal to 1.

Usage

```
snp_simuPheno(
  G,
  h2,
  M,
  K = NULL,
  alpha = -1,
  ind.row = rows_along(G),
  ind.possible = cols_along(G),
  prob = NULL,
  effects.dist = c("gaussian", "laplace"),
  ncores = 1
)
```

Arguments

G	A FBM.code256 (typically <bigSNP>$genotypes). **You shouldn't have missing values.** Also, remember to do quality control, e.g. some algorithms in this package won't work if you use SNPs with 0 MAF.
h2	Heritability.
M	Number of causal variants.
K	Prevalence. Default is NULL, giving a continuous trait.
alpha	Assumes that the average contribution (e.g. heritability) of a SNP of frequency p is proportional to $[2p(1-p)]^{1+\alpha}$. Default is -1.
ind.row	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
ind.possible	Indices of possible causal variants.

prob	Vector of probability weights for sampling causal indices. It can have 0s (discarded) and is automatically scaled to sum to 1. Default is NULL (all indices have the same probability).
effects.dist	Distribution of effects. Either "gaussian" (the default) or "laplace".
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().

Value

A list with 3 elements:

- $pheno: vector of phenotypes,
- $set: indices of causal variants,
- $effects: effect sizes (of scaled genotypes) corresponding to set.
- $allelic_effects: effect sizes, but on the allele scale (0|1|2).

---

snp_split *Split-parApply-Combine*

Description

A Split-Apply-Combine strategy to parallelize the evaluation of a function on each SNP, independently.

Usage

```
snp_split(infos.chr, FUN, combine, ncores = 1, ...)
```

Arguments

infos.chr	Vector of integers specifying each SNP's chromosome. Typically <bigSNP>mapchromosome.
FUN	The function to be applied. It must take a FBM.code256 as first argument and ind.chr, an another argument to provide subsetting over SNPs. You can access the number of the chromosome by using attr(ind.chr, "chr").
combine	function that is used by foreach::foreach to process the tasks results as they generated. This can be specified as either a function or a non-empty character string naming the function. Specifying 'c' is useful for concatenating the results into a vector, for example. The values 'cbind' and 'rbind' can combine vectors into a matrix. The values '+' and '*' can be used to process numeric data. By default, the results are returned in a list.
ncores	Number of cores used. Default doesn't use parallelism. You may use bigstatsr::nb_cores().
...	Extra arguments to be passed to FUN.

Details

This function splits indices for each chromosome, then apply a given function to each part (chromosome) and finally combine the results.

Value

The result of foreach::foreach.

Examples

```
# parallelize over chromosomes made easy
# examples of functions from this package
snp_pruning
snp_clumping
snp_fastImpute
```

---

snp_subset *Subset a bigSNP*

Description

Subset (copy) of a bigSNP, also stored on disk.

Usage

```
snp_subset(
  x,
  ind.row = rows_along(x$genotypes),
  ind.col = cols_along(x$genotypes),
  backingfile = NULL
)

## S3 method for class 'bigSNP'
subset(
  x,
  ind.row = rows_along(x$fam),
  ind.col = rows_along(x$map),
  backingfile = NULL,
  ...
)
```

Arguments

x	A bigSNP.
ind.row	Indices of the rows (individuals) to keep. Negative indices **can** be used to exclude row indices. Default: keep them all.
ind.col	Indices of the columns (SNPs) to keep. Negative indices **can** be used to exclude column indices. Default: keep them all.
backingfile	Prefix of the two new files created (".bk" and ".rds"). By default, it is automatically determined by appending "_sub" and a number to the prefix of the input bigSNP backing files.
...	Not used.

Value

The path to the RDS file that stores the bigSNP object.

See Also

bigSNP

Examples

```
str(test <- snp_attachExtdata())

# keep only first 50 samples and SNPs
rdsfile <- snp_subset(test, ind.row = 1:50, ind.col = 1:50)
str(snp_attach(rdsfile))

# remove only first 50 samples and SNPs
rdsfile2 <- snp_subset(test, ind.row = -(1:50), ind.col = -(1:50))
str(snp_attach(rdsfile2))
```

---

snp_thr_correct *Thresholding and correction*

Description

P-value thresholding and correction of summary statistics for winner's curse.

Usage

```
snp_thr_correct(beta, beta_se, lpS, thr_lpS)
```

Arguments

beta	Vector of effect sizes.
beta_se	Vector of standard errors for beta. Either beta_se or lpS must be provided.
lpS	Vector of -log10(p-value) associated with beta. Either beta_se or lpS must be provided.
thr_lpS	Threshold on lpS (-log10(p-value) at which variants are excluded if they not significant enough.

Value

beta after p-value thresholding and shrinkage.

References

Zhong, H., & Prentice, R. L. (2008). Bias-reduced estimators and confidence intervals for odds ratios in genome-wide association studies. Biostatistics, 9(4), 621-634.

Examples

```
beta <- rnorm(1000)
beta_se <- runif(1000, min = 0.3, max = 0.5)
new_beta <- snp_thr_correct(beta, beta_se = beta_se, thr_lpS = 1)
plot(beta / beta_se, new_beta / beta_se, pch = 20); abline(0, 1, col = "red")
plot(beta, new_beta, pch = 20); abline(0, 1, col = "red")

# Can provide -log10(p-values) instead of standard errors
lpval <- -log10(pchisq((beta / beta_se)^2, df = 1, lower.tail = FALSE))
new_beta2 <- snp_thr_correct(beta, lpS = lpval, thr_lpS = 1)
all.equal(new_beta2, new_beta)
```

---

snp_writeBed *Write PLINK files from a "bigSNP"*

Description

Function to write bed/bim/fam files from a bigSNP. This will use the slot `code` **rounded** to write 0s, 1s, 2s or NAs.

Usage

```
snp_writeBed(x, bedfile, ind.row = rows_along(G), ind.col = cols_along(G))
```

Arguments

`x`	A bigSNP.
`bedfile`	Path to file with extension ".bed" to create.
`ind.row`	An optional vector of the row indices (individuals) that are used. If not specified, all rows are used. **Don't use negative indices.**
`ind.col`	An optional vector of the column indices (SNPs) that are used. If not specified, all columns are used. **Don't use negative indices.**

Value

The input `bedfile` path.

Examples

```
N <- 17
M <- 911

fake <- snp_fake(N, M)
G <- fake$genotypes
```

```
G[] <- sample(as.raw(0:3), size = length(G), replace = TRUE)

# Write the object as a bed/bim/fam object
tmp <- tempfile(fileext = ".bed")
bed <- snp_writeBed(fake, tmp)

# Read this new file for the first time
rds <- snp_readBed(bed, backingfile = tempfile())
# Attach object in R session
fake2 <- snp_attach(rds)

# Same content
all.equal(fake$genotypes[], fake2$genotypes[])
all.equal(fake$fam, fake2$fam)
all.equal(fake$map, fake2$map)

# Two different backingfiles
fake$genotypes$backingfile
fake2$genotypes$backingfile
```

---

sub_bed *Replace extension '.bed'*

Description

Replace extension '.bed'

Usage

```
sub_bed(path, replacement = "", stop_if_not_ext = TRUE)
```

Arguments

path	String with extension '.bed'.
replacement	Replacement of '.bed'. Default replaces by nothing. Can be useful to replace e.g. by '.bim' or '.fam'.
stop_if_not_ext	If `replacement != ""`, whether to error if replacement is not an extension (starting with a '.').

Value

String with extension '.bed' replaced by `replacement`.

Examples

```
path <- "toto.bed"
sub_bed(path)
sub_bed(path, ".bim")
sub_bed(path, ".fam")
sub_bed(path, "_QC", stop_if_not_ext = FALSE)
```

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