Package 'ApplyPolygenicScore'

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Type Package

Title Utilities for the Application of a Polygenic Score to a VCF

Version 4.0.2

Description Simple and transparent parsing of genotype/dosage data
from an input Variant Call Format (VCF) file, matching of genotype
coordinates to the component Single Nucleotide Polymorphisms (SNPs)
of an existing polygenic score (PGS), and application of SNP weights
to dosages for the calculation of a polygenic score for each individual
in accordance with the additive weighted sum of dosages model. Methods
are designed in reference to best practices described by
Collister, Liu, and Clifton (2022) <doi:10.3389/fgene.2022.818574>.

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Author Paul Boutros [cre],
Nicole Zeltser [aut] (ORCID: <https://orcid.org/0000-0001-7246-2771>),
Rachel Dang [ctb],
Raag Agrawal [ctb]

Maintainer Paul Boutros <PBoutros@sbpdiscovery.org>

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Contents

`analyze.pgs.binary.predictiveness`
Analyze PGS Predictiveness for Binary Phenotypes

Description

This function performs logistic regression to evaluate the predictiveness of polygenic scores for binary or continuous phenotypes. For continuous phenotypes, it converts them to binary based on a specified cutoff threshold. It calculates and returns AUC, Odds Ratios (OR), and p-values for each PGS. Corresponding ROC curves are plotted automatically.

Usage

```
analyze.pgs.binary.predictiveness(
  pgs.data,
  pgs.columns,
  phenotype.columns,
  covariate.columns = NULL,
  phenotype.type = "binary",
  cutoff.threshold = NULL,
  output.dir = NULL,
  filename.prefix = NULL,
```

```
  file.extension = "png",
  width = 8,
  height = 8,
  xaxes.cex = 1.5,
  yaxes.cex = 1.5,
  titles.cex = 1.5
)
```

Arguments

pgs.data	A data frame containing the PGS, phenotype, and covariate columns.
pgs.columns	A character vector specifying the names of the PGS columns in pgs.data to be analyzed. All specified columns must be numeric.
phenotype.columns	A character vector specifying the names of the phenotype columns in data to be analyzed. If binary phenotypes are specified, they must be factors with two levels (0 and 1).
covariate.columns	A character vector specifying the names of covariate columns in data to be included in the regression model. Default is NULL.
phenotype.type	A character string specifying the type of phenotype. Must be either 'continuous' or 'binary'. All provided phenotype columns must match this type.
cutoff.threshold	A numeric value or a named list specifying the cutoff threshold for converting continuous phenotypes to binary. If a named list, it must contain entries for each continuous phenotype.
output.dir	A character string specifying the directory where the ROC plots will be saved. If NULL, no plots are saved.
filename.prefix	A character string specifying the prefix for the output filenames. If NULL, defaults to 'ApplyPolygenicScore-Plot'.
file.extension	A character string specifying the file extension for the output plots. Default is 'png'.
width	Numeric value specifying the width of the output plot in inches.
height	Numeric value specifying the height of the output plot in inches.
xaxes.cex	Numeric size for all x-axis labels.
yaxes.cex	Numeric size for all y-axis labels.
titles.cex	Numeric size for all plot titles.

Value

A list containing a data frame of logistic regression results and a plot object of corresponding ROC curves.

Output Formatting

results.df	A data frame with columns:

- phenotype: Name of the phenotype column.
- PGS: Name of the PGS column.
- AUC: Area Under the Reciever Operator Curve.
- OR: Odds Ratio for the PGS from logistic regression.
- OR.Lower.CI: Lower 95
- OR.Upper.CI: Upper 95
- p.value: P-value for the PGS coefficient.

Values for AUC, OR, OR.Lower.CI, OR.Upper.CI, and p.value may be NA if model fitting or ROC calculation fails (e.g., due to no complete cases, no variance in PGS, or ROC calculation errors).

roc.plot A multipanelplot object (from BoutrosLab.plotting.general) if output.dir is NULL, otherwise NULL if plots are saved to file.

Each phenotype is plotted in a separate panel, with ROC curves for each PGS specified in pgs.columns.

Examples

```
set.seed(100);

pgs.data <- data.frame(
    PGS = rnorm(100, 0, 1),
    continuous.phenotype = rnorm(100, 2, 1),
    binary.phenotype = sample(c(0, 1), 100, replace = TRUE),
    covariate1 = rnorm(100, 0, 1)
    );
 temp.dir <- tempdir();

# Basic analysis with binary phenotype
analyze.pgs.binary.predictiveness(
    pgs.data,
    output.dir = temp.dir,
    filename.prefix = 'basic-plot',
    pgs.columns = 'PGS',
    phenotype.columns = 'binary.phenotype',
    phenotype.type = 'binary',
    covariate.columns = 'covariate1',
    width = 6,
    height = 6
    );

# Analysis with continuous phenotype and cutoff threshold
analyze.pgs.binary.predictiveness(
   pgs.data,
   output.dir = temp.dir,
   filename.prefix = 'continuous-plot',
   pgs.columns = 'PGS',
   phenotype.columns = 'continuous.phenotype',
   phenotype.type = 'continuous',
   cutoff.threshold = 1.5, # Convert to binary using this threshold
   covariate.columns = NULL,
```

```
  width = 6,
  height = 6
  );
```

`apply.polygenic.score` *Apply polygenic score to VCF data*

Description

Apply a polygenic score model to VCF data.

Usage

```
apply.polygenic.score(
  vcf.data,
  vcf.long.format = FALSE,
  pgs.weight.data,
  phenotype.data = NULL,
  phenotype.analysis.columns = NULL,
  correct.strand.flips = TRUE,
  remove.ambiguous.allele.matches = FALSE,
  max.strand.flips = 0,
  remove.mismatched.indels = FALSE,
  output.dir = NULL,
  file.prefix = NULL,
  missing.genotype.method = "mean.dosage",
  use.external.effect.allele.frequency = FALSE,
  n.percentiles = NULL,
  analysis.source.pgs = NULL,
  validate.inputs.only = FALSE
)
```

Arguments

`vcf.data`	VCF genotype data as formatted by `import.vcf()`. Two formats are accepted: wide format (a list of elements named `genotyped.alleles` and `vcf.fixed.fields`) or long format(a data frame). See `vcf.import` for more details.
`vcf.long.format`	A logical indicating whether `vcf.data` is provided in long format. Default is `FALSE`.
`pgs.weight.data`	A data.frame containing PGS weight data as formatted by `import.pgs.weight.file()`.
`phenotype.data`	A data.frame containing phenotype data. Must have an Indiv column matching vcf.data. Default is `NULL`.

phenotype.analysis.columns
: A character vector of phenotype columns from phenotype.data to analyze in a regression analsyis. Default is NULL. Phenotype variables are automatically classified as continuous, binary, or neither based on data type and number of unique values. The calculated PGS is associated with each phenotype variable using linear or logistic regression for continuous or binary phenotypes, respectively. See run.pgs.regression for more details. If no phenotype.analysis.columns are provided, no regression analysis is performed.

correct.strand.flips
: A logical indicating whether to check PGS weight data/VCF genotype data matches for strand flips and correct them. Default is TRUE. The PGS catalog standard column other_allele in pgs.weight.data is required for this check.

remove.ambiguous.allele.matches
: A logical indicating whether to remove PGS variants with ambiguous allele matches between PGS weight data and VCF genotype data. Default is FALSE. The PGS catalog standard column other_allele in pgs.weight.data is required for this check.

max.strand.flips
: An integer indicating the number of unambiguous strand flips that need to be detected in order to discard all variants with ambiguous allele matches. Only applies if return.ambiguous.as.missing == TRUE. Default is 0 which means that all ambiguous variants are removed regardless of the status of any other variant.

remove.mismatched.indels
: A logical indicating whether to remove indel variants that are mismatched between PGS weight data and VCF genotype data. Default is FALSE. The PGS catalog standard column other_allele in pgs.weight.data is required for this check.

output.dir
: A character string indicating the directory to write output files. Separate files are written for per-sample pgs results and optional regression results. Files are tab-separate .txt files. Default is NULL in which case no files are written.

file.prefix
: A character string to prepend to the output file names. Default is NULL.

missing.genotype.method
: A character string indicating the method to handle missing genotypes. Options are "mean.dosage", "normalize", or "none". Default is "mean.dosage".

use.external.effect.allele.frequency
: A logical indicating whether to use an external effect allele frequency for calculating mean dosage when handling missing genotypes. Default is FALSE. Provide allele frequency as a column is pgs.weight.data named allelefrequency_effect.

n.percentiles
: An integer indicating the number of percentiles to calculate for the PGS. Default is NULL.

analysis.source.pgs
: A character string indicating the source PGS for percentile calculation and regression analyses. Options are "mean.dosage", "normalize", or "none". When not specified, defaults to missing.genotype.method choice and if more than one PGS missing genotype method is chosen, calculation defaults to the first selection.

validate.inputs.only
: A logical indicating whether to only perform input data validation checks without running PGS application. If no errors are triggered, a message is printed and TRUE is returned. Default is FALSE.

Value

A list containing per-sample PGS output and per-phenotype regression output if phenotype analysis columns are provided.

Output Structure

The outputed list contains the following elements:

- pgs.output: A data.frame containing the PGS per sample and optional phenotype data.
- regression.output: A data.frame containing the results of the regression analysis if phenotype.analysis.columns are provided, otherwise NULL.

pgs.output columns:

- Indiv: A character string indicating the sample ID.
- PGS: A numeric vector indicating the PGS per sample. (only if missing.genotype.method includes "none")
- PGS.with.normalized.missing: A numeric vector indicating the PGS per sample with missing genotypes normalized. (only if missing.genotype.method includes "normalize")
- PGS.with.replaced.missing: A numeric vector indicating the PGS per sample with missing genotypes replaced by mean dosage. (only if missing.genotype.method includes "mean.dosage")
- percentile: A numeric vector indicating the percentile rank of the PGS.
- decile: A numeric vector indicating the decile rank of the PGS.
- quartile: A numeric vector indicating the quartile rank of the PGS.
- percentile.X: A numeric vector indicating the user-specified percentile rank of the PGS where "X" is substituted by n.percentiles. (only if n.percentiles is specified)
- n.missing.genotypes: A numeric vector indicating the number of missing genotypes per sample.
- percent.missing.genotypes: A numeric vector indicating the percentage of missing genotypes per sample.
- All columns in phenotype.data if provided.

regression.output columns:

- phenotype: A character vector of phenotype names.
- model: A character vector indicating the regression model used. One of "logistic.regression" or "linear.regression".
- beta: A numeric vector indicating the beta coefficient of the regression analysis.
- se: A numeric vector indicating the standard error of the beta coefficient.
- p.value: A numeric vector indicating the p-value of the beta coefficient.

- `r.squared`: A numeric vector indicating the r-squared value of linear regression analysis. NA for logistic regression.
- `AUC`: A numeric vector indicating the area under the curve of logistic regression analysis. NA for linear regression.

PGS Calculation

PGS for each individual *i* is calculated as the sum of the product of the dosage and beta coefficient for each variant in the PGS:

$$PGS_i = \sum_{m=1}^{M} (\beta_m \times dosage_{im})$$

Where *m* is a PGS component variant out of a total *M* variants.

Missing Genotype Handling

VCF genotype data are matched to PGS data by chromosome and position. If a SNP cannot be matched by genomic coordinate, an attempt is made to match by rsID (if available). If a SNP from the PGS weight data is not found in the VCF data after these two matching attempts, it is considered a cohort-wide missing variant.

Missing genotypes (in individual samples) among successfully matched variants are handled by three methods:

`none`: Missing genotype dosages are excluded from the PGS calculation. This is equivalent to assuming that all missing genotypes are homozygous for the non-effect allele, resulting in a dosage of 0.

`normalize`: Missing genotypes are excluded from score calculation but the final score is normalized by the number of non-missing alleles. The calculation assumes a diploid genome:

$$PGS_i = \frac{\sum (\beta_m \times dosage_{im})}{P_i * M_{non-missing}}$$

Where *P* is the ploidy and has the value `2` and $M_{non-missing}$ is the number of non-missing genotypes.

`mean.dosage`: Missing genotype dosages are replaced by the mean population dosage of the variant which is calculated as the product of the effect allele frequency *EAF* and the ploidy of a diploid genome:

$$\overline{dosage_k} = EAF_k * P$$

where *k* is a PGS component variant that is missing in between 1 and n-1 individuals in the cohort and *P* = ploidy = 2 This dosage calculation holds under assumptions of Hardy-Weinberg equilibrium. By default, the effect allele frequency is calculated from the provided VCF data. For variants that are missing in all individuals (cohort-wide), dosage is assumed to be zero (homozygous non-reference) for all individuals. An external allele frequency can be provided in the `pgs.weight.data` as a column named `allelefrequency_effect` and by setting `use.external.effect.allele.frequency` to `TRUE`.

Multiallelic Site Handling

If a PGS weight file provides weights for multiple effect alleles, the appropriate dosage is calculated for the alleles that each individual carries. It is assumed that multiallelic variants are encoded in the same row in the VCF data. This is known as "merged" format. Split multiallelic sites are not

accepted. VCF data can be formatted to merged format using external tools for VCF file manipulation.

Allele Mismatch Handling Variants from the PGS weight data are merged with records in the VCF data by genetic coordinate. After the merge is complete, there may be cases where the VCF reference (REF) and alternative (ALT) alleles do not match their conventional counterparts in the PGS weight data (other allele and effect allele, respectively). This is usually caused by a strand flip: the variant in question was called against opposite DNA reference strands in the PGS training data and the VCF data. Strand flips can be detected and corrected by flipping the affected allele to its reverse complement. `apply.polygenic.score` uses `assess.pgs.vcf.allele.match` to assess allele concordance, and is controlled through the following arguments:

- `correct.strand.flips`: When `TRUE`, detected strand flips are corrected by flipping the affected value in the `effect_allele` column prior to dosage calling.
- `remove.ambiguous.allele.matches`: Corresponds to the `return.ambiguous.as.missing` argument in `assess.pgs.vcf.allele.match`. When `TRUE`, non-INDEL allele mismatches that cannot be resolved (due to palindromic alleles or causes other than strand flips) are removed by marking the affected value in the `effect_allele` column as missing prior to dosage calling and missing genotype handling. The corresponding dosage is set to NA and the variant is handled according to the chosen missing genotype method.
- `max.strand.flips`: This argument only applies when `remove.ambiguous.allele.matches` is on and modifies its behavior. In cases where none or very few unambiguous strand flips are detected, it is likely that all ambiguous allele matches are simply palindromic effect size flips. This option facilitates handling of ambiguous allele matches conditional on a maximum number of unambiguous strand flips. Variants with ambiguous strand flips will be marked as missing only if the number of unambiguous strand flips is greater than or equal to `max.strand.flips`.
- `remove.mismatched.indels`: Corresponds to the `return.indels.as.missing` argument in `assess.pgs.vcf.allele.match`. When `TRUE`, INDEL allele mismatches (which cannot be assessed for strand flips) are removed by marking the affected value in the `effect_allele` column as missing prior to dosage calling and missing genotype handling. The corresponding dosage is set to NA and the variant is handled according to the chosen missing genotype method.

Note that an allele match assessment requires the presence of both the `other_allele` and `effect_allele` in the PGS weight data. The `other_allele` column is not required by the PGS Catalog, and so is not always available.

Examples

```
# Example VCF
vcf.path <- system.file(
    'extdata',
    'HG001_GIAB.vcf.gz',
    package = 'ApplyPolygenicScore',
    mustWork = TRUE
    );
vcf.import <- import.vcf(vcf.path, long.format = TRUE);

# Example pgs weight file
```

```
pgs.weight.path <- system.file(
    'extdata',
    'PGS000662_hmPOS_GRCh38.txt.gz',
    package = 'ApplyPolygenicScore',
    mustWork = TRUE
    );
pgs.import <- import.pgs.weight.file(pgs.weight.path);

pgs.data <- apply.polygenic.score(
    vcf.data = vcf.import$split.wide.vcf.matrices,
    pgs.weight.data = pgs.import$pgs.weight.data,
    missing.genotype.method = 'none'
    );

# Use long format
pgs.data <- apply.polygenic.score(
    vcf.data = vcf.import$combined.long.vcf.df$dat,
    vcf.long.format = TRUE,
    pgs.weight.data = pgs.import$pgs.weight.data,
    missing.genotype.method = 'none'
    );

# Specify different methods for handling missing genotypes
pgs.import$pgs.weight.data$allelefrequency_effect <- rep(0.5, nrow(pgs.import$pgs.weight.data));
pgs.data <- apply.polygenic.score(
    vcf.data = vcf.import$split.wide.vcf.matrices,
    pgs.weight.data = pgs.import$pgs.weight.data,
    missing.genotype.method = c('none', 'mean.dosage', 'normalize'),
    use.external.effect.allele.frequency = TRUE
    );

# Specify allele mismatch handling
pgs.data <- apply.polygenic.score(
   vcf.data = vcf.import$split.wide.vcf.matrices,
   pgs.weight.data = pgs.import$pgs.weight.data,
   correct.strand.flips = TRUE,
   remove.ambiguous.allele.matches = TRUE,
   remove.mismatched.indels = FALSE
   );

# Provide phenotype data for basic correlation analysis
n.samples <- length(colnames(vcf.import$split.wide.vcf.matrices$genotyped.alleles))
phenotype.data <- data.frame(
    Indiv = colnames(vcf.import$split.wide.vcf.matrices$genotyped.alleles),
    continuous.phenotype = rnorm(n.samples),
    binary.phenotype = sample(
        c('a', 'b'),
        n.samples,
        replace = TRUE
        )
    );

pgs.data <- apply.polygenic.score(
```

```
    vcf.data = vcf.import$split.wide.vcf.matrices,
    pgs.weight.data = pgs.import$pgs.weight.data,
    phenotype.data = phenotype.data
    );

# Only run validation checks on input data and report back
apply.polygenic.score(
    vcf.data = vcf.import$split.wide.vcf.matrices,
    pgs.weight.data = pgs.import$pgs.weight.data,
    validate.inputs.only = TRUE
    );
```

`assess.pgs.vcf.allele.match` *Assess PGS allele match to VCF allele*

Description

Assess whether PGS reference and effect alleles match provided VCF reference and alternative alleles. Mismatches are checked for potential switching of effect and reference PGS alleles (cases where the effect allele is the REF VCF allele) and are evaluated for DNA strand flips (by flipping the PGS alleles). INDEL alleles are not supported for strand flip assessment.

Usage

```
assess.pgs.vcf.allele.match(
  vcf.ref.allele,
  vcf.alt.allele,
  pgs.ref.allele,
  pgs.effect.allele,
  return.indels.as.missing = FALSE,
  return.ambiguous.as.missing = FALSE,
  max.strand.flips = 0
)
```

Arguments

`vcf.ref.allele`	A character vector of singular VCF reference (REF) alleles.
`vcf.alt.allele`	A character vector of VCF alternative (ALT) alleles. Multiple alleles at a multi-allelic site must be separated by commas.
`pgs.ref.allele`	A character vector of singular PGS reference alleles aka "non-effect" or "other" alleles.
`pgs.effect.allele`	A character vector of singular PGS effect alleles.
`return.indels.as.missing`	A logical value indicating whether to return NA for INDEL alleles with detected mismatches. Default is `FALSE`.

`return.ambiguous.as.missing`
: A logical value indicating whether to return NA for ambiguous cases where both a strand flip and effect switch are possible, or no strand flip is detected and a mismatch cannot be resolved. Default is `FALSE`.

`max.strand.flips`
: An integer indicating the number of non-ambiguous strand flips that must be present to implement the discarding all allele matches labeled "ambiguous_flip". Only applies if `return.ambiguous.as.missing == TRUE`. Defaults to `0`, meaning that no strand flips are allowed. Allele matches labeled "unresolved_mismatch" are not affected by this parameter.

Value

A list containing the match assessment, a new PGS effect allele, and a new PGS other allele.

Output Structure

The outputed list contains the following elements:

- `match.status`: A character vector indicating the match status for each pair of allele pairs. Possible values are `default_match`, `effect_switch`, `strand_flip`, `effect_switch_with_strand_flip`, `ambiguous_flip`, `indel_mismatch`, and `unresolved_mismatch`.
- `new.pgs.effect.allele`: A character vector of new PGS effect alleles based on the match status. If the match status is `default_match`, `effect_switch` or `missing_allele`, the original PGS effect allele is returned. If the match status is `strand_flip` or `effect_switch_with_strand_flip` the flipped PGS effect allele is returned. If the match status is `ambiguous_flip`, `indel_mismatch`, or `unresolved_mismatch`, the return value is either the original allele or NA as dictated by the `return.indels.as.missing`, `return.ambiguous.as.missing`, and `max.strand.flips` parameters.
- `new.pgs.other.allele`: A character vector of new PGS other alleles based on the match status, following the same logic as `new.pgs.effect.allele`.

The match.status output indicates the following:

- `default_match`: The default PGS reference allele matches the VCF REF allele and the default PGS effect allele matches one of the VCF ALT alleles.
- `effect_switch`: The PGS effect allele matches the VCF REF allele and the PGS reference allele matches one of the VCF ALT alleles.
- `strand_flip`: The PGS reference and effect alleles match their respective VCF pairs when flipped.
- `effect_switch_with_strand_flip`: The PGS effect allele matches the VCF REF allele and the PGS reference allele matches one of the VCF ALT alleles when flipped.
- `ambiguous_flip`: Both an effect switch and a strand flip have been detected. This is an ambiguous case caused by palindromic SNPs.
- `indel_mismatch`: A mismatch was detected between pairs of alleles where at least one was an INDEL. INDEL alleles are not supported for strand flip assessment.
- `unresolved_mismatch`: A mismatch was detected between pairs of non-INDEL alleles that could not be resolved by an effect switch or flipping the PGS alleles.
- `missing_allele`: One of the four alleles is missing, making it impossible to assess the match.

Examples

```
# Example data demonstrating the following cases in each vector element:
# 1. no strand flips
# 2. effect allele switch
# 3. strand flip
# 4. effect allele switch AND strand flip
# 5. palindromic (ambiguous) alleles
# 6. unresolved mismatch
vcf.ref.allele <- c('A', 'A', 'A', 'A', 'A', 'A');
vcf.alt.allele <- c('G', 'G', 'G', 'G', 'T', 'G');
pgs.ref.allele <- c('A', 'G', 'T', 'C', 'T', 'A');
pgs.effect.allele <- c('G', 'A', 'C', 'T', 'A', 'C');
assess.pgs.vcf.allele.match(vcf.ref.allele, vcf.alt.allele, pgs.ref.allele, pgs.effect.allele);
```

---

check.pgs.weight.columns

Check PGS weight file columns

Description

Check that a PGS weight file contains the required columns for PGS application with `apply.polygenic.score`.

Usage

```
check.pgs.weight.columns(pgs.weight.colnames, harmonized = TRUE)
```

Arguments

`pgs.weight.colnames`	A character vector of column names.
`harmonized`	A logical indicating whether the presence of harmonized columns should be checked.

Value

A logical indicating whether the file contains the required columns.

`combine.pgs.bed` *Combine PGS BED files*

Description

Merge overlapping PGS coordinates in multiple BED files.

Usage

```
combine.pgs.bed(
  pgs.bed.list,
  add.annotation.data = FALSE,
  annotation.column.index = 4,
  slop = 0
)
```

Arguments

`pgs.bed.list`	A named list of data.frames containing PGS coordinates in BED format.
`add.annotation.data`	A logical indicating whether an additional annotation data column should be added to the annotation column.
`annotation.column.index`	An integer indicating the index of the column in the data frames in `pgs.bed.list` that should be added to the annotation column.
`slop`	An integer indicating the number of base pairs to add to the BED interval on either side.

Value

A data.frame containing the merged PGS coordinates in BED format with an extra annotation column containing the name of the PGS and data from one additional column optionally selected by the user.

Examples

```
bed1 <- data.frame(
    chr = c(1, 2, 3),
    start = c(1, 2, 3),
    end = c(2, 3, 4),
    annotation = c('a', 'b', 'c')
    );
bed2 <- data.frame(
    chr = c(1, 2, 3),
    start = c(1, 20, 30),
    end = c(2, 21, 31),
    annotation = c('d', 'e', 'f')
    );
```

```
bed.input <- list(bed1 = bed1, bed2 = bed2);
combine.pgs.bed(bed.input);
```

`combine.vcf.with.pgs` *Combine VCF with PGS*

Description

Match PGS SNPs to corresponding VCF information by genomic coordinates or rsID using a merge operation.

Usage

```
combine.vcf.with.pgs(vcf.data, pgs.weight.data)
```

Arguments

`vcf.data`	A data frame/table containing VCF data. Required columns: `CHROM`, `POS`.
`pgs.weight.data`	A data frame/table containing PGS data. Required columns: `CHROM`, `POS`.

Value

A list containing a data.table of merged VCF and PGS data and a data.table of PGS SNPs missing from the VCF.

A primary merge is first performed on chromosome and base pair coordinates. For SNPs that could not be matched in the first mergs, a second merge is attempted by rsID if available. This action can account for short INDELs that can have coordinate mismatches between the PGS and VCF data. The merge is a left outer join: all PGS SNPs are kept as rows even if they are missing from the VCF, and all VCF SNPs that are not a component of the PGS are dropped. If no PGS SNPs are present in the VCF, the function will terminate with an error.

Examples

```
# Example VCF
vcf.path <- system.file(
    'extdata',
    'HG001_GIAB.vcf.gz',
    package = 'ApplyPolygenicScore',
    mustWork = TRUE
    );
vcf.import <- import.vcf(vcf.path);

# Example pgs weight file
pgs.weight.path <- system.file(
    'extdata',
    'PGS000662_hmPOS_GRCh38.txt.gz',
    package = 'ApplyPolygenicScore',
```

```
    mustWork = TRUE
    );
pgs.import <- import.pgs.weight.file(pgs.weight.path);

merge.data <- combine.vcf.with.pgs(
    vcf.data = vcf.import$split.wide.vcf.matrices$vcf.fixed.fields,
    pgs.weight.data = pgs.import$pgs.weight.data
    );
```

`convert.allele.frequency.to.dosage` *Convert allele frequency to mean dosage*

Description

Convert a population allele frequency to a mean dosage for that allele.

Usage

```
convert.allele.frequency.to.dosage(allele.frequency)
```

Arguments

`allele.frequency` A numeric vector of allele frequencies.

Value

A numeric vector of mean dosages for the allele frequencies.

Examples

```
allele.frequency <- seq(0.1, 0.9, 0.1);
convert.allele.frequency.to.dosage(allele.frequency);
```

`convert.alleles.to.pgs.dosage` *Convert alleles to dosage*

Description

Convert genotype calls in the form of witten out alleles (e.g. 'A/T') to dosages (0, 1, 2) based on provided risk alleles from a PGS.

Usage

```
convert.alleles.to.pgs.dosage(called.alleles, risk.alleles)
```

Arguments

called.alleles	A vector of genotypes in allelic notation separated by a slash or pipe.
risk.alleles	A vector of risk alleles from a polygenic score corresponding to each genotype (by locus) in called.alleles.

Value

A vector of dosages corresponding to each genotype in called.alleles. Hemizygous genotypes (one allele e.g. 'A') are counted as 1.

Examples

```
called.alleles <- c('A/A', 'A/T', 'T/T');
risk.alleles <- c('T', 'T', 'T');
convert.alleles.to.pgs.dosage(called.alleles, risk.alleles);
```

---

convert.pgs.to.bed *Convert PGS data to BED format*

Description

Convert imported and formatted PGS compnent SNP coordinate data to BED format.

Usage

```
convert.pgs.to.bed(
  pgs.weight.data,
  chr.prefix = TRUE,
  numeric.sex.chr = FALSE,
  slop = 0
)
```

Arguments

pgs.weight.data	A data.frame containing SNP coordinate data with standardized CHROM and POS columns.
chr.prefix	A logical indicating whether the 'chr' prefix should be used when formatting chromosome name.
numeric.sex.chr	A logical indicating whether the sex chromosomes should be formatted numerically, as opposed to alphabetically.
slop	An integer indicating the number of base pairs to add to the BED interval on either side.

Value

A data.frame containing the PGS component SNP coordinate data in BED format and any other columns provided in pgs.weight.data.

Examples

```
pgs.weight.data <- data.frame(
    CHROM = c('chr1', 'chrX'),
    POS = c(10, 20)
    );
convert.pgs.to.bed(pgs.weight.data);

# Switch between different chromosome notations
convert.pgs.to.bed(pgs.weight.data, chr.prefix = FALSE, numeric.sex.chr = TRUE);

# Add slop to BED intervals
convert.pgs.to.bed(pgs.weight.data, slop = 10);
```

---

create.pgs.boxplot *Plot PGS Boxplots*

Description

Plot boxplots of PGS data outputted by `apply.polygenic.score`. If phenotype columns are provided, multiple boxplots are plotted for automatically detected categories for each categorical variable.

Usage

```
create.pgs.boxplot(
  pgs.data,
  pgs.columns = NULL,
  phenotype.columns = NULL,
  add.stripplot = TRUE,
  jitter.factor = 1,
  output.dir = NULL,
  filename.prefix = NULL,
  file.extension = "png",
  tidy.titles = FALSE,
  alpha = 0.5,
  width = 10,
  height = 10,
  xaxes.cex = 1.5,
  yaxes.cex = 1.5,
  titles.cex = 1.5,
  border.padding = 1
)
```

Arguments

pgs.data	data.frame PGS data as formatted by apply.polygenic.score(). Required columns are at least one of PGS, PGS.with.replaced.missing, or PGS.with.normalized.missing. This function is designed to work with the output of apply.polygenic.score().
pgs.columns	character vector of column names indicating which columns in pgs.data to plot as PGSs. If NULL, defaults to recognized PGS columns: PGS, PGS.with.replaced.missing, and PGS.with.normalized.missing.
phenotype.columns	character vector of phenotype columns in pgs.data to plot (optional)
add.stripplot	logical whether to add a stripplot to the boxplot, defaults to TRUE
jitter.factor	numeric factor by which to scale the jitter (noise) applied to stripplot points, defaults to 1
output.dir	character directory to save output plots
filename.prefix	character prefix for output filenames
file.extension	character file extension for output plots
tidy.titles	logical whether to reformat PGS plot titles to remove periods
alpha	numeric alpha value for stripplot points, defaults to 0.5
width	numeric width of output plot in inches
height	numeric height of output plot in inches
xaxes.cex	numeric size for all x-axis labels
yaxes.cex	numeric size for all y-axis labels
titles.cex	numeric size for all plot titles
border.padding	numeric padding for plot borders

Value

If no output directory is provided, a multipanel lattice plot object is returned, otherwise a plot is written to the indicated path and NULL is returned.

Examples

```
set.seed(100);
pgs.data <- data.frame(
    PGS = rnorm(100, 0, 1)
    );
temp.dir <- tempdir();

# Basic Plot
create.pgs.boxplot(
   pgs.data,
   output.dir = temp.dir,
   filename.prefix = 'basic-plot',
   width = 6,
   height = 6
```

```
   );

# Plot multiple PGS outputs
pgs.data$PGS.with.normalized.missing <- rnorm(100, 1, 1);
create.pgs.boxplot(pgs.data, output.dir = temp.dir);

# Plot non-default PGS columns
pgs.data$PGS.custom <- rnorm(100, 2, 1);
create.pgs.boxplot(pgs.data, pgs.columns = 'PGS.custom', output.dir = temp.dir);
# Plot phenotype categories
pgs.data$sex <- sample(c('male', 'female'), 100, replace = TRUE);

create.pgs.boxplot(
    pgs.data,
    output.dir = temp.dir,
    filename.prefix = 'multiple-pgs',
    phenotype.columns = 'sex'
    );

# Plot multiple phenotypes
pgs.data$letters <- sample(letters[1:5], 100, replace = TRUE);

create.pgs.boxplot(
   pgs.data,
   output.dir = temp.dir,
   filename.prefix = 'multiple-phenotypes',
   phenotype.columns = c('sex', 'letters')
   );
```

`create.pgs.density.plot` *Plot PGS Density*

Description

Plot density curves of PGS data outputted by `apply.polygenic.score`. If phenotype columns are provided, multiple density curves are plotted for automatically detected categories for each categorical variable.

Usage

```
create.pgs.density.plot(
  pgs.data,
  pgs.columns = NULL,
  phenotype.columns = NULL,
  output.dir = NULL,
  filename.prefix = NULL,
  file.extension = "png",
```

```
  tidy.titles = FALSE,
  width = 10,
  height = 10,
  xaxes.cex = 1.5,
  yaxes.cex = 1.5,
  titles.cex = 1.5,
  key.cex = 1,
  border.padding = 1
)
```

Arguments

pgs.data	data.frame PGS data as formatted by apply.polygenic.score(). Required columns are at least one of PGS, PGS.with.replaced.missing, or PGS.with.normalized.missing. This function is designed to work with the output of apply.polygenic.score().
pgs.columns	character vector of column names indicating which columns in pgs.data to plot as PGSs. If NULL, defaults to recognized PGS columns: PGS, PGS.with.replaced.missing, and PGS.with.normalized.missing.
phenotype.columns	character vector of phenotype columns in pgs.data to plot (optional)
output.dir	character directory to save output plots
filename.prefix	character prefix for output filenames
file.extension	character file extension for output plots
tidy.titles	logical whether to reformat PGS plot titles to remove periods
width	numeric width of output plot in inches
height	numeric height of output plot in inches
xaxes.cex	numeric size for all x-axis labels
yaxes.cex	numeric size for all y-axis labels
titles.cex	numeric size for all plot titles
key.cex	numeric size of color key legend
border.padding	numeric padding for plot borders

Value

If no output directory is provided, a multipanel lattice plot object is returned, otherwise a plot is written to the indicated path and NULL is returned.

Examples

```
set.seed(100);
pgs.data <- data.frame(
    PGS = rnorm(100, 0, 1)
    );
 temp.dir <- tempdir();
```

```
# Basic Plot
create.pgs.density.plot(
    pgs.data,
    output.dir = temp.dir,
    filename.prefix = 'basic-plot',
    width = 6,
    height = 6
    );

# Plot multiple PGS outputs
pgs.data$PGS.with.normalized.missing <- rnorm(100, 1, 1);
create.pgs.density.plot(pgs.data, output.dir = temp.dir);

# Plot non-default PGS columns
pgs.data$PGS.custom <- rnorm(100, 2, 1);
create.pgs.density.plot(pgs.data, pgs.columns = 'PGS.custom', output.dir = temp.dir);

# Plot phenotype categories
pgs.data$sex <- sample(c('male', 'female'), size = 100, replace = TRUE);

create.pgs.density.plot(
    pgs.data,
    output.dir = temp.dir,
    filename.prefix = 'multiple-pgs',
    phenotype.columns = 'sex'
    );


# Plot multiple phenotypes
pgs.data$letters <- sample(letters[1:5], size = 100, replace = TRUE);

create.pgs.density.plot(
    pgs.data,
    output.dir = temp.dir,
    filename.prefix = 'multiple-phenotypes',
    phenotype.columns = c('sex', 'letters')
    );
```

`create.pgs.rank.plot` *Plot PGS Rank*

Description

Plot PGS percentile rank of each sample outputted by `apply.polygenic.score()` as a barplot, plot missing genotypes if any are present, plot corresponding decile and quartile markers as a heatmap, optionally plot phenotype covariates as color bars.

Usage

```
create.pgs.rank.plot(
  pgs.data,
  phenotype.columns = NULL,
  missing.genotype.style = "count",
  categorical.palette = NULL,
  binary.palette = NULL,
  output.dir = NULL,
  filename.prefix = NULL,
  file.extension = "png",
  width = 8,
  height = 8,
  xaxis.cex = 1.2,
  yaxis.cex = 1,
  titles.cex = 1.2,
  border.padding = 1
)
```

Arguments

pgs.data	data.frame PGS data as formatted by apply.polygenic.score() Required columns: Indiv, percentile, decile, quartile, n.missing.genotypes, percent.missing.genotypes, and optionally user-defined percentiles and phenotype covariates. This function is designed to work with the output of the function apply.polygenic.score().
phenotype.columns	character vector of column names in pgs.data containing phenotype covariates to plot as color bars. Default is NULL.
missing.genotype.style	character style of missing genotype barplot. Default is "count". Options are "count" or "percent".
categorical.palette	character vector of colors to use for categorical phenotype covariates. Default is NULL in which case the default palette is used, which contains 12 unique colors. If the number of unique categories exceeds the number of colors in the color palette, an error will be thrown.
binary.palette	character vector of colors to use for binary and continuous phenotype covariates. Each color is contrasted with white to create a color ramp or binary categories. Default is NULL in which case the default palette is used, which contains 9 unique colors paired with white. If the number of binary and continuous phenotype covariates exceeds the number of colors in the color palette, an error will be thrown.
output.dir	character directory path to write plot to file. Default is NULL in which case the plot is returned as lattice multipanel object.
filename.prefix	character prefix for plot filename.
file.extension	character file extension for plot file. Default is "png".

width	numeric width of plot in inches.
height	numeric height of plot in inches.
xaxis.cex	numeric size of x-axis labels.
yaxis.cex	numeric size of y-axis labels.
titles.cex	numeric size of plot titles.
border.padding	numeric padding around plot border.

Value

If no output directory is provided, a multipanel lattice plot object is returned, otherwise a plot is written to the indicated path and NULL is returned.

For clarity, certain plot aspects change when sample size exceeds 50:

- x-axis labels are no longer displayed
- missing (NA) values are not labeled with text in heatmaps but are color-coded with a legend

Colors for continuous and binary phenotypes are chosen from the binary color palettes in BoutrosLab.plotting.general::
Colors for categorical phenotypes are chosen by default from the qualitative color palette in BoutrosLab.plotting.general

Examples

```
set.seed(200);
percentiles <- get.pgs.percentiles(rnorm(200, 0, 1));
pgs.data <- data.frame(
    Indiv = paste0('sample', 1:200),
    percentile = percentiles$percentile,
    decile = percentiles$decile,
    quartile = percentiles$quartile,
    n.missing.genotypes = sample(1:10, 200, replace = TRUE),
    percent.missing.genotypes = sample(1:10, 200, replace = TRUE) / 100,
    continuous.pheno = rnorm(200, 1, 1),
    categorical.pheno = sample(letters[1:5], 200, replace = TRUE),
    binary.pheno = sample(c(0,1), 200, replace = TRUE)
    );

temp.dir <- tempdir();

create.pgs.rank.plot(
    pgs.data,
    phenotype.columns = c('continuous.pheno', 'categorical.pheno', 'binary.pheno'),
    missing.genotype.style = 'percent',
    output.dir = temp.dir,
    filename.prefix = 'example-rank-plot'
    );
```

`create.pgs.with.continuous.phenotype.plot` *Plot PGS Scatterplots*

Description

Create scatterplots for PGS data outputed by `apply.polygenic.score()` with continuous phenotype variables

Usage

```
create.pgs.with.continuous.phenotype.plot(
  pgs.data,
  pgs.columns = NULL,
  phenotype.columns,
  hexbin.threshold = 1000,
  hexbin.colour.scheme = NULL,
  hexbin.colourkey = TRUE,
  hexbin.colourcut = seq(0, 1, length = 11),
  hexbin.mincnt = 1,
  hexbin.maxcnt = NULL,
  hexbin.xbins = 30,
  hexbin.aspect = 1,
  output.dir = NULL,
  filename.prefix = NULL,
  file.extension = "png",
  tidy.titles = FALSE,
  compute.correlation = TRUE,
  corr.legend.corner = c(0, 1),
  corr.legend.cex = 1.5,
  include.origin = FALSE,
  width = 10,
  height = 10,
  xaxes.cex = 1.5,
  yaxes.cex = 1.5,
  titles.cex = 1.5,
  point.cex = 0.75,
  border.padding = 1
)
```

Arguments

`pgs.data`	data.frame PGS data as formatted by `apply.polygenic.score()`. Required columns are at least one of PGS, PGS.with.replaced.missing, or PGS.with.normalized.missing, and at least one continuous phenotype column. This function is designed to work with the output of `apply.polygenic.score()`.

pgs.columns character vector of column names indicating which columns in pgs.data to plot as PGSs. If NULL, defaults to recognized PGS columns: PGS, PGS.with.replaced.missing, and PGS.with.normalized.missing.

phenotype.columns
character vector of continuous phenotype column names in pgs.data to plot

hexbin.threshold
numeric threshold (exclusive) for cohort size at which to switch from scatterplot to hexbin plot.

hexbin.colour.scheme
character vector of colors for hexbin plot bins. Default is NULL which uses gray/black.

hexbin.colourkey
logical whether a legend should be drawn for a hexbinplot, defaults to TRUE.

hexbin.colourcut
numeric vector of values covering [0, 1] that determine hexagon colour class boundaries and hexagon legend size boundaries. Alternatively, an integer (<= hexbin.maxcnt) specifying the number of equispaced colourcut values in [0,1].

hexbin.mincnt integer, minimum count for a hexagon to be plotted. Default is 1.

hexbin.maxcnt integer, maximum count for a hexagon to be plotted. Cells with more counts are not plotted. Default is NULL.

hexbin.xbins integer, number of bins in the x direction for hexbin plot. Default is 30.

hexbin.aspect numeric, aspect ratio of hexbin plot to control plot dimensions. Default is 1.

output.dir character directory to save output plots

filename.prefix
character prefix for output filenames

file.extension character file extension for output plots

tidy.titles logical whether to reformat PGS plot titles to remove periods

compute.correlation
logical whether to compute correlation between PGS and phenotype and display in plot

corr.legend.corner
numeric vector indicating the corner of the correlation legend e.g. c(0,1) for top left

corr.legend.cex
numeric cex for correlation legend

include.origin logical whether to include the origin (zero) in plot axes

width numeric width of output plot in inches

height numeric height of output plot in inches

xaxes.cex numeric size for x-axis labels

yaxes.cex numeric size for y-axis labels

titles.cex numeric size for plot titles

point.cex numeric size for plot points

border.padding numeric padding for plot borders

Value

If no output directory is provided, a multipanel lattice plot object is returned, otherwise a plot is written to the indicated path and NULL is returned. If no continuous phenotype variables are detected, a warning is issued and NULL is returned.

Examples

```
set.seed(100);

pgs.data <- data.frame(
    PGS = rnorm(100, 0, 1),
    continuous.phenotype = rnorm(100, 2, 1)
    );
 temp.dir <- tempdir();

# Basic Plot
create.pgs.with.continuous.phenotype.plot(
    pgs.data,
    output.dir = temp.dir,
    filename.prefix = 'basic-plot',
    phenotype.columns = 'continuous.phenotype',
    width = 6,
    height = 6
    );

# Plot multiple PGS outputs

pgs.data$PGS.with.normalized.missing <- rnorm(100, 1, 1);
create.pgs.with.continuous.phenotype.plot(
    pgs.data,
    output.dir = temp.dir,
    filename.prefix = 'multiple-pgs',
    phenotype.columns = 'continuous.phenotype'
    );


# Plot non-default PGS columns

pgs.data$PGS.custom <- rnorm(100, 2, 1);
create.pgs.with.continuous.phenotype.plot(
   pgs.data,
   pgs.columns = 'PGS.custom',
   output.dir = temp.dir,
   filename.prefix = 'custom-pgs',
   phenotype.columns = 'continuous.phenotype'
   );


# Plot multiple phenotypes

pgs.data$continuous.phenotype2 <- rnorm(100, 10, 1);
create.pgs.with.continuous.phenotype.plot(
```

```
    pgs.data,
    pgs.columns = 'PGS',
    output.dir = temp.dir,
    filename.prefix = 'multiple-phenotypes',
    phenotype.columns = c('continuous.phenotype', 'continuous.phenotype2')
    );
```

`flip.DNA.allele` *Flip DNA allele*

Description

Flip single base pair DNA alleles to their reverse complement. INDEL flipping is not supported.

Usage

```
flip.DNA.allele(alleles, return.indels.as.missing = FALSE)
```

Arguments

`alleles`	A character vector of DNA alleles.
`return.indels.as.missing`	A logical value indicating whether to return NA for INDEL alleles. Default is `FALSE`.

Value

A character vector of flipped DNA alleles. INDEL alleles are returned as is unless `return.indels.as.missing` is `TRUE`.

Examples

```
alleles <- c('A', 'T', 'C', 'G', 'ATG', NA);
flip.DNA.allele(alleles);
```

format.chromosome.notation *Format chromosome names*

Description

Format chromosome names according to user specifications.

Usage

```
## S3 method for class 'chromosome.notation'
format(chromosome, chr.prefix, numeric.sex.chr)
```

Arguments

chromosome	A character vector of chromosome names.
chr.prefix	A logical indicating whether the 'chr' prefix should be used when formatting chromosome name.
numeric.sex.chr	A logical indicating whether the sex chromosomes should be formatted numerically, as opposed to alphabetically.

Value

A character vector of chromosome names formatted according to user specifications.

Examples

```
numeric.chr <- c(1,2,23,24);
chr.with.prefix <- c('chr1', 'chr2', 'chrX', 'chrY');
format.chromosome.notation(numeric.chr, chr.prefix = TRUE, numeric.sex.chr = FALSE);
format.chromosome.notation(chr.with.prefix, chr.prefix = FALSE, numeric.sex.chr = TRUE);
```

get.pgs.percentiles *get.pgs.percentiles*

Description

Calculate percentiles and report decile and quartile ranks for a vector of polygenic scores

Usage

```
get.pgs.percentiles(pgs, n.percentiles = NULL)
```

Arguments

pgs	numeric vector of polygenic scores
n.percentiles	integer number of percentiles to calculate (optional)

Value

data frame with columns for percentile, decile, quartile, and optional n.percentiles

Examples

```
x <- rnorm(100);
get.pgs.percentiles(x, n.percentiles = 20);
```

---

import.pgs.weight.file

Import PGS weight file

Description

Import a PGS weight file formatted according to PGS catalog guidelines, and prepare for PGS application with `apply.polygenic.score()`.

Usage

```
import.pgs.weight.file(pgs.weight.path, use.harmonized.data = TRUE)
```

Arguments

pgs.weight.path	A character string indicating the path to the pgs weight file.
use.harmonized.data	A logical indicating whether the file should be formatted to indicate harmonized data columns for use in future PGS application.

Value

A list containing the file metadata and the weight data.

Examples

```
# Example pgs weight file
pgs.weight.path <- system.file(
    'extdata',
    'PGS000662_hmPOS_GRCh38.txt.gz',
    package = 'ApplyPolygenicScore',
    mustWork = TRUE
    );
import.pgs.weight.file(pgs.weight.path);
```

```
# Note, harmonized data is used by default. To disable set `use.harmonized.data = FALSE`
import.pgs.weight.file(pgs.weight.path, use.harmonized.data = FALSE);
```

`import.vcf` *Import VCF file*

Description

A wrapper for the VCF import function in the vcfR package that formats VCF data for PGS application with `apply.polygenic.score()`.

Usage

```
import.vcf(
  vcf.path,
  long.format = FALSE,
  info.fields = NULL,
  format.fields = NULL,
  verbose = FALSE
)
```

Arguments

`vcf.path`	A character string indicating the path to the VCF file to be imported.
`long.format`	A logical indicating whether the VCF import should be converted into long format (one row per sample-variant combination)
`info.fields`	A character vector indicating the INFO fields to be imported, only applicable when long format is `TRUE`.
`format.fields`	A character vector indicating the FORMAT fields to be imported, only applicable when long format is `TRUE`.
`verbose`	A logical indicating whether verbose output should be printed by vcfR.

Value

A list of two elements containing imported VCF information in wide format and in long format if requested.

Output Structure

The outputed list contains the following elements:

- split.wide.vcf.matrices: A list with two elements: a `data.table` of fixed VCF fields and a `matrix` of genotyped alleles.
- combined.long.vcf.df: Default is `NULL` otherwise if `long.format == TRUE` a list with two elements inherited from vcfR: a data frame meta data from the VCF header and a data frame of all requested VCF fields (including INFO and FORMAT fields) in long format. Number of rows is equal to the number of samples times the number of sites in the VCF.

The split.wide.vcf.matrices list contains the following elements:

- genotyped.alleles: A matrix of genotyped alleles (e.g. "A/C"). Rows are unique sites and columns are unique samples in the input VCF.
- vcf.fixed.fields: A data table of the following fixed (not varying by sample) VCF fields: CHROM, POS, ID, REF, ALT. Also one additional column allele.matrix.row.index indicating the corresponding row in genotyped.alleles

The combined.long.vcf.df list contains the following elements:

- meta: A data frame of meta data parsed from the VCF header
- dat: A data frame of all default VCF fields and all requested INFO and FORMAT fields in long format. Number of rows is equal to the number of unique samples times the number of unique sites in the VCF.

The wide format is intended to efficiently contain the bare minimum information required for PGS application. It intentionally excludes much of the additional information included in a typical VCF, and splits off genotypes into a separate matrix for easy manipulation. If users wish to maintain additional information in the INFO and FORMAT fields for e.g. variant filtering, the long format allows this. However, the long format requires substantially more memory to store, and is not recommended for large input files.

Examples

```
# Example VCF
vcf <- system.file(
    'extdata',
    'HG001_GIAB.vcf.gz',
    package = 'ApplyPolygenicScore',
    mustWork = TRUE
    );
vcf.data <- import.vcf(vcf.path = vcf, long.format = TRUE);
```

---

parse.pgs.input.header

Parse PGS input file header

Description

Parse metadata from a PGS input file header.

Usage

```
parse.pgs.input.header(pgs.weight.path)
```

Arguments

pgs.weight.path
: A character string indicating the path to the pgs weight file.

Value

A data frame containing the metadata from the file header.

Examples

```
# Example pgs weight file
pgs.weight.path <- system.file(
    'extdata',
    'PGS000662_hmPOS_GRCh38.txt.gz',
    package = 'ApplyPolygenicScore',
    mustWork = TRUE
    );
parse.pgs.input.header(pgs.weight.path);
```

---

run.pgs.regression *Run linear and logistic regression on a polygenic score and a set of phenotypes*

Description

Phenotype data variables are automatically classified as continuous or binary and a simple linear regression or logistic regression, respectively, is run between the polygenic score and each phenotype. Categorical phenotypes with more than two category are ignored. If a binary variable is not formatted as a factor, it is converted to a factor using `as.factor()` defaults. For logistic regression, the first level is classified as "failure" and the second "success" by `glm()` defaults.

Usage

```
run.pgs.regression(pgs, phenotype.data)
```

Arguments

`pgs`	numeric vector of polygenic scores
`phenotype.data`	data.frame of phenotypes

Value

data frame with columns for phenotype, model, beta, se, p.value, r.squared, and AUC

Examples

```
set.seed(200);
pgs <- rnorm(200, 0, 1);
phenotype.data <- data.frame(
    continuous.pheno = rnorm(200, 1, 1),
    binary.pheno = sample(c(0, 1), 200, replace = TRUE)
    );
run.pgs.regression(pgs, phenotype.data);
```

`write.apply.polygenic.score.output.to.file` *Write apply.polygenic.score output to file*

Description

A utility function that writes the two data frames outputted by apply.polygenic.score to two tab-delimited text files.

Usage

```
write.apply.polygenic.score.output.to.file(
  apply.polygenic.score.output,
  output.dir,
  file.prefix = NULL
)
```

Arguments

`apply.polygenic.score.output`	list of two data frames: `pgs.output` and `regression.output`
`output.dir`	character string of the path to write both output files
`file.prefix`	character string of the file prefix to use for both output files

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