Package: RMR.ICP (via r-universe)

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Description Robust Mendelian Randomization method to account for Idiosyncratic and Correlated Pleiotropy.

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`RMR.ICP-package` *Robust Mendelian Randomization to account for Idiosyncratic and Correlated Pleiotropy*

Description

Implements a robust Mendelian Randomization method (RMR-ICP) that accounts for both idiosyncratic and correlated pleiotropy using a Gibbs sampler.

Author(s)

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`gamma1_Indep` *Example datasets for RMR-ICP*

Description

Simulated GWAS summary statistics and LD reference data for demonstrating the RMR-ICP method.

- `gamma1_Indep`, `gamma1_LD`: SNP-exposure effect estimates (independent and LD-structured scenarios, respectively).
- `Gamma2_Indep`, `Gamma2_LD`: SNP-outcome effect estimates (independent and LD-structured scenarios, respectively).
- `se1_Indep`, `se1_LD`: Standard errors for the exposure effect estimates.
- `se2_Indep`, `se2_LD`: Standard errors for the outcome effect estimates.
- `R`: LD correlation matrix (2000 x 2000) for the LD scenario.
- `block_inf1`: Block boundary matrix (200 x 2) giving the start and end indices of each LD block (0-indexed).

Usage

```
data(gamma1_Indep)
data(gamma1_LD)
data(Gamma2_Indep)
data(Gamma2_LD)
data(se1_Indep)
data(se1_LD)
data(se2_Indep)
data(se2_LD)
data(R)
data(block_inf1)
```

Format

Numeric matrices. The `_Indep` datasets have 100 rows (SNPs); the `_LD` datasets have 2000 rows. `R` is a 2000 x 2000 matrix. `block_inf1` is a 200 x 2 integer matrix of block boundaries.

Examples

```
data(gamma1_Indep)
data(Gamma2_Indep)
data(se1_Indep)
data(se2_Indep)
res <- RMRICPindep(gamma1_Indep, Gamma2_Indep, se1_Indep, se2_Indep)
```

`genRawGeno` *Simulation helpers for RMR-ICP*

Description

`genRawGeno` simulates a genotype matrix with a block correlation structure.

`genSumStat` takes a genotype matrix and generates GWAS summary statistics under a specified causal and pleiotropic model.

`traceplot` plots the Gibbs sampler trace of the causal effect estimate.

Usage

```
genRawGeno(maf, L, M, rho, n)

genSumStat(x12, n1, n2, M, L, b1, Alrate, sigma2g, dfA, delta, h2a, h2g)

traceplot(bhatpoint)
```

Arguments

`maf`	Numeric vector of minor allele frequencies (length `L * M`).
`L`	Number of LD blocks.
`M`	Number of SNPs per block.
`rho`	Within-block LD correlation parameter (AR(1) structure).
`n`	Total sample size.
`x12`	Genotype matrix (`(n1+n2)` rows, `L*M` columns).
`n1`	Sample size for exposure GWAS.
`n2`	Sample size for outcome GWAS.
`b1`	True causal effect of exposure on outcome.
`Alrate`	Proportion of blocks with correlated pleiotropic effects.
`sigma2g`	Variance of genetic effects.

`dfA`	Degrees of freedom for the t-distributed correlated pleiotropy.
`delta`	Scaling factor for correlated pleiotropy.
`h2a`	Heritability explained by pleiotropic effects.
`h2g`	Heritability of the exposure explained by genetics.
`bhatpoint`	Numeric vector of posterior samples of the causal effect.

Value

`genRawGeno` returns a numeric genotype matrix with `n` rows and `L*M` columns.

`genSumStat` returns a list with components `gammah`, `se1`, `se2`, `Gammah`, and `CHPindex`.

`traceplot` returns a `ggplot` object.

`RcppArmadillo-Functions`

Set of functions in example RcppArmadillo package

Description

These four functions are created when `RcppArmadillo.package.skeleton()` is invoked to create a skeleton packages.

Usage

```
rcpparma_hello_world()
rcpparma_outerproduct(x)
rcpparma_innerproduct(x)
rcpparma_bothproducts(x)
```

Arguments

`x`	a numeric vector

Details

These are example functions which should be largely self-explanatory. Their main benefit is to demonstrate how to write a function using the Armadillo C++ classes, and to have to such a function accessible from R.

Value

`rcpparma_hello_world()` does not return a value, but displays a message to the console.

`rcpparma_outerproduct()` returns a numeric matrix computed as the outer (vector) product of `x`.

`rcpparma_innerproduct()` returns a double computer as the inner (vector) product of `x`.

`rcpparma_bothproducts()` returns a list with both the outer and inner products.

Author(s)

Dirk Eddelbuettel

References

See the documentation for Armadillo, and RcppArmadillo, for more details.

Examples

```
x <- sqrt(1:4)
rcpparma_innerproduct(x)
rcpparma_outerproduct(x)
```

`ReadSummaryStat` *Read and prepare GWAS summary statistics for RMR-ICP*

Description

`ReadSummaryStat` reads GWAS summary statistics for the exposure and outcome, performs quality control (MHC region removal, allele filtering), aligns to a reference panel, and organises data into LD blocks ready for `RMRICP`.

`EstRho` estimates the correlation between exposure and outcome GWAS using null SNPs via a truncated Gibbs sampler.

Usage

```
ReadSummaryStat(fileexp, fileout, filepan, snpinfo, pva_cutoff, lambad)

EstRho(fileexp, fileout, filepan, snpinfo, ld_r2_thresh, lambad, pth)
```

Arguments

`fileexp`	Path to the exposure GWAS summary statistics file.
`fileout`	Path to the outcome GWAS summary statistics file.
`filepan`	Named list (by chromosome) of paths to LD panel RDS files.
`snpinfo`	Path to reference SNP information RDS file.
`pva_cutoff`	p-value threshold for selecting instruments from the exposure GWAS.
`lambad`	Shrinkage factor applied to off-diagonal LD correlations.
`ld_r2_thresh`	LD r-squared threshold for clumping (used in `EstRho`).
`pth`	Numeric vector of z-score thresholds used to define null SNPs for rho estimation.

Value

`ReadSummaryStat` returns a list of LD-block-structured summary statistics suitable for passing to `RMRICP`.

`EstRho` returns a list with components `rhohat`, `pvalue`, `pres`, and `Rhores`.

`RMRICP` *Robust Mendelian Randomization accounting for Idiosyncratic and Correlated Pleiotropy*

Description

Perform robust Mendelian Randomization using a Gibbs sampler that accounts for both idiosyncratic and correlated horizontal pleiotropy. `RMRICP` handles the general case with LD structure; `RMRICPindep` assumes independent instruments; `RMRICPSim` works with a pre-specified LD matrix and block structure.

Usage

```
RMRICP(F4gammah, F4Gammah, F4se1, F4se2, F4Rblock, opts = NULL)

RMRICPindep(gammah, Gammah, se1, se2, opts = NULL)

RMRICPSim(gammah, Gammah, se1, se2, R, block_inf, opts = NULL)
```

Arguments

`F4gammah`	List of numeric vectors of SNP-exposure effect estimates per LD block.
`F4Gammah`	List of numeric vectors of SNP-outcome effect estimates per LD block.
`F4se1`	List of numeric vectors of standard errors for `F4gammah`.
`F4se2`	List of numeric vectors of standard errors for `F4Gammah`.
`F4Rblock`	List of LD correlation matrices per block.
`gammah`	Numeric vector of SNP-exposure effect estimates.
`Gammah`	Numeric vector of SNP-outcome effect estimates.
`se1`	Numeric vector of standard errors for `gammah`.
`se2`	Numeric vector of standard errors for `Gammah`.
`R`	LD correlation matrix.
`block_inf`	Matrix of block boundary indices.
`opts`	Optional list of MCMC options (e.g., iterations, burn-in, thinning).

Value

A list containing posterior samples and summary estimates of the causal effect.

Examples

```
data(gamma1_Indep)
data(Gamma2_Indep)
data(se1_Indep)
data(se2_Indep)
res <- RMRICPindep(gamma1_Indep, Gamma2_Indep, se1_Indep, se2_Indep)
```

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