Package 'MR.DEEM'

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| Title Debiased Estimating Equation Method for Mendelian Randomization |
| Version 0.1.0 |
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| Description Implements the DEEM method for MR analysis with summary data. |
| License `use_mit_license()`, `use_gpl3_license()` or friends to pick a license |
| Encoding UTF-8 |
| Roxygen list(markdown = TRUE) |
| RoxygenNote 7.3.1 |
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| R topics documented: est.os.DEEM 1 est.ts.DEEM 2 prepare.DEEM 3 |
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| est.os.DEEM Calculate the DEEM estimator and its estimated standard error in the |

Description

This function implements the Debiased Estimating Equation Method (DEEM) for Mendelian randomization in the one-sample setting, producing consistent causal effect estimates even when instruments are weak or correlated. Inputs of this function are the outputs of the function "prepare.DEEM" Examples for the required summary statistics can be downloaded from https://osf.io/j25rc/files/osfstorage (the LD matrix is approximately 6GB after decompression).

one-sample setting

est.ts.DEEM

Usage

```
est.os.DEEM(
  index,
  Gamma_h_lst,
  gamma_h_lst,
  gamma_s_lst,
  Sig_y,
  Sig_x,
  Sig_alpha,
  R_sel
)
```

Arguments

| index | Number of LD blocks included. |
|-------------|--|
| Gamma_h_lst | A list of vectors of estimated SNP-outcome associations within different LD blocks from the outcome sample. |
| gamma_h_lst | A list of vectors of estimated SNP-exposure associations within different LD blocks from the exposure sample. |
| gamma_s_lst | A list of vectors of estimated SNP-exposure associations within different LD blocks from the supplemental exposure sample (used to select SNPs). |
| Sig_y | A list of estimated variance-covariance matrix for the estimated SNP-outcome associations within different LD blocks from the outcome sample. |
| Sig_x | A list of estimated variance-covariance matrix for the estimated SNP-exposure associations within different LD blocks from the exposure sample. |
| Sig_alpha | A list of estimated variance-covariance matrix for the pleiotropic effects within different LD blocks. |
| R_sel | A list of estimated LD matrix within different LD blocks. |

Value

A vector containing:

- beta_hat: the estimated causal effect.
- se: the estimated standard error.

| est.ts.DEEM | Calculate the DEEM estimator and its estimated standard error in the |
|-------------|--|
| | two-sample setting |

Description

This function implements the Debiased Estimating Equation Method (DEEM) for Mendelian randomization in the two-sample setting, producing consistent causal effect estimates even when instruments are weak and/or correlated. Inputs of this function are the outputs of the function "prepare.DEEM". Examples for the required summary statistics can be downloaded from https://osf.io/j25rc/files/osfstorage (the LD matrix is approximately 6GB after decompression).

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Usage

```
est.ts.DEEM(
  index,
  Gamma_h_lst,
  gamma_h_lst,
  gamma_s_lst,
  Sig_y,
  Sig_x,
  Sig_alpha,
  R_sel
)
```

Arguments

| index | Number of LD blocks included. |
|-------------|--|
| Gamma_h_lst | A list of vectors of estimated SNP-outcome associations within different LD blocks from the outcome sample. |
| gamma_h_lst | A list of vectors of estimated SNP–exposure associations within different LD blocks from the exposure sample. |
| gamma_s_lst | A list of vectors of estimated SNP–exposure associations within different LD blocks from the supplemental exposure sample (used to select SNPs). |
| Sig_y | A list of estimated variance-covariance matrix for the estimated SNP-outcome associations within different LD blocks from the outcome sample. |
| Sig_x | A list of estimated variance-covariance matrix for the estimated SNP-exposure associations within different LD blocks from the exposure sample. |
| Sig_alpha | A list of estimated variance-covariance matrix for the pleiotropic effects within different LD blocks. |
| R_sel | A list of estimated LD matrix within different LD blocks. |

Value

A vector containing:

- beta_hat: the estimated causal effect.
- se: the estimated standard error.

| prepare.DEEM | Prepare the data required by DEEM, outputs of this function are the |
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| le contraction of the contractio | inputs of "est.ts.DEEM" and "est.os.DEEM" |

Description

The function prepares the data required by DEEM, outputs of this function are the inputs of "est.ts.DEEM" and "est.os.DEEM" Examples for the required summary statistics can be downloaded from https://osf.io/j25rc/files/osfsto (the LD matrix is approximately 6GB after decompression)

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Usage

```
prepare.DEEM(
   SumData,
   com_list,
   LD_Ref,
   Blocks,
   ns,
   ne,
   no,
   p_thr = 0.1,
   r2_thr = 0.81
)
```

Arguments

SumData

A data frame consists of eight variables:

- chr: the chromosome.
- pos: the position.
- gamma_s: a vector of estimated SNP-exposure associations from the supplemental exposure sample used to select the SNPs.
- sigma_s: a vector of estimated standard error for the estimated SNP–exposure associations from the supplemental exposure sample used to select the SNPs.
- gamma_h: a vector of estimated SNP-exposure associations from the exposure sample.
- sigma_x: a vector of estimated standard error for the estimated SNP–exposure associations from the exposure sample.
- Gamma_h: a vector of estimated SNP-outcome associations from the outcome sample.
- sigma_y: a vector of estimated standard error for the estimated SNP–outcome associations from the outcome sample.

SNPs in the three samples should be the same (possible preprocessing required).

com_list A vector of characters in the form "chr:pos" of the SNPs in the SumData.

LD_Ref A list of LD matrix in each LD blocks from the reference sample.

ns sample size of the supplemental exposure sample that generates gamma_s.

ne sample size of the exposure sample that generates gamma_h.

no sample size of the outcome sample that generates Gamma_h.

p_thr p-value threshold, default 0.1.

r2_thr r2 threshold, default 0.81.

Block data.frame consists of three variables:

- chr: a vector of character in the form "chr?" where "?" is the chromosome that the LD block locates on.
- start: a vector of int indicates where the LD block starts.
- stop: a vector of int indicates where the LD block ends.

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Value

A list containing:

- index: Number of LD blocks included.
- Gamma_h_lst: A list of vectors of estimated SNP-outcome associations within different LD blocks from the outcome sample.
- gamma_h_1st: A list of vectors of estimated SNP-exposure associations within different LD blocks from the exposure sample.
- gamma_s_lst: A list of vectors of estimated SNP-exposure associations within different LD blocks from the supplemental exposure sample (used to select SNPs).
- Sig_y: A list of estimated variance-covariance matrix for the estimated SNP-outcome associations within different LD blocks from the outcome sample.
- Sig_x: A list of estimated variance-covariance matrix for the estimated SNP-exposure associations within different LD blocks from the exposure sample.
- Sig_alpha: A list of estimated variance-covariance matrix for the pleiotropic effects within different LD blocks.
- R_sel: A list of estimated LD matrix within different LD blocks.

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