Package: MVMRcMLSuSiE (via r-universe)

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Title Implementation of MVMR-cML-SuSiE

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Description Implements the first three steps of constrained Maximum Likelihood (cML) based Mendelian randomization approach for highly correlated exposures

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Contents

`mvmr.cml.susie.step1` *Step 1 of MVMR-cML-SuSiE*

Description

This function performs the first step of the MVMR-cML-SuSiE approach to obtain each exposure's univariable Mendelian randomization (UVMR) p-value, used for initial filtering of exposures. You can choose to pull GWAS data using `OpenGWAS` (by setting `use.openGWAS = TRUE`) or provide your own summary statistics (by setting `use.openGWAS = FALSE`)

Usage

```
mvmr.cml.susie.step1(
  exposure.ids = NULL,
  outcome.id = NULL,
  sample.sizes,
  beta.exposure.ls = NULL,
  se.exposure.ls = NULL,
  beta.outcome.ls = NULL,
  se.outcome.ls = NULL,
  use.openGWAS = TRUE
)
```

Arguments

`exposure.ids`	A length L character vector of openGWAS IDs corresponding to the exposures, where L is the number of intended exposures
`outcome.id`	A character corresponding to the outcome openGWAS ID
`sample.sizes`	A numeric vector of sample sizes corresponding to each exposure and outcome If `use.openGWAS = TRUE`, the length should be L (exposures only). Otherwise, the length should be $L + 1$, with the last element for the outcome sample size
`beta.exposure.ls`	A list (length L) of numeric vectors with effect sizes (betas) for each SNP on exposure
`se.exposure.ls`	A list (length L) of numeric vectors with standard errors for each SNP on exposure
`beta.outcome.ls`	A list (length L) of numeric vectors with effect sizes (betas) for each SNP on outcome
`se.outcome.ls`	A list (length L) of numeric vectors with standard errors for each SNP on outcome
`use.openGWAS`	A logical indicating whether to use `OpenGWAS` to extract GWAS data based on `exposure.ids` and `outcome.id`. If `FALSE`, requires user-provided summary statistics (lists for `beta.exposure.ls`, `se.exposure.ls`, `beta.outcome.ls`, and `se.outcome.ls`) Default is `TRUE`

Value

A numeric vector (length L) of p-values, each corresponding to the UVMR p-value for one exposure

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`mvmr.cml.susie.step2` *Step 2 of MVMR-cML-SuSiE*

Description

This function performs the second step of the MVMR-cML-SuSiE approach. After identifying exposures of interest in Step 1 (e.g., by filtering UVMR p-values), step 2 extracts the relevant instruments for those exposures, identifies invalid instruments (if any), and obtains an initial estimate from univariable Mendelian randomization (UVMR) for each exposure

Usage

```
mvmr.cml.susie.step2(
  exposure.ids.subset = NULL,
  outcome.id = NULL,
  sample.sizes.subset,
  beta.exposure.mat = NULL,
  se.exposure.mat = NULL,
  beta.outcome.vec = NULL,
  se.outcome.vec = NULL,
  pval.exposure.mat = NULL,
  use.openGWAS = TRUE,
  cutoff = 5e-08
)
```

Arguments

`exposure.ids.subset`
: A length L^* character vector of exposure IDs (a subset from step 1)

`outcome.id`
: A character specifying the outcome ID

`sample.sizes.subset`
: A length L^* numeric vector of sample sizes corresponding to `exposure.ids.subset` (and optionally the outcome as the last element if user-provided data)

`beta.exposure.mat`
: A size $m^* \times L^*$ matrix of exposure effect sizes, where m^* is the number of SNPs

`se.exposure.mat`
: A size $m^* \times L^*$ matrix of exposure standard errors

`beta.outcome.vec`
: A length m^* numeric vector of outcome effect sizes for the same SNPs

`se.outcome.vec`
: A length m^* numeric vector of standard errors for `beta.outcome.vec`

`pval.exposure.mat`
: A $m^* \times L^*$ matrix of exposure p-values

use.openGWAS	A logical indicating whether to extract data via OpenGWAS. If FALSE, you must supply the *.mat and *.vec arguments. Default is TRUE
cutoff	A numeric threshold for instrument selection. Default is 5×10^{-8}

Value

A list containing:

mvdat	A list containing the relevant data (exposure/outcome betas, SEs, etc)
invalid.idx	A vector of indices of invalid instruments identified based off the UVMR procedure
theta.vec	A numeric vector of initial values for each exposure

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mvmr.cml.susie.step3 *Step 3 of MVMR-cML-SuSiE (Iterative SuSiE)*

Description

This function performs the iterative SuSiE algorithm to identify potential exposure signal clusters

Usage

```
mvmr.cml.susie.step3(
  mvdat,
  invalid.idx,
  theta.vec,
  rho.mat,
  S = 10,
  max.iter = 200,
  tol = 1e-10
)
```

Arguments

mvdat	A list returned by mvmr.cml.susie.step2, containing exposure and outcome summary statistics
invalid.idx	An integer vector of invalid IV indices as identified in step 2
theta.vec	A numeric vector of initial exposure effect estimates from step 2
rho.mat	A genetic correlation matrix of size $(L^*+1)\times(L^*+1)$, where L^* is the number of exposures. The last row/column corresponds to the outcome
S	The number of single effects (signal clusters) in SuSiE. Default is 10.
max.iter	The maximum number of iterations for SuSiE. Default is 200.
tol	A numeric value indicating the convergence threshold for the iterative procedure. Default is 1×10^{-10}.

Value

A fitted `susie` object. The key SuSiE output is the posterior inclusion probability (PIP) matrix `alpha` used for determining signal clusters

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