Package ‘EMAS’

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Type Package

Title Epigenome-Wide Mediation Analysis Study

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Imports mediation, parallel, multilevel, minfi, ggplot2, qqman,
lavaan, IlluminaHumanMethylationEPICanno.ilm10b4.hg19,
IlluminaHumanMethylation450kanno.ilmn12.hg19

Description
DNA methylation is essential for human, and environment can change the DNA methylation and affect body status. Epigenome-Wide Mediation Analysis Study (EMAS) can find potential mediator CpG sites between exposure (x) and outcome (y) in epigenome-wide. For more information on the methods we used, please see the following references:
Tingley, D. (2014) <doi:10.18637/jss.v059.i05>,
Turner, S. D. (2018) <doi:10.21105/joss.00731>,
Rosseel, D. (2012) <doi:10.18637/jss.v048.i02>.

License GPL-3

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LazyData true

RoxygenNote 7.1.2

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Contents

`data.m` *A data for 221 participants*

Description

A data for 221 participants. The data were fabricated.

Usage

```
data.m
```

Format

A data.frame contains 221 obs of 7 variables. The variables are:

ID The ID of these 221 people.

age A numeric.

gender A two level factor: "1" or "2"

CD8T A numeric.

CD4T A numeric.

x A numeric.

y A numeric.

`E.result` *An `Emas` results data.*

Description

An `Emas` results data for 2000 CpGs. The data were fabricated.

Usage

```
E.result
```

Format

A data.frame produced by `Emas` contains 2000 obs of 13 variables.

`Emas` *Epigenome-Wide Mediation Analysis Study*

Description

This function can perform the Epigenome-Wide Mediation Analysis Study (EMAS).

Usage

```
Emas(
  data,
  M.matrix,
  id = "",
  x = "",
  y = "",
  x.cov = c(),
  y.cov = c(),
  m.cov = c(),
  mem.sav = FALSE,
  p.th = 0.1,
  ini.sims = 100,
  boot = FALSE,
  cl.n = 1,
  ...
)
```

Arguments

`data`	A data.frame included id, x, y, x.cov, y.cov, m.cov.
`M.matrix`	A matrix with the epigenome-wide CpG information, maybe a M-value matrix or a beta value matrix.
`id`	Variable name of the id.
`x, y`	Variable name of exposure(x) and outcome(y).
`x.cov`	Variable names of covariates related to exposure(x).
`y.cov`	Variable names of covariates related to outcome(y).
`m.cov`	Variable names of covariates related to mediator(m).
`mem.sav`	A logical value. If 'TRUE', the memory required for the function will decrease, but the speed will also decrease.
`p.th`	Sobel indirect effects P-value threshold for subsequent nonparametric bootstrap or quasi-Bayesian approximation mediation analyses.
`ini.sims`	Initial number of Monte Carlo draws for nonparametric bootstrap or quasi-Bayesian approximation.
`boot`	A logical value. If 'FALSE' a quasi-Bayesian approximation is used for confidence intervals; if 'TRUE' nonparametric bootstrap will be used. Default is 'FALSE'.

`cl.n`	Number of cores used for parallel computing.
`...`	Other arguments passed to `makeCluster`.

Details

This function can perform the Epigenome-Wide Mediation Analysis Study (EMAS) to explore the potential mediating CpG sites of exposure variables affecting outcome variables within the epigenome-wide.

Value

`Emas` returns a data.frame with the average mediation effects(AME), average direct effects(ADE), total effects, mediation proportion.

- AMEEst: Point estimates for average mediation effects under the exposure conditions.
- AMElow95, AMEupp95: 95 percentage confidence intervals for average mediation effects.
- AME.P: Two-sided p-values for average mediation effects.
- ADEEst: Point estimates for average direct effect under the exposure conditions.
- ADElow95, ADEupp95: 95 percentage confidence intervals for average direct effects.
- ADE.P: Two-sided p-values for average direct effects.
- TotEst: Point estimate for total effect.
- Totlow95, Totupp95: 95 percentage confidence interval for total effect.
- Tot.P: Two-sided p-values for total effect.
- PropEst: The "proportions mediated", or the size of the average mediation effects relative to the total effect.

Author(s)

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References

Tingley, D., Yamamoto, T., Hirose, K., Imai, K. and Keele, L. (2014). mediation: R package for Causal Mediation Analysis. *Journal of Statistical Software*, 59(5), 1–38. doi: 10.18637/jss.v059.i05.

Examples

```
data(data.m)
data(Mvalue)
E.result <- Emas(data.m, Mvalue, id = "ID", x = "x", y = "y",
                 x.cov = c("age", "gender"),
                 y.cov = c("age", "gender"),
                 m.cov = c("age", "gender", "CD8T", "CD4T"),
                 p.th = 0.1, ini.sims = 100, boot = FALSE, cl.n = 1)
```

`EMAS.manhattan` *Plotting the manhattan plot from the EMAS results*

Description

Function to plot a manhattan plot from the `Emas` results.

Usage

```
EMAS.manhattan(E.result, type = "EPIC", ...)
```

Arguments

`E.result`	A data.frame produced by `Emas`.
`type`	A character string indicating the type of annotation, only "EPIC" and "450k" are available.
`...`	Other arguments passed to `manhattan`.

Details

This function can plot a manhattan plot from the `Emas` results according to the annotation from 450k or EPIC.

Value

No return value, called for side effects.

Author(s)

Xiuquan Nie, niexiuquan1995@foxmail.com

References

Turner, (2018). qqman: an R package for visualizing GWAS results using Q-Q and manhattan plots. *Journal of Open Source Software*, 3(25), 731. doi: 10.21105/joss.00731.

Examples

```
data(E.result)
EMAS.manhattan(E.result, type = "EPIC",
               genomewideline = -log10(0.05/2000),
               suggestiveline = -log10(1/100), ylim=c(0,5))
```

`Emas.parallel` *Epigenome-Wide Mediation Analysis Study: Parallel multiple mediation model*

Description

This function can perform the parallel multiple mediation model after the Epigenome-Wide Mediation Analysis Study (EMAS).

Usage

```
Emas.parallel(
  data,
  M.matrix,
  id = "",
  x = "",
  y = "",
  x.cov = c(),
  y.cov = c(),
  m.cov = c(),
  m.cor = TRUE,
  boot = FALSE,
  lavaan = FALSE,
  ...
)
```

Arguments

`data`	A data.frame included id, x, y, x.cov, y.cov, m.cov.
`M.matrix`	A matrix with the CpG information screened from EMAS., maybe a M-value matrix or a beta value matrix.
`id`	Variable name of the id.
`x, y`	Variable name of exposure(x) and outcome(y).
`x.cov`	Variable names of covariates related to exposure(x).
`y.cov`	Variable names of covariates related to outcome(y).
`m.cov`	Variable names of covariates related to mediator(m).
`m.cor`	A logical value. If 'TRUE', the mediators in the parallel multiple mediation model are set to correlate with each other.
`boot`	A logical value or a numeric value. If a numeric value, the number for bootstrap.
`lavaan`	A logical value. If 'TRUE', a lavaan object will be given.
`...`	Other arguments passed to `sem` from `lavaan` package.

Details

This function can perform the parallel multiple mediation model after the Epigenome-Wide Mediation Analysis Study (EMAS) to further explore the potential parallel mediating CpG sites of exposure variables affecting outcome variables.

Value

`Emas.parallel` returns a data.frame with the average mediation effects(AME), average direct effects(ADE), and total effects(Tot). If `lavaan` is 'TRUE', a lavaan object will be given.

Author(s)

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References

Rosseel, Y. (2012). lavaan: An R Package for Structural Equation Modeling. *Journal of Statistical Software*, 48(2), 1–36. doi: 10.18637/jss.v048.i02.

Examples

```
data(data.m)
data(Mvalue)
EP.result <- Emas.parallel(data.m, Mvalue,
                           id = "ID", x = "x", y = "y",
                           x.cov = c("age", "gender"),
                           y.cov = c("age", "gender"),
                           m.cov = c("age", "gender", "CD8T", "CD4T"),
                           m.cor = TRUE, boot = FALSE, lavaan = FALSE)
```

`EMAS.volcano` *Plotting the volcano plot from the EMAS results*

Description

Function to plot a volcano plot from the `Emas` results.

Usage

```
EMAS.volcano(
  E.result,
  epiwideline = -log10(1e-07),
  suggestiveline = -log10(1e-05)
)
```

Arguments

`E.result`	A data.frame produced by `Emas`.
`epiwideline`	Where to draw a "epigenome-wide sigificant" line. Default -log10(1.0e-7).
`suggestiveline`	Where to draw a "suggestive" line. Default -log10(1.0e-5). Set to FALSE to disable.

Details

This function can plot a volcano plot from the `Emas` results.

Value

No return value, called for side effects.

Author(s)

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Examples

```
data(E.result)
EMAS.volcano(E.result,
             epiwideline = -log10(0.05/2000),
             suggestiveline = -log10(1/100))
```

`Mvalue` *A M-value matrix for 221 participants*

Description

A M-value matrix for 221 participants. The data were fabricated.

Usage

```
Mvalue
```

Format

A matrix contains 221 obs of 10 CpGs.

Index