Package 'EMAS'

October 12, 2022

Type Package

Title Epigenome-Wide Mediation Analysis Study

Version 0.2.2

Date 2022-08-08

Author Xiuquan Nie [aut, cph, cre],
Mengyi Wang [ctb, rev],
Weihong Chen [fnd]

Maintainer Xiuquan Nie <niexiuquan1995@foxmail.com>

Depends R (>= 4.1.0)

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

Encoding UTF-8

LazyData true

RoxygenNote 7.1.2

NeedsCompilation no

Repository CRAN

Date/Publication 2022-08-11 13:50:07 UTC

R topics documented:

---

  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)

Xiuquan Nie, niexiuquan1995@foxmail.com

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)

Xiuquan Nie, niexiuquan1995@foxmail.com

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)

Xiuquan Nie, niexiuquan1995@foxmail.com

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