

# Package ‘microHIMA’

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**Type** Package

**Title** High-dimensional mediation analysis in microbiome data

**Version** 0.1.1

**Authors** Haixiang Zhang, Jun Chen, Yang Feng and Lei Liu

**Maintainer** Haixiang Zhang <haixiang.zhang@tju.edu.cn>

**Description** We use the isometric logratio (ilr) transformations of the relative abundances as the mediator variables. Moreover, we propose a novel closed testing-based selection procedure for the mediation effects in microbiome compositional data with desirable confidence.

**Depends** R (>= 3.3), ncvreg, MASS, stats, Compositional, nloptr, glmnet, Matrix, hommel

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ilr Isometric Logratio Transformation

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## Description

ilr is used to transform the compositional data from the simplex  $S^p$  to Euclidean space  $R^{p-1}$ .

## Usage

ilr (ID, M)

## Arguments

ID the index of targeted mediator

M a matrix of high-dimensional compositional mediators. Rows represent samples, columns represent variables

## Value

MT a matrix after *ilr*-based transformation

## References

- [1] Egozcue, J., Pawlowsky-Glahn, V., Mateu-Figueras, G. and BarcelÓ-Vidal, C. (2003). Isometric logratio transformations for compositional data analysis. *Mathematical Geology*, 35, 279-300.
- [2] Haixiang Zhang, Jun Chen, Zhigang Li, Lei Liu (2019). Testing for mediation effect with application to human microbiome data. *Statistics in Biosciences*. DOI: <https://doi.org/10.1007/s12561-019-09253-3>

## Examples

```
library(MASS)
Ind <- 3 # The index of targeted mediator
n <- 100 # sample size
p <- 200 # the number of mediators
E <- matrix(rexp(n*p,1),n,p)
M <- matrix(0,n,p)
for (i in 1:n){
  M[i,] <- E[i,]/sum(E[i,]) # generate compositional mediators
}

MT <- ilr(ID =Ind, M) # the ilr-based transformation for M_ID
```

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mhima	Microbiome High-Dimensional Mediation Analysis
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## Description

mhima is used to select significant mediation effects in high-dimensional and compositional microbiome data

## Usage

```
mhima (exposure, covariates, otu.com, outcome)
```

## Arguments

exposure	a vector of exposure
covariates	a matrix of covariates. Rows represent samples, columns represent variables
otu.com	a matrix of compositional OTUs. Rows represent samples, columns represent variables
outcome	a vector of outcome

## Value

ID	the index of selected significant mediator
alpha_hat	coefficient estimate of exposure (X) $\rightarrow$ significant mediator (M)
alpha_hat_SE	the standard error for alpha_hat
beta_hat	coefficient estimate of the significant mediator (M) $\rightarrow$ outcome (Y) (adjusted for exposure, covariates, and high-dimensional nuisance mediators)
beta_hat_SE	the standard error for beta_hat

## References

Haixiang Zhang, Jun Chen, Yang Feng and Lei Liu (2020). Mediation Effect Selection in High-Dimensional and Compositional Microbiome Data. *Submitted*.

## Examples

```
library(stats)
library(Compositional)
library(nlptr)
library(glmnet)
library(ncvreg)
library(MASS)
library(Matrix)
library(hommel)
library(microHIMA)
# ##### generation data
# ### Sample size and number of mediators
n <- 200
p <- 25

sample.num=n
otu.num=p
Treatment = rbinom(n,1,0.2)
#####Two covariates
covariates=cbind(sample(c(1,0),sample.num,replace = TRUE),rnorm(sample.num))

# ### parameters
beta0 <- matrix(0,1,p)
beta0 <- as.numeric(beta0)
betaT=rep(0,otu.num)
betaT[c(1,2,3)]=c(1,1.2,1.5) # the first three are non-zero
betaX=matrix(0,otu.num,2)
alpha0=0
alphaT=1
alphaZ=alphaC=rep(0,otu.num)
alphaZ[c(1,2,3)]=c(1.3,-0.7, -0.6) # the first three are non-zero for response
```

```

alphaX=c(0.5,0.5)
# #####Microbiome data
library(dirmult)
X=cbind(rep(1,sample.num),covariates,Treatment) #n*(1+q+p)
b=cbind(beta0,betaX,betaT) #num.otu*(1+q+p)
gamma.simu=exp(X %*% t(b)) # n * num.otu
otu.com=t(apply(gamma.simu,1,rdirichlet,n=1))

#####Outcome data
X=cbind(rep(1,sample.num),Treatment,covariates,log(otu.com),log(otu.com)*Treatment)
b=c(alpha0,alphaT,alphaX,alphaZ,alphaC)
outcome=c(b%*%t(X)+rnorm(sample.num,mean = 0, sd =1))
exposure <- t(t(Treatment))

#####

mhima.fit <- mhima(exposure,covariates,otu.com,outcome)
print(mhima.fit)

```