Package ‘LUCIDus’

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**boot.lucid**  
*Inference of LUCID model based on bootstrap resampling*

**Description**

Generate R bootstrap replicates of LUCID parameters and derive confidence interval (CI) base on bootstrap. Bootstrap replicates are generated based on nonparameteric resampling, implemented by ordinary method of Codeboot::boot function.

**Usage**

```r
boot.lucid(G, Z, Y, CoG = NULL, CoY = NULL, model, conf = 0.95, R = 100)
```

**Arguments**

- **G**  
  Exposures, a numeric vector, matrix, or data frame. Categorical variable should be transformed into dummy variables. If a matrix or data frame, rows represent observations and columns correspond to variables.

- **Z**  
  Omics data, a numeric matrix or data frame. Rows correspond to observations and columns correspond to variables.

- **Y**  
  Outcome, a numeric vector. Categorical variable is not allowed. Binary outcome should be coded as 0 and 1.

- **CoG**  
  Optional, covariates to be adjusted for estimating the latent cluster. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

- **CoY**  
  Optional, covariates to be adjusted for estimating the association between latent cluster and the outcome. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

- **model**  
  A LUCID model fitted by est.lucid.
est.lucid

Fit LUCID model to conduct integrated clustering

Description

The Latent Unknown Clustering with Integrated Data (LUCID) performs integrative clustering using multi-view data. LUCID model is estimated via EM algorithm for model-based clustering. It also features variable selection, integrated imputation, bootstrap inference and visualization via Sankey diagram.

conf

A numeric scalar between 0 and 1 to specify confidence level(s) of the required interval(s).

R

An integer to specify number of bootstrap replicates for LUCID model. If feasible, it is recommended to set R > 1000. However, the convergence speed of LUCID varies greatly depending on data. If it takes very long time to run 1000 replicates, it is recommend to set smaller values for R, such as 200.

Value

A list, containing the following components:

- beta: effect estimate for each exposure
- mu: cluster-specific mean for each omics feature
- gamma: effect estimate for the association between latent cluster and outcome
- bootstrap: The boot object returned by boot::boot

Examples

```r
## Not run:
# use simulated data
G <- sim_data$G
Z <- sim_data$Z
Y_normal <- sim_data$Y_normal

# fit lucid model
fit1 <- est.lucid(G = G, Z = Z, Y = Y_normal, family = "normal", K = 2,
                 seed = 1008)

# conduct bootstrap resampling
boot1 <- boot.lucid(G = G, Z = Z, Y = Y_normal, model = fit1, R = 100)

# check distribution for bootstrap replicates of the variable of interest
plot(boot1$bootstrap, 1)

# use 90% CI
boot2 <- boot.lucid(G = G, Z = Z, Y = Y_normal, model = fit1, R = 100, conf = 0.9)

## End(Not run)
```
Usage

est.lucid(  
  G,  
  Z,  
  Y,  
  CoG = NULL,  
  CoY = NULL,  
  K = 2,  
  family = c("normal", "binary"),  
  useY = TRUE,  
  tol = 0.001,  
  max_itr = 1000,  
  max_tot.itr = 10000,  
  Rho_G = 0,  
  Rho_Z_Mu = 0,  
  Rho_Z_Cov = 0,  
  modelName = "VVV",  
  seed = 123,  
  init_impute = c("mclust", "lod"),  
  init_par = c("mclust", "random"),  
  verbose = FALSE  
)

Arguments

G  Exposures, a numeric vector, matrix, or data frame. Categorical variable should be transformed into dummy variables. If a matrix or data frame, rows represent observations and columns correspond to variables.

Z  Omics data, a numeric matrix or data frame. Rows correspond to observations and columns correspond to variables.

Y  Outcome, a numeric vector. Categorical variable is not allowed. Binary outcome should be coded as 0 and 1.

CoG  Optional, covariates to be adjusted for estimating the latent cluster. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

CoY  Optional, covariates to be adjusted for estimating the association between latent cluster and the outcome. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

K  Number of latent clusters. An integer greater or equal to 2. User can use lucid to determine the optimal number of latent clusters.

family  Distribution of outcome. For continuous outcome, use "normal"; for binary outcome, use "binary". Default is "normal".

useY  Flag to include information of outcome when estimating the latent cluster. Default is TRUE.

tol  Tolerance for convergence of EM algorithm. Default is 1e-3.

max_itr  Max number of iterations for EM algorithm.
est.lucid

max_tot.itr  Max number of total iterations for est.lucid function. est.lucid may conduct EM algorithm for multiple times if the algorithm fails to converge.

Rho_G  A scalar. Penalty to conduct LASSO regularization and obtain a sparse estimation for effect of exposures. If user wants to tune the penalty, use the wrapper function lucid

Rho_Z_Mu  A scalar. Penalty to conduct LASSO regularization and obtain a sparse estimation of cluster-specific mean for omics data. If user wants to tune the penalty, use the wrapper function lucid

Rho_Z_Cov  A scalar. Penalty to conduct graphic LASSO regularization and obtain a sparse estimation of cluster-specific variance-covariance matrices for omics data. If user wants to tune the penalty, use the wrapper function lucid

modelName  The variance-covariance structure for omics data. See mclust::mclustModelNames for details.

seed  An integer to initialize the EM algorithm or imputing missing values. Default is 123.

init_impute  Method to initialize the imputation of missing values in LUCID. "mclust" will use mclust::imputeData to implement EM Algorithm for Unrestricted General Location Model to impute the missing values in omics data; lod will initialize the imputation via replacing missing values by LOD / sqrt(2). LOD is determined by the minimum of each variable in omics data.

init_par  Method to initialize the EM algorithm. "mclust" will use mclust model to initialize parameters; "random" initialize parameters from uniform distribution.

verbose  A flag indicates whether detailed information for each iteration of EM algorithm is printed in console. Default is FALSE.

Value

A list which contains the several features of LUCID, including:

pars  Estimates of parameters of LUCID, including beta (effect of exposure), mu (cluster-specific mean for omics data), sigma (cluster-specific variance-covariance matrix for omics data) and gamma (effect estimate of association between latent cluster and outcome)

K  Number of latent cluster

modelName  Geometric model to estimate variance-covariance matrix for omics data

likelihood  The log likelihood of the LUCID model

post.p  Posterior inclusion probability (PIP) for assigning observation i to latent cluster j

Z  If missing values are observed, this is the complete dataset for omics data with missing values imputed by LUCID

References

Examples

```r
## Not run:
# use simulated data
G <- sim_data$G
Z <- sim_data$Z
Y_normal <- sim_data$Y_normal
Y_binary <- sim_data$Y_binary
cov <- sim_data$Covariate

# fit LUCID model with continuous outcome
fit1 <- est.lucid(G = G, Z = Z, Y = Y_normal, family = "normal", K = 2,
seed = 1008)

# fit LUCID model with block-wise missing pattern in omics data
Z_miss_1 <- Z
Z_miss_1[sample(1:nrow(Z), 0.3 * nrow(Z)), ] <- NA
fit2 <- est.lucid(G = G, Z = Z_miss_1, Y = Y_normal, family = "normal", K = 2)

# fit LUCID model with sporadic missing pattern in omics data
Z_miss_2 <- Z
index <- arrayInd(sample(length(Z_miss_2), 0.3 * length(Z_miss_2)), dim(Z_miss_2))
Z_miss_2[index] <- NA
# initialize imputation by imputing
fit3 <- est.lucid(G = G, Z = Z_miss_2, Y = Y_normal, family = "normal", K = 2,
seed = 1008, init_impute = "lod")

# initialize imputation by mclust
fit4 <- est.lucid(G = G, Z = Z_miss_2, Y = Y, family = "normal", K = 2,
seed = 123, init_impute = "mclust")

# fit LUCID model with binary outcome
fit5 <- est.lucid(G = G, Z = Z, Y = Y_binary, family = "binary", K = 2,
seed = 1008)

# fit LUCID model with covariates
fit6 <- est.lucid(G = G, Z = Z, Y = Y_binary, CoY = cov, family = "binary",
K = 2, seed = 1008)

# use LUCID model to conduct integrated variable selection
# select exposure
fit6 <- est.lucid(G = G, Z = Z, Y = Y_normal, CoY = NULL, family = "normal",
K = 2, seed = 1008, Rho_G = 0.1)
# select omics data
fit7 <- est.lucid(G = G, Z = Z, Y = Y_normal, CoY = NULL, family = "normal",
K = 2, seed = 1008, Rho_Z_Mu = 90, Rho_Z_Cov = 0.1, init_par = "random")

## End(Not run)
```

**fill_data**

Impute missing data by optimizing the likelihood function
**gen_ci**

**Description**

Impute missing data by optimizing the likelihood function

**Usage**

```
fill_data(obs, mu, sigma, p, index)
```

**Arguments**

- `obs` a vector of length M
- `mu` a matrix of size M x K
- `sigma` a matrix of size M x M x K
- `p` a vector of length K
- `index` a vector of length M, indicating whether a value is missing or not in the raw data

**Value**

an observation with updated imputed value

---

**gen_ci**  
*generate bootstrap ci (normal, basic and percentile)*

---

**Description**

generate bootstrap ci (normal, basic and percentile)

**Usage**

```
gen_ci(x, conf = 0.95)
```

**Arguments**

- `x` an object return by boot function
- `conf` A numeric scalar between 0 and 1 to specify confidence level(s) of the required interval(s).

**Value**

a matrix, the first column is t0 statistic from original model
helix_data  HELIX data

Description

The Human Early-Life Exposome (HELIX) project is multi-center research project that aims to characterize early-life environmental exposures and associate these with omics biomarkers and child health outcomes (Vrijheid, 2014, doi: 10.1289/ehp.1307204). We used a subset of HELIX data from Exposome Data Challenge 2021 (hold by ISGlobal) as an example to illustrate LUCID model.

Usage

helix_data

Format

A list with 4 matrices corresponding to exposures (G), omics data (Z), outcome (Y) and covariates (CoY)

- **exposure**: 8 variables, representing children/maternal exposure to environmental pollutants
- **omics**: 10 proteins
- **outcome**: A continuous outcome for BMI-z score based on WHO standard. A binary outcome for body mass index categories at 6-11 years old based on WHO reference (0: Thinness or Normal; 1: Overweight or Obese)
- **covariate**: 3 covariates including mother's bmi, child sex, maternal age

lucid  A wrapper function to perform model selection for LUCID

Description

Given a grid of K and L1 penalties (including Rho_G, Rho_Z_mu and Rho_Z_Cov), fit LUCID model over all combinations of K and L1 penalties to determine the optimal penalty.

Usage

lucid(
  G,
  Z,
  Y,
  CoG = NULL,
  CoY = NULL,
  family = "normal",
  useY = TRUE,
  K = 2:5,
)
Rho_G = 0, 
Rho_Z_Mu = 0, 
Rho_Z_Cov = 0, 
...
)

**Arguments**

G  
Exposures, a numeric vector, matrix, or data frame. Categorical variable should be transformed into dummy variables. If a matrix or data frame, rows represent observations and columns correspond to variables.

Z  
Oomics data, a numeric matrix or data frame. Rows correspond to observations and columns correspond to variables.

Y  
Outcome, a numeric vector. Categorical variable is not allowed. Binary outcome should be coded as 0 and 1.

CoG  
Optional, covariates to be adjusted for estimating the latent cluster. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

CoY  
Optional, covariates to be adjusted for estimating the association between latent cluster and the outcome. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

family  
Distribution of outcome. For continuous outcome, use "normal"; for binary outcome, use "binary". Default is "normal".

useY  
Flag to include information of outcome when estimating the latent cluster. Default is TRUE.

K  
Number of latent clusters. An integer greater or equal to 2.

Rho_G  
A scalar or a vector. Penalty to conduct LASSO regularization and obtain a sparse estimation for effect of exposures. If a vector, lucid will fit lucid model over the grid of penalties.

Rho_Z_Mu  
A scalar or a vector. Penalty to conduct LASSO regularization and obtain a sparse estimation of cluster-specific mean for omics data. If a vector, lucid will fit lucid model over the grid of penalties.

Rho_Z_Cov  
Penalty to conduct graphic LASSO regularization and obtain a sparse estimation of cluster-specific variance-covariance matrices for omics data. If a vector, lucid will fit lucid model over the grid of penalties.

...  
Other parameters passed to est.lucid

**Value**

A list:

- **best_model**: the best model over different combination of tuning parameters
- **tune_list**: a data frame contains combination of tuning parameters and corresponding BIC
- **res_model**: a list of LUCID models corresponding to each combination of tuning parameters
Examples

## Not run:
# use simulated data
G <- sim_data$G
Z <- sim_data$Z
Y_normal <- sim_data$Y_normal

# find the optimal model over the grid of K
tune_K <- lucid(G = G, Z = Z, Y = Y_normal, useY = FALSE, tol = 1e-3, seed = 1, K = 2:5)

# tune penalties
tune_Rho_G <- lucid(G = G, Z = Z, Y = Y_normal, useY = FALSE, tol = 1e-3, seed = 1, K = 2, Rho_G = c(0.1, 0.2, 0.3, 0.4))
tune_Rho_Z_mu <- lucid(G = G, Z = Z, Y = Y_normal, useY = FALSE, tol = 1e-3, seed = 1, K = 2, Rho_Z_mu = c(10, 20, 30, 40))
tune_Rho_Z_Cov <- lucid(G = G, Z = Z, Y = Y_normal, useY = FALSE, tol = 1e-3, seed = 1, K = 2, Rho_Z_Cov = c(0.1, 0.2, 0.3))

## End(Not run)
predict_lucid

G_color  Color of node for exposure
X_color  Color of node for latent cluster
Z_color  Color of node for omics data
Y_color  Color of node for outcome
pos_link_color  Color of link corresponds to positive association
neg_link_color  Color of link corresponds to negative association
fontsize  Font size for annotation

Value

A DAG graph created by sankeyNetwork

Examples

```r
## Not run:
# prepare data
G <- sim_data$G
Z <- sim_data$Z
Y_normal <- sim_data$Y_normal
Y_binary <- sim_data$Y_binary
cov <- sim_data$Covariate

# plot lucid model
fit1 <- est.lucid(G = G, Z = Z, Y = Y_normal, CoY = NULL, family = "normal",
                  K = 2, seed = 1008)
plot_lucid(fit1)

# change node color
plot_lucid(fit1, G_color = "yellow")
plot_lucid(fit1, Z_color = "red")

# change link color
plot_lucid(fit1, pos_link_color = "red", neg_link_color = "green")

## End(Not run)
```

predict_lucid

Predict cluster assignment and outcome based on LUCID model

Description

Predict cluster assignment and outcome based on LUCID model

Usage

predict_lucid(model, G, Z, Y = NULL, CoG = NULL, CoY = NULL, response = TRUE)
Arguments

- **model**: A model fitted and returned by `est.lucid`.

- **G**: Exposures, a numeric vector, matrix, or data frame. Categorical variable should be transformed into dummy variables. If a matrix or data frame, rows represent observations and columns correspond to variables.

- **Z**: Omics data, a numeric matrix or data frame. Rows correspond to observations and columns correspond to variables.

- **Y**: Outcome, a numeric vector. Categorical variable is not allowed. Binary outcome should be coded as 0 and 1.

- **CoG**: Optional, covariates to be adjusted for estimating the latent cluster. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

- **CoY**: Optional, covariates to be adjusted for estimating the association between latent cluster and the outcome. A numeric vector, matrix or data frame. Categorical variable should be transformed into dummy variables.

- **response**: If TRUE, when predicting binary outcome, the response will be returned. If FALSE, the linear predictor is returned.

Value

A list contains predicted latent cluster and outcome for each observation.

Examples

```r
## Not run:
# prepare data
G <- sim_data$G
Z <- sim_data$Z
Y_normal <- sim_data$Y_normal

# fit lucid model
fit1 <- est.lucid(G = G, Z = Z, Y = Y_normal, K = 2, family = "normal")

# prediction on training set
pred1 <- predict_lucid(model = fit1, G = G, Z = Z, Y = Y_normal)
pred2 <- predict_lucid(model = fit1, G = G, Z = Z)
## End(Not run)
```

Print the output of `est.lucid`

Print the output of `est.lucid`
print.sumlucid

Usage

```r
## S3 method for class 'lucid'
print(x, ...)
```

Arguments

- `x`: An object of LUCID model, returned by `est.lucid`
- `...`: Other arguments to be passed to `print`

---

print.sumlucid

*Print the output of LUCID in a nicer table*

Description

Print the output of LUCID in a nicer table

Usage

```r
## S3 method for class 'sumlucid'
print(x, ...)
```

Arguments

- `x`: An object returned by `summary.lucid`
- `...`: Other parameters to be passed to `print`

---

sim_data

*A simulated dataset for LUCID*

Description

This is an example dataset to illustrate LUCID model. It is simulated by assuming there are 2 latent clusters in the data. We assume the exposures are associated with latent cluster which ultimately affects the PFAS concentration and liver injury in children. The latent clusters are also characterized by differential levels of metabolites.

Usage

```r
sim_data
```
Format

A list with 5 matrices corresponding to exposures (G), omics data (Z), a continuous outcome, a binary outcome and 2 covariates (can be used either as CoX or CoY). Each matrix contains 2000 observations.

G 10 exposures  
Z 10 metabolites  
Y_normal Outcome, PFAS concentration in children  
Y_binary Binary outcome, liver injury status  
Covariates 2 continous covariates, can be treated as either CoX or CoY  
X Latent clusters

summary_lucid  Summarize results of LUCID model

Description

Summarize results of LUCID model

Usage

summary_lucid(object, boot.se = NULL)

Arguments

object A LUCID model fitted by est.lucid  
boot.se An object returned by boot.lucid, which contains the bootstrap confidence intervals

Examples

## Not run:  
# use simulated data  
G <- sim_data$G  
Z <- sim_data$Z  
Y_normal <- sim_data$Y_normal  

# fit lucid model  
fit1 <- est.lucid(G = G, Z = Z, Y = Y_normal, family = "normal", K = 2, seed = 1008)  

# conduct bootstrap resampling  
boot1 <- boot.lucid(G = G, Z = Z, Y = Y_normal, model = fit1, R = 100)  

# summarize lucid model  
summary_lucid(fit1)
# summarize lucid model with bootstrap CIs
summary_lucid(fit1, boot.se = boot)

## End(Not run)
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