Package ‘bipd’

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Description
We use a Bayesian approach to run individual patient data meta-analysis and network meta-analysis using 'JAGS'. The methods incorporate shrinkage methods and calculate patient-specific treatment effects as described in Seo et al. (2021) <DOI:10.1002/sim.8859>. This package also includes user-friendly functions that impute missing data in an individual patient data using mice-related packages.

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bipd-package

bipd: A package for individual patient data meta-analysis using 'JAGS'

Description

A package for individual patient data meta-analysis using 'JAGS'

Details

We use a Bayesian approach to run individual patient data meta-analysis and network meta-analysis using 'JAGS'. The methods incorporate shrinkage methods and calculate patient-specific treatment effects as described in Seo et al. (2021) [DOI:10.1002/sim.8859]. This package also includes user-friendly functions that impute missing data in an individual patient data using mice-related packages.

References


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### add.mcmc

#### Convenient function to add results (i.e. combine mcmc.list)

**Description**

This is a convenient function to add results (i.e. combine mcmc.list). This can be useful when combining results obtained from multiple imputation.

**Usage**

```
add.mcmc(x, y)
```

**Arguments**

- `x` first result in a format of mcmc.list
- `y` second result in a format of mcmc.list

**Examples**

```r
ds <- generate_ipdma_example(type = "continuous")
ls2 <- generate_ipdma_example(type = "continuous")
ipd <- with(ds, ipdma.model.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2), response = "normal", shrinkage = "none"))
ipd2 <- with(ds2, ipdma.model.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2), response = "normal", shrinkage = "none"))
samples <- ipd.run(ipd, pars.save = c("beta", "gamma", "delta"), n.chains = 3, n.burnin = 500, n.iter = 5000)
samples2 <- ipd.run(ipd2, pars.save = c("beta", "gamma", "delta"), n.chains = 3, n.burnin = 500, n.iter = 5000)
combined <- add.mcmc(samples, samples2)
```
**Description**

Find missing data pattern in a given data i.e. whether variables are systematically missing or sporadically missing. Also calculates missing count and percentage for exploratory purposes.

**Usage**

```r
findMissingPattern(
  dataset = NULL,
  covariates = NULL,
  typeofvar = NULL,
  studyname = NULL,
  treatmentname = NULL,
  outcome name = NULL
)
```

**Arguments**

- `dataset`: data which contains variables of interests
- `covariates`: vector of variable names that the user is interested in finding a missing data pattern
- `typeofvar`: type of covariate variables; should be a vector of these values: "continuous", "binary", or "count". Order should follow that of covariates parameter.
- `studyname`: study name in the data specified
- `treatmentname`: treatment name in the data specified
- `outcome name`: outcome name in the data specified

**Value**

- `missingcount`: missing number of patients for each study and covariate
- `missingpercent`: missing percentage of patients for each study and covariate
- `sys_missing`: a vector indicating whether each covariate is systematically missing
- `spor_missing`: a vector indicating whether each covariate is sporadically missing
- `sys_covariates`: a vector of systematically missing covariates
- `spor_covariates`: a vector of sporadically missing covariates
- `without_sys_covariates`: a vector of covariates that are not systematically missing
- `covariates`: vector of variable names that the user is interested in finding a missing data pattern
- `studyname`: study name in the data specified
- `treatmentname`: treatment name in the data specified
- `outcome name`: outcome name in the data specified
Examples

```r
simulated_dataset <- generate_sysmiss_ipdma_example(Nstudies = 10, Ncov = 5, sys_missing_prob = 0.3, magnitude = 0.2, heterogeneity = 0.1)

missP <- findMissingPattern(simulated_dataset, covariates = c("x1", "x2", "x3", "x4", "x5"), typeofvar = c("continuous", "binary", "binary", "continuous", "continuous"), studyname = "study", treatmentname = "treat", outcomename = "y")
missP
```

---

**generate_ipdma_example**

*Generate a simulated IPD-MA data for demonstration*

**Description**

Generate a simulated IPD-MA data for demonstration

**Usage**

```r
generate_ipdma_example(type = "continuous")
```

**Arguments**

- `type` : "continuous" for continuous outcome and "binary" for binary outcome

**Value**

returns simulated IPD-MA data

**Examples**

```r
ds <- generate_ipdma_example(type = "continuous")
head(ds)
```

---

**generate_ipdnma_example**

*Generate a simulated IPD-NMA data for demonstration*

**Description**

Generate a simulated IPD-NMA data for demonstration

**Usage**

```r
generate_ipdnma_example(type = "continuous")
```

**Value**

returns simulated IPD-NMA data

**Examples**

```r
ds <- generate_ipdnma_example(type = "continuous")
```
Arguments

- **type**: "continuous" for continuous outcome and "binary" for binary outcome.

Value

- return simulated IPD-NMA data `ds <- generate_ipdnma_example(type = "continuous")` `head(ds)`

Description

Generate a simulated IPD-MA data with systematically missing covariates.

Usage

```r
generate_sysmiss_ipdma_example(
  Nstudies = 10,
  Ncov = 5,
  sys_missing_prob = 0.1,
  magnitude = 0.3,
  heterogeneity = 0.1,
  interaction = TRUE
)
```

Arguments

- **Nstudies**: number of studies. Default is 10.
- **Ncov**: number of covariates in total. Options are 5 or 10 studies. Default is set to 5.
- **sys_missing_prob**: probability of systematically missing studies for each covariates. Default is set to 0.3.
- **magnitude**: magnitude of the regression estimates (the mean). Default is set to 0.2.
- **heterogeneity**: heterogeneity of regression estimates across studies. Default is set to 0.1.
- **interaction**: whether to include treatment indicator and treatment

Value

- returns simulated IPD-MA data with systematically missing covariates

Examples

```r
simulated_dataset <- generate_sysmiss_ipdma_example(Nstudies = 10, Ncov = 5, sys_missing_prob = 0.3,
magnitude = 0.2, heterogeneity = 0.1)
head(simulated_dataset)
```
Run the model using the ipd object

Description

This is the core function that runs the model in our program. Before running this function, we need to specify data, prior, JAGS code, etc. using ipd.model type function.

Usage

ipd.run(
  ipd,
  pars.save = NULL,
  inits = NULL,
  n.chains = 3,
  n.adapt = 1000,
  n.burnin = 1000,
  n.iter = 10000
)

Arguments

- **ipd**: ipd object created from ipd.model type function
- **pars.save**: parameters to save. For instance, "beta" - coefficients for main effects; "gamma" - coefficients for effect modifiers; "delta" - average treatment effect
- **inits**: initial values specified for the parameters to save
- **n.chains**: number of MCMC chains to sample
- **n.adapt**: number of iterations for adaptation (Note that the samples from adaptation phase is non-Markovian and do not constitute a Markov chain)
- **n.burnin**: number of iterations for burn-in
- **n.iter**: number of iterations to run after the adaptation

Value

MCMC samples stored using JAGS. The returned samples have the form of mcmc.list and coda functions can be directly applied.

Examples

ds <- generate_ipdma_example(type = "continuous")
ipd <- with(ds, ipdma.model.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2),
  response = "normal", shrinkage = "none"))

samples <- ipd.run(ipd, n.chains = 3, n.burnin = 500, n.iter = 5000)
ipd.run.parallel Run the model using the ipd object with parallel computation

Description
This function runs the model through parallel computation using dclone R package. Before running this function, we need to specify data, prior, JAGS code, etc. using ipd.model type function.

Usage

```
ipd.run.parallel(
ipd,
pars.save = NULL,
inits = NULL,
n.chains = 2,
n.adapt = 1000,
n.burnin = 1000,
n.iter = 10000
)
```

Arguments

- **ipd**: ipd object created from ipd.model type function
- **pars.save**: parameters to save. For instance, "beta" - coefficients for main effects; "gamma" - coefficients for effect modifiers; "delta" - average treatment effect
- **inits**: initial values specified for the parameters to save
- **n.chains**: number of MCMC chains to sample
- **n.adapt**: number of iterations for adaptation (Note that the samples from adaptation phase is non-Markovian and do not constitute a Markov chain)
- **n.burnin**: number of iterations for burn-in
- **n.iter**: number of iterations to run after the adaptation

Value

MCMC samples stored using JAGS. The returned samples have the form of mcmc.list and coda functions can be directly applied.

Examples

```
ds <- generate_ipdma_example(type = "continuous")
ipd <- with(ds, ipdma.model.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2), response = "normal", shrinkage = "none"))
samples <- ipd.run.parallel(ipd, n.chains = 2, n.burnin = 500, n.iter = 5000)
```
ipdma.impute

Impute missing data in individual participant data with two treatments (i.e. placebo and a treatment).

Description

Impute missing data in individual participant data with two treatments. Data is clustered by different studies. In the presence of systematically missing variables, the function defaults to 2l.2stage.norm, 2l.2stage.bin, and 2l.2stage.pois methods in micemd package. If there are no systematically missing variables, the function defaults to use 2l.pmm in miceadds package which generalizes predictive mean matching using linear mixed model. If there is only one study available, the function defaults to use pmm in mice package.

Usage

ipdma.impute(
  dataset = NULL,
  covariates = NULL,
  typeofvar = NULL,
  sys_impute_method = "2l.2stage",
  interaction = NULL,
  meth = NULL,
  pred = NULL,
  studyname = NULL,
  treatmentname = NULL,
  outcomename = NULL,
  m = 5
)

Arguments

dataset data which contains variables of interests
covariates vector of variable names to find missing data pattern
typeofvar type of covariate variables; should be a vector of these values: "continuous", "binary", or "count". Order should follow that of covariates parameter specified. Covariates that are specified "binary" are automatically factored.
sys_impute_method method used for systematically missing studies. Options are "2l.glm", "2l.2stage", or "2l.jomo". Default is set to "2l.2stage". There is also an option to ignore all the clustering level and impute using predictive mean matching by setting this parameter to "pmm".
interaction indicator denoting whether treatment-covariate interactions should be included. Default is set to true.
meth imputation method to be used in the mice package. If left unspecified, function picks a reasonable one.
pred correct prediction matrix to be used in the mice package. If left unspecified, function picks a reasonable one.
studyname study name in the data specified.
treatmentname treatment name in the data specified.
outcomename outcome name in the data specified.
m number of imputed datasets. Default is set to 5.

Value

missingPattern missing pattern object returned by running findMissingPattern function
meth imputation method used with the mice function
pred prediction matrix used with the mice function
imp imputed datasets that is returned from the mice function
imp.list imputed datasets in a list format

Examples

simulated_dataset <- generate_sysmiss_ipdma_example(Nstudies = 10, Ncov = 5, sys_missing_prob = 0.3, magnitude = 0.2, heterogeneity = 0.1)

# load in mice packages
library(mice) #for datasets with only one study level
library(miceadds) #for multilevel datasets without systematically missing predictors
library(micemd) #for multilevel datasets with systematically missing predictors.
imputation <- ipdma.impute(simulated_dataset, covariates = c("x1", "x2", "x3", "x4", "x5"),
typeofvar = c("continuous", "binary", "binary", "continuous", "continuous"), interaction = TRUE,
studyname = "study", treatmentname = "treat", outcomename = "y", m = 5)
response = "normal",
type = "random",
mean.alpha = 0,
prec.alpha = 0.001,
mean.beta = 0,
prec.beta = 0.001,
mean.gamma.within = 0,
prec.gamma.within = 0.001,
mean.gamma.across = 0,
prec.gamma.across = 0.001,
mean.delta = 0,
prec.delta = 0.001,
hy.prior = list("dhnorm", 0, 1)
)

Arguments

y            outcome of the study. Can be continuous or binary.
study        vector indicating which study the patient belongs to. Please change the study names into numbers (i.e. 1, 2, 3, etc)
treat        vector indicating which treatment the patient was assigned to (i.e. 1 for treatment, 0 for placebo)
X             matrix of covariate values for each patient. Dimension would be number of patients x number of covariates.
response     specification of the outcome type. Must specify either "normal" or "binomial".
type         assumption on the treatment effect: either "random" for random effects model or "fixed" for fixed effects model. Default is "random".
mean.alpha   prior mean for the study intercept
prec.alpha   prior precision for the study intercept
mean.beta    prior mean for the regression coefficients of the main effects of the covariates; main effects are assumed to have common effect.
prec.beta    prior precision for the regression coefficients of the main effects of the covariates
mean.gamma.within prior mean for effect modifiers of within study information.
prec.gamma.within prior precision for the effect modifiers of within study information.
mean.gamma.across prior mean for the effect modifiers of across study information; effect modification is assumed to have common effect.
prec.gamma.across prior precision for the effect modifiers of across study information
mean.delta    prior mean for the average treatment effect
prec.delta    prior precision for the average treatment effect
hy.prior prior for the heterogeneity parameter. Supports uniform, gamma, and half normal for normal and binomial response. It should be a list of length 3, where the first element should be the distribution (one of dunif, dgamma, dhnorm) and the next two are the parameters associated with the distribution. For example, list(“dunif”, 0, 5) gives uniform prior with lower bound 0 and upper bound 5 for the heterogeneity parameter.

Value

data.JAGS data organized in a list so that it can be used when running code in JAGS

code JAGS code that is used to run the model. Use cat(code) to see the code in a readable format

model.JAGS JAGS code in a function. This is used when running model in parallel

Xbar study specific averages of covariates

References


Examples

ds <- generate_ipdma_example(type = "continuous")
ipd <- with(ds, ipdma.model.deft.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2), response = "normal"))

samples <- ipd.run(ipd)
treatment.effect(ipd, samples, newpatient = c(1, 0.5), reference = c(0, 0))

ipdma.model.onestage Make an one-stage individual patient data meta-analysis object containing data, priors, and a JAGS model code

Description

This function sets up data and JAGS code that is needed to run one-stage IPD-MA models in JAGS.

Usage

ipdma.model.onestage(
  y = NULL,
  study = NULL,
  treat = NULL,
  X = NULL,
  response = "normal",
  type = "random",
  hy.prior = list("dunif", 0, 5))
shrinkage = "none",
scale = TRUE,
mean.alpha = 0,
prec.alpha = 0.001,
mean.beta = 0,
prec.beta = 0.001,
mean.gamma = 0,
prec.gamma = 0.001,
mean.delta = 0,
prec.delta = 0.001,
hy.prior = list("dhnorm", 0, 1),
lambda.prior = NULL,
p.ind = NULL,
g = NULL,
hy.prior.eta = NULL
)

Arguments

y
outcome of the study. Can be continuous or binary.

study
vector indicating which study the patient belongs to. Please change the study
names into numbers (i.e. 1, 2, 3, etc)

treat
vector indicating which treatment the patient was assigned to (i.e. 1 for treat-
ment, 0 for placebo)

X
matrix of covariate values for each patient. Dimension would be number of
patients x number of covariates.

response
specification of the outcome type. Must specify either "normal" or "binomial".

type
assumption on the treatment effect: either "random" for random effects model
or "fixed" for fixed effects model. Default is "random".

shrinkage
shrinkage method applied to the effect modifiers. "none" correspond to no
shrinkage. "laplace" corresponds to a adaptive shrinkage with a Laplacian prior
(ie often known as Bayesian LASSO). "SSVS" corresponds to the Stochastic
Search Variable Selection method. SSVS is not strictly a shrinkage method, but
pulls the estimated coefficient toward zero through variable selection in each

scale
indicator for scaling the covariates by the overall average; default is TRUE.

mean.alpha
prior mean for the study intercept

prec.alpha
prior precision for the study intercept

mean.beta
prior mean for the regression coefficients of the main effects of the covariates;
main effects are assumed to have common effect.

prec.beta
prior precision for the regression coefficients of the main effects of the covariates

mean.gamma
prior mean for the effect modifiers. This parameter is not used if penalization is
placed on effect modifiers.

prec.gamma
prior precision for the effect modifiers. This parameter is not used if penalization
is placed on effect modifiers.
mean.delta  prior mean for the average treatment effect
prec.delta  prior precision for the average treatment effect
hy.prior  prior for the heterogeneity parameter. Supports uniform, gamma, and half normal for normal and binomial response. It should be a list of length 3, where first element should be the distribution (one of dunif, dgamma, dhnorm) and the next two are the parameters associated with the distribution. For example, list("dunif", 0, 5) gives uniform prior with lower bound 0 and upper bound 5 for the heterogeneity parameter.

lambda.prior  (only for shrinkage = "laplace") two options for laplace shrinkage. We can put a gamma prior on the lambda (i.e. list("dgamma",2,0.1)) or put a uniform prior on the inverse of lambda (i.e. list("dunif",0,5))
p.ind  (only for shrinkage = "SSVS") prior probability of including each of the effect modifiers. Length should be same as the total length of the covariates.
g  (only for shrinkage = "SSVS") multiplier for the precision of spike. Default is g = 1000.
hy.prior.eta  (only for shrinkage = "SSVS") standard deviation of the slab prior. Currently only support uniform distribution. Default is list("dunif", 0, 5)

Value
data.JAGS  data organized in a list so that it can be used when running code in JAGS
code  JAGS code that is used to run the model. Use cat(code) to see the code in a readable format
model.JAGS  JAGS code in a function. This is used when running model in parallel
scale.mean  mean used in scaling covariates
scale.sd  standard deviation used in scaling covariates

References

Examples
ds <- generate_ipdma_example(type = "continuous")
ipd <- with(ds, ipdma.model.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2), response = "normal", shrinkage = "none"))
samples <- ipd.run(ipd)
treatment.effect(ipd, samples, newpatient= c(1,0.5))
ipdnma.model.onestage Make an one-stage individual patient data network meta-analysis object containing data, priors, and a JAGS model code

Description

This function sets up data and JAGS code that is needed to run one-stage IPD-NMA models in JAGS.

Usage

ipdnma.model.onestage(
  y = NULL,
  study = NULL,
  treat = NULL,
  X = NULL,
  response = "normal",
  type = "random",
  shrinkage = "none",
  scale = TRUE,
  mean.alpha = 0,
  prec.alpha = 0.001,
  mean.beta = 0,
  prec.beta = 0.001,
  mean.gamma = 0,
  prec.gamma = 0.001,
  mean.delta = 0,
  prec.delta = 0.001,
  hy.prior = list("dhnorm", 0, 1),
  lambda.prior = NULL,
  p.ind = NULL,
  g = NULL,
  hy.prior.eta = NULL
)

Arguments

y outcome of the study. Can be continuous or binary.
study vector indicating which study the patient belongs to. Please change the study names into numbers (i.e. 1, 2, 3, etc)
treat vector indicating which treatment the patient was assigned to. Since this is a network meta-analysis and there would be more than 2 treatments, careful naming of treatment is needed. This vector needs to be a sequence from 1:NT where NT is the total number of treatments. Treatment that is assigned 1 would be the baseline treatment.
matrix of covariate values for each patient. Dimension would be number of patients x number of covariates.

specification of the outcome type. Must specify either "normal" or "binomial".

assumption on the treatment effect: either "random" for random effects model or "fixed" for fixed effects model. Default is "random".

shrinkage method applied to the effect modifiers. "none" correspond to no shrinkage. "laplace" corresponds to a adaptive shrinkage with a Laplacian prior (ie often known as Bayesian LASSO). "SSVS" corresponds to the Stochastic Search Variable Selection method. SSVS is not strictly a shrinkage method, but pulls the estimated coefficient toward zero through variable selection in each iteration of the MCMC. See O'hara et al (2009) for more details.

indicator for scaling the covariates by the overall average; default is TRUE.

prior mean for the study intercept

prior precision for the study intercept

prior mean for the regression coefficients of the main effects of the covariates; main effects are assumed to have common effect.

prior precision for the regression coefficients of the main effects of the covariates

prior mean for the effect modifiers. This parameter is not used if penalization is placed on effect modifiers.

prior precision for the effect modifiers. This parameter is not used if penalization is placed on effect modifiers.

prior mean for the average treatment effect

prior precision for the average treatment effect

prior for the heterogeneity parameter. Supports uniform, gamma, and half normal for normal and binomial response It should be a list of length 3, where first element should be the distribution (one of dunif, dgamma, dhnorm) and the next two are the parameters associated with the distribution. For example, list("dunif", 0, 5) gives uniform prior with lower bound 0 and upper bound 5 for the heterogeneity parameter.

(only for shrinkage = "laplace") two options for laplace shrinkage. We can put a gamma prior on the lambda (i.e. list("dgamma",2,0.1)) or put a uniform prior on the inverse of lambda (i.e. list("dunif",0,5))

(only for shrinkage = "SSVS") prior probability of including each of the effect modifiers. Length should be same as the total length of the covariates.

(only for shrinkage = "SSVS") multiplier for the precision of spike. Default is g = 1000.

(only for shrinkage = "SSVS") standard deviation of the slab prior. Currently only support uniform distribution. Default is list("dunif", 0, 5)

Value

data.JAGS data organized in a list so that it can be used when running code in JAGS

code JAGS code that is used to run the model. Use cat(code) to see the code in a readable format
treatment.effect  

model.JAGS  JAGS code in a function. This is used when running model in parallel  
scale.mean  mean used in scaling covariates  
scale.sd  standard deviation used in scaling covariates  

References  


Examples  

ds <- generate_ipdnma_example(type = ’continuous’)  
ipd <- with(ds, ipdnma.model.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2), response = ”normal”, shrinkage = ”none”))  
samples <- ipd.run(ipd)  
treatment.effect(ipd, samples, newpatient= c(1,0.5))

--------------------------------------------------------------------------------

treatment.effect  Calculate patient-specific treatment effect  

Description  

Function for calculating the patient-specific treatment effect. Patient-specific treatment effect includes the main effect of treatment and treatment-covariate interaction effect (i.e. effect modification). Reports odds ratio for the binary outcome.  

Usage  

treatment.effect(  
  ipd = NULL,  
samples = NULL,  
newpatient = NULL,  
scale_mean = NULL,  
scale_sd = NULL,  
reference = NULL,  
quantiles = c(0.025, 0.5, 0.975)  
)
Arguments

- `ipd`  
  IPD object created from running `ipdma.model` type function

- `samples`  
  MCMC samples found from running `ipd.run` function

- `newpatient`  
  Covariate values of patients that you want to predict treatment effect on. Must have length equal to total number of covariates.

- `scale_mean`  
  Option to specify different overall mean compared to what was calculated in IPD object. Can be useful when using multiple imputation.

- `scale_sd`  
  Option to specify different overall standard deviation compared to what was calculated in IPD object.

- `reference`  
  Reference group used for finding patient-specific treatment effect. This is only used for deft approach.

- `quantiles`  
  Quantiles for credible interval of the patient-specific treatment effect

Value

Patient-specific treatment effect with credible interval at specified quantiles

References


Examples

```r
ds <- generate_ipdma_example(type = "continuous")
ipd <- with(ds, ipdma.model.onestage(y = y, study = studyid, treat = treat, X = cbind(z1, z2), response = "normal", shrinkage = "none"))
samples <- ipd.run(ipd, pars.save = c("beta", "gamma", "delta"), n.chains = 3, n.burnin = 500, n.iter = 5000)
treatment.effect(ipd, samples, newpatient = c(1,0.5))
```
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