Package 'MetaStan'

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Version 0.4.0

Title Bayesian Meta-Analysis via 'Stan'

Description Performs Bayesian meta-analysis and model-based meta-analysis using 'Stan'. Includes binomial-normal hierarchical models and option to use weakly informative priors for the heterogeneity parameter and the treatment effect parameter which are described in Guenhan, Roever, and Friede (2020) <doi:10.1002/jrsm.1370>.

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LazyData true

ByteCompile true

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Imports rstan (>= 2.18.1), rstantools (>= 1.5.0)

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LinkingTo StanHeaders (>= 2.18.0), rstan (>= 2.18.1), BH (>= 1.66.0-1), Rcpp (>= 0.12.17), RcppEigen (>= 0.3.3.4.0)

SystemRequirements GNU make

NeedsCompilation yes

RoxygenNote 7.1.1

URL https://github.com/gunhanb/MetaStan

BugReports https://github.com/gunhanb/MetaStan/issues

VignetteBuilder knitr

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R topics documented:

`MetaStan-package` *The 'MetaStan' package.*

Description

Fitting Bayesian meta-analysis models via Rstan.

Details

To fit meta-analysis models using frequentist methods, there are many R packages available including 'metafor'. On the other hand, Bayesian estimation methods such as Markov chain Monte Carlo (MCMC) are very attractive for meta-analysis, especially because they can be used to fit more complicated models. These include binomial-normal hierarchical models and beta-binomial models which are based on the exact distributional assumptions unlike (commonly used) normal-normal hierarchical model. Another advantage of Bayesian methods to be able to use informative prior distributions for example to regularize heterogeneity estimates in case of low number of studies. Thus, we developed 'MetaStan' which uses Stan (a modern MCMC engine) to fit several pairwise meta-analysis models including binomial-normal hierarchical model and beta-binomial model. This package is also the accompanying package of Guenhan et al (2018).

Author(s)

Burak Kuersad Guenhan <burak.gunhan@med.uni-goettingen.de>

References

Stan Development Team (2018). RStan: the R interface to Stan. R package version 2.17.3. http://mc-stan.org

Günhan, B and Röver, C and Friede, T (2018). Meta-analysis of few studies involving rare events. arXiv.org E-print Archive. https://arxiv.org/abs/1809.04407.

convert_data_arm *Convert contrast-based dataset to arm-based dataset*

Description

convert_data_arm creates a dataframe to fit a Binomial-Normal Hierarchical model using glmer function.

Usage

```
convert_data_arm(nt, nc, pt, pc)
```

Arguments

nt	Number of subjects in treatment arm
nc	Number of subjects in control arm
pt	Number of events in treatment arm
pc	Number of events in treatment arm

Value

A dataframe object

Examples

```
data('dat.Crins2014', package = "MetaStan")
## Subset of dataset where PTLD outcomes available
dat.Crins2014.PTLD = subset(dat.Crins2014, is.finite(exp.PTLD.events))
## Create arm-based dataset
dat.Crins2014.PTLD.arm <- convert_data_arm(dat.Crins2014.PTLD$exp.total,
dat.Crins2014.PTLD$cont.total,dat.Crins2014.PTLD$exp.PTLD.events,
dat.Crins2014.PTLD$cont.PTLD.events)
```

create_MBMA_dat *Prepare model-based meta-analysis dataset for Stan.*

Description

create_MBMA_dat converts datasets in the one-study-per-row format to one-arm-per-row format,

Usage

```
create_MBMA_dat(
  dat = dat,
  armVars = c(dose = "t", responders = "r", sampleSize = "n"),
  nArmsVar = "nd"
)
```

Arguments

dat	Data in one-study-per-row format.
armVars	Vector of per-arm variables The name of each component will be the column name in the resulting dataset.
nArmsVar	Variable holding the number of arms for each study.

Details

The resulting data.frame can be used as data argument in MBMA_stan.

Value

A data frame with the generated coloumns.

Author(s)

Burak Kuersad Guenhan, <burak.gunhan@med.uni-goettingen.de> and Gert van Valkenhoef

See Also

gemtc::mtc.data.studyrow and nmaINLA::create_INLA_dat

Examples

```
data('dat.Eletriptan')
## Create the dataset suitable for MBMA_stan
EletriptanDat <- create_MBMA_dat(dat = dat.Eletriptan,
armVars = c("dose" = "d", "r" = "r", "n" = "n"), nArmsVar = 'nd')
## Check that the data are correct
print(EletriptanDat)
```

dat.Berkey1995 *Trials investigating effectiveness of the BCG vaccine against TB*

Description

A dataset containing the results from 13 trials examining the efficacy of Bacillus Calmette-Guerin (BCG) vaccine against tuberculosis (TB).

Usage

```
dat.Berkey1995
```

Format

A data frame with following coloumns

Trial Trial number

rt number of TB events in treatment arm

nt number of subjects in treatment arm

rc number of TB events in control arm

nc number of subjects in control arm

Latitude absolute latitude of the study location

Source

Berkey, C.S., Hoaglin, D.C., Mosteller, F. and Colditz, G.A., 1995. A random-effects regression model for meta-analysis. Statistics in medicine, 14(4), pp.395-411

dat.Crins2014 *Pediatric liver transplant example data*

Description

Numbers of cases and events (PTLDs or deaths) in experimental and control groups of six studies.

Usage

```
dat.Crins2014
```

Format

A data frame with following coloumns

publication publication identifier (first author and publication year)

year publication year

randomized randomization status (y/n)

control.type type of control group ("concurrent" or "historical")

comparison type of comparison ("IL-2RA only", "delayed CNI", or "no/low steroids")

followup t follow-up time in months

exp.PTLD.events number of PTLD events in experimental group

exp.death.events number of deaths in experimental group

exp.total number of patients in experimental group

cont.PTLD.events number of PTLD events in control group

cont.death.events number of deaths in control group

cont.total number of patients in control group

Source

N.D. Crins, C. Roever, A.D. Goralczyk, T. Friede. Interleukin-2 receptor antagonists for pediatric liver transplant recipients: A systematic review and meta-analysis of controlled studies. Pediatric Transplantation, 18(8):839-850, 2014.

`dat.Eletriptan` *Migraine pain relief example (Eletriptan)*

Description

Numbers of patients and events (headcahe free at 2 hours) in experimental and control groups of 12 studies. It is in one-study-per-row format.

Usage

```
dat.Eletriptan
```

Format

A data frame with following coloumns

ID trial ID

d1 dose (mg) in the first arm (placebo)

r1 number of events in the first arm (placebo)

n1 number of patients in the first arm (placebo)

d2 dose (mg) in the second arm

r2 number of events in the second arm

n2 number of patients in the second arm

d3 dose (mg) in the third arm

r3 number of events in the third arm

n3 number of patients in the third arm

d4 dose (mg) in the fourth arm

r4 number of events in the fourth arm

n4 number of patients in the fourth arm

nd number of treatment arms

Source

Thorlund, K., Mills, E., Wu, P., Ramos, E., Chatterjee, A., Druyts, E., and Goadsby, P. (2014). Comparative efficacy of triptans for the abortive treatment of migraine: A multiple treatment comparison meta-analysis. Cephalalgia, 34(4):258-267.

`MBMA_stan` *Fitting a model-based meta-analysis model using Stan*

Description

'MBMA_stan' fits a model-based meta-analysis model using Stan.

Usage

```
MBMA_stan(
  data = NULL,
  Pred_doses = NULL,
  model = "AB_Emax",
  mu_prior = c(0, 10),
  Emax_prior = c(0, 10),
  ED50_prior = c(0, 10),
  tau_prior = 0.5,
  tau_prior_dist = "half-normal",
  chains = 4,
  iter = 2000,
  warmup = 1000,
  adapt_delta = 0.95
)
```

Arguments

data	An object of 'create_MBMA_dat'.
Pred_doses	A numerical vector specfying the doses which prediction will be made. Default is NULL.
model	A string specifying the model used. Available options are 'Baseline_Emax' (Baseline random effects model (*Boucher and Bennets, 2016)*), 'CB_Emax' (contrast-based random effects model (*Mawdsley et al ,2016)*), 'AB_Emax' (arm-based random effects model, adapted from (*Zhang et al ,2017)*), 'CBPlusBaseline_Emax' (contrast-based plus baseline random effects model, adapted from (*Dias et al ,2013)*). Default is 'AB_Emax'.
mu_prior	A numerical vector specifying the parameter of the normal prior density for baseline risks, first value is parameter for mean, second is for variance. Default is c(0, 10).
Emax_prior	A numerical vector specifying the parameter of the normal prior density for Emax parameter, first value is parameter for mean, second is for standard deviation. Default is c(0, 10).
ED50_prior	A numerical vector specifying the parameter of the normal prior density for ED50 parameter, first value is parameter for mean, second is for standard deviation. Default is c(0, 10).
tau_prior	A numerical value specifying the standard dev. of the prior density for heterogenety stdev. Default is 0.5.
tau_prior_dist	A string specifying the prior density for the heterogeneity standard deviation, option is 'half-normal' for half-normal prior, 'uniform' for uniform prior, 'half-cauchy' for half-cauchy prior.
chains	A positive integer specifying the number of Markov chains. The default is 4.
iter	A positive integer specifying the number of iterations for each chain (including warmup). The default is 2000.
warmup	A positive integer specifying the number of warmup (aka burnin) iterations per chain. The default is 1000.
adapt_delta	A numerical value specfying the target average proposal acceptance probability for adaptation. See Stan manual for details. Default is 0.95. In general you should not need to change adapt_delta unless you see a warning message about divergent transitions, in which case you can increase adapt_delta from the default to a value closer to 1 (e.g. from 0.95 to 0.99, or from 0.99 to 0.999, etc).

Value

an object of class 'stanfit' returned by 'rstan::sampling'

References

Boucher M, et al. The many flavors of model-based meta-analysis: Part I-Introduction and landmark data. *CPT: Pharmacometrics & Systems Pharmacology*. 2016;5:54–64.

Mawdsley D, et al. Model-based network meta-analysis: A framework for evidence synthesis of clinical trial data. *CPT: Pharmacometrics & Systems Pharmacology*. 2016;5:393-401.

Zhang J, et al. (2014). Network meta-analysis of randomized clinical trials: Reporting the proper summaries. *Clinical Trials*. 11(2), 246–262.

Dias S, et al. Absolute or relative effects? Arm-based synthesis of trial data. *Research Synthesis Methods*. 2016;7:23–28.

Examples

```
## Not run:
## Load the dataset
data('dat.Eletriptan', package = "MetaStan")
## Fitting a Binomial-Normal Hierarchial model using WIP priors
datMBMA = create_MBMA_dat(dat = dat.Eletriptan,
                          armVars = c(dose = "d", responders = "r",
                                      sampleSize = "n"),
                          nArmsVar = "nd")

MBMA.AB.Emax  <- MBMA_stan(data = datMBMA,
                           model = "AB_Emax",
                           Pred_doses = seq(0, 80, length.out = 11),
                           Emax_prior = c(0, 10),
                           tau_prior_dist = "half-normal",
                           tau_prior = 0.5)

## End(Not run)
```

`meta_stan` *Fitting a meta-analysis model using Stan*

Description

'meta_stan' fits a meta-analysis model using Stan.

Usage

```
meta_stan(
  ntrt,
  nctrl,
  rtrt,
  rctrl,
  data = NULL,
  model = "BNHM1",
  mu_prior = c(0, 10),
  theta_prior = NULL,
  tau_prior = 0.5,
  tau_prior_dist = "half-normal",
  delta = NULL,
  chains = 4,
```

```
  iter = 2000,
  warmup = 1000,
  adapt_delta = 0.95
)
```

Arguments

ntrt	Number of subjects in treatment arm
nctrl	Number of subjects in control arm
rtrt	Number of events in treatment arm
rctrl	Number of events in contrl arm
data	Optional data frame containing the variables given to the arguments above
model	A string specifying the model used. Available options are 'FE' (fixed-effect model using binomial lielihood) 'BNHM1' (Model 4 from *Jackson et al (2018)*), 'BNHM2' (Model 2 from *Jackson et al (2018)*), and 'Beta-binomial' (Beta-binomial model from *Kuss (2014)*). Default is 'BNHM1'.
mu_prior	A numerical vector specifying the parameter of the normal prior density for baseline risks, first value is parameter for mean, second is for variance. Default is c(0, 10).
theta_prior	A numerical vector specifying the parameter of the normal prior density for treatment effect estimate, first value is parameter for mean, second is for variance. Default is NULL.
tau_prior	A numerical value specifying the standard dev. of the prior density for heterogenety stdev. Default is 0.5.
tau_prior_dist	A string specifying the prior density for the heterogeneity standard deviation, option is 'half-normal' for half-normal prior, 'uniform' for uniform prior, 'half-cauchy' for half-cauchy prior.
delta	A numerical value specifying the upper bound of the a priori interval for treatment effect on odds ratio scale *Guenhan et al (2018)*. This is used to calculate a normal weakly informative prior for theta. Thus when this argument is pecified, 'theta' should be left empty. Default is NULL.
chains	A positive integer specifying the number of Markov chains. The default is 4.
iter	A positive integer specifying the number of iterations for each chain (including warmup). The default is 2000.
warmup	A positive integer specifying the number of warmup (aka burnin) iterations per chain. The default is 1000.
adapt_delta	A numerical value specfying the target average proposal acceptance probability for adaptation. See Stan manual for details. Default is 0.95. In general you should not need to change adapt_delta unless you see a warning message about divergent transitions, in which case you can increase adapt_delta from the default to a value closer to 1 (e.g. from 0.95 to 0.99, or from 0.99 to 0.999, etc).

Value

an object of class 'stanfit' returned by 'rstan::sampling'

References

Guenhan BK, Roever C, Friede T. Meta-analysis of few studies involving rare events *arXiv preprint* 2018;https://arxiv.org/abs/1809.04407.

Jackson D, Law M, Stijnen T, Viechtbauer W, White IR. A comparison of 7 random-effects models for meta-analyses that estimate the summary odds ratio. *Stat Med* 2018;37:1059–1085.

Kuss O.Statistical methods for meta-analyses including information from studies without any events-add nothing to nothing and succeed nevertheless, *Stat Med*, 2015; 4; 1097–1116, doi: 10.1002/sim.6383.

Examples

```
## Not run:
data('dat.Crins2014', package = "MetaStan")
## Subset of dataset where PTLD outcomes available
dat.Crins2014.PTLD = subset(dat.Crins2014, is.finite(exp.PTLD.events))
## Fitting a Binomial-Normal Hierarchial model using vague priors for theta
bnhm.vague.PTLD.stan  <- meta_stan(ntrt = dat.Crins2014.PTLD$exp.total,
                                   nctrl = dat.Crins2014.PTLD$cont.total,
                                   rtrt = dat.Crins2014.PTLD$exp.PTLD.events,
                                   rctrl = dat.Crins2014.PTLD$cont.PTLD.event,
                                   mu_prior = c(0, 10), theta_prior = c(0, 100),
                                   tau_prior =  0.5)
## Obatining a small summary
print(bnhm.vague.PTLD.stan)
## Extract the rstan fit for post-processing, eg convergence diagnostics
bnhm.vague.PTLD.stanfit = bnhm.vague.PTLD.stan$fit
 ## see `?rstan::sampling` for for post-processing of the `stanfit` object
## Fitting a Binomial-Normal Hierarchial model using WIP for theta
bnhm.wip.PTLD.stan  <- meta_stan(ntrt = dat.Crins2014.PTLD$exp.total,
                                   nctrl = dat.Crins2014.PTLD$cont.total,
                                   rtrt = dat.Crins2014.PTLD$exp.PTLD.events,
                                   rctrl = dat.Crins2014.PTLD$cont.PTLD.event,
                                   mu_prior = c(0, 10),
                                   theta_prior = c(0, 2.82),
                                   tau_prior =  0.5)
## Fitting a fixed-effect Binomial model using vague priors for theta
bm.vague.PTLD.stan  <- meta_stan(ntrt = dat.Crins2014.PTLD$exp.total,
                                   nctrl = dat.Crins2014.PTLD$cont.total,
                                   rtrt = dat.Crins2014.PTLD$exp.PTLD.events,
                                   rctrl = dat.Crins2014.PTLD$cont.PTLD.event,
                                   mu_prior = c(0, 10), theta_prior = c(0, 100),
                                   model = "FE")

## Fitting a Beta-binomial model using vague priors
bnhm.wip.PTLD.stan  <- meta_stan(ntrt = dat.Crins2014.PTLD$exp.total,
                                   nctrl = dat.Crins2014.PTLD$cont.total,
                                   rtrt = dat.Crins2014.PTLD$exp.PTLD.events,
                                   rctrl = dat.Crins2014.PTLD$cont.PTLD.event,
                                   model = "Beta-binomial")

## End(Not run)
```

print.meta_stan *Print meta_stan object*

Description

Takes an meta_stan object which is obtained by function meta_stan and print the model and data information such as model type used in the model.

Usage

```
## S3 method for class 'meta_stan'
print(x, digits = 2, ...)
```

Arguments

x	A meta_stan object.
digits	An integer indicating the number of decimal places.
...	Further arguments passed to or from other methods.

Details

The resulting data.frame can be used as data argument in meta_stan.

Value

The return value is invisible NULL

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