Package 'basket'

February 17, 2019

Title Basket Trial Analysis

Version 0.0.18

Description
Implemention of multisource exchangeability models for basket trial design and monitoring.

License LGPL-2

Maintainer Michael J. Kane <mkane@presagia.ai>

Encoding UTF-8

Imports foreach, GenSA, rjags, ggplot2, stats, GGally, tibble, tidyr, dplyr, igraph, gridExtra, itertools

LazyData true

RoxygenNote 6.1.1

Suggests knitr, rmarkdown, testthat,

VignetteBuilder knitr

Author Brian Hobbs [aut], Michael Kane [aut, cre]

R topics documented:

eb_reference *Reference Outputs for Testing*

Description

There are three reference data sets used for testing: eb_reference, eb_reference ub, and fb_reference. These are the the outputs generated by the reference code (in inst/code-from-brian) and are used to detect changes in the output of our implementation.

mem_full_bayes_exact *MEM Full Bayes Exact*

Description

Fit the MEM model using full Bayesian inference.

Usage

```
mem_full_bayes_exact(responses, size, name, p0 = 0.15, shape1 = 0.5,
  shape2 = 0.5, prior_inclusion = diag(length(responses))/2 +
  matrix(0.5, nrow = length(responses), ncol = length(responses)),
  hpd_alpha = 0.05, alternative = "greater", seed = 1000,
  call = NULL)
```

Arguments

responses	the number of responses in each basket.
size	the size of each basket.
name	the name of each basket.
p0	the null response rate for the poster probability calculation (default 0.15).
shape1	the first shape parameter(s) for the prior of each basket (default 0.5).
shape2	the second shape parameter(s) for the prior of each basket (default 0.5).
prior_inclusion	the matrix giving the prior inclusion probability for each pair of baskets. The default is on on the main diagonal and 0.5 elsewhere.
hpd_alpha	the highest posterior density trial significance.
call	the call of the function (default NULL).

Examples

```
# 5 baskets, each with enrollement size 5
trial_sizes <- rep(5, 5)

# The response rates for the baskets.
resp_rate <- 0.15

# The trials: a column of the number of responses and a column of the
# the size of each trial.
```

```
trials <- data.frame(
  responses = rbinom(trial_sizes, trial_sizes, resp_rate),
  size = trial_sizes
)

mem_full_bayes(trials$responses, trials$size)
```

`mem_full_bayes_mcmc` *MEM Full Bayes MCMC method*

Description

Fit the MEM model using full Bayesian Metropolis-Hasting MCMC inference.

Usage

```
mem_full_bayes_mcmc(responses, size, name, p0 = 0.15, shape1 = 0.5,
  shape2 = 0.5, Prior = diag(length(responses))/2 + matrix(0.5, nrow =
  length(responses), ncol = length(responses)), HPD.alpha = 0.05,
  alternative = "greater", niter.MCMC = 10000, Initial = NA,
  seed = 1000, call = NULL)
```

Arguments

`responses`	the number of responses in each basket.
`size`	the size of each basket.
`name`	the name of each basket.
`p0`	the null response rate for the poster probability calculation (default 0.15).
`shape1`	the first shape parameter(s) for the prior of each basket (default 0.5).
`shape2`	the second shape parameter(s) for the prior of each basket (default 0.5).
`alternative`	the alternative case defination (default greater)
`niter.MCMC`	the number of MCMC iterations.
`Initial`	the initial MEM matrix.
`seed`	the random number seed.
`call`	the call of the function.
`prior`	the matrix giving the prior inclusion probability for each pair of baskets. The default is on on the main diagonal and 0.5 elsewhere.
`hpd_alpha`	the highest posterior density trial significance.

Examples

```
# 5 baskets, each with enrollement size 5
trial_sizes <- rep(5, 5)

# The response rates for the baskets.
resp_rate <- 0.15

# The trials: a column of the number of responses and a column of the
# the size of each trial.
```

```
trials <- data.frame(
  responses = rbinom(trial_sizes, trial_sizes, resp_rate),
  size = trial_sizes
)
mem_full_bayes_mcmc(trials$responses, trials$size)
```

`plot_all_exchangeability` *Plot the Prior, MAP, and PEP of a Basket Trial*

Description

Plot the Prior, MAP, and PEP of a Basket Trial

Usage

```
plot_all_exchangeability(x, plotList, ...)
```

Arguments

`x`	the exchangeability model.
`...`	other options. See Details for more information.

Details

TODO: WRITE THIS

`plot_density` *Plot the Densities of Baskets in a Trial*

Description

TODO: WRITE THIS

Usage

```
plot_density(x, ...)
```

Arguments

`x`	the exchangeability model.
`...`	other options. See Details for more information.

Details

TODO WRITE THIS TALK ABOUT ... OPTIONS

Examples

```
# TODO: WRITE THIS
```

plot_exchangeability *Plot the Map Exchangeability of a Basket Trial*

Description

TODO: WRITE THIS

Usage

```
plot_exchangeability(x, ...)
```

Arguments

x	the exchangeability model.
...	other options. See Details for more information.

Details

TODO: WRITE THIS

Examples

```
# WRITE THIS
```

plot_posterior_exchangeability *Plot the Posterior Exchangeability of a Basket Trial*

Description

TODO: WRITE THIS

Usage

```
plot_posterior_exchangeability(x, ...)
```

Arguments

x	the exchangeability model.
...	other options. See Details for more information.

Details

TODO: WRITE THIS

Examples

```
# WRITE THIS
```

summary.full_bayes *Make the summary table*

Description

From the input full_bayes class object, summarize the CDF, HPD, ESS, Mean, and Median results.

Usage

```
## S3 method for class 'full_bayes'
summary(res)
```

Arguments

res	the full_bayes class object..

update_result *Update Full Bayes results with different p0 values*

Description

Update Full Bayes results with different p0 values and alternative

Usage

```
update_result(res, p0 = 0.15, alternative = "greater")
```

Arguments

p0	the null response rate for the poster probability calculation (default 0.15).
alternative	the alternative case defination (default greater)

Examples

```
MHResult1New <- updateResult(MHResult1, 0.25)
```

vemu *Summary Data from the Vemurafinib Study*

Description

The 'vemu' and 'vemu_wide' data sets provides response information taken from the "Vemurafenib in multiple nonmelanoma cancers with braf v600 mutations" study where, in total, 18 responders were observed among the 84 patients contributing evaluable outcomes for statistical estimation. Observed response rates varied from $42%$ and $43%$ for baskets of NSCLC and ECD or LCH to 0 and $4%,$ for CRC with vemurafenib mono and combination therapies, respectively. Two responders of seven patients, ATC was associated with a $29%$ response rate, while one responder of eight patients was observed in the cholangiocarcinoma basket. Contrasting favorable results for preliminary vemurafenib activity among NSCLC and ECD or LCH patients with less favorable results for CRC patients, the authors concluded that nonmelanoma tumor types harboring $BRAF^V600$ mutations failed to respond uniformly to BRAF-targeted therapy giving credence to more conventional organ-specific nosology when compared to molecular tumor nosology.

Later, in the "Statistical challenges posed by basket trials: sensitivity analysis of the Vemurafenib study" it was shown that patient-enrollment types we likely drove the negative results for several targets, rather than Vemurafinib itself.

References

Hyman DM, Puzanov I, Subbiah V, Faris JE, Chau I, Blay JY, Wolf J, Raje NS, Diamond EL, Hollebecque A, et al. Vemurafenib in multiple nonmelanoma cancers with braf v600 mutations. New England Journal of Medicine 2015; **373**(8):726–736.

Hobbs BP, Kane MJ, Hong DS, and Landin R. Statistical challenges posed by basket trials: sensitivity analysis of the Vemurafenib study. *Accepted to the Annals of Clinical Oncology* 2018.

Index