Package ‘BHTSpack’

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**Type** Package

**Title** Bayesian Multi-Plate High-Throughput Screening of Compounds

**Version** 0.5

**Description** Can be used for joint identification of candidate compound hits from multiple assays, in drug discovery. This package implements the framework of I. D. Shterev, D. B. Dunson, C. Chan and G. D. Sempowski. "Bayesian Multi-Plate High-Throughput Screening of Compounds", Scientific Reports 8(1):9551, 2018. This project was funded by the Division of Allergy, Immunology, and Transplantation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract No. HHSN272201400054C entitled "Adjuvant Discovery For Vaccines Against West Nile Virus and Influenza", awarded to Duke University and lead by Drs. Herman Staats and Soman Abraham.

**Depends** R (>= 3.2.3), R2HTML (>= 2.3.2), xtable (>= 1.8-2)

**VignetteBuilder** knitr

**Suggests** knitr

**License** GPL-3

**LazyLoad** yes

**NeedsCompilation** yes

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**Repository** CRAN

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### R topics documented:

- BHTSpack-package
- abfun
- alpha.u

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## Description

Can be used for joint identification of candidate hits from multiple assays, in drug discovery. This package implements the framework of I. D. Shterev, D. B. Dunson, C. Chan and G. D. Sempowski. "Bayesian Multi Plate High Throughput Screening of Compounds", arXiv:1709.10041, September 2017. This project was funded by the Division of Allergy, Immunology, and Transplantation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract No. HHSN272201400054C entitled "Adjuvant Discovery For Vaccines Against West Nile Virus and Influenza", awarded to Duke University and lead by Drs. Herman Staats and Soman Abraham.

## Details

The DESCRIPTION file:

```
Package: BHTSpack
Type: Package
Title: Bayesian Multi-Plate High-Throughput Screening of Compounds
Version: 0.5
Authors@R: c(person(c("Ivo", "D."), "Shterev", role = c("aut", "cre"), email = "i.shterev@duke.edu"), person(c("David", "B."), "Dunson", role = "aut"), person("Cliburn", "Chan", role = "aut"), person(c("Gregory", "D."), "Sempowski", role = "aut"))
Description: Can be used for joint identification of candidate compound hits from multiple assays, in drug discovery. This project was funded by the Division of Allergy, Immunology, and Transplantation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract No. HHSN272201400054C entitled "Adjuvant Discovery For Vaccines Against West Nile Virus and Influenza", awarded to Duke University and lead by Drs. Herman Staats and Soman Abraham.
Depends: R (>= 3.2.3), R2HTML (>= 2.3.2), xtable (>= 1.8-2)
VignetteBuilder: knitr
Suggests: knitr
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**Author(s)**

I. D. Shterev, D. B. Dunson, C. Chan and G. D. Sempowski

Maintainer: I. D. Shterev <i.shterev@duke.edu>

**References**

Usage

abfun(m, v)

Arguments

m Description
v Description

Examples

abfun(0.26, 10^-4)

alpha.u package internal function

Description

package internal function

Usage

alpha.u(nu, a0, b0, H)

Arguments

nu Description
a0 Description
b0 Description
H Description

Examples

M = 5
H = 10
a = 10^-6
b = 10^-6
nu = lapply(1:M, function(x){rbeta(H, a, b)})
alpha.u(nu, a, b, H)
b.u

package internal function

Description

package internal function

Usage

b.u(hatpai)

Arguments

hatpai Description

Examples

pai = 0.5
M = 10
H = 10
K = 5
n = 100

z = abs(rnorm(n))

sigma1 = abs(rnorm(K))
sigma0 = abs(rnorm(K))

mu1 = abs(rnorm(K))
mu0 = abs(rnorm(K))

hk0 = matrix(sample(K, M*H, replace=TRUE), M, H)
hk1 = matrix(sample(K, M*H, replace=TRUE), M, H)

nu.h0 = lapply(1:H, function(x)(rbeta(1,5,5)))
nu.h1 = lapply(1:H, function(x)(rbeta(1,5,5)))

ph0 = lapply(nu.h0, lambda.u)
ph1 = lapply(nu.h1, lambda.u)

b.u(hatpai.u(z, hk1, hk0, ph1, ph0, sigma1, sigma0, mu1, mu0, pai, H, n))
bhts

Bayesian High-Throughput Screening

Description

This is the package main function.

Usage

\texttt{bhts(Z, iters, H, K, mu00=NULL, mu10=NULL, a.alpha, b.alpha, a.tau, b.tau, pnorm=FALSE, s=NULL, store=FALSE)}

Arguments

\begin{itemize}
  \item \texttt{Z} \hspace{1em} A list of compounds.
  \item \texttt{iters} \hspace{1em} Number of iterations to perform.
  \item \texttt{H} \hspace{1em} Number of local DP components.
  \item \texttt{K} \hspace{1em} Number of global DP components.
  \item \texttt{mu00} \hspace{1em} Activity level (mean) of non-hit compounds
  \item \texttt{mu10} \hspace{1em} Activity level (mean) of hit compounds
  \item \texttt{a.alpha} \hspace{1em} Gamma shape parameter specifying local DP concentration prior.
  \item \texttt{b.alpha} \hspace{1em} Gamma rate parameter specifying local DP concentration prior.
  \item \texttt{a.tau} \hspace{1em} Gamma shape parameter specifying global DP concentration prior.
  \item \texttt{b.tau} \hspace{1em} Gamma rate parameter specifying global DP concentration prior.
  \item \texttt{pnorm} \hspace{1em} Plate normalization. If \texttt{TRUE}, each plate is normalized to zero mean and unit variance, prior to analysis. Default is \texttt{FALSE}.
  \item \texttt{s} \hspace{1em} Random seed (for reproducibility purposes). Default is \texttt{NULL}.
  \item \texttt{store} \hspace{1em} If \texttt{TRUE}, all samples of certain latent variables are stored in the output object. Default is \texttt{FALSE}.
\end{itemize}

Value

This function returns a list consisting of the following elements:

\begin{itemize}
  \item \texttt{hatpai} \hspace{1em} A list of vectors of posterior probabilities, estimating the probability of a compound being a hit.
  \item \texttt{dat.store} \hspace{1em} If \texttt{store = TRUE} (default is \texttt{FALSE}), the output contains a list of \texttt{iters×K} matrices of samples. Each matrix contains the samples of a separate latent variable. At each iteration, the following six variables are stored in a different row of their corresponing matrix, \((\lambda_1^{(0)}, \ldots, \lambda_K^{(0)}), (\lambda_1^{(1)}, \ldots, \lambda_K^{(1)}), (\mu_0, \ldots, \mu_K), (\mu_1, \ldots, \mu_{1K}), (\sigma_0^2, \ldots, \sigma_0^2_K)\) and \((\sigma_1^2, \ldots, \sigma_{1K}^2)\).
\end{itemize}
Examples

```r
set.seed(1234)
Nmax = 100
M = 100
n = sample(Nmax, M, replace=TRUE)
Z = lapply(n, function(x){abs(rnorm(x)})
  bhts(Z, iters=100, H=10, K=5, mu0=0, mu1=10, a.alpha=10, b.alpha=5, a.tau=10, b.tau=5)
```

bhts2HTML

Convert to HTML

**Description**

This function creates an HTML file.

**Usage**

```r
bhts2HTML(dat, dir, fname, title=NULL, bgcolor="#B8B8B8")
```

**Arguments**

- `dat`: An object which is the output of `bhts()`.  
- `dir`: Directory in which to store the file.  
- `fname`: File name.  
- `title`: The title of the html file.  
- `bgcolor`: Color for the html background.

**Examples**

```
#See package vignette
```

data.create

Create Synthetic Data

**Description**

This function generates synthetic compound data.

**Usage**

```r
data.create(N, nr, nc, M, p, s=NULL, covrow=NULL, covcol=NULL, c=0.0001, mat=FALSE)
```
Arguments

N  Number of compounds per plate.
nr Number of plate rows.
nc Number of plate columns.
M  Number of plates.
p  Probability of a compound being a hit.
s  Random seed (for reproducibility purposes). Default is NULL.
covrow Noise plate row-covariance matrix. Default is NULL.
covcol Noise plate column-covariance matrix. Default is NULL.
c  Constant for scaling plate noise. Default is 0.0001.
mat Specifies a matrix (TRUE) or a vector (FALSE) plate format. Default is FALSE.

Value

This function returns a list consisting of the following elements:

Z  A list of matrices (mat = TRUE) or vectors (mat = FALSE) of compounds.
B  A list of compound indicators specifying a hit (1) or a non-hit (0).
I  A list of compound indicators specifying the mixture component (from 1 to K).

Examples

#See package vignette

---

fdr.r  package internal function

Description

package internal function

Usage

fdr.r(r, hatpai, fdr)

Arguments

r  Description
hatpai  Description
fdr  Description

Examples

#See package vignette
h.pr.u

package internal function

Description

package internal function

Usage

h.pr.u(z, ih, mu, sigma, pk, K, H, n)

Arguments

z
ih
mu
sigma
pk
K
H
n

Examples

Nmax = 100
K = 5
H = 10
M = 20
n = sample(Nmax, M, replace=TRUE)

z = abs(rnorm(sum(n)))
mu = abs(rnorm(K))
sigma = 1/rgamma(n=K, shape=10, rate=10)

ih = sample(H, sum(n), replace=TRUE)

pk = lambda.u(rbeta(K, 1, 1))

h.pr.u(z, ih, mu, sigma, pk, K, H, n)
Description
package internal function

Usage
hatpai.u(z, hk1, hk0, ph1, ph0, sigma1, sigma0, mu1, mu0, pai, H, n)

Arguments
z
hk1
hk0
ph1
ph0
sigma1
sigma0
mu1
mu0
pai
H
n

Value
value

Examples
pai = 0.5
M = 10
H = 10
K = 5
n = 100
z = abs(rnorm(n))
sigma1 = abs(rnorm(K))
sigma0 = abs(rnorm(K))
mu1 = abs(rnorm(K))
mu0 = abs(rnorm(K))
\begin{verbatim}
ind.u = matrix(sample(K, M+H, replace=TRUE), M, H)

nu.h0 = lapply(1:H, function(x){rbeta(1,5,5)})

nu.h1 = lapply(1:H, function(x){rbeta(1,5,5)})

ph0 = lapply(nu.h0, lambda.u)

ph1 = lapply(nu.h1, lambda.u)

hatpai.u(z, hk1, hk0, ph1, ph0, sigma1, sigma0, mu1, mu0, pai, H, n)
\end{verbatim}

---

**Description**

package internal function

**Usage**

\texttt{ind.u(pr)}

**Arguments**

\texttt{pr}

**Examples**

\begin{verbatim}
Nmax = 100
K = 5
H = 10
M = 20
n = sample(Nmax, M, replace=TRUE)

z = abs(rnorm(sum(n)))

mu = abs(rnorm(K))

sigma = 1/rgamma(n=K, shape=10, rate=10)

hk = sample(K, M+H, replace=TRUE)

ph = as.vector(sapply(1:M, function(x){lambda.u(rbeta(H, 1, 1))}))

ind.u(z, pr, z, hk, mu, sigma, ph, H, n))
\end{verbatim}
### lambda.u

**package internal function**

**Description**
package internal function

**Usage**

```r
lambda.u(nu)
```

**Arguments**

- `nu`

**Examples**

```r
H = 5
nu = rbeta(H, 1, 1)
lambda.u(nu)
```

---

### lg.mu.sig

**package internal function**

**Description**
package internal function

**Usage**

```r
lg.mu.sig(m, v)
```

**Arguments**

- `m`  
  Description
- `v`  
  Description

**Examples**

```r
#See package vignette
```
mu.k.u

package internal function

Description
package internal function

Usage
mu.k.u(k, ik, z, sigma, mu0)

Arguments
k
ik
z
sigma
mu0

Value
Describe

Examples
K = 5
n = 100
z = abs(rnorm(n))
sigma = sapply(1:K, function(x){rgamma(n=1, shape=10, rate=10)})
mu0 = 0
ik = sample(K, n, replace=TRUE)
sapply(1:K, mu.k.u, ik, z, sigma, mu0)

nu.u

package internal function

Description
package internal function

Usage
nu.u(ind, tau, H)
Arguments

\hspace{1cm} \text{ind}
\hspace{1cm} \text{tau}
\hspace{1cm} \text{H}

Value

\hspace{1cm} \text{Describe}

Examples

\hspace{1cm} H = 5
\hspace{1cm} n = 100
\hspace{1cm} tau = rgamma(1, 1, 1)
\hspace{1cm} ind = sample(H, n, replace=TRUE)
\hspace{1cm} nu.u(ind, tau, H)

\hspace{1cm} \text{package internal function}

Description

\hspace{1cm} \text{package internal function}

Usage

\hspace{1cm} pai.u(b, a.pai, b.pai)

Arguments

\hspace{1cm} b
\hspace{1cm} a.pai
\hspace{1cm} b.pai

Value

\hspace{1cm} \text{Describe}

Examples

\hspace{1cm} n = 100
\hspace{1cm} b = rbinom(n, 1, 0.5)
\hspace{1cm} a.pai = 10^{-6}
\hspace{1cm} b.pai = 10^{-6}
\hspace{1cm} pai.u(b, a.pai, b.pai)
ptrace  

Trace (ACF) Plots

Description

This function outputs trace plots of certain latent variables.

Usage

ptrace(res, var, ndisc, nr, nc, type="trace")

Arguments

 rés  An output object from bhts().
 var  Variable for which to display convergence diagnostic plots. Current options are mu0 (displaying $\mu_0$, $\mu_{0K}$), mu1 (displaying $\mu_1$, $\mu_{1K}$), sigma0 (displaying $\sigma_0^2$, $\sigma_{0K}^2$), sigma1 (displaying $\sigma_1^2$, $\sigma_{1K}^2$), pk0 (displaying $\lambda_{01}$, $\lambda_{0K}$), and pk1 (displaying $\lambda_{11}$, $\lambda_{1K}$).
 ndisc  Number of iterations for which to discard samples.
 nr  Number of rows in the resulting composite plot.
 nc  Number of columns in the resulting composite plot.
 type  Type of convergence diagnostic. Currently implemented are trace plots (default type = "trace") and ACF plots (type = "acf")

Examples

#See package vignette

r.fdr  

Significant Hits

Description

This function determines significant hits, based on a specified expected FDR.

Usage

r.fdr(res, fdr=0.05)

Arguments

 rés  An output object from bhts().
 fdr  Expected FDR (default is 0.05).
Value

This function returns a list consisting of the following elements:

- `res` A data frame containing significant hits and their probabilities.
- `r` The computed significant hit probability threshold.

Examples

```r
# See package vignette
```

Description

package internal function

Usage

```r
sig.k.u(k, ik, z, mu0, a0, b0)
```

Arguments

- `k`
- `ik`
- `z`
- `mu0`
- `a0`
- `b0`

Examples

```r
K = 5
n = 100
z = abs(rnorm(n))
mu0 = 0
ik = sample(K, n, replace=TRUE)
a0 = 5
b0 = 5
sapply(1:K, sig.k.u, ik, z, mu0, a0, b0)
```
**tau.u**

*package internal function*

**Description**

package internal function

**Usage**

`tau.u(nu, a0, b0)`

**Arguments**

- `nu` Description
- `a0` Description
- `b0` Description

**Examples**

```r
K = 5
a = 10^-6
b = 10^-6
nu = rbeta(K, a, b)
tau.u(nu, a, b)
```

---

**z.pr.u**

*package internal function*

**Description**

package internal function

**Usage**

`z.pr.u(z, hk, mu, sigma, ph, H, n)`

**Arguments**

- `z`
- `hk`
- `mu`
- `sigma`
- `ph`
- `H`
- `n`
Examples

Nmax = 100
K = 5
H = 10
M = 20
n = sample(Nmax, M, replace=TRUE)

z = abs(rnorm(sum(n)))
mu = abs(rnorm(K))
sigma = 1/rgamma(n=K, shape=10, rate=10)

hk = sample(K,M*H, replace=TRUE)

ph = as.vector(sapply(1:M, function(x){lambda.u(rbeta(H, 1, 1))}))

z.pr.u(z, hk, mu, sigma, ph, H, n)
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