Package ‘corrcoverage’

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Type Package

Title Correcting the Coverage of Credible Sets from Bayesian Genetic Fine Mapping

Version 1.2.1

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Description Using a computationally efficient method, the package can be used to find the corrected coverage estimate of a credible set of putative causal variants from Bayesian genetic fine-mapping. The package can also be used to obtain a corrected credible set if required; that is, the smallest set of variants required such that the corrected coverage estimate of the resultant credible set is within some user defined accuracy of the desired coverage.

Maller et al. (2012) <doi:10.1038/ng.2435>,
Wakefield (2009) <doi:10.1002/gepi.20359>,

URL https://annahutch.github.io/corrcoverage

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BugReports https://github.com/annahutch/corrcoverage/issues

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\begin{tabular}{ll}
\textbf{.zj_abf} & \textit{Internal function: Simulate nrep ABFs from joint Z-score vector} \\
\end{tabular}
\end{table}

\textbf{Description}

Does not include posterior probabilities for null model
**.zj_pp**

Usage

```
.zj_abf(Zj, int.Sigma, int.nrep, int.ERR, int.r)
```

Arguments

- **Zj**: joint z vector
- **int.Sigma**: internal sigma
- **int.nrep**: internal nrep
- **int.ERR**: internal error matrix
- **int.r**: internal r

Value

Matrix of simulated ABFs, one simulation per row

---

**Description**

Internal function: Simulate nrep posterior probabilities of causality from joint Z-score vector

Usage

```
.zj_pp(Zj, int.Sigma, int.nrep, int.ERR, int.r)
```

Arguments

- **Zj**: joint z vector
- **int.Sigma**: internal sigma
- **int.nrep**: internal nrep
- **int.ERR**: internal error matrix
- **int.r**: internal r

Details

Does not include posterior probabilities for null model

Value

Matrix of simulated posterior probabilities of causality, one simulation per row
approx.bf.p

Find approx. Bayes factors (ABFs)

Description

Wakefield’s log asymptotic Bayes factor (lABF) with prior standard deviation of effect size as a parameter

Usage

approx.bf.p(pvals, f, type, N, s, W = 0.2)

Arguments

pvals P-values
f Minor allele frequencies
type Type of experiment (‘quant’ or ’cc’)
N Total sample size
s Proportion of cases (N1/N0+N1), ignored if type==‘quant’
W Prior for the standard deviation of the effect size parameter beta (W=0.2 default)

Details

([Wakefield et al. 2009](https://onlinelibrary.wiley.com/doi/abs/10.1002/gepi.20359) This function converts p-values to log ABFs, also reporting intermediate calculations

Value

data.frame containing lABF and intermediate calculations

Examples

```r
set.seed(1)
snps = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(snps, 0, 3)
p_values <- 2 * pnorm( - abs( z_scores ) )
```

`## generate example LD matrix and MAFs`

```r
library(mvtnorm)
nsamples = 1000

simx <- function(snps, nsamples, S, maf=0.1) {
  mu <- rep(0, snps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  ```
bf_func <- pnorm(rawvars)
x <- qbinom(1-pvars, 1, maf)
}
S <- (1 - (abs(outer(1:nsnps,1:nsnps, 
/grave.Var
/grave.Var
))/nsnps))^4
X <- simx(nsnps,nsamples,S)
maf <- colMeans(X)
approx.bf.p(pvals = p_values, f = maf, type = “cc”, N = N0+N1, s = N1/(N0+N1))

bf_func Calculate ABFs from Z scores

Description
Calculate ABFs from Z scores

Usage
bf_func(z, V, W = 0.2)

Arguments
z Vector of Z-scores
V Variance of the estimated effect size
W Prior for the standard deviation of the effect size parameter, beta (default 0.2)

Details
Note, z and V should both be vectors or both be matrices

Value
ABFs

Examples
set.seed(1)
nsnps = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(nsnps, 0, 3)

## generate example LD matrix and MAFs
library(mvtnorm)
nsamples = 1000
cor2 <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0, nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps, '/grave.Var'))/nsnps))^4
X <- simx(nsnps,nsamples,S)
maf <- colMeans(X)
varbeta = Var.data.cc(f = maf, N = N0 + N1, s = 0.5)
bf_func(z_scores, V = varbeta)

---

cor2  
Correlation matrix of SNPS

Description

Correlation matrix of SNPs

Usage

cor2(x)

Arguments

x  Phased haplotype matrix, rows as samples and columns as SNPs

Details

Quick function to find a correlation matrix

Value

Correlation matrix

Author(s)

Chris Wallace
Corrected coverage estimate using Z-scores and MAFs

**Usage**

```r
corrcov(z, f, N0, N1, Sigma, thr, W = 0.2, nrep = 1000, pp0min = 0.001)
```

**Arguments**

- `z`: Marginal Z-scores
- `f`: Minor allele frequencies
- `N0`: Number of controls
- `N1`: Number of cases
- `Sigma`: SNP correlation matrix
- `thr`: Minimum threshold for fine-mapping experiment
- `W`: Prior for the standard deviation of the effect size parameter, beta (default 0.2)
- `nrep`: The number of simulated posterior probability systems to consider for the corrected coverage estimate (default 1000)
- `pp0min`: Only average over SNPs with pp0 > pp0min

**Details**

This function only requires the marginal summary statistics from GWAS

**Value**

Corrected coverage estimate

**Author(s)**

Anna Hutchinson

**Examples**

```r
set.seed(1)
nSNPs = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(nSNPs, 0, 3) # simulate a vector of Z-scores

## generate example LD matrix
```
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,/-))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)
corrcov(z = z_scores, f = maf, N0, N1, Sigma = LD, thr = 0.95)

corrcov_bhat

Corrected coverage estimate using estimated effect sizes and their standard errors

Description
Corrected coverage estimate using estimated effect sizes and their standard errors

Usage
corrcov_bhat(bhat, V, N0, N1, Sigma, thr, W = 0.2, nrep = 1000, pp0min = 0.001)

Arguments

bhat Estimated effect sizes from single-SNP logistic regressions
V Variance of estimated effect sizes
N0 Number of controls
N1 Number of cases
Sigma SNP correlation matrix
thr Minimum threshold for fine-mapping experiment
W Prior for the standard deviation of the effect size parameter, beta (default 0.2)
nrep The number of simulated posterior probability systems to consider for the corrected coverage estimate (default 1000)
pp0min Only average over SNPs with pp0 > pp0min

Details
This function only requires the marginal summary statistics from GWAS
**corrcov_CI**

**Value**

Corrected coverage estimate

**Author(s)**

Anna Hutchinson

**Examples**

```r
set.seed(1)
nsnps <- 100
N0 <- 1000 # number of controls
N1 <- 1000 # number of cases

## generate example LD matrix
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,`-`))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)

varbeta <- Var.data.cc(f = maf, N = N0 + N1, s = N1/(N0+N1))

bhats = rnorm(nsnps, 0, 0.2) # log OR
corrcov_bhat(bhat = bhats, V = varbeta, N0, N1, Sigma = LD, thr = 0.95)
```

---

**corrcov_CI**

*Confidence interval for corrected coverage estimate using Z-scores and MAFs*

**Description**

Obtain confidence interval for corrected coverage estimate using Z-scores and mafs
corrcov_CI

Usage

```r
corrcov_CI(
  z,
  f,
  N0,  
  N1,
  Sigma,
  thr, 
  W = 0.2, 
  nrep = 1000,
  CI = 0.95, 
  pp0min = 0.001
)
```

Arguments

- `z`: Marginal Z-scores
- `f`: Minor allele frequencies
- `N0`: Number of controls
- `N1`: Number of cases
- `Sigma`: SNP correlation matrix
- `thr`: Minimum threshold for fine-mapping experiment
- `W`: Prior for the standard deviation of the effect size parameter, beta (default 0.2)
- `nrep`: The number of simulated posterior probability systems to consider for the corrected coverage estimate (nrep = 1000 default)
- `CI`: The size of the confidence interval (as a decimal)
- `pp0min`: Only average over SNPs with pp0 > pp0min

Value

- CI for corrected coverage estimate

Author(s)

Anna Hutchinson

Examples

```r
# this is a long running example
set.seed(1)
nsnps = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(nsnps, 0, 3) # simulate a vector of Z-scores
```
## generate example LD matrix

```r
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,"-"))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)
corrcov_CI(z = z_scores, f = maf, N0, N1, Sigma = LD, thr = 0.95)
```

---

**corrcov_CI_bhat**  
*Confidence interval for corrected coverage estimate using estimated effect sizes and their standard errors*

### Description

Obtain confidence interval for corrected coverage estimate using estimated effect sizes and their standard errors

### Usage

```r
corrcov_CI_bhat(
  bhat,
  V,
  N0,
  N1,
  Sigma,
  thr,
  W = 0.2,
  nrep = 1000,
  CI = 0.95,
  pp0min = 0.001
)
```

### Arguments

- **bhat**: Estimated effect sizes from single-SNP logistic regressions
- **V**: Variance of estimated effect sizes
N₀  Number of controls
N₁  Number of cases
Sigma SNP correlation matrix
thr Minimum threshold for fine-mapping experiment
W Prior for the standard deviation of the effect size parameter beta
nrep The number of simulated posterior probability systems to consider for the corrected coverage estimate (nrep = 1000 default)
CI The size of the confidence interval (as a decimal)
pp₀min Only average over SNPs with pp₀ > pp₀min

Value
CI for corrected coverage estimate

Author(s)
Anna Hutchinson

Examples

# this is a long running example
set.seed(1)
nsnps <- 100
N₀ <- 5000  # number of controls
N₁ <- 5000  # number of cases

## generate example LD matrix
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,`-`))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)

varbeta <- Var.data.cc(f = maf, N = N₀ + N₁, s = N₁/(N₀+N₁))
bhats = rnorm(nsnps,0,0.2)  # log OR
corccov_CI_bhat(bhat = bhats, V = varbeta, N₀, N₁, Sigma = LD)
**corrcov_nvar**  
*Corrected coverage estimate using Z-scores and MAFs (fixing nvar)*

**Description**

Obtain corrected coverage estimate using Z-scores and MAFs (limiting simulations used for estimation to those with correct nvar)

**Usage**

```r
corrcov_nvar(
  z,  # Marginal Z-scores
  f,  # Minor allele frequencies
  N0,  # Number of controls
  N1,  # Number of cases
  Sigma,  # SNP correlation matrix
  nvar,  # The number of variants that simulated credible sets used for estimation should contain
  thr,  # Minimum threshold for fine-mapping experiment
  W = 0.2,  # Prior for the standard deviation of the effect size parameter, beta (default 0.2)
  nrep = 10000,  # The number of simulated posterior probability systems to consider for the corrected coverage estimate (nrep = 10000 default due to trimming)
  pp0min = 0.001  # Only average over SNPs with pp0 > pp0min
)
```

**Arguments**

- `z`: Marginal Z-scores
- `f`: Minor allele frequencies
- `N0`: Number of controls
- `N1`: Number of cases
- `Sigma`: SNP correlation matrix
- `nvar`: The number of variants that simulated credible sets used for estimation should contain
- `thr`: Minimum threshold for fine-mapping experiment
- `W`: Prior for the standard deviation of the effect size parameter, beta (default 0.2)
- `nrep`: The number of simulated posterior probability systems to consider for the corrected coverage estimate (nrep = 10000 default due to trimming)
- `pp0min`: Only average over SNPs with pp0 > pp0min

**Details**

This function requires the marginal summary statistics from GWAS and an nvar value. It should only be used when nvar is very low (<3) and there is some evidence to suggest that only simulated credible sets with this nvar value should be used to derive the corrected coverage estimate.
**Value**

Corrected coverage estimate

**Author(s)**

Anna Hutchinson

**Examples**

```r
set.seed(1)
nsnps = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(nsnps, 0, 3) # simulate a vector of Z-scores

## generate example LD matrix
library(mvtnorm)
samples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,'/'))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)

corrcov_nvar(z = z_scores, f = maf, N0, N1, Sigma = LD, thr = 0.95, nvar = 1, nrep = 100)

# note that nrep should be at least the default value (nrep = 10000) but is
# lower here for speed of computation
```

---

**corrcov_nvar_bhat**

**Corrected coverage estimate using estimated effect sizes and their standard errors (fixing nvar)**

**Description**

Obtain corrected coverage estimate using estimated effect sizes and their standard errors (limiting simulations used for estimation to those with correct nvar)
corrcov_nvar_bhat

Usage

```r
corrcov_nvar_bhat(
bhat,
    V,
    N0,
    N1,
    Sigma,
    nvar,
    thr,
    W = 0.2,
    nrep = 10000,
    pp0min = 0.001
)
```

Arguments

- `bhat`: Estimated effect sizes from single-SNP logistic regressions
- `V`: Variance of estimated effect sizes
- `N0`: Number of controls
- `N1`: Number of cases
- `Sigma`: SNP correlation matrix
- `nvar`: The number of variants that simulated credible sets used for estimation should contain
- `thr`: Minimum threshold for fine-mapping experiment
- `W`: Prior for the standard deviation of the effect size parameter, beta (default 0.2)
- `nrep`: The number of simulated posterior probability systems to consider for the corrected coverage estimate (nrep = 10000 default due to trimming)
- `pp0min`: Only average over SNPs with pp0 > pp0min

Details

This function requires the marginal summary statistics from GWAS and an nvar value. It should only be used when nvar is very low (\$<3\$) and there is some evidence to suggest that only simulated credible sets with this nvar value should be used to derive the corrected coverage estimate.

Value

Corrected coverage estimate

Author(s)

Anna Hutchinson
Examples

```r
set.seed(1)
nsnps <- 100
N0 <- 5000 # number of controls
N1 <- 5000 # number of cases

# generate example LD matrix
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,/) / grave.Var - grave.Var)) / nsnps)^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)

varbeta <- Var.data.cc(f = maf, N = N0 + N1, s = N1/(N0+N1))
bhats = rnorm(nsnps,0,0.2) # log OR
corrcoverage_nvar_bhat(bhat = bhats, V = varbeta, N0, N1, Sigma = LD, thr = 0.95, nvar = 1, nrep = 1000)

# note that nrep should be at least the default value (nrep = 10000) but is
# lower here for speed of computation
```

---

**corrected_cov**

Corrected coverage estimate of the causal variant in the credible set

**Description**

Corrected coverage estimate of the causal variant in the credible set

**Usage**

```r
corrected_cov(pp0, mu, V, Sigma, thr, W = 0.2, nrep = 1000, pp0min = 0.001)
```

**Arguments**

- **pp0**  
  Posterior probabilities of SNPs

- **mu**  
  The true effect at the CV (estimate using corrcoverage::est_mu function)
**corrected_cov**

Variance of the estimated effect size (can be obtained using coloc::Var.beta.cc function)

**Sigma**
SNP correlation matrix

**thr**
Minimum threshold for fine-mapping experiment

**W**
Prior for the standard deviation of the effect size parameter, beta (W=0.2 default)

**nrep**
Number of posterior probability systems to simulate for each variant considered causal (nrep = 1000 default)

**pp0min**
Only average over SNPs with pp0 > pp0min

**Details**
Requires an estimate of the true effect at the CV (e.g. use maximum absolute z-score or output from corrcoverage::est_mu function)

**Value**
Corrected coverage estimate

**Author(s)**
Anna Hutchinson

**Examples**

```r
set.seed(1)
nsnps <- 100
N0 <- 5000
N1 <- 5000

## generate example LD matrix
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,`-`))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)

## generate V (variance of estimated effect sizes)
varbeta <- Var.data.cc(f = maf, N = 5000, s = 0.5)

pp <- rnorm(nsnps, 0.2, 0.05)
```
Corrected credible set using Z-scores and MAFs

Description
Corrected credible set using Z-scores and MAFs

Usage
corrected_cs(
z, f, N0, N1, Sigma, W = 0.2, lower = 0, upper = 1, desired.cov, acc = 0.005, max.iter = 20, pp0min = 0.001)

Arguments
z Z-scores
f Minor allele frequencies
N0 Number of controls
N1 Number of cases
Sigma Correlation matrix of SNPs
W Prior for the standard deviation of the effect size parameter, beta (default 0.2)
lower Lower threshold (default = 0)
upper Upper threshold (default = 1)
desired.cov The desired coverage of the causal variant in the credible set
acc Accuracy of corrected coverage to desired coverage (default = 0.005)
max.iter Maximum iterations (default = 20)
pp0min Only average over SNPs with pp0 > pp0min
**Value**

List of variants in credible set, required threshold, the corrected coverage and the size of the credible set

**Author(s)**

Anna Hutchinson

**Examples**

```r
# this is a long running example

# In this example, the function is used to find a corrected 95% credible set
# using Z-scores and MAFs, that is the smallest set of variants
# required such that the resultant credible set has coverage close to (within
# some accuracy of) the "desired coverage" (here set to 0.95). Max.iter parameter
# defines the maximum number of iterations to try in the root bisection algorithm,
# this should be increased to ensure convergence to the desired coverage, but is set
# to 1 here for speed (and thus the resultant credible set will not be accurate).

set.seed(2)
snps = 200
N0 = 1000
N1 = 1000
z_scores <- rnorm(snps, 0, 1) # simulate a vector of Z-scores

## generate example LD matrix
library(mvtnorm)
nsamples = 1000
S <- (1 - (abs(outer(1:nsnps,1:nsnps,"-"))/nsnps))^4
X <- simx(snps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)
names(z_scores) <- seq(1,length(z_scores))

corrected_cs(z = z_scores, f = maf, N0, N1, Sigma = LD, desired.cov = 0.9, max.iter = 1) # max.iter set low for speed, should be set to at least
# the default to ensure convergence to desired coverage
```
Corrected credible set using estimated effect sizes and their standard errors

Usage

```r
corrected_cs_bhat(
  bhat,
  V,
  N0,
  N1,
  Sigma,
  W = 0.2,
  lower = 0,
  upper = 1,
  desired.cov,
  acc = 0.005,
  max.iter = 20,
  pp0min = 0.001
)
```

Arguments

- `bhat`: Estimated effect sizes
- `V`: Prior variance of estimated effect sizes
- `N0`: Number of controls
- `N1`: Number of cases
- `Sigma`: Correlation matrix of SNPs
- `W`: Prior for the standard deviation of the effect size parameter, beta (default 0.2)
- `lower`: Lower threshold (default = 0)
- `upper`: Upper threshold (default = 1)
- `desired.cov`: The desired coverage of the causal variant in the credible set
- `acc`: Accuracy of corrected coverage to desired coverage (default = 0.005)
- `max.iter`: Maximum iterations (default = 20)
- `pp0min`: Only average over SNPs with pp0 > pp0min

Value

List of variants in credible set, required threshold, the corrected coverage and the size of the credible set
Author(s)
Anna Hutchinson

Examples

# this is a long running example

# In this example, the function is used to find a corrected 95% credible set
# using bhats and their standard errors, that is the smallest set of variants
# required such that the resultant credible set has coverage close to (/within
# some accuracy of) the "desired coverage" (here set to 0.95). Max.iter parameter
# defines the maximum number of iterations to try in the root bisection algorithm,
# this should be increased to ensure convergence to the desired coverage, but is set
# to 1 here for speed (and thus the resultant credible set will not be accurate).

set.seed(18)
nsnps <- 100
N0 <- 500 # number of controls
N1 <- 500 # number of cases

# simulate fake haplotypes to obtain MAFs and LD matrix
## generate example LD matrix
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,'/'))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)

varbeta <- Var.data.cc(f = maf, N = N0 + N1, s = N1/(N0+N1))

bhats = rnorm(nsnps,0,0.2) # log OR

names(bhats) <- seq(1,length(bhats))

corrected_cs_bhat(bhat = bhats, V = varbeta, N0, N1, Sigma = LD, desired.cov = 0.9, max.iter = 1)
# max.iter set low for speed, should be set to at
# least the default to ensure convergence to desired coverage
credset

Credible set of genetic variants

**Description**

Credible set of putative causal variants

**Usage**

`credset(pp, CV, thr)`

**Arguments**

- `pp` Vector of posterior probabilities of causality
- `CV` Optional parameter: Index of CV
- `thr` Minimum threshold for credible set size

**Details**

If the CV parameter is supplied (index of causal variant) then the output includes a binary indicator of whether the CV is contained in the set

**Value**

List of the variants in the credible set, the `claimed.cov` (cumulative sum of the posterior probabilities of the variants forming the credible set), binary covered indicator (1 if CV is contained in the credible set) and `nvar` (number of variants in the set)

**Author(s)**

Anna Hutchinson

**Examples**

```r
set.seed(1)
nsnps <- 100
pp <- rnorm(nsnps, 0.3, 0.05)
pp <- pp/sum(pp)
credset(pp, thr = 0.9)
iCV <- 71
credset(pp, CV = iCV, thr = 0.9)
```
credsetC

Credible set of variants from matrix of PPs

Description

Quick credset function for matrix of posterior probabilities (using RCpp)

Usage

credsetC(pp, CV, thr)

Arguments

pp          Matrix of posterior probabilities of causality (one row per system)
CV          Vector of CV indices (one per system/row)
thr         Minimum threshold for credible set size

Value

Data.frame of claimed coverage (sum of posterior probabilities of variants in the set), binary covered indicator and number of variants (nvar).

Examples

```R
set.seed(1)
nsnps <- 100

# simulate matrix of posterior probabilities
# 1 simulation per row
pp <- matrix(rnorm(nsnps*100, 0.3, 0.05), ncol = nsnps)
pp <- pp/rowSums(pp)
iCV <- rep(71, times = dim(pp)[1])
credsetC(pp, CV = iCV, thr = 0.9)
```
credsetmat

*Obtain credible sets from a matrix of posterior probabilities*

**Description**

Obtain credible sets from a matrix of posterior probabilities

**Usage**

```r
credsetmat(pp, iCV, threshold)
```

**Arguments**

- `pp`: Matrix of posterior probabilities (one row for each simulation)
- `iCV`: A vector of the indices of the CV
- `threshold`: The threshold to use to generate the credible set

---

est_mu

*Estimate the true effect at the causal variant using Z-scores and MAFs*

**Description**

Estimate the true effect at the causal variant using Z-scores and MAFs

**Usage**

```r
est_mu(z, f, N0, N1, W = 0.2)
```

**Arguments**

- `z`: Vector of marginal Z-scores
- `f`: Minor allele frequencies
- `N0`: Number of controls
- `N1`: Number of cases
- `W`: Prior for the standard deviation of the effect size parameter, beta, default 0.2

**Value**

Estimate of the true effect at the causal variant

**Author(s)**

Anna Hutchinson
est_mu_bhat

Examples

nsnps <- 100
z_scores <- rnorm(nsnps, 0, 3) # simulate a vector of Z-scores
N0 <- 5000 # number of controls
N1 <- 5000 # number of cases
maf <- runif(nsnps, 0.05, 0.5)
est_mu(z = z_scores, f = maf, N0 = N0, N1 = N1)

est_mu_bhat

Estimate the true effect at the causal variant using estimated effect sizes and their standard errors

Description

Estimate the true effect at the causal variant using estimated effect sizes and their standard errors

Usage

est_mu_bhat(bhat, V, N0, N1, p1 = 1e-04, W = 0.2)

Arguments

bhat Vector of estimated effect sizes
V Prior variance for estimated effect sizes
N0 Number of controls
N1 Number of cases
p1 Prior probability a SNP is associated with the trait, default 1e-4
W Prior for the standard deviation of the effect size parameter, beta

Value

Estimate of the true effect at the causal variant

Author(s)

Anna Hutchinson
Examples

```r
nsnps <- 100
N0 <- 5000 # number of controls
N1 <- 5000 # number of cases
maf <- runif(nsnps, 0.05, 0.3)
varbeta <- Var.data.cc(f = maf, N = N0 + N1, s = N1/(N0+N1))
bhats = rnorm(nsnps,0,0.2) # log(OR)
est_mu_bhat(bhat = bhats, V = varbeta, N0 = N0, N1 = N1)
```

Description

Internal function, logsum

Usage

```r
logsum(x)
```

Arguments

- `x` numeric vector

Details

This function calculates the log of the sum of the exponentiated logs taking out the max, i.e. insuring that the sum is not Inf

Value

```r
max(x) + log(sum(exp(x - max(x))))
```

Author(s)

Chris Wallace
logsum_matrix

logsum_matrix

Description

matrix-ified version of logsum to avoid needing apply()

Usage

logsum_matrix(x)

Arguments

x numeric matrix

Value

rowwise sums

Author(s)

Chris Wallace

ppfunc

Find PPs of SNPs from Z-scores

Description

Posterior probabilities of causality from marginal Z-scores

Usage

ppfunc(z, V, W = 0.2)

Arguments

z Vector of marginal Z-scores
V Variance of the estimated effect size (can be obtained using Var.beta.cc function)
W Prior for the standard deviation of the effect size parameter, beta (W = 0.2 default)

Details

This function converts Z-scores to posterior probabilities of causality i.e. not including the null model of no genetic effects, so that the sum of the posterior probabilities for all variants is 1
ppfunc.mat

Value

Vector of posterior probabilities

Examples

```r
set.seed(1)
snps = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(snps, 0, 3)

## generate example LD matrix and MAFs
library(mvtnorm)
nsamples = 1000

simx <- function(snps, nsamples, S, maf=0.1) {
  mu <- rep(0,snps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:snps,1:snps, "/")/snps))/snps)^4
X <- simx(snps,nsamples,S)
maf <- colMeans(X)

varbeta <- Var.data.cc(f = maf, N = N0+N1, s = N1/(N0+N1))

res <- ppfunc(z = z_scores, V = varbeta)
sum(res)
res
```

---

**ppfunc.mat**

*Find PPs of SNPs from matrix of Z-scores*

### Description

Posterior probabilities of causality from matrix of marginal Z-scores (1 simulation per row)

### Usage

```r
ppfunc.mat(zstar, V, W = 0.2)
```

### Arguments

- **zstar**: Matrix of marginal z-scores, one replicate per row
- **V**: Variance of the estimated effect size, one element per column of zstar
- **W**: Prior for the standard deviation of the effect size parameter, beta
Details

This function converts a matrix of Z-scores (one row per simulation) to posterior probabilities of causality, not including the null model of no genetic effects, so that the sum of the posterior probabilities for each simulation (each row) is 1.

Value

Matrix of posterior probabilities of causality

Author(s)

Chris Wallace

Examples

```r
set.seed(1)
nsnps = 100
N0 = 5000
N1 = 5000

## generate example LD matrix and MAFs
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,`-`))/nsnps))^4
X <- simx(nsnps,nsamples,S)
maf <- colMeans(X)

varbeta <- Var.data.cc(f = maf, N = N0+N1, s = N1/(N0+N1))

# simulate matrix of Z scores
# 1 simulation per row
z_scores <- matrix(rnorm(nsnps*100, 0, 3), ncol = nsnps)

# each row is a vector of simulated PPs
res <- ppfunc.mat(zstar = z_scores, V = varbeta)
rowSums(res)
```
prop_cov

Proportion of credible sets containing the causal variant

Description
Proportion of simulated credible sets containing the causal variant

Usage
prop_cov(x)

Arguments

x data.frame with a binary 'covered' column

Value
Proportion of x with x = 1

Author(s)
Anna Hutchinson

pvals_pp
Find PPs for SNPs and null model from P-values and MAFs

Description
Posterior probabilities of causality from P-values

Usage
pvals_pp(pvals, f, type, N, s, W = 0.2, p1 = 1e-04)

Arguments

pvals P-values of SNPs
f Minor allele frequencies
type Type of experiment ('quant' or 'cc')
N Total sample size
s Proportion of cases (N1/N0+N1), ignored if type=='quant'
W Prior for the standard deviation of the effect size parameter, beta (default 0.2)
p1 Prior probability a SNP is associated with the trait (default 1e-4)
Details
This function converts p-values to posterior probabilities of causality, including the null model of no genetic effect.

Value
Posterior probabilities of null model (no genetic effect) and causality for each SNP

Author(s)
Anna Hutchinson

Examples

```r
set.seed(1)
nsnps = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(nsnps, 0, 3)
p_values <- 2 * pnorm(-abs(z_scores))

## generate example LD matrix and MAFs
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps, `-$`))/nsnps))^4
X <- simx(nsnps,nsamples,S)
maf <- colMeans(X)

res <- pvals_pp(pvals = p_values, f = maf, type = "cc", N = N0+N1, s = N1/(N0+N1))
sum(res)
res
```

---

<table>
<thead>
<tr>
<th>Var.data.cc</th>
<th>Variance of the estimated effect size for case-control data</th>
</tr>
</thead>
</table>

Description
Variance of the estimated effect size for case-control data
Usage

Var.data.cc(f, N, s)

Arguments

- **f**: Minor allele frequencies
- **N**: Total sample size (N0+N1)
- **s**: Proportion of cases (N1/N0+N1)

Value

Variance of estimated effect size \( \hat{\beta} \), \( V \).

Author(s)

Chris Wallace

Examples

```r
maf = runif(100, 0.05, 0.5)
N0 = 5000 # number of controls
N1 = 5000 # number of cases
Var.data.cc(f = maf, N = N0 + N1, s = N1/(N0+N1))
```

---

### z0_pp

Find PPs for SNPs and null model from Z-scores and MAFs

Description

Posterior probabilities of causality from marginal Z-scores with prior SD as a parameter

Usage

z0_pp(z, f, type, N, s, W = 0.2, p1 = 1e-04)

Arguments

- **z**: Marginal Z-scores of SNPs
- **f**: Minor allele frequencies
- **type**: Type of experiment (‘quant’ or ‘cc’)
- **N**: Total sample size
- **s**: Proportion of cases (N1/N0+N1), ignored if type=='quant'
- **W**: Prior for the standard deviation of the effect size parameter, beta (default 0.2)
- **p1**: Prior probability a SNP is associated with the trait (default 1e-4)
Details

Converts Z-scores to posterior probabilities of causality, including the null model of no genetic effects

Value

Posterior probabilities of null model (no genetic effect) and causality for each SNP

Author(s)

Anna Hutchinson

Examples

```r
set.seed(1)
nsnps = 100
N0 = 5000
N1 = 5000
z_scores <- rnorm(nsnps, 0, 3)

## generate example LD matrix and MAFs
library(mvtnorm)
nsamples = 1000

S <- (1 - (abs(outer(1:nsnps,1:nsnps,'-''))/nsnps))^4
X <- simx(nsnps,nsamples,S)
maf <- colMeans(X)
res <- z0_pp(z = z_scores, f = maf, type = "cc", N = N0+N1, s = N1/(N0+N1))
sum(res)
res
```

**zj_pp**  
*Simulate posterior probabilities of causality from joint Z-score vector*

Description

Simulate nrep marginal Z-scores from joint Z-scores and convert these to posterior probabilities of causality
Usage

\texttt{zj_pp(Zj, V, nrep = 1000, W = 0.2, Sigma)}

Arguments

- **Zj**: Vector of joint Z-scores (0s except at CV)
- **V**: Variance of the estimated effect size (can be obtained using \texttt{Var.beta.cc} function)
- **nrep**: Number of posterior probability systems to simulate (default 1000)
- **W**: Prior for the standard deviation of the effect size parameter, beta (default 0.2)
- **Sigma**: SNP correlation matrix

Details

Does not include posterior probabilities for null model

Value

Matrix of simulated posterior probabilities, one simulation per row

Author(s)

Anna Hutchinson

Examples

```
set.seed(1)
nsnps <- 100
Zj <- rep(0, nsnps)
iCV <- 4  # index of CV
mu <- 5  # true effect at CV
Zj[iCV] <- mu

## generate example LD matrix and MAFs
library(mvtnorm)
nsamples = 1000

simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}
S <- (1 - (abs(outer(1:nsnps,1:nsnps,`-`))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)
maf <- colMeans(X)

## generate V (variance of estimated effect sizes)
```
```
varbeta <- Var.data.cc(f = maf, N = 5000, s = 0.5)
res <- zj_pp(Zj, V = varbeta, nrep = 5, W = 0.2, Sigma = LD)
res[c(1:5), c(1:5)]
```

---

**Simulation**

Simulate marginal Z-scores from joint Z-score vector

**Description**

Simulate marginal z-scores \((Z_m)\) from the joint z-scores \((Z_j)\) using \(E(Z_m) = Z_j \times \Sigma\) and \(Z * \sim MVN(E(Z_m), \Sigma)\)

**Usage**

```r
z_sim(Zj, Sigma, nrep)
```

**Arguments**

- **Zj**: Vector of joint Z-scores (a vector of 0s except at the CV)
- **Sigma**: SNP correlation matrix
- **nrep**: Number of Z-score systems to simulate

**Value**

Matrix of simulated posterior probabilities, one simulation per row

**Author(s)**

Anna Hutchinson

**Examples**

```r
set.seed(1)
nsnps <- 100

# derive joint Z score vector
Zj <- rep(0, nsnps)
iCV <- 4 # index of CV
mu <- 5 # true effect at CV
Zj[iCV] <- mu

## generate example LD matrix
library(mvtnorm)
nsamples = 1000
```
```r
simx <- function(nsnps, nsamples, S, maf=0.1) {
  mu <- rep(0,nsnps)
  rawvars <- rmvnorm(n=nsamples, mean=mu, sigma=S)
  pvars <- pnorm(rawvars)
  x <- qbinom(1-pvars, 1, maf)
}

S <- (1 - (abs(outer(1:nsnps,1:nsnps,'-''))/nsnps))^4
X <- simx(nsnps,nsamples,S)
LD <- cor2(X)

res <- z_sim(Zj, Sigma = LD, nrep = 100)
res[c(1:5), c(1:5)]
```
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