

Package: ReAD (via r-universe)

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Type Package

Title Powerful Replicability Analysis of Genome-Wide Association Studies

Version 1.0.1

Description A robust and powerful approach is developed for replicability analysis of two Genome-wide association studies (GWASs) accounting for the linkage disequilibrium (LD) among genetic variants. The LD structure in two GWASs is captured by a four-state hidden Markov model (HMM). The unknowns involved in the HMM are estimated by an efficient expectation-maximization (EM) algorithm in combination with a non-parametric estimation of functions. By incorporating information from adjacent locations via the HMM, this approach identifies the entire clusters of genotype-phenotype associated signals, improving the power of replicability analysis while effectively controlling the false discovery rate.

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Encoding UTF-8

Depends Rcpp (>= 1.0.10), qvalue

LinkingTo Rcpp, RcppArmadillo

RoxygenNote 7.2.3

NeedsCompilation yes

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em_hmm	<i>EM algorithm in combination with a non-parametric algorithm for estimation of the rLIS statistic.</i>
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Description

Estimate the rLIS values accounting for the linkage disequilibrium across two genome-wide association studies via the four-state hidden Markov model. Apply a step-up procedure to control the FDR of replicability null.

Usage

```
em_hmm(pa_in, pb_in, pi0a_in, pi0b_in)
```

Arguments

pa_in	A numeric vector of p-values from study 1.
pb_in	A numeric vector of p-values from study 2.
pi0a_in	An initial estimate of the null probability in study 1.
pi0b_in	An initial estimate of the null probability in study 2.

Value

rLIS	The estimated rLIS for replicability null.
fdr	The adjusted values based on rLIS for FDR control.
loglik	The log-likelihood value with converged estimates of the unknowns.
pi	An estimate of the stationary probabilities of four states (0,0), (0,1), (1,0), (1,1).
A	An estimate of the 4-by-4 transition matrix.
f1	A non-parametric estimate for the non-null probability density function in study 1.
f2	A non-parametric estimate for the non-null probability density function in study 2.

ReAD	<i>Replicability analysis across two genome-wide association studies accounting for the linkage disequilibrium structure.</i>
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Description

Replicability analysis across two genome-wide association studies accounting for the linkage disequilibrium structure.

Usage

```
ReAD(pa, pb)
```

Arguments

pa	A numeric vector of p-values from study 1.
pb	A numeric vector of p-values from study 2.

Value

A list:

rLIS	The estimated rLIS for replicability null.
fdr	The adjusted values based on rLIS for FDR control.
loglik	The log-likelihood value with converged estimates of the unknowns.
pi	An estimate of the stationary probabilities of four states (0,0), (0,1), (1,0), (1,1).
A	An estimate of the 4-by-4 transition matrix.
f1	A non-parametric estimate for the non-null probability density function in study 1.
f2	A non-parametric estimate for the non-null probability density function in study 2.

Examples

```
# Simulate p-values in two studies locally dependent via a four-state hidden Markov model
data <- SimuData(J = 10000)
p1 = data$pa; p2 = data$pb; theta1 = data$theta1; theta2 = data$theta2
# Run ReAD to identify replicable signals
res.read = ReAD(p1, p2)
sig.idx = which(res.read$fdr <= 0.05)
```

SimuData	<i>Simulate two sequences of p-values by accounting for the local dependence structure via a hidden Markov model.</i>
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Description

Simulate two sequences of p-values by accounting for the local dependence structure via a hidden Markov model.

Usage

```
SimuData(
  J = 10000,
  pi = c(0.25, 0.25, 0.25, 0.25),
  A = 0.6 * diag(4) + 0.1,
  muA = 2,
  muB = 2,
  sdA = 1,
  sdB = 1
)
```

Arguments

J	The number of features to be tested in two studies.
pi	The stationary probabilities of four hidden joint states.
A	The 4-by-4 transition matrix.
muA	Mean of the normal distribution generating the p-value in study 1.
muB	Mean of the normal distribution generating the p-value in study 2.
sdA	The standard deviation of the normal distribution generating the p-value in study 1.
sdB	The standard deviation of the normal distribution generating the p-value in study 2.

Value

A list:

pa	A numeric vector of p-values from study 1.
pb	A numeric vector of p-values from study 2.
theta1	The true states of features in study 1.
theta2	The true states of features in study 2.

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