

# Package ‘ReAD’

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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.

**License** GPL-3

**Encoding** UTF-8

**Depends** Rcpp ( $\geq 1.0.10$ ), 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.

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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)
```

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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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