

Package ‘CARMAX’

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Title CARMA-X: A novel fine-mapping method for admixed population

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Description We propose here a novel fine-mapping method (CARMA-X) for admixed settings that improves upon existing methods in several directions, including: (1) flexible prior distributions that can model heterogeneity in effects across ancestries, (2) a new method to estimate cross-ancestry LD, and (3) a Bayesian hypothesis test to detect and correct for discrepancies between summary statistics and external LD to avoid false positives.

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Encoding UTF-8

Imports methods, stats, dplyr, Matrix, MASS, Rcpp

LinkingTo Rcpp, RcppArmadillo, RcppGSL

RoxygenNote 7.3.2

NeedsCompilation yes

R topics documented:

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CARMAX-package	<i>A short title line describing what the package does</i>
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Description

A more detailed description of what the package does. A length of about one to five lines is recommended.

Details

This section should provide a more detailed overview of how to use the package, including the most important functions.

Author(s)

Your Name, email optional.

Maintainer: Your Name <your@email.com>

References

This optional section can contain literature or other references for background information.

See Also

Optional links to other man pages

Examples

```
## Not run:
## Optional simple examples of the most important functions
## These can be in \dontrun{} and \donttest{} blocks.

## End(Not run)
```

CARMAX

CARMA-X

Description

Implements the CARMA-X model, a Bayesian fine-mapping method specifically designed for admixed populations. The model identifies putative causal variants at GWAS loci using summary statistics of SNPs within the loci of interest, along with corresponding ancestral LD matrices for admixed fine-mapping and an estimated variance of traits. CARMA-X includes an LD estimation procedure to correct for inconsistencies introduced by external LD reference panels, which is important for admixed populations where reference LD structures may be less accurate to the results of local ancestry inferences on admixed cohorts. Additionally, CARMA-X offers a robust outlier detection procedure that resolves discrepancies between the summary statistics and the LD matrix derived from reference panels.

Usage

```
CARMAX(
  z.list,
  ld.list,
  lambda.list = NULL,
  output.labels = ".",
  label.list = NULL,
  LD.estimation = T,
  effect.size.prior = "Spike-slab",
  rho.index = 0.99,
```

```

    BF.index = 10,
    Max.Model.Dim = 2e+05,
    all.iter = 3,
    all.inner.iter = 10,
    epsilon.threshold = 1e-04,
    num.causal = 10,
    y.var = 1,
    tau = 0.04,
    outlier.switch = T,
    outlier.BF.index = 1/3.2,
    purity.index = 0.5
)

```

Arguments

<code>z.list</code>	Input list of the summary statistics of the testing loci, and each element of the list is the summary statistics of each ancestry of the admixed cohort.
<code>ld.list</code>	Input list of the LD correlation matrix of the testing loci, and each element of the list is the LD matrix of each ancestry of the admixed cohort. The last element of the list is the overall LD matrix that captures correlations across ancestries.
<code>lambda.list</code>	Input list of the hyper-parameter η of the testing loci, and each element of the list is the hyper-parameter of each ancestry of the admixed cohort.
<code>output.labels</code>	Output directory where output will be written while CARMA is running. Default is the OS root directory ".".
<code>label.list</code>	Input list of the names of the testing loci. Default is NULL.
<code>LD.estimation</code>	he indicator variable of whether turn on the LD estimation of cross-ancestry correlations. We suggest that the LD estimation is used if using external LD matrix.
<code>effect.size.prior</code>	The prior of the effect size, where the 'Spike-slab' prior is the default prior.
<code>rho.index</code>	A number between 0 and 1 specifying ρ of the estimated credible sets.
<code>BF.index</code>	A number smaller than 1 to specifying the threshold of the Bayes factor of the estimated credible models. The default setting is 10.
<code>Max.Model.Dim</code>	Maximum number of the top candidate models based on the unnormalized posterior probability.
<code>all.iter</code>	Maximum iterations for EM algorithm to run.
<code>all.inner.iter</code>	Maximum iterations for Shotgun algorithm to run per iteration within EM algorithm.
<code>epsilon.threshold</code>	Convergence threshold measured by average of Bayes factors.
<code>num.causal</code>	The maximum number of causal variants assumed per locus, which is 10 causal SNPs per locus by default.
<code>y.var</code>	The input variance of the summary statistics, the default value is 1 as the summary statistics are standardized.
<code>outlier.switch</code>	The indicator variable of whether turn on the outlier detection. We suggest that the detection should always turn on if using external LD matrix.
<code>outlier.BF.index</code>	The threshold of the Bayes factor of the hypothesis testing of determining outliers, which is 1/3.2 by default.

Details

The function performs a Bayesian fine-mapping method.

Value

The form of the return is a list, for each list:

- pip - The posterior inclusion probability.
- Credibleset - The information regarding the credible set given a threshold ρ .
- Credible model - The information regarding the credible model given a threshold of the Bayes factor.
- Outliers - The information regarding the detected outliers.

Examples

```
# Example
set.seed(1)
n = 400
p = 500
beta = rep(0,p)
beta[1] = 1
X = matrix(rnorm(n*p),nrow = n,ncol = p)
X = scale(X,center = TRUE,scale = TRUE)
y = drop(X %*% beta + rnorm(n))
SS=compute_summary_statistics(X,y)
z.list<-list()
z.list[[1]]<-(SS$betahat/SS$sebetahat)
ld.list<-list()
ld.list[[1]]<-cov(X)
lambda.list<-list()
lambda.list[[1]]<-1/sqrt(p)
CARMA.result<-CARMA_fixed_sigma(z.list,ld.list=ld.list,
lambda.list = lambda.list,effect.size.prior='Hyper-g')
```

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