Package 'ACAT'

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Title Aggregaged Cauchy Associaion Test (ACAT)

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Description This package implemented ACAT, a generic method for combing p-values, and ACAT-V, a variant set test for rare variant analysis using ACAT.

Depends R (>= 3.2.0)

Imports Matrix

License GPLv3

Encoding UTF-8

LazyData true

RoxygenNote 7.1.1

R topics documented:

ACAT   *Aggregated Cauchy Assocaition Test*

Description

A p-value combination method using the Cauchy distribution.

Usage

```
ACAT(Pvals, weights = NULL, is.check = TRUE)
```

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Arguments

Pvals	a numeric vector/matrix of p-values. When it is a matrix, each column of p-values is combined by ACAT.
weights	a numeric vector/matrix of non-negative weights for the combined p-values. When it is NULL, the equal weights are used.
is.check	logical. Should the validity of *Pvals* (and *weights*) be checked? When the size of *Pvals* is large and one knows *Pvals* is valid, then the checking part can be skipped to save memory.

Value

The p-value(s) of ACAT.

Author(s)

Yaowu Liu

References

Liu, Y., & Xie, J. (2019). Cauchy combination test: a powerful test with analytic p-value calculation under arbitrary dependency structures. *Journal of American Statistical Association*,115(529), 393-402. (pub)

Examples

```
p.values<-c(2e-02,4e-04,0.2,0.1,0.8);ACAT(Pvals=p.values)
ACAT(matrix(runif(1000),ncol=10))
```

ACAT_V	*A set-based test that uses ACAT to combine the variant-level p-values.*

Description

A set-based test that uses ACAT to combine the variant-level p-values.

Usage

```
ACAT_V(G, obj, weights.beta = c(1, 25), weights = NULL, mac.thresh = 10)
```

Arguments

G	a numeric matrix or dgCMatrix with each row as a different individual and each column as a separate gene/snp. Each genotype should be coded as 0, 1, 2.
obj	an output object of the NULL_Model function.
weights.beta	a numeric vector of parameters for the beta weights for the weighted kernels. If you want to use your own weights, please use the "weights" parameter. It will be ignored if "weights" parameter is not null.
weights	a numeric vector of weights for the SNP p-values. When it is NULL, the beta weight with the "weights.beta" parameter is used.
mac.thresh	a threshold of the minor allele count (MAC). The Burden test will be used to aggregate the SNPs with MAC less than this thrshold.

Details

The Burden test is first used to aggregate very rare variants with Minor Allele Count (MAC) < *mac.thresh* (e.g., 10), and a Burden p-value is obtained. For each of the variants with MAC >= *mac.thresh*, a variant-level p-value is calculated. Then, ACAT is used to combine the variant-level p-values and the Burden test p-value of very rare variants.

If *weights.beta* is used, then the weight for the Burden test p-value is demetermined by the average Minor Allele Frequency (MAF) of the variants with MAC < *mac.thresh*; if the user-specified *weights* is used, then the weight for the Burden test p-value is the average of *weights* of the variants with MAC < *mac.thresh*.

Note that the *weights* here are for the SNP p-vlaues. In SKAT, the weights are for the SNP score test statistics. To transfrom the SKAT weights to the *weights* here, one can use the formula that *weights* = (skat_weights)^2*MAF*(1-MAF).

Value

The p-value of ACAT-V.

Author(s)

Yaowu Liu

References

Liu, Y., et al. (2019). ACAT: A fast and powerful p value combination method for rare-variant analysis in sequencing studies. *American Journal of Humann Genetics 104*(3), 410-421. (pub)

Examples

```
data(Geno)
G<-Geno[,1:100] # Geno is a dgCMatrix of genotypes
Y<-rnorm(nrow(G)); Z<-matrix(rnorm(nrow(G)*4),ncol=4)
obj<-NULL_Model(Y,Z)
ACAT_V(G,obj)
```

NULL_Model *Get parameters and residuals from the NULL model*

Description

Compute model parameters and residuals for ACAT-V

Usage

```
NULL_Model(Y, Z = NULL)
```

Arguments

Y
: a numeric vector of outcome phenotypes.

Z
: a numeric matrix of covariates. Z must be full-rank. Do not include intercept in Z. The intercept will be added automatically.

Details

Y could only be continuous or binary. If *Y* is continuous, a linear regression model is fitted. If *Y* is binary, it must be coded as 0,1 and a logistic model is fitted.

Value

This function returns an object that has model parameters and residuals of the NULL model of no association between genetic variables and outcome phenotypes. After obtaining it, please use ACAT_V function to conduct the association test.

Author(s)

Yaowu Liu

Examples

```
Y<-rnorm(10000)
Z<-matrix(rnorm(10000*4),ncol=4)
obj<-NULL_Model(Y,Z)
```

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