

Package ‘RNOMni’

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Title Rank Normal Transformation Omnibus Test

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Description Genetic association tests that use the rank-based inverse normal transformation (INT). These tests are recommend for continuous traits with non-normally distributed residuals. INT-based tests robustly control the type I error in settings where standard linear regression does not. Moreover, INT-based tests dominate standard linear regression in terms of power. INT-based tests may be classified into two types: tests that directly transform the phenotype (D-INT) and tests that transform phenotypic residuals (I-INT). Our omnibus test (O-INT) adaptively combines D-INT and I-INT into a single robust and statistically powerful approach.

Depends R (>= 3.2.2)

Imports abind, foreach, plyr, Rcpp

License GPL-3

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 BAT

Basic Association Test

Description

Conducts tests of association between the loci in G and the untransformed phenotype y, adjusting for the model matrix X.

Usage

```
BAT(y, G, X = NULL, test = "Score", simple = FALSE,
    parallel = FALSE)
```

Arguments

y	Numeric phenotype vector.
G	Obs by snp genotype matrix.
X	Model matrix of covariates and structure adjustments. Should include an intercept. Omit to perform marginal tests of association.
test	Either Score or Wald.
simple	Return the p-values only?
parallel	Logical indicating whether to run in parallel. Must register parallel backend first.

Value

If simple=T, returns a vector of p-values, one for each column of G. If simple=F, returns a numeric matrix, including the Wald or Score statistic, its standard error, the Z-score, and the p-value.

See Also

Direct INT [DINT](#), indirect INT [IINT](#), omnibus INT [OINT](#).

Examples

```
## Not run:
set.seed(100);
# Design matrix
X = cbind(1,rnorm(1e3));
# Genotypes
G = replicate(1e3,rbinom(n=1e3,size=2,prob=0.25));
storage.mode(G) = "numeric";
# Phenotype
y = as.numeric(X%%c(1,1))+rnorm(1e3);
# Association test
p = BAT(y=y,G=G,X=X,simple=T);

## End(Not run)
```

cov

*Correlation***Description**

Calculates the correlation between two vectors.

Usage

```
cov(A, B, cor = FALSE)
```

Arguments

A	First matrix.
B	Second matrix.
cor	Return correlation matrix?

Value

Numeric matrix.

DINT

*Direct-INT***Description**

Applies the rank-based inverse normal transformation ([rankNorm](#)) to the phenotype y . Conducts tests of association between the loci in G and transformed phenotype, adjusting for the model matrix X .

Usage

```
DINT(y, G, X = NULL, k = 3/8, test = "Score", simple = FALSE,
     parallel = FALSE)
```

Arguments

<code>y</code>	Numeric phenotype vector.
<code>G</code>	Obs by snp genotype matrix.
<code>X</code>	Model matrix of covariates and structure adjustments. Should include an intercept. Omit to perform marginal tests of association.
<code>k</code>	Offset applied during rank-normalization. See rankNorm .
<code>test</code>	Either Score or Wald.
<code>simple</code>	Return the p-values only?
<code>parallel</code>	Logical indicating whether to run in parallel. Must register parallel backend first.

Value

If `simple=T`, returns a vector of p-values, one for each column of `G`. If `simple=F`, returns a numeric matrix, including the Wald or Score statistic, its standard error, the Z-score, and the p-value.

See Also

Basic association test [BAT](#), indirect INT [IINT](#), omnibus INT [OINT](#).

Examples

```
## Not run:
set.seed(100);
# Design matrix
X = cbind(1,rnorm(1e3));
# Genotypes
G = replicate(1e3,rbinom(n=1e3,size=2,prob=0.25));
storage.mode(G) = "numeric";
# Phenotype
y = exp(as.numeric(X%*%c(1,1))+rnorm(1e3));
# Association test
p = DINT(y=y,G=G,X=X,simple=T);

## End(Not run)
```

fitOLS	<i>Univariate OLS model.</i>
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Description

Fits the standard OLS model.

Usage

```
fitOLS(y, X)
```

Arguments

y	Numeric vector.
X	Numeric matrix.

Value

List containing the following:

Beta	Regression coefficient.
V	Outcome variance.
Ibb	Information matrix for beta.
Resid	Outcome residuals.

IINT	<i>Indirect-INT</i>
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Description

Two-stage association testing procedure. In the first stage, phenotype y and genotype G are each regressed on the model matrix X to obtain residuals. The phenotypic residuals are transformed using [rankNorm](#). In the next stage, the INT-transformed residuals are regressed on the genotypic residuals.

Usage

```
IINT(y, G, X = NULL, k = 3/8, simple = FALSE, parallel = FALSE)
```

Arguments

y	Numeric phenotype vector.
G	Obs by snp genotype matrix.
X	Model matrix of covariates and structure adjustments. Should include an intercept. Omit to perform marginal tests of association.
k	Offset applied during rank-normalization. See rankNorm .
simple	Return the p-values only?
parallel	Logical indicating whether to run in parallel. Must register parallel backend first.

Value

If simple=T, returns a vector of p-values, one for each column of G. If simple=F, returns a numeric matrix, including the Wald or Score statistic, its standard error, the Z-score, and the p-value.

See Also

Basic association test [BAT](#), direct INT [DINT](#), omnibus INT [OINT](#).

Examples

```
## Not run:
set.seed(100);
# Design matrix
X = cbind(1,rnorm(1e3));
# Genotypes
G = replicate(1e3,rbinom(n=1e3,size=2,prob=0.25));
storage.mode(G) = "numeric";
# Phenotype
y = exp(as.numeric(X%*%c(1,1))+rnorm(1e3));
# Association test
p = IINT(y=y,G=G,X=X,simple=T);

## End(Not run);
```

matInv

Matrix Inverse

Description

Calculates A^{-1} .

Usage

```
matInv(A)
```

Arguments

A Numeric matrix.

Value

A numeric matrix.

matIP *Matrix Inner Product*

Description

Calculates the inner product $A'B$.

Usage

matIP(A, B)

Arguments

A Numeric matrix.

B Numeric matrix.

Value

Numeric matrix.

OINT *Omnibus-INT*

Description

Association test that synthesizes the [DINT](#) and [IINT](#) tests. The first approach is most powerful for traits that could have arisen from a rank-preserving transformation of a latent normal trait. The second approach is most powerful for traits that are linear in covariates, yet have skewed or kurtotic residual distributions. During the omnibus test, the direct and indirect tests are separately applied then

Usage

OINT(y, G, X = NULL, k = 3/8, simple = FALSE, parallel = FALSE)

Arguments

y	Numeric phenotype vector.
G	Obs by locus genotype matrix.
X	Model matrix of covariates and structure adjustments. Should include an intercept. Omit to perform marginal tests of association.
k	Offset applied during rank-normalization. See rankNorm .
simple	Return the OINT p-values only?
parallel	Logical indicating whether to run in parallel. Must register parallel backend first.

Value

A numeric matrix of p-values, three for each column of G.

See Also

Basic association test [BAT](#), direct INT [DINT](#), indirect INT [IINT](#).

Examples

```
## Not run:
set.seed(100);
# Design matrix
X = cbind(1,rnorm(1e3));
# Genotypes
G = replicate(1e3,rbinom(n=1e3,size=2,prob=0.25));
storage.mode(G) = "numeric";
# Phenotype
y = exp(as.numeric(X%*%c(1,1))+rnorm(1e3));
# Omnibus
p = OINT(y=y,G=G,X=X,simple=T);

## End(Not run)
```

OINTp

Omnibus p-value

Description

Omnibus p-value

Usage

OINTp(p)

Arguments

p Vector of p-values

Value

OINT p-value.

rankNorm

Rank-Normalize

Description

Applies the rank based inverse normal transform (INT) to a numeric vector. The INT can be broken down into a two-step procedure. In the first, the observations are transformed onto the probability scale using the empirical cumulative distribution function (ECDF). In the second, the observations are transformed onto the real line, as Z-scores, using the probit function.

Usage

```
rankNorm(u, k = 3/8)
```

Arguments

u Numeric vector.
k Offset. Defaults to (3/8), correspond to the Blom transform.

Value

Numeric vector of rank normalized measurements.

See Also

Direct INT [DINT](#), indirect INT [IINT](#), omnibus INT [OINT](#).

Examples

```
## Not run:  
# Draw from chi-1 distribution  
y = rchisq(n=1e3,df=1);  
# Rank normalize  
z = rankNorm(y);  
# Plot density of transformed measurement  
plot(density(z));  
  
## End(Not run)
```

 RNOmni-help

RNOmni: Rank-Normal Omnibus Association Testing

Description

Implementation of genetic association tests that incorporate the rank-based inverse normal transformation (INT) [rankNorm](#). The direct-INT [DINT](#) test directly transforms the outcome, whereas the indirect-INT [IINT](#) test forms residuals prior to transformation. The omnibus INT [OINT](#) test adaptively combines the D-INT and I-INT tests into a single robust and statistically powerful procedure.

Author(s)

Zachary R. McCaw

 SchurC

Schur complement

Description

Calculates the efficient information $I_{bb} - I_{ba}I_{aa}^{-1}I_{ab}$.

Usage

SchurC(Ibb, Iaa, Iba)

Arguments

Ibb	Information of target parameter
Iaa	Information of nuisance parameter
Iba	Cross information between target and nuisance parameters

Value

Numeric matrix.

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