Package ‘RNOmni’

April 28, 2019

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.

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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

```r
## 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**

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**

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

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.
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

Basic association test BAT, indirect INT IINT, omnibus INT OINT.

Examples

```r
## 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**  
*Univariate OLS model.*

**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**  
*Indirect-INT*

**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

```r
# 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 = OINT(y=y, G=G, X=X, simple=T);

## End(Not run);
```

---

### matInv

**Matrix Inverse**

**Description**

Calculates \( A^{-1} \).

**Usage**

`matInv(A)`
**matIP**

**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

```r
## 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 = OINTp(y=y,G=G,X=X,simple=T);
## End(Not run)
```

---

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Description

Omnibus p-value

Usage

`OINTp(p)`
Arguments

p  Vector of p-values

Value

OINT p-value.

---

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

```r
# 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 0INT test directly transforms the outcome, whereas the indirect-INT 1INT test forms residuals prior to transformation. The omnibus INT 0INT test adaptively combines the D-INT and I-INT tests into a single robust and statistically powerful procedure.

**Author(s)**

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**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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