

Package: RNOmni (via r-universe)

October 14, 2026

Title Rank Normal Transformation Omnibus Test

Version 1.0.1.4

Date 2024-11-09

Author Zachary R. McCaw [aut, cre]

Maintainer Zachary R. McCaw <zmccaw@alumni.harvard.edu>

Description Inverse normal transformation (INT) based genetic association testing. These tests are recommended 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, as when the residual distribution exhibits excess skew or kurtosis. Moreover, INT-based tests outperform standard linear regression in terms of power. These tests may be classified into two types. In direct INT (D-INT), the phenotype is itself transformed. In indirect INT (I-INT), phenotypic residuals are transformed. The omnibus test (O-INT) adaptively combines D-INT and I-INT into a single robust and statistically powerful approach. See McCaw ZR, Lane JM, Saxena R, Redline S, Lin X. ``Operating characteristics of the rank-based inverse normal transformation for quantitative trait analysis in genome-wide association studies" <doi:10.1111/biom.13214>.

Depends R (>= 3.2.2)

Imports plyr, Rcpp, stats

LinkingTo Rcpp, RcppArmadillo

License GPL-3

URL <https://github.com/zrmacc/RNOmni>

BugReports <https://github.com/zrmacc/RNOmni/issues>

Encoding UTF-8

RoxygenNote 7.3.3

Suggests testthat (>= 3.0.0), withr, R.rsp

VignetteBuilder R.rsp

Config/testthat/edition 3
Repository <https://zrmacc.r-universe.dev>
Date/Publication 2026-02-25 03:22:10 UTC
RemoteUrl <https://github.com/zrmacc/rnomni>
RemoteRef HEAD
RemoteSha abd120809a5764db5f879a6b631a3b240a87aa23

Contents

RNOmni-package	2
BasicInputChecks	3
BAT	4
CauchyToP	5
DINT	5
FitOLS	6
IINT	7
OINT	8
OmniP	9
PartitionData	10
PtoCauchy	11
RankNorm	11

Index	13
--------------	-----------

RNOmni-package	<i>RNOmni: Rank normal transformation omnibus association test</i>
----------------	--

Description

INT-based tests control type I error when standard linear regression does not (e.g. skewed or kurtotic residuals) and typically outperform linear regression in power. The package provides:

- [BAT](#): Basic association test (no transformation).
- [DINT](#): Direct INT (phenotype is rank-normalized).
- [IINT](#): Indirect INT (phenotypic residuals are rank-normalized).
- [OINT](#): Omnibus test combining D-INT and I-INT via Cauchy combination ([OmniP](#)).

Helper functions include [RankNorm](#) (rank-based INT) and [FitOLS](#) (OLS fit).

Details

Genetic association tests based on the rank-based inverse normal transformation (INT). Recommended for continuous traits with non-normally distributed residuals.

Use [OINT](#) for a single robust test that adapts to the trait distribution. Use [DINT](#) when the trait may be a rank-preserving transform of a normal trait, and [IINT](#) when the trait is linear in covariates but has non-normal residuals.

Author(s)

Maintainer: Zachary McCaw <zmccaw@alumni.harvard.edu> ([ORCID](#))

References

McCaw ZR, Lane JM, Saxena R, Redline S, Lin X (2020). Operating characteristics of the rank-based inverse normal transformation for quantitative trait analysis in genome-wide association studies. *Biometrics*, doi:[10.1111/biom.13214](https://doi.org/10.1111/biom.13214).

See Also

[OINT](#), [DINT](#), [IINT](#), [BAT](#), [RankNorm](#), [OmniP](#)

BasicInputChecks

Basic Input Checks

Description

Stops evaluation if inputs are improperly formatted.

Usage

```
BasicInputChecks(y, G, X)
```

Arguments

y	Numeric phenotype vector.
G	Genotype matrix with observations as rows, SNPs as columns.
X	Covariate matrix.

Value

None; called for side effects (stops on invalid input).

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)
```

Arguments

<i>y</i>	Numeric phenotype vector.
<i>G</i>	Genotype matrix with observations as rows, SNPs as columns.
<i>X</i>	Model matrix of covariates and structure adjustments. Should include an intercept. Omit or set to NULL for marginal tests of association.
<i>test</i>	Character: "Score" or "Wald".
<i>simple</i>	If TRUE, return only the p-values; if FALSE, return the full matrix of statistic, SE, Z, and p-value.

Value

If *simple* = TRUE, returns a vector of p-values, one for each column of *G*. If *simple* = FALSE, 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

```
set.seed(100)
# Design matrix
X <- cbind(1, stats::rnorm(1e3))
# Genotypes
G <- replicate(1e3, stats::rbinom(n = 1e3, size = 2, prob = 0.25))
storage.mode(G) <- "numeric"
# Phenotype
y <- as.numeric(X %*% c(1, 1)) + stats::rnorm(1e3)
# Association test
p <- BAT(y = y, G = G, X = X)
```

CauchyToP*Convert Cauchy Random Variable to P*

Description

Convert Cauchy Random Variable to P

Usage

CauchyToP(z)

Arguments

z Numeric Cauchy random variable.

Value

Numeric p-value.

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 = 0.375,  
  test = "Score",  
  ties.method = "average",  
  simple = FALSE  
)
```

Arguments

<code>y</code>	Numeric phenotype vector.
<code>G</code>	Genotype matrix with observations as rows, SNPs as columns.
<code>X</code>	Model matrix of covariates and structure adjustments. Should include an intercept. Omit or set to NULL for marginal tests of association.
<code>k</code>	Offset for rank-normalization; see RankNorm .
<code>test</code>	Character: "Score" or "Wald".
<code>ties.method</code>	Method for breaking ties, passed to rank .
<code>simple</code>	If TRUE, return only p-values; if FALSE, return the full matrix of statistic, SE, Z, and p-value.

Value

If `simple = TRUE`, returns a vector of p-values, one for each column of `G`. If `simple = FALSE`, 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 test [IINT](#).
- Omnibus INT test [OINT](#).

Examples

```
set.seed(100)
# Design matrix
X <- cbind(1, stats::rnorm(1e3))
# Genotypes
G <- replicate(1e3, stats::rbinom(n = 1e3, size = 2, prob = 0.25))
storage.mode(G) <- "numeric"
# Phenotype
y <- exp(as.numeric(X %*% c(1, 1)) + stats::rnorm(1e3))
# Association test
p <- DINT(y = y, G = G, X = X)
```

FitOLS

Ordinary least squares

Description

Fits the linear model $y = X\beta + \epsilon$ by OLS.

Usage

```
FitOLS(y, X)
```

Arguments

y	Numeric response vector (length n).
X	Numeric design matrix ($n \times p$); typically includes an intercept column.

Value

A list:	
Beta	Estimated coefficient vector $\hat{\beta}$.
V	Residual variance $\hat{\sigma}^2$ (residual sum of squares divided by $n - p$).
Ibb	Information matrix for β (scaled $X'X$).
Resid	Residual vector $y - X\hat{\beta}$.

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

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 = 0.375, ties.method = "average", simple = FALSE)
```

Arguments

y	Numeric phenotype vector.
G	Genotype matrix with observations as rows, SNPs as columns.
X	Model matrix of covariates and structure adjustments. Should include an intercept. Omit or set to NULL for marginal tests of association.
k	Offset for rank-normalization; see RankNorm .
ties.method	Method for breaking ties, passed to rank .
simple	If TRUE, return only p-values; if FALSE, return the full matrix of Score statistic, SE, Z, and p-value.

Value

If `simple = TRUE`, returns a vector of p-values, one for each column of G . If `simple = FALSE`, 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 test [DINT](#).
- Omnibus INT test [OINT](#).

Examples

```
set.seed(100)
# Design matrix
X <- cbind(1, stats::rnorm(1e3))
# Genotypes
G <- replicate(1e3, stats::rbinom(n = 1e3, size = 2, prob = 0.25))
storage.mode(G) <- "numeric"
# Phenotype
y <- exp(as.numeric(X %*% c(1,1)) + stats::rnorm(1e3))
# Association test
p <- IINT(y = y, G = G, X = X)
```

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 the p-values are combined via the Cauchy combination method.

Usage

```
OINT(
  y,
  G,
  X = NULL,
  k = 0.375,
  ties.method = "average",
  weights = c(1, 1),
  simple = FALSE
)
```

Arguments

y	Numeric phenotype vector.
G	Genotype matrix with observations as rows, SNPs as columns.
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 .
ties.method	Method of breaking ties, passed to <code>base::rank</code> .
weights	Numeric length-2 vector of weights for the D-INT and I-INT p-values in the Cauchy combination. Default <code>c(1, 1)</code> gives equal weight.
simple	If TRUE, return only the omnibus p-values; if FALSE, return a matrix with D-INT, I-INT, and OINT p-values.

Value

If `simple = TRUE`, a named numeric vector of omnibus p-values (one per column of `G`). If `simple = FALSE`, a numeric matrix with columns DINT-p, IINT-p, OINT-p and one row per SNP.

See Also

- Basic association test [BAT](#).
- Direct INT test [DINT](#).
- Indirect INT test [IINT](#).

Examples

```
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 = TRUE)
```

OmniP	<i>Omnibus P-value (Cauchy combination)</i>
-------	---

Description

Combines a vector of potentially dependent p-values into a single p-value using the Cauchy combination method: p-values are converted to Cauchy random deviates, then weighted and summed; the sum is again Cauchy, and is converted back to a p-value.

Usage

```
OmniP(p, w = NULL)
```

Arguments

p	Numeric vector of p-values (each in [0, 1]; cannot mix 0 and 1).
w	Optional numeric weight vector of the same length as p. If NULL, equal weights are used.

Value

A single numeric p-value.

References

Liu Y, Xie J (2020). Cauchy combination test: a powerful test with bimodal distributions. *J Am Stat Assoc*, doi:[10.1080/01621459.2018.1554485](https://doi.org/10.1080/01621459.2018.1554485).

See Also

[OINT](#), which uses OmniP to combine D-INT and I-INT p-values.

 PartitionData

Partition Data

Description

Partition y and X according to the missingness pattern of g.

Usage

```
PartitionData(e, g, X)
```

Arguments

e	Numeric residual vector.
g	Genotype vector.
X	Model matrix of covariates.

Value

List containing:

- "g_obs", observed genotype vector.
- "X_obs", covariates for subjects with observed genotypes.
- "X_mis", covariates for subjects with missing genotypes.
- "e_obs", residuals for subjects with observed genotypes.

PtoCauchy	<i>Convert P-value to Cauchy Random</i>
-----------	---

Description

Convert P-value to Cauchy Random

Usage

PtoCauchy(p)

Arguments

p	Numeric p-value.
---	------------------

Value

Numeric Cauchy random variable.

RankNorm	<i>Rank-Normalize</i>
----------	-----------------------

Description

Applies the rank-based inverse normal transform (INT) to a numeric vector. Observations are first mapped to the (0, 1) scale via the empirical cumulative distribution function (ECDF), then to the real line via the probit (inverse normal CDF).

Usage

RankNorm(u, k = 0.375, ties.method = "average")

Arguments

u	Numeric vector. Must not contain NA.
k	Offset in the probability scale; must be in (0, 0.5). Default 0.375 corresponds to the Blom transform.
ties.method	Method for breaking ties, passed to rank .

Value

Numeric vector of rank-normalized values (same length as u).

See Also

- Direct INT test [DINT](#).
- Indirect INT test [IINT](#).
- Omnibus INT test [OINT](#).

Examples

```
# Draw from chi-1 distribution
y <- stats::rchisq(n = 1e3, df = 1)
# Rank normalize
z <- RankNorm(y)
# Plot density of transformed measurement
plot(stats::density(z))
```

Index

BasicInputChecks, [3](#)

BAT, [2](#), [3](#), [4](#), [6](#), [8](#), [9](#)

CauchyToP, [5](#)

DINT, [2–4](#), [5](#), [8](#), [9](#), [12](#)

FitOLS, [2](#), [6](#)

IINT, [2–4](#), [6](#), [7](#), [8](#), [9](#), [12](#)

OINT, [2–4](#), [6](#), [8](#), [8](#), [10](#), [12](#)

OmniP, [2](#), [3](#), [9](#)

PartitionData, [10](#)

PtoCauchy, [11](#)

rank, [6](#), [7](#), [11](#)

RankNorm, [2](#), [3](#), [5–7](#), [9](#), [11](#)

RNOmni (RNOmni-package), [2](#)

RNOmni-package, [2](#)