

Package ‘pleio’

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Type Package

Title Pleiotropy Test for Multiple Traits on a Genetic Marker

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Description Perform tests for pleiotropy of multiple traits on genotypes for a genetic marker.

License GPL (>= 2)

Depends R (>= 3.2.0), Matrix, stats, utils

Suggests R.rsp

VignetteBuilder R.rsp

NeedsCompilation no

Repository CRAN

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pleio.q.fit

Compute Intermediate Statistics for Testing Pleiotropy

Description

Pre-compute statistics for testing pleiotropy, to be used in pleio.q.test and pleio.q.sequential

Usage

```
pleio.q.fit(y, geno)
```

Arguments

y	matrix of multiple quantitative traits to test for pleiotropy on genotype vector. Rows are for subjects and columns are for traits.
geno	vector of genotypes coded as dosage of a minor allele, 0,1,2.

Details

The matrix y of traits is expected to have rows for subjects and columns for traits. The number of rows of y should match the length of vector geno. This function computes intermediate statistics that are subsequently used to test various hypotheses about pleiotropy. For technical details, Schaid et al. (Genetics, 2016)

Value

A list containing

x	the de-correlated genotype design matrix
xx.inv	inverse of $x'x$
beta.ols	estimated unconstrained beta coefficients for y traits based on ordinary least squares
n.traits	number of traits (columns) in y

Author(s)

Dan Schaid, Jason Sinnwell.

References

Schaid DJ, Tong X, Larrabee B, Kennedy RB, Poland GA, Sinnwell JP. Statistical Methods for Testing Genetic Pleiotropy. To appear in Genetics, 2016.

pleio.q.sequential *Perform sequential tests of pleiotropy*

Description

Perform sequential tests of pleiotropy to determine the number of traits, and which traits, are associated with a vector of genotypes.

Usage

```
pleio.q.sequential(obj.fit, pval.threshold)
```

Arguments

obj.fit	result of pleio.q.fit
pval.threshold	p-value for rejecting the null hypothesis of the specified number of non-zero beta's.

Details

Perform sequential tests of pleiotropy, starting at the usual multivariate null hypothesis that all beta's = 0. If this test rejects because the p-value < pval.threshold, then allow one beta to be non-zero in order to test whether the remaining beta's = 0. If the test of one non-zero beta rejects, then allow two non-zero beta's, and continue this sequential testing until the p-value for a test is greater than the specified pval.threshold.

Value

A list containing:

pval	p-value of the final test from the sequential testing
index.beta	index of trait(s) in y that have non-zero beta's. These indices indicate which traits are associated with the genotype, accounting for the correlations among the traits.

Author(s)

Dan Schaid and Jason Sinnwell

References

Schaid DJ, Tong X, Larrabee B, Kennedy RB, Poland GA, Sinnwell JP. Statistical Methods for Testing Genetic Pleiotropy. To appear in *Genetics*, 2016.

Examples

```
data(pleio.qsim)
fit <- pleio.q.fit(y, geno)
test.seq <- pleio.q.sequential(fit, pval.threshold=.05)
test.seq
```

pleio.q.test

Single tests of the number of traits associated with genotype

Description

Perform single test of the number of traits associated with a genotype, by allowing a specified number of regression beta's to be unconstrained.

Usage

```
pleio.q.test(obj.fit, count.nonzero.beta = 0)
```

Arguments

`obj.fit` result of `pleio.q.fit`
`count.nonzero.beta` Number of non-zero betas. A non-zero beta is allowed to be unconstrained, while all other beta's are constrained to be zero.

Details

By specifying the number of non-zero beta's, the algorithm evaluates all possible ways of choosing unconstrained and constrained beta's, and for each configuration a statistic (tk) is computed. This tk statistic can be considered a measure of fit of a model. The minimum tk over all possible configurations provides a global test of whether one of the models fits well.

Value

A list containing:

`stat` global test statistic
`df` degrees of freedom of the statistic
`pval` p-value for the test
`index.nonzero.beta` index of the non-zero beta(s) that provide the minimum tk goodness of fit statistic - this configuration is assumed to have beta's for all other indices equal to zero.
`tests` data.frame containing the tests performed. For m traits, and $k=count.nonzero.beta$, there are m -choose- k tests considered in the null hypothesis. The data.frame provides the indices of the unconstrained beta's and the corresponding tk test statistic for the configuration.

Author(s)

Dan Schaid and Jason Sinnwell

References

Schaid DJ, Tong X, Larrabee B, Kennedy RB, Poland GA, Sinnwell JP. Statistical Methods for Testing Genetic Pleiotropy. To appear in *Genetics*, 2016.

Examples

```
data(pleio.qsim)
fit <- pleio.q.fit(y, geno)
## usual multivariate test of whether all beta's = 0
test0 <- pleio.q.test(fit, count.nonzero.beta = 0)
test0
## test whether allowing 2 beta's to be non-zero fits data
test2 <- pleio.q.test(fit, count.nonzero.beta = 2)
test2
```

pleio.qsim

Simulated dataset for quantitative pleiotropy tests

Description

A simulated dataset with 6 y variables simulated from multivariate normal distribution with common correlation structure, correlation of 0.5, and genotypes simulated based on minor allele frequency of 0.2, and assume that betas for traits 2 and 3 have non-zero values, while all other traits are not associated with dose of minor allele.

Usage

```
data("pleio.qsim")
```

Format

y is a data.frame with 500 observations and 6 quantitative traits, t1-t6, while geno is a single SNP of dosage of a minor allele, simulated from frequency of 0.2.

Examples

```
data(pleio.qsim)
str(y)
table(geno)
```

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