Package 'segregatr'

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Title Segregation Analysis for Variant Interpretation

Version 0.3.0

Description An implementation of the full-likelihood Bayes factor (FLB) for evaluating segregation evidence in clinical medical genetics. The method was introduced by Thompson et al. (2003) <doi:10.1086/378100>, and further popularised by Bayrak-Toydemir et al. (2008) <doi:10.1016/j.yexmp.2008.03.006>. This implementation allows custom penetrance values and liability classes, and includes specialised pedigree visualisations.

License GPL-3

URL https://github.com/magnusdv/segregatr

BugReports https://github.com/magnusdv/segregatr/issues

Encoding UTF-8

Language en-GB

Depends pedtools (>= 2.2.0), R (>= 4.1.0)

Imports pedprobr

Suggests testthat

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NeedsCompilation no

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R topics documented:

FLB *Full-likelihood Bayes factor*

Description

Computes the Bayes factor for co-segregation, as originally described by Thompson et al. (2003).

Usage

```
FLB(
  x,
  carriers = NULL,
  homozygous = NULL,
  noncarriers = NULL,
  freq = NULL,
  affected = NULL,
  unknown = NULL,
  proband = NULL,
  penetrances = NULL,
  liability = NULL,
  loopBreakers = NULL,
  Xchrom = FALSE,
  details = FALSE,
  plot = FALSE,
  ...
)
```

Arguments

x	A pedtools::ped() object.
carriers	A character vector (or coercible to such), containing the ID labels of pedigree members known to carry one copy of the variant in question.
homozygous	A character vector (or coercible to such), containing the ID labels of pedigree members known to carry two copies of the variant in question.
noncarriers	A character vector (or coercible to such), containing the ID labels of pedigree members known *not* to carry the variant in question.
freq	A single number strictly between 0 and 1: the population frequency of the observed allele.
affected	The affected pedigree members.
unknown	Pedigree members with unknown affection status.
proband	The ID label of the proband. This person must also be in both carriers and affected.

penetrances	For autosomal models, a numeric vector of length 3 (f0, f1, f2), or a matrix-like with 3 columns, where row i contains the penetrances of liability class i. For X-linked models, a list of two vectors named "male" and "female", of lengths 2 (f0, f1) and 3 (f0, f1, f2) respectively. Alternatively, each list entry may be matrix-like (with the same number of columns) where each row represents a liability class.
liability	A vector of length pedsize(x), containing for each pedigree member the row number of penetrances which should be used for that individual. (If penetrances is just a vector (or one for each sex in X-linked models), it will be used for all classes.) If liability is NULL (the default), it is set to 1 for all individuals.
loopBreakers	(Relevant only if x has loops.) A vector of ID labels indicating loop breakers. The default value (NULL) initiates automatic loop breaking, which is recommended in most cases.
Xchrom	A logical, indicating if a model of X-linked inheritance should be applied.
details	A logical, indicating if detailed output should be returned (for debugging purposes).
plot	A logical.
...	Optional plot parameters passed on to pedtools::plot.ped().

Value

A positive number, the FLB score. If details = TRUE, a list including intermediate results.

References

Thompson D, Easton DF, Goldgar DE. *A full-likelihood method for the evaluation of causality of sequence variants from family data.* Am J Hum Genet, 2003. doi:10.1086/378100.

Examples

```
### Autosomal dominant

x = nuclearPed(2)

FLB(x, carriers = 3:4, aff = 3:4, unknown = 1:2,
    freq = 0.0001, penetrances = c(0, 1, 1), proband = 3)


### Autosomal recessive with phenocopies and reduced penetrance

y = nuclearPed(4)

FLB(y, carriers = 4:5, homozygous = 3, noncarriers = 6,
    aff = 3, unknown = 1:2, freq = 0.0001, proband = 3,
    penetrances = c(0.01, 0.01, 0.99), plot = TRUE)


### X-linked recessive
```

```
z = nuclearPed(3, sex = c(1, 1, 2)) |>
  addChildren(mother = 5, nch = 2, sex = 1:2)

FLB(z, carriers = c(3, 7), nonc = 4, aff = c(3, 7), unknown = 1:2,
    freq = 0.0001, penetrances = list(male = c(0, 1), female = c(0, 0, 1)),
    proband = 7, Xchrom = TRUE, plot = TRUE)
```

`plotSegregation` *Pedigree plot for segregation analysis*

Description

Plots a pedigree showing the segregation of a variant.

Usage

```
plotSegregation(
  x,
  affected = NULL,
  unknown = NULL,
  proband = NULL,
  carriers = NULL,
  homozygous = NULL,
  noncarriers = NULL,
  cex = 1,
  margins = 1,
  pos.geno = "bottom",
  pos.arrow = "bottomleft",
  ...
)
```

Arguments

`x`	A `pedtools::ped()` object.
`affected`	The affected pedigree members.
`unknown`	Pedigree members with unknown affection status.
`proband`	The ID label of the proband. This person must also be in both `carriers` and `affected`.
`carriers`	A character vector (or coercible to such), containing the ID labels of pedigree members known to carry one copy of the variant in question.
`homozygous`	A character vector (or coercible to such), containing the ID labels of pedigree members known to carry two copies of the variant in question.
`noncarriers`	A character vector (or coercible to such), containing the ID labels of pedigree members known *not* to carry the variant in question.

`cex, margins`	Arguments passed on to `pedtools::plot.ped()`.
`pos.geno`	Position of genotype labels relative to pedigree symbols; either "bottom" (default), "topleft" or "topright".
`pos.arrow`	Position of the proband arrow; either "bottomleft", "bottomright", "topleft" or "topright".
`...`	Optional plot parameters passed on to `pedtools::plot.ped()`.

Examples

```
x = nuclearPed(2)
plotSegregation(x, proband = 3, carriers = 3:4, noncarriers = 1,
                aff = 3:4, unknown = 1:2)

# Same with various options
plotSegregation(x, proband = 3, carriers = 3:4, noncarriers = 1,
                aff = 3:4, unknown = 1:2,
                pos.geno = "topright", pos.arrow = "topleft",
                labs = NULL, title = "Family 1", cex.main = 1.5)

# Recessive example
y = cousinPed(1, child = TRUE)
plotSegregation(y, affected = 9, unknown = 1:6, carrier = 7:8,
                homozygous = 9, noncarriers = c(4,6), proband = 9)

# Different symbol placements
plotSegregation(y, affected = 9, unknown = 1:6, carrier = 7:8,
                homozygous = 9, noncarriers = c(4,6), proband = 9,
                pos.geno = "topleft", pos.arrow = "bottomright")

# Incest case
y = nuclearPed() |> addChildren(father = 3, mother = 2, nch = 3)

plotSegregation(y, proband = 4, aff = 4:6, unknown = 2, carrier = 4:6, deceased = 1,
                pos.geno = "topleft", pos.arrow = "bottomright")
```

`segregatr` *segregatr: Segregation Analysis for Identifying Pathogenic Variants*

Description

An implementation of the full-likelihood Bayes factor (FLB) for evaluating segregation evidence in clinical medical genetics. The method was introduced by Thompson et al. (2003), and further popularised by Bayrak-Toydemir et al. (2008). This implementation allows custom penetrance values and liability classes, and includes specialised pedigree visualisations.

References

Thompson D, Easton DF, Goldgar DE. *A full-likelihood method for the evaluation of causality of sequence variants from family data.* Am J Hum Genet, 2003. doi:10.1086/378100.

Bayrak-Toydemir et al. *Likelihood ratios to assess genetic evidence for clinical significance of uncertain variants: Hereditary hemorrhagic telangiectasia as a model.* Exp Mol Pathol, 2008. doi:10.1016/j.yexmp.2008.03.006.

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