Package 'ASPBay'

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Type Package

Title Bayesian Inference on Causal Genetic Variants using Affected Sib-Pairs Data

Depends hexbin, Rcpp

LinkingTo Rcpp, RcppArmadillo

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Description This package allows to make inference on the properties of causal genetic variants in linkage disequilibrium with genotyped markers. In a first step, we select a subset of variants using a score statistic for affected sib-pairs. In a second step, on the selected subset, we make inference on causal genetic variants in the considered region.

License GPL-2

NeedsCompilation yes

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R topics documented:

ASPBay-package *Bayesian method with affected sib pairs*

Description

This package permits to select in a genomic region a subset of SNPs which is likely to contain the true causal SNPs or a SNPs which tag them. Then, we exploite the linkage information contained in affected sib-pairs data to make inference on the causal SNPs in the region using Bayesian method.

Author(s)

Claire Dandine-Roulland

References

Perdry, Herve, Muller-Myhsok, Bertram, et Clerget-Darpoux, Francoise. *Using affected sib-pairs to uncover rare disease variants.* Hum Hered, 2013.

Dandine-Roulland, Claire and Perdry, Herve. *Where is the causal variant? On the advantage of the family design over the case-control design in genetic association studies.* Submitted to Eur J Hum Genet

ASP.Bayesian *Samples in the posterior distribution of the frequencies and OR*

Description

Samples using Metropolis-Hasting Algorithm in the posterior distribution of the four haplotype frequencies and OR

Usage

```
ASP.Bayesian(N, Tem_Gen, Index_Gen, IBD, snp, thin = 1, sd.freq = 0.05,
                    sd.psi = 0.05, p0 = c(rep(1/4, 4), 1), psi.prior = 0)
```

Arguments

N	Number of Metropolis-Hastings iterations
Tem_Gen	Genotypes of controls (denoted by the number of alternative allele)
Index_Gen	Genotypes of index cases
IBD	IBD states for each affected sib-pair
snp	Names or number column of the SNP to consider
thin	Thinning parameter (keep only every thin-th draw)
sd.freq	Random walk standard deviation of the frequency logarithms
sd.psi	Random walk standard deviation of the OR
p0	The initial point of random walk
psi.prior	Precision of gaussian log(OR) prior (0 = improper flat prior)

Details

Samples using Metropolis-Hasting and likelihood defined by data. More precisely, give the frequency samples of haplotypes for observed SNP and unobserved causal SNP and give the sample of the odds ratio associated to the causal SNP.

Value

List of 5 vectors of length `N/thin` with components:

`f_ab`	Sample of the haplotype composed by the two alternative alleles
`f_Ab`	Sample of the haplotype composed by the reference allele for the causal (unobserved) locus and the alternative alleles for the observed locus
`f_aB`	Sample of the haplotype composed by the alternative allele for the causal (unobserved) locus and the reference alleles for the observed locus
`f_AB`	Sample of the haplotype composed by the two reference alleles
`OR`	Sample of the OR

Author(s)

Claire Dandine-Roulland

References

Dandine-Roulland, Claire and Perdry, Herve. *Where is the causal variant? On the advantage of the family design over the case-control design in genetic association studies.* Submitted to Eur J Hum Genet

See Also

`ASP.Selection`, `Graphs.Bayesian`

Examples

```
data(ASPData)
B <- ASP.Bayesian(1e5, ASPData$Control, ASPData$Index,
                  ASPData$IBD, 15 )
```

ASP.Score *Score test of association*

Description

Calculate score statistics and the associated P-value for each SNPs

Usage

```
ASP.Score(Tem_Gen, Index_Gen, IBD)
```

Arguments

Tem_Gen	Genotypes of controls (denoted by the number of alternative allele)
Index_Gen	Genotypes of Index cases
IBD	IBD states for each affected sib pair

Details

Give the values of statistic and p-value of the association score test.

Value

List of 2 vectors of length the number of SNPs:

Value	Statistic values for each SNPs
Pvalue	P-values of the score test for each SNPs

Author(s)

Claire Dandine-Roulland

References

Perdry, Herve, Muller-Myhsok, Bertram, et Clerget-Darpoux, Francoise. *Using affected sib-pairs to uncover rare disease variants.* Hum Hered, 2013.

See Also

ASP.Selection

Examples

```
data(ASPData)
ASP.Score(ASPData$Control, ASPData$Index, ASPData$IBD )
```

ASP.Selection *Select a subset of SNPs*

Description

Select a subset of SNPs using discrimination method for affected sib pairs

Usage

```
ASP.Selection(Tem_Gen, Index_Gen, IBD, k = log(10000))
```

Arguments

Tem_Gen	Genotypes of controls (denoted by the number of alternative allele)
Index_Gen	Genotypes of index cases
IBD	IBD states for each affected sib pair
k	Selection threshold (by default log(1e4))

Details

Take the genotypes of controls and index cases and the IBD states. Give the score statistics, discrimination statistics and the subset of selected SNPs with the chosen threshold.

Value

List of 4 vectors with components:

score	The values of the score statistic for each SNPs
stat	The values of discrimination statistic comparing each SNPs with the most associated SNP
SNP_subset	The indexes (numbers of columns) of selected SNPs
SNPname_subset	The names (names of columns) of selected SNPs

Author(s)

Claire Dandine-Roulland

References

Dandine-Roulland, Claire and Perdry, Herve. *Where is the causal variant? On the advantage of the family design over the case-control design in genetic association studies.* Submitted to Eur J Hum Genet

See Also

ASP.Score, ASP.Bayesian

Examples

```
data(ASPData)
ASP.Selection(ASPData$Control, ASPData$Index, ASPData$IBD )
```

ASPData *Simulated dataset*

Description

Simulations of 1000 controls and 1000 affected sib pairs with 22 SNPs. There is one causal SNP with an OR of 2.

Usage

```
data(ASPData)
```

Format

A list with the following elements.

`Control` 21 genotypes of controls no including causal SNP

`Index` 21 genotypes of index cases no including causal SNP

`IBD` Vector of IBD states for each affected sib pairs

`Causal` The name of the causal SNP

Details

See `vignette("ASPBay")`.

Examples

```
data(ASPData)
```

Graphs.Bayesian *Graphs*

Description

Plot graphs to visualize the results of `ASP.Bayesian`

Usage

```
Graphs.Bayesian(M, burn=0, xbins=200, ORlim=c(1,5),
        conf.int=c(0.2,0.3,0.4,0.5,0.6,0.7,0.8,0.9,0.95), print=TRUE)
```

Arguments

M	Object given by the function ASP.Bayesian
burn	The first burn values of the sampling are removed
xbins	The number of bins which partition the range of graph variables
ORlim	OR limits in graphs
conf.int	Chosen credibility intervals
print	Logical, if TRUE the plots are printed

Details

Plot two graphs and give associated hexbinplot objects. This two graphs summarize the results of the Bayesian method. The first graph shows the linkage disequilibrium between observed and causal SNPs in abscissae and the OR of causal SNP in ordinates. The second graph displays the alternative allele frequency of causal SNP in abscissae and the alternative allele frequency of observed SNP in ordinates. Before plotting the graphs, the causal odds ratio is transformed. The value of OR is kept if it is superior to 1, otherwise it is inversed. The alternative causal allele frequency is transformes accordingly: if the OR is inferior to 1, the frequency is replaced by its complement to 1. With this transformations, we avoid to obtain two peaks corresponding to equivalent parameter values.

Value

List of 2 hexbin objects:

hex_r2_OR	Hexbinplot object with the linkage disequilibrium between observed and causal SNPs in abscissae and the OR of causal SNP in ordinates.
hex_fa_fb	Hexbinplot object with the alternative allele frequency of causal SNP in abscissae and the alternative allele frequency of observed SNP in ordinates.

Author(s)

Claire Dandine-Roulland

References

Dandine-Roulland, Claire and Perdry, Herve. *Where is the causal variant? On the advantage of the family design over the case-control design in genetic association studies.* Submitted to Eur J Hum Genet

See Also

ASP.Bayesian

Examples

```
data(ASPData)
B <- ASP.Bayesian(1e5, ASPData$Control, ASPData$Index,
                  ASPData$IBD, 15)
G <- Graphs.Bayesian(B, burn = 5000, xbins=100)
```

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