Package ‘RVsharing’

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Description Computes estimates of the probability of related individuals sharing a rare variant.
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ComputeKinshipPropCoef-method

Description

Computes, for each pair of final descendants in the pedigree structure contained in the pedigree object, the ratio of the difference between the inferred and expected kinship coefficient for the pair over the mean kinship among founders.

Usage

```r
## S4 method for signature 'RVsharingProb'
ComputeKinshipPropCoef(obj)
```

Arguments

- `obj`  
  obj is a RVsharingProb object returned by the function RVsharing

Details

The ratio for each pair of final descendants is computed using equation (A1) of Bureau et al. Dividing the difference between the inferred and expected kinship coefficient for each pair by this ratio gives a pair-specific estimate of the mean kinship among founders, which can then be averaged over all pairs of final descendants from the same population to obtain a global estimate of the mean kinship among founders.

Value

A symmetric matrix of ratios for all pair of final descendants in the pedigree structure contained in the pedigree object.

Author(s)

Alexandre Bureau <alexandre.bureau@msp.ulaval.ca>

References

GeneDrop-method

See Also

pedigree

Examples

data(ped.list)
plot(ped.list[[1]])
obj = RVsharing(ped.list[[1]])
ComputeKinshipPropCoeff(obj)

Description

Simulate transmission of alleles from the parents to their offspring according to Mendel's laws.

Usage

## S4 method for signature 'Trio, numeric'
GeneDrop(trio, geno.vec)

Arguments

trio A Trio object.

geno.vec A named genotype vector.

Details

Simulate transmission of alleles from the parents to their offspring in a trio object according to Mendel's laws.

Value

A numeric genotype vector.

Author(s)

Samuel G. Younkin <syounkin@stat.wisc.edu>
**GeneDropSim.fn**

*Estimation of the probability of sharing of a rare variant by gene dropping in a pedigree*

**Description**

Estimates the probability that all subjects in a subset of pedigree members share a rare variant given that it occurred in any of them by performing a Monte Carlo simulation of the transmission of the genotypes of the variant from the founders down the pedigree.

**Usage**

GeneDropSim.fn(trio.list, id, dt.vec, fd.indices, n = 1e3, k = 10, nf = 1)

**Arguments**

- **trio.list**: a list of trio objects encoding the pedigree structure.
- **id**: a vector of identifiers of the pedigree members.
- **dt.vec**: a vector of identifiers of the subset of pedigree members for which to estimate the sharing probability. Must be a subset of the id vector.
- **fd.indices**: a vector of the indices of the founders of the pedigree.
- **n**: minimal number of gene dropping replicates where the rare variant occurs in at least one member of dt.vec.
- **k**: this number times n gives the maximal number of gene dropping replicates.
- **nf**: number of founders introducing the rare variant into the pedigree.

**Details**

The transmission of the RV down the pedigree from the nf founders introducing it is simulated according to Mendel’s laws. The events that the variant was observed in any of the subjects from dt.vec and in all of them are then recorded. The simulation continues until the number of replicates where the RV was observed in any of the subjects from dt.vec reaches n or the number of replicates reaches k n. The RV sharing probability is then estimated as the number of replicates where the RV was observed in all subjects from dt.vec over n (or the number of replicates where the RV was observed in any of the subjects when k n replicates are reached).

**Value**

Estimate of the probability that all subjects in a subset of pedigree members share a rare variant given that it occurred in any of them

**Author(s)**

Samuel G. Younkin <syounkin@stat.wisc.edu> and Alexandre Bureau <alexandre.bureau@msp.ulaval.ca>
References

See Also
ped2trio, GeneDropSimExcessSharing.fn

Examples

```r
data(ped.list)
plot(ped.list[[54]])
trio.obj = ped2trio(ped.list[[54]])

GeneDropSim(fn( trio.list = trio.obj$object, id=ped.list[[54]]$id, dt.vec = c("40","47"), fd.indices = trio.obj$fd.indices, n = 5e3)

# Result should be very close to exact value
RVsharing(ped.list[[54]]))
```

GeneDropSimExcessSharing.fn

Estimation of the probability of sharing of a rare variant by gene dropping in a pedigree

Description
Estimates the probability that all subjects in a subset of pedigree members share a rare variant (RV) given that it occurred in any of them by performing a Monte Carlo simulation of the transmission of the genotypes of the variant from the founders down the pedigree.

Usage

```
GeneDropSimExcessSharing.fn(trio.list, id, dt.vec, fd.indices, phihat, RVfreq, ord=5, n = 1e3, k = 10)
```

Arguments

- `trio.list`: a list of trio objects encoding the pedigree structure.
- `id`: a vector of identifiers of the pedigree members.
- `dt.vec`: a vector of identifiers of the subset of pedigree members for which to estimate the sharing probability. Must be a subset of the `id` vector.
- `fd.indices`: a vector of the indices of the founders of the pedigree.
- `phihat`: a vector of values of the mean kinship coefficient between founders. Must be non-negative.
**RVfreq**

frequency of the variant in the population (optional). When missing, the variant frequency tends to 0.

**ord**

order of the polynomial approximation of the number of distinct alleles among pedigree founders.

**n**

minimal number of gene dropping replicates where the rare variant occurs in at least one member of `dt.vec`.

**k**

this number times `n` gives the maximal number of gene dropping replicates.

### Details

The function performs the following steps. It first determines the probability `w` that the RV was introduced only once in the pedigree and its complement `1-w` that it was introduced twice based on the mean kinship among founders `phi.hat`. It then samples an indicator variable of whether one or two copies of the RV were introduced into the family with probability `w` and `1-w` respectively. In practice, this is done by sampling the number of distinct alleles `a` from an approximate distribution derived from `phi.hat`, then sampling the RV among the `$a$` alleles. The RV is introduced twice if it is one of the first `$2n_f - a$` alleles, and introduced once otherwise. If it is introduced twice, the pair of founders introducing the RV is sampled with equal probability for all pairs. If it is introduced once, the sole founder introducing it is sampled instead. Then the transmission of the RV down the pedigree from the one or two founders introducing it is simulated according to Mendel’s laws. The events that the variant was observed in any of the subjects from `dt.vec` and in all of them are then recorded. The simulation continues until the number of replicates where the RV was observed in any of the subjects from `dt.vec` reaches `n` or the number of replicates reaches `k` times `n`. The RV sharing probability is then estimated as the number of replicates where the RV was observed in all subjects from `dt.vec` over `n` (or the number of replicates where the RV was observed in any of the subjects when `k` times `n` replicates are reached).

### Value

Estimate of the probability that all subjects in a subset of pedigree members share a rare variant given that it occurred in any of them

### Author(s)

Samuel G. Younkin <syounkin@stat.wisc.edu> and Alexandre Bureau <alexandre.bureau@msp.ulaval.ca>

### References


### See Also

`ped2trio`, `GeneDropSim.fn`
Examples

data(ped.list)
plot(ped.list[[54]])
trio.obj = ped2trio(ped.list[[54]])

GeneDropSimExcessSharing.fn(trio.list = trio.obj$object, id = ped.list[[54]]$id,
dt.vec = c("40","47"), fd.indices = trio.obj$fd.indices, phiHat=0.005,RVfreq=0.01,
ord=5, n = 2e3)

# Result should be higher than exact value under the assumption of a variant frequency
# tending to 0 and no unknown relationship among founders
RVsharing(ped.list[[54]])

Description

List of example pedigree objects

Usage

ped.list
data(ped.list)
plot(ped.list)

Conversion of a pedigree object into a list of trio objects

Description

Creates trio objects representing the pedigree structure contained in the pedigree object.

Usage

ped2trio(ped)

Arguments

ped a pedigree object

Details

The function processes the pedigree from the bottom generation to the top, adding new trio objects for each non-founder in a generation, with in their offspring list the trio objects associated to their children. At the top generation, there are as many trio objects as the number of founder couples, and these are returned as a list of trio objects. For now, only founders are allowed to have more than one spouse, non-founders can only have one spouse.
Value

object list of Trio objects, one list for each founder couple of the pedigree
fd.indices Vector of the IDs of the founders of the pedigree

Author(s)

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See Also

pedigree, Trio

Examples

data(ped.list)
ped.trio1 = ped2trio(ped.list[[1]])

RVsharing Probability of sharing a rare variant among relatives

Description

Computing probability that a rare variant is shared by a set of subjects in a pedigree using equation (1) of Bureau et al.

Usage

RVsharing(data, dad.id, mom.id)

Arguments

data a pedigree object or character/numeric vector of subject IDs.
dad.id if data is a vector, character or numeric vector of father IDs. Founders’ parents should be coded to NA or 0.
mom.id if data is a vector, character or numeric vector of mother IDs. Founders’ parents should be coded to NA or 0.

Details

The function RV sharing computes the probability that all final descendants in the pedigree share a rare variant given that a rare variant has been detected in any one of these final descendants. For now, there can only be one lineage of branching individuals (intermediate ancestors) with more than one child each. Multiple marriages can only involve one of the top founders. Branching individuals can have only one spouse. All final descendants must share a common ancestor or couple of ancestors, otherwise an erroneous response may be obtained.

The function recursively processes branching individuals (intermediate ancestors) from the lowest one in the pedigree to the one who is a top founder, applying the formulas in Bureau et al. to
compute the terms of $P[C_1 = \ldots = C_n = 1]$ and $P[C_1 = \ldots = C_n = 0]$ involving each branching individual.

Value

An object of class RVsharingProb

Author(s)

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References


See Also

pedigree, RVsharingProb, GeneDropSim.fn, GeneDropSimExcessSharing.fn

Examples

data(ped.list)
plot(ped.list[[1]])
RVsharing(ped.list[[1]])

RVsharingProb-class  RVsharingProb Class

Description

An object created by RVsharing

Arguments

- **p.share**  probability that all final descendants in the pedigree share a rare variant given that a rare variant has been detected in any one of these final descendants.
- **ancestors**  Character vector of the IDs of branching individuals (intermediate ancestors): subjects who are ancestors to final descendants through two or more of their children and have ancestors above them in the pedigree. The only exception is that one of the top founders is designated as the last branching individual.
- **desfounders**  List of vectors. Each final descendant has a vector in the list containing the distances to the founders above him.
- **id**  Character vector of subject IDs.
- **dad.id**  Character vector of father IDs for the subjects in `id`.
- **mom.id**  Character vector of mother IDs for the subjects in `id`. 
Trio-class

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Trio-class
Trio Class

Description
An object containing a character subject identifier ID, a character identifier of his/her spouse and a list of their offspring.

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