Package 'paramlink'

July 21, 2025

Title Parametric Linkage and Other Pedigree Analysis in R

Version 1.1-6

Maintainer Magnus Dehli Vigeland <m.d.vigeland@medisin.uio.no>

Description NOTE: 'PARAMLINK' HAS BEEN SUPERSEDED BY THE 'PEDSUITE' PACKAGES (https://magnusdv.github.io/pedsuite/). 'PARAMLINK' IS

MAINTAINED ONLY FOR LEGACY PURPOSES AND SHOULD NOT BE USED IN NEW

PROJECTS. A suite of tools for analysing pedigrees with marker data, including parametric linkage analysis, forensic computations, relatedness analysis and marker simulations. The core of the package is an implementation of the Elston-Stewart algorithm for pedigree likelihoods, extended to allow mutations as well as complex inbreeding. Features for linkage analysis include singlepoint LOD scores, power analysis, and multipoint analysis (the latter through a wrapper to the 'MERLIN' software). Forensic applications include exclusion probabilities, genotype distributions and conditional simulations. Data from the 'Familias' software can be imported and analysed in 'paramlink'. Finally, 'paramlink' offers many utility functions for creating, manipulating and plotting pedigrees with or without marker data (the actual plotting is done by the 'kinship2' package).

License GPL (>= 2)

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

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

Depends R (>= 3.3)

Imports assertthat, graphics, kinship2, maxLik, stats, utils

Suggests igraph
Encoding UTF-8
Language en-GB
LazyData Yes

RoxygenNote 7.3.2

SystemRequirements For multipoint linkage analysis, 'MERLIN' (http://csg.sph.umich.edu/abecasis/merlin/index.html).

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NeedsCompilation no

Author Magnus Dehli Vigeland [aut, cre], Thore Egeland [ctb], Guro Doerum [ctb]

Repository CRAN

Date/Publication 2025-07-21 20:21:05 UTC

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allGenotypes

Genotype combinations

Description

Auxiliary functions computing possible genotype combinations in a pedigree. These are not normally intended for end users.

Usage

```
allGenotypes(n)
fast.grid(argslist, as.list = FALSE)
geno.grid.subset(x, partialmarker, ids, chrom, make.grid = T)
```

Arguments

a positive integer. argslist a list of vectors. as.list

if TRUE, the output is a list, otherwise a matrix.

a linkdat object.

partialmarker a marker object compatible with x.

ids a numeric with ID labels of one or more pedigree members.

chrom a character, either 'X' or 'AUTOSOMAL'. If missing, the 'chrom' attribute of

partialmarker is used. If this is also missing, then 'AUTOSOMAL' is taken

as the default value.

a logical. If FALSE, a list is returned, otherwise fast.grid is applied to the list make.grid

before returning it.

Value

allGenotypes returns a matrix with 2 columns and n + n*n(n-1)/2 rows containing all possible (unordered) genotypes at a biallelic locus with alleles 1,2,...{},n. fast.grid is basically a stripped down version of expand.grid.

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Examples

```
m = allGenotypes(2)
stopifnot(m == rbind(c(1,1), c(2,2), 1:2))
```

```
as.data.frame.linkdat linkdat to data.frame conversion
```

Description

Convert a linkdat object to data.frame for pretty printing.

Usage

```
## S3 method for class 'linkdat'
as.data.frame(
    x,
    ...,
    famid = F,
    markers = seq_len(x$nMark),
    alleles = NULL,
    missing = NULL,
    singleCol = FALSE,
    sep = ""
)
```

Arguments

x	a linkdat object.
	further arguments (not used).
famid	a logical indicating if the family identifier should be included as the first column.
markers	a numeric indicating which markers should be included/printed.
alleles	a character containing allele names, e.g. alleles=c('A', 'B').
missing	the character (of length 1) used for missing alleles. Defaults to '0'.
singleCol	a logical: Should the two alleles for each marker be pasted into one column or kept in separate columns?
sep	a single character to be used as allele separator if singleCol=TRUE.

Details

This function is mainly intended for pretty-printing linkdat objects (for instance it is called by print.linkdat). For direct manipulation of the pedigree and/or marker matrices, it is better to use as.matrix.linkdat.

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Value

```
A data.frame.
```

See Also

```
as.matrix.linkdat
```

Examples

```
x = linkdat(toyped)
x

# Printing x as above is equivalent to:
as.data.frame(x, sep = '/', missing = '-', singleCol = TRUE)
```

as.matrix.linkdat

linkdat to matrix conversion

Description

Converts a linkdat object to a matrix (basically following a pre-makeped LINKAGE format), with marker annotations and other info attached as attributes.

Usage

```
## S3 method for class 'linkdat'
as.matrix(x, include.attrs = TRUE, ...)
restore_linkdat(x, attrs = NULL, checkped = TRUE)
```

Arguments

X	a $\mbox{linkdat}$ object. In $\mbox{restore_linkdat}$: A numerical matrix in LINKAGE format.
include.attrs	a logical indicating if marker annotations and other info should be attached as attributes. See value.
	not used.
attrs	a list containing marker annotations and other linkdat info compatible with x , in the format produced by as.matrix. If NULL, the attributes of x itself are used.
checkped	a logical, forwarded to linkdat. If FALSE, no checks for pedigree errors are performed.

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Details

restore_linkdat is the reverse of as.matrix.

The way linkdat objects are created in paramlink, marker data are stored as a list of marker objects. Each of these is essentially a matrix with various attributes like allele frequencies, map info a.s.o.. This format works well for marker-by-marker operations (e.g. likelihoods and LOD scores), but makes it somewhat awkward to operate 'horizontally', i.e. individual-by-individual, for instance if one wants to delete all genotypes of a certain individual, or rearrange the pedigree in some way.

It is therefore recommended to convert the linkdat object to a matrix first, do the necessary manipulations on the matrix, and finally use restore_linkdat. Attributes are often deleted during matrix manipulation, so it may be necessary to store them in a variable and feed them manually to restore_linkdat using the attrs argument.

With default parameters, restore_linkdat(as.matrix(x)) should reproduce x exactly.

Value

For as.matrix: A matrix with x\$nInd rows and 6 + 2*x\$nMark columns. The 6 first columns describe the pedigree in LINKAGE format, and the remaining columns contain marker alleles, using the internal (numerical) allele coding and 0 for missing alleles. If include.attrs = TRUE the matrix has the following attributes:

- markerattr (a list of marker annotations)
- available (the availability vector)
- model (the disease model, if present)
- plot.labels (plot labels, if present)
- orig.ids (original individual IDs)

For restore_linkdat: A linkdat object.

See Also

```
linkdat, as.data.frame.linkdat
```

```
x = linkdat(toyped, model=1)
y = restore_linkdat(as.matrix(x))
stopifnot(all.equal(x,y))

# If attributes are lost during matrix manipulation: Use the 'attrs' argument.
xmatr = as.matrix(x)
newmatr = xmatr[-4, ] # NB: attributes are lost here
z = restore_linkdat(newmatr, attrs = attributes(xmatr))

# Should be the same as:
z2 = removeIndividuals(x, 4)
stopifnot(all.equal(z, z2))
```

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dominant

Example pedigree for linkage analysis

Description

Medical pedigree with 23 individuals of which 15 are genotyped with 650 SNP markers. Eleven family members are affected by a disease, showing an autosomal dominant inheritance pattern.

Usage

dominant

Format

A data frame with 23 rows and 1306 columns, describing the pedigree and marker data in premakeped format. The first 6 columns contain the pedigree structure and affection status, while the final 1300 columns hold the marker alleles.

- FAMID. Family ID
- ID. Individual ID
- FID. Father ID
- MID. Mother ID
- SEX. Gender (male=1, female=2)
- AFF. Affection status (unaffected=1, affected=2, unknown=0)
- M1_1. First allele of marker 1
- M1_2. Second allele of marker 1
- ..
- M650_1. First allele of marker 650
- M650 2. Second allele of marker 650

All markers are SNPs, whose alleles are written as 1 and 2. Missing alleles are denoted by 0.

```
x = linkdat(dominant)
summary(x)
```

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examineKinships

Check pedigree for relationship errors

Description

This function provides a convenient way to check for pedigree errors in a linkage project or other situations where marker data is available for several members. The function calls IBDestimate to estimate IBD coefficients for all indicated pairs of pedigree members and produces a colour-coded plot where wrong relationships are easy to spot.

Usage

```
examineKinships(
  х,
 who = "all",
  interfam = c("founders", "none", "all"),
 makeplot = T,
 pch = 4,
)
```

Arguments

A linkdat object, or a list of such. Х A character vector of one or more of the words 'parents', 'siblings', 'hugs' (= who halfsibs/uncles/grandparents), 'cousins' and 'unrelated'. Two additional single-

word values are possible: 'all' (all of the above, plus 'other') and 'close' (=

'parents', 'siblings', 'hugs', 'cousins').

interfam A character; either 'founders', 'none' or 'all', indicating which interfamiliar

pairs of individuals should be included. Only relevant if x is a list of several

linkdat objects.

A logical. makeplot

Plotting symbol (default: cross). pch

Other plot arguments passed on to showInTriangle.

Value

A list of data.frames (one for each relation category) with IBD estimates.

See Also

IBDestimate, IBDtriangle, showInTriangle

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Examples

```
x = cousinsPed(1)
x = simpleSim(x, 500, alleles=1:2)
examineKinships(x)

# Pretend we didn't know the brothers (3 and 6) were related
x1 = branch(x, 3)
x2 = branch(x, 6)
x2$famid = 2

# Notice the error: An 'unrelated' dot close to the sibling point
examineKinships(list(x1, x2))
```

exclusionPower

Power of exclusion

Description

Computes the power (of a single marker) of excluding a claimed relationship, given the true relationship.

Usage

```
exclusionPower(
  ped_claim,
  ped_true,
  ids,
  markerindex = NULL,
  alleles = NULL,
  afreq = NULL,
  known_genotypes = list(),
  Xchrom = FALSE,
  plot = TRUE
)
```

Arguments

ped_claim a linkdat object, or a list of several linkdat and/or singleton objects, describing

the claimed relationship. If a list, the sets of ID labels must be disjoint, that is,

all ID labels must be unique.

ped_true a linkdat object, or a list of several linkdat and/or singleton objects, describing

the true relationship. ID labels must be consistent with ped_claim.

ids individuals available for genotyping.

markerindex NULL, or a single numeric indicating the index of a marker of ped_claim from

which alleles, afreq and known_genotypes will be extracted.

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alleles a numeric or character vector containing marker alleles names. Ignored if marker index

is non-NULL.

afreq a numerical vector with allele frequencies. An error is given if they don't sum

to 1 (rounded to 3 decimals). Ignored if markerindex is non-NULL.

known_genotypes

list of triplets (a, b, c), indicating that individual a has genotype b/c. Must be

NULL if markerindex is non-NULL.

Xchrom a logical: Is the marker on the X chromosome? Ignored if markerindex is

non-NULL.

plot either a logical or the character 'plot_only', controlling if a plot should be pro-

duced. If 'plot only', a plot is drawn, but no further computations are done.

Details

This function computes the 'Power of exclusion', as defined and discussed in (Egeland et al., 2014).

Value

A single numeric value. If plot='plot_only', the function returns NULL after producing the plot.

References

T. Egeland, N. Pinto and M. D. Vigeland, *A general approach to power calculation for relationship testing*. Forensic Science International: Genetics 9 (2014): 186-190. DOI:10.1016/j.fsigen.2013.05.001

```
### A standard case paternity case:
### Compute the power of exclusion when the claimed father is in fact unrelated to the child.
claim = nuclearPed(noffs=1, sex=2)
                                  # Specifies individual 1 as the father of 3
true = list(singleton(id=1,sex=1), singleton(id=3, sex=2))
                                                    # Specifies 1 and 3 as unrelated
available = c(1, 3)
                    # Individuals 1 and 3 are available for genotyping
# Equifrequent autosomal SNP:
PE1 = exclusionPower(claim, true, available, alleles = 2, afreq=c(0.5,0.5))
# If the child is known to have genotype 1/1:
PE2 = exclusionPower(claim, true, available, alleles = 2, afreq=c(0.5,0.5),
                  known\_genotypes=list(c(3,1,1)))
# Equifrequent SNP on the X chromosome:
PE3 = exclusionPower(claim, true, available, alleles = 2, afreq=c(0.5,0.5), Xchrom=TRUE)
stopifnot(PE1==0.125, PE2==0.25, PE3==0.25)
### Example from Egeland et al. (2012):
```

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```
### Two females claim to be mother and daughter. Below we compute the power of various
### markers to reject this claim if they in reality are sisters.
mother_daughter = nuclearPed(1, sex = 2)
sisters = relabel(nuclearPed(2, sex = c(2, 2)), c(101, 102, 2, 3))
# Equifrequent SNP:
PE1 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters, ids = c(2, 3),
                    alleles = 2)
# SNP with MAF = 0.1:
PE2 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters, ids = c(2, 3),
                    alleles = 2, afreq=c(0.9, 0.1))
# Equifrequent tetra-allelic marker:
PE3 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters, ids = c(2, 3),
                    alleles = 4)
# Tetra-allelic marker with one major allele:
PE4 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters, ids = c(2, 3),
                    alleles = 4, afreq=c(0.7, 0.1, 0.1, 0.1)
stopifnot(round(c(PE1,PE2,PE3,PE4), 5) == c(0.03125, 0.00405, 0.08203, 0.03090))
###### How does the power change if the true pedigree is inbred?
sisters_LOOP = addParents(sisters, 101, father = 201, mother = 202)
sisters_LOOP = addParents(sisters_LOOP, 102, father = 201, mother = 203)
# Equifrequent SNP:
PE5 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters_LOOP,
                    ids = c(2, 3), alleles = 2)
# SNP with MAF = 0.1:
PE6 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters_LOOP,
                     ids = c(2, 3), alleles = 2, afreq=c(0.9, 0.1))
stopifnot(round(c(PE5, PE6), 5) == c(0.03125, 0.00765))
## Not run:
# Equifrequent tetra-allelic marker:
PE7 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters_LOOP,
                    ids = c(2, 3), alleles = 4)
# Tetra-allelic marker with one major allele:
PE8 = exclusionPower(ped_claim = mother_daughter, ped_true = sisters_LOOP,
                    ids = c(2, 3), alleles = 4, afreq=c(0.7, 0.1, 0.1, 0.1))
stopifnot(round(c(PE7,PE8), 5) == c(0.07617, 0.03457))
## End(Not run)
```

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Familias2linkdat Convert 'Familias' output to linkdat objects	
---	--

Description

Familias is a widely used program for computations in forensic genetics. The function documented here facilitates the use of paramlink for specialized computations which are not implemented in Familias, e.g. conditional simulations.

Usage

```
Familias2linkdat(familiasped, datamatrix, loci)
readFamiliasLoci(loci)
connectedComponents(ID, FID, MID)
```

Arguments

familiasped	A FamiliasPedigree object or a list of such.
datamatrix	A data frame with two columns per marker (one for each allele) and one row per individual.
loci	A FamiliasLocus object or a list of such.
ID	An integer vector: Individual ID.
FID	An integer vector: ID of father.
MID	An integer vector: ID of mother.

Details

The Familias program represents pedigrees and marker data in a way that differs from paramlink in several ways, mostly because of paramlink's stricter definition of a 'pedigree'. In paramlink, a pedigree must be connected, have numerical IDs, and each member must have either 0 or 2 parents present in the pedigree. None of this is required by FamiliasPedigree objects. The conversion function Familias2linkdat takes care of all of these potential differences: It converts each FamiliasPedigree into a list of connected linkdat objects, additional parents are added where needed, and non-numerical ID labels are stored in the plot.labels slot of the linkdat object(s).

Value

A linkdat object, or a list of such.

Author(s)

Magnus Dehli Vigeland, Thore Egeland

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References

Windows Familias is freely available from https://familias.name.

Examples

```
x = nuclearPed(1)
```

hasCA

Pairwise common ancestors

Description

Computes a matrix A whose entry A[i,j] is TRUE if pedigree members i and j have a common ancestor, and FALSE otherwise.

Usage

hasCA(x)

Arguments

Х

a linkdat object.

Examples

```
x = fullSibMating(3)
A = hasCA(x)
stopifnot(A[1,1], !A[1,2], all(A[3:8, 3:8]))
```

IBDestimate

Relatedness estimation

Description

Estimate the pairwise IBD coefficients $(\kappa_0, \kappa_1, \kappa_2)$ for specified pairs of pedigree members, using maximum likelihood methods. The optimization machinery is imported from the maxLik package.

Usage

```
IBDestimate(x, ids, markers = NULL, start = c(0.99, 0.001), tol = 1e-07)
```

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Arguments

Х	A single linkdat object or a list of linkdat and/or singleton objects.
ids	Either a vector of length 2, or a matrix with two columns, indicating the pair(s) of individuals for which IBD estimates should be computed. If a matrix, each row corresponds to a pair. The entries can be either characters (matching the plot.labels of the linkdat object(s)) or integers (matching the orig.ids identifiers of the linkdat object(s)).
markers	A numeric indicating which marker(s) to include. If NULL (default), all markers are used.
start	Numeric of length 2, indicating the initial value of (κ_0, κ_2) in the optimisation (passed on to maxLik).
tol	A single numeric: the optimising tolerance value; passed on to maxLik).

Details

This function optimises the log-likelihood function first described in (Thompson, 1975). Optimisation is done in the (κ_0, κ_2) -plane and restricted to the probability triangle defined by $\kappa_0 \geq 0, \kappa_2 \geq 0, \kappa_0 + \kappa_2 \leq 1$.

Value

A data.frame with 8 columns: ID1, ID2 (numeric IDs), Name1, Name2 (plot labels, if present), N (#markers with no missing alleles), κ_0 , κ_1 , κ_2 .

References

E. A. Thompson (2000). *Statistical Inferences from Genetic Data on Pedigrees*. NSF-CBMS Regional Conference Series in Probability and Statistics. Volume 6.

See Also

examineKinships, IBDtriangle, maxLik

```
if (requireNamespace("maxLik", quietly = TRUE)) {

# Simulate marker data for two siblings
x = nuclearPed(2)
x = setPlotLabels(x, c("Sib1", "Sib2"), c(3,4))
x = simpleSim(x, 200, 1:2) # 200 equifrequent SNPs

# Estimate the IBD coefficients for the siblings
est1 = IBDestimate(x, ids=c(3,4))

# Estimate should be the same if pedigree structure is unknown
xlist = list(branch(x, 3), branch(x, 4))
est2 = IBDestimate(xlist, ids=c(3,4))
stopifnot(identical(est1, est2))
```

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```
# If the pedigree has plot.labels, they can be used as IDs
est3 = IBDestimate(x, ids=c("Sib1", "Sib2"))
stopifnot(identical(est1, est3))
}
```

IBDtriangle

IBD triangle plot

Description

The IBD triangle is typically used to visualize the pairwise relatedness of non-inbred individuals. Various annotations are available, including points marking the most common relationships, contour lines for the kinship coefficients, and shading of the unattainable region.

Usage

```
IBDtriangle(
  relationships = c("UN", "PO", "MZ", "S", "H,U,G", "FC", "SC", "DFC", "Q"),
  kinship.lines = numeric(),
  shading = "lightgray",
  pch = 16,
  cex_points = 1.2,
  cex_text = 1,
  axes = FALSE
)
```

Arguments

relationships A character vector indicating relationships points to be included in the plot. By

default all of the following are included: UN=unrelated; PO=parent/offspring; MZ=monozygotic twins; S=full siblings; H=half siblings; U=uncle/niece and similar; G=grandparent/grandchild; FC=first cousins; SC=second cousins; DFC=double

first cousins; Q=quadruple first half cousins.

kinship.lines A numeric vector. (See Details.)

shading The shading colour for the unattainable region.

pch Symbol used for the relationship points (see par).

cex_points A single numeric controlling the symbol size for the relationship points.

cex_text A single numeric controlling the font size for the relationship labels.

axes Draw surrounding axis box?

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Details

For any pair of non-inbred individuals A and B, their genetic relationship can be summarized by the IBD coefficients $(\kappa_0, \kappa_1, \kappa_2)$, where

```
\kappa_i = P(AandBshareiallelesIBDatrandomautosomallocus).
```

Since $\kappa_0 + \kappa_1 + \kappa_2 = 1$, any relationship corresponds to a point in the triangle in the (κ_0, κ_2) -plane defined by $\kappa_0 \geq 0$, $\kappa_2 \geq 0$, $\kappa_0 + \kappa_2 \leq 1$. The choice of κ_0 and κ_2 as the axis variables is done for reasons of symmetry and is not significant (other authors have used different views of the triangle).

As shown in (Thompson, 1976) points in the subset of the triangle defined by $4\kappa_0\kappa_2 > \kappa_1^2$ is unattainable for pairwise relationships. By default this region in shaded in a 'lightgray' colour.

The IBD coefficients are linearly related to the kinship coefficient ϕ by the formula

$$\phi = 0.25\kappa_1 + 0.5\kappa_2.$$

By indicating values for ϕ in the kinship.lines argument, the corresponding contour lines are shown as dashed lines in the triangle plot.

References

E. A. Thompson (1975). The estimation of pairwise relationships. Annals of Human Genetics 39.

E. A. Thompson (1976). A restriction on the space of genetic relationships. Annals of Human Genetics 40.

See Also

examineKinships

Examples

```
IBDtriangle()
IBDtriangle(kinship=c(0.25, 0.125), shading=NULL, cex_text=0.8)
```

is.linkdat

Is an object a linkdat object?

Description

Functions for checking whether an object is a linkdat object, a singleton or a list of such.

Usage

```
is.linkdat(x)
is.singleton(x)
is.linkdat.list(x)
```

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Arguments

Χ

Any R object.

Details

Note that the singleton class inherits from linkdat, so if x is a singleton, is.linkdat(x) returns TRUE.

Value

```
For is.linkdat: TRUE if x is a linkdat (or singleton) object, and FALSE otherwise. For is.singleton: TRUE if x is a singleton object, and FALSE otherwise. For is.linkdat.list: TRUE if x is a list of linkdat/singleton objects.
```

See Also

linkdat

Examples

likelihood

Pedigree likelihood

Description

Calculates various forms of pedigree likelihoods.

Usage

```
likelihood(x, ...)
## S3 method for class 'linkdat'
likelihood(
    x,
    locus1,
    locus2 = NULL,
    theta = NULL,
    startdata = NULL,
    eliminate = 0,
    logbase = NULL,
    loop_breakers = NULL,
```

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```
## S3 method for class 'singleton'
likelihood(x, locus1, logbase = NULL, ...)

## S3 method for class 'list'
likelihood(x, locus1, locus2 = NULL, ..., returnprod = TRUE)

likelihood_LINKAGE(
    x,
    marker,
    theta = NULL,
    afreq = NULL,
    logbase = NULL,
    TR.MATR = NULL,
    initialCalc = NULL,
    singleNum.geno = NULL,
    loop_breakers = NULL
)
```

Arguments

x a linkdat object, a singleton object, or a list of such objects. In likelihood_LINKAGE,

x must be a linkdat object, with x\$model different from NULL.

... further arguments.

locus1 a marker object compatible with x. If x is a list, then locus1 must be a list of

corresponding marker objects.

locus2 either NULL, the character 'disease', or a marker object compatible with x. See

Details.

theta the recombination rate between locus1 and locus2 (in likelihood_LINKAGE:

between the marker and the disease locus). To make biological sense theta

should be between 0 and 0.5.

startdata for internal use.

eliminate mostly for internal use: a non-negative integer indicating the number of itera-

tions in the internal genotype-compatibility algorithm. Positive values can save

time if partialmarker is non-empty and the number of alleles is large.

logbase a numeric, or NULL. If numeric the log-likelihood is returned, with logbase as

basis for the logarithm.

loop_breakers a numeric containing IDs of individuals to be used as loop breakers. If NULL,

automatic selection of loop breakers will be performed. See breakLoops.

returnprod a logical; if TRUE, the product of the likelihoods is returned, otherwise a vector

with the likelihoods for each pedigree in the list.

marker an integer between 0 and x\$nMark, indicating which marker to use in the calcu-

lation.

afreq a numeric containing the marker allele frequencies.

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```
TR.MATR, initialCalc, singleNum.geno
```

for internal use, speeding up linkage computations with few-allelic markers.

Details

All likelihoods are calculated using the Elston-Stewart algorithm.

If locus2 = NULL, the result is simply the likelihood of the genotypes observed at the marker in locus1.

If locus2 = 'disease', the result is the likelihood of the marker genotypes in locus1, given the affection statuses of the pedigree members, the disease model and the recombination rate theta between the marker and disease loci. The main use of this is for computation of LOD scores in parametric linkage analysis.

If locus 2 is a marker object, the result is the likelihood of the genotypes at the two markers, given the recombination rate theta between them.

The function likelihood_LINKAGE is a fast version of likelihood.linkdat in the case where locus2 = 'disease' and the marker in locus1 has less than 5 alleles.

Value

The likelihood of the data. If the parameter logbase is a positive number, the output is log(likelihood, logbase).

See Also

1od

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linkage.power

Power of a linkage study

Description

Power analysis of parametric linkage studies

Usage

```
linkage.power(
    x,
    N = 100,
    available = x$available,
    afreq = c(0.5, 0.5),
    loop_breakers = NULL,
    threshold = NULL,
    seed = NULL,
    verbose = FALSE
)

## S3 method for class 'powres'
summary(object, threshold = NULL, ...)
```

Arguments

Χ

N	an integer; the number of markers to simulate.
available	a vector containing IDs of the available individuals, i.e. those whose genotypes should be simulated.
afreq	a numerical vector with sum 1; the population frequencies for the marker alleles.
loop_breakers	a numeric containing IDs of individuals to be used as loop breakers. Relevant only if the pedigree has loops. See breakLoops.
threshold	NULL, or a single numeric. If numeric, the output includes the percentage of simulated markers having LOD larger than threshold.
seed	NULL, or a numeric seed for the random number generator.
verbose	a logical passed on to linkageSim. If TRUE, some details are shown during the marker simulation.
object	a powres object, normally produced by linkage.power.
	not used.

a linkdat object with a valid model. (See setModel.)

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Value

The function prints a summary and returns invisibly a powres object, which is a list with the following entries:

sim A linkdat object with the simulated markers

1od The LOD scores (computed with recombination fraction theta=0) of the simu-

lated markers

maxlod The highest LOD score of the simulated markers elod The average LOD score for the simulated markers

returns the maximum LOD score for each element of values.

References

Marker simulation is inspired by the SLINK algorithm.

See Also

```
linkdat, linkageSim
```

Examples

```
# Note: In the examples below N is set very low in order to reduce time consumption.
# Increase N to get more interesting results.

x = nuclearPed(3)
x = swapAff(x, c(1,3,4))
x = setModel(x, 1) # Autosomal dominant
linkage.power(x, N=1)

# X-linked recessive example:
y = linkdat(Xped, model=4)
linkage.power(y, N=1)

# Power of homozygosity mapping:
z = addOffspring(cousinPed(1), father=7, mother=8, noffs=1, aff=2)
z = setModel(z, 2) # Autosomal recessive model
pow = linkage.power(z, N=1, loop_breaker=7, seed=123)
stopifnot(round(pow$maxlod, 1) == 1.2)
```

linkageSim

Simulate markers linked to a disease locus.

Description

Simulates markers (with up to 4 alleles) conditional on the pedigree structure, affection statuses and disease model.

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Usage

```
linkageSim(
    x,
    N = 1,
    available = x$available,
    afreq = NULL,
    partialmarker = NULL,
    loop_breakers = NULL,
    unique = FALSE,
    seed = NULL,
    verbose = TRUE
)
```

Arguments

x a linkdat object

N a positive integer: the number of markers to be simulated

available a vector containing IDs of the available individuals, i.e. those whose genotypes

should be simulated.

afreq a vector of length < 5 containing the population frequencies for the marker alle-

les.

partialmarker Either NULL (indicating no given marker data), or a marker object.

loop_breakers a numeric containing IDs of individuals to be used as loop breakers. Relevant

only if the pedigree has loops. See breakLoops.

unique a logical indicating if duplicates among the simulated markers should be re-

moved.

seed NULL, or a numeric seed for the random number generator.

verbose a logical.

Details

All markers are simulated under the condition that the recombination fraction between the marker and the disease locus is 0. This is an implementation of the algorithm used in SLINK of the LINK-AGE/FASTLINK suite.

Value

a linkdat object equal to x except its markerdata entry, which consists of the N simulated markers.

References

G. M. Lathrop, J.-M. Lalouel, C. Julier, and J. Ott (1984). *Strategies for Multilocus Analysis in Humans*, PNAS 81, pp. 3443-3446.

See Also

```
linkage.power
```

Examples

```
x = linkdat(toyped, model=1)
y = linkageSim(x, N=10, afreq=c(0.5, 0.5))
stopifnot(length(mendelianCheck(y))==0)

z = addOffspring(cousinPed(1), father=7, mother=8, noffs=1, aff=2)
z = setModel(z, 2)
linkageSim(z, N=1, afreq = c(0.1, 0.2, 0.7))
```

linkdat

Linkdat objects

Description

Functions to create and display 'linkdat' objects.

Usage

```
linkdat(
  ped,
 model = NULL,
 map = NULL,
  dat = NULL,
  freq = NULL,
  annotations = NULL,
 missing = 0,
 header = FALSE,
  checkped = TRUE,
  verbose = TRUE,
)
singleton(id, sex = 1, famid = 1, verbose = FALSE, ...)
## S3 method for class 'linkdat'
print(x, ..., markers)
## S3 method for class 'linkdat'
summary(object, ...)
write.linkdat(
 prefix = "",
 what = c("ped", "map", "dat", "freq", "model"),
 merlin = FALSE
)
```

```
## S3 method for class 'linkdat'
subset(x, subset = x$orig.ids, ..., markers = seq_len(x$nMark))
```

Arguments

ped a matrix, data.frame or a character with the path to a pedigree file in standard

LINKAGE format. (See details)

model either a linkdat.model object (typically y\$model for some linkdat object y), or

a single integer with the following meaning: 1 = autosomal dominant; 2 = autosomal recessive; 3 = X-linked dominant; 4 = X-linked recessive. In each of these cases, the disease is assumed fully penetrant and the disease allele frequency is

set to 0.00001. If model=NULL, no model is set.

map a character with the path to a map file in MERLIN format, or NULL. If non-

NULL, a dat file must also be given (next item).

dat a character with the path to a dat file in MERLIN format, or NULL. (Only

needed if map is non-NULL.)

freq a character with the path to a allele frequency file in MERLIN (short) format, or

NULL. If NULL, all markers are interpreted as equifrequent.

annotations a list (of the same length and in the same order as the marker columns in x) of

marker annotations. If this is non-NULL, then all of map, dat, freq should be

NULL.

missing the character (of length 1) used for missing alleles. Defaults to '0'.

header a logical, relevant only if ped points to a ped file: If TRUE, the first line of the

ped file is skipped.

checkped a logical. If FALSE, no checks for pedigree errors are performed.

verbose a logical: verbose output or not.

... further arguments.

id, sex single numerics describing the individual ID and gender of the singleton.

famid a numeric: the family ID of the singleton.

x, object a linkdat object.

markers a numeric indicating which markers should be included/printed.

prefix a character string giving the prefix of the files. For instance, if prefix='fam1'

and what=c('ped', 'map'), the files 'fam1.ped' and 'fam1.map' will be cre-

ated.

what a character vector forming a subset of c('ped', 'map', 'dat', 'freq', 'model'),

indicating which files should be created. All files are written in MERLIN style

(but see the next item!)

merlin a logical. If TRUE, the marker alleles are relabeled to 1,2,..., making sure

that the generated files are readable by MERLIN (which does not accept nonnumerical allele labels in the frequency file.) If FALSE (the default) the allele labels are unchanged. In this case, x should be exactly reproducible from the

files. (See examples.)

subset a numeric containing the individuals in the sub-pedigree to be extracted. NB:

No pedigree checking is done here, so make sure the subset form a meaningful,

closed pedigree.

Details

The file (or matrix or data.frame) ped must describe one or several pedigrees in standard LINKAGE format, i.e. with the following columns in correct order:

- 1 Family id (optional) (FAMID)
- 2 Individual id (ID),
- 3 Father id (FID),
- 4 Mother id (MID),
- 5 Gender (SEX): 1 = male, 2 = female,
- 6 Affection status (AFF): 1 = unaffected, 2 = affected, 0 = unknown,
- 7 First allele of first marker,
- 8 Second allele of first marker,
- 9 First allele of second marker,

a.s.o.

Only columns 2-6 are mandatory. The first column is automatically interpreted as family id if it has repeated elements.

Internally the individuals are relabeled as 1,2,..., but this should rarely be of concern to the end user. Some pedigree checking is done, but it is recommended to plot the pedigree before doing any analysis.

Details on the formats of map, dat and frequency files can be found in the online MERLIN tutorial: http://csg.sph.umich.edu/abecasis/Merlin/

A singleton is a special linkdat object whose pedigree contains 1 individual. The class attribute of a singleton is c('singleton', 'linkdat')

Value

A linkdat object, or a list of linkdat objects. A linkdat object is essentially a list with the following entries, some of which can be NULL.

pedigree data.frame with 5 columns (ID, FID, MID, SEX, AFF) describing the pedigree

in linkage format. (NB: Internal labeling used.)

orig.ids the original individual id labels.

nInd the number of individuals in the pedigree.

founders vector of the founder individuals. (NB: Internal labeling used.)
nonfounders vector of the nonfounder individuals (NB: Internal labeling used.)

hasLoops a logical: TRUE if the pedigree is inbred.

subnucs list containing all (maximal) nuclear families in the pedigree. Each nuclear fam-

ily is given as a vector of the form c(pivot, father, mother, child1, ...), where the pivot is either the id of the individual linking the nuclear family to the rest of the

pedigree, or 0 if there are none. (NB: Internal labeling used.)

markerdata a list of marker objects.

nMark the number of markers.

available a numeric vector containing IDs of available individuals. Used for simulations and plots.

a linkdat.model object, essentially a list containing the model parameters. See

setModel for details.

loop_breakers a matrix with original loop breaker ID's in the first column and their duplicates

in the second column. This is set by breakLoops.

See Also

model

pedCreate, pedModify, pedParts, setModel

```
x = linkdat(toyped, model=1)
summary(x)
#### test read/write:
x = modifyMarker(x, 1, alleles=c('B','C'), afreq=c(.9, .1), chrom=2, name='SNP1', pos=123)
write.linkdat(x, prefix='toy')
y = linkdat('toy.ped', map='toy.map', dat='toy.dat', freq='toy.freq', model=1)
unlink(c('toy.ped', 'toy.map', 'toy.dat', 'toy.freq', 'toy.model'))
stopifnot(isTRUE(all.equal(x,y)))
#### test singletons:
w = singleton(id=3, sex=2)
T1 = all.equal(w, linkdat(ped=rbind(c(3,0,0,2,1))))
w = markerSim(w, N=5, alleles=2, afreq=c(0.1, .9))
T2 = all.equal(w, relabel(relabel(w, 10), 3))
T3 = all.equal(w, swapSex(swapSex(w, 3), 3))
T4 = all.equal(w, swapAff(swapAff(w, 3), 3))
stopifnot(T1, T2, T3, T4)
#### several ways of creating the same linkdat object:
alleles = c(157, 160, 163)
afreq = c(0.3, 0.3, 0.4)
gt10 = c(160, 160)
gt14 = c(160, 163)
z1 = relabel(addOffspring(nuclearPed(1), father=3, noffs=1, aff=2), 10:14)
z1 = addMarker(z1, marker(z1, 10, gt10, 14, gt14, alleles=alleles, afreq=afreq))
z1 = setModel(z1, 2)
z2 = addParents(relabel(nuclearPed(1), 12:14), 12, father=10, mother=11)
z2 = addMarker(z2, rbind(gt10, 0, 0, 0, gt14), alleles=alleles, afreq=afreq)
z2 = setModel(swapAff(z2, 14), 2)
z3 = linkdat(data.frame(ID=10:14, FID=c(0,0,10,0,12), MID=c(0,0,11,0,13),
             SEX=c(1,2,1,2,1), AFF=c(1,1,1,1,2),
             M=c('160/160', '0/0', '0/0', '0/0', '160/163')), model=2)
z3 = modifyMarker(z3, 1, alleles=alleles, afreq=afreq)
```

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linkres

S3 methods for class 'linkres'.

Description

Functions for printing, summarizing and plotting the results of a linkage analysis.

Usage

```
## S3 method for class 'linkres'
print(x, ...)

## S3 method for class 'linkres'
summary(object, ...)

## S3 method for class 'linkres'
as.data.frame(x, ..., sort = TRUE)

peakSummary(x, threshold, width = 1, physmap = NULL)

## S3 method for class 'linkres'
plot(x, chrom = NULL, ylim = NULL, ...)
```

Arguments

x, object	a linkres object (normally produced by lod or merlin).
	further arguments.
sort	a logical, indicating if the data frame should be sorted according to map position.
threshold	a single numeric. A peak is defined as a regions of at least width consecutive markers LOD score above threshold.
width	a single numeric.

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physmap a matrix or data frame with three columns: Marker name, chromosome and physical position. This argument is optional.

chrom NULL, or a numeric containing chromosome numbers. In the latter case only

results for the markers on the indicated chromosomes will be plotted.

ylim NULL, or a numeric of length 2: to be passed on to plot.default.

See Also

```
lod, merlin
```

Examples

```
x = linkdat(toyped, model=1)
lods = lod(x, theta='max')
summary(lods)
as.data.frame(lods)
```

lod

Two-point LOD score

Description

Calculates the two-point LOD scores of a pedigree for the specified markers. The recombination ratio between the disease and marker loci can be either fixed at specific values, or optimized.

Usage

```
lod(
   x,
   markers = seq_len(x$nMark),
   theta = 0,
   loop_breakers = NULL,
   max.only = FALSE,
   verbose = FALSE,
   tol = 0.01
)
```

Arguments

x a linkdat object.

markers an integer vector denoting which markers to use.

theta either a numeric containing specific recombination ratio(s), or the word 'max',

indicating that the recombination ratio should be optimized by the program.

loop_breakers a numeric containing IDs of individuals to be used as loop breakers. Relevant

only if the pedigree has loops. See breakLoops.

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max.only a logical indicating whether only the maximum LOD score should be returned.

verbose a logical: verbose output or not.

tol a numeric passed on to optimize as its tolerance parameter.

Details

The LOD score of a marker is defined as

$$LOD(\theta) = \log[10] \frac{L(\theta)}{L(0.5)}$$

where $L(\theta)$ denotes the likelihood of the observed marker genotypes given a recombination ratio θ between the marker and the disease locus.

Value

If max.only=TRUE, the highest computed LOD score is returned, as a single number.

Otherwise a linkres object, which is essentially a matrix containing the LOD scores. The details depend on the other parameters:

If theta is numeric, the matrix has dimensions length(theta) * length(markers), and the entry in row t, column m is the lod score of the pedigree for marker m assuming a recombination rate of t.

If theta='max', the linkres matrix has one column per marker and two rows: The first containing the LOD score and the second the optimal recombination ratio for each marker.

If a marker has incompatible values (i.e. if a child of homozygous 1/1 parents has a 2 allele), the corresponding output entries are NaN.

See Also

likelihood, optimize, breakLoops

```
x = linkdat(toyped, model=1)
res = lod(x)
res_theta = lod(x, theta=c(0, 0.1, 0.2, 0.5))
res_max = lod(x, theta='max')
stopifnot(all(0.3 == round(c(res, res_theta['0',], res_max['LOD',]), 1))))
# bigger pedigree with several markers
y = linkdat(dominant)
y = setModel(y, model=1, penetrances=c(.001, .9, .99))
lod(y, markers=305:310)
lod(y, markers=305:310, theta='max')
# Example with pedigree with loops:
z = linkdat(twoloops, model=2) # fully penetrant autosomal recessive model.
# add SNP for which individuals 15 and 16 are homozygous for the rare allele.
m = marker(z, 15:16, c(1,1), alleles=1:2, afreq=c(0.001, 0.999))
z = addMarker(z, m)
```

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```
res1 = lod(z)
# manual specification of loop breakers gives same result
res2 = lod(z, loop_breakers=c(8,12))
# making the marker triallelic and adding some genotypes.
z = modifyMarker(z, marker=1, ids=c(7,9,11,13), genotype=3, alleles=1:3, afreq=c(0.001, 0.499, 0.5))
plot(z, 1)
res3 = lod(z)
z = modifyMarker(z, marker=1, alleles=1:4, afreq=c(0.001, 0.499, 0.25, 0.25))
res4 = lod(z)
stopifnot(all(3 == round(c(res1, res2, res3, res4), 1)))
```

lod.peaks

LOD score peaks

Description

Identify LOD score peaks

Usage

```
lod.peaks(x, threshold, width = 1)
```

Arguments

x a linkres objectthreshold a single numericwidth a positive integer

Details

The function first transforms x to a data frame (using as.data.frame.linkres with sort=T. A peak is defined a run of at least width consecutive markers with LOD score above or equal to threshold. If possible, one flanking marker is included on each side of the peak.

Value

A list of data frames.

See Also

```
linkres, lod, merlin,
```

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Examples

```
## minimal example
x = linkdat(toyped, model=1)
res = lod(x)
peak1 = lod.peaks(res, threshold=0)
peak2 = lod.peaks(res, threshold=0, width=2)
peak3 = lod.peaks(res, threshold=1)
stopifnot(length(peak1)==1, nrow(peak1[[1]])==1, length(peak2)==0, length(peak3)==0)
```

LR

Likelihood ratios of pedigree hypotheses

Description

This function computes likelihood ratios for a given a list of pedigrees (linkdat/singletons objects), one of which is the 'reference', with genotype data from the same set of markers. Data exported from the 'Familias' software can be analysed by using Familias2linkdat prior to calling this function.

Usage

```
LR(x, ref, markers)
```

Arguments

x A list of pedigrees. Each pedigree is either a single linkdat/singleton object, or

a list of such objects (the latter is necessary if the pedigree is disconnected).

ref A single integer, indicating the index of the reference pedigree. This is used in

the denominator of each LR.

markers A vector of integers, indexing which markers should be included. If NULL (the

default) all markers are used.

Value

A list with entries

LR Likelihood ratios

LRperMarker Likelihood ratios for each marker

likelihoodsPerSystem

Likelihoods for each marker

time user, system and elapsed time

Author(s)

Magnus Dehli Vigeland and Thore Egeland

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See Also

IBDtriangle, examineKinships

Examples

```
# Simulate genotypes for 5 tetraallelic markers for a pair of full sibs
set.seed(123)
sibs = simpleSim(nuclearPed(2), N=5, alleles=1:4, available=3:4)

# Create two alternative hypotheses and transfer the simulated genotypes to them
halfsibs = addOffspring(nuclearPed(1),father=1,noffs=1,id=4)
halfsibs = transferMarkerdata(sibs, halfsibs)

unrel = list(singleton(3), singleton(4))
unrel = transferMarkerdata(sibs, unrel)

# Compute LR with 'unrelated' as reference
LR(list(sibs, halfsibs, unrel), ref=3)
```

markers

Marker functions

Description

Functions for setting and manipulating marker genotypes for 'linkdat' objects.

Usage

```
marker(
    x,
    ...,
    allelematrix,
    alleles = NULL,
    afreq = NULL,
    missing = 0,
    chrom = NA,
    pos = NA,
    name = NA,
    mutmat = NULL
)

addMarker(x, m, ...)

setMarkers(x, m, annotations = NULL, missing = 0)

modifyMarker(x, marker, ids, genotype, alleles, afreq, chrom, name, pos)
```

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```
getMarkers(x, markernames = NULL, chroms = NULL, fromPos = NULL, toPos = NULL)

removeMarkers(
    x,
    markers = NULL,
    markernames = NULL,
    chroms = NULL,
    fromPos = NULL,
    toPos = NULL
)

swapGenotypes(x, ids)

modifyMarkerMatrix(x, ids, new.alleles)
```

Arguments

x a linkdat object

an even number of vectors, indicating individuals and their genotypes. See ex-

amples.

allelematrix a matrix with one row per pedigree member and two columns per marker, con-

taining the alleles for a single marker.

alleles a numeric or character vector containing allele names.

afreq a numerical vector with allele frequencies. An error is given if they don't sum

to 1 (rounded to 3 decimals).

missing a numeric - or character - of length 1, indicating the code for missing alleles.

chrom NA or an integer (the chromosome number of the marker).

pos NA or a non-negative real number indicating the genetic position (in cM) of the

marker.

name NA or a character (the name of the marker).

mutmat a mutation matrix, or a list of two such matrices named 'female' and 'male'.

The matrix/matrices must be square, with the allele labels as dimnames, and

each row must sum to 1 (after rounding to 3 decimals).

m a marker object or a matrix with alleles. (In setMarkers this matrix can contain

data of several markers.)

annotations a list of marker annotations.

marker, markers a numeric indicating which marker(s) to use/modify.

ids a numeric indicating individual(s) to be modified. In swapGenotypes this must

have length 2.

genotype a vector of length 1 or 2, containing the genotype to be given the ids individuals.

See examples.

markernames NULL or a character vector.

chroms NULL or a numeric vector of chromosome numbers.

fromPos, toPos NULL or a single numeric.

new.alleles a numerical matrix of dimensions length(ids), 2*x\$nMark. Entries refer to

the internal allele numbering.

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Value

The marker function returns an object of class marker: This is a numerical 2-column matrix with one row per individual, and attributes 'alleles' (a character vector with allele names), 'nalleles' (the number of alleles) and 'missing' (the input symbol for missing marker alleles), 'chrom' (chromosome number), 'name' (marker identifier), 'pos' (chromosome position in cM).

For addMarker, setMarkers, removeMarkers, modifyMarker, modifyMarkerMatrix and swapGenotypes, a linkdat object is returned, whose markerdata element has been set/modified.

For getMarkers a numeric vector containing marker numbers (i.e. their indices in x\$markerdata) for the markers whose 'name' attribute is contained in markernames, 'chrom' attribute is contained in chroms, and 'pos' attribute is between from and to. NULL arguments are skipped, so getMarkers(x) will return seq_len(x\$nMark) (i.e. all markers).

See Also

linkdat

```
x = linkdat(toyped)
x = removeMarkers(x, 1) # removing the only marker.
# Creating and adding a SNP marker with alleles 'a' and 'b', for which
# individual 1 is heterozygous, individuals 2 and 4 are homozygous for the
# 'b' allele, and individual 3 has a missing genotype.
m1 = marker(x, 1, c('a', 'b'), c(2,4), c('b', 'b'))
x = addMarker(x, m1)
# A rare SNP for which both children are heterozygous.
# The 'alleles' argument can be skipped, but is recommended to ensure
# correct order of the frequencies.
m2 = marker(x, 3:4, 1:2, alleles=1:2, afreq=c(0.99, 0.01))
x = addMarker(x, m2)
# Modifying the second marker:
# Making it triallelic, and adding a genotype to the father.
x = modifyMarker(x, marker=2, alleles=1:3, ids=1, genotype=2:3)
# Adding an empty SNP (all genotypes are missing):
x = addMarker(x, 0, alleles=c('A', 'B'))
# Similar shortcut for creating a marker for which all
# pedigree members are homozygous for an allele (say 'b'):
x = addMarker(x, 'b')
# Alternative: m = marker(x, 'b'); addMarker(x, m)
```

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markerSim Marker simulation

Description

Simulates marker genotypes conditional on the pedigree structure, affection statuses and disease model.

Usage

```
markerSim(
    x,
    N = 1,
    available = NULL,
    alleles = NULL,
    afreq = NULL,
    partialmarker = NULL,
    loop_breakers = NULL,
    eliminate = 0,
    seed = NULL,
    verbose = TRUE
)
```

a logical.

Arguments

verbose

x	a linkdat object
N	a positive integer: the number of markers to be simulated
available	a vector containing IDs of the available individuals, i.e. those whose genotypes should be simulated. By default, all individuals are included.
alleles	a vector containing the alleles for the marker to be simulation. If a single integer is given, this is interpreted as the number of alleles, and the actual alleles as 1:alleles. Must be NULL if partialmarker is non-NULL.
afreq	a vector of length 2 containing the population frequencies for the marker alleles. Must be NULL if partialmarker is non-NULL.
partialmarker	Either NULL (resulting in unconditional simulation), a marker object (on which the simulation should be conditioned) or the index of an existing marker of x.
loop_breakers	a numeric containing IDs of individuals to be used as loop breakers. Relevant only if the pedigree has loops, and only if partialmarker is non-NULL. See breakLoops.
eliminate	A non-negative integer, indicating the number of iterations in the internal genotype-compatibility algorithm. Positive values can save time if partialmarker is non-NULL and the number of alleles is large.
seed	NULL, or a numeric seed for the random number generator.

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Details

This implements (with various time savers) the algorithm used in SLINK of the LINKAGE/FASTLINK suite. If partialmarker is NULL, genotypes are simulated by simple gene dropping, using simpleSim.

Value

a linkdat object equal to x except its markerdata entry, which consists of the N simulated markers.

References

G. M. Lathrop, J.-M. Lalouel, C. Julier, and J. Ott, *Strategies for Multilocus Analysis in Humans*, PNAS 81(1984), pp. 3443-3446.

See Also

```
simpleSim, linkage.power
```

Examples

```
x = nuclearPed(2)
partial = marker(x, 3, 1, alleles=1:3)
markerSim(x, N=1, alleles=1:3)
markerSim(x, N=1, partialmarker=partial)
markerSim(x, N=1, partialmarker=partial)
markerSim(x, N=1, available=4, partialmarker=partial)
```

mendelianCheck

Check for Mendelian errors

Description

Check marker data for Mendelian inconsistencies

Usage

```
mendelianCheck(x, remove = FALSE, verbose = !remove)
```

Arguments

x a linkdat object

remove a logical. If FALSE, the function returns the indices of markers found to incor-

rect. If TRUE, a new linkdat object is returned, where the incorrect markers

have been deleted.

verbose a logical. If TRUE, details of the markers failing the tests are shown.

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Value

A numeric containing the indices of the markers that did not pass the tests, or (if remove=TRUE) a new linkdat object where the failing markers are removed.

Examples

```
x = nuclearPed(3)
# Adding a SNP with a mendelian error:
# Individual 3 has an allele 'c' not carried by either parents
m1 = marker(x, 1, c('a', 'a'), 2, c('a', 'b'), 3, c('a', 'c'))
# Another erroneous marker: The siblings carry more than 4 different alleles.
m2 = marker(x, 3, c(1,2), 4, c(3,4), 5, c(1,5))
# Another marker with incosistent genotypes among the siblings:
m3 = marker(x, 3, c(1,1), 4, c(2,2), 5, c(3,3))
# Another marker with incosistent genotypes among the siblings:
m4 = marker(x, 3, c(1,1), 4, c(2,3), 5, c(1,4))
# A correct marker (all homozygous for allele 'A')
m5 = marker(x, 1:5, 'A')
# An empty marker
m6 = marker(x)
x = setMarkers(x, list(m1, m2, m3, m4, m5, m6))
# Finding the errors
err_index = mendelianCheck(x, remove=FALSE)
stopifnot(all.equal(err_index, 1:4))
x_remove = mendelianCheck(x, remove=TRUE)
stopifnot(x_remove$nMark == 2)
```

mergePed

Merge two pedigrees

Description

This function merges two linkdat objects, joining them at the individuals with equal ID labels. This is especially useful for building 'top-heavy' pedigrees. Only linkdat objects without marker data are supported.

Usage

```
mergePed(x, y, quick = FALSE)
```

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Arguments

x, y linkdat objects
quick a single logical. If TRUE, no pedigree checks are performed, and the individual ordering may be unfortunate.

Value

A linkdat object.

Examples

```
# Creating a trio where each parent have first cousin parents.
# (Alternatively, this could be built using many calls to addParents().)

x = cousinPed(1)
x = addOffspring(x, father=7, mother=8, noffs=1, id=9)
x = addOffspring(x, father=9, mother=10, noffs=1, id=11)

y = relabel(cousinPed(1), 101:108)
y = addOffspring(y, father=107, mother=108, noffs=1, sex=2, id=10)
y = addOffspring(y, father=9, mother=10, noffs=1, id=11)

# Joining x and y at the common individuals 9,10,11:
z = mergePed(x,y)

# plot all three pedigrees
op = par(mfrow = c(1,3))
plot(x); plot(y); plot(z)
par(op)
```

merlin

MERLIN wrappers

Description

Wrappers for the MERLIN software, providing multipoint LOD scores and other computations on pedigrees with marker data. These functions require MERLIN to be installed and correctly pointed to in the PATH environment variable.

Usage

```
merlin(
   x,
   markers = seq_len(x$nMark),
   model = TRUE,
   theta = NULL,
   options = "",
```

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```
verbose = FALSE,
  generate.files = TRUE,
  cleanup = generate.files,
  logfile = ""
)
merlinUnlikely(x, remove = FALSE, verbose = !remove)
```

Arguments

x a linkdat object

markers an integer vector indicating which markers to use (default: all).

model a logical: If TRUE (and x\$model is not NULL), the file 'merlin.model' is created

and '-model merlin.model' is included to the MERLIN command.

theta a numeric with values between 0 and 0.5: The recombination value(s) for which

the LOD score is computed. The values of theta are converted to centiMorgan positions using the Haldane map function and included in the MERLIN command using the --position parameter. Works only for single markers (i.e.

markers must consist of a single integer).

options a character with additional options to the MERLIN command. See details.

verbose a logical: Show MERLIN output and other information, or not.

generate.files a logical. If TRUE, the files 'merlin.ped', 'merlin.dat', 'merlin.map', 'mer-

lin.freq' and (if model=TRUE) 'merlin.model' are created in the working direc-

tory.

cleanup a logical: Should the MERLIN files be deleted automatically?

logfile a character. If this is given, the MERLIN screen output will be written to a file

with this name.

remove a logical. If FALSE, the function returns the indices of markers found to un-

likely. If TRUE, a new linkdat object is returned, where the unlikely markers

have been deleted.

Details

For these functions to work, MERLIN must be installed and the path to merlin.exe included in the PATH variable. The merlin function is first and foremost a wrapper to the parametric linkage functionality of MERLIN.

By default the following MERLIN command is run (via a call to system) after creating appropriate files in the current working directory:

```
_merlin.freg --model _merlin.model --tabulate --markerNames --quiet
```

The resulting multipoint LOD scores are extracted from the output and returned in R as a linkres object.

Additional command parameters can be passed on using the options argument (this is simply pasted onto the MERLIN command, so dashes must be included). For example, to obtain single-point LOD scores instead of multipoint, set options='--singlepoint'. (The singlepoint scores

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should agree with the results of lod(x), except in cases where some individuals have partial genotypes (see Examples).)

If model=FALSE the --model merlin.model part is removed from the MERLIN command above. This is necessary for some calculations, e.g. likelihoods (see Examples).

The merlinUnlikely function is a wrapper for MERLIN's '-error' command. The syntax is similar to that of mendelianCheck.

Value

If model=TRUE, a linkres object. Otherwise a character containing the complete MERLIN output.

For merlinUnlikely, a numeric containing the indices of the unlikely, or (if remove=TRUE) a new linkdat object where the unlikely markers are removed.

References

```
http://csg.sph.umich.edu/abecasis/Merlin/
```

Examples

```
## Not run:
x = linkdat(toyped, model=1)
x

# MERLIN treats partial genotypes (i.e. one known and one unknown allele) as missing:
lod_merlin = merlin(x)
lod_partial = lod(x)
x = modifyMarker(x, marker=1, ids=1, genotype=0)
lod_missing = lod(x)
stopifnot(lod_merlin == round(lod_missing, 4))

# Likelihood computation by MERLIN:
merlin(x, model=F, options='--lik')

## End(Not run)
```

 $one {\tt MarkerDistribution} \ \ \textit{Genotype probability distribution}$

Description

Computes the (joint) genotype probability distribution of one or several pedigree members, possibly conditional on partial marker data.

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Usage

```
oneMarkerDistribution(
    x,
    ids,
    partialmarker,
    theta = NULL,
    grid.subset = NULL,
    loop_breakers = NULL,
    eliminate = 0,
    ignore.affection.status = FALSE,
    verbose = TRUE
)
```

Arguments

x A linkdat object.

ids A numeric with ID labels of one or more pedigree members.

partialmarker Either a marker object compatible with x, or the index (a single integer) of an

existing marker of x.

theta The recombination fraction between marker and disease locus. Only relevant if

at least one individual is affected by disease. In that case an error is raised if

theta is NULL, and if x does not have a disease model.

grid. subset (Not relevant for most end users.) A numeric matrix describing a subset of all

marker genotype combinations for the ids individuals. The matrix should have one column for each of the ids individuals, and one row for each combination: The genotypes are described in terms of the matrix M = allGenotypes(n), where n is the number of alleles for the marker. If the entry in column j is the

integer k, this means that the genotype of individual ids[j] is row k of M.

A numeric containing IDs of individuals to be used as loop breakers. Relevant only if the pedigree has loops. See breakLoops.

eliminate A non-negative integer, indicating the number of iterations in the internal genotype-

compatibility algorithm. Positive values can save time if partialmarker is

non-empty and the number of alleles is large.

ignore.affection.status

loop_breakers

A logical indicating if the 'AFF' column should be ignored (only relevant if

some family members are marked as affected).

verbose A logical.

Value

A named array (of dimension length(ids)) giving the joint marker genotype distribution for the ids individuals, conditional on 1) the marker allele frequencies given in partialmarker, 2) non-missing alleles in partialmarker, and 3) the disease model of x (if the pedigree is affected).

See Also

twoMarkerDistribution, allGenotypes

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```
x = nuclearPed(2)
x_aff = swapAff(x, c(1,3))
x_aff = setModel(x_aff, model=1) # dominant model
snp = marker(x, 1, c(1,1), 2, c(1,0), alleles=1:2, afreq=c(0.1, 0.9))
res1 = oneMarkerDistribution(x, ids=3:4, partialmarker=snp)
res2 = oneMarkerDistribution(x_aff, ids=3:4, partialmarker=snp, theta=0.5)
# should give same result, since theta=0.5 implies that marker is independent of disease.
stopifnot(all.equal(res1, res2))
#### Different example for the same pedigree. A marker with 4 alleles:
m2 = marker(x, 3:4, c('C', 'D'), alleles=LETTERS[1:4])
oneMarkerDistribution(x, ids=1, partialmarker=m2)
# Same as above, but computing only the cases where individual 1 is heterozygous.
# (The numbers 5:10 refer to the 6 last rows of allGenotypes(4),
# which contain the heterozygous genotypes.)
oneMarkerDistribution(x, ids=1, partialmarker=m2, grid.subset=matrix(5:10, ncol=1))
#### Expanding on the previous example:
# Joint genotype probabilities of the parents, but including only the combinations
# where the father is heterozygous and the mother is homozygous:
grid = expand.grid(5:10, 1:4)
oneMarkerDistribution(x, ids=1:2, partialmarker=m2, grid.subset=grid)
#### Something else:
# The genotype distribution of an individual whose half cousin is homozygous
# for a rare allele.
y = halfCousinPed(degree=1)
snp = marker(y, 9, c('a', 'a'), alleles=c('a', 'b'), afreq=c(0.01, 0.99))
oneMarkerDistribution(y, ids=8, partialmarker=snp)
#### X-linked example:
z = linkdat(Xped, model=4) # X-linked recessive model
z2 = swapAff(z, 1:z$nInd, 1) # disease free version of the same pedigree
snpX = marker(z, c(5,15), c('A', 'A'), alleles=c('A', 'B'), chrom=23)
r1 = oneMarkerDistribution(z, ids=13, partialmarker=snpX, theta=0.5) # results: A - 0.8; B - 0.2
r2 = oneMarkerDistribution(z2, ids=13, partialmarker=snpX)
                                                                 # should be same as above
r3 = oneMarkerDistribution(z, ids=13, partialmarker=snpX, theta=0) # results: A - 0.67; B - 0.33
stopifnot(all.equal(r1,r2), round(r1[1], 2)==0.8, round(r3[1], 2) == 0.67)
```

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Description

These are utility functions for creating some common pedigree structures as linkdat objects.

Usage

```
nuclearPed(noffs, sex)

cousinsPed(degree, removal = 0, degree2 = NULL, child = FALSE)

halfCousinsPed(degree, removal = 0, degree2 = NULL, child = FALSE)

doubleCousins(degree1, degree2, removal1 = 0, removal2 = 0, child = FALSE)

doubleFirstCousins()

quadHalfFirstCousins()

fullSibMating(generations)

halfSibStack(generations)

cousinPed(degree)

halfCousinPed(degree)
```

Arguments

noffs A positive integer, the number of offspring in the nuclear family.

sex A vector of length noffs; indicating the genders (1=male, 2=female) of the

offspring. If missing, all offspring are taken to be males.

degree, degree1, degree2

Non-negative integers, indicating the degree of cousin-like relationships: 0=sib-

lings, 1=first cousins; 2=second cousins, a.s.o. See Details and Examples.

removal, removal1, removal2

Non-negative integers, indicating removals of cousin-like relationships. See De-

tails and Examples.

child A logical: Should an inbred child be added to the two cousins?

generations A positive integer indicating the number of crossings.

Details

All individuals are created as unaffected. Use swapAff to edit this (see Examples). Use swapSex to change gender of pedigree members.

The call cousinsPed(degree=n, removal=k) creates a pedigree with two n'th cousins, k times removed. By default, removals are added on the right side. To override this, the parameter degree2 can be used to indicate explicitly the number of generations on the right side of the pedigree. When degree2 is given removal is ignored. (Similarly for halfCousinsPed.)

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The function doubleCousins creates two individuals whose fathers are cousins (degree1, removal1) as well as their mothers (degree2, removal2). For simplicity, a wrapper doubleFirstCousins is provided for the most common case, double first cousins. Finally quadHalfFirstCousins produces a pedigree with quadruple half first cousins.

fullSibMating crosses full sibs continuously for the indicated number of generations.

halfSibStack produces a breeding scheme where the two individuals in the final generation are simultaneously half siblings and half n'th cousins, where n=1,...,generations.

cousinPed and halfCousinPed (written without the 's') are depreciated functions kept for backwards compatibility. They create cousin pedigrees, but without possibility for removals, and with a different ordering than their replacements cousinsPed and halfCousinsPed.

Value

A linkdat object.

See Also

```
swapAff, swapSex, removeIndividuals, addOffspring, relabel
```

```
# A nuclear family with 2 boys and 3 girls,
# where the father and the two boys are affected.
x = nuclearPed(noffs=5, sex=c(1,1,2,2,2))
x = swapAff(x, ids=c(1,3,4))
# Half sibs:
halfCousinsPed(degree=0)
# Grand aunt:
cousinsPed(degree=0, removal=2)
# Second cousins once removed.
cousinsPed(degree=2, removal=1)
# Again second cousins once removed,
# but with the 'removal' on the left side.
cousinsPed(degree=3, degree2=2)
# A child of first cousin parents.
cousinsPed(degree=1, child=TRUE)
# Consecutive brother-sister matings.
fullSibMating(3)
# Simultaneous half siblings and half first cousins
halfSibStack(2)
# Double first cousins
doubleFirstCousins()
```

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```
# Quadruple half first cousins
# Weird plotting behaviour for this pedigree.
x = quadHalfFirstCousins()
#plot(x)
```

pedigreeLoops

Pedigree loops

Description

Functions for identifying, breaking and restoring loops in pedigrees.

Usage

```
pedigreeLoops(x)
breakLoops(x, loop_breakers = NULL, verbose = TRUE)
tieLoops(x)
findLoopBreakers(x)
findLoopBreakers2(x)
```

Arguments

x a linkdat object.

loop_breakers either NULL (resulting in automatic selection of loop breakers) or a numeric

containing IDs of individuals to be used as loop breakers.

verbose a logical: Verbose output or not?

Details

Most of paramlink's handling of pedigree loops is done under the hood - using the functions described here - without need for explicit action from end users. When a linkdat object x is created, an internal routine detects if the pedigree contains loops, in which case x\$hasLoops is set to TRUE. In analyses of x where loops must be broken (e.g. lod score computation or marker simulation), this is done automatically by calling breakLoops.

In some cases with complex inbreeding, it can be instructive to plot the pedigree after breaking the loops. Duplicated individuals are plotted with appropriate labels (see examples).

The function findLoopBreakers identifies a set of individuals breaking all inbreeding loops, but not marriage loops. These require more machinery for efficient detection, and paramlink does this is a separate function, findLoopBreakers2, utilizing methods from the igraph package. Since this is rarely needed for most users, igraph is not imported when loading paramlink, only when findLoopBreakers2 is called.

In practice, breakLoops first calls findLoopBreakers and breaks at the returned individuals. If the resulting linkdat object still has loops, findLoopBreakers2 is called to break any marriage loops.

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Value

For breakLoops, a linkdat object in which the indicated loop breakers are duplicated. The returned object will also have a non-null loop_breakers entry, namely a matrix with the IDs of the original loop breakers in the first column and the duplicates in the second.

For tieLoops, a linkdat object in which any duplicated individuals (as given in the x\$loop_breakers entry) are merged. For any linkdat object x, the call tieLoops(breakLoops(x)) should return x.

For pedigreeLoops, a list containing all inbreeding loops (not marriage loops) found in the pedigree. Each loop is represented as a list with elements 'top', a 'bottom' individual, 'pathA' (individuals forming a path from top to bottom) and 'pathB' (creating a different path from top to bottom, with no individuals in common with pathA). Note that the number of loops reported here counts all closed paths in the pedigree and will in general be larger than the genus of the underlying graph.

For findLoopBreakers and findLoopBreakers2, a numeric vector of individual ID's.

Examples

```
x = cousinsPed(1, child=TRUE)
# Make the child affected, and homozygous for rare allele.
x = swapAff(x, 9)
x = setMarkers(x, marker(x, 9, c(2,2), alleles=1:2, afreq=c(0.99, 0.01)))
# Compute the LOD score under a recessive model. Loops are automatically broken in lod().
x = setModel(x, 2)
LOD1 = lod(x, theta=0.1)
stopifnot(round(LOD1, 2) == 0.88)
# Or we can break the loop manually before computing the LOD:
loopfree = breakLoops(x, loop_breaker=8)
plot(loopfree)
LOD2 = lod(loopfree, theta=0.1)
stopifnot(all.equal(x, tieLoops(loopfree)))
stopifnot(all.equal(LOD1, LOD2))
# Pedigree with marriage loop: Double first cousins
if(requireNamespace("igraph", quietly = TRUE)) {
    y = doubleCousins(1, 1, child=TRUE)
    findLoopBreakers(y) # --> 9
    findLoopBreakers2(y) # --> 9 and 4
    breakLoops(y) # uses both 9 and 4
}
```

pedModify

Modify the pedigree of 'linkdat' objects

Description

Functions to modify the pedigree of a 'linkdat' object.

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Usage

```
swapSex(x, ids, verbose = TRUE)
swapAff(x, ids, newval = NULL)
addOffspring(
 х,
 father,
 mother,
 noffs,
 ids = NULL,
 sex = 1,
 aff = 1,
 verbose = TRUE
)
addSon(x, parent, id = NULL, aff = 1, verbose = TRUE)
addDaughter(x, parent, id = NULL, aff = 1, verbose = TRUE)
addParents(x, id, father, mother, verbose = TRUE)
removeIndividuals(x, ids, verbose = TRUE)
branch(x, id)
trim(x, keep = c("available", "affected"), return.ids = FALSE, verbose = TRUE)
relabel(x, new, old)
```

Arguments

x	A linkdat object
verbose	A logical: Verbose output or not.
newval	A numeric, indicating affection status values for the ids individuals: 1=unaffected, 2=affected, 0=unknown. If NULL, the affection statuses are swapped 1 <-> 2, hence the main use of the newval argument is to assign 0's.
father, mother	Integers indicating the IDs of parents. If missing, a new founder individual is created (whose ID will be 1+the largest ID already in the pedigree).
noffs	A single integer indicating the number of offspring to be created.
sex, aff	Integer vectors indicating the gender and affection statuses of the offspring to be created (recycled if less than noffs elements).
parent	Integer ID of any pedigree member, which will be the father or mother (depending on its gender) of the new child.
id, ids	Individual ID label(s). In addOffspring the (optional) ids argument is used to specify ID labels for the offspring to be created.

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keep	A character, either 'available' (trimming the pedigree for unavailable members) or 'affected' (trimming for unaffected members).
return.ids	A logical. If FALSE, the trimmed pedigree is returned as a new linkdat object. If TRUE, a vector containing the IDs of 'removable' individuals is returned
new	a numeric containing new labels to replace those in old.
old	a numeric containing ID labels to be replaced by those in new. If missing, old is set to x\$orig.ids, i.e. all members in their original order.

Details

When removing an individual, all descendants are also removed as well as founders remaining without offspring.

The branch() function extracts the pedigree subset consisting of all descendants of id, including id itself and all relevant spouses.

Value

The modified linkdat object.

See Also

```
linkdat, nuclearPed
```

```
x = linkdat(toyped)
# To see the effect of each command below, use plot(x) in between.
x = addParents(x, id=2, father=5, mother=6)

x = swapSex(x, c(1,5))
x = swapSex(x, c(2,6))

x = addOffspring(x, mother=6, noffs=2, id=c(7,10))
x = removeIndividuals(x, 3)
x = swapAff(x, c(4,10))

stopifnot(setequal(x$orig.ids, c(1,2,4,5,6,7,10,11)))
# Trimming a pedigree
x = linkdat(dominant)
x_affectedOnly = trim(x, keep='affected')

unavail = trim(x, keep='available', return.ids=TRUE)
nonaff = trim(x, keep='affected', return.ids=TRUE)
stopifnot(setequal(unavail, c(5, 19:23)), setequal(nonaff, c(6:7, 12:13, 19:23)))
```

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pedParts

Pedigree subsets

Description

Utility functions for 'linkdat' objects, mainly for extracting various pedigree information.

Usage

```
offspring(x, id, original.id = TRUE)
spouses(x, id, original.id = TRUE)
related.pairs(
 Х,
 relation = c("parents", "siblings", "grandparents", "nephews_nieces", "cousins",
    "spouses", "unrelated"),
  available = F,
  interfam = c("none", "founders", "all"),
)
unrelated(x, id, original.id = TRUE)
leaves(x)
parents(x, id, original.id = TRUE)
grandparents(x, id, degree = 2, original.id = TRUE)
siblings(x, id, half = NA, original.id = TRUE)
cousins(x, id, degree = 1, removal = 0, half = NA, original.id = TRUE)
nephews_nieces(x, id, removal = 1, half = NA, original.id = TRUE)
ancestors(x, id)
descendants(x, id, original.id = TRUE)
```

Arguments

x a linkdat object. In related pairs possibly a list of linkdat objects.

id a numerical ID label.

original.id a logical indicating whether 'id' refers to the original ID label or the internal labeling.

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 $relation \hspace{1cm} one of the words \hspace{0.5cm} (possibly \hspace{0.5cm} truncated) \hspace{0.5cm} parents, \hspace{0.5cm} siblings, \hspace{0.5cm} grandparents, \hspace{0.5cm} nephews_nieces, \hspace{0.5cm} and \hspace{0.5cm} parents, \hspace{0.5cm} and \hspace{$

cousins, spouses, unrelated.

available a logical, if TRUE only pairs of available individuals are returned.

interfam one of the words (possibly truncated) none, founders or all, specifying which

interfamiliar pairs should be included as unrelated in the case where x is a list of several pedigrees. If none, only intrafamiliar pairs are considered; if founders all interfamiliar pairs of (available) founders are included; if all, all interfamil-

iar (available) pairs are included.

... further parameters

degree a non-negative integer.

half a logical or NA. If TRUE (resp FALSE), only half (resp. full) siblings/cousins/nephews/nieces

are returned. If NA, both categories are included.

removal a non-negative integer

Value

For ancestors(x,id), a vector containing the ID's of all ancestors of the individual id. For descendants(x,id), a vector containing the ID's of all descendants (i.e. children, grandchildren, a.s.o.) of individual id.

The functions cousins, grandparents, nephews_nieces, offspring, parents, siblings, spouses, unrelated, each returns an integer vector containing the ID's of all pedigree members having the specified relationship with id.

For related pairs a matrix with two columns. Each row gives of a pair of pedigree members with the specified relation. If the input is a list of multiple pedigrees, the matrix entries are characters of the form 'X-Y' where X is the family ID and Y the individual ID of the person.

For leaves, a vector of IDs containing all pedigree members without children.

```
p = cbind(ID=2:9, FID=c(0,0,2,0,4,4,0,2), MID=c(0,0,3,0,5,5,0,8),
        SEX=c(1,2,1,2,1,2,2,2), AFF=c(2,1,2,1,2,1,1,2))
x = linkdat(p)
stopifnot(setequal(spouses(x, 2), c(3,8)),
          setequal(offspring(x, 2), c(4,9)),
          setequal(descendants(x, 2), c(4,6,7,9)),
          setequal(leaves(x), c(6,7,9)))
# Creating a loop and detecting it with 'pedigreeLoops'
# (note that we get two loops, one for each inbred child):
loopx = addOffspring(x, father=4, mother=9, noffs=2)
lps = pedigreeLoops(loopx)
stopifnot(lps[[1]]$top == 2, setequal(sapply(lps, '[[', 'bottom'), 10:11))
# We add genotypes for a single SNP marker and compute a LOD score under a dominant model.
loopx = setMarkers(loopx, cbind(1,c(2,1,2,1,2,1,1,2,1,1)))
loopx = setModel(loopx, 1)
# Loops are automatically broken in lod():
```

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```
LOD1 = lod(loopx, theta=0.1)
stopifnot(round(LOD1, 3) == 1.746)

# Or we can break the loop manually before computing the LOD:
loopfree = breakLoops(loopx, loop_breaker=4)
LOD2 = lod(loopfree, theta=0.1)
stopifnot(all.equal(loopx, tieLoops(loopfree)))
stopifnot(all.equal(LOD1, LOD2))
```

plot.linkdat

Plot pedigrees with genotypes

Description

This is the main function for pedigree plotting, with many options for controlling the appearance of pedigree symbols, labels and marker genotypes. Most of the work is done by the plotting functionality in the 'kinship2' package.

Usage

```
## S3 method for class 'linkdat'
plot(
  Х,
 marker = NULL,
  alleles = NULL,
  sep = "/",
 missing = "-",
  skip.empty.genotypes = FALSE,
  id.labels = NULL,
  title = NULL,
  available = FALSE,
  col = 1,
  deceased = numeric(0),
  starred = numeric(0),
  aff2 = NULL,
 margins = c(0.6, 1, 4.1, 1),
)
## S3 method for class 'singleton'
plot(
  Х,
 marker = NULL,
  alleles = NULL,
  sep = "/",
 missing = "-",
  skip.empty.genotypes = FALSE,
```

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```
id.labels = NULL,
title = NULL,
available = FALSE,
col = 1,
deceased = numeric(0),
starred = numeric(0),
aff2 = NULL,
margins = c(8, 0, 0, 0),
...
)
```

Arguments

x a linkdat object.

marker either NULL, a vector of positive integers, a marker object, or a list of marker

objects. If NULL, no genotypes are plotted. If a marker object (or a list of such), the genotypes are written below each individual in the pedigree, in the format determined by alleles, sep and missing. If a vector of integers is given, the

corresponding marker objects are extracted from x\$markerdata.

alleles a character vector with allele names.

sep a character of length 1 separating alleles for diploid markers.

missing the symbol (integer or character) for missing alleles.

skip.empty.genotypes

a logical. If TRUE, and marker is non-NULL, empty genotypes (which by

default looks like '-/-') are not printed.

id.labels a vector with labels for each pedigree member. This defaults to x\$plot.labels

is this is set (see setPlotLabels), otherwise to as.character(x\$orig.ids).

title the plot title. If NULL or ", no title is added to the plot.

available either a logical, a colour name, or the word 'shaded'. If a colour name is

given, the available individuals (as defined by x\$available) are plotted in this colour. If available=F no colouring is used, while (for backwards compatibility) available=T is equivalent to available='red'. The 'shaded' option

results in diagonal shading.

col a vector with colour indicators for the pedigree members. Recycled if necessary.

By default everyone is drawn black.

deceased a numeric containing ID's of deceased pedigree members.

starred a numeric containing ID's of pedigree members that should be marked with a

star in the pedigree plot.

aff2 NULL, or a numeric with affection statuses (2=affected, 1=unaffected, 0=un-

known) for a second trait.

margins a numeric of length 4 indicating the plot margins. For singletons only the first

element (the 'bottom' margin) is used.

... arguments passed on to plot.pedigree in the kinship2 package. In particular

symbolsize and cex can be useful.

plotPedList 53

Details

plot.linkdat is in essence a wrapper for 'plot.pedigree()' in the kinship2 package.

Author(s)

Magnus Dehli Vigeland, Guro Doerum

See Also

```
plot.pedigree, setPlotLabels
```

Examples

```
data(toyped)
x = linkdat(toyped)
plot(x, marker=1, alleles=c('a1','a2'), sep=' | ', deceased=2)

y = singleton(id=1)
m = marker(y, 1, c('A',0), alleles=c('A','B'))
plot(y, marker=m, id='indiv 1', title='Singleton', available=TRUE)
```

plotPedList

Plot a list of pedigrees.

Description

This function creates a row of pedigree plots, each created by plot.linkdat. Each parameter accepted by plot.linkdat can be applied here. Some effort is made to guess a reasonable window size and margins, but in general the user must be prepared to do manual resizing of the plot window.

Usage

```
plotPedList(
  plot.arg.list,
  widths = NA,
  frames = TRUE,
  frametitles = NULL,
  fmar = NA,
  newdev = FALSE,
  dev.height = NA,
  dev.width = NA,
  ...
)
```

54 plotPedList

Arguments

plot.arg.list A list of lists. Each element of plot.arg.list is a list, where the first element

is the linkdat object to be plotted, and the remaining elements are passed on to plot.linkdat. These elements must be correctly named. See examples below.

widths A numeric vector of relative widths of the subplots. Recycled to length(plot.arg.list)

if necessary, before passed on to layout. Note that the vector does not need to

sum to 1.

frames Either a single logical (FALSE = no frames; TRUE = automatic framing) or a list

of numeric vectors: Each vector must consist of consecutive integers, indicating subplots to be framed together. By default the framing follows the list structure

of plot.arg.list.

frametitles A character vector of titles for each frame. If this is non-NULL, titles for indi-

viduals subplots are ignored.

fmar A single number in the interval [0,0.5) controlling the position of the frames.

newdev A logical, indicating if a new plot window should be opened.

dev.height, dev.width

The dimensions of the new device (only relevant if newdev is TRUE). If these

are NA suitable values are guessed from the pedigree sizes.

Further arguments passed on to each call to plot.linkdat.

Details

See various examples in the Examples section below.

Note that for tweaking dev.height and dev.width the function dev.size is useful to determine the size of the active device.

See Also

```
plot.linkdat
```

```
# Simplest use: Just give a list of linkdat objects.
# To guess suitable plot window dimensions, use 'newdev=T'
peds = list(nuclearPed(3),cousinPed(2), singleton(12), halfCousinsPed(0))
plotPedList(peds) # try with newdev=TRUE

## Not run:
# Modify the relative widths (which are not guessed)
widths = c(2, 3, 1, 2)
plotPedList(peds, widths=widths)

# In most cases the guessed dimensions are not perfect.
# Resize plot window manually, and then plot again with newdev=F (default)
# plotPedList(peds, widths=widths)

## Remove frames
```

randomPed 55

```
plotPedList(peds, widths=widths, frames=F)
# Non-default frames
frames = list(1, 2:3)
plotPedList(peds, widths=widths, frames=frames, frametitles=c('First', 'Second'))
# To give *the same* parameter to all plots, it can just be added at the end:
margins=c(2,4,2,4)
title='Same title'
id.labels=''
symbolsize=1.5 # note: doesn't work as expected for singletons
plotPedList(peds, widths=widths, frames=frames, margins=margins, title=title,
            id.labels=id.labels, symbolsize=symbolsize)
# For more control of individual plots, each plot and all its parameters
# can be specified in its own list:
x1 = nuclearPed(3)
x1$available = 3:5
m1 = marker(x1, 3, 1:2)
marg1 = c(5,4,5,4)
plot1 = list(x1, marker=m1, margins=marg1, title='Plot 1', deceased=1:2)
x2 = cousinsPed(2)
x2$available = leaves(x2)
m2 = marker(x2, leaves(x2), 'A')
marg2 = c(3,4,2,4)
plot2 = list(x2, marker=m2, margins=marg2, title='Plot 2', symbolsize=1.2,
             skip.empty.genotypes=T)
x3 = singleton(12)
x3 = setAvailable(x3, 12)
marg3 = c(10,0,0,0)
plot3 = list(x3, margins=marg3, title='Plot 3', available='shaded', symbolsize=2)
x4 = halfCousinsPed(0)
names4 = c(Father=1, Brother=3, Sister=5)
marg4 = marg1
plot4 = list(x4, margins=marg4, title='Plot 4', id.labels=names4)
plotPedList(list(plot1, plot2, plot3, plot4), widths=c(2,3,1,2),
            frames=list(1,2:3,4), available=T, newdev=T)
# Different example:
plotPedList(list(halfCousinPed(4), cousinsPed(7)), title='Many generations',
    new=T, dev.height=9, dev.width=9)
## End(Not run)
```

56 randomPed

Description

Creates a random medical pedigree with specified number of generations.

Usage

```
randomPed(
  gen,
  lambda = 2,
  penetrances = c(0, 1, 1),
  naff = "last.gen",
  founder.mut = 1
)
```

Arguments

gen an integer in the interval [2,5] indicating the number of generations.

lambda a positive numeric. For each descendant of the first generation, the number of

offspring is sampled from a Poisson distribution with parameter lambda.

penetrances a numeric of length 3, as in setModel.

naff an integer specifying a lower bound on the number of affected individuals, or

the character 'last.gen'. The latter produce a pedigree where at least one in the

youngest generation is affected.

founder.mut an integer, the number of disease alleles to be distributed among the founders.

Details

The function produces a random simple pedigree. Each founder is given at most one disease allele. At least one of the two top founders carries a disease allele.

Value

A linkdat object.

See Also

linkdat

```
plot(randomPed(3))
# gives error message: Not enough founder mutations
## Not run:
randomPed(gen=4, penetrances=c(0,0,1), naff=2, founder.mut=1)
## End(Not run)
```

readDatfile 57

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Read dat file in LINKAGE format

Description

Converts dat files in LINKAGE format to dat/map/freq files in MERLIN format

Usage

```
readDatfile(datfile, chrom, comment_string = "<<", write_to = NULL)</pre>
```

Arguments

datfile character. The path to the dat file.

chrom integer chromosome number (needed to create the MERLIN map).

comment_string character indicating comments (which are removed before processing).

write_to a character prefix used for naming the output files, or NULL if no files should

be written.

Value

If write_to is NULL, a list of data.frames named dat, map and freq.

Examples

```
# No example given.
```

relatednessCoeff

Relatedness coefficients

Description

Computes inbreeding coefficients for all pedigree members, and Jacquard's condensed identity coefficients for any pair of members. These are simple wrappers for functions in other packages or external programs.

Usage

```
inbreeding(x)
kinship_coefs(x, ids = NULL)
jacquard(x, ids)
jacquard2(x, ids, verbose = FALSE, cleanup = TRUE)
```

58 relatednessCoeff

Arguments

x a linkdat object.

ids a integer vector of length 2.

verbose a logical, indicating if messages from IdCoefs should be printed.

cleanup a logical: If TRUE, the pedfile and sample file created for the IdCoefs run are

deleted automatically.

Details

Both inbreeding and kinship_coefs are thin wrappers of kinship. jacquard2, executes an external call to the C program IdCoefs (Abney, 2009). For this to function, IdCoefs must be installed on the computer (see link in the References section below) and the executable placed in a folder included in the PATH variable. The jacquard2 wrapper works by writing the necessary files to disk and calling IdCoefs via system.

Value

For inbreeding, a numerical vector with the inbreeding coefficients, with names according to the ID labels x\$orig.ids.

For kinship_coefs, either a single numeric (if ids is a pair of pedigree members) or the whole kinship matrix, with x\$orig.ids as dimnames.

For jaquard and jaquard2, a numerical vector of length 9 (in the standard order of Jacquard's condensed identity coefficients).

References

The IdCoefs program: Abney, Mark (2009). A graphical algorithm for fast computation of identity coefficients and generalized kinship coefficients. Bioinformatics, 25, 1561-1563. http://home.uchicago.edu/~abney/abney_web/Software.html

See Also

kinship

```
# Offspring of first cousins
x = cousinsPed(1, child=TRUE)
inb = inbreeding(x)
stopifnot(inb[9] == 1/16)

# if ID labels are not 1:9, care must be taken in extracting correct elements.
set.seed(1357)
y = relabel(x, sample(1:9))
child = leaves(y)
inbreeding(y)[child] #wrong
inb = inbreeding(y)[as.character(child)] #correct
inb
# the inbreeding coeff of the child equals the kinship coeff of parents
```

relationLR 59

```
kin = kinship_coefs(y, parents(y, child))
stopifnot(inb==kin, inb==1/16)
```

relationLR

Relationship Likelihood Ratio

Description

Computes likelihood for two pedigrees and their ratio, the likelihood ratio (LR).

Usage

```
relationLR(
  ped_numerator,
  ped_denominator,
  ids,
  alleles,
  afreq = NULL,
  known_genotypes = list(),
  loop_breakers = NULL,
  Xchrom = FALSE,
  plot = TRUE,
  title1 = "",
  title2 = ""
)
```

Arguments

ped_numerator

a linkdat object, or a list of several linkdat and/or singleton objects, describing the relationship corresponding to the hypothesis H1 (numerator). If a list, the sets of ID labels must be disjoint, that is, all ID labels must be unique.

ped_denominator

a linkdat object, or a list of several linkdat and/or singleton objects, describing the relationship corresponding to the hypothesis H2 (denominator). ID labels must be consistent with ped_claim.

ids genotyped individuals.

alleles a numeric or character vector containing marker alleles names

afreq a numerical vector with allele frequencies. An error is given if they don't sum

to 1 (rounded to 3 decimals).

known_genotypes

list of triplets (a, b, c), indicating that individual a has genotype b/c. Missing

value is 0.

loop_breakers Not yet implemented, only default value NULL currently handled

Xchrom a logical: Is the marker on the X chromosome?

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plot	either a logical or the character 'plot_only', controlling if a plot should be produced. If 'plot_only', a plot is drawn, but no further computations are done.
title1	a character, title of leftmost plot.
title2	a character, title of rightmost plot.

Details

This function computes the likelihood of two pedigrees (each corresponding to a hypothesis describing a family relationship). The likelihood ratio is also reported. Unlike other implementations we are aware of, partial DNA profiles are allowed here. For instance, if the genotype of a person is reported as 1/0 (0 is 'missing') for a triallelic marker with uniform allele frequencies, the possible ordered genotypes (1,1), (2,1), (1,2), (1,3) and (3,1) are treated as equally likely. (For general allele frequencies, genotype probabilities are obtained by assuming Hardy-Weinberg equilibrium.) A reasonable future extension would be to allow the user to weigh these genotypes; typically (1,1) may be more likely than the others. If plot='plot_only', the function returns NULL after producing the plot.

Value

```
lik.numerator likelihood of data given ped_numerator
lik.denominator likelihood of data given ped_denominator
LR likelihood ratio lik.numerator/lik.denominator
```

Author(s)

Thore Egeland, Magnus Dehli Vigeland

See Also

exclusionPower

```
# A partial DNA profile is obtained from the person
# denoted 4 in the figure produced below
# There are two possibilities:
# H1: 4 is the missing relative of 3 and 6 (as shown to the left) or
# H2: 4 is unrelated to 3 and 6.
p = c(0.2, 0.8)
alleles = 1:length(p)
g3 = c(1,1); g4 = c(1,0); g6 = c(2,2)
x1 = nuclearPed(2)
x1 = addOffspring(x1, father = 4, sex = 1, noff = 1)
m = marker(x1, 3, g3, 4, g4, 6, g6, alleles = alleles, afreq = p)
x1 = addMarker(x1, m)
x2 = nuclearPed(2)
x2 = addOffspring(x2, father = 4, sex = 1, noff = 1)
```

setAvailable 61

setAvailable

Functions for modifying availability vectors

Description

Functions to set and modify the availability vector of a 'linkdat' object. This vector is used in 'linkage.power' and 'linkageSim', indicating for whom genotypes should be simulated.

Usage

```
setAvailable(x, available)
swapAvailable(x, ids)
```

Arguments

```
    a linkdat object
    available a numeric containing the IDs of available individuals.
    ids the individual(s) whose availability status should be swapped.
```

Value

The modified linkdat object.

See Also

```
plot.linkdat, linkage.power, linkageSim
```

62 setModel

Examples

```
data(toyped)
x = linkdat(toyped)
x = setAvailable(x, 3:4)
x = swapAvailable(x, 2:3)
x$available
```

setModel

Set, change or display the model parameters for 'linkdat' objects

Description

Functions to set, change and display model parameters involved in parametric linkage analysis.

Usage

```
setModel(x, model = NULL, chrom = NULL, penetrances = NULL, dfreq = NULL)
## S3 method for class 'linkdat.model'
print(x, ...)
```

Arguments

X	in setModel: a linkdat object. In print.linkdat.model: a linkdat.model object.
model	NULL, or an object of class linkdat.model, namely a list with elements chrom, penetrances and dfreq. In the setModel function, the model argument can be one of the integers 1-4, with the following meanings:
	1 = autosomal dominant; fully penetrant, dfreq=1e-5
	2 = autosomal recessive; fully penetrant, dfreq=1e-5
	3 = X-linked dominant; fully penetrant, dfreq=1e-5
	4 = X-linked recessive; fully penetrant, dfreq=1e-5
chrom	a character, either 'AUTOSOMAL' or 'X'. Lower case versions are allowed and will be converted automatically.
penetrances	if chrom=='AUTOSOMAL': a numeric of length 3 - (f0, f1, f2) - where fi is the probability of being affected given i disease alleles.
	If chrom=='X': a list of two vectors, containing the penetrances for each sex: penetrances = list(male=c(f0, f1), female=c(f0, f1, f2)).

Value

dfreq

. . .

setModel returns a new linkdat object, whose model entry is a linkdat.model object: A list containing the given chrom, penetrances and dfreq.

the population frequency of the disease allele.

further parameters

setPlotLabels 63

See Also

linkdat

Examples

setPlotLabels

Attach plot labels to a linkdat object

Description

This function attaches (or modifies) a character vector of plotting labels for the pedigree members of a linkdat object. This is useful since only numerical ID's are allowed in defining pedigrees in paramlink.

Usage

```
setPlotLabels(x, labels, ids = x$orig.ids)
```

Arguments

x A linkdat object.

labels A character vector of the same length as ids.

ids A numeric vector of numerical IDs. Must be a subset of x\$orig.ids.

Value

A new linkdat object, differing from x only in x\$plot.labels.

showInTriangle

See Also

```
plot.linkdat
```

Examples

```
x = nuclearPed(1)
x = setPlotLabels(x, labels=c('Father', 'Mother', 'Son'))
plot(x)
```

showInTriangle

Add points to the IBD triangle

Description

Utility function for plotting points in the IBD triangle.

Usage

```
showInTriangle(
  k0,
  k2 = NULL,
  new = T,
  col = "blue",
  cex = 1,
  pch = 4,
  lwd = 2,
  labels = NULL,
  col_labels = col,
  cex_labels = 0.8,
  pos = 1,
  adj = NULL,
  ...
)
```

Arguments

```
k0, k2 Numerical vectors giving coordinates for points to be plotted in the IBDtriangle.

new Logical indicating if a new IBDtriangle should be drawn.

col, cex, pch, lwd

Parameters passed onto points.

labels A character of same length as k0, or NULL.

col_labels, cex_labels, pos, adj

Parameters passed onto text (if labels is non-NULL).

... Plot arguments passed on to IBDtriangle.
```

simpleSim 65

See Also

```
IBDtriangle, examineKinships
```

Examples

```
showInTriangle(k0=3/8, k2=1/8, label="3/4 siblings", pos=1)
```

simpleSim

Unconditional marker simulation

Description

Unconditional simulation of unlinked markers

a logical.

Usage

```
simpleSim(
    X,
    N,
    alleles,
    afreq,
    available,
    Xchrom = FALSE,
    mutmat = NULL,
    seed = NULL,
    verbose = T
)
```

Arguments

verbose

x	a linkdat object
N	a positive integer: the number of markers to be simulated
alleles	a vector containing the allele names. If missing, the alleles are taken to be $seq_along(afreq)$.
afreq	a vector of length 2 containing the population frequencies for the alleles. If missing, the alleles are assumed equifrequent.
available	a vector containing IDs of the available individuals, i.e. those whose genotypes should be simulated.
Xchrom	a logical: X linked markers or not?
mutmat	a mutation matrix, or a list of two such matrices named 'female' and 'male'. The matrix/matrices must be square, with the allele labels as dimnames, and each row must sum to 1 (after rounding to 3 decimals).
seed	NULL, or a numeric seed for the random number generator.

66 toyped

Details

This simulation is done by distributing alleles randomly to all founders, followed by unconditional gene dropping down throughout the pedigree (i.e. for each non-founder a random allele is selected from each of the parents). Finally the genotypes of any individuals not included in available are removed.

Value

a linkdat object equal to x in all respects except its markerdata entry, which consists of the N simulated markers.

See Also

```
markerSim, linkageSim
```

Examples

```
x = nuclearPed(1)
simpleSim(x, N=3, afreq=c(0.5, 0.5))

y = addOffspring(cousinPed(1), father=7, mother=8, noffs=1)
simpleSim(y, N=3, alleles=LETTERS[1:10])
```

toyped

Toy pedigree for linkage analysis

Description

Toy pedigree with 4 individuals typed at a single SNP marker. Individual 1 is missing one allele.

Usage

toyped

Format

A data frame with 4 rows and 8 columns

Details

The format is standard LINKAGE (pre-makeped) format, with columns as follows:

- FAMID. Family ID
- ID. Individual ID
- FID. Father ID
- MID. Mother ID

transferMarkerdata 67

- SEX. Gender (male=1, female=2)
- AFF. Affection status (unaffected=1, affected=2, unknown=0)
- M_A1. First allele of marker 1
- M_A2. Second allele of marker 1

Examples

```
toyped
linkdat(toyped)
```

transferMarkerdata

Transfer marker data

Description

Transfer marker data between pedigrees (in the form of linkdat objects). Both the source and target can be lists of linkdat and/or singleton objects (these must have disjoint ID sets). Any previous marker data of the target is overwritten.

Usage

```
transferMarkerdata(from, to)
```

Arguments

```
from a linkdat or singleton object, or a list of such objects.

to a linkdat or singleton object, or a list of such objects.
```

Value

A linkdat object (or a list of such) similar to to, but where all individuals also present in from have marker genotypes copied over. Any previous marker data is erased.

See Also

linkdat

```
x = list(singleton(id=5), nuclearPed(noffs=2))
x = markerSim(x, N=5, alleles=1:5, verbose=FALSE, available=4:5)
y = nuclearPed(noffs=3)
y = transferMarkerdata(x, y)
stopifnot(all.equal(x[[1]], branch(y,5)))
stopifnot(all.equal(x[[2]], subset(y,1:4)))
```

68 twoMarkerDistribution

twoloops

A consanguineous pedigree

Description

A consanguineous pedigree with two inbreeding loops.

Usage

twoloops

Format

A data frame with 17 rows and 6 columns. See toyped for details about the format.

Examples

```
x = linkdat(twoloops)
plot(x)
```

twoMarkerDistribution Genotype probability distribution

Description

Computes the joint genotype distribution of two markers for a specified pedigree member, conditional on existing genotypes and pedigree information.

Usage

```
twoMarkerDistribution(
    X,
    id,
    partialmarker1,
    partialmarker2,
    theta,
    loop_breakers = NULL,
    eliminate = 99,
    verbose = TRUE
)
```

Xped 69

Arguments

X	A linkdat object.
id	The individual in question.
partialmarker1, partialmarker2	
	Either a single integer indicating the number of one of x's existing markers, or a marker object.
theta	A single numeric in the interval $[0, 0.5]$ - the recombination fraction between the two markers.
loop_breakers	A numeric containing IDs of individuals to be used as loop breakers. Relevant only if the pedigree has loops. See breakLoops.
eliminate	A non-negative integer, indicating the number of iterations in the internal genotype-compatibility algorithm. Positive values can save time if partialmarker is non-empty and the number of alleles is large.

Value

verbose

A named matrix giving the joint genotype distribution.

A logical.

See Also

```
oneMarkerDistribution
```

Examples

```
x = nuclearPed(2)
emptySNP = marker(x, alleles=c('a','b'))
SNP1 = marker(x, 1, c(1,1), 2, c(1,0), alleles=1:2, afreq=c(0.1, 0.9))
twoMarkerDistribution(x, id=2, emptySNP, SNP1, theta=0)
twoMarkerDistribution(x, id=2, emptySNP, SNP1, theta=0.5)
twoMarkerDistribution(x, id=3, emptySNP, SNP1, theta=0.5)

# X-linked example
SNPX_1 = marker(x, 2, c('a','b'), 3, 'b', alleles=c('a','b'), chrom=23)
SNPX_2 = marker(x, 2, c('a','b'), 3, 'b', alleles=c('a','b'), chrom=23)
r1 = twoMarkerDistribution(x, id=4, SNPX_1, SNPX_2, theta=0)
r2 = twoMarkerDistribution(x, id=4, SNPX_1, SNPX_2, theta=0.5)
stopifnot(all(r1==c(.5,0,0,.5)), all(r2==c(.25,.25,.25,.25)))
```

Xped

Example pedigree with X-linked disease pattern.

Description

A complex pedigree with an X-linked recessive disease pattern

70 Xped

Usage

Xped

Format

A data frame with 15 rows and 6 columns. See toyped for details about the format.

Details

The format is standard LINKAGE (pre-makeped) format.

```
Xped
```

```
# Convert to a 'linkdat' object and set a recessive X-linked model: x = linkdat(Xped, model=4) summary(x)
```

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