## Package 'rNeighborQTL'

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Title Interval Mapping for Quantitative Trait Loci Underlying Neighbor Effects

Version 1.1.0

**Description** To enable quantitative trait loci mapping of neighbor effects, this package extends a single-marker regression to interval mapping. The theoretical background of the method is described in Sato et al. (2020) <doi:10.1101/2020.05.20.089474>.

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## calc\_neiprob

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calc\_neiprob Calculating a set of neighbor QTL effects from conditional genotype probabilities

## Description

A function to calculate self QTL effects for all individuals, with given deviation coefficients and conditional genotype probabilities.

## Usage

```
calc_neiprob(
  genoprobs,
  a2,
  d2,
  contrasts = NULL,
  smap,
  scale,
  grouping = rep(1, nrow(smap)),
  d2sq0 = FALSE
)
```

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
a2	A numeric scalar indicating additive deviation.
d2	A numeric scalar indicating dominance deviation.
contrasts	A vector composed of three TRUE/FALSE values, which represents the pres- ence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE, TRUE/FALSE) = AA, AB, BB.
smap	A matrix showing a spatial map for individuals. The first and second column include spatial positions along an x-axis and y-axis, respectively.
scale	A numeric scalar indicating the maximum spatial distance between a focal indi- vidual and neighbors to define neighbor effects.

## calc\_pve

grouping	An integer vector assigning each individual to a group. This argument can
	be used when smap contains different experimental replicates. Default setting
	means that all individuals are belong to a single group.
d2sq0	An option to make AB/AB interaction effects zero.

#### Value

A numeric matrix containing individuals x marker elements for neighbor QTL effects.

## Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

calc\_pve

Calculating phenotypic variation explained by neighbor effects

#### Description

A function to calculate the proportion or ratio of phenotypic variation explained (PVE or RVE) by neighbor effects for a series of neighbor distance (s\_seq) using mixed models.

## Usage

```
calc_pve(
  genoprobs,
  pheno,
  smap,
  s_seq,
  addcovar = NULL,
  grouping = rep(1, nrow(smap)),
  response = c("quantitative", "binary"),
  fig = TRUE,
  contrasts = NULL
)
```

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
pheno	A vector of individual phenotypes.
smap	A matrix showing a spatial map for individuals. The first and second column include spatial positions along an x-axis and y-axis, respectively.
s_seq	A numeric vector including a set of the maximum spatial distance between a fo- cal individual and neighbors to define neighbor effects. A scalar is also allowed.
addcovar	An optional matrix including additional non-genetic covariates. It contains no. of individuals x no. of covariates.

grouping	An optional integer vector assigning each individual to a group. This argument can be used when smap contains different experimental replicates. Default set- ting means that all individuals are belong to a single group.
response	An optional argument to select trait types. The "quantitative" or "binary" applies the "lmm.aireml()" or "logistic.mm.aireml()" for a mixed model, respectively.
fig	TRUE/FALSE to add a figure of Delta PVE or not.
contrasts	An optional vector composed of three TRUE/FALSE values, which represents the presence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE, TRUE/FALSE) = AA, AB, BB. If NULL, it is compiled from genoprobs automatically.

#### Details

This function calls linear or logistic mixed models via the gaston package (Perdry & Dandine-Roulland 2020). If "binary" is selected, Var\_nei in the output is given by the proportion of phenotypic variation explained (PVE) by neighbor effects as PVEnei  $=\sigma_2^2/(\sigma_1^2 + \sigma_2^2 + \sigma_e^2)$ . If "binary" is selected, Var\_nei is given by the ratio of phenotypic variation explained (RVE) by neighbor effects as RVEnei  $=\sigma_2^2/\sigma_1^2$  and p-values are not available. This is because a logistic mixed model logistic.mm.airem1() called via the gaston package does not provide  $\sigma_e^2$  and log-likelihood (see Chen et al. 2016 for the theory).

#### Value

A matrix containing the maximum neighbor distance, phenotypic variation explained by neighbor effects, and p-value by a likelihood ratio test.

- · scale Maximum neighbor distance given as an argument
- Var\_nei Proportion or ratio of phenotypic variation explained (PVE or RVE) by neighbor effects for linear or logistic mixed models, respectively
- p-value p-value by a likelihood ratio test between models with or without neighbor effects

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

#### References

- Perdry H, Dandine-Roulland C (2019) gaston: Genetic Data Handling (QC, GRM, LD, PCA) & Linear Mixed Models. R package version 1.5.5. https://CRAN.R-project.org/package=gaston
- Chen H, Wang C, Conomos M. et al. (2016) Control for population structure and relatedness for binary traits in genetic association studies via logistic mixed models. The American Journal of Human Genetics 98: 653-666.

#### decompose\_genoprobs

#### Examples

decompose\_genoprobs Decomposition of conditional genotype probabilities

#### Description

A function to decompose qtl's object of conditional genotype probabilities.

#### Usage

```
decompose_genoprobs(genoprobs, contrasts = NULL)
```

## Arguments

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
contrasts	A vector composed of three TRUE/FALSE values, which represents the pres- ence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE, TRUE/FALSE) = AA, AB, BB.

#### Value

A list of three numeric matrices for genotype probabilities AA, AB, and BB. Each contains elements of individuals x markers.

- AA Homozygote AA probabilities.
- AB Heterozygote AB probabilities for. NA if inbred lines
- BB Homozygote BB probabilities. NA if backcross lines

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

eff\_neighbor

#### Description

A function to estimate additive and dominance deviation for self and neighbor QTL effects by a simple regression.

## Usage

```
eff_neighbor(
  genoprobs,
  pheno,
  smap,
  scale,
  addcovar = NULL,
  addQTL = NULL,
  grouping = rep(1, nrow(smap)),
  response = c("quantitative", "binary"),
  fig = TRUE,
  contrasts = NULL
)
```

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
pheno	A vector of individual phenotypes.
smap	A matrix showing a spatial map for individuals. The first and second column include spatial position along an x-axis and y-axis, respectively.
scale	A numeric scalar indicating the maximum spatial distance between a focal indi- vidual and neighbors to define neighbor effects.
addcovar	An optional matrix including additional non-genetic covariates. It contains no. of individuals x no. of covariates.
addQTL	An optional vector containing marker names that are considered covariates. Namely, this option allows composite interval mapping (Jansen 1993).
grouping	An optional integer vector assigning each individual to a group. This argument can be used when smap contains different experimental replicates. Default set- ting means that all individuals are belong to a single group.
response	An optional argument to select trait types. The "quantitative" or "binary" calls the "gaussian" or "binomial" family in glm(), respectively.
fig	TRUE/FALSE to plot the effects or not.
contrasts	An optional vector composed of three TRUE/FALSE values, which represents the presence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE) = AA, AB, BB. If NULL, it is compiled from genoprobs automatically.

#### eff\_neighbor

#### Details

Similar to Haley-Knott regression (Haley & Knott 1992), the additive and dominance deviations are approximated by a regression of trait values on conditional genotype probabilities. The self QTL effects a1 and d1 are estimated in the same way as the qtl package performs the Haley-Knott regression. If contrasts = c(TRUE, TRUE, TRUE), neighbor QTL effects a1 and d1 are estimated using a quadratic regression; otherwise, the additive neighbor effects are estimated using a linear regression. See also Sato, Takeda & Nagano (2020) for the rationale behind the approximation.

#### Value

A matrix of estimated additive and dominance deviation for self and neighbor effects, with the chromosome numbers and positions. The row names correspond to marker names.

- chr Chromosome number
- pos Marker position
- · a1 Additive deviation for self effects
- d1 Dominance deviation for self effects
- a2 Additive deviation for neighbor effects
- · d2 Dominance deviation for neighbor effects

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

#### References

- Haley CS, Knott SA (1992) A simple regression method for mapping quantitative trait loci in line crosses using flanking markers. Heredity 69:315-324.
- Jansen RC (1993) Interval mapping of multiple quantitative trait loci. Genetics 135:205-211.
- Sato Y, Takeda K, Nagano AJ (2020) Neighbor QTL: an interval mapping method for quantitative trait loci underlying neighbor effects. bioRxiv https://doi.org/10.1101/2020.05. 20.089474

#### Examples

genoprobs2selfprobs Calculating a set of self QTL effects from conditional genotype probabilities

## Description

A function to reshape qtl's object of conditional genotype probabilities, and to calculate self QTL effects for all individuals with given deviation coefficients and conditional genotype probabilities.

## Usage

```
genoprobs2selfprobs(genoprobs, a1, d1, contrasts = NULL)
```

## Arguments

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
a1	A numeric scalar indicating additive deviation.
d1	A numeric scalar indicating dominance deviation.
contrasts	A vector composed of three TRUE/FALSE values, which represents the pres- ence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE, TRUE/FALSE) = AA, AB, BB.

## Value

A numeric matrix containing individuals x marker elements for self QTL effects.

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

get\_markers Reshaping marker information

#### Description

A function to get marker information from a genetic map including observed and pseudo markers

#### Usage

```
get_markers(genoprobs)
```

#### Arguments

genoprobs Conditional genotype probabilities as taken from qtl::calc.genoprob().

## int\_neighbor

#### Value

A matrix showing the chromosome numbers (the first column) and positions (the second column) for all markers (row names).

## Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

int\_neighbor

Testing marker-by-marker epistasis in neighbor QTL effects

## Description

A function to test interaction terms between one focal marker and the other markers across a genome.

## Usage

```
int_neighbor(
  genoprobs,
  pheno,
  smap,
  scale,
  addcovar = NULL,
  addQTL,
  intQTL,
  grouping = rep(1, nrow(smap)),
  response = c("quantitative", "binary"),
  contrasts = NULL
)
```

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
pheno	A vector of individual phenotypes.
smap	A matrix showing a spatial map for individuals. The first and second column include spatial positions along an x-axis and y-axis, respectively.
scale	A numeric scalar indicating the maximum spatial distance between a focal indi- vidual and neighbors to define neighbor effects.
addcovar	An optional matrix including additional non-genetic covariates. It contains no. of individuals x no. of covariates.
addQTL	A vector containing marker names that are considered covariates. This argument is necessary for int_neighbor(), and must match the marker names of gmap.
intQTL	A name of a focal marker to be tested for its epistasis with the other markers in neighbor effects. The marker name must be included by addQTL.

grouping	An optional integer vector assigning each individual to a group. This argument can be used when smap contains different experimental replicates. Default set- ting means that all individuals are belong to a single group.
response	An optional argument to select trait types. The "quantitative" or "binary" calls the "gaussian" or "binomial" family in glm(), respectively.
contrasts	An optional vector composed of three TRUE/FALSE values, which represents the presence/absence of specific genotypes as $c(TRUE/FALSE, TRUE/FALSE) = AA$ , AB, BB. If NULL, it is compiled from genoprobs automatically.

#### Details

This is an optimal function to test two-way interactions between the main neighbor effect of a focal marker given by intQTL and the others. All the main neighbor effects are first estimated using eff\_neighbor(), and then a two-way interaction term between the focal marker effect and its counterpart was considered an additional explanatory variable. LOD score was compared between models with or without the two-way interaction.

#### Value

A matrix of LOD scores for neighbor epistasis effects, with the chromosome numbers and positions. The row names correspond to marker names.

- chr Chromosome number
- pos Marker position
- LOD\_int LOD score for epistasis in neighbor effects between a focal and the other markers

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

#### See Also

scan\_neighbor eff\_neighbor

#### Examples

logLik\_glm.fit Calculating log-likelihood in generalized linear models

#### Description

An utility function to extract log-likelihood based on AIC of glm.fit()

#### Usage

```
logLik_glm.fit(...)
```

#### Arguments

. . .

Arguments to be passed to glm.fit().

#### Value

Log-likelihood

min_dist Calculating the minimum distance
---

## Description

A function to calculate a Euclidian distance including at least one neighbor for all individuals.

#### Usage

min\_dist(smap, grouping = rep(1, nrow(smap)))

## Arguments

smap	A matrix showing a spatial map. The first and second column include spatial points along a x-axis and y-axis, respectively.
grouping	A integer vector assigning each individual to a group. This argument can be useful when a "smap" contains different experimental replicates. Default setting means that all individuals are belong to a single group.

## Value

Return a scalar of the minimum Euclidian distance that allows all individuals to have at least one neighbor.

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

neiprob

## Description

A function to calculate neighbor QTL effects between two individuals, with given deviation coefficients and conditional genotype probabilities.

## Usage

neiprob(i, j, a2, d2, AA, AB, BB, d2sq0 = FALSE)

## Arguments

i	ID of a target individual.
j	ID of an interacting neighbor.
a2	A numeric scalar indicating additive deviation.
d2	A numeric scalar indicating dominance deviation.
AA	An individual x marker matrix of conditional probabilities for AA genotype.
AB	An individual x marker matrix of conditional probabilities for AB genotype. Input NA if heterozygotes are absent.
BB	An individual x marker matrix of conditional probabilities for BB genotype. Input NA for backcross lines.
d2sq0	An option to make AB/AB interaction effects zero.

#### Value

A numeric vector containing each marker effect for individual i.

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

perm\_neighbor

Permutation tests for neighbor effects with a QTL model

## Description

A function to calculate a genome-wide LOD threshold using permutation tests for self or neighbor effects.

## perm\_neighbor

## Usage

```
perm_neighbor(
  genoprobs,
  pheno,
  smap,
  scale,
  addcovar = NULL,
  addQTL = NULL,
  intQTL = NULL,
  grouping = rep(1, nrow(smap)),
  response = c("quantitative", "binary"),
  type = c("neighbor", "self", "int"),
  times = 99,
  p_val = 0.05,
  n_core = 1L,
  contrasts = NULL
)
```

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
pheno	A vector of individual phenotypes.
smap	A matrix showing a spatial map for individuals. The first and second column include spatial positions along an x-axis and y-axis, respectively.
scale	A numeric scalar indicating the maximum spatial distance between a focal indi- vidual and neighbors to define neighbor effects.
addcovar	An optional matrix including additional non-genetic covariates. It contains no. of individuals x no. of covariates.
addQTL	An optional vector containing marker names that are considered covariates. Namely, this option allows composite interval mapping (Jansen 1993).
intQTL	An option when using int_neighbor(). A name of a focal marker to be tested for its epistasis with the other markers in neighbor effects. The marker name must be included by addQTL.
grouping	An optional integer vector assigning each individual to a group. This argument can be used when smap contains different experimental replicates. Default set- ting means that all individuals are belong to a single group.
response	An optional argument to select trait types. The "quantitative" or "binary" calls the "gaussian" or "binomial" family in glm(), respectively.
type	Select "self", "neighbor", or "int" to perform permutation tests for self effects, neighbor effects, or neighbor epistasis, respectively.
times	No. of permutation iterations. Default at 99 times
p_val	A vector indicating upper quantiles for permutation LOD scores
n_core	No. of cores for a parallel computation. This does not work for Windows OS. Default is a single-core computation.

```
contrasts An optional vector composed of three TRUE/FALSE values, which represents
the presence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE,
TRUE/FALSE) = AA, AB, BB. If NULL, it is compiled from genoprobs auto-
matically.
```

#### Value

LOD thresholds at given quantiles by p-val

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

#### See Also

plot\_nei scan\_neighbor int\_neighbor

#### Examples

```
plot_eff
```

Plot self and neighbor QTL effects across a genome

## Description

Plot estimated additive and dominance deviation for self or neighbor effects across a genome

#### Usage

plot\_eff(res, type = c("neighbor", "self"))

res	Output results of eff_neighbor().
type	An option to select "self" or "neighbor" effects to be shown. Default is "neighbor".

## plot\_nei

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

## See Also

eff\_neighbor

plot\_nei

Plot LOD score for self or neighbor QTL effects

## Description

Plot LOD curves for a genome scan of self and neighbor QTL effects.

#### Usage

```
plot_nei(res, type = c("neighbor", "self", "int"), chr = NULL, th = NULL, ...)
```

## Arguments

res	Output results of scan_neighbor().
type	Plot "self", "neighbor" or "int" effects. Default is "neighbor" effects.
chr	An optional vector to select chromosome numbers to be plotted. If NULL, shown are all chromosomes.
th	Add genome-wide threshold by user-defined vectors or Bonferroni correction. Default is no thresholds added.
	Arguments to be passed to plot().

#### Details

For the type argument, "int" can be selected to draw the results of int\_neighbor(). In this case, the res object and type must match, otherwise it returns an error message.

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

#### See Also

scan\_neighbor int\_neighbor perm\_neighbor

```
scan_neighbor
```

## Description

Genome scan using a QTL model for self and neighbor effects, with possible allowance for additional covariates and non-normal traits. Theoretical background is described in Sato, Takeda & Nagano (2020).

## Usage

```
scan_neighbor(
  genoprobs,
  pheno,
  smap,
  scale,
  addcovar = NULL,
  addQTL = NULL,
  grouping = rep(1, nrow(smap)),
  response = c("quantitative", "binary"),
  contrasts = NULL
)
```

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
pheno	A vector of individual phenotypes.
smap	A matrix showing a spatial map for individuals. The first and second column include spatial positions along an x-axis and y-axis, respectively.
scale	A numeric scalar indicating the maximum spatial distance between a focal indi- vidual and neighbors to define neighbor effects.
addcovar	An optional matrix including additional non-genetic covariates. It contains no. of individuals x no. of covariates.
addQTL	An optional vector containing marker names that are considered covariates. Namely, this option allows composite interval mapping (Jansen 1993).
grouping	An optional integer vector assigning each individual to a group. This argument can be used when smap contains different experimental replicates. Default set- ting means that all individuals are belong to a single group.
response	An optional argument to select trait types. The "quantitative" or "binary" calls the "gaussian" or "binomial" family in glm(), respectively.
contrasts	An optional vector composed of three TRUE/FALSE values, which represents the presence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE) = AA, AB, BB. If NULL, it is compiled from genoprobs automatically.

#### scan\_neighbor

#### Details

This function calculates LOD score after the additive and dominance deviation are estimated using eff\_neighbor(). As it adopts a stepwise testing from self to neighbor effects, LOD\_self are the same as standard QTL mapping. Note that the results return 0 LOD scores for covariate markers when using addQTL option.

## Value

A matrix of LOD scores for self and neighbor effects, with the chromosome numbers and positions. The row names correspond to marker names.

- chr Chromosome number
- pos Marker position
- LOD\_self LOD score for self effects
- LOD\_nei LOD score for neighbor effects

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

#### References

- Jansen RC (1993) Interval mapping of multiple quantitative trait loci. Genetics 135:205-211.
- Sato Y, Takeda K, Nagano AJ (2020) Neighbor QTL: an interval mapping method for quantitative trait loci underlying neighbor effects. bioRxiv https://doi.org/10.1101/2020.05. 20.089474

#### See Also

eff\_neighbor

#### Examples

plot\_nei(test\_scan)

selfprob

## Description

A function to calculate self QTL effects for an individual, with given deviation coefficients and conditional genotype probabilities.

## Usage

selfprob(i, a1, d1, AA, AB, BB)

## Arguments

i	ID of a target individual.
a1	A numeric scalar indicating additive deviation.
d1	A numeric scalar indicating dominance deviation.
AA	An individual x marker matrix of conditional probabilities for AA genotype.
AB	An individual x marker matrix of conditional probabilities for AB genotype. Input NA if heterozygotes are absent.
BB	An individual x marker matrix of conditional probabilities for BB genotype. Input NA for backcross lines.

## Value

A numeric vector containing each marker effect for individual i.

#### Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

sim\_nei\_qtl

Phenotype simulation for neighbor QTL effects

## Description

A function to simulate neighbor effects with given QTL effects, distance scale, and causal markers.

## sim\_nei\_qtl

## Usage

```
sim_nei_qtl(
  genoprobs,
  a2,
  d2,
  smap,
  scale,
  grouping = rep(1, nrow(smap)),
  n_QTL = 1,
  contrasts = NULL
)
```

#### Arguments

genoprobs	Conditional genotype probabilities as taken from qtl::calc.genoprob().
a2	A numeric scalar indicating additive deviation.
d2	A numeric scalar indicating dominance deviation.
smap	A matrix showing a spatial map for individuals. The first and second column include spatial positions along an x-axis and y-axis, respectively.
scale	A numeric scalar indicating the maximum spatial distance between a focal indi- vidual and neighbors to define neighbor effects.
grouping	An integer vector assigning each individual to a group. This argument can be used when smap contains different experimental replicates. Default setting means that all individuals are belong to a single group.
n_QTL	A positive integer indicating the number of causal markers.
contrasts	An optional vector composed of three TRUE/FALSE values, which represents the presence/absence of specific genotypes as c(TRUE/FALSE, TRUE/FALSE) = AA, AB, BB. If NULL, it is compiled from genoprobs automatically.

### Details

Major genetic effects, a2 and d2, are allocated to causal loci randomly selected by  $n_QTL$ , while minor polygenic effects (i.e., 1% of a2) are allocated to the other loci.

#### Value

A numeric matrix containing individuals x marker elements for neighbor QTL effects.

- true\_scale True distance scale of simulated neighbor effects
- true\_marker The name(s) of causal markers
- nei\_y Simulated neighbor effects standardized to have zero mean and one variance

## Author(s)

Yasuhiro Sato (<sato.yasuhiro.36c@kyoto-u.jp>)

## Examples

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