

Package ‘gpmmap’

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Depends isotone, plyr, ggplot2, foreach

Description This package contains tools for studying genotype-phenotype (GP) maps for bi-allelic loci underlying quantitative phenotypes. The 0.1 version is released in connection with the publication of Gjuvsland et al. (2003) and implements basic line plots and the monotonicity measures for GP maps presented in the paper. Reference: Gjuvsland AB, Wang Y, Plahte E and Omholt SW (2013) Monotonicity is a key feature of genotype-phenotype maps. *Front. Genet.* 4:216. doi: 10.3389/fgene.2013.00216 [[\{ \}href{http://www.frontiersin.org/Journal/10.3389/](http://www.frontiersin.org/Journal/10.3389/)

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gpmmap-package

Tools for analysing and plotting genotype-phenotype maps

Description

The **gpmmap** package deals with genotype-phenotype maps for biallelic loci underlying quantitative phenotypes. The package provides a class `gpmmaps`, analysis functions and basic lineplots. The package is designed for studying the properties of GP maps without reference to any particular population, i.e. the physiological (Cheverud & Routman, 1995) or functional (Hansen, 2001) properties of the GP map. This is opposed to statistical effects underlying most of quantitative genetics, where the GP-map is analysed together with genotype frequencies in a given population (e.g. Lynch & Walsh, 1998).

In version 0.1 which is released as part of the publication of Gjuvsland *et al.* (2013) we have implemented functionality for studying monotonicity Gjuvsland *et al.* (2011) of GP maps. The package utilizes the **isotone** package for monotone regression, and the **foreach** package for parallel computation.

The package consists of the following high-level functions : `enumerate_genotypes`, `generate_gpmmap`, `degree_of_monotonicity`, `decompose_monotone` and `plot.gpmmap`

Author(s)

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References

- Cheverud JM & Routman EJ (1995) Epistasis and Its Contribution to Genetic Variance Components. *Genetics* 139:1455-1461 [[link](#)]
- Gjuvsland AB, Vik JO, Woolliams JA, Omholt SW (2011) Order-preserving principles underlying genotype-phenotype maps ensure high additive proportions of genetic variance. *Journal of Evolutionary Biology* 24(10):2269-2279 [[link](#)]
- Gjuvsland AB, Wang Y, Plahte E and Omholt SW (2013) Monotonicity is a key feature of genotype-phenotype maps. *Front. Genet.* 4:216. doi: 10.3389/fgene.2013.00216 [[link](#)]
- Hansen T & Wagner GP (2001) Modeling genetic Architecture: A Multilinear Theory of gene Interaction. *Theoretical Population Biology* 59:61-86 [[link](#)]
- Leeuw J, Hornik K and Mair P (2009) Isotone Optimization in R: Pool-Adjacent-Violators Algorithm (PAVA) and Active Set Methods. *Journal of Statistical Software* 32(5) [[link](#)]
- Lynch M & Walsh B (1998) *Genetics and Analysis of Quantitative Traits*, Sunderland, MA: Sinauer Associates

decompose_monotone	<i>Decompose genotype-phenotype map(s) using monotone regression</i>
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Description

Functions for decomposing genotype-phenotype (GP) maps with N biallelic loci using monotone regression from the `isotone` package.

Usage

```
decompose_monotone(gpmap)
decompose_monotone_single(gpmap)
```

Arguments

gpmap	A <code>gpmap</code> object
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Details

`decompose_monotone` works for any `gpmap` object (values is $(3^N) \times K$ matrix of genotypic values) and calls the internal function `decompose_monotone_single` for each column. `decompose_monotone_single` takes a `gpmap` object with a single set of genotypic values ($K = 1$), loops through all 2^N possible combinations of plusalleles, calls `monotone_regression` and identifies the best fit. The code uses the `foreach` package and will run in parallel if a *parallel backend* is registered (see `foreach` documentation).

Value

The input `gpmap` is returned with two added elements

monoR2	The coefficient of determination of the monotone regression
values.mono	A matrix of genotypic values for the monotone component of genotype-phenotype map(s)

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References

- Leeuw J, Hornik K and Mair P (2009) Isotone Optimization in R: Pool-Adjacent-Violators Algorithm (PAVA) and Active Set Methods. *Journal of Statistical Software* 32(5) [[link](#)]
- Gjuvsland AB, Wang Y, Plahte E and Omholt SW (2013) Monotonicity is a key feature of genotype-phenotype maps. *Front. Genet.* 4:216. doi: 10.3389/fgene.2013.00216 [[link](#)]

Examples

```

data(GPmaps)

#Additive GP map is monotone so monoR2=1 and values.mono=values
decompose_monotone(A)

#Pure AxA epistasis map
decompose_monotone(AA)

#two-locus example in Cheverud & Routman (1995)
decompose_monotone(mouseweight)

#decompose four random 3-locus GP maps
set.seed(0)
randomGP <- rnorm(3^2*4)
dim(randomGP) <- c(9,4)
decompose_monotone(generate_gpmap(randomGP))

```

degree_of_monotonicity

Degree of monotonicity of GP map

Description

Functions for computing degree of monotonicity m for [gpmap](#) objects.

Usage

```

degree_of_monotonicity(gpmap)
degree_of_monotonicity_single(gpmap)

```

Arguments

gpmap A [gpmap](#) object

Details

degree_of_monotonicity works for any [gpmap](#) object (values is $(3^N) \times K$ matrix of genotypic values) and calls the internal function degree_of_monotonicity_single for each column. degree_of_monotonicity_single computes substitution effect, locus weights and per-locus and overall degree of monotonicity as described in Gjuvslund *et al.* (2013).

Value

degree_of_monotonicity returns the input gmap with the following added fields:

- degree.monotonicity Overall degree of monotonicity for the K GP maps
- degree.monotonicity.locus Data frame with per locus degree of monotonicity for the K GP maps
- locus.weight Data frame with locus weights

Author(s)

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References

Gjuvsland AB, Wang Y, Plahte E and Omholt SW (2013) Monotonicity is a key feature of genotype-phenotype maps. *Front. Genet.* 4:216. doi: 10.3389/fgene.2013.00216 [[link](#)]

Examples

```
data(GPmaps)

#Additive GP map is monotone
degree_of_monotonicity(A)

#Pure AxA epistasis map
degree_of_monotonicity(AA)

#two-locus example in Cheverud & Routman (1995)
degree_of_monotonicity(mouseweight)
```

enumerate_genotypes *Function for enumerating genotypes for N biallelic loci*

Description

Function for enumerating all 3^N genotypes for N biallelic loci. Optional specification of names of loci and alleles. `genotypes`. Generates a data frame of multilocus genotypes in the sequence used for objects of class `gmap`.

Usage

```
enumerate_genotypes(nloci=1, locinames=NULL, allelenames=NULL)
```

Arguments

- `nloci` The number of loci N
- `locinames` An optional character vector with N names of loci
- `allelenames` An optional character object specifying allele names

Details

Unless specified locinames default to "Locus 1", "Locus 2", ..., "Locus N".

If allelenames is not specified then the alleles will be named "1" and "2".

Value

Returns a data frame with locinames as colnames, and with 3^N rows specifying all possible genotypes in the sequence used for all GP maps in the package (the same sequence as used in Gjuvsland *et al.* (2011)), where the genotype at the first locus varies fastest, then the second locus, and so on:

	Locus_1	Locus_2
1	11	11
2	12	11
3	22	11
4	11	12
5	12	12
6	22	12
7	11	22
8	12	22
9	22	22

Author(s)

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References

Gjuvsland AB, Vik JO, Woolliams JA, Omholt SW (2011) Order-preserving principles underlying genotype-phenotype maps ensure high additive proportions of genetic variance. *Journal of Evolutionary Biology* 24(10):2269-2279 [[link](#)]

Examples

```
#genotypes for a single locus
enumerate_genotypes()

#genotypes for two loci "A" and "B", with alleles named "H" and "L"
enumerate_genotypes(2,c("A", "B"),c("H", "L"))

#genotypes for the two-locus example in Cheverud & Routman (1995)
enumerate_genotypes(2,c("D7Mit17", "D1Mit7"),rbind(c('A1', 'A2'),c('B1', 'B2')))
```

generate_gpmap	<i>Function for creating genotype-phenotype (GP) maps</i>
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Description

Function for creating a `gpmap` object representing a genotype-phenotype (GP) map for N biallelic loci or more generally K such maps, from a matrix of genotypic values.

Usage

```
generate_gpmap(y, locinames = NULL, allelenames = NULL, mapnames = NULL)
```

Arguments

<code>y</code>	A ($3^N \times K$) matrix or numeric with each column specifying the 3^N genotypic values for K GP maps
<code>locinames</code>	An optional character vector with N names of loci
<code>allelenames</code>	An optional character object specifying allele names
<code>mapnames</code>	An optional character vector with K names of GP maps / phenotypes

Details

Arguments `locinames` and `allelenames` are passed on to `enumerate_genotypes`, and the genotypic values in `y` should be given in the same sequence as the sequence of genotypes returned by `enumerate_genotypes`. If `mapnames` is not specified then the GP maps will be named "GPmap_1", "GPmap_2", ..., "GPmap_K".

Value

The function returns an object of class `gpmap` containing the following components

<code>values</code>	The vector or matrix of genotypic values
<code>nloci</code>	The number of loci in the map
<code>genotypes</code>	Data frame with enumeration of genotypes
<code>locinames</code>	Character vector with names for all loci
<code>mapname</code>	The name(s) of the GP map

Author(s)

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References

Gjuvslund AB, Vik JO, Woolliams JA, Omholt SW (2011) Order-preserving principles underlying genotype-phenotype maps ensure high additive proportions of genetic variance. *Journal of Evolutionary Biology* 24(10):2269-2279 [[link](#)]

Examples

```
#inter- and intra-locus additive GPmap with two loci
generate_gpmap(c(-2,1,0,-1,0,1,0,1,2),mapnames="Additive")

#two-locus GP map with AxA epistasis for loci named A and B
generate_gpmap(c(-1,0,1,0,0,0,1,0,-1),locinames=c("A","B"),mapnames="AxA")

#random GP map with 3 loci
set.seed(0)
generate_gpmap(rnorm(27))
```

 GPmaps

Dataset containing example GP maps

Description

Example GP maps with two loci including: The orthogonal GP maps A, D, AA, AD, DA and DD used in decomposition of genetic variance (Zeng *et al.* 2005). The GP map mouseweight for body weight studied by Cheverud *et al.* (1995).

Usage

GPmaps

Format

Objects of class [gpmap](#)

References

Cheverud JM & Routman EJ (1995) Epistasis and Its Contribution to Genetic Variance Components. *Genetics* 139:1455-1461 [[link](#)]

Zeng ZB, Wang T, Zou W. (2005). Modelling quantitative trait loci and interpretation of models. *Genetics* 169: 1711-1725. [[link](#)]

 monotone_regression

Perform monotone regression on a genotype-phenotype (GP) map

Description

The function uses [partial_genotype_order](#) and [activeSet](#) from the [isotone](#) package to do monotone regression (Leeuw *et al.*, 2009) on a GP map.

Usage

```
monotone_regression(gpmap, plusallele)
```


Arguments

gmap	An object of class gmap
plusallele	An N vector of allele indexes (1 or 2)

Details

Element i in `plusallele` specifies the ordering of the genotypes at locus i , if the element is 1 then $11 < 12 < 22$ and conversely if it is 2 then $22 < 12 < 11$. `monotone_regression` calls [partial_genotype_order](#) to obtain the partial ordering of genotypic values for the given `plusalleles`. This partial ordering is then used together with the GP map itself as input to the [activeSet](#) function from the package [isotone](#).

Value

`monotone_regression` returns the output from [activeSet](#) directly.

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References

- Leeuw J, Hornik K and Mair P (2009) Isotone Optimization in R: Pool-Adjacent-Violators Algorithm (PAVA) and Active Set Methods. *Journal of Statistical Software* 32(5) [[link](#)]
- Gjuvsland AB, Wang Y, Plahte E and Omholt SW (2013) Monotonicity is a key feature of genotype-phenotype maps. *Front. Genet.* 4:216. doi: 10.3389/fgene.2013.00216 [[link](#)]

Examples

```
data(GPmaps)

#Additive GP map is monotone
monotone_regression(A,c(2,2))

#Pure AxA epistasis map
monotone_regression(AA,c(2,2))

#two-locus example in Cheverud & Routman (1995)
monotone_regression(mouseweight,c(1,1))
```

partial_genotype_order

Generate partial ordering of genotype space based from allele content of genotypes

Description

Generate the strict partial order on genotype space specified in eq. (13) in Gjuvsland *et al.* (2011). For a genotype space with N biallelic loci a minimal description of this partial order is given by $2N * 3^{(N-1)}$ inequalities.

Usage

```
partial_genotype_order(plusallele)
```

Arguments

plusallele A N -vector with indexes (1 or 2) for the +allele for each locus

Details

In short a partial order on a set is a binary relation defining a pairwise ordering of some pairs of elements in the set, for a formal definition see http://en.wikipedia.org/wiki/Partial_order. In the partial order on the set of genotypes defined in Gjuvsland *et al.* (2011) the comparable pairs of genotypes are equal at every locus except one, while all other pairs of genotypes are incomparable. This partial ordering of genotype space is implicit in the regression on gene content (the number of alleles with a given index in each genotype) used for decomposition of the genotypic value in quantitative genetics (see e.g. Lynch and Walsh page 65).

Value

Returns a $(2N * 3^{(N-1)}) \times 2$ matrix of genotype indexes. The genotype indexes refer to row number in the genotype sequence set up in [enumerate_genotypes](#). Each row vector in the matrix contains the genotype indexes of one comparable pair, and if the first index is k and the second is l then $genotype[k] < genotype[l]$.

Author(s)

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References

Gjuvsland AB, Vik JO, Woolliams JA, Omholt SW (2011) Order-preserving principles underlying genotype-phenotype maps ensure high additive proportions of genetic variance. *Journal of Evolutionary Biology* 24(10):2269-2279 [[link](#)]

Lynch M & Walsh B (1998) *Genetics and Analysis of Quantitative Traits*, Sunderland, MA: Sinauer Associates

`plot.gpmap`*Functions for creating lineplots of genotype-phenotype (GP) maps*

Description

Function for creating lineplots for genotype-phenotype (GP) map (an object of class `gpmap`) with 1-3 biallelic loci.

Usage

```
## S3 method for class 'gpmap'  
plot(x, show=1, decomposed=FALSE, ...)
```

Arguments

<code>x</code>	A <code>gpmap</code> object
<code>show</code>	Which map (only used if >1 map in <code>gpmap</code> object) to plot
<code>decomposed</code>	Decomposition into monotone and non-monotone component plotted if TRUE
<code>...</code>	ignored

Author(s)

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Examples

```
data(GPmaps)  
  
#plot additive gpmap  
plot(A)  
  
#plot decomposition of GPmap from Cheverud & Routman (1995)  
decomp <- decompose_monotone(mouseweight)  
plot(decomp, decomposed=TRUE)
```

`print.gpmap`*Print function for `gpmap` objects*

Description

Print a summary of a genotype-phenotype (GP) map (an object of class `gpmap`) with 1-3 N biallelic loci.

Usage

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

Arguments

x	A gpmap object
...	ignored

Details

Prints name(s) of GP map(s) and loci, a summary of genotypic values. Monotonicity measures are printed if available.

Author(s)

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Examples

```
data(GPmaps)  
print(A)
```

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