

Package ‘HWEBayes’

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Type Package

Title Bayesian investigation of Hardy-Weinberg Equilibrium via estimation and testing.

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Description Estimation and testing of HWE using Bayesian methods.
Three models are currently considered: HWE, a model parameterized in terms of the allele frequencies and a single inbreeding coefficient f , and the saturated model. Testing is based on Bayes factors.

License GPL-2

LazyLoad yes

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| | |
|-----------|--|
| baselogit | <i>Calculates a set of baseline logits from a set of probabilities</i> |
|-----------|--|

Description

Calculates a set of $k - 1$ baseline logits $\log(p_1/p_k), \dots, \log(p_{k-1}/p_k)$, from a set of probabilities p_1, \dots, p_k .

Usage

baselogit(probs)

Arguments

probs A set of probabilities, p_1, \dots, p_k , where k is the number of alleles.

Details

This function is used by a number of other functions in the package, for example, to provide a parameterization for maximization and for importance sampling in the single f model.

Value

baselogit Returns the set of $k - 1$ baseline logits, where k is the number of alleles.

Author(s)

Jon Wakefield (jonno@u.washington).

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

invbaselogit

Examples

```
baselogit(probs=c(0.5,0.4,0.1))
```

DiabRecess

Data on diabetes patients antigen classes

Description

Data are from Thomson et al. (1986) and describe the counts of combinations of four different antigen classes in 45 French type I diabetes patients. HWE is equivalent to a recessive model, see Thomson (1983) and Wakefield (2009) for more details.

Usage

```
data(DiabRecess)
```

Format

A vector with 10 observations in the order $n_{11}, n_{11}, n_{13}, n_{14}, n_{22}, n_{23}, n_{24}, n_{33}, n_{34}, n_{44}$.

Source

Thomson, G. et al (1986). HLA and IDDM predisposition: new aspects. *Genetic Epidemiology*, 1, 262-368.

References

Thomson, G. (1983). Investigation of the mode of inheritance of the HLA associated diseases by the method of antigen genotype frequencies among diseased individuals. *Tissue Antigens*, 21, 81-104.

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

Examples

```
data(DiabRecess)
```

| | |
|---------------|---|
| DirichNormHWE | <i>Evaluates the normalizing constant under the HWE model, with a conjugate prior</i> |
|---------------|---|

Description

Function to evaluate the normalizing constant given a conjugate Dirichlet prior and the HWE model.

Usage

```
DirichNormHWE(nvec, bvec0)
```

Arguments

| | |
|-------|---|
| nvec | vector of genotype frequencies in the order $n_{11}, n_{12}, \dots, n_{1k}, n_{22}, \dots, n_{2k}, \dots, n_{kk}$. |
| bvec0 | vector of length k Dirichlet prior parameters, where k is the number of alleles. |

Value

The normalizing constant.

Author(s)

Jon Wakefield (jonno@u.washington).

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium.

See Also

DirichNormSat

Examples

```
data(DiabRecess)
DirichNormHWE(nvec=DiabRecess, bvec0=rep(1, 4))
```

| | |
|---------------|--|
| DirichNormSat | <i>Evaluates the normalizing constant (as used in the denominator of a Bayes factor) for a conjugate prior</i> |
|---------------|--|

Description

Function to evaluate the normalizing constant given a conjugate Dirichlet prior and a saturated model.

Usage

```
DirichNormSat(nvec, bvec)
```

Arguments

| | |
|------|---|
| nvec | vector of genotype frequencies in the order $n_{11}, n_{12}, \dots, n_{1k}, n_{22}, \dots, n_{2k}, \dots, n_{kk}$. |
| bvec | vector of length $k(k + 1)/2$ Dirichlet prior parameters, where k is the number of alleles. |

Value

The normalizing constant.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

DirichSampSat, DirichSampHWE, DirichNormSat, DirichNormHWE, HWEDirichBF2

Examples

```
data(DiabRecess)
DirichNormSat(nvec=DiabRecess, bvec=rep(1, 10))
```

DirichSampHWE

Simulate samples from a Dirichlet prior or posterior under HWE

Description

Function to simulate samples from the HWE Dirichlet model. Can be used for samples from the prior or the (conjugate) Dirichlet posterior, both in the k allele case. Samples are generated for the allele frequencies in the order p_1, p_2, \dots, p_k .

Usage

```
DirichSampHWE(nvec, bvec0, nsim)
```

Arguments

| | |
|-------|---|
| nvec | vector of genotype frequencies in the order $n_{11}, n_{12}, \dots, n_{1k}, n_{22}, \dots, n_{2k}, \dots, n_{kk}$. |
| bvec0 | vector of length k Dirichlet prior parameters, where k is the number of alleles. |
| nsim | number of samples to simulate from the prior/posterior. |

Details

Uses the `rdirichlet` function from the `MCMCpack` library.

Value

| | |
|------|--|
| pvec | matrix of size $nsim \times k$ containing samples for the genotype frequencies, in the order p_1, p_{12}, \dots, p_k . |
|------|--|

Author(s)

Jon Wakefield (jonno@u.washington).

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

`DirichSampSat`, `DirichNormSat`, `DirichNormHWE`

Examples

```
# First sample from the prior
PriorSampHWE <- DirichSampHWE(nvec=rep(0,10),bvec0=rep(1,4),nsim=1000)
par(mfrow=c(1,1))
hist(PriorSampHWE$pvec[,1],xlab="p1",main="")
# Now sample from the posterior
data(DiabRecess)
```

```
PostSampHWE <- DirichSampHWE(nvec=DiabRecess,bvec0=rep(1,4),nsim=1000)
par(mfrow=c(1,1))
hist(PostSampHWE$pvec[,1],xlab="p1",main="")
```

| | |
|---------------|---|
| DirichSampSat | <i>Simulate samples from a Dirichlet prior or posterior under the saturated model</i> |
|---------------|---|

Description

Function to simulate samples from the saturated Dirichlet model. Can be used for samples from the prior or the (conjugate) Dirichlet posterior, both in the k allele case. Samples are generated for the genotype frequencies in the order $p_{11}, p_{12}, \dots, p_{1k}, p_{22}, \dots, p_{2k}, \dots, p_{kk}$, the allele frequencies, and the fixation indices.

Usage

```
DirichSampSat(nvec, bvec, nsim)
```

Arguments

| | |
|------|---|
| nvec | vector of genotype frequencies in the order $n_{11}, n_{12}, \dots, n_{1k}, n_{22}, \dots, n_{2k}, \dots, n_{kk}$. |
| bvec | vector of length $k(k+1)/2$ Dirichlet prior parameters, where k is the number of alleles. |
| nsim | number of samples to simulate from the prior/posterior. |

Details

Uses the `rdirichlet` function from the `MCMCpack` library.

Value

| | |
|--------|--|
| pvec | matrix of size $nsim \times k(k+1)/2$ containing samples for the genotype frequencies, in the order $p_{11}, p_{12}, \dots, p_{1k}, p_{22}, \dots, p_{2k}, \dots, p_{kk}$. |
| pmat | matrix of size $nsim \times k(k+1)/2 \times k(k+1)/2$ containing samples for the genotype probabilities. |
| pmarg | matrix of size $nsim \times k$ containing samples for the allele frequencies, in the order p_1, \dots, p_k . |
| fixind | matrix of size $nsim \times k(k+1)/2 \times k(k+1)/2$ containing samples for the fixation indices, contained in the lower diagonal, i.e. <code>fixind[i, j]</code> for $[i > j]$. |

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

DirichSampHWE, DirichNormSat, DirichNormHWE

Examples

```
# First sample from the prior
PriorSampSat <- DirichSampSat(nvec=rep(0,10),bvec=rep(1,10),nsim=1000)
par(mfrow=c(1,2))
hist(PriorSampSat$pvec[,1],xlab="p1",main="")
hist(PriorSampSat$fixind[,2,1],xlab="f21",main="")
# Now sample from the posterior
data(DiabRecess)
PostSampSat <- DirichSampSat(nvec=DiabRecess,bvec=rep(1,10),nsim=1000)
par(mfrow=c(1,2))
hist(PostSampSat$pvec[,1],xlab="p1",main="")
hist(PostSampSat$fixind[,2,1],xlab="f21",main="")
```

HWEDirichBF2

Evaluates the Bayes factor in the $k=2$ allele case under conjugate priors

Description

Function to evaluate the Bayes factor $\Pr(n | \text{HWE}) / \Pr(n | \text{saturated model})$ in the $k = 2$ allele case and with conjugate (Dirichlet) priors under HWE and saturated models.

Usage

```
HWEDirichBF2(nvec, bvec0, bvec1)
```

Arguments

nvec vector of genotype frequencies in the order n_{11}, n_{21}, n_{22} .

bvec0 vector of length $k = 2$ Dirichlet prior parameters for the prior under the null, where k is the number of alleles.

bvec1 vector of length $k(k + 1)/2 = 3$ Dirichlet prior parameters for the prior under the saturated model, where k is the number of alleles.

Value

Bayes factor is returned.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

DirichNormHWE, DirichNormSat, DirichSampHWE, DirichSampSat, HWETriangBF2, TriangNormHWE

Examples

```
HWEDirichBF2(nvec=c(88,10,2),bvec0=c(1,1),bvec1=c(1,1,1))
```

| | |
|---------------|---|
| HWEImportSamp | <i>Importance sampling to calculate the normalizing constant under the single f model</i> |
|---------------|---|

Description

Importance sampling to calculate the normalizing constant under the single f model. Two proposals are available, either sampling from the prior or sampling from a normal distribution whose mean vector and variance-covariance matrix must be specified. The latter may be taken from an MCMC analysis using, for example, WinBUGS. In all cases the likelihood is multinomial and the prior is Dirichlet on the allele frequencies, and normal on λ where $\lambda = \log(f - f_{\min})/(1 - f)$. See Weir (1996) for a description of HWE and different models/parameterizations.

Usage

```
HWEImportSamp(nsim, nvec, ischoice, lambdamu, lambdasd, alpha,
gmu = rep(0, length(alpha)), gsigma = diag(0, nrow = length(alpha),
ncol = length(alpha)))
```

Arguments

| | |
|----------|--|
| nsim | the number of points to sample to calculate the estimate. |
| nvec | vector of genotype frequencies in the order $n_{11}, n_{12}, \dots, n_{1k}, n_{22}, \dots, n_{2k}, \dots, n_{kk}$. |
| ischoice | choice of importance sampling proposal, =1 gives a normal distribution with mean and variance that must be specified (as gmu and gsigma) and =2 is from the prior. |
| lambdamu | the mean of the prior for λ . |
| lambdasd | the variance of the prior for λ . |
| alpha | the vector of k parameters for the Dirichlet prior on the allele frequencies. |
| gmu | the mean of the importance sampling proposal, of length k , where k is the number of alleles. |
| gsigma | the variance of the importance sampling proposal, a matrix of dimension $k \times k$, where k is the number of alleles. |

Value

PrnH1 the estimate of the normalizing constant
 varest the variance of the estimate of the normalizing constant

Warning

As always with importance sampling the procedure can be very unstable, particularly for large k . Hence rerunning the function with different simulation sample sizes, and different $g\mu$ and $g\sigma$ is recommended

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.
 Weir, B.S. (1996). *Genetic Data Analysis II*. Sunderland MA: Sinauer.

See Also

LambdaOptim, DirichNormSat, DirichNormHWE, TriangNormHWE

Examples

```
alpha <- c(1,1,1,1) # prior on allele frequencies
# gmu and gsigma were obtained from a WinBUGS run
gmu <- c(-0.4633092,0.3391625,0.3397936,-3.5438008)
gsigma <- matrix(c(
  0.07937341,0.02819656,0.02766583,0.04607996,
  0.02819656,0.07091320,0.04023827,0.01657028,
  0.02766583,0.04023827,0.07042278,0.01752266,
  0.04607996,0.01657028,0.01752266,0.57273683),nrow=4,ncol=4)
data(DiabRecess)
HWEImportSamp(nsim=5000,nvec=DiabRecess,ischoice=1,lambdamu=-2.95,
  lambdasd=1.07,alpha=alpha,gmu,gsigma)
HWEImportSamp(nsim=5000,nvec=DiabRecess,ischoice=2,lambdamu=-2.95,
  lambdasd=1.07,alpha=alpha)
```

HWEmodelsMLE

Evaluates the maximum likelihood estimates of the parameters of various models in the k allele case

Description

Function to obtain the MLEs of parameters under the HWE, single f and saturated models. For the single f model numerical maximization is required if $k > 2$, where k is the number of alleles.

Usage

```
HWEmodelsMLE(nvec)
```

Arguments

nvec vector of genotype frequencies in the order $n_{11}, n_{21}, n_{22}, \dots, n_{k1}, n_{k2}, \dots, n_{kk}$.

Value

phat matrix of $k \times k$ MLEs of genotype frequencies
qhat MLEs of k allele frequencies under the HWE model
fqhat MLEs of k allele frequencies under the single f model
fsingle MLE of single f
fmaxloglik maximized log-likelihood (without the normalizing constant), under the single f model
fmin estimated lower bound of f_{\min} in the single f model. Under the single f model $f_{\min} < f < 1$ where $f_{\min} = -p_{\min}/(1 - p_{\min})$ and p_{\min} is the minimum of the allele frequencies.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.
Weir, B.S. (1996). *Genetic Data Analysis II*. Sunderland MA: Sinauer.

Examples

```
data(DiabRecess)
HWEmodelsMLE(nvec=DiabRecess)
```

HWEsimdat

Simulate data under the single f model with k alleles.

Description

Simulate data under the single f model with k alleles (so $f = 0$ gives data under HWE).

Usage

```
HWEsimdat(npop, q, f)
```

Arguments

npop population size.
 q vector of k allele frequencies.
 f value of inbreeding coefficient

Value

nvec vector of genotype counts, in the order $n_{11}, n_{21}, n_{22}, \dots, n_{k1}, n_{k2}, \dots, n_{kk}$.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.
 Weir, B.S. (1996). *Genetic Data Analysis II*. Sunderland MA: Sinauer.

Examples

```
counts <- HWEsimdat(100,q=c(0.1,0.8,.1),f=0.1)
```

| | |
|--------------|--|
| HWETriangBF2 | <i>Evaluates the Bayes factor in the $k=2$ allele case with a "triangular" prior under the null</i> |
|--------------|--|

Description

Function to evaluate the Bayes factor $\Pr(n | \text{HWE}) / \Pr(n | \text{saturated model})$ in the $k = 2$ allele case and with a conjugate (Dirichlet) priors under the saturated model and a "triangular" distribution under the null. the latter is the marginal prior distribution under the (1,1,1) Dirichlet prior under the saturated model.

Usage

```
HWETriangBF2(nvec)
```

Arguments

nvec vector of genotype frequencies in the order n_{11}, n_{21}, n_{22} .

Value

Bayes factor is returned.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

TriangNormHWE

Examples

```
HWETriangBF2(nvec=c(88,10,2))
```

invbaselogit

Converts a set of $k-1$ baseline logits into a set of probabilities

Description

Converts a set of $k - 1$ baseline logits $\log(p_1/p_k), \dots, \log(p_{k-1}/p_k)$ into a set of probabilities p_1, \dots, p_k , where k is the number of alleles.

Usage

```
invbaselogit(baselogit)
```

Arguments

baselogit A set of $k - 1$ baseline logits, where k is the number of alleles.

Details

This is used by a number of other functions in the package, for example, to provide a parameterization for maximization and for importance sampling in the single f model.

Value

invbaselogit the probability vector corresponding to the baseline logit

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

baselogit

Examples

```
invbaselogit(baselogit=c(0,0))
```

LambdaOptim

Obtains values for the prior specification for lambda

Description

In the single f model we may parameterize in terms of the allele frequencies and $\lambda = \log((f - f_{\min})/(1 - f))$ where $f_{\min} = -p_{\min}/(1 - p_{\min})$ and p_{\min} is the minimum allele frequency. The prior for λ is assumed normal and this function finds the mean and standard deviation of this normal, given two values for f , with associated probabilities.

Usage

```
LambdaOptim(nsim, bvec, f1, f2, p1, p2, init)
```

Arguments

| | |
|------|---|
| nsim | the optimization is carried out by simulating from the joint prior on allele frequencies and λ , and this argument gives the number of simulations to take from the prior |
| bvec | vector of length k of prior specification for the HWE Dirichlet prior, where k is the number of alleles. |
| f1 | first quantile for inbreeding coefficient f |
| f2 | second quantile for inbreeding coefficient f |
| p1 | probability associated with f1 |
| p2 | probability associated with f2 |
| init | initial values for <code>lambdamu</code> and <code>lambdasd</code> |

Value

| | |
|----------|--|
| lambdamu | prior mean for λ |
| lambdasd | prior standard deviation for λ |

Warning

This function can be unstable and good starting values may be needed. It is also recommended to check the output by simulating from the given prior to see if the empirical quantiles match with those desired; the function `SinglefPrior` may be used for this

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

HWEImportSamp

Examples

```
bvec <- c(1,1,1,1)
init <- c(-3,log(1.1))
lampr <- LambdaOptim(nsim=10000,bvec=bvec,f1=0,f2=0.26,p1=0.5,p2=0.95,init)
```

LambdaPriorChoice *Called by LambaOptim*

Description

Internal function, should not be needed. It is the function that is minimized when the mean and standard deviation for λ are being found.

Usage

```
LambdaPriorChoice(x, nsim, bvec, f1, f2, p1, p2, init)
```

Arguments

| | |
|------|--|
| x | Proposal for λ and $\exp(\lambda)$. |
| nsim | number of points to simulate from the prior |
| bvec | k vector of Dirichlet prior parameters. |
| f1 | first quantile for inbreeding coefficient f |
| f2 | second quantile for inbreeding coefficient f |
| p1 | probability associated with f1 |
| p2 | probability associated with f2 |
| init | initial values for λ and $\exp(\lambda)$ |

Value

Returns the sum of squares that is being minimized.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

LambdaOptim

MultLogLik

Evaluates the Multinomial likelihood under the single f model

Description

Evaluates the Multinomial likelihood under the single f model. The normalizing constant is not included. This function is called by a number of other functions, and should not be needed.

Usage

```
MultLogLik(x, nvec, paramch = 1)
```

Arguments

| | |
|---------|--|
| x | a set of $k - 1$ baseline logits, where k is the number of alleles), and a transformed version of f . Hence a vector of length k . The transformation adopted depends on the value of paramch. |
| nvec | vector of genotype frequencies in the order $n_{11}, n_{21}, n_{22}, \dots, n_{k1}, n_{k2}, \dots, n_{kk}$. |
| paramch | a variable that if =1 assumes f is on the range $(-1, +1)$ before transformation, and if =2 assumes on the range $(f_{\min}, +1)$. |

Value

MultLogLik The value of the (unnormalized) multinomial log-likelihood.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.
 Weir, B.S. (1996). *Genetic Data Analysis II*. Sunderland MA: Sinauer.

See Also

SinglefReject

 SinglefReject

Samples from the posterior for the single f model

Description

Function to generate samples from the posterior for allele frequencies and f , under the single f model. Samples are generated using a rejection algorithm that simulates from the prior.

Usage

```
SinglefReject(nsim, bvec, lambdamu, lambdasd, nvec)
```

Arguments

| | |
|----------|--|
| nsim | number of samples to generate from the prior. |
| bvec | vector of size k that is the specification for the Dirichlet prior on the allele frequencies. |
| lambdamu | prior mean for λ . |
| lambdasd | prior standard deviation for λ . |
| nvec | vector of genotype frequencies in the order $n_{11}, n_{21}, n_{22}, \dots, n_{k1}, n_{k2}, \dots, n_{kk}$. |

Value

| | |
|---------|--|
| psamp | samples for k allele frequencies. |
| fsamp | samples for inbreeding coefficient f . |
| accrate | acceptance rate of the rejection algorithm. |
| PrnH1 | estimate of normalizing constant (which may be used in Bayes factor calculations). Calculated by averaging the likelihood over the sampled points. |
| varest | estimated variance of the estimate of the normalizing constant. |

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

Examples

```
data(DiabRecess)
postsampf1 <- SinglefReject(nsim=100, bvec=rep(1, 4), lambdamu=-2.95,
  lambdasd=1.07, nvec=DiabRecess)
```

| | |
|---------------|--|
| TriangNormHWE | <i>Evaluates the normalizing constant under the HWE model, for the "triangular" prior distribution</i> |
|---------------|--|

Description

Function to evaluate the normalizing constant given a "triangular" prior and the HWE model, in the $k = 2$ allele case. This prior results from marginalizing the conjugate Dirichlet prior with parameters (1,1,1) on the genotype frequencies under the alternative.

Usage

```
TriangNormHWE(nvec)
```

Arguments

nvec vector of genotype frequencies in the order n_{11}, n_{21}, n_{22} .

Value

Normalizing constant is returned.

Author(s)

Jon Wakefield (jonno@u.washington.edu)

References

Wakefield, J. (2009). Bayesian methods for examining Hardy-Weinberg equilibrium. *Biometrics*.

See Also

DirichNormHWE, DirichNormSat, DirichSampHWE, DirichSampSat, HWEDirichBF2, TriangNormHWE

Examples

```
nvec <- c(88,10,2)
TriangNormHWE(nvec)
```

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