

# Package 'lclGWAS'

February 21, 2017

**Type** Package

**Title** Efficient Estimation of Discrete-Time Multivariate Frailty Model  
Using Exact Likelihood Function for Grouped Survival Data

**Version** 1.0.3

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**Description** The core of this 'Rcpp' based package is several functions to estimate the baseline hazard, frailty variance, and fixed effect parameter for a discrete-time shared frailty model with random effects. The functions are designed to analyze grouped time-to-event data accounting for family structure of related individuals (i.e., trios). The core functions include two processes: (1) evaluate the multivariable integration to compute the exact proportional hazards model based likelihood and (2) estimate the desired parameters using maximum likelihood estimation. The integration is evaluated by the 'Cuhre' algorithm from the 'Cuba' library (Hahn, T., Cuba-a library for multidimensional numerical integration, Comput. Phys. Commun. 168, 2005, 78-95 <doi:10.1016/j.cpc.2005.01.010>), and the source files of the 'Cuhre' function are included in this package. The maximization process is carried out using Brent's algorithm, with the 'C++' code file from John Burkardt and John Denker (Brent, R., Algorithms for Minimization without Derivatives, Dover, 2002, ISBN 0-486-41998-3).

**License** GPL (>= 2)

**Imports** Rcpp (>= 0.12.4)

**LinkingTo** Rcpp, BH

**Suggests** knitr

**VignetteBuilder** knitr

**BuildVignettes** yes

**NeedsCompilation** yes

**Repository** CRAN

**Date/Publication** 2017-02-21 00:03:26

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lclGWAS-package	<i>Efficient Estimation of Multivariate Frailty Model Using Exact Likelihood Function for Grouped Survival Data</i>
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### Description

The core of this Rcpp based package is several functions to estimate the baseline hazard, frailty variance, and fixed effect parameter for a discrete-time shared frailty model with random effects. The functions are designed to analyze grouped time-to-event data accounting for family structure of related individuals (i.e., trios). The core functions include two processes: (1) evaluate the multivariable integration to compute the exact proportional hazards model based likelihood and (2) estimate the desired parameters using maximum likelihood estimation. The integration is evaluated by the Cuhre algorithm from the Cuba library (Hahn, T., Cuba-a library for multidimensional numerical integration, *Comput. Phys. Commun.* 168, 2005, 78-95), and the source files of the Cuhre function are included in this package. The maximization process is carried out using Brent's algorithm, with the C++ code file from John Burkardt and John Denker (Brent, R., *Algorithms for Minimization without Derivatives*, Dover, 2002). License: GPL ( $\geq 2$ )

### Details

```
Package: lclGWAS
Type: Package
Version: 1.0.2
Date: 2017-02-20
License: GPL-3
```

Please refer to the individual function documentation or the included vignette for more information. The package vignette serves as a tutorial for using this package.

### Author(s)

Jiaxing Lin, Alexander Sibley, Tracy Truong, Nancy Cox, Eileen Dolan, Yu Jiang, Janice McCarthy, Andrew Allen, Kouros Owzar, Zhiguo Li Maintainer: Jiaxing Lin <jiaxing.lin@duke.edu>

### References

Ripatti, S. and Palmgren, J., Estimation of Multivariate Frailty Models Using Penalized Partial Likelihood. *Biometrics*, 56, 2000, 1016-1022.

Hahn, T., Cuba-a library for multidimensional numerical integration, Computer Physics Communications, 168, 2005, 78-95.

Brent, R., Algorithms for Minimization without Derivatives, Dover, 2002.

### See Also

[Rcpp](#)

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alphaEst	<i>Estimate the Interval Baseline Survival Rates for Discrete-Time Multivariate Frailty Model for Grouped Survival Data</i>
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### Description

A method to estimate the baseline survival rate for each time interval for a multivariate frailty model. The estimation is conducted under the null hypothesis, i.e., that there is no fixed effect.

### Usage

```
alphaEst(dtime, delta)
```

### Arguments

dtime	Vector of observed discrete survival times for each sample.
delta	Event indicator vector: 1 indicates observed event, 0 indicates censored.

### Value

A list with one object:

alphaEst	Vector of estimates of the baseline survival rates.
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### Examples

```
# Generate dummy data
dtime <- c(1, 3, 3, 2, 1, 1, 2, 3, 1)
delta <- c(1, 0, 1, 1, 1, 0, 1, 0, 1)
res <- alphaEst(dtime, delta)
res
```

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betaEst	<i>Estimate the Fixed Effect Parameter for Discrete-Time Multivariate Frailty Model for Grouped Survival Data</i>
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### Description

A method to estimate the fixed effect parameter for a multivariate frailty model accounting for family structure of related individuals (i.e., trios). The input data is assumed to be organized such that records for each family occur consecutively, and that records for offspring precede those for parents. The variance matrix for the random effects is assumed to be of the form  $\text{var} * \mathbf{K}$ , where  $\mathbf{K}$  is a matrix of kinship coefficients between family members. The following groupings are permitted: (Individual), (Offspring, Offspring), (Offspring, Parent), (Offspring, Parent, Parent), and (Offspring, Offspring, Parent, Parent). Other family structures have not been implemented.

### Usage

```
betaEst(fam_group, alpha, dtime, delta, g, var, lower, upper)
```

### Arguments

fam_group	Vector of family indicators for each sample.
alpha	Vector of baseline survival rates for each time interval.
dtime	Vector of observed discrete survival times for each sample.
delta	Event indicator vector: 1 indicates observed event, 0 indicates censored.
g	Vector of numeric genotypes for each sample.
var	Scalar for frailty variance.
lower	Scalar for the lower bound of the fixed effect parameter estimation search region.
upper	Scalar for the upper bound of the fixed effect parameter estimation search region.

### Value

A list with one object:

betaEst	Scalar estimate of the fixed effect parameter.
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### Examples

```
# Generate dummy data
fam_group <- rep(1:3,each=3)
alpha <- c(0.7500000, 0.6666667, 0.5000000, 0.0000000)
dtime <- c(1, 3, 3, 2, 1, 1, 2, 3, 1)
delta <- c(1, 0, 1, 1, 1, 0, 1, 0, 1)
g <- c(0, 1, 1, 1, 2, 2, 0, 0, 0)
var <- 0.2
res <- betaEst(fam_group, alpha, dtime, delta, g, var, lower = 0, upper = 2)
res
```

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varEst	<i>Estimate the Frailty Variance for Discrete-Time Multivariate Frailty Model for Grouped Survival Data</i>
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### Description

A method to estimate the frailty variance for a multivariate frailty model accounting for family structure of related individuals (i.e., trios). The input data is assumed to be organized such that records for each family occur consecutively, and that records for offspring precede those for parents. The variance matrix for the random effects is assumed to be of the form  $\text{var} * K$ , where  $K$  is a matrix of kinship coefficients between family members. The following groupings are permitted: (Individual), (Offspring, Offspring), (Offspring, Parent), (Offspring, Parent, Parent), and (Offspring, Offspring, Parent, Parent). Other family structures have not been implemented.

### Usage

```
varEst(fam_group, alpha, dtime, delta, g, beta, lower, upper)
```

### Arguments

fam_group	Vector of family indicators for each sample.
alpha	Vector of baseline survival rates for each time interval.
dtime	Vector of observed discrete survival times for each sample.
delta	Event indicator vector: 1 indicates observed event, 0 indicates censored.
g	Vector of numeric genotypes for each sample.
beta	Scalar for the fixed effect size.
lower	Scalar for the lower bound of the variance estimation search region.
upper	Scalar for the upper bound of the variance estimation search region.

### Value

A list with one object:

varEst	Scalar estimate of the frailty variance.
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### Examples

```
# Generate dummy data
fam_group <- rep(1:3,each=3)
alpha <- c(0.7500000, 0.6666667, 0.5000000, 0.0000000)
dtime <- c(1, 3, 3, 2, 1, 1, 2, 3, 1)
delta <- c(1, 0, 1, 1, 1, 0, 1, 0, 1)
g <- c(0, 1, 1, 1, 2, 2, 0, 0, 0)
beta <- 1
res <- varEst(fam_group, alpha, dtime, delta, g, beta, lower = 0, upper = 2)
res
```

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