

Package ‘mixedBayes’

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Type Package

Title Bayesian Longitudinal Regularized Quantile Mixed Model

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Description In longitudinal studies, the same subjects are measured repeatedly over time, leading to correlations among the repeated measurements. Properly accounting for the intra-cluster correlations in the presence of data heterogeneity and long tailed distributions of the disease phenotype is challenging, especially in the context of high dimensional regressions. In this package, we developed a Bayesian quantile mixed effects model with spike- and -slab priors dissect important gene - environment interactions under longitudinal genomics studies. An efficient Gibbs sampler has been developed to facilitate fast computation. The Markov chain Monte Carlo algorithms of the proposed and alternative methods are efficiently implemented in 'C++'. The development of this software package and the associated statistical methods have been partially supported by an Innovative Research Award from Johnson Cancer Research Center, Kansas State University.

Depends R (>= 4.2.0)

License GPL-2

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URL <https://github.com/kunfa/mixedBayes>

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LinkingTo Rcpp, RcppArmadillo

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Author Kun Fan [aut, cre],
Cen Wu [aut]

Maintainer Kun Fan <kfan@ksu.edu>

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mixedBayes-package	<i>Bayesian Longitudinal Regularized Quantile Mixed Model</i>
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Description

In this package, we provide a set of Bayesian regularized variable selection methods under the mixed effect models (random intercept and slope model, random intercept model) to dissect important gene - environment interactions for longitudinal studies. A Bayesian quantile regression has been adopted to accommodate data contamination and heavy-tailed distributions in the response/phenotype. The default method (the proposed method) conducts variable selection by accounting the group level selection on the interaction effects under random intercept and slope model. In particular, the spike-and-slab priors are imposed on both individual and group levels to identify important main and interaction effects. In addition to the default method, users can also choose different selection structures for the interaction effects (group-level or individual-level), random intercept model, methods without spike-and-slab priors and non-robust methods. In total, *mixedBayes* provides 16 different methods (8 robust and 8 non-robust) under both mixed effects models. Among them, robust methods with spike-and-slab priors and the robust method for both individual level selection and group level selection under both mixed effects models have been developed for the first time. Please read the Details below for how to configure the method used.

Details

The user friendly, integrated interface **mixedBayes()** allows users to flexibly choose the fitting methods by specifying the following parameter:

- slope: whether to use random intercept and slope model.
- robust: whether to use robust methods for modelling.
- quant: to specify different quantiles when using robust methods.
- structure: structure for interaction effects.
- sparse: whether to use the spike-and-slab priors to impose sparsity.

The function **mixedBayes()** returns a **mixedBayes** object that contains the posterior estimates of each coefficients. S3 generic functions **selection()** and **print()** are implemented for **mixedBayes** objects. **selection()** takes a **mixedBayes** object and returns the variable selection results.

References

- Fan, K., Wang, W. and Wu, C. (2022). Bayesian Regularized Quantile Mixed Model for Lipid - Environment Interactions in a Longitudinal Study. (to be submitted)
- Zhou, F., Ren, J., Li, G., Jiang, Y., Li, X., Wang, W. and Wu, C. (2019). Penalized Variable Selection for Lipid-Environment Interactions in a Longitudinal Lipidomics Study. *Genes*, 10(12), 1002 [doi:10.3390/genes10121002](https://doi.org/10.3390/genes10121002)
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- Wu, C., and Ma, S. (2015). A selective review of robust variable selection with applications in bioinformatics. *Briefings in Bioinformatics*, 16(5), 873–883 [doi:10.1093/bib/bbu046](https://doi.org/10.1093/bib/bbu046)
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- Ren, J., Zhou, F., Li, X., Wu, C. and Jiang, Y. (2019) spinBayes: Semi-Parametric Gene-Environment Interaction via Bayesian Variable Selection. R package version 0.1.0. <https://CRAN.R-project.org/package=spinBayes>
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- Wu, C., Cui, Y., and Ma, S. (2014). Integrative analysis of gene–environment interactions under a multi–response partially linear varying coefficient model. *Statistics in Medicine*, 33(28), 4988–4998 [doi:10.1002/sim.6287](https://doi.org/10.1002/sim.6287)
- Wu, C., Zhong, P.S. and Cui, Y. (2013). High dimensional variable selection for gene-environment interactions. *Technical Report. Michigan State University*.

See Also

[mixedBayes](#)

data

simulated data for demonstrating the features of mixedBayes

Description

Simulated gene expression data for demonstrating the features of mixedBayes.

Format

The data object consists of seven components: y, e, X, g, w, k and coeff. coeff contains the true values of parameters used for generating Y.

Details

The data and model setting

Consider a longitudinal study on n subjects with k repeated measurement for each subject. Let Y_{ij} be the measurement for the i th subject at each time point j ($1 \leq i \leq n, 1 \leq j \leq k$). We use a m -dimensional vector G_{ij} to denote the genetics factors, where $G_{ij} = (G_{ij1}, \dots, G_{ijm})^\top$. Also, we use p -dimensional vector E_{ij} to denote the environment factors, where $E_{ij} = (E_{ij1}, \dots, E_{ijp})^\top$. $X_{ij} = (1, T_{ij})^\top$, where T_{ij}^\top is a vector of time effects. Z_{ij} is a $h \times 1$ covariate associated with random effects and α_i is a $h \times 1$ vector of random effects. At the beginning, the interaction effects is modeled as the product of genomics features and environment factors with 4 different levels. After representing the environment factors as three dummy variables, the identification of the gene by environment interaction needs to be performed as group level. Combing the genetics factors, environment factors and their interactions that associated with the longitudinal phenotype, we have the following mixed-effects model:

$$Y_{ij} = X_{ij}^\top \gamma_0 + E_{ij}^\top \gamma_1 + G_{ij}^\top \gamma_2 + (G_{ij} \otimes E_{ij})^\top \gamma_3 + Z_{ij}^\top \alpha_i + \epsilon_{ij}.$$

where $\gamma_1, \gamma_2, \gamma_3$ are p, m and mp dimensional vectors that represent the coefficients of the environment effects, the genetics effects and interactions effects, respectively. Accommodating the Kronecker product of the m -dimensional vector G_{ij} and the p -dimensional vector E_{ij} , the interactions between genetics and environment factors can be expressed as a mp -dimensional vector, denoted as the following form:

$$G_{ij} \otimes E_{ij} = [E_{ij1}E_{ij1}, E_{ij2}E_{ij2}, \dots, E_{ij1}E_{ijp}, E_{ij2}E_{ij1}, \dots, E_{ijm}E_{ijp}]^\top.$$

For random intercept and slope model, $Z_{ij}^\top = (1, j)$ and $\alpha_i = (\alpha_{i1}, \alpha_{i2})^\top$. For random intercept model, $Z_{ij}^\top = 1$ and $\alpha_i = \alpha_{i1}$.

See Also

[mixedBayes](#)

Examples

```
data(data)
length(y)
dim(g)
dim(e)
dim(w)
print(k)
print(X)
print(coeff)
```

mixedBayes

*fit a Bayesian longitudinal regularized quantile mixed model***Description**

fit a Bayesian longitudinal regularized quantile mixed model

Usage

```
mixedBayes(
  y,
  e,
  X,
  g,
  w,
  k,
  iterations = 10000,
  burn.in = NULL,
  slope = TRUE,
  robust = TRUE,
  quant = 0.5,
  sparse = TRUE,
  structure = c("group", "individual")
)
```

Arguments

y	the vector of response variable. The current version of mixedBayes only supports continuous response.
e	the matrix of a group of dummy environmental factors variables.
X	the matrix of the intercept and time effects (time effects are optional).
g	the matrix of predictors (genetic factors) without intercept. Each row should be an observation vector.
w	the matrix of interactions between genetic factors and environmental factors.
k	the total number of time points.
iterations	the number of MCMC iterations.
burn.in	the number of iterations for burn-in.
slope	logical flag. If TRUE, random intercept and slope model will be used.
robust	logical flag. If TRUE, robust methods will be used.
quant	specify different quantiles when applying robust methods.
sparse	logical flag. If TRUE, spike-and-slab priors will be used to shrink coefficients of irrelevant covariates to zero exactly.
structure	structure for interaction effects, two choices are available. "group" for selection on group-level only. "individual" for selection on individual-level only.

Details

Consider the data model described in "[data](#)":

$$Y_{ij} = X_{ij}^\top \gamma_0 + E_{ij}^\top \gamma_1 + \sum_{l=1}^p G_{ijl} \gamma_{2l} + \sum_{l=1}^p W_{ijl}^\top \gamma_{3l} + Z_{ij}^\top \alpha_i + \epsilon_{ij}.$$

where γ_{2l} is the main effect of the l th genetic variant. The interaction effects is corresponding to the coefficient vector $\gamma_{3l} = (\gamma_{3l1}, \gamma_{3l2}, \dots, \gamma_{3lm})^\top$.

When 'structure="group"', group-level selection will be conducted on $\|\gamma_{3l}\|_2$. If 'structure="individual"', individual-level selection will be conducted on each γ_{3lq} , ($q = 1, \dots, m$).

When 'slope=TRUE' (default), random intercept and slope model will be used as the mixed effects model.

When 'sparse=TRUE' (default), spike-and-slab priors are imposed on individual and/or group levels to identify important main and interaction effects. Otherwise, Laplacian shrinkage will be used.

When 'robust=TRUE' (default), the distribution of ϵ_{ij} is defined as a Laplace distribution with density.

$f(\epsilon_{ij}|\theta, \tau) = \theta(1 - \theta) \exp\{-\tau\rho_\theta(\epsilon_{ij})\}$, ($i = 1, \dots, n, j = 1, \dots, k$), which leads to a Bayesian formulation of quantile regression. If 'robust=FALSE', ϵ_{ij} follows a normal distribution.

Please check the references for more details about the prior distributions.

Value

an object of class 'mixedBayes' is returned, which is a list with component:

posterior	the posteriors of coefficients.
coefficient	the estimated coefficients.
burn.in	the total number of burn-ins.
iterations	the total number of iterations.

See Also

[data](#)

Examples

```
data(data)

## default method
fit = mixedBayes(y,e,X,g,w,k,structure=c("group"))
fit$coefficient

## Compute TP and FP
b = selection(fit,sparse=TRUE)
index = which(coeff!=0)
pos = which(b != 0)
tp = length(intersect(index, pos))
```

```

fp = length(pos) - tp
list(tp=tp, fp=fp)

## alternative: robust individual selection
fit = mixedBayes(y,e,X,g,w,k,structure=c("individual"))
fit$coefficient

## alternative: non-robust group selection
fit = mixedBayes(y,e,X,g,w,k,robust=FALSE, structure=c("group"))
fit$coefficient

## alternative: robust group selection under random intercept model
fit = mixedBayes(y,e,X,g,w,k,slope=FALSE, structure=c("group"))
fit$coefficient

```

selection	<i>Variable selection for a mixedBayes object</i>
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Description

Variable selection for a mixedBayes object

Usage

```
selection(obj, sparse)
```

Arguments

obj	mixedBayes object.
sparse	logical flag. If TRUE, spike-and-slab priors will be used to shrink coefficients of irrelevant covariates to zero exactly..

Details

If sparse, the median probability model (MPM) (Barbieri and Berger, 2004) is used to identify predictors that are significantly associated with the response variable. Otherwise, variable selection is based on 95% credible interval. Please check the references for more details about the variable selection.

Value

an object of class ‘selection’ is returned, which is a list with component:

inde	a vector of indicators of selected effects.
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References

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- Barbieri, M.M. and Berger, J.O. (2004). Optimal predictive model selection. *Ann. Statist.*, 32(3):870–897

See Also

[mixedBayes](#)

Examples

```
data(data)
## sparse
fit = mixedBayes(y,e,X,g,w,k,structure=c("group"))
selected=selection(fit,sparse=TRUE)
selected

## non-sparse
fit = mixedBayes(y,e,X,g,w,k,sparse=FALSE,structure=c("group"))
selected=selection(fit,sparse=FALSE)
selected
```


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