Package ‘EMMREML’

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Title Fitting Mixed Models with Known Covariance Structures

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Description The main functions are 'emmreml', and 'emmremlMultiKernel'. 'emmreml' solves a mixed model with known covariance structure using the 'EMMA' algorithm. 'emmremlMultiKernel' is a wrapper for 'emmreml' to handle multiple random components with known covariance structures. The function 'emmremlMultivariate' solves a multivariate gaussian mixed model with known covariance structure using the 'ECM' algorithm.

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`EMMREML` *Fitting mixed models with known covariance structures.*

Description

The main functions are emmreml, and emmremlMultiKernel.emmreml solves a mixed model with known covariance structure using the EMMA algorithm in Kang et.al. (2008). emmremlMultiKernel is a wrapper for emmreml to handle multiple random components with known covariance structures. The function emmremlMultivariate solves a multivariate gaussian mixed model with known covariance structure using the ECM algorithm in Zhou and Stephens (2012).

Details

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Author(s)

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References

Efficient control of population structure in model organism association mapping. Kang, Hyun Min and Zaitlen, Noah A and Wade, Claire M and Kirby, Andrew and Heckerman, David and Daly, Mark J and Eskin, Eleazar. Genetics, 2008.

Genome-wide efficient mixed-model analysis for association studies. Zhou, Xiang and Stephens, Matthew. Nature genetics, 2012.

`emmreml` *Solver for Gaussian mixed model with known covariance structure.*

Description

This function estimates the parameters of the model

$$y = X\beta + Zu + e$$

where y is the n vector of response variable, X is a nxq known design matrix of fixed effects, Z is a nxl known design matrix of random effects, β is $qx1$ vector of fixed effects coefficients and u and e are independent variables with $N_l(0, \sigma_u^2 K)$ and $N_n(0, \sigma_e^2 I_n)$ correspondingly. It also produces the BLUPs and some other useful statistics like large sample estimates of variances and PEV.

Usage

```
emmreml(y, X, Z, K,varbetahat=FALSE,varuhat=FALSE, PEVuhat=FALSE, test=FALSE)
```

Arguments

`y`	$nx1$ numeric vector
`X`	nxq matrix
`Z`	nxl matrix
`K`	lxl matrix of known relationships
`varbetahat`	TRUE or FALSE
`varuhat`	TRUE or FALSE
`PEVuhat`	TRUE or FALSE
`test`	TRUE or FALSE

Value

`Vu`	Estimate of σ_u^2
`Ve`	Estimate of σ_e^2
`betahat`	BLUEs for β
`uhat`	BLUPs for u
`Xsqtestbeta`	χ^2 test statistics for testing whether the fixed effect coefficients are equal to zero.
`pvalbeta`	pvalues obtained from large sample theory for the fixed effects. We report the pvalues adjusted by the "padjust" function for all fixed effect coefficients.
`Xsqtestu`	χ^2 test statistic values for testing whether the BLUPs are equal to zero.
`pvalu`	pvalues obtained from large sample theory for the BLUPs. We report the pvalues adjusted by the "padjust" function.
`varuhat`	Large sample variance for the BLUPs.
`varbetahat`	Large sample variance for the β's.
`PEVuhat`	Prediction error variance estimates for the BLUPs.
`loglik`	loglikelihood for the model.

Examples

```
n=200
M1<-matrix(rnorm(n*300), nrow=n)
K1<-cov(t(M1))
K1=K1/mean(diag(K1))
```

```
covY<-2*K1+1*diag(n)

Y<-10+crossprod(chol(covY),rnorm(n))


#training set
Trainset<-sample(1:n, 150)

funout<-emmreml(y=Y[Trainset], X=matrix(rep(1, n)[Trainset], ncol=1),
 Z=diag(n)[Trainset,], K=K1)

cor(Y[-Trainset], funout$uhat[-Trainset])
```

`emmremlMultiKernel` *Function to fit Gaussian mixed model with multiple mixed effects with known covariances.*

Description

This function is a wrapper for the emmreml to fit Gaussian mixed model with multiple mixed effects with known covariances. The model fitted is $y = X\beta + Z_1 u_1 + Z_2 u_2 + ...Z_k u_k + e$ where y is the n vector of response variable, X is a nxq known design matrix of fixed effects, Z_j is a nxl_j known design matrix of random effects for $j = 1, 2, ..., k$, β is $nx1$ vector of fixed effects coefficients and $U = (u_1^t, u_2^t, ..., u_k^t)^t$ and e are independent variables with $N_L(0, blockdiag(\sigma^2_{u_1} K_1, \sigma^2_{u_2} K_2, ..., \sigma^2_{u_k} K_k))$ and $N_n(0, \sigma^2_e I_n)$ correspondingly. The function produces the BLUPs for the $L = l_1 + l_2 + ... + l_k$ dimensional random effect U. The variance parameters for random effects are estimated as $(\hat{w}_1, \hat{w}_2, ..., \hat{w}_k) * \hat{\sigma^2_u}$ where $w = (w_1, w_2, ..., w_k)$ are the kernel weights. The function also provides some useful statistics like large sample estimates of variances and PEV.

Usage

```
emmremlMultiKernel(y, X, Zlist, Klist,
varbetahat=FALSE,varuhat=FALSE, PEVuhat=FALSE, test=FALSE)
```

Arguments

`y`	$nx1$ numeric vector
`X`	nxq matrix
`Zlist`	list of random effects design matrices of dimensions nxl_1,...,nxl_k
`Klist`	list of known relationship matrices of dimensions l_1xl_1,...,l_kxl_k
`varbetahat`	TRUE or FALSE
`varuhat`	TRUE or FALSE
`PEVuhat`	TRUE or FALSE
`test`	TRUE or FALSE

Value

Vu	Estimate of σ_u^2
Ve	Estimate of σ_e^2
betahat	BLUEs for β
uhat	BLUPs for u
weights	Estimates of kernel weights
Xsqtestbeta	A χ^2 test statistic based for testing whether the fixed effect coefficients are equal to zero.
pvalbeta	pvalues obtained from large sample theory for the fixed effects. We report the pvalues adjusted by the "padjust" function for all fixed effect coefficients.
Xsqtestu	A χ^2 test statistic based for testing whether the BLUPs are equal to zero.
pvalu	pvalues obtained from large sample theory for the BLUPs. We report the pvalues adjusted by the "padjust" function.
varuhat	Large sample variance for the BLUPs.
varbetahat	Large sample variance for the β's.
PEVuhat	Prediction error variance estimates for the BLUPs.
loglik	loglikelihood for the model.

Examples

```
####example
#Data from Gaussian process with three
#(total four, including residuals) independent
#sources of variation

n=80
M1<-matrix(rnorm(n*10), nrow=n)

M2<-matrix(rnorm(n*20), nrow=n)

M3<-matrix(rnorm(n*5), nrow=n)


#Relationship matrices
K1<-cov(t(M1))
K2<-cov(t(M2))
K3<-cov(t(M3))
K1=K1/mean(diag(K1))
K2=K2/mean(diag(K2))
K3=K3/mean(diag(K3))


#Generate data
covY<-2*(.2*K1+.7*K2+.1*K3)+diag(n)

Y<-10+crossprod(chol(covY),rnorm(n))
```

```
#training set
Trainsamp<-sample(1:80, 60)

funout<-emmremlMultiKernel(y=Y[Trainsamp], X=matrix(rep(1, n)[Trainsamp], ncol=1),
Zlist=list(diag(n)[Trainsamp,], diag(n)[Trainsamp,], diag(n)[Trainsamp,]),
Klist=list(K1,K2, K3),
varbetahat=FALSE,varuhat=FALSE, PEVuhat=FALSE, test=FALSE)
#weights
funout$weights
#Correlation of predictions with true values in test set
uhatmat<-matrix(funout$uhat, ncol=3)
uhatvec<-rowSums(uhatmat)

cor(Y[-Trainsamp], uhatvec[-Trainsamp])
```

`emmremlMultivariate` *Function to fit multivariate Gaussian mixed model with with known covariance structure.*

Description

This function estimates the parameters of the model

$$Y = BX + GZ + E$$

where Y is the dxn matrix of response variable, X is a qxn known design matrix of fixed effects, Z is a lxn known design matrix of random effects, B is dxq matrix of fixed effects coefficients and G and E are independent matrix variate variables with $N_{dxl}(0, V_G, K)$ and $N_{dxn}(0, V_E, I_n)$ correspondingly. It also produces the BLUPs for the random effects G and some other statistics.

Usage

```
emmremlMultivariate(Y, X, Z, K,varBhat=FALSE,varGhat=FALSE,
PEVGhat=FALSE, test=FALSE,tolpar=1e-06, tolparinv=1e-06)
```

Arguments

`Y`	dxn matrix of response variable
`X`	qxn known design matrix of fixed effects
`Z`	lxn known design matrix of random effects
`K`	lxl matrix of known relationships
`varBhat`	TRUE or FALSE
`varGhat`	TRUE or FALSE
`PEVGhat`	TRUE or FALSE
`test`	TRUE or FALSE
`tolpar`	tolerance parameter for convergence
`tolparinv`	tolerance parameter for matrix inverse

Value

Vg	Estimate of V_G
Ve	Estimate of V_E
Bhat	BLUEs for B
Gpred	BLUPs for G
XsqtestB	χ^2 test statistics for testing whether the fixed effect coefficients are equal to zero.
pvalB	pvalues obtained from large sample theory for the fixed effects. We report the pvalues adjusted by the "padjust" function for all fixed effect coefficients.
XsqtestG	χ^2 test statistic values for testing whether the BLUPs are equal to zero.
pvalG	pvalues obtained from large sample theory for the BLUPs. We report the pvalues adjusted by the "padjust" function.
varGhat	Large sample variance for BLUPs.
varBhat	Large sample variance for the elements of B.
PEVGhat	Prediction error variance estimates for the BLUPs.

Examples

```
l=20
n<-15
m<-40

M<-matrix(rbinom(m*l,2,.2),nrow=l)
rownames(M)<-paste("l",1:nrow(M))
beta1<-rnorm(m)*exp(rbinom(m,5,.2))
beta2<-rnorm(m)*exp(rbinom(m,5,.1))
beta3<- rnorm(m)*exp(rbinom(m,5,.1))+beta2

g1<-M%*%beta1
g2<-M%*%beta2
g3<-M%*%beta3
e1<-sd(g1)*rnorm(l)
e2<-(-e1*2*sd(g2)/sd(g1)+.25*sd(g2)/sd(g1)*rnorm(l))
e3<-1*(e1*.25*sd(g2)/sd(g1)+.25*sd(g2)/sd(g1)*rnorm(l))

y1<-10+g1+e1
y2<--50+g2+e2
y3<--5+g3+e3

Y<-rbind(t(y1),t(y2), t(y3))

colnames(Y)<-rownames(M)
cov(t(Y))
Y[1:3,1:5]

K<-cov(t(M))
K<-K/mean(diag(K))
rownames(K)<-colnames(K)<-rownames(M)
X<-matrix(1,nrow=1,ncol=l)
```

```
colnames(X)<-rownames(M)
Z<-diag(l)
rownames(Z)<-colnames(Z)<-rownames(M)
SampleTrain<-sample(rownames(Z),n)
Ztrain<-Z[rownames(Z)%in%SampleTrain,]
Ztest<-Z[!(rownames(Z)%in%SampleTrain),]


##For a quick answer, tolpar is set to 1e-4.  Correct this in practice.
outfunc<-emmremlMultivariate(Y=Y%*%t(Ztrain),
X=X%*%t(Ztrain), Z=t(Ztrain),
K=K,tolpar=1e-4,varBhat=FALSE,
varGhat=FALSE, PEVGhat=FALSE, test=FALSE)

Yhattest<-outfunc$Gpred%*%t(Ztest)

cor(cbind(Ztest%*%Y[1,],Ztest%*%outfunc$Gpred[1,],
Ztest%*%Y[2,],Ztest%*%outfunc$Gpred[2,],Ztest%*%Y[3,],Ztest%*%outfunc$Gpred[3,]))


outfuncRidgeReg<-emmremlMultivariate(Y=Y%*%t(Ztrain),X=X%*%t(Ztrain), Z=t(Ztrain%*%M),
K=diag(m),tolpar=1e-5,varBhat=FALSE,varGhat=FALSE,
PEVGhat=FALSE, test=FALSE)

Gpred2<-outfuncRidgeReg$Gpred%*%t(M)
cor(Ztest%*%Y[1,],Ztest%*%Gpred2[1,])
cor(Ztest%*%Y[2,],Ztest%*%Gpred2[2,])
cor(Ztest%*%Y[3,],Ztest%*%Gpred2[3,])
```

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