Package 'cpgen'

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Type Package

Title Parallel genomic evaluations

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Description Frequently used methods in genomic applications with emphasis on parallel computing	
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cpgen-package

cpgen - Parallel genomic evaluations

Description

The package offers a variety of functions that are frequently being used in genomic prediction and genomewide association studies. The package is based on Rcpp and RcppEigen, hence all routines are implemented using the matrix algebra library Eigen. The main emphasis of the package lies in parallel computing which is realized by C++ functions making use of OpenMP.

Details

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License: GPL (>= 2)

Author(s)

Claas Heuer

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References

Guennebaud, G., Jacob, B., et al.: "Eigen v3". http://eigen.tuxfamily.org (2010)

Dirk Eddelbuettel and Romain Francois (2011). "Rcpp: Seamless R and C++ Integration". Journal of Statistical Software, 40(8), 1-18. URL http://www.jstatsoft.org/v40/i08/.

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Douglas Bates, Dirk Eddelbuettel (2013). "Fast and Elegant Numerical Linear Algebra Using the RcppEigen Package". Journal of Statistical Software, 52(5), 1-24. URL http://www.jstatsoft.org/v52/i05/.

ccolmv

Colwise means or variances

Description

Computes the colwise means or variances of a matrix - internal use

Usage

```
ccolmv(X,var=FALSE)
```

Arguments

X matrix of type: matrix or dgCMatrix

var boolean, defines whether the colwise variances rather than the means will be

returned

Value

Numeric Vector of colwise means or variances of X

Examples

```
X <- matrix(rnorm(1000*500),1000,500)
means <- ccolmv(X)
vars <- ccolmv(X,var=TRUE)</pre>
```

ccov

ccov

Description

Computation of covariance- or correlation-matrix. Shrinkage estimate through the use of 'lambda'. Weights for observations can be passed.

Usage

```
ccov(X,lambda=0, w=NULL, cor=FALSE)
```

4 ccross

Arguments

X matrix

lambda numeric scalar, shrinkage parameter

w numeric vector of weights with same lengths as rows in X

cor boolean - defines whether the functions returns a correlation- rather than a co-

variance matrix

Value

Covariance matrix with dimension ncol(X)

Examples

```
## Not run:
# generate random data
rand_data(500,5000)
# compute correlation matrix of t(M)
corM <- ccov(t(M),cor=T)
## End(Not run)</pre>
```

ccross ccross

Description

Computation of the following matrix-product: $\mathbf{XDX'}$ Where \mathbf{D} is a diagonal matrix, which is being passed to the function as a vector.

Usage

```
ccross(X,D=NULL)
```

Arguments

X matrix

D numeric vector, will be used as a weighting diagonal matrix of dimension ncol(X).

If omitted an identity matrix will be assigned.

Value

Square matrix of dimension nrow(X)

cCV 5

Examples

```
# Computing the matrix-square-root of a positive definite square matrix:
## Not run:
# generate random data
rand_data(500,5000)

W <- ccross(M)

# this is the implementation of the matrix power-operator '%**%'
W_sqrt <- with(eigen(W), ccross(vectors,values**0.5))

## End(Not run)</pre>
```

cCV

Generate phenotype vectors for cross validation

Description

This function takes a phenotype vector and generates folds * reps masked vectors for cross validation. Every vector has as many additional missing values as length(y) / folds.

Usage

```
cCV(y,folds=5,reps=1,matrix=FALSE,seed=NULL)
```

Arguments

		1	. 1 1		1
١	vector of	phenotypes - may	aiready c	ontain missin	o valiles
	vector or	pricinot, pes may	un cua y c	Ontain missin	Svaracs

folds integer, number of folds

reps integer, number of replications

matrix boolean, if TRUE function returns a matrix rather than a list

seed numeric scalar, seed for sample

Value

List (matrix) with as many items (columns) as folds * reps

See Also

```
clmm, get_pred, get_cor
```

6 cGBLUP

Examples

```
## Not run:
# generate random data
rand_data(500,5000)

y_CV <- cCV(y,folds=5,reps=20)
## End(Not run)</pre>
```

cGBLUP

Genomic BLUP

Description

This function allows fitting a mixed model with one random effect besides the residual using clmm. The random effect ${\bf a}$ follows some covariance-structure ${\bf G}$

Usage

```
cGBLUP(y,G,X=NULL, scale_a = 0, df_a = -2, scale_e = 0, df_e = -2, niter = 10000, burnin = 5000, seed = NULL, verbose=TRUE)
```

Arguments

у		vector of phenotypes
G		Relationship matrix / covariance structure for random effects
Χ		Optional Design Matrix for fixed effects. If omitted a column-vector of ones will be assigned
sca	le_a	prior scale parameter for a
df_	a	prior degrees of freedom for a
sca	le_e	prior scale parameter for e
df_	е	prior degrees of freedom for e
nit	er	Number of iterations
bur	nin	Burnin
see	d	Seed
ver	bose	Prints progress to the screen

Details

Kang et al. (2008):

$$y = Xb + a + e$$
 with: $a \sim MVN(0, G\sigma_a^2)$

By finding the decomposition: G = UDU' and premultiplying the model equation by U' we get:

$$\mathbf{U}'\mathbf{y} = \mathbf{U}'\mathbf{X}\mathbf{b} + \mathbf{U}'\mathbf{a} + \mathbf{U}'\mathbf{e}$$

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with:

$$Var(\mathbf{U'y}) = \mathbf{U'G'U}\sigma_a^2 + \mathbf{U'U}\sigma_e^2$$

$$\mathbf{U'UDU'U}\sigma_a^2 + \mathbf{I}\sigma_e^2$$

$$\mathbf{D}\sigma_a^2 + \mathbf{I}\sigma_e^2$$

After diagonalization of the variance-covariance structure the transformed model is being fitted by passing $\mathbf{D}^{1/2}$ as the design matrix for the random effects to clmm. The results are subsequently backtransformed and returned by the function.

Value

List of 6:

var_e Posterior mean of the residual variance
var_a Posterior mean of the random-effect variance
b Posterior means of the fixed effects
a Posterior means of the random effects
posterior_var_e
Posterior of the residual variance
posterior_var_u

Posterior of the random variance

Author(s)

Claas Heuer

References

Kang, H. M., N. A. Zaitlen, C. M. Wade, A. Kirby, D. Heckerman, M. J. Daly, and E. Eskin. "Efficient Control of Population Structure in Model Organism Association Mapping." Genetics 178, no. 3 (February 1, 2008): 1709-23. doi:10.1534/genetics.107.080101.

See Also

```
clmm, cgrm, cGWAS.emmax
```

```
## Not run:
# generate random data
rand_data(500,5000)

# compute a genomic relationship-matrix
G <- cgrm(M,lambda=0.01)

# run model
mod <- cGBLUP(y,G)

## End(Not run)</pre>
```

8 cgrm

cgrm

Genomic Relationship Matrices

Description

Based on a coefficient-matrix (i.e. marker matrix) X that will be scaled column-wise, a weight-vector w and a shrinkage parameter λ , cgrm returns the following similarity matrix:

$$\mathbf{G} = (1 - \lambda) \frac{\mathbf{X} \mathbf{D} \mathbf{X}'}{\sum \mathbf{w}} + \mathbf{I} \lambda$$

where $\mathbf{D} = diag(\mathbf{w})$. A weighted genomic relationship matrix allows running TA-BLUP as described in Zhang et al. (2010).

Usage

```
cgrm(X, w = NULL, lambda=0)
```

Arguments

X coefficient matrix

w numeric vector of weights for every column in X

lambda numeric scalar, shrinkage parameter

Details

...

Value

Similarity matrix with dimension nrow(X)

Author(s)

Claas Heuer

References

de los Campos, G., Vazquez, A.I., Fernando, R., Klimentidis, Y.C., Sorensen, D., 2013. "Prediction of Complex Human Traits Using the Genomic Best Linear Unbiased Predictor". PLoS Genetics 9, e1003608. doi:10.1371/journal.pgen.1003608

Zhang Z, Liu J, Ding X, Bijma P, de Koning D-J, et al. (2010) "Best Linear Unbiased Prediction of Genomic Breeding Values Using a Trait-Specific Marker-Derived Relationship Matrix". PLoS ONE 5(9): e12648. doi:10.1371/journal.pone.0012648

See Also

cgrm.A, cgrm.D.

cgrm.A

Examples

```
## Not run:
# generate random data
rand_data(500,5000)
weights <- (cor(M,y)**2)[,1]
G <- cgrm(M,weights,lambda=0.01)
## End(Not run)</pre>
```

cgrm.A

Additive Genomic Relationship Matrix

Description

Based on a marker matrix X with $\{-1,0,1\}$ - coding that will be centered column-wise and a shrinkage parameter λ , cgrm. A returns the following additive genomic relationship matrix according to VanRaden (2008):

$$\mathbf{G} = (1 - \lambda) \frac{\mathbf{X} \mathbf{X}'}{\sum_{i=1}^{n} 2p_i q_i} + \mathbf{I} \lambda$$

Usage

```
cgrm.A(X, lambda=0, yang=FALSE)
```

Arguments

X marker matrix

lambda numeric scalar, shrinkage parameter

yang boolean, diagonal elements of A according to Yang et al. (2010)

Details

•••

Value

Additive genomic relationship matrix with dimension nrow(X)

Author(s)

Claas Heuer

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References

VanRaden, P.M. "Efficient Methods to Compute Genomic Predictions". Journal of Dairy Science 91, no. 11 (November 2008): 4414-23. doi:10.3168/jds.2007-0980.

Yang, Jian, Beben Benyamin, Brian P McEvoy, Scott Gordon, Anjali K Henders, Dale R Nyholt, Pamela A Madden, et al. "Common SNPs Explain a Large Proportion of the Heritability for Human Height". Nature Genetics 42, no. 7 (July 2010): 565-69. doi:10.1038/ng.608.

See Also

```
cgrm, cgrm.D
```

Examples

```
## Not run:
# generate random data
rand_data(500,5000)

### compute the additive genomic relationship matrix
A <- cgrm.A(M,lambda=0.01)
## End(Not run)</pre>
```

cgrm.D

Dominance Genomic Relationship Matrix

Description

Based on a marker matrix X with $\{-1,0,1\}$ - out of which a column-wise centered dominance coefficient matrix will be constructed and a shrinkage parameter λ , cgrm.D returns the following dominance genomic relationship matrix according to Su et al. (2012):

$$\mathbf{G} = (1 - \lambda) \frac{\mathbf{X} \mathbf{X}'}{\sum_{i=1}^{n} 2p_i q_i (1 - 2p_i q_i)} + \mathbf{I} \lambda$$

The additive marker coefficients will be used to compute dominance coefficients as: 1-abs(X)

Usage

```
cgrm.D(X, lambda=0)
```

Arguments

X marker matrix

lambda numeric scalar, shrinkage parameter

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Details

...

Value

Dominance relationship matrix with dimension nrow(X)

Author(s)

Claas Heuer

References

Su G, Christensen OF, Ostersen T, Henryon M, Lund MS (2012) "Estimating Additive and Non-Additive Genetic Variances and Predicting Genetic Merits Using Genome-Wide Dense Single Nucleotide Polymorphism Markers". PLoS ONE 7(9): e45293. doi:10.1371/journal.pone.0045293

See Also

```
cgrm, cgrm. A.
```

Examples

```
## Not run:
# generate random data
rand_data(500,5000)

D <- cgrm.D(M,lambda=0.01)
## End(Not run)</pre>
```

cGWAS

Genomewide Association Study

Description

This function runs GWAS for continuous traits. Population structure that can lead to false positive association signals can be accounted for by passing a Variance-covariance matrix of the phenotype vector (Kang et al., 2010). The GLS-solution for fixed effects is computed as:

$$\hat{\boldsymbol{\beta}} = (\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^{-1}\mathbf{X}'\mathbf{V}^{-1}\mathbf{y}$$

Equivalent solutions are obtained by premultiplying the design matrix X for fixed effects and the phenotype vector y by $V^{-1/2}$:

$$\hat{eta} = (\mathbf{X}^{*\prime}\mathbf{X}^{*})^{-1}\mathbf{X}^{*\prime}\mathbf{y}^{*}$$

$$\mathbf{X}^{*} = \mathbf{V}^{-1/2}\mathbf{X}$$

$$\mathbf{v}^{*} = \mathbf{V}^{-1/2}\mathbf{v}$$

with

cGWAS

Usage

cGWAS(y,M,X=NULL,V=NULL,dom=FALSE, verbose=TRUE)

Arguments

У	vector of phenotypes
М	Marker matrix
X	Optional Design Matrix for additional fixed effects. If omitted a column-vector of ones will be assigned
V	Inverse square root of the Variance-covariance matrix for the phenotype vector of type: matrix or dgCMatrix. Used for computing the GLS-solution of fixed effects. If omitted an identity-matrix will be assigned
dom	Defines whether to include an additional dominance coefficient for every marker. Note: only useful if the genotype-coding in M follows {-1,0,1} The dominance coefficient is computed as: 1-abs(M)
verbose	prints progress to the screen

Details

...

Value

List of 3 vectors or matrices. If dom=TRUE every element of the list will be a matrix with two columns. First column additive, second dominance:

p-value Vector of p-values for every marker
beta GLS solution for fixed marker effects
se Standard Errors for values in beta

Author(s)

Claas Heuer

References

Kang, Hyun Min, Jae Hoon Sul, Susan K Service, Noah A Zaitlen, Sit-yee Kong, Nelson B Freimer, Chiara Sabatti, and Eleazar Eskin. "Variance Component Model to Account for Sample Structure in Genome-Wide Association Studies." Nature Genetics 42, no. 4 (April 2010): 348-54. doi:10.1038/ng.548.

See Also

cGWAS.emmax

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Examples

```
## Not run:
# generate random data
rand_data(500,5000)
### GWAS without accounting for population structure
mod <- cGWAS(y,M)</pre>
### GWAS - accounting for population structure
## Estimate variance covariance matrix of y
G <- cgrm.A(M,lambda=0.01)
fit <- cGBLUP(y,G,verbose=FALSE)</pre>
### construct V
V <- G*fit$var_a + diag(length(y))*fit$var_e</pre>
### get the inverse square root of V
V2inv <- V %**% -0.5
### run GWAS again
mod2 <- cGWAS(y,M,V=V2inv,verbose=TRUE)</pre>
## End(Not run)
```

cGWAS.emmax

Genomewide Association Study - EMMAX

Description

This is a convenience function that uses the function cGWAS but estimates the variance-covariance matrix of the phenotype vector in advance using clmm. This method was termed EMMAX (Kang et al., 2010).

Usage

```
cGWAS.emmax(y,M,A=NULL,X=NULL,dom=FALSE,verbose=TRUE,scale_a = 0, df_a = -2, scale_e = 0, df_e = -2,niter=15000,burnin=7500,seed=NULL)
```

Arguments

y vector of phenotypes

M Marker matrix

A Relationship matrix that is being used to estimate V - if omitted, A will be constructed using M and cgrm

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X Optional Design Matrix for additional fixed effects. If omitted a column-vector

of ones will be assigned

dom Defines whether to include an additional dominance coefficient for every marker.

Note: only useful if the genotype-coding in M follows {-1,0,1} The dominance

coefficient is computed as: 1-abs(M)

verbosePrints progress to the screenscale_aprior scale parameter for adf_aprior degrees of freedom for ascale_eprior scale parameter for edf_eprior degrees of freedom for eniterNumber of iterations used by clmm

burnin Burnin for clmm
seed Seed used by clmm

Details

...

Value

List of 3 vectors or matrices. If dom=TRUE every element of the list will be a matrix with two columns. First column additive, second dominance:

p-value Vector of p-values for every marker
beta GLS solution for fixed marker effects
se Standard Errors for values in beta

marker_variance

Estimate of the marker variance reported by clmm

residual_variance

Estimate of the residual variance reported by clmm

Author(s)

Claas Heuer

References

Kang, H. M., N. A. Zaitlen, C. M. Wade, A. Kirby, D. Heckerman, M. J. Daly, and E. Eskin. "Efficient Control of Population Structure in Model Organism Association Mapping." Genetics 178, no. 3 (February 1, 2008): 1709-23. doi:10.1534/genetics.107.080101.

Kang, Hyun Min, Jae Hoon Sul, Susan K Service, Noah A Zaitlen, Sit-yee Kong, Nelson B Freimer, Chiara Sabatti, and Eleazar Eskin. "Variance Component Model to Account for Sample Structure in Genome-Wide Association Studies." Nature Genetics 42, no. 4 (April 2010): 348-54. doi:10.1038/ng.548.

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See Also

cGWAS

Examples

```
## Not run:
# generate random data
rand_data(500,5000)

# run EMMAX
res <- cGWAS.emmax(y,M,verbose=TRUE)
## End(Not run)</pre>
```

check_openmp

Check OpenMP-support.

Description

Checks whether the C++ binaries have been compiled with OpenMP-support.

Usage

```
check_openmp()
```

Value

Returns a message telling you whether OpenMP is available for the cpgen-functions or not.

See Also

```
set_num_threads, get_num_threads, get_max_threads
```

```
# check whether openmp is available or not
check_openmp()
```

c1mm

Linear Mixed Models using Gibbs Sampling

Description

This function runs linear mixed models of the following form:

$$y = Xb + Z_1u_1 + Z_2u_2 + Z_3u_3 + ... + Z_ku_k + e$$

The function allows to include an arbitrary number of independent random effects with each of them being assumed to follow: $MVN(\mathbf{0}, \mathbf{I}\sigma_{u_k}^2)$. If the covariance structure of one random effect is assumed to follow some \mathbf{G} then it is necessary to construct the design matrix for that random effect as described in Waldmann et al. (2008): $\mathbf{F} = \mathbf{Z}\mathbf{G}^{1/2}$.

Usage

```
clmm(y, X = NULL , random = NULL, par_random = NULL, niter=10000, burnin=5000, scale_e=0,
df_e=-2, beta_posterior = FALSE, verbose = TRUE, timings = FALSE, seed = NULL)
```

Arguments

У

guments			

X Fixed effects design matrix of type: matrix or dgCMatrix. If omitted a column-

vector of ones will be assigned

vector or list of phenotypes

random list of design matrices for random effects - every element of the list represents

one random effect and may be of type: matrix or dgCMatrix

par_random list of options for random effects. If passed, the list must have as many elements

as random. Every element may be a list of 4:

• scale - (vector of) scale parameters for the inverse chi-square prior

• df - (vector of) degrees of freedom for the inverse chi-square prior

 method - method to be used for the random effects, may be: ridge or BayesA

• name - name for that effect

• GWAS - list of options for conducting GWAS using window variance proportions (Fernando et al, 2013):

window_size - number of markers used to form a single window

 threshold - window porportion of total variance, used to determine presents of association

niter number of iterations

burnin number of iterations to be discarded as burnin

verbose prints progress to the screen

beta_posterior save all posterior samples of regression coefficients

timings prints time per iteration to the screen - sets verbose = FALSE

scale_e scale parameter for the inverse chi-square prior for the residuals

df_e degrees of freedom for the inverse chi-square prior for the residuals

seed seed for the random number generator. If omitted, a seed will be generated based on machine and time

Details

Single Model run

At this point the function allows to specify the method for any random term as: 'ridge' or 'BayesA'. In Ridge Regression the prior distribution of the random effects is assumed to be normal with a constant variance component, while in BayesA the marginal prior is a t-distribution, resulting from locus specific variances with inverse chi-square priors (Gianola et al., 2009). A wider range of methods is available in the excellent BGLR-package, which also allows phenotypes to be discrete (de los Campos et al. 2013).

The focus of this function is to allow solving high-dimensional problems that are mixtures of sparse and dense features in the design matrices. The computational expensive parts of the Gibbs Sampler are parallelized as described in Fernando et al. (2014). Note that the parallel performance highly depends on the number of observations and features present in the design matrices. It is highly recommended to set the number of threads for less than 10000 observations (length of phenotype vector) to 1 using: set_num_threads(1) before running a model. Even for larger sample sizes the parallel performance still depends on the dimension of the feature matrices. Good results in terms of parallel scaling were observed starting from 50000 observations and more than 10000 features (i.e. number of markers). Single threaded performance is very good thanks to smart computations during gibbs sampling (Fernando, 2013 (personal communication), de los Campos et al., 2009) and the use of efficient Eigen-methods for dense and sparse algebra.

Parallel Model runs

In the case of multiple phenotypes passed to the function as a list, the main advantage of the function is that several threads can access the very same data once assigned, which means that the design matrices only have to be allocated once. The parallel scaling of this function using multiple phenotypes is almost linear.

In C++:

For every element of the phenotype list a new instance of an MCMC-object will be created. All the memory allocation needed for running the model is done by the major thread. The function then iterates over all objects and runs the gibbs sampler. This step is parallelized, which means that as many models are being run at the same time as threads available. All MCMC-objects are totally independent from each other, they only share the same design-matrices. Every object has its own random-number generator with its own seed which allows perfectly reproducible results.

GWAS using genomic windows

The function allows to specify options to any random effect for conducting genomewide association studies using prediction vector variances of marker windows as described in Fernando et al. (2013). In every effective sample of the Gibbs Sampler the sampling variance of the genotypic value vector $\mathbf{g} = \mathbf{Z}\mathbf{u}$ of the particular random effect is computed as: $\tilde{\sigma}_g^2 = \left(\sum_{j=1}^n (g_j - \mu_g)^2\right)(n-1)^{-1}$, with μ_g being the mean of \mathbf{g} and n the number of observations. Then for any window w the sampling variance of $\mathbf{g}_{\mathbf{w}} = \mathbf{Z}_w \mathbf{u}_w$ is obtained as: $\tilde{\sigma}_{g_w}^2 = \left(\sum_{j=1}^n (g_{w_j} - \mu_{g_w})^2\right)(n-1)^{-1}$, where w indicates the range over the columns of \mathbf{Z} that forms the window w. The posterior probability

that a window exceeds a specified proportion δ of the total variance is estimated by the number of samples in which $\frac{\tilde{\sigma}_{gw}^2}{\tilde{\sigma}_g^2} > \delta$ divided by the total number of samples. It can be shown that among marker windows that have a posterior probability p or greater for having a variance greater than δ of the total variance, the proportion of false positive signals (PFP) are expected to be lower than 1-p (Fernando et al. 2004, Fernando et al., 2013).

Value

List of 4 + number of random effects:

Residual_Variance

List of 4:

- Posterior_Mean Mean estimate of the residual variance
- Posterior posterior samples of residual variance
- scale_prior scale parameter that has been assigned
- df_prior degrees of freedom that have been assigned

Predicted

numeric vector of predicted values

fixed_effects List of 4:

- type dense or sparse design matrix
- method method that has been used = "fixed"
- posterior list of 1 + 1 (if beta_posterior=TRUE)
 - estimates_mean mean solutions for random effects
 - estimates posterior samples of random effects

Susequently as many additional items as random effects of the following form

Effect_k List of 4 + 1 (if GWAS options were specified):

- type dense or sparse design matrix
- method method that has been used
- scale_prior scale parameter that has been assigned
- df_prior degrees of freedom that have been assigned
- posterior list of 3 + 1 (if beta_posterior=TRUE)
 - estimates_mean mean solutions for random effects
 - variance_mean mean variance
 - variance posterior samples of variance
 - estimates posterior samples of random effects
- GWAS list of 9 (if specified)
 - window_size number of features (markers) used to form a single window
 - threshold window porportion of total variance, used to determine presents of association
 - mean_variance mean variance of prediction vector using all windows
 - windows identifier
 - start starting column for window
 - end ending column for window

- window_variance mean variance of prediction vector using this window
- window_variance_proportion mean window proportion of total variance
- prob_window_var_bigger_threshold mean probability that window variance exceeds threshold

mcmc

List of 4 + 1 (if timings=TRUE):

- niter number of iterations
- burnin number of samples discarded as burnin
- number_of_samples number of samples used to estimate posterior means
- · seed seed used for the random number generator
- time_per_iter average seconds per iteration

Author(s)

Claas Heuer

Credits: Xiaochen Sun (Iowa State University, Ames) gave strong assistance in the theoretical parts and contributed in the very first implementation of the Gibbs Sampler. Essential parts were adopted from the BayesC-implementation of Rohan Fernando and the BLR-package of Gustavo de los Campos. The idea of how to parallelize the single site Gibbs Sampler came from Rohan Fernando (2013).

References

Gianola, D., de Los Campos, G., Hill, W.G., Manfredi, E., Fernando, R.: "Additive genetic variability and the bayesian alphabet." Genetics 183(1), 347<e2><80><93>363 (2009)

de los Campos, G., H. Naya, D. Gianola, J. Crossa, A. Legarra, E. Manfredi, K. Weigel, and J. M. Cotes. "Predicting Quantitative Traits With Regression Models for Dense Molecular Markers and Pedigree." Genetics 182, no. 1 (May 1, 2009): 375-85. doi:10.1534/genetics.109.101501.

Waldmann, Patrik, Jon Hallander, Fabian Hoti, and Mikko J. Sillanpaa. "Efficient Markov Chain Monte Carlo Implementation of Bayesian Analysis of Additive and Dominance Genetic Variances in Noninbred Pedigrees." Genetics 179, no. 2 (June 1, 2008): 1101-12. doi:10.1534/genetics.107.084160.

Meuwissen, T., B. J. Hayes, and M. E. Goddard. "Prediction of Total Genetic Value Using Genome-Wide Dense Marker Maps." Genetics 157, no. 4 (2001): 1819-29.

de los Campos, Gustavo, Paulino Perez Rodriguez, and Maintainer Paulino Perez Rodriguez. "Package 'BGLR,'" 2013. ftp://128.31.0.28/pub/CRAN/web/packages/BGLR/BGLR.pdf.

Fernando, R.L., Dekkers, J.C., Garrick, D.J. "A class of bayesian methods to combine large numbers of genotyped and non-genotyped animals for whole-genome analyses." Genetics Selection Evolution 46(1), 50 (2014)

Fernando, R., Nettleton, D., Southey, B., Dekkers, J., Rothschild, M., Soller, M. "Controlling the proportion of false positives in multiple dependent tests." Genetics 166(1), 611<e2><80><93>619 (2004)

Fernando, Rohan L., and Dorian Garrick. "Bayesian methods applied to GWAS." Genome-Wide Association Studies and Genomic Prediction. Humana Press, 2013. 237-274.

See Also

```
cGBLUP, cSSBR, cGWAS.emmax
```

```
## Not run:
### Running a model with an additive and dominance effect ###
# generate random data
rand_data(500,5000)
### compute the relationship matrices
G.A <- cgrm.A(M,lambda=0.01)</pre>
G.D \leftarrow cgrm.D(M,lambda=0.01)
### generate the list of design matrices for clmm
random = list(t(chol(G.A)),t(chol(G.D)))
### specify options
par_random = list(list(method="ridge",scale=var(y)/2 ,df=5, name="add"),
 list(method="ridge",scale=var(y)/10,df=5, name="dom"))
### run
set_num_threads(1)
fit <- clmm(y,random=random,par_random=par_random,niter=5000,burnin=2500)</pre>
### inspect results
str(fit)
### Cross Validation ###
### 4-fold cross-validation with one repetition:
# generate random data
rand_data(500,5000)
### compute the list of masked phenotype-vectors for CV
y_CV <- cCV(y,fold=4,reps=1)</pre>
### Cross Validation using GBLUP
G.A <- cgrm.A(M,lambda=0.01)</pre>
### generate the list of design matrices for clmm
```

```
random = list(t(chol(G.A)))
### specify options
h2 = 0.3
scale = unlist(lapply(y_CV,function(x)var(x,na.rm=T))) * h2
df = rep(5,length(y_CV))
par_random = list(list(method="ridge", scale=scale, df=df, name="animal"))
### run model with 4 threads
set_num_threads(4)
fit <- clmm(y_CV,random=random,par_random=par_random,niter=5000,burnin=2500)</pre>
### inspect results
str(fit)
### obtain predictions
pred <- get_pred(fit)</pre>
### prediction accuracy
get_cor(pred,y_CV,y)
### GWAS using Bayesian Regression on marker windows ###
# generate random data
rand_data(500,5000)
### generate the list of design matrices for clmm
random = list(M)
### specify options
h2 = 0.3
scale = var(y) * h2
df = 5
# specifying the model
# Here we use ridge regression on the marker covariates
# and define a window size of 100 and a threshold of 0.01
# which defines the proportion of genetic variance accounted
# for by a single window
par_random = list(list(method="ridge",scale=scale,df=df,
            GWAS=list(window_size=100, threshold=0.01), name="markers"))
### run
set_num_threads(1)
fit <- clmm(y,random=random,par_random=par_random,niter=2000,burnin=1000)</pre>
### inspect results
str(fit)
### extract GWAS part
gwas <- fit$markers$GWAS</pre>
```

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```
# plot window variance proportions
plot(gwas$window_variance_proportion)

## End(Not run)
```

cmaf

cmaf

Description

Computes the minor allele frequencies of a marker-matrix.

Usage

cmaf(X)

Arguments

Χ

Marker matrix with $\{-1,0,1\}$ coding

Value

Numeric Vector of minor allele frequencies for every column in X

Examples

```
# generate random data
rand_data(500,5000)
# compute minor allele frequencies
mafs <- cmaf(M)</pre>
```

cscanx

Read in a matrix from a file

Description

Reads in a matrix from file (no header, no row-names, no NA's, space or tab-delimiter) and returns the according R-matrix. No Need to specify dimensions.

Usage

```
cscanx(path)
```

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Arguments

path

character - location of the file to be read ("/path/to/file")

Value

Matrix shaped as in the file

Examples

```
# random matrix
X <- matrix(rnorm(10,5),10,5)

# write that matrix to a file
write.table(X,file="X",col.names=FALSE,row.names=FALSE,quote=FALSE)

# read in the matrix to object Z
Z <- cscanx("X")</pre>
```

csolve

csolve

Description

This is a wrapper for the Cholesky-solvers 'LLT' (dense case) or 'Simplicial-LLT' (sparse case) from Eigen. The function computes the solution:

$$\mathbf{b} = \mathbf{X}^{-1}\mathbf{y}$$

If no vector y is passed, an identity matrix will be assigned and the function returns the inverse of X. In the case of multiple right hand sides (as is the case when computing an inverse matrix) multiple threads will solve equal parts of it.

Usage

```
csolve(X,y=NULL)
```

Arguments

X positive definite square matrix of type matrix or dgCMatrix

y numeric vector of length equal to columns/rows of X

Value

Solution vector/matrix

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Examples

```
# Least Squares Solving

# Generate random data

n = 1000
p = 500

M <- matrix(rnorm(n*p),n,p)
y <- rnorm(n)

# least squares solution:

b <- csolve(t(M) %c% M, t(M) %c% y)</pre>
```

cSSBR

Single Step Bayesian Regression

Description

This function runs Single Step Bayesian Regression (SSBR) for the prediction of breeding values in a unified model that incorporates genotyped and non genotyped individuals (Fernando et al., 2014).

Usage

```
cSSBR(data, M, M.id, X=NULL, par_random=NULL, scale_e=0, df_e=0,
    niter=5000, burnin=2500, seed=NULL, verbose=TRUE)
```

Arguments

data	data.frame with four columns: id, sire, dam, y
М	Marker Matrix for genotyped individuals
M.id	Vector of length nrow(M) representing rownames for M
X	Fixed effects design matrix of type: matrix or dgCMatrix. If omitted a column-vector of ones will be assigned. Must have as many rows as data
par_random	as in clmm
niter	as in clmm
burnin	as in clmm
verbose	as in clmm
scale_e	as in clmm
df_e	as in clmm
seed	as in clmm

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Details

The function sets up the following model using cSSBR. setup:

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{M}\alpha + \mathbf{Z}\epsilon + \mathbf{e}$$

The matrix \mathbf{M} denotes a combined marker matrix consisting of actual and imputed marker covariates. Best linear predictions of gene content (Gengler et al., 2007) for the non-genotyped individuals are obtained using: $\mathbf{A}^{11}\hat{\mathbf{M}}_1 = -\mathbf{A}^{12}\mathbf{M}_2$ (Fernando et al., 2014). \mathbf{A}^{11} and \mathbf{A}^{12} are submatrices of the inverse of the numerator relationship matrix, which is easily obtained (Henderson, 1976). The subscripts 1 and 2 denote non genotyped and genotyped individuals respectively. The very sparse equation system is being solved using a sparse cholesky solver provided by the Eigen library. The residual imputation error has variance: $(\mathbf{A}^{11})^{-1}\sigma_{\epsilon}^2$ and is modelled by constructing the design matrix as $\mathbf{Z} = \mathbf{L}_{11}$, where $\mathbf{A} = \mathbf{L}\mathbf{L}'$ and $(\mathbf{A}^{11})^{-1} = \mathbf{L}_{11}\mathbf{L}'_{11}$.

Value

List of 4 + number of random effects as in clmm +

SSBR List of 4:

- ids ids used in the model (ordered as in other model terms)
- y phenotype vector
- X Design matrix for fixed effects
- Marker_Matrix Combined Marker Matrix including imputed and genotyped individuals
- Z_residual Design Matrix used to model the residual error for the imputed individuals
- Breeding_Values Predicted Breeding Values for all animals in data that have genotypes and/or phenotypes

Author(s)

Claas Heuer

References

Fernando, R.L., Dekkers, J.C., Garrick, D.J.: A class of bayesian methods to combine large numbers of genotyped and non-genotyped animals for whole-genome analyses. Genetics Selection Evolution 46(1), 50 (2014)

Gengler, N., Mayeres, P., Szydlowski, M.: A simple method to approximate gene content in large pedigree populations: application to the myostatin gene in dual-purpose belgian blue cattle. animal 1(01), 21 (2007)

Henderson, C.R.: A simple method for computing the inverse of a numerator relationship matrix used in prediction of breeding values. Biometrics 32(1), 69-83 (1976)

See Also

cSSBR.setup, clmm

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```
# example dataset
id <- 1:6
sire <- c(rep(NA,3),rep(1,3))</pre>
dam <- c(rep(NA,3),2,2,3)
# phenotypes
y \leftarrow c(NA, 0.45, 0.87, 1.26, 1.03, 0.67)
dat <- data.frame(id=id,sire=sire,dam=dam,y=y)</pre>
# Marker genotypes
M \leftarrow rbind(c(1,2,1,1,0,0,1,2,1,0),
           c(2,1,1,1,2,0,1,1,1,1),
           c(0,1,0,0,2,1,2,1,1,1))
M.id <- 1:3
var_y <- var(y,na.rm=TRUE)</pre>
var_e <- (10*var_y / 21)</pre>
var_a <- var_e
var_m <- var_e / 10</pre>
# put emphasis on the prior
df = 500
par_random=list(list(method="ridge",scale=var_m,df = df),list(method="ridge",scale=var_a,df=df))
set_num_threads(1)
mod<-cSSBR(data = dat,</pre>
           M=M,
           M.id=M.id,
            par_random=par_random,
            scale_e = var_e,
            df_e=df,
            niter=50000,
            burnin=30000)
# check marker effects
print(round(mod[[4]]$posterior$estimates_mean,digits=2))
# check breeding value prediction:
print(round(mod$SSBR$Breeding_Values,digits=2))
```

cSSBR.setup 27

Description

This function prepares all model terms for SSBR using pedigree and marker information. The function is particularly useful for using the reported model terms on multiple phenotypes, for cross validation (clmm), for genomewide association studies or to pass them to alternative software.

Usage

```
cSSBR.setup(data, M, M.id, verbose=TRUE)
```

Arguments

data data.frame with four columns: id, sire, dam, y

M Marker Matrix for genotyped individuals

M.id Vector of length nrow(M) representing rownames for M

verbose Prints progress to the screen

Details

...

Value

List of 4:

ids ids for the model (ordered as in other model terms)

y phenotype vector

Marker_Matrix Combined Marker Matrix including imputed and genotyped individuals

Z_residual Design Matrix used to model the residual error for the imputed individuals

Author(s)

Claas Heuer

References

Fernando, R.L., Dekkers, J.C., Garrick, D.J.: A class of bayesian methods to combine large numbers of genotyped and non-genotyped animals for whole-genome analyses. Genetics Selection Evolution 46(1), 50 (2014)

See Also

```
cSSBR.setup, clmm
```

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```
# example dataset
id <- 1:6
sire <- c(rep(NA,3),rep(1,3))</pre>
dam <- c(rep(NA,3),2,2,3)
# phenotypes
y \leftarrow c(NA, 0.45, 0.87, 1.26, 1.03, 0.67)
dat <- data.frame(id=id,sire=sire,dam=dam,y=y)</pre>
# Marker genotypes
M \leftarrow rbind(c(1,2,1,1,0,0,1,2,1,0),
           c(2,1,1,1,2,0,1,1,1,1),
           c(0,1,0,0,2,1,2,1,1,1))
M.id <- 1:3
model_terms <- cSSBR.setup(dat,M, M.id)</pre>
var_y <- var(y,na.rm=TRUE)</pre>
var_e <- (10*var_y / 21)</pre>
var_a <- var_e
var_m <- var_e / 10</pre>
# put emphasis on the prior
df = 500
par_random=list(list(method="ridge",scale=var_m,df = df),list(method="ridge",scale=var_a,df=df))
set_num_threads(1)
# passing model terms to 'clmm'
mod<-clmm(y=model_terms$y,</pre>
          random=list(model_terms$Marker_Matrix,model_terms$Z_residual),
          par_random=par_random,
           scale_e = var_e,
           df_e=df,
           niter=50000,
          burnin=30000)
# check marker effects
print(round(mod[[4]]$posterior$estimates_mean,digits=2))
```

get_cor 29

Description

Takes a matrix of predictions returned by get_pred, a list of masked phenotypes returned by cCV and the original phenotype vector and returns the correlation between predicted and observed values

Usage

```
get_cor(predictions,cv_pheno,y)
```

Arguments

predictions Prediction matrix returned by get_pred cv_pheno List of masked phenotypes returned by cCV

y Original unmasked phenotype vector that has been used in cCV

Value

Numeric scalar - Mean prediction accuracy measured as correlation between predicted and observed phenotypes

See Also

```
clmm, get_pred, cCV
```

```
### Running a 4-fold cross-validation with one repetition:
# generate random data
rand_data(500,5000)
### compute the list of masked phenotype-vectors for CV
y_CV <- cCV(y,fold=4,reps=1)</pre>
### Cross Validation using GBLUP
G.A <- cgrm.A(M,lambda=0.01)</pre>
### generate the list of design matrices for clmm
random = list(t(chol(G.A)))
### specify options
h2 = 0.3
scale = unlist(lapply(y_CV,function(x)var(x,na.rm=T))) * h2
df = rep(5, length(y_CV))
par_random = list(list(method="ridge",scale=scale,df=df))
### run
fit <- clmm(y_CV,random=random,par_random=par_random,niter=5000,burnin=2500)</pre>
```

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```
### inspect results
str(fit)

### obtain predictions
pred <- get_pred(fit)

### prediction accuracy
get_cor(pred,y_CV,y)

## End(Not run)</pre>
```

get_max_threads

Get the maximum number of threads available

Description

This is a wrapper for the OpenMP-function omp_get_max_threads(), hence the function will report the result of the according omp-function. Note: The returned value does not necessarily reflect the number of physical cores present but in most cases it will.

Usage

```
get_max_threads()
```

Value

Returns the value reported by omp_get_max_threads()

See Also

```
set_num_threads, get_num_threads, check_openmp
```

```
# set number of threads to the value reported by get_max_threads()
n_threads <- get_max_threads()
set_num_threads(n_threads)
# check
get_num_threads()</pre>
```

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get_num_threads	Get the number of threads for cpgen

Description

Check the variable that specifies the number of threads being used by cpgen-functions

Usage

```
get_num_threads()
```

Value

Returns the value of the global variable cpgen. threads

See Also

```
set_num_threads, get_max_threads, check_openmp
```

Examples

```
# set the number of threads to 1
set_num_threads(1)

# check
get_num_threads()

# set number of threads to the value reported by get_max_threads()
n_threads <- get_max_threads()
set_num_threads(n_threads)

# check
get_num_threads()</pre>
```

get_pred

Extract predictions vectors of an object returned by clmm using multpile phenotypes

Description

Takes an object returned by clmm using multpile phenotypes and returns a matrix of predicted values from every model. Every column represents the prediction vector of one model

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Usage

```
get_pred(mod)
```

Arguments

mod

List returned by clmm using multpile phenotypes

Value

Matrix of prediction vectors in columns

See Also

```
clmm, get_cor, cCV
```

```
### Running a 4-fold cross-validation with one repetition:
## Not run:
# generate random data
rand_data(500,5000)
### compute the list of masked phenotype-vectors for CV
y_CV <- cCV(y,fold=4,reps=1)</pre>
### Cross Validation using GBLUP
G.A <- cgrm.A(M,lambda=0.01)</pre>
### generate the list of design matrices for clmm
random = list(t(chol(G.A)))
### specify options
h2 = 0.3
scale = unlist(lapply(y_CV, function(x)var(x,na.rm=T))) * h2
df = rep(5, length(y_CV))
par_random = list(list(method="ridge",scale=scale,df=df))
fit <- clmm(y_CV,random=random,par_random=par_random,niter=5000,burnin=2500)</pre>
### inspect results
str(fit)
### obtain predictions
pred <- get_pred(fit)</pre>
### prediction accuracy
get_cor(pred,y_CV,y)
```

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End(Not run)

Parallelization

Multithreading using cpgen

Description

The package cpgen makes use of shared memory multi-threading using OpenMP. R is of single-threaded nature, hence almost the entire package is written in C++. The package offers a variety of functions that lets you control and check the number of threads that are being used by the functions of the package. Internally every function uses the global variable cpgen.threads which is stored in options()\$cpgen.threads. The value can be changed using the function set_num_threads(). When the package is loaded in an R-session cpgen.threads will be set to the value returned by get_max_threads() which is a wrapper for the OpenMP-header function omp_get_max_threads()

Details

The following functions are multithreaded and access the variable cpgen. threads:

- cGWAS
- cGWAS.emmax
- clmm
- cGBLUP
- ccross
- %c%
- cgrm
- cgrm.A
- cgrm.D
- ccov
- csolve
- cSSBR.setup
- cSSBR

See Also

```
set_num_threads, get_num_threads, get_max_threads, check_openmp
```

rand_data

rand_data	Generate random data for test purposes	

Description

Generates a random marker-matrix in {-1,0,1} coding and a phenotype vector. Phenotypic variance times h2 (variance explained by markers) is equally spread among all markers (sampled from uniform distribution).

Usage

```
rand_data(n=500,p_marker=10000,h2=0.3,prop_qtl=0.01,seed=NULL)
```

Arguments

	Number of ober	a a museti a ma
n	Number of ober	servations

p_marker Number of markers

h2 Heritability of the trait

prop_qtl Proportion of QTL of total number of markers

seed Seed for RNG

Value

No return value. Generates two objects globally (M and y) that can be used after the execution of the function. M is the marker matrix and y the phenotype vector

```
# Generate random data with 100 observations and 500 markers
rand_data(100,500)
# check that objects have been created
str(M)
str(y)
```

set_num_threads 35

set_num_threads	Set the number of OpenMP threads used by the functions of package
	cpgen

Description

This function sets the value of the global variable stored in options()\$cpgen.threads to the assigned integer. Note_1: The assigned value may exceed the number of physical cores present but that might lead to dramatical decrease in performance. Note_2: The function can override the global variable 'OMP_NUM_THREADS' (if global=TRUE and hence also other non-cpgen functions are affected by a call to set_num_threads().

Usage

```
set_num_threads(x,silent=FALSE, global=FALSE)
```

Arguments

Х	Integer scalar that specifies the number of threads to be used by cpgen-functions
silent	boolean, controls whether to print a message
global	boolean, change openmp threads globally (might effect other libraries)

Value

Changes the global variable cpgen. threads to the value in x

See Also

```
get_num_threads, get_max_threads, check_openmp
```

```
# Control the number of threads being used in an R-session:
# set the number of threads to 1
## Not run:
set_num_threads(1)
#### Use a parallelized cpgen-function
# generate random data
rand_data(1000,10000)
# check single-threaded performance
system.time(W <- M%c%t(M))
# set number of threads to 2</pre>
```

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```
set_num_threads(2)
# check multi-threaded performance
system.time(W <- M%c%t(M))
## End(Not run)</pre>
```

%**%

Square matrix power operator

Description

This operator computes an arbitrary power of a positive definite square matrix using an Eigendecomposition: $\mathbf{X}^p = \mathbf{U}\mathbf{D}^p\mathbf{U}'$

Usage

```
X %**% power
```

Arguments

X Positive definite square matrix
power numeric scalar - desired power of X

Value

Matrix X to the power p

```
## Not run:
# Inverse Square Root of a positive definite square matrix
X <- matrix(rnorm(100*5000),100,1000)

XX <- ccross(X)

XX_InvSqrt <- XX %*** -0.5

# check result: ((XX')^-0.5 (XX')^-0.5)^-1 = XX'
table(round(csolve(XX_InvSqrt %c% XX_InvSqrt),digits=2) == round(XX,digits=2) )

## End(Not run)</pre>
```

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%c%

(Parallel) Matrix product operator

Description

This operator computes the matrix-product between two matrices. It can be used as a replacement for %*% in many cases. The operator only accepts matrices of types: matrix or dgCMatrix. In the case of two dense matrices the operator will compute the crossproduct in parallel (Eigen + OpenMP)

Usage

X%c%Y

Arguments

```
X Matrix or vector (treated as column-vector) of type: matrix or dgCMatrix
Y as X
```

Value

Matrix of type: matrix or dgCMatrix

```
# Least Squares Solving

# Generate random data

n = 1000
p = 500

M <- matrix(rnorm(n*p),n,p)
y <- rnorm(n)

# least squares solution:

b <- csolve(t(M) %c% M, t(M) %c% y)</pre>
```

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