

# Changes and FAQs for the sommer package

Giovanny Covarrubias-Pazaran

2021-05-05

The sommer package was developed to provide R users a powerful and reliable multivariate mixed model solver. The package is focused in problems of the type  $p > n$  (more effects to estimate than observations) and its core algorithm is coded in C++ using the Armadillo library. This package allows the user to fit mixed models with the advantage of specifying the variance-covariance structure for the random effects, and specify heterogeneous variances, and obtain other parameters such as BLUPs, BLUEs, residuals, fitted values, variances for fixed and random effects, etc.

Recently, I decided to code the main algorithm (Newton-Raphson & Average-Information) in C++ which encouraged me to refactor all the machinery including special functions and specification of the models. For a more in depth explanation of how the machinery works please read the “Quick start for the sommer package” vignette [i.e. typing `vignette(‘sommer.start’)`]. Here I will focus in just making a translation of the old specification to the new specification.

The purpose of this vignette is to first show the changes in syntax for sommer and frequently asked question.

## SECTION 1: The new syntax of sommer

- 1) The specification of multiresponse model
- 2) The specification of multivariate unknown covariance structures
- 3) The specification of additional unknown covariance structures
- 4) The specification of unknown covariance structures in the residuals
- 5) Special models

## SECTION 2: Frequently asked questions

- 1) I got an error similar to...
- 2) My model runs very slow
- 3) Can I run both; rrBLUP for markers and GBLUP for individuals in sommer?
- 4) I am missing BLUPs for individuals even when I provided them in the relationship matrix
- 5) How can I use the AR1(), CS() and ARMA() functions
- 6) Can I run GWAS in MET experiments with replicates?
- 7) How can I constrain the value of specific random effects?
- 8) How can I constrain two variance components to be equal?

## SECTION 1: The new syntax of sommer

### 1) The specification of multiresponse model

In past versions (depending how old your version) there was an argument called `MVM` which had to be set to `TRUE` if the user wanted to run a true multi-trait model since the specification

```
fixed= cbind(y1,y2)-x
```

would by default fit 2 univariate models in parallel. That is no longer the case, the `MVM` argument doesn't exist and if a model like the one above is specified it will run a true multi-trait model.

## 2) The specification of multivariate unknown covariance structures

In the previous versions when I introduced the multivariate solver I decided to follow the asreml syntax to specify the unknown covariance structured that needed to be estimated. For example, a diagonal model for the multitrait model, assuming a random effect called ‘re’ looked something like this:

```
fixed= cbind(y1,y2)~x
random= ~ diag(trait):re
```

and an unstructured multitrait model was:

```
random= ~ us(trait):re
```

Although this was easier for users adapted to asreml a good thing, it put a lot of limitations on the way constraints for variance components where specified. The same model in the new versions looks like this:

```
random= ~ vs(re, Gtc=unsm(2))
```

where the `Gtc` argument helps us to indicate what type of structure this random effect represents. Here I specified an unstructured model with the function `unsm()` with a number 2 for 2 traits. The user can use either `diag()` or `unsm()`, or any customized matrix with dimensions  $t \times t$  ( $t$  being the number of traits) containing the number 0,1,2,3 that specify the constraint:

0: not to be estimated 1: estimated and constrained to be positive (i.e. variance component) 2: estimated and unconstrained (can be negative or positive, i.e. covariance component) 3: not to be estimated but fixed (value has to be provided in the `Gti` argument)

All this models fit a model with the following variance for `re`:

$$\text{var}(u) = T \otimes A$$

where:

$$\text{var}(\mathbf{u}) = \begin{bmatrix} \sigma_{g_{t1,t1}}^2 & \sigma_{g_{t1,t2}} \\ \sigma_{g_{t2,t1}} & \sigma_{g_{t2,t2}}^2 \end{bmatrix} \otimes A$$

By doing this change now the user has full control on the constraints applied to the estimation of variance components and can provide initial values easily using the `Gti` argument.

## 3) The specification of additional unknown covariance structures

If we focus for a moment in an univariate mixed model we can also have other unknown covariance structures specified.

$$\text{var}(u) = E \otimes \dots \otimes F \otimes A$$

where:

$$\text{var}(\mathbf{u}) = \begin{bmatrix} \sigma_{g_{e1,e1}}^2 & \sigma_{g_{e1,e2}} & \sigma_{g_{e1,e3}} \\ \sigma_{g_{e2,e1}} & \sigma_{g_{e2,e2}}^2 & \sigma_{g_{e2,e3}} \\ \sigma_{g_{e3,e1}} & \sigma_{g_{e3,e2}} & \sigma_{g_{e3,e3}}^2 \end{bmatrix} \otimes \dots \otimes \begin{bmatrix} \sigma_{g_{f1,f1}}^2 & \sigma_{g_{f1,f2}} \\ \sigma_{g_{f2,f1}} & \sigma_{g_{f2,f2}}^2 \end{bmatrix} \otimes A$$

If we think in the multi trait model this is very similar but with an additional kroneker product for the multivariate version:

$$\text{var}(u) = T \otimes E \otimes \dots \otimes F \otimes A$$

where:

$$\mathbf{var}(\mathbf{u}) = \begin{bmatrix} \sigma_{g_{t1,t1}}^2 & \sigma_{g_{t1,t2}} \\ \sigma_{g_{t2,t1}} & \sigma_{g_{t2,t2}}^2 \end{bmatrix} \otimes \begin{bmatrix} \sigma_{g_{e1,e1}}^2 & \sigma_{g_{e1,e2}} & \sigma_{g_{e1,e3}} \\ \sigma_{g_{e2,e1}} & \sigma_{g_{e2,e2}}^2 & \sigma_{g_{e2,e3}} \\ \sigma_{g_{e3,e1}} & \sigma_{g_{e3,e2}} & \sigma_{g_{e3,e3}}^2 \end{bmatrix} \otimes \dots \otimes \begin{bmatrix} \sigma_{g_{f1,f1}}^2 & \sigma_{g_{f1,f2}} \\ \sigma_{g_{f2,f1}} & \sigma_{g_{f2,f2}}^2 \end{bmatrix} \otimes A$$

Going back to the point. The additional unknown covariance structures besides the multi-trait (T) before were specified with asreml syntax. For example an univariate diagonal and unstructured model, assumed a random effect called 'id' representing the treatments planted in different environments coded in a second random effect called 'env'. The model used to look like:

```
fixed= y1~x
```

```
random= ~ diag(env):id or random= ~ us(env):id
```

and now it would be specified as:

```
fixed= y1~x
```

```
random= ~ vs(ds(env),id) or random= ~ vs(us(env),id)
```

where the `ds()` and `us()` functions specify a diagonal and unstructured models respectively. Now in addition `cs()` for a customized structure is available. The main gain from having changed the formulation is that the new specification through the `vs()` function allows to construct more complex models. For example, assume individuals specified in a column called 'id' tested in three environments in a column called 'env' measured at two different time points specified in a column called 'time'. We may want something more flexible than:

```
fixed= y1~x
```

```
random= ~ id
```

We could actually assume that individuals are correlated within the environments for the different time points but want to consider environments independent. The variance for such random effects is the following:

$$\mathbf{var}(\mathbf{u}) = \begin{bmatrix} \sigma_{g_{e1,e1}}^2 & \sigma_{g_{e1,e2}} & \sigma_{g_{e1,e3}} \\ \sigma_{g_{e2,e1}} & \sigma_{g_{e2,e2}}^2 & \sigma_{g_{e2,e3}} \\ \sigma_{g_{e3,e1}} & \sigma_{g_{e3,e2}} & \sigma_{g_{e3,e3}}^2 \end{bmatrix} \otimes \begin{bmatrix} \sigma_{g_{t1,t1}}^2 & \sigma_{g_{t1,t2}} \\ \sigma_{g_{t2,t1}} & \sigma_{g_{t2,t2}}^2 \end{bmatrix} \otimes A$$

which was not possible in previous versions of sommer and now can be specified as:

```
random= ~ vs(us(env),ds(time),id)
```

and the same logic can be extended to as many factors interacting as desired.

#### 4) The specification of unknown covariance structures in the residuals

Before sommer was limited to only diagonal models in the residuals (unstructured available only for multi-trait before). Now all the same applications discussed for the random term also applies for the residual term. Just keep in mind that the residual term is always called units.

Previous versions:

```
random= ~ diag(trait):diag(env):units
```

```
random= ~ us(trait):diag(env):units # limit
```

New versions (>3.7):

```
random= ~ vs(ds(env),units, Gtc=mm) ## can be extended to more interacting factors
```

```
random= ~ vs(us(env),units, Gtc=mm) ## can be extended to more interacting factors
```

```
random= ~ vs(at(env),units, Gtc=mm) ## can be extended to more interacting factors
```

`random= ~ vs(cs(env),units, Gtc=mm) ##` can be extended to more interacting factors

where `mm` can be any matrix specifying the type of multi-trait model (constraints). For example we could use `unsm()` `diag()`, `uncm()` or any other customized matrix.

## 5) Special models

In previous version the use of `asreml` formulation really limited the expansion of `sommer` to more sophisticated models. Now there's many more possible models

Previous versions:

**Overlay models** Previous version: limited to 2 columns and only random and no covariance structures.

```
random= ~ x + and(y)
```

New versions (>3.7): in theory no limits. Can be extended to more interacting factors in the unknown covariance structures and can overlay as many columns as needed. Plus is fully functional with the multivariate models.

```
random=~ vs(..., overlay(x1,...,xn), Gtc=mm)
```

**Random regression models** Previous version: Not available before

New versions (>3.7): in theory no limits. Can be extended to more interacting factors in the unknown covariance structures and only requires the use of the `leg()` function. Plus is fully functional with the multivariate models.

```
random=~ vs(us(leg(v,1)),x)
```

```
random=~ vs(ds(leg(v,1)),x)
```

```
random=~ vs(leg(v,1),x)
```

**GWAS models** Previous version: Only univariate models available

New versions (>3.7): all the power of the `mmer` function is available plus you can fit multivariate GWAS models. See details in the `sommer.start` vignettes.

**Spatial models** Previous version: It was called directly in the formula

```
random=~ sp12D(Row,Col,at=?)
```

New versions (>3.7): It has to be called within the `vs()` function but now it can be combined with all the unknown covariance structures available.

```
random=~ vs(...,sp12D(Row,Col,at=?), Gtc=mm) # being mm any multi-trait constraint-structure.
```

**Customized random effects** Previous version: It was provided in the grouping argument

```
random=~ grp(x),
```

```
grouping=list(x=Z)
```

New versions (>3.7): It has to be called within the `vs()` function but now it can be combined with all the unknown covariance structures available.

```
random=~vs(..., Z, Gtc=mm) # being mm any multi-trait constraint-structure.
```

## SECTION 2: Frequently asked questions

### 1) I got an error similar to:

```
# iteration   LogLik      wall   cpu(sec)  restrained
#      1      -224.676  18:11:23    3          0
# System is singular. Aborting the job. You could try a bigger tolparinv value.
```

This error indicates that your model is singular (phenotypic variance  $V$  matrix is not invertible) and therefore the model is stopped throwing the error message and returning an empty list. Whether you can try a simpler model or just modify the argument `tolparinv` in the `mmer` function. The default is  $1e-3$ , which means that it will try to invert  $V$  and if it fails it will try to add a small value to the diagonal of  $V$  of  $1e-3$  to make it invertible and try bigger and bigger numbers. If this fails then the program will return the empty list.

Sometimes the model becomes singular when you use variance covariance matrices (i.e. genomic relationship matrices) that are not full-rank. You can try to make it full-rank and try again.

### 2) My model runs very slow

Keep in mind that `sommer` uses direct inversion (DI) algorithm which can be very slow for large datasets. The package is focused in problems of the type  $p > n$  (more random effect levels than observations) and models with dense covariance structures. For example, for experiment with dense covariance structures with low-replication (i.e. 2000 records from 1000 individuals replicated twice with a covariance structure of  $1000 \times 1000$ ) `sommer` will be faster than MME-based software. Also for genomic problems with large number of random effect levels, i.e. 300 individuals ( $n$ ) with 100,000 genetic markers ( $p$ ). For highly replicated trials with small covariance structures or  $n > p$  (i.e. 2000 records from 200 individuals replicated 10 times with covariance structure of  $200 \times 200$ ) `asreml` or other MME-based algorithms will be much faster and we recommend you to opt for those software.

### 3) Can I run both; rrBLUP for markers and GBLUP for individuals in sommer?

Both types of models can be fitted in `sommer`. The only thing that it changes is what is the random effect of interest; the marker matrix or the identifier for the individual. Here there is a complex example using multi-trait models but can be used with only one trait.

```
library(sommer)
## rrBLUP for makers
data(DT_cpdata)
DT <- DT_cpdata
GT <- GT_cpdata
MP <- MP_cpdata
mix.rrblup <- mmer(fixed=color~1,
                  random=~vs(GT,Gtc=unsm(1), buildGu = FALSE) + vs(Rowf,Gtc=diag(1)),
                  rcov=~vs(units,Gtc=unsm(1)), getPEV = FALSE,
                  data=DT, verbose = FALSE)
summary(mix.rrblup)
```

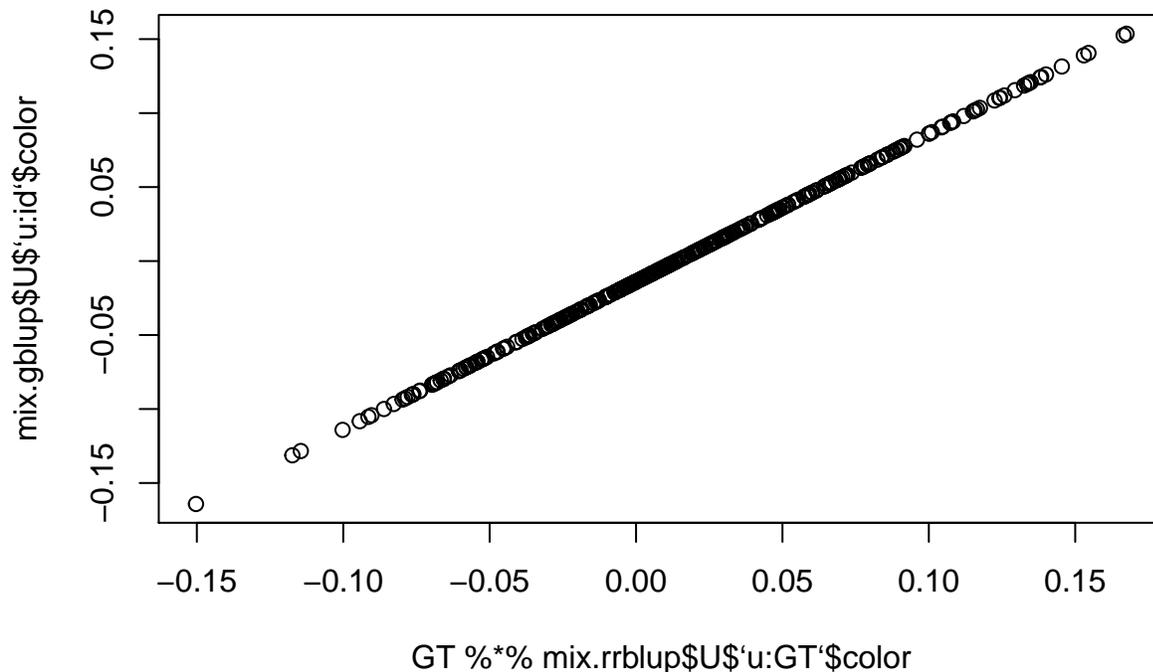
```
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -108.1202  218.2403  222.132      NR      TRUE
```

```

## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## u:GT.color-color  4.213e-06 8.581e-07  4.909   Positive
## u:Rowf.color-color 1.963e-04 1.355e-04  1.449   Positive
## u:units.color-color 2.612e-03 2.926e-04  8.928   Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 color (Intercept)  0.1692  0.03908  4.329
## =====
## Groups and observations:
##      color
## u:GT    2889
## u:Rowf   13
## =====
## Use the '$' sign to access results and parameters
## GBLUP for individuals
A <- A.mat(GT)
mix.gblup <- mmer(fixed=color~1,
                 random=~vs(id,Gu=A, Gtc=unsm(1)) + vs(Rowf,Gtc=diag(1)),
                 rcov=~vs(units,Gtc=unsm(1)),
                 data=DT, verbose = FALSE)
summary(mix.gblup)

## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -108.1201 218.2403 222.1319      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## u:id.color-color  0.0049524 0.0010082  4.912   Positive
## u:Rowf.color-color 0.0001965 0.0001359  1.446   Positive
## u:units.color-color 0.0026123 0.0002926  8.928   Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 color (Intercept)  0.1831  0.004732  38.7
## =====
## Groups and observations:
##      color
## u:id    363
## u:Rowf   13
## =====
## Use the '$' sign to access results and parameters
## Equivalence
plot(GT*%mix.rtblup$U$`u:GT`$color, mix.gblup$U$`u:id`$color)

```



Please notice that when specifying the marker matrix as a random effect we used the argument ‘buildGu=FALSE’ to inform the ‘mmer’ function that a covariance matrix for the levels of the random effect shouldn’t be built. Imagine a model with 100,000 markers, that would imply a relationship matrix of 100,000 x 100,000. If that matrix is a diagonal it would only compromise the speed and memory of the function. By setting ‘buildGu=FALSE’ the mmer solver will avoid the matrix multiplications using that huge diagonal matrix. If you want to specify a relationship matrix for the marker matrix then you cannot use that ‘buildGu’ argument.

#### 4) I am missing BLUPs for individuals even when I provided them in the relationship matrix

I got this good question in the past: “when I want to fit an animal model with sommer package using additive relationship matrix(A), this A matrix would contain parents. But the random effects only contains animals in the random effect but not including parents in the A matrix. How can I get the random effects for parents?”

Answer: The easy way to do it is to make sure that even if the parents don’t show up in the dataset, you need to make sure that they are present in the levels of the column that contains the individuals (i.e. animal IDs), in addition they have to be provided in the relationship matrix and that’s it. They should be returned in the blups.

```
library(sommer)

data(DT_cpdata)
DT <- DT_cpdata
GT <- GT_cpdata
MP <- MP_cpdata
#### create the variance-covariance matrix
A <- A.mat(GT) # additive relationship matrix
#### look at the data and fit the model
set.seed(12)
DT2 <- droplevels(DT[sample(1:nrow(DT),100),]) # we simulate a dataset with only 100 animals
nrow(DT2); length(levels(DT2$id))

## [1] 100
```

```
## [1] 100
# we fit a model with the reduced dataset where only 100 blups will be returned since only
# 100 levels exist in the "id" column
mix1 <- mmer(Yield~1,
             random=~vs(id,Gu=A)
               + Rowf + Colf,
             rcov=~units,
             data=DT2, verbose = FALSE)
```

```
## Adding additional levels of Gu in the model matrix of 'id'
```

```
summary(mix1)
```

```
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
##           logLik      AIC      BIC Method Converge
## Value -47.00674 96.01348 98.61865      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## u:id.Yield-Yield 1531.7    1000.9 1.530  Positive
## Rowf.Yield-Yield  157.1     297.5 0.528  Positive
## Colf.Yield-Yield   0.0     396.4 0.000  Positive
## units.Yield-Yield 3358.4     883.6 3.801  Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept) 127.4      7.214 17.66
## =====
## Groups and observations:
##   Yield
## u:id  363
## Rowf  13
## Colf  35
## =====
## Use the '$' sign to access results and parameters
```

```
length(mix1$U$`u:id`$Yield) # only 100 levels
```

```
## [1] 363
# we add additional levels to the "id" column and also provide them in the relationship matrix
levels(DT2$id) <- c(levels(DT2$id), setdiff(levels(DT$id), levels(DT2$id)))
mix2 <- mmer(Yield~1,
             random=~vs(id,Gu=A)
               + Rowf + Colf,
             rcov=~units,
             data=DT2, verbose = FALSE)
```

```
summary(mix2)
```

```
## =====
##           Multivariate Linear Mixed Model fit by REML
## ***** sommer 4.1 *****
## =====
```

```
##           logLik      AIC      BIC Method Converge
## Value -47.00674 96.01348 98.61865      NR      TRUE
## =====
## Variance-Covariance components:
##           VarComp VarCompSE Zratio Constraint
## u:id.Yield-Yield  1531.7    1000.9  1.530    Positive
## Rowf.Yield-Yield   157.1     297.5  0.528    Positive
## Colf.Yield-Yield     0.0     396.4  0.000    Positive
## units.Yield-Yield  3358.4     883.6  3.801    Positive
## =====
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)    127.4     7.214   17.66
## =====
## Groups and observations:
##      Yield
## u:id   363
## Rowf   13
## Colf   35
## =====
## Use the '$' sign to access results and parameters
```

```
length(mix2$U$`u:id`$Yield) # now 363 levels
```

```
## [1] 363
```

Since 4.1.2 this shouldn't be a problem since internally the mmer solver adds the missing levels but we leave this for reference for people using older versions of sommer.

## 5) How can I use the AR1(), CS() and ARMA() functions

Sommer doesn't support the estimation of additional correlation components like AR1 in the way asreml does. Still, if the user know the correlation value or can do an iterative approach to find the best value then these functions can be used to specify the variance covariance structure for a given random effect.

For example, in the DT\_cpdata dataset we have a field with row and column coordinates. This allows to fit row and column as random effects:

```
library(sommer)
data(DT_cpdata)
DT <- DT_cpdata
mix1 <- mmer(Yield~1,
             random=~ Rowf + Colf,
             rcov=~units,
             data=DT, verbose = FALSE)
summary(mix1)$varcomp
```

```
##           VarComp VarCompSE   Zratio Constraint
## Rowf.Yield-Yield  832.2879  393.8951  2.112968    Positive
## Colf.Yield-Yield  153.9201  126.7582  1.214281    Positive
## units.Yield-Yield 3647.3486  290.4910 12.555804    Positive
```

If the user wants to relax the independence between rows and define an AR1 covariance structure among rows then the model could be fitted as:

```
library(sommer)
data(DT_cpdata)
```

```
DT <- DT_cpdata
mixAR1row <- mmer(Yield~1,
  random=~ vs(Rowf, Gu=AR1(Rowf, rho=0.3)) + Colf,
  rcov=~units,
  data=DT, verbose = FALSE)
summary(mixAR1row)$varcomp
```

##		VarComp	VarCompSE	Zratio	Constraint
##	u:Rowf.Yield-Yield	791.8219	387.8695	2.041465	Positive
##	Colf.Yield-Yield	154.5660	126.8094	1.218885	Positive
##	units.Yield-Yield	3643.6027	290.1689	12.556834	Positive

Same could be done for the column random effect:

```
library(sommer)
data(DT_cpdata)
DT <- DT_cpdata
mixAR1col <- mmer(Yield~1,
  random=~ Rowf + vs(Colf, Gu=AR1(Colf, rho=0.3)),
  rcov=~units,
  data=DT, verbose = FALSE)
summary(mixAR1col)$varcomp
```

##		VarComp	VarCompSE	Zratio	Constraint
##	Rowf.Yield-Yield	830.3623	392.8264	2.113815	Positive
##	u:Colf.Yield-Yield	178.7490	134.2703	1.331262	Positive
##	units.Yield-Yield	3624.6074	287.6072	12.602629	Positive

If on the other hand, you would like to establish the presence of correlation in row and columns at the same time the model would look like this:

```
library(sommer)
data(DT_cpdata)
DT <- DT_cpdata
mixAR1rowcol <- mmer(Yield~1,
  random=~ vs(Rowf:Colf,
    Gu=kronecker(AR1(Rowf, rho=0.3),AR1(Colf, rho=0.3),make.dimnames = TRUE)
  ),
  rcov=~units,
  data=DT, verbose = FALSE)
summary(mixAR1rowcol)$varcomp
```

##		VarComp	VarCompSE	Zratio	Constraint
##	u:Rowf:Colf.Yield-Yield	2474.339	730.1474	3.388821	Positive
##	units.Yield-Yield	2025.584	622.1023	3.256030	Positive

Notice that if you specify a random effect that is the interaction between 2 random effects the covariance structure to be specified in the `Gu` argument has to be built using the `kronecker()` function. The same applies to the `ARMA()` and `CS()` functions. Please keep in mind that the correlation values (`rho` argument) is a fixed value not estimated by REML like `asreml` does but you can always follow an iterative approach.

## 6) Can I run GWAS in MET experiments with replicates?

Although the direct-inversion algorithm that `sommer` uses in the background is not the best choice to solve GWAS models for the  $n > p$  scenario it is still possible to perform GWAS in MET models.

For example, assume a MET model that has 41 lines with 1000 SNP markers, tested in 3 environments. The genetic term in a MET can be modeled as CS, DIAG or US covariance. The whole point of the GWAS function in sommer is to provide the name of the gTerm (random effect) that will match the marker data provided.

We first make up marker data for the MET data for example purposes

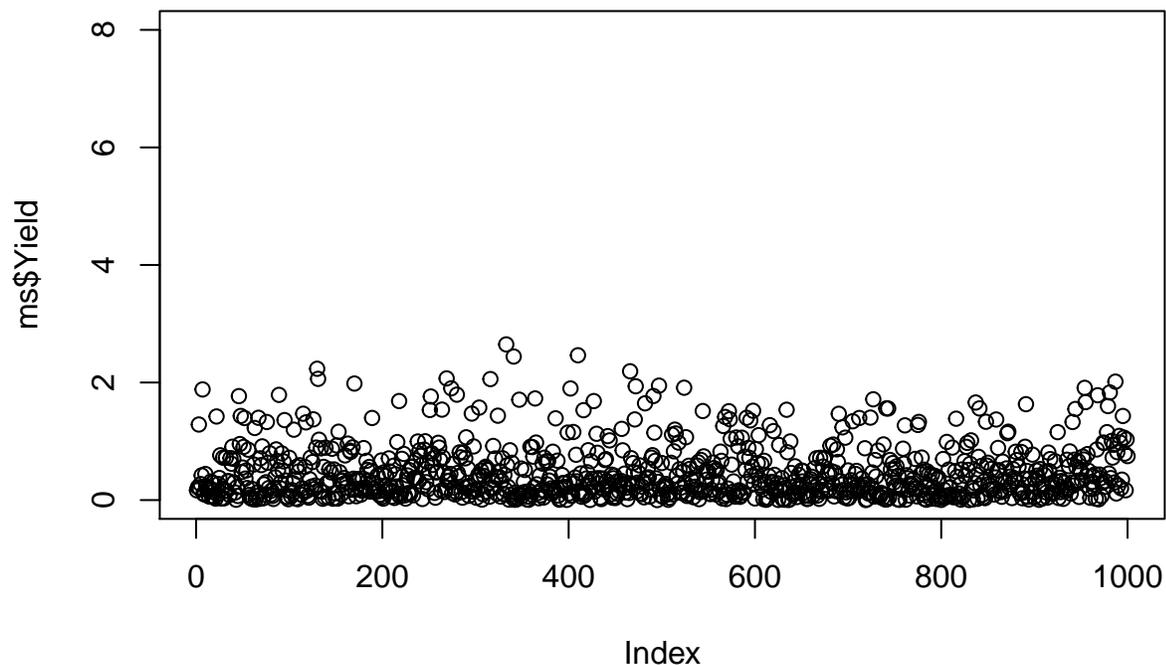
```
library(sommer)
data(DT_example)
DT <- DT_example
A <- A_example
M <- matrix(rep(0,41*1000),1000,41)
for (i in 1:41) {
  M[,i] <- ifelse(runif(1000)<0.5,-1,1)
}
tM <- t(M)
```

We then fit the MET model of the type compound symmetry (CS) and evaluate the GWAS for the main genetic term “Name”:

```
## GWAS for main term in CS model
ansx <- GWAS(Yield~Env,
             random= ~ Name + Env:Name,
             rcov= ~ units,
             data=DT,
             M=tM,
             gTerm = "Name", verbose = FALSE)
```

```
## Performing GWAS evaluation
```

```
ms <- as.data.frame(ansx$scores)
plot(ms$Yield, ylim=c(0,8))
```



We could do the same but evaluate the GWAS considering the genetic term as the interaction term “Env:Name”

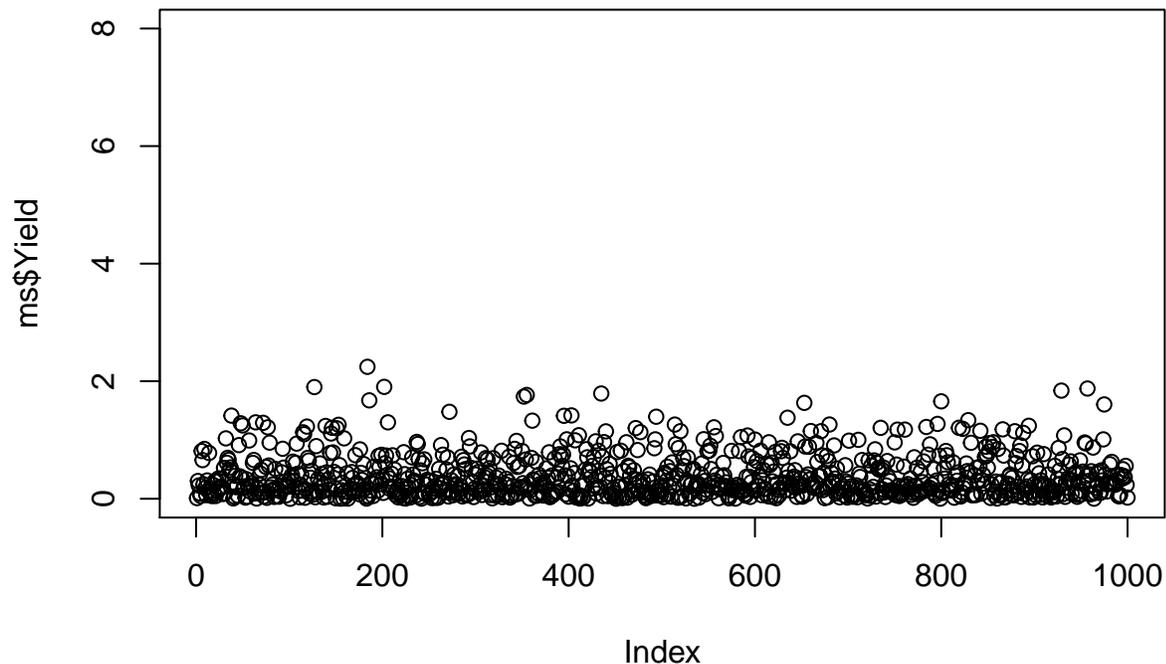
```
## GWAS for the interaction term in CS model
E <- matrix(1,nrow = length(unique(DT$Env)));E
```

```
##      [,1]
## [1,]  1
## [2,]  1
## [3,]  1
```

```
EtM <- kronecker(E,tM)
ansx <- GWAS(Yield~Env,
             random= ~ Name + Env:Name,
             rcov= ~ units,
             data=DT,
             M=EtM,
             gTerm = "Env:Name", verbose = FALSE)
```

```
## Performing GWAS evaluation
```

```
ms <- as.data.frame(ansx$scores)
plot(ms$Yield, ylim=c(0,8))
```



If the MET is a diagonal model, there's a variance components and BLUPs for each environment. Therefore we can evaluate the GWAS at any environment, here for example we evaluate the GWAS at the genetic term in the environment 'CA.2011'.

```
## GWAS for the interaction term in DIAG model
E <- matrix(1,nrow = length(unique(DT$Env)));E
```

```
##      [,1]
## [1,]  1
## [2,]  1
## [3,]  1
```

```
EtM <- kronecker(E,tM)
ansx <- GWAS(Yield~Env,
```

```

random= ~Name + vs(ds(Env),Name),
rcov= ~ vs(ds(Env),units),
data=DT,
M=tM,
gTerm = "CA.2011:Name", verbose = FALSE )

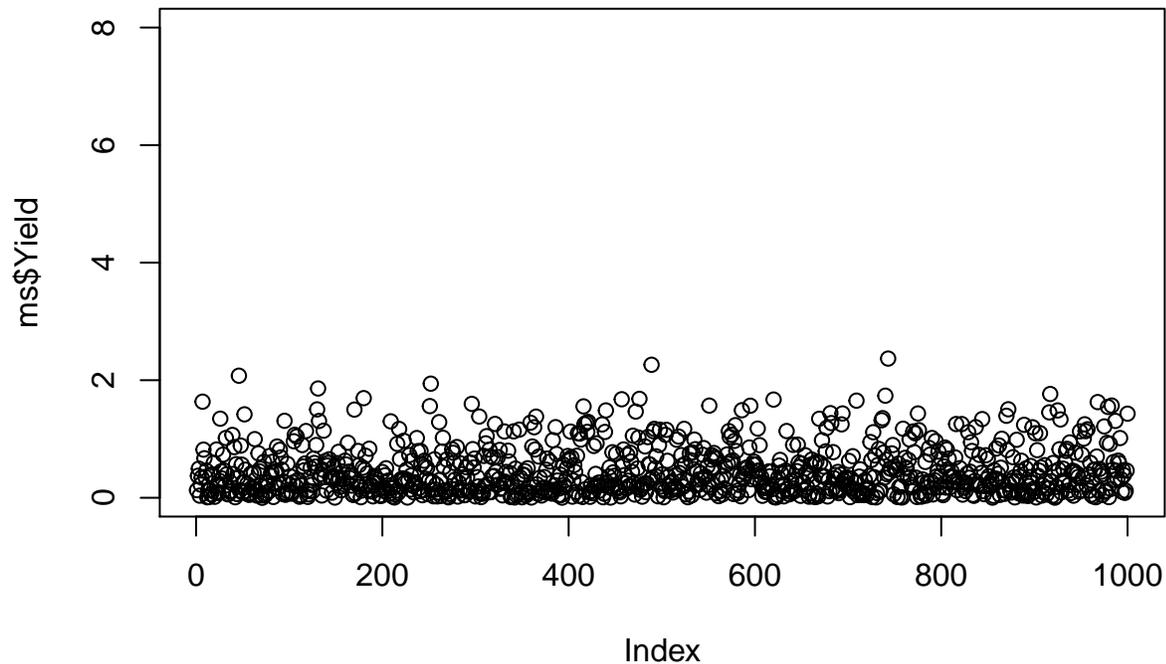
```

```
## Performing GWAS evaluation
```

```

ms <- as.data.frame(ansx$scores)
plot(ms$Yield, ylim=c(0,8))

```



If the MET is an unstructured model, there's a variance components and BLUPs for each environment and a covariance component among the different combinations of environments. Therefore we can evaluate the GWAS at any environment as before, here for example we evaluate the GWAS at the genetic term in the environment 'CA.2011'. The difference with the previous model is that here we expect a greater accuracy in the environment CA.2011 since it has borrowed information from the other environments given the covariance fitted among environments.

```

## GWAS for main term in US model
ansx <- GWAS(Yield~Env,
  random= ~vs(us(Env),Name),
  rcov= ~ vs(us(Env),units),
  data=DT,
  M=tM,
  gTerm = "CA.2011:Name", verbose = FALSE)

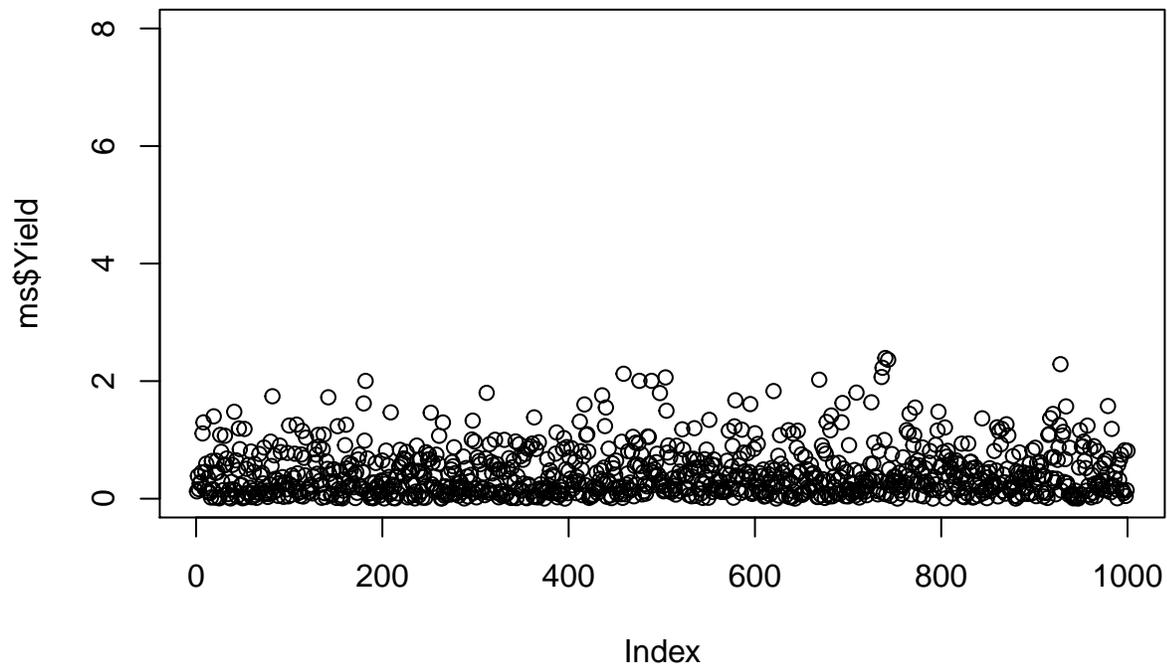
```

```
## Performing GWAS evaluation
```

```

ms <- as.data.frame(ansx$scores)
plot(ms$Yield, ylim=c(0,8))

```

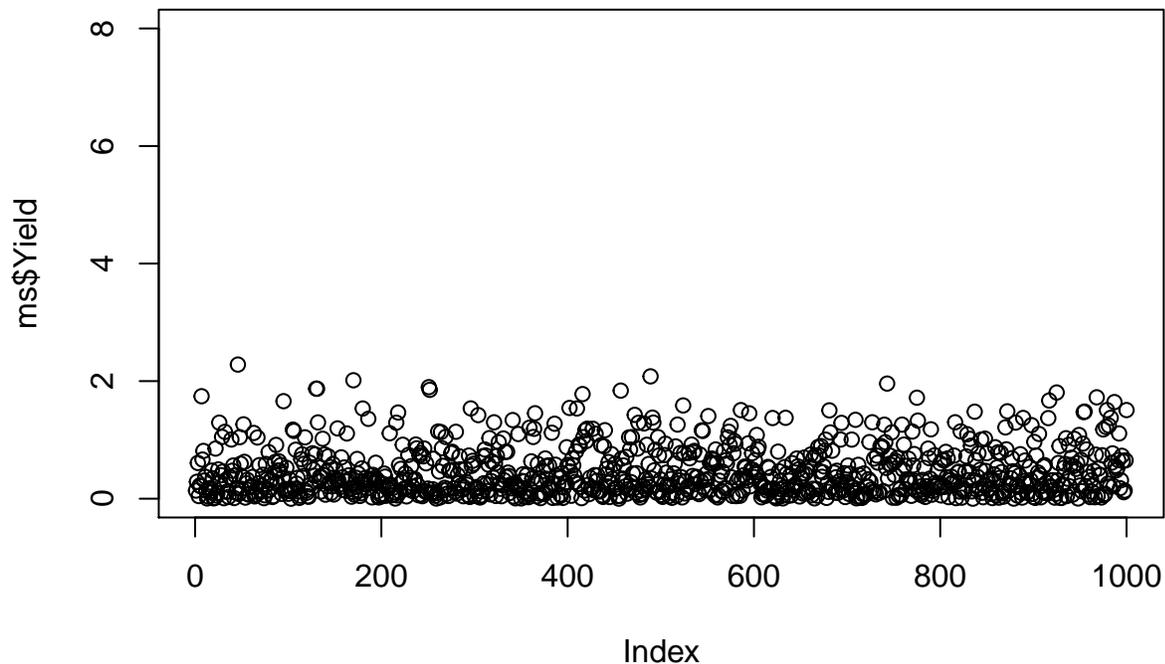


Same theory applies for the multitrait model:

```
## GWAS for main term in multitrait DIAG model
ansx <- GWAS(cbind(Weight,Yield)~Env,
             random= ~vs(ds(Env),Name, Gtc=unsm(2)),
             rcov= ~ vs(ds(Env),units, Gtc=diag(2)),
             data=DT,
             M=tM,
             gTerm = "CA.2011:Name", verbose = FALSE)
```

## Performing GWAS evaluation

```
ms <- as.data.frame(ansx$scores)
plot(ms$Yield, ylim=c(0,8))
```



## 7) How can I constrain the value of specific random effects?

When using the `vs` function three additional arguments help to control the following:

Gu: matrix for covariances among levels for the  $u$ .th random effect  
 Gti: matrix of initial values for the variance-covariance components  
 Gtc: matrix of constraints for the variance-covariance components

Since each random effect can be seen as a multi-trait variance covariance structure, the univariate models are just an extension where the multi-trait variance covariance structure is a  $1 \times 1$  matrix. When inspecting the results for the mixed models fitted by the `mmer()` function corresponding to the variance components stored in the `sigma` element, you will notice that each random effect contains a  $t \times t$  matrix which corresponds to the multi-trait structure we referred to. For example:

```
data(DT_cpdata)
DT <- DT_cpdata
GT <- GT_cpdata
MP <- MP_cpdata
#### create the variance-covariance matrix
A <- A.mat(GT) # additive relationship matrix
#### look at the data and fit the model
mix1 <- mmer(Yield~1,
             random=~vs(id,Gu=A),
             rcov=~units,
             data=DT, verbose = FALSE)
mix1$sigma$`u:id`
```

```
##          Yield
## Yield 650.4145
```

Here the `sigma` element contains the random effects for `id` and `units` (error). Each of these contains a matrix of 1 by 1, but in a multi trait model would look like this:

```
data(DT_cpdata)
DT <- DT_cpdata
```

```

GT <- GT_cpdata
MP <- MP_cpdata
#### create the variance-covariance matrix
A <- A.mat(GT) # additive relationship matrix
#### look at the data and fit the model
mix2 <- mmer(cbind(Yield,color)~1,
             random=~vs(id,Gu=A, Gtc=unsm(2)),
             rcov=~vs(units,Gtc=diag(2)),
             data=DT, verbose = FALSE)
mix2$sigma$`u:id`

```

```

##           Yield      color
## Yield 634.6295932 0.471715518
## color  0.4717155 0.005126228

```

Notice that for 2 traits this becomes a 2 by 2 matrix. In order to put constraints in some of these random effect matrices you can use the `Gtc` argument as show above. For the `id` random effect we have specified that variance components should be estimated and be positive (diagonals with a 1), whereas covariance components should be estimated and unconstrained to be positive or negative (off-diagonals with a 2).

```
unsm(2)
```

```

##      [,1] [,2]
## [1,]    1    2
## [2,]    2    1

```

```
mix2$sigma$`u:id`
```

```

##           Yield      color
## Yield 634.6295932 0.471715518
## color  0.4717155 0.005126228

```

On the other hand, for the `units` (error) random effect we have specified in the `Gtc` argument that variance components should be estimated and be positive (diagonals), whereas covariance components should not be estimated (off-diagonals with a 0)

```
diag(2)
```

```

##      [,1] [,2]
## [1,]    1    0
## [2,]    0    1

```

```
mix2$sigma$`u:units`
```

```

##           Yield      color
## Yield 4009.336 0.000000000
## color   0.000 0.002563711

```

If the user would like to constraint a value to be fixed and don't change through the estimation process of other random effects the user needs to provide the initial value (scaled with respect to the error variance) of those variance-covariance components in the `Gti` argument and use a matrix with the value 3 in the `Gtc` constraint matrix.

```

mm <- matrix(3,1,1) ## matrix to fix the var comp
initialVal <- mix1$sigma_scaled$`u:id`/2 # we want to fix the vc to be half of the previous univariate
mix3 <- mmer(Yield~1,
            random=~vs(id, Gu=A, Gti=initialVal, Gtc=mm), # constrained
            rcov=~vs(units), # unconstrained

```

```

data=DT, verbose = FALSE)

# analyze variance components
summary(mix1)$varcomp

##                VarComp VarCompSE    Zratio Constraint
## u:id.Yield-Yield  650.4145  325.5562  1.997856   Positive
## units.Yield-Yield 4031.0153  344.6051 11.697493   Positive

summary(mix3)$varcomp

##                VarComp VarCompSE    Zratio Constraint
## u:id.Yield-Yield   325.2072  259.0889  1.255196     Fixed
## u:units.Yield-Yield 4051.3786  352.4804 11.493912   Positive

```

### 8) How can I constrain two variance components to be equal?

Sometimes the built-in capacities of sommer are not flexible enough to do all what users want. One of those situations is to fix variance components to be equal. Let's simulate some multitrait data:

```

library("MASS") ## needed for mvrnorm
n <- 100
mu <- c(1,2)
Sigma <- matrix(c(10,5,5,10),2,2)
Y <- mvrnorm(n,mu,Sigma); colnames(Y) <- c("y1","y2")
## this simulates multivariate normal rvs
y <- as.vector(t(Y))
df1 <- data.frame(Y)
df2 <- data.frame(y)

```

Now lets assume that we want to fit a multitrait model with an unstructured error variance structure with the built-in capacity. That would be as easy as this:

```

mix1 <- mmer(cbind(y1,y2)~1, rcov=~vs(units, Gtc=unsm(2)), data=df1, verbose = FALSE)
mix1$sigma

## $`u:units`
##          y1          y2
## y1 8.804435  5.324279
## y2 5.324279 10.806112

```

But now assume that you would like to constraint the variance of y1 and y2 to be equal. This requires the user to take a different approach. The user can build externally the multitrait matrices and fit them directly. Let's do this to recreate the exact same result than using the bil-in capabilities:

```

X <- kronecker(rep(1,n),diag(1,2))
V1 <- matrix(c(1,0,0,0),2,2)
V2 <- matrix(c(0,0,0,1),2,2)
V3 <- matrix(c(0,1,1,0),2,2)
sig1 <- kronecker(diag(1,n),V1) # variance component 1
sig2 <- kronecker(diag(1,n),V2) # variance component 2
gam <- kronecker(diag(1,n),V3) # covariance component
# now fit the model
mix2 <- mmer(y~X-1, rcov = ~vs(sig1)+vs(sig2)+vs(gam), data=df2, verbose = FALSE)
mix2$sigmaVector

```

```
## u:sig1.y-y u:sig2.y-y u:gam.y-y
## 8.804453 10.806046 5.324242
```

Notice that we fitted a univariate model but we built the kernels and fitted those kernels one by one.

Now we will constraint the two variance components to be equal. This is done the following way:

```
sig <- sig1+sig2
mix3 <- mmer(y~X-1, rcov = ~vs(sig)+vs(gam), data=df2, iters=30, verbose = FALSE)
mix3$sigmaVector
```

```
## u:sig.y-y u:gam.y-y
## 9.805147 5.324050
```

## Literature

Covarrubias-Pazaran G. 2016. Genome assisted prediction of quantitative traits using the R package sommer. PLoS ONE 11(6):1-15.

Covarrubias-Pazaran G. 2018. Software update: Moving the R package sommer to multivariate mixed models for genome-assisted prediction. doi: <https://doi.org/10.1101/354639>

Bernardo Rex. 2010. Breeding for quantitative traits in plants. Second edition. Stemma Press. 390 pp.

Gilmour et al. 1995. Average Information REML: An efficient algorithm for variance parameter estimation in linear mixed models. Biometrics 51(4):1440-1450.

Henderson C.R. 1975. Best Linear Unbiased Estimation and Prediction under a Selection Model. Biometrics vol. 31(2):423-447.

Kang et al. 2008. Efficient control of population structure in model organism association mapping. Genetics 178:1709-1723.

Lee, D.-J., Durban, M., and Eilers, P.H.C. (2013). Efficient two-dimensional smoothing with P-spline ANOVA mixed models and nested bases. Computational Statistics and Data Analysis, 61, 22 - 37.

Lee et al. 2015. MTG2: An efficient algorithm for multivariate linear mixed model analysis based on genomic information. Cold Spring Harbor. doi: <http://dx.doi.org/10.1101/027201>.

Maier et al. 2015. Joint analysis of psychiatric disorders increases accuracy of risk prediction for schizophrenia, bipolar disorder, and major depressive disorder. Am J Hum Genet; 96(2):283-294.

Rodriguez-Alvarez, Maria Xose, et al. Correcting for spatial heterogeneity in plant breeding experiments with P-splines. Spatial Statistics 23 (2018): 52-71.

Searle. 1993. Applying the EM algorithm to calculating ML and REML estimates of variance components. Paper invited for the 1993 American Statistical Association Meeting, San Francisco.

Yu et al. 2006. A unified mixed-model method for association mapping that accounts for multiple levels of relatedness. Genetics 38:203-208.

Tunncliffe W. 1989. On the use of marginal likelihood in time series model estimation. JRSS 51(1):15-27.