Quick start for the sommer package

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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.

The purpose of this quick start guide is to show the flexibility of the package under certain common scenarios:

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SECTION 1: Introduction

1) Background on mixed models

The core of the package is the `mmer` function which solve the mixed model equations. The functions are an interface to call the `NR` Direct-Inversion Newton-Raphson or Average Information algorithms (Tunnicliffe 1989; Gilmour et al. 1995; Lee et al. 2016). From version 2.0, sommer can handle multivariate models. Following Maier et al. (2015), the multivariate (and by extension the univariate) mixed model implemented has the form:

$y_1 = X_1\beta_1 + Z_1u_1 + \epsilon_1$

$y_2 = X_2\beta_2 + Z_2u_2 + \epsilon_2$

...

$y_i = X_i\beta_i + Z_iu_i + \epsilon_i$

where y_i is a vector of trait phenotypes, β_i is a vector of fixed effects, u_i is a vector of random effects for individuals and e_i are residuals for trait 'i' (i = 1, ..., t). The random effects ($u_1 \ldots u_i$ and e_i) are assumed to be normally distributed with mean zero. X and Z are incidence matrices for fixed and random effects respectively. The distribution of the multivariate response and the phenotypic variance covariance (V) are:

$Y = X\beta + ZU + \epsilon_i$

Y ~ MVN($X\beta$, V)

$$\mathbf{Y} = \begin{bmatrix} y_1 \\ y_2 \\ ... \\ y_t \end{bmatrix}$$

$$\mathbf{X} = \begin{bmatrix} X_1 & 0 & 0 \\ \vdots & \ddots & \vdots \\ 0 & 0 & X_t \end{bmatrix}$$

$$\mathbf{V} = \begin{bmatrix} Z_1K\sigma^2_{g_1}Z'_1 + H\sigma^2_{\epsilon_1} & ... & Z_1K\sigma_{g_{1,t}}Z'_t + H\sigma_{\epsilon_{1,t}} \\ \vdots & \ddots & \vdots \\ Z_1K\sigma_{g_{1,t}}Z'_t + H\sigma_{\epsilon_{1,t}} & ... & Z_tK\sigma^2_{g_t}Z'_t + H\sigma^2_{\epsilon_t} \end{bmatrix}$$

where K is the relationship or covariance matrix for the kth random effect (u=1,...,k), and H=I is an identity matrix or a partial identity matrix for the residual term. The terms $\sigma^2_{g_i}$ and $\sigma^2_{\epsilon_i}$ denote the genetic (or any of the kth random terms) and residual variance of trait 'i', respectively and $\sigma_{g_{ij}}$ and $\sigma_{\epsilon_{ij}}$ the genetic (or any of the kth random terms) and residual covariance between traits 'i' and 'j' (i=1,...,t, and j=1,...,t). The algorithm implemented optimizes the log likelihood:

$logL = 1/2 * ln(|V|) + ln(X'|V|X) + Y'PY$

where || is the determinant of a matrix. And the REML estimates are updated using a Newton optimization algorithm of the form:

$\theta^{k+1} = \theta^k + (H^k)^{-1} * \frac{dL}{d\sigma^2_i}|\theta^k$

Where, θ is the vector of variance components for random effects and covariance components among traits, H^{-1} is the inverse of the Hessian matrix of second derivatives for the kth cycle, $\frac{dL}{d\sigma_i^2}$ is the vector of first derivatives of the likelihood with respect to the variance-covariance components. The Eigen decomposition of the relationship matrix proposed by Lee and Van Der Werf (2016) was included in the Newton-Raphson algorithm to improve time efficiency. Additionally, the popular vpredict function to estimate standard errors for linear combinations of variance components (i.e. heritabilities and genetic correlations) was added to the package as well.

Please refer to the canonical papers listed in the Literature section to check how the algorithms work. We have tested widely the methods to make sure they provide the same solution when the likelihood behaves well but for complex problems they might lead to slightly different answers. If you have any concern please contact me at cova_ruber@live.com.mx.

In the following section we will go in detail over several examples on how to use mixed models in univariate and multivariate case and their use in quantitative genetics.

2) Background on covariance structures

One of the major strenghts of linear mixed models is the flexibility to specify variance-covariance structures at all levels. In general, variance structures of mixed models can be seen as tensor (kronecker) products of multiple variance-covariance stuctures. For example, a multi-response model (i.e. 2 traits) where "g" individuals (i.e. 100 individuals) are tested in "e" treatments (i.e. 3 environments), the variance-covariance for the random effect "individuals" can be seen as the following multiplicative model:

T ⊗ G ⊗ A

where:

$$\mathbf{T} = \begin{bmatrix} \sigma^2_{g_{t1,t1}} & \sigma_{g_{t1,t2}} \\ \sigma_{g_{t2,t1}} & \sigma^2_{g_{t2,t2}} \end{bmatrix}$$

is the covariance structure for individuals among traits.

$$\mathbf{G} = \begin{bmatrix} \sigma^2_{g_{e1,e1}} & \sigma_{g_{e1,e2}} & \sigma_{g_{e1,e3}} \\ \sigma_{g_{e2,e1}} & \sigma^2_{g_{e2,e2}} & \sigma_{g_{e2,e3}} \\ \sigma_{g_{e3,e1}} & \sigma_{g_{e3,e2}} & \sigma^2_{g_{e3,e3}} \end{bmatrix}$$

is the covariance structure for individuals among environments.

and A is a square matrix representing the covariance among the levels of the individuals (any known relationship matrix).

The T and G covariance structures shown above are unknown matrices to be estimated whereas A is known. The T and G matrices shown above are called as unstructured (US) covariance matrices, although this type is just one example from several covariance structures that the linear mixed models enable. For example, other popular covariance structures are:

Diagonal (DIAG) covariance structures

$$\mathbf{\Sigma} = \begin{bmatrix} \sigma^2_{g_{e1,e1}} & 0 & 0 \\ \vdots & \ddots & \vdots \\ 0 & 0 & \sigma^2_{g_{ei,ei}} \end{bmatrix}$$

Compound simmetry (CS) covariance structures

$$
\mathbf{\Sigma} = \begin{bmatrix} \sigma^2_g + \sigma^2_{ge} & \sigma^2_g & \sigma^2_g & \sigma^2_g \\ \sigma^2_g & \sigma^2_g + \sigma^2_{ge} & \sigma^2_g & \sigma^2_g \\ \vdots & \vdots & \ddots & \vdots \\ \sigma^2_g & \sigma^2_g & \sigma^2_g & \sigma^2_g + \sigma^2_{ge} \end{bmatrix}
$$

First order autoregressive (AR1) covariance structures

$$
\mathbf{\Sigma} = \sigma^2 \begin{bmatrix} 1 & \rho & \rho^2 & \rho^3 \\ \rho & 1 & \rho & \rho^2 \\ \rho^2 & \rho & 1 & \rho \\ \rho^3 & \rho^2 & \rho & 1 \end{bmatrix}
$$

or the already mentioned Unstructured (US) covariance structures

$$
\mathbf{\Sigma} = \begin{bmatrix} \sigma^2_{g_{e1,e1}} & \sigma_{g_{e1,e2}} & \sigma_{g_{e1,e3}} \\ \vdots & \ddots & \vdots \\ \sigma_{g_{e3,e1}} & \sigma_{g_{e3,e2}} & \sigma^2_{g_{e3,e3}} \end{bmatrix}
$$

among others. Sommer has the capabilities to fit some of these covariance structures in the mixed model machinery.

SECTION 2: Different models enabled in sommer

1) Univariate homogeneous variance models

This type of models refer to single response models where a variable of interest (i.e. genotypes) needs to be analized as interacting with a 2nd random effect (i.e. environments), but you assume that across environments the genotypes have the same variance component. This is the so-called compound simmetry (CS) model.

```r
library(sommer)
data(DT_example)
DT <- DT_example

ans1 <- mmer(Yield~Env,
             random= ~ Name + Env:Name,
             rcov= ~ units,
             data=DT, verbose = FALSE)
summary(ans1)
```

```
## ============================================================
##          Multivariate Linear Mixed Model fit by REML
## **********************  sommer 4.1  **********************
## ============================================================
##          logLik      AIC      BIC Method Converge
## Value -20.14538 46.29075 55.95182     NR     TRUE
## ============================================================
## Variance-Covariance components:
##                      VarComp VarCompSE Zratio Constraint
## Name.Yield-Yield       3.682     1.691  2.177   Positive
## Env:Name.Yield-Yield   5.173     1.495  3.460   Positive
## units.Yield-Yield      4.366     0.647  6.748   Positive
```

```
## ============================================================
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)   16.496    0.6855  24.065
## 2 Yield  EnvCA.2012   -5.777    0.7558  -7.643
## 3 Yield  EnvCA.2013   -6.380    0.7960  -8.015
## ============================================================
## Groups and observations:
##          Yield
## Name        41
## Env:Name   123
## ============================================================
## Use the '$' sign to access results and parameters
```

2) Univariate heterogeneous variance models

Very often in multi-environment trials, the assumption that the genetic variance or the residual variance is the same across locations may be too naive. Because of that, specifying a general genetic component and a location specific genetic variance is the way to go. This requires a CS+DIAG model (also called heterogeneous CS model).

```r
data(DT_example)
DT <- DT_example

ans2 <- mmer(Yield~Env,
              random= ~Name + vs(ds(Env),Name),
              rcov= ~ vs(ds(Env),units),
              data=DT, verbose = FALSE)
summary(ans2)
```

```
## ============================================================
##          Multivariate Linear Mixed Model fit by REML
## **********************  sommer 4.1  **********************
## ============================================================
##          logLik      AIC      BIC Method Converge
## Value -15.42983 36.85965 46.52072     NR     TRUE
## ============================================================
## Variance-Covariance components:
##                           VarComp VarCompSE Zratio Constraint
## Name.Yield-Yield            2.963     1.496  1.980   Positive
## CA.2011:Name.Yield-Yield   10.146     4.507  2.251   Positive
## CA.2012:Name.Yield-Yield    1.878     1.870  1.004   Positive
## CA.2013:Name.Yield-Yield    6.629     2.503  2.649   Positive
## CA.2011:units.Yield-Yield   4.942     1.525  3.242   Positive
## CA.2012:units.Yield-Yield   5.725     1.312  4.363   Positive
## CA.2013:units.Yield-Yield   2.560     0.640  4.000   Positive
## ============================================================
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)   16.508    0.8268  19.965
## 2 Yield  EnvCA.2012   -5.817    0.8575  -6.783
## 3 Yield  EnvCA.2013   -6.412    0.9356  -6.854
## ============================================================
## Groups and observations:
```

```
##                Yield
## Name              41
## CA.2011:Name      41
## CA.2012:Name      41
## CA.2013:Name      41
## ===============================================================
## Use the '$' sign to access results and parameters
```

As you can see the special function `at` or `diag` can be used to indicate that there's a different variance for the genotypes in each environment. Same was done for the residual. The difference between `at` and `diag` is that the `at` function can be used to specify the levels or specific environments where the variance is different.

3) Unstructured variance models

A more relaxed asumption than the CS+DIAG model is the unstructured model (US) which assumes that among the levels of certain factor (i.e. Environments) there's a covariance struture of a second random effect (i.e. Genotypes). This can be done in sommer using the `us(.)` function:

```
data(DT_example)
DT <- DT_example

ans3 <- mmer(Yield~Env,
             random=~ vs(us(Env),Name),
             rcov=~vs(us(Env),units),
             data=DT, verbose = FALSE)
summary(ans3)
```

```
## ======================================================================
##              Multivariate Linear Mixed Model fit by REML
## **************************  sommer 4.1  **************************
## ======================================================================
##          logLik      AIC      BIC Method Converge
## Value -11.49971 28.99943 38.66049     NR     TRUE
## ======================================================================
## Variance-Covariance components:
##                                    VarComp VarCompSE    Zratio Constraint
## CA.2011:Name.Yield-Yield            15.665 5.421e+00 2.890e+00   Positive
## CA.2012:CA.2011:Name.Yield-Yield     6.110 2.485e+00 2.459e+00   Unconstr
## CA.2012:Name.Yield-Yield             4.530 1.821e+00 2.488e+00   Positive
## CA.2013:CA.2011:Name.Yield-Yield     6.384 3.066e+00 2.082e+00   Unconstr
## CA.2013:CA.2012:Name.Yield-Yield     0.393 1.523e+00 2.580e-01   Unconstr
## CA.2013:Name.Yield-Yield             8.597 2.484e+00 3.461e+00   Positive
## CA.2011:units.Yield-Yield            4.970 1.532e+00 3.243e+00   Positive
## CA.2012:CA.2011:units.Yield-Yield    4.087 3.360e-16 1.217e+16   Unconstr
## CA.2012:units.Yield-Yield            5.673 1.301e+00 4.361e+00   Positive
## CA.2013:CA.2011:units.Yield-Yield    4.087 0.000e+00       Inf   Unconstr
## CA.2013:CA.2012:units.Yield-Yield    4.087 0.000e+00       Inf   Unconstr
## CA.2013:units.Yield-Yield            2.557 6.393e-01 4.000e+00   Positive
## ======================================================================
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)   16.331    0.8137  20.070
## 2 Yield  EnvCA.2012   -5.696    0.7404  -7.693
## 3 Yield  EnvCA.2013   -6.271    0.8191  -7.656
```

```
## ======================================================================
## Groups and observations:
##                      Yield
## CA.2011:Name            41
## CA.2012:CA.2011:Name    82
## CA.2012:Name            41
## CA.2013:CA.2011:Name    82
## CA.2013:CA.2012:Name    82
## CA.2013:Name            41
## ======================================================================
## Use the '$' sign to access results and parameters
```

As can be seen the `us(Env)` indicates that the genotypes (Name) can have a covariance structure among environments (Env).

4) Multivariate homogeneous variance models

Currently there's a great push for multi-response models. This is motivated by the correlation that certain variables hide and that could benefit in the prediction perspective. In sommer to specify multivariate models the response requires the use of the `cbind()` function in the response, and the `us(trait)`, `diag(trait)`, or `at(trait)` functions in the random part of the model.

```r
data(DT_example)
DT <- DT_example
DT$EnvName <- paste(DT$Env,DT$Name)

ans4 <- mmer(cbind(Yield, Weight) ~ Env,
              random= ~ vs(Name, Gtc=unsm(2)) + vs(EnvName, Gtc=unsm(2)),
              rcov= ~ vs(units, Gtc=unsm(2)),
              data=DT, verbose = FALSE)
summary(ans4)
```

```
## ============================================================
##          Multivariate Linear Mixed Model fit by REML
## **********************  sommer 4.1  **********************
## ============================================================
##          logLik       AIC       BIC Method Converge
## Value 167.0252 -322.0505 -298.5695     NR     TRUE
## ============================================================
## Variance-Covariance components:
##                            VarComp VarCompSE Zratio Constraint
## u:Name.Yield-Yield          3.7089   1.68117  2.206   Positive
## u:Name.Yield-Weight         0.9071   0.37944  2.391   Unconstr
## u:Name.Weight-Weight        0.2243   0.08775  2.557   Positive
## u:EnvName.Yield-Yield       5.0921   1.47879  3.443   Positive
## u:EnvName.Yield-Weight      1.0269   0.30767  3.338   Unconstr
## u:EnvName.Weight-Weight     0.2101   0.06661  3.154   Positive
## u:units.Yield-Yield         4.3837   0.64941  6.750   Positive
## u:units.Yield-Weight        0.9077   0.14145  6.417   Unconstr
## u:units.Weight-Weight       0.2280   0.03377  6.751   Positive
## ============================================================
## Fixed effects:
##    Trait      Effect Estimate Std.Error t.value
## 1  Yield (Intercept)  16.4093    0.6783  24.191
```

```
## 2 Weight (Intercept)   0.9806    0.1497   6.550
## 3  Yield  EnvCA.2012  -5.6844    0.7474  -7.606
## 4 Weight  EnvCA.2012  -1.1846    0.1593  -7.439
## 5  Yield  EnvCA.2013  -6.2952    0.7850  -8.019
## 6 Weight  EnvCA.2013  -1.3559    0.1681  -8.065
## =============================================================
## Groups and observations:
##           Yield Weight
## u:Name       41     41
## u:EnvName    94     94
## =============================================================
## Use the '$' sign to access results and parameters
```

You may notice that we have added the `us(trait)` behind the random effects. This is to indicate the structure that should be assume in the multivariate model. The `diag(trait)` used behind a random effect (i.e. Name) indicates that for the traits modeled (Yield and Weight) there's no a covariance component and should not be estimated, whereas `us(trait)` assumes that for such random effect, there's a covariance component to be estimated (i.e. covariance between Yield and Weight for the random effect Name). Same applies for the residual part (rcov).

5) Multivariate heterogeneous variance models

This is just an extension of the univariate heterogeneous variance models but at the multivariate level. This would be a CS+DIAG multivariate model:

```r
data(DT_example)
DT <- DT_example
DT$EnvName <- paste(DT$Env,DT$Name)

ans5 <- mmer(cbind(Yield, Weight) ~ Env,
              random= ~ vs(Name, Gtc=unsm(2)) + vs(ds(Env),Name, Gtc=unsm(2)),
              rcov= ~ vs(ds(Env),units, Gtc=unsm(2)),
              data=DT, verbose = FALSE)
summary(ans5)
```

```
## ==============================================================
##           Multivariate Linear Mixed Model fit by REML
## **********************  sommer 4.1  **********************
## ==============================================================
##         logLik       AIC       BIC Method Converge
## Value 177.8154 -343.6308 -320.1497     NR     TRUE
## ==============================================================
## Variance-Covariance components:
##                             VarComp VarCompSE Zratio Constraint
## u:Name.Yield-Yield          3.31936   1.45269 2.2850   Positive
## u:Name.Yield-Weight         0.79393   0.32621 2.4338   Unconstr
## u:Name.Weight-Weight        0.19085   0.07503 2.5438   Positive
## CA.2011:Name.Yield-Yield    8.70657   4.01470 2.1687   Positive
## CA.2011:Name.Yield-Weight   1.77892   0.83926 2.1196   Unconstr
## CA.2011:Name.Weight-Weight  0.35966   0.17903 2.0089   Positive
## CA.2012:Name.Yield-Yield    2.57109   1.94951 1.3188   Positive
## CA.2012:Name.Yield-Weight   0.33245   0.39840 0.8345   Unconstr
## CA.2012:Name.Weight-Weight  0.03842   0.08595 0.4470   Positive
## CA.2013:Name.Yield-Yield    5.46908   2.16307 2.5284   Positive
```

```
## CA.2013:Name.Yield-Weight   1.34713   0.50479 2.6687   Unconstr
## CA.2013:Name.Weight-Weight  0.32902   0.12208 2.6952   Positive
## CA.2011:units.Yield-Yield   4.93852   1.52318 3.2422   Positive
## CA.2011:units.Yield-Weight  0.99447   0.32150 3.0932   Unconstr
## CA.2011:units.Weight-Weight 0.23982   0.07394 3.2433   Positive
## CA.2012:units.Yield-Yield   5.73887   1.31533 4.3631   Positive
## CA.2012:units.Yield-Weight  1.28009   0.30157 4.2448   Unconstr
## CA.2012:units.Weight-Weight 0.31806   0.07286 4.3652   Positive
## CA.2013:units.Yield-Yield   2.56127   0.63993 4.0024   Positive
## CA.2013:units.Yield-Weight  0.44569   0.12645 3.5246   Unconstr
## CA.2013:units.Weight-Weight 0.12232   0.03057 4.0009   Positive
## ===============================================================
## Fixed effects:
##    Trait      Effect Estimate Std.Error t.value
## 1  Yield (Intercept)  16.4243    0.7891  20.815
## 2 Weight (Intercept)   0.9866    0.1683   5.863
## 3  Yield  EnvCA.2012  -5.7339    0.8266  -6.937
## 4 Weight  EnvCA.2012  -1.1998    0.1698  -7.066
## 5  Yield  EnvCA.2013  -6.3128    0.8757  -7.209
## 6 Weight  EnvCA.2013  -1.3621    0.1915  -7.114
## ===============================================================
## Groups and observations:
##              Yield Weight
## u:Name          41     41
## CA.2011:Name    41     41
## CA.2012:Name    41     41
## CA.2013:Name    41     41
## ===============================================================
## Use the '$' sign to access results and parameters
```

6) Multivariate unstructured variance models

This is just an extension of the univariate unstructured variance models but at the multivariate level. This would be a US multivariate model:

```r
data(DT_example)
DT <- DT_example
DT$EnvName <- paste(DT$Env,DT$Name)

ans6 <- mmer(cbind(Yield, Weight) ~ Env,
              random= ~ vs(us(Env),Name, Gtc=unsm(2)),
              rcov= ~ vs(ds(Env),units, Gtc=unsm(2)),
              data=DT, verbose = FALSE)
summary(ans6)
```

```
## ======================================================================
##             Multivariate Linear Mixed Model fit by REML
## **************************  sommer 4.1  **************************
## ======================================================================
##         logLik       AIC       BIC Method Converge
## Value 181.7945 -351.5889 -328.1079     NR     TRUE
## ======================================================================
## Variance-Covariance components:
##                                  VarComp VarCompSE Zratio Constraint
```

```
## CA.2011:Name.Yield-Yield           15.6451   5.35692  2.921   Positive
## CA.2011:Name.Yield-Weight           3.3586   1.14633  2.930   Unconstr
## CA.2011:Name.Weight-Weight          0.7182   0.24871  2.888   Positive
## CA.2012:CA.2011:Name.Yield-Yield    6.5289   2.48615  2.626   Positive
## CA.2012:CA.2011:Name.Yield-Weight   1.3505   0.52388  2.578   Unconstr
## CA.2012:CA.2011:Name.Weight-Weight  0.2842   0.11259  2.524   Positive
## CA.2012:Name.Yield-Yield            4.7893   1.86183  2.572   Positive
## CA.2012:Name.Yield-Weight           0.8640   0.38377  2.251   Unconstr
## CA.2012:Name.Weight-Weight          0.1693   0.08354  2.027   Positive
## CA.2013:CA.2011:Name.Yield-Yield    5.9934   2.93830  2.040   Positive
## CA.2013:CA.2011:Name.Yield-Weight   1.4232   0.64973  2.190   Unconstr
## CA.2013:CA.2011:Name.Weight-Weight  0.3379   0.14680  2.302   Positive
## CA.2013:CA.2012:Name.Yield-Yield    2.0987   1.44034  1.457   Positive
## CA.2013:CA.2012:Name.Yield-Weight   0.5240   0.32356  1.619   Unconstr
## CA.2013:CA.2012:Name.Weight-Weight  0.1342   0.07572  1.772   Positive
## CA.2013:Name.Yield-Yield            8.6257   2.47811  3.481   Positive
## CA.2013:Name.Yield-Weight           2.1048   0.58748  3.583   Unconstr
## CA.2013:Name.Weight-Weight          0.5125   0.14285  3.588   Positive
## CA.2011:units.Yield-Yield           4.9516   1.52694  3.243   Positive
## CA.2011:units.Yield-Weight          0.9993   0.32286  3.095   Unconstr
## CA.2011:units.Weight-Weight         0.2411   0.07432  3.244   Positive
## CA.2012:units.Yield-Yield           5.7790   1.32423  4.364   Positive
## CA.2012:units.Yield-Weight          1.2914   0.30408  4.247   Unconstr
## CA.2012:units.Weight-Weight         0.3212   0.07356  4.366   Positive
## CA.2013:units.Yield-Yield           2.5567   0.63883  4.002   Positive
## CA.2013:units.Yield-Weight          0.4452   0.12631  3.524   Unconstr
## CA.2013:units.Weight-Weight         0.1223   0.03056  4.001   Positive
## ===================================================================
## Fixed effects:
##    Trait      Effect Estimate Std.Error t.value
## 1  Yield (Intercept)  16.3342    0.8254  19.790
## 2 Weight (Intercept)   0.9677    0.1770   5.466
## 3  Yield  EnvCA.2012  -5.6637    0.7449  -7.604
## 4 Weight  EnvCA.2012  -1.1855    0.1604  -7.390
## 5  Yield  EnvCA.2013  -6.2153    0.8340  -7.453
## 6 Weight  EnvCA.2013  -1.3406    0.1806  -7.425
## ===================================================================
## Groups and observations:
##                      Yield Weight
## CA.2011:Name            41     41
## CA.2012:CA.2011:Name    82     82
## CA.2012:Name            41     41
## CA.2013:CA.2011:Name    82     82
## CA.2013:CA.2012:Name    82     82
## CA.2013:Name            41     41
## ===================================================================
## Use the '$' sign to access results and parameters
```

Any number of random effects can be specified with different structures.

7) Details on special functions for variance models

the major vs() function for special variance models and its auxiliars The sommer function `vs()` allows to construct complex variance models that are passed to the `mmer()` function it constitutes one of the most important features of the sommer package. Its specification of the `vs()` function has the form:

```
random=~vs(..., Gu, Gti, Gtc)
```

The idea is that the `vs()` function reflects the special variance structure that each random effect could have in the matrix notation:

$var(u) = T \bigotimes E \bigotimes ... \bigotimes A$

where the ... argument in the `vs()` function is used to specify the kronecker products from all matrices that form the variance for the random effect , where the auxiliar function ds(), us(), cs(), at(), can be used to define such structure variance structure. The idea is that a variance model for a random effect x (i.e. individuals) might require a more flexible model than just:

```
random=~x
```

For example, if individuals are tested in different time-points and environment, we can assume a different variance and covariance components among the individuals in the different environment-timepoint combinations. An example of variance structure of the type:

$var(u) = T \bigotimes E \bigotimes S \bigotimes A$

would be specified in the `vs()` function as:

```
random=~vs(us(e),us(s),x, Gu=A, Gtc=T)
```

where the `e` would be a column vector in a data frame for the environments, `s` a column vector in the dataframe for the time points, `x` is the vector in the datrame for the identifier of individuals, `A` is a known square variance covariance matrix among individuals (usually an identity matrix; default if not specified), and T is a square matrices with as many rows and columns as the number of traits that specifyies the trait covariance structure.

The auxiliar function to build the variance models for the random effect are: + ds() diagonal covariance structure + us() unstructured covariance + at() specific levels heterogeneous variance structure + cs() customized covariance structure

ds() to specify a diagonal (DIAG) covariance structures A diagonal covariance structure looks like this:

$$\mathbf{\Sigma} = \left[\begin{array}{ccc} \sigma^2_{g_{e1,e1}} & 0 & 0 \\ \vdots & \ddots & \vdots \\ 0 & 0 & \sigma^2_{g_{ei,ei}} \end{array}\right]$$

Considering an example for one random effect (g; indicating i.e. individuals) evaluated in different treatment levels (e; indicating i.e. the different treatments) the model would look like:

```
random=~vs(ds(e),g)
```

us() to specify an unstructured (US) covariance A unstructured covariance looks like this:

$$\mathbf{G} = \left[\begin{array}{ccc} \sigma^2_{g_{e1,e1}} & \sigma_{g_{e1,e2}} & \sigma_{g_{e1,e3}} \\ \sigma_{g_{e2,e1}} & \sigma^2_{g_{e2,e2}} & \sigma_{g_{e2,e3}} \\ \sigma_{g_{e3,e1}} & \sigma_{g_{e3,e2}} & \sigma^2_{g_{e3,e3}} \end{array}\right]$$

Considering same example for one random effect (g; indicating i.e. individuals) evaluated in different treatment levels (e; indicating i.e. the different treatments) the model would look like:

```
random=~vs(us(e),g)
```

at() to specify a level-specific heterogeneous variance A diagonal covariance structure for specific levels of the second random effect looks like this:

$$\mathbf{\Sigma} = \begin{bmatrix} \sigma^2_{g_{e1,e1}} & 0 & 0 \\ \vdots & \ddots & \vdots \\ 0 & 0 & \sigma^2_{g_{ei,ei}} \end{bmatrix}$$

Considering same example for one random effect (g; indicating i.e. individuals) evaluated in different treatment levels (e; indicating i.e. the different treatments A,B,C) the model would look like:

`random=~vs(at(e,c("A","B")),g)`

where the variance component for g is only fitted at levels A and B.

cs() to specify a level-specific variance-covariance structure A customized covariance structure for specific levels of the second random effect (variance and covariances) looks i.e. like this:

$$\mathbf{\Sigma} = \begin{bmatrix} \sigma^2_{g_{e1,e1}} & \sigma_{g_{e1,e2}} & 0 \\ \vdots & \ddots & \vdots \\ 0 & 0 & \sigma^2_{g_{ei,ei}} \end{bmatrix}$$

Considering same example for one random effect (g; indicating i.e. individuals) evaluated in different treatment levels (e; indicating i.e. the different treatments A,B,C) the model would look like:

`random=~vs(cs(e,mm),g)`

where mm indicates which variance and covariance components are estimated for g.

8) The specification of constraints in the variance components (Gtc argument)

One of the major strengths of sommer is its extreme flexibility to specify variance-covariance structures in the multi-trait framework. Since sommer 3.7 this is easily achieved by the use of the `vs()` function and it's argument `Gtc`. The `Gtc` argument expects a matrix of constraints for the variance-covariance components for the random effect filled with numbers according to the following rules:

0: parameter not to be estimated 1: estimated and constrained to be positive 2: estimated and unconstrained 3: not to be estimated but fixed value provided in Gti

Some useful function to specify quickly the contraint matrices are `unsm()` for unstructured, `uncm` for unconstrained, `fixm()` for fixed constraint, and `fcm()` for fixed effect constrains.

Consider a multi-trait model with 4 traits (y1,. . . ,y4) and 1 random effects (u) and 1 fixed effect (x)

`fixed=cbind(y1,y2,y3,y4)~x`

`random= ~vs(u, Gtc=?)`

The constraint for the 4 x 4 matrix of variance covariance components to be estimated can be an:

a) unstructured (variance components have to be positive and covariances either positive or negative) `random= ~vs(u, Gtc=unsm(4))`

```
unsm(4)
```

```
##      [,1] [,2] [,3] [,4]
## [1,]    1    2    2    2
## [2,]    2    1    2    2
## [3,]    2    2    1    2
## [4,]    2    2    2    1
```

b) unconstrained (any component variance or covariance can be positive or negative) `random= ~vs(u, Gtc=uncm(4))`

```
uncm(4)
```

```
##      [,1] [,2] [,3] [,4]
## [1,]    2    2    2    2
## [2,]    2    2    2    2
## [3,]    2    2    2    2
## [4,]    2    2    2    2
```

c) fixed (variance or covariance components indicated with a 3 are considered fixed and values are provided in the Gti argument) `random= ~vs(u, Gtc=fixm(4), Gti=mm)`

```
fixm(4)
```

```
##      [,1] [,2] [,3] [,4]
## [1,]    3    3    3    3
## [2,]    3    3    3    3
## [3,]    3    3    3    3
## [4,]    3    3    3    3
```

where mm is a 4 x 4 matrix with initial values for the variance components.

d) constraints for fixed effects `fixed= cbind(y1,y2,y3,y4)~vs(x, Gtc=fcm(c(1,0,1,0)))`

```
fcm(c(1,0,1,0))
```

```
##      [,1] [,2]
## [1,]    1    0
## [2,]    0    0
## [3,]    0    1
## [4,]    0    0
```

where 1's and 0's indicate the traits where the fixed effect will be estimated (1's) and where it won't (0's).

9) Special functions for special models

Random regression models In order to fit random regression models the user can use the `leg()` function to fit Legendre polynomials. This can be combined with other special covariance structures such as `ds()`, `us()`, etc.

```
library(orthopolynom)
```

```
## Loading required package: polynom
```

```
data(DT_legendre)
DT <- DT_legendre

mRR2<-mmer(Y~ 1 + Xf
           , random=~ vs(us(leg(X,1)),SUBJECT)
           , rcov=~vs(units)
```

```
          , data=DT, verbose = FALSE)
summary(mRR2)$varcomp
```

```
##                           VarComp VarCompSE   Zratio Constraint
## leg0:SUBJECT.Y-Y      2.5782969 0.6717242 3.838326   Positive
## leg1:leg0:SUBJECT.Y-Y 0.4765431 0.2394975 1.989763   Unconstr
## leg1:SUBJECT.Y-Y      0.3497299 0.2183229 1.601893   Positive
## u:units.Y-Y           2.6912226 0.3825197 7.035513   Positive
```

Here, a numeric covariate X is used to explain the trajectory of the SUBJECT's and combined with an unstructured covariance matrix. The details can be found in the theory.

GWAS models Although genome wide association studies can be conducted through a variety of approaches, the use of mixed models to find association between markers and phenotypes still one of the most popular approaches. Two of the most classical and popular approaches is to test marker by marker trough mixed modeling (1 model by marker) to obtain the marker effect and an statistic reflecting the level of association usually provided as the -log10 p-value. The second most popular approach is to assume that the genetic variance component is similar for all markers and therefore the variance components are only estimated once (1 model for all markers) and use the inverse of the phenotypic variance matrix (V.inverse) to test all markers in the generalized linear model b=(XV-X)-XV-y. This makes the GWAS much faster and efficient without major loses. Given the straight forward extension, sommer provides the `GWAS` function which can fit both type of approaches (be aware that these are 2 among many existant in the literature) in univariate and multivariate models, that way genetically correlated traits can be tested together to increase the power of detection. In summary the GWAS model implemented in sommer to obtain marker effect is a generalized linear model of the form:

b = (X'V-X)X'V-y

with X = ZMi

where: b is the marker effect (dimensions 1 x mt) y is the response variable (univariate or multivariate) (dimensions 1 x nt) V- is the inverse of the phenotypic variance matrix (dimensions nt x nt) Z is the incidence matrix for the random effect selected (gTerm argument) to perform the GWAS (dimensions nt x ut) Mi is the ith column of the marker matrix (M argument) (dimensions u x m)

for t traits, n observations, m markers and u levels of the random effect. Depending if P3D is TRUE or FALSE the V- matrix will be calculated once and used for all marker tests (P3D=TRUE) or estimated through REML for each marker (P3D=FALSE).

Here we show a simple GWAS model for an univariate 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
head(DT,3)
```

```
##        id Row Col Year      color  Yield FruitAver Firmness Rowf Colf
## P003 P003   3   1 2014 0.10075269 154.67     41.93  588.917    3    1
## P004 P004   4   1 2014 0.13891940 186.77     58.79  640.031    4    1
## P005 P005   5   1 2014 0.08681502  80.21     48.16  671.523    5    1
```

```
head(MP,3)
```

```
##                  Locus Position Chrom
```

```
## 1   scaffold_77830_839        0     1
## 2   scaffold_39187_895        0     1
## 3 scaffold_50439_2379         0     1
```

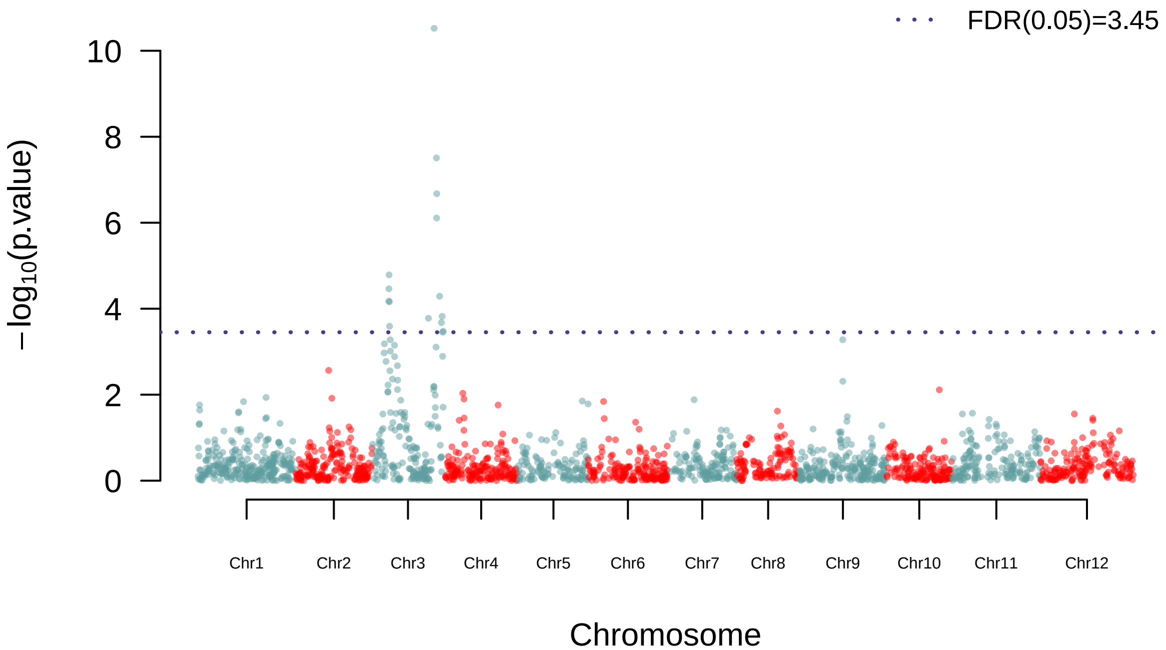
```
GT[1:3,1:4]
```

```
##      scaffold_50439_2381 scaffold_39344_153 uneak_3436043 uneak_2632033
## P003                   0                  0             0             1
## P004                   0                  0             0             1
## P005                   0                 -1             0             1
```

```
mix1 <- GWAS(color~1,
             random=~vs(id,Gu=A)
             + Rowf + Colf,
             rcov=~units,
             data=DT,
             M=GT, gTerm = "u:id",
             verbose = FALSE)
```

```
## Performing GWAS evaluation
```

```
ms <- as.data.frame(mix1$scores)
ms$Locus <- rownames(ms)
MP2 <- merge(MP,ms,by="Locus",all.x = TRUE);
manhattan(MP2, pch=20,cex=.5, PVCN = "color")
```



Be aware that the marker matrix M has to be imputed (no missing data allowed) and make sure that the number of rows in the M matrix is equivalent to the levels of the gTerm specified (i.e. if the gTerm is "id" and has 300 levels or in other words 300 individuals, then M has dimensions 300 x m, being m the number of markers).

Overlayed models [the overlay() function] Another very useful function is the `overlay` function, which allows to overlay matrices of different random effects and estimate a single variance component for the overlayed terms.

```r
data("DT_halfdiallel")
DT <- DT_halfdiallel
head(DT)
```

```
##   rep geno male female     sugar
## 1   1   12    1      2 13.950509
## 2   2   12    1      2  9.756918
## 3   1   13    1      3 13.906355
## 4   2   13    1      3  9.119455
## 5   1   14    1      4  5.174483
## 6   2   14    1      4  8.452221
```

```r
DT$femalef <- as.factor(DT$female)
DT$malef <- as.factor(DT$male)
DT$genof <- as.factor(DT$geno)
#### model using overlay
modh <- mmer(sugar~1,
             random=~vs(overlay(femalef,malef))
             + genof,
             data=DT,verbose = FALSE)
```

here the femalef and malef random effects are overlayed becoming a single random effect that has the same variance component.

Spatial models (using the 2-dimensional spline) We will use the CPdata to show the use of 2-dimensional splines for accomodating spatial effects in field experiments. In early generation variety trials the availability of seed is low, which makes the use of unreplicated design a neccesity more than anything else. Experimental designs such as augmented designs and partially-replicated (p-rep) designs become every day more common this days.

In order to do a good job modeling the spatial trends happening in the field special covariance structures have been proposed to accomodate such spatial trends (i.e. autoregressive residuals; ar1). Unfortunately, some of these covariance structures make the modeling rather unstable. More recently other research groups have proposed the use of 2-dimensional splines to overcome such issues and have a more robust modeling of the spatial terms (Lee et al. 2013; Rodríguez-Álvarez et al. 2018).

In this example we assume an unreplicated population where row and range information is available which allows us to fit a 2 dimensional spline model.

```r
data(DT_cpdata)
DT <- DT_cpdata
GT <- GT_cpdata
MP <- MP_cpdata
### mimic two fields
A <- A.mat(GT)
mix <- mmer(Yield~1,
            random=~vs(id, Gu=A) +
              vs(Rowf) +
              vs(Colf) +
              vs(spl2D(Row,Col)),
            rcov=~vs(units),
            data=DT,verbose = FALSE)
summary(mix)
```

```
## ============================================================
##          Multivariate Linear Mixed Model fit by REML
```

```
## **********************  sommer 4.1  **********************
## ============================================================
##          logLik      AIC      BIC Method Converge
## Value -151.2011 304.4021 308.2938     NR     TRUE
## ============================================================
## Variance-Covariance components:
##                      VarComp VarCompSE Zratio Constraint
## u:id.Yield-Yield       783.4     319.3 2.4536   Positive
## u:Rowf.Yield-Yield     814.7     390.5 2.0863   Positive
## u:Colf.Yield-Yield     182.2     129.7 1.4053   Positive
## u:Row.Yield-Yield      513.6     694.7 0.7393   Positive
## u:units.Yield-Yield   2922.6     294.1 9.9368   Positive
## ============================================================
## Fixed effects:
##   Trait      Effect Estimate Std.Error t.value
## 1 Yield (Intercept)    132.1     8.791   15.03
## ============================================================
## Groups and observations:
##        Yield
## u:id     363
## u:Rowf    13
## u:Colf    36
## u:Row    168
## ============================================================
## Use the '$' sign to access results and parameters
```

Notice that the job is done by the `spl2D()` function that takes the Row and Col information to fit a spatial kernel.

Customized random effects One of the most powerful features of sommer is the ability to provide any customized matrix and estimate any random effect. For example:

```r
data(DT_cpdata)
DT <- DT_cpdata
GT <- GT_cpdata
MP <- MP_cpdata

#### look at the data and fit the model
mix1 <- mmer(Yield~1,
              random=~vs(list(GT)),
              rcov=~units,
              data=DT,verbose = FALSE)
```

the matrix GT is provided as a random effect by encapsulating the matrix in a list and provided in the `vs()` function.

10) Genomic selection

In this section I decided to show the way you can fit an rrBLUP and GBLUP model in sommer using some wheat example data from CIMMYT in the genomic selection framework. This is the case of prediction of specific individuals within a population. It basically uses a similar model of the form:

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

and takes advantage of the variance covariance matrix for the genotype effect known as the additive relationship matrix (A) and calculated using the `A.mat` function to establish connections among all individuals and predict the BLUPs for individuals that were not measured. In case the interest is to get BLUPs for markers the random effect is the actual marker matrix and the relationship among markers can be specified as well but in this example is assume a diagonal.

```
data(DT_wheat)
DT <- DT_wheat
GT <- GT_wheat
colnames(DT) <- paste0("X",1:ncol(DT))
DT <- as.data.frame(DT);DT$id <- as.factor(rownames(DT))
# select environment 1
rownames(GT) <- rownames(DT)
K <- A.mat(GT) # additive relationship matrix
colnames(K) <- rownames(K) <- rownames(DT)
# GBLUP pedigree-based approach
set.seed(12345)
y.trn <- DT
vv <- sample(rownames(DT),round(nrow(DT)/5))
y.trn[vv,"X1"] <- NA

## GBLUP
ans <- mmer(X1~1,
            random=~vs(id,Gu=K),
            rcov=~units,
            data=y.trn,verbose = FALSE) # kinship based
ans$U$`u:id`$X1 <- as.data.frame(ans$U$`u:id`$X1)
rownames(ans$U$`u:id`$X1) <- gsub("id","",rownames(ans$U$`u:id`$X1))
cor(ans$U$`u:id`$X1[vv,],DT[vv,"X1"], use="complete")
```

```
## [1] 0.5737594
```

```
## rrBLUP
ans2 <- mmer(X1~1,
             random=~vs(list(GT)),
             rcov=~units,
             data=y.trn,verbose = FALSE) # kinship based

u <- GT %*% as.matrix(ans2$U$`u:GT`$X1) # BLUPs for individuals
rownames(u) <- rownames(GT)
cor(u[vv,],DT[vv,"X1"]) # same correlation
```

```
## [1] 0.5737681
```

```
# the same can be applied in multi-response models in GBLUP or rrBLUP
```

11) Likelihood ratio tests

The Likelihood ratio tests (LRT) is a good way to investigate the significance of random effects or specific variance-covariance components.

11.1) Testing the significance of a variance component For example, imagine that a researcher would like to know if his model improves when adding the effect of a spatial kernel to capture the spatial trend in the field, his base model may look like this:

```r
data(DT_cpdata)
DT <- DT_cpdata
GT <- GT_cpdata
MP <- MP_cpdata
### mimic two fields
A <- A.mat(GT)

mix1 <- mmer(Yield~1,
            random=~vs(id, Gu=A) +
              vs(Rowf) +
              vs(Colf),
            rcov=~vs(units),
            data=DT, verbose = FALSE)
```

And the model with the spatial kernel is the following:

```r
mix2 <- mmer(Yield~1,
            random=~vs(id, Gu=A) +
              vs(Rowf) +
              vs(Colf) +
              vs(spl2D(Row,Col)),
            rcov=~vs(units),
            data=DT,verbose = FALSE)
```

Then to test if the second model brings value let us fit the likelihood ratio test as follows:

```r
lrt <- anova(mix1, mix2)
```

```
## Likelihood ratio test for mixed models
## ==============================================================
##      Df      AIC      BIC     loLik   Chisq ChiDf  PrChisq
## mod2  8 304.4021 308.2938 -151.2011
## mod1  7 305.0477 308.9393 -151.5238 0.64554     1 0.42171
## ==============================================================
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

As can be seen the test turns out to not be very significant despite the increase in the likelihood.

11.2) Testing the significance of a covariance component Sometimes the researcher is more interested in knowing if a covariance structure is relevant or not. Assume we have two multi-trait models, 1) fitting no-covariance (independent) among traits, and 2) one fitting the genetic covariance among yield and color in the following population:

```r
data(DT_example)
DT <- DT_example

DT$EnvName <- paste(DT$Env,DT$Name)
modelBase <- mmer(cbind(Yield, Weight) ~ Env,
              random= ~ vs(Name, Gtc=diag(2)), # here is diag()
              rcov= ~ vs(units, Gtc=unsm(2)),
              data=DT,verbose = FALSE)

modelCov <- mmer(cbind(Yield, Weight) ~ Env,
              random= ~ vs(us(Env),Name, Gtc=unsm(2)), # here is unsm()
              rcov= ~ vs(ds(Env),units, Gtc=unsm(2)),
              data=DT,verbose = FALSE)
```

```
lrt <- anova(modelBase, modelCov)
```

```
## Likelihood ratio test for mixed models
## ==============================================================
##      Df       AIC       BIC    loLik    Chisq ChiDf                  PrChisq
## mod2 45 -351.5889 -328.1079 181.7945
## mod1 23 -253.4383 -229.9573 132.7192 98.15058    22 1.35527471041289e-11 ***
## ==============================================================
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

As can be seen, in this case fitting the covariance among the genotypes improves the model fit considerably and the probablity fro the Chi-square distribution is < 0.05. Then you the model with the covariance is the preferred model.

SECTION 3: The predict function

1) Background on prediction

In a linear mixed model where y is nx1 vector of observations, the linear mixed model can be written as:

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

where τ is a vector tx1 of fixed effects, X is an nxt design matrix which associates observations with the appropriate combinations of fixed effects, u is the qx1 vector of random effects, Z is the nxq matrix which associates observations with the appropriate random effects, and e is the nx1 vectors of residual errors. For shorthand W and β represent the combined design matrix and vector of eefects, respectively. It is assumed:

$$\begin{bmatrix} u \\ e \end{bmatrix} = N(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} G(\gamma) & 0 \\ 0 & R(\phi) \end{bmatrix})$$

where the covariance matrices G and R for random effects and residuals are functions of parameters γ and ϕ respectively. The covariance matrix of data can be written as:

$var(y) = \sigma^2(ZGZ' + R)$

The variance parameters γ and ϕ are usually estimated by maximum likelihood or REML (Patterson and Thompson, 1971).

The BLUP of a linear combination for known D, γ, and ϕ is then:

$$\mathbf{D}\overline{\beta} = \begin{bmatrix} D_\tau & D_u \end{bmatrix} \begin{bmatrix} \overline{\tau} \\ \overline{u} \end{bmatrix} = D\overline{\tau} + D_u\overline{u}$$

where $\overline{\beta} = (\tau, u)$ is the solution of the mixed moel equations:

$$\begin{bmatrix} X^TR^{-1}X & X^TR^{-1}Z \\ Z^TR^{-1}X & Z^TR^{-1}Z + G^{-1} \end{bmatrix} \begin{bmatrix} \tau \\ u \end{bmatrix} = \begin{bmatrix} X^TR^{-1}y \\ Z^TR^{-1}X \end{bmatrix}$$

These can also be written as $C\overline{\beta} = W^TR^{-1}y$. The $\overline{\tau}$ is the best linear unbiased estimator (BLUE) of τ and $\overline{u}$ is the best linear unbiased predictor (BLUP) of u, this with variance $var(\overline{\beta} - \beta) = C^{-1}$. Consideration of the values required to form the confidence intervals make it clear that is the prediction error variance (PEV or $var(\overline{\beta} - \beta)$), rather than the variance of the estimator $var(\overline{\beta})$ that is usually of interest. The prediction error variance for a linear combination $D\overline{\beta}$ is then $DC^{-1}D^T$. Since the variance parameters are unknown, we replace the unknown variance parameters by their REML estimates and use the empirical values.

The predict function of the sommer package then builts the C^{-1} matrix from the mixed model equations and the D matrix of linear combinations to obtain the PEV and SEs for the predictions. For the means it uses the D matrix of linear combinations times the vector of required fixed and random effects $X\overline{\tau} + Z\overline{u}$ or $D\overline{\beta}$, where the matrix D is a linear combination of specific fixed and/or random effects from matrices X and/or Z.

2) Predicting means

The sommer package is equiped with a predict() function that can be used to calculate means and standard errors for fixed and random effects specified in the models fitted with the mmer function. Using the yatesoats dataset we will will fit some fixed and random effects.

```
library(sommer)
data(DT_yatesoats)
DT <- DT_yatesoats
m3 <- mmer(fixed=Y ~ V + N + V:N,
           random = ~ B + B:MP,
           rcov=~units,
           data = DT, verbose=FALSE)
summary(m3)$varcomp
```

```
##             VarComp VarCompSE   Zratio Constraint
## B.Y-Y      214.4477 168.62790 1.271722   Positive
## B:MP.Y-Y   106.0508  67.83280 1.563415   Positive
## units.Y-Y 177.0883  37.34293 4.742217   Positive
```

Now, the model can be used together with the classify argument to obtain means for the classify argument. For example, the model includes in the fixed formula the terms "V" for variety, "N" for nitrogen treatments, and "V:N" for the interaction between variety and nitrogen. The classify argument can be used to specify the term for which means are desired. In the following example the means for the nitrogen treatments are obtained as follows:

```
p0 <- predict.mmer(object=m3, classify = "N")
```

```
## iteration    LogLik     wall    cpu(sec)   restrained
##     1      -0.745921   15:7:54      0           0
##     2      -0.745921   15:7:54      0           0
##     3      -0.745921   15:7:54      0           0
##     4      -0.745921   15:7:54      0           0
```

```
p0$pvals
```

```
##   trait   N predicted.value standard.error
## 1     Y   0        79.38889       9.006796
## 2     Y 0.2        98.88889       9.006796
## 3     Y 0.4       114.22222       9.006796
## 4     Y 0.6       123.38889       9.006796
```

Final remarks

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 1000x1000) 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 200x200) asreml or other MME-based algorithms will be much faster and we recommend you to opt for those software.

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.

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